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## Association Between Breastfeeding and Childhood Cardiovascular Disease Risk Factors

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### Abstract

**Introduction**—The immediate benefits of breastfeeding are well-established but the long-term health benefits are less well-known. West Virginia (WV) has a higher prevalence of cardiovascular disease (CVD) and lower breastfeeding rates compared to national averages. There is a paucity of research examining the relationship between breastfeeding and subsequent childhood CVD risk factors, an issue of particular relevance in WV.

**Methods**—This study used longitudinally linked data from three cross-sectional datasets in WV (N = 11,980). The information on breastfeeding was obtained retrospectively via parental recall when the child was in the fifth grade. The outcome variables included blood pressure measures [systolic blood pressure (SBP), diastolic blood pressure (DBP)] and lipid profile [total cholesterol (TC), low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), non-HDL, and triglycerides (TG)]. Multiple regression analyses were performed, adjusting for childhood body mass index (BMI) and additional covariates.

**Results**—Only 43% of mothers self-reported ever breastfeeding. The unadjusted analysis showed that children who were ever vs. never breastfed had significantly lower SBP (b = - 1.39 mmHg; 95% CI - 1.97, - 0.81), DBP (b = - 0.79 mmHg; 95% CI - 1.26, - 0.33), log-TG (b = - 0.08; 95% CI - 0.1, - 0.05), and higher HDL (b = 0.95 mg/dL; 95% CI 0.33, 1.56). After adjustment for

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Compliance with Ethical Standards

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the child's BMI, socio-demographic and lifestyle factors, log-TG remained significantly associated with breastfeeding ( $b = -0.04$ ; 95% CI  $-0.06, -0.01$ ;  $p = 0.01$ ).

**Conclusion**—The observed protective effect of any breastfeeding on childhood TG level was small but significant. This finding provides some support for a protective effect of breastfeeding on later CVD risk.

### Keywords

Breastfeeding; Cardiovascular disease; Childhood; Blood pressure; Lipid(s); Triglycerides; Rural

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## Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in the United States (U.S.) (Mensah and Brown 2007). Importantly, CVD mortality rates are approximately 20% higher in the rural Appalachian population compared to the rest of the nation (Liburd et al. 2006). West Virginia (WV), a state entirely within the Appalachian region, has some of the highest rates of CVD mortality in the nation, ranking 45th, and CVD risk factors, ranking 50th in high blood pressure and 48th in high total cholesterol (TC) levels in the nation (UHF 2014). Although CVD typically develops in adulthood, the risk factors for CVD may be present in children and adolescents as well (Rodrigues et al. 2013). These risk factors have the propensity to persist from childhood into adulthood, and the association between childhood and adult CVD risk has been shown to rise in magnitude with increasing age (Chen and Wang 2008; Juhola et al. 2011). Data on early life determinants of CVD risk suggests that breastfeeding is protective for cardiovascular health (Gartner et al. 2005; Martin et al. 2005).

The American Academy of Pediatrics recommends 6 months of exclusive breastfeeding and continuation of breastfeeding until the infant is 1 year old while gradually introducing solid foods after 6 months (AAP 2012). Unfortunately, results from the 2013 National Immunization Survey show that only 22.3% of U.S. mothers exclusively breastfeed for the first 6 months while in WV, the prevalence is even lower (14.1%) (CDC 2016). Bartick and colleagues performed a pediatric cost analysis and concluded that the annual cost of morbidity and mortality associated with suboptimal breastfeeding in the U.S. was approximately \$13 billion (Bartick and Reinhold 2010).

Breastfeeding has been shown to be protective against childhood obesity (Umer et al. 2015). Results from a recent meta-analysis found a 15% decrease in the odds of childhood obesity in children who were ever vs. never breastfed (Weng et al. 2012). In addition to childhood adiposity, breastfeeding has been shown to have protective effects on other childhood CVD risk factors as well (Plagemann and Harder 2005).

Previous research examining the associations between breastfeeding and later childhood CVD risk factors has yielded conflicting results. For example, while some studies have found a significant protective effect of breastfeeding on child CVD risk factors such as systolic blood pressure (SBP) (Amorim Rde et al. 2014; Hosaka et al. 2013; Lawlor et al. 2004), diastolic blood pressure (DBP) (Martin et al. 2005, 2004; Owen et al. 2003), and lipid

levels in childhood (Plagemann and Harder 2005; Plancoulaine et al. 2000; Thorsdottir et al. 2003), others have not (Bekkers et al. 2011; de Jonge et al. 2010; Fall et al. 2011; Horta et al. 2006, 2015; Izadi et al. 2013; Kramer 2010; Kramer et al. 2007; Kwok et al. 2013; Owen et al. 2002, 2008; Rudnicka et al. 2007). These discrepancies may in part reflect the role of childhood adiposity, a factor associated with blood pressure and cholesterol (McMurray et al. 1995). Some studies that did adjust for childhood obesity found that the association between breastfeeding and childhood CVD risk factors became non-significant in the adjusted models (Bekkers et al. 2011), whereas others found that even after controlling for body mass index (BMI) the association attenuated but remained statistically significant (Amorim Rde et al. 2014; Lawlor et al. 2004; Martin et al. 2004). These conflicting results suggest that childhood obesity could potentially be a partial or full mediator between the observed effects. Furthermore, some studies have found this association to be gender specific (Kolacek et al. 1993; Plancoulaine et al. 2000; Thorsdottir et al. 2003), or specific to one or two components of CVD risk factors (Kolacek et al. 1993; Victora et al. 2006). Moreover, studies examining this association use varying definitions of breastfeeding, with very few studies examining the association of ever breastfeeding compared to never breastfeeding (Horta et al. 2015). Given the former, the purpose of this study was to examine the association between ever breastfeeding and SBP, DBP, TC, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), non-HDL, and triglycerides (TG) after controlling for childhood BMI.

## Methods and Materials

### Data Sources

The current study utilized data from three sources: (1) WV Birth Certificates (WVDHHR), (2) the Working in Appalachia to Track High Birth Score, Critical Congenital Heart Disease and Hearing Loss (WATCH)/Birth Score project (WATCH 2013), and (3) the Coronary Artery Risk Detection in Appalachian Communities (CARDIAC) project (Muratova et al. 2002). The Birth Score project collects data on every newborn in WV prior to discharge in order to identify infants who are at a high risk of poor health outcomes in the first year of life. The CARDIAC project collects data using an active-consent process in fifth grade children in all 55 counties in WV. Area coordinators employed by the project, along with health science student volunteers, school nurses, and volunteer phlebotomists conducted blood pressure, anthropometric measurements, and blood lipid testing in local schools. Blood samples were analyzed by local area hospitals or by LabCorp Inc. (Burlington, NC). Further details of the data collection procedure are described elsewhere (Muratova et al. 2002). For the current study, children participating in the CARDIAC Project from 2008 to 2014 (N = 20,531) were matched with Birth Score project participants (merged with Birth Certificate data) born between 1997 and 2004. Overall, a nearly 60% data match was achieved (N = 11,980, 58.4%). Reasons for non-matches included CARDIAC participants born out of state, BirthScore participants who were not named at the time the BirthScore was filled out, CARDIAC participants who use a different name than that given at birth (e.g., middle names as first name, nicknames), CARDIAC participants who were legally adopted, and lastly use of out-of-state hospital by the rural populations living near state borders. The WVU IRB approved the data merging and subsequent analyses of the de-identified dataset.

The final analyses excluded infants born preterm, i.e., < 37 weeks of gestation (N = 1190, 10.2%) because preterm and term infants are considered two separate populations with different morbidity and mortality risk profiles in later life (Wilcox 2001).

## Variables

**Dependent Variables**—The main outcome variables included blood pressure and lipid profile (SBP, DBP, TC, LDL, HDL, non-HDL, and TG) for the child in fifth grade. Blood pressure was taken in a sitting position with the arm resting on a table at the level of the heart after the child had rested for 5 min. The first and fifth Korotkoff sound was used to record SBP and DBP in mmHg respectively. Lipids were mostly fasting values, although when the student forgot to fast the non-fasting values were used. All lipid values were measured in mg/dl. LabCorp Inc. (Burlington, NC) estimated LDL using the Friedewald equation (Friedewald et al. 1972).

**Independent Variable**—The main exposure variable was the one question on reported history of breastfeeding. Information related to breastfeeding was obtained using the CARDIAC questionnaire retrospectively via parental recall when the child was in fifth grade, and stated as, “Was your child breastfed?”

**Mediator (BMI Percentile)**—The children’s height and weight were measured using SECA Road Rod stadiometers (78”/200 cm) and the SECA 840 Personal Digital Scales (Seca Corp, Hanover, MD, USA). The current study used BMI percentile as a measure of the child’s adiposity status. BMI percentiles represent a measure of relative weight adjusted for the child’s height, age and sex corresponding to the 2000 CDC growth charts (Kuczmarski et al. 2002).

### Covariates

**Socio-demographic Variables:** Socio-demographic variables included the child’s age, sex, race, maternal age, education, and health insurance status at time of delivery. The child’s age, sex, and race was recorded by the CARDIAC project in fifth grade. For this study, race was dichotomized as white and other based on the population distribution of WV, i.e., 94% white (US-Census-Bureau 2011). Though not conclusive, several studies have suggested a link between advanced maternal age and children’s negative health outcomes in later life (Myrskylä and Fenelon 2012). Thus, maternal age at the time of birth was included. Maternal socio-economic status (SES) has also been shown to be associated with CVD risk factors in childhood (van den Berg et al. 2013) and also a predictor of maternal breastfeeding practices (van Rossem et al. 2009). Two proxy assessments of maternal SES were included: (1) maternal education at the time of delivery, recorded as a continuous variable (number of years of education ranging from 1 to 17), and (2) maternal health insurance at the time of delivery, categorized as a binary variable (Medicaid and non-Medicaid).

**Family History of CVD and Dyslipidemia:** The CARDIAC project collects parent-reported information on family history (parent or grandparent) of heart disease, coronary heart disease, heart attack, open-heart surgery, angioplasty, and death from heart diseases.

For the current study, we created one variable for family history of CVD (yes or no) based on having a family history of any one of these six outcomes. The CARDIAC project also collects information on family history of high cholesterol (yes or no) that we included.

**Other Infant and Maternal Characteristics:** Additional covariates based on the literature included (1) number of previous pregnancies (0 or 1) (Gaillard et al. 2014), (2) smoking during pregnancy (yes or no) (Huang et al. 2012), (3) self-reported weight gain during pregnancy (measured in pounds) (Mamun et al. 2009), and (4) birth weight of the child (measured in grams) (Huang et al. 2012).

### Statistical Analysis

All statistical analyses were conducted using SAS, version 9.3 (SAS Institute, Cary NC). Frequency and percentage were reported for categorical variables and mean  $\pm$  standard deviation for the continuous data. If any of the continuous CVD risk factors had a skewed distribution they were log transformed for all analyses. Independent sample t-tests were used to compare the means of dependent variables (DV) for women who responded 'yes' vs. 'no' to the question about breastfeeding their index child. The magnitude of this association was calculated using Cohen's effect size (d). Seven separate multiple-regression analyses were performed for the seven continuous DVs (SBP, DBP, TC, LDL, HDL, non-HDL, and TG). All CVD outcomes were first regressed on reported breastfeeding (model 1) and then BMI percentile was included (model 2). For the outcomes where the association was statistically significant between breastfeeding and CVD outcomes independent of obesity, additional covariates were added to the model (model 3). The covariates were removed one at a time from the regression model if they were not statistically significant (highest p-value greater than  $p > 0.05$ ). We also performed the regression analysis with and without breastfeeding to calculate the amount of variance shared between breastfeeding and CVD risk factors (change in  $R^2$ , model 3).

**Sensitivity Analyses**—To explore whether there were gender differences, we performed Chi square tests on breastfeeding groups in addition to including the interaction term between gender and reported breastfeeding in the linear regression analysis.

### Results

A total of 11,980 participants were available for analysis after merging the data. After excluding the infants born preterm the final number of participants included for analysis was 10,457 (Table 1). The percentage of children who were parent-reported as having been ever breastfed was 43.2% in children who had been born full-term. The mean age of the children in fifth grade was  $11.0 \pm 0.5$  years. 55% were female and 94% were white. The mean BMI percentile of fifth graders was  $72.6 \pm 28.0$ . Only serum TG measurements had a skewed distribution and were log transformed (log-TG) for all analyses.

Children who were ever vs. never breastfed had significantly lower mean SBP, DBP, and log-TG levels, and significantly higher HDL levels in fifth grade. The mean differences were:  $-1.3$  mmHg (95% CI  $-1.97, -0.81$ ) for SBP,  $-0.81$  mmHg (95% CI  $-1.26, -0.33$ ) for DBP,  $-0.08$  (95% CI  $-0.10, -0.05$ ) for log-TG levels, and  $0.9$  mg/dL (95% CI  $0.33,$

1.56) for HDL levels (Table 2). Effect sizes using Cohen's *d* ranged from 0.07 to 0.16 for the statistically significant outcomes (SBP, DBP, TG and HDL). No statistically significant differences were observed for TC, LDL, and non-HDL levels.

The unadjusted regression analysis showed that children who were ever vs. never breastfed had significantly lower SBP ( $b = -1.39$  mmHg; 95% CI  $-1.97, -0.81$ ;  $p < 0.0001$ ), DBP ( $b = -0.79$  mmHg; 95% CI  $-1.26, -0.33$ ;  $p = 0.0009$ ), log-TG ( $b = -0.08$ ; 95% CI  $-0.1, -0.05$ ;  $p < 0.0001$ ), and higher HDL ( $b = 0.95$  mg/dL; 95% CI  $0.33, 1.56$ ;  $p < 0.0001$ ) (Table 3, model 1). However, adjustments for the child's current BMI decreased the associations of ever vs. never breastfeeding for SBP ( $b = -0.77$  mmHg; 95% CI  $-1.32, -0.23$ ;  $p = 0.005$ ) and log-TG ( $b = -0.05$ ; 95% CI  $-0.07, -0.03$ ;  $p = 0.048$ ), while eliminating the statistically significant association for DBP ( $b = -0.44$  mmHg; 95% CI  $-0.89, 0.02$ ;  $p = 0.06$ ) and HDL ( $b = 0.28$  mg/dL; 95% CI  $-0.29, 0.86$ ;  $p = 0.335$ ) (Table 3, model 2). Further adjustments for additional covariates eliminated the significant association between ever breastfeeding and SBP ( $b = -0.43$  mmHg; 95% CI  $-0.98, -0.13$ ;  $p = 0.1349$ ) and attenuated the association with log-TG but remained statistically significant ( $b = -0.04$ ; 95% CI  $-0.06, -0.01$ ;  $p = 0.01$ ) (Table 3, model 3).

Ever breastfeeding (yes vs. no) was significantly and inversely associated with log-TG of children after adjustment for BMI percentile in fifth grade, child's age, gender, race, maternal education at birth, number of previous pregnancies, and family history of cholesterol ( $F(8, 5339) = 118.84$ ;  $p < 0.0001$ ; adjusted  $R^2 = 0.15$ ) (Table 4). Children who had a reported history of ever vs. never being breastfed showed a 0.04 ( $b = -0.04$ ; 95% CI  $-0.06, -0.01$ ,  $t = -2.65$ ,  $p = 0.008$ ) decrease in the log-TG levels. The amount of variance shared between ever breastfeeding and a childhood log-TG level was 0.13%.

No sex differences were observed in the additional sensitivity analysis that examined the interaction of reported history of breastfeeding by sex on blood pressure and lipid levels of children ( $b = -0.03$ ; 95% CI  $-0.08, 0.02$ ,  $t = -1.15$ ,  $p = 0.2495$ ).

## Discussion

Reported breastfeeding rates in this study were low; only 43% of the mothers reported ever breastfeeding their index child in this sample of WV children born between the years 1997–2004. State-specific breastfeeding data for these years are not available, but nationally, ever breastfeeding rates increased from 71.4% in 2002 to 81.1% in 2013 (NIS, 2002–2013). However, in 2013, WV ranked third lowest (64.6%) for ever breastfeeding rates in the nation (CDC 2016).

Overall, the results showed that children who were ever breastfed had significantly lower SBP, DBP, and TG levels, and higher HDL levels. After adjustment for the child's current BMI percentile in fifth grade, only SBP and TG remained significantly and positively associated with breastfeeding, although the associations were attenuated. Further adjustment for socio-demographic and lifestyle variables did not alter the inverse association with childhood TG levels, but eliminated that with SBP. These results suggest that BMI may in

part mediate the observed association of breastfeeding with TG levels, and possibly SBP in childhood.

### **SBP and DBP**

Our results are consistent with those of several previous studies that found no differences in the mean SBP and DBP of children who were breastfed as compared to those not breastfed during infancy (de Jonge et al. 2010; Fall et al. 2011; Horta et al. 2006; Izadi et al. 2013; Kramer 2010; Kramer et al. 2007; Kwok et al. 2013; Rudnicka et al. 2007). However, several studies have found the opposite, (Amorim Rde et al. 2014; Hosaka et al. 2013; Lawlor et al. 2004; Martin et al. 2004) including two earlier systematic reviews with meta-analysis (Martin et al. 2005; Owen et al. 2003). These systematic reviews concluded that the pooled mean difference in SBP (but not DBP) was significantly lower among children who had been breastfed as infants (Owen et al. 2003), while the later systematic review with meta-analysis found a statistically significant reduction in both SBP and DBP (Martin et al. 2005). Our results for both SBP and DBP are consistent with the evidence provided by the most recent systematic review published in 2015 (Horta et al. 2015), which demonstrated that for age groups 10–19, SBP was lower but not significant among those subjects who had been breastfed, whereas no association was observed for DBP. One of the possible explanations for the variation in results may be that previous studies that found a significant association focused on younger children less than 10 years old (Amorim Rde et al. 2014; Hosaka et al. 2013; Lawlor et al. 2004; Martin et al. 2004). Our study demonstrated that the association between breastfeeding and childhood blood pressure during 11 years is not independent of the child's current BMI and socio-demographic variables, thus suggesting the role of the child's current BMI as a potential mediator. Breastfeeding has shown to be inversely related to childhood obesity in several studies (Weng et al. 2012) including our earlier investigation in WV fifth grade children (Umer et al. 2015).

### **Lipid Levels**

In this study, we found a statistically significant association between log-TG levels among fifth grade children who were ever breastfed independent of the child's BMI, socio-demographic, and lifestyle characteristics. To our knowledge, very few studies have examined this association in children. One study found a significant negative association in 17-year-old boys but not among girls (Kark et al. 1984) while another study among 18-year-old boys did not find any difference in ever vs. never breastfed adolescents (Victoria et al. 2006). Conversely, another population-based study found that among 6 year old children the association was not significant after adjusting for age, sex, family-based socio-demographic, maternal lifestyle-related, and childhood factors (Durmus et al. 2014). We did not find any gender differences for the association between breastfeeding and log-TG levels. The standardized regression coefficient of the unadjusted association attenuated but remained statistically significant after adjusting for childhood BMI percentile and additional covariates. Based on these results, it would appear reasonable to suggest that this association is partially mediated by the child's current BMI levels. However, the change in  $R^2$  showed that ever breastfeeding accounted for less than 0.2% of the unique variance in log-TG levels of fifth grade children, suggesting a small effect size.

The results of the current study are also consistent with studies that found no association between TC (Bekkers et al. 2011; Horta et al. 2015; Owen et al. 2002), LDL (Owen et al. 2002), and non-HDL levels among breastfed vs. non-breastfed children. The results of two systematic reviews with meta-analysis using random effects models showed that the mean TC and LDL levels in children were not significantly different when comparing breastfed infants to non-breastfed infants (Owen et al. 2002). The most recent meta-analysis also found no significant difference in the mean TC levels between breastfed and non-breastfed infants in children 10–19 years of age (Horta et al. 2015). For HDL, our study found a statistically significant positive association among children who were ever vs. never breastfed. However, the association was attenuated after adjustment for the child's BMI and became non-significant. The results are consistent with other studies (Bekkers et al. 2011) (Victora et al. 2006) that also adjusted for the child's current BMI (Bekkers et al. 2011).

### Strengths, Limitations and Potential Implications

This study has several strengths. First, this study used a large sample size and population-based design. Second, the use of linked data from different time points allowed us to assess the influence of broad array of demographic, lifestyle, and health-related factors on the association between breastfeeding and childhood CVD risk factors. Third, while the effect size for the association between breastfeeding and log-TG levels was small, we believe that it is a novel finding in 11-year-old children that may be important from a population health perspective and worthy of additional examination with different study designs.

In addition to strengths, this study also has some potential limitations. These include a lack of information on certain potential confounders such as parental adiposity status, maternal pre-pregnancy weight, rapid weight gain during the first year of life, pubertal status, family history of hypertension, physical activity, and dietary behaviors. Additionally, information on history of breastfeeding was obtained retrospectively, and thus, subject to recall and social desirability bias. Furthermore, the fact that the question regarding breastfeeding asked “was your child breastfed?” and did not explicitly ask “was your child EVER breastfed?” As a result, this may have led to a misinterpretation of the question by the mothers. In addition, our data did not capture the method, extent, or duration of lactation, precluding examination of these factors. Furthermore, the investigative team was also unable to match data on ~ 40% of CARDIAC participants due to the fact that many participants were not born in WV and thus, did not have information available in the Birth Score database. Finally, as the study population was restricted to residents of a rural Appalachian state, the results may not be generalizable to other populations.

Potential implications and future recommendations based on the results of this study include designing large prospective studies that include comprehensive, carefully worded questions on breastfeeding in order to confirm the current findings in diverse populations. In addition, it appears plausible to suggest that biomedical research is needed to explore and understand the mechanism(s) underlying these findings at the molecular level. Focusing on preterm infants may also be worth exploring, as the causal mechanism may differ in that particular group given that they have different growth patterns and later CVD risk. As the breastfeeding rates in WV are one of the lowest in the nation, the current findings highlight



the need to increase breastfeeding rates in the state so as to achieve both short and long-term health benefits. Finally, although the observed effects of breastfeeding on childhood TG lipid levels were small, the distal protective effects with respect to adult CVD risk may be nonetheless practically significant as these small changes are likely to not only to persist, but also amplify with age.

## Conclusion

Breastfeeding has numerous health benefits for both the mother and the child. Our earlier work has shown that breastfeeding is protective for childhood obesity (Umer et al. 2015). This study further suggests that breastfeeding is inversely associated with childhood TG levels at 11 years of age independent of childhood obesity. However, significant associations were not observed with other childhood CVD risk factors examined. Future large prospective studies designed specifically to address this topic are needed to fully assess and understand the association of breastfeeding and CVD risks factors at various life stages.

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### Significance

Despite the well-known immediate benefits of breastfeeding on infants' health, the long term influence of breastfeeding on childhood cardiovascular disease (CVD) risk factors show inconsistent results. Limited research exists on this topic in West Virginia (WV); a state characterized by high CVD burden and low breastfeeding rates. This study gathered retrospective data on breastfeeding when the child was in the fifth grade. The results showed that less than half of the mothers ever breastfed their child. Children who were reported as ever being breastfed had significantly lower triglyceride levels in fifth grade compared to those who were not breastfed. These findings offer some support for the long-term health benefits of breastfeeding, and highlight the need to increase breastfeeding rates in WV.

**Table 1**  
Maternal and child characteristics at birth and in fifth grade using merged data from the Birth Score Project (1998–2003) and the CARDIAC Project (2010–2013) for all infants who were born full-term (N = 10,457)

| Variable                              | N      | Missing | Frequency (%) / mean (SD) |
|---------------------------------------|--------|---------|---------------------------|
| Sex                                   | 10,457 |         |                           |
| Female                                |        |         | 5740 (54.89)              |
| Male                                  |        |         | 4717 (45.11)              |
| Race                                  | 10,070 | 387     |                           |
| Others                                |        |         | 630 (6.26)                |
| White                                 |        |         | 9440 (93.74)              |
| Marital status (at birth)             | 10,457 |         |                           |
| Single                                |        |         | 2788 (26.66)              |
| Married                               |        |         | 7669 (73.34)              |
| No. of previous pregnancy (at birth)  | 10,457 |         |                           |
| 0                                     |        |         | 3651 (34.91)              |
| 1                                     |        |         | 6806 (65.09)              |
| Health insurance of mother (at birth) | 10,457 |         |                           |
| Medicaid                              |        |         | 4841 (46.29)              |
| Non-Medicaid                          |        |         | 5616 (53.71)              |
| Family history of cholesterol         | 8879   | 1578    |                           |
| No                                    |        |         | 6119 (68.92)              |
| Yes                                   |        |         | 2760 (31.08)              |
| Family history of CVD                 | 10,457 |         |                           |
| No                                    |        |         | 6114 (58.47)              |
| Yes                                   |        |         | 4343 (41.53)              |
| Smoking during pregnancy              | 10,395 | 62      |                           |
| Yes                                   |        |         | 2580 (24.82)              |
| No                                    |        |         | 7815 (75.18)              |
| No. of prenatal care visits           | 10,457 |         |                           |
| <12                                   |        |         | 4641 (44.38)              |
| 12                                    |        |         | 5816 (55.62)              |

| Variable                            | N      | Missing | Frequency (%)    | mean (SD) |
|-------------------------------------|--------|---------|------------------|-----------|
| Breastfeeding                       | 6833   | 3624    |                  |           |
| No                                  |        |         | 3883 (56.83)     |           |
| Yes                                 |        |         | 2950 (43.17)     |           |
| Age of child (years)                | 10,457 | 0       | 10.97 (0.47)     |           |
| Maternal age at birth (years)       | 10,424 | 33      | 25.79 (5.5)      |           |
| Maternal education at birth         | 10,405 | 52      | 12.87 (2.12)     |           |
| Weight gain during pregnancy (lbs.) | 9597   | 860     | 30.79 (14.66)    |           |
| Gestational age (weeks)             | 10,457 | 0       | 39.07 (1.12)     |           |
| Birth weight (grams)                | 10,452 | 5       | 3352.64 (481.55) |           |
| BMI-percentile                      | 10,444 | 13      | 72.58 (28)       |           |
| Child SBP (mmHg)                    | 10,254 | 203     | 108.43 (11.75)   |           |
| Child DBP (mmHg)                    | 10,255 | 202     | 67.49 (9.53)     |           |
| Child TC (mg/dL)                    | 9740   | 717     | 157.7 (27.51)    |           |
| Child LDL (mg/dL)                   | 9725   | 732     | 89.99 (24.41)    |           |
| Child HDL (mg/dL)                   | 9740   | 717     | 50.14 (12.37)    |           |
| Child NON-HDL (mg/dL)               | 9740   | 717     | 107.56 (27.86)   |           |
| Child TG (mg/dL)                    | 9739   | 718     | 92.28 (54.99)    |           |
| Child log TG                        | 9739   | 718     | 4.38 (0.52)      |           |

CVD cardiovascular disease, SBP systolic blood pressure, DBP diastolic blood pressure, TC total cholesterol, LDL low-density lipoprotein cholesterol, HDL high-density lipoprotein, non-HDL non-high-density lipoprotein cholesterol, TG triglycerides

Results of the Independent Sample *T* test for the mean difference in blood pressure and lipid levels in both fifth grade children who were breastfed vs. not breastfed and mothers who breastfed vs. did not breastfed for children born Full-Term using merged data from the Birth Score Project (1998–2003) and the CARDIAC Project (2010–2013)

**Table 2**

|                         | <b>Childhood CVD risk factors</b> |                      |                                 |                |                              |
|-------------------------|-----------------------------------|----------------------|---------------------------------|----------------|------------------------------|
|                         | <b>Breastfed</b>                  | <b>Not breastfed</b> | <b>Mean difference (95% CI)</b> | <b>P-value</b> | <b>Cohen's d effect size</b> |
| <b>BMI (percentile)</b> |                                   |                      |                                 |                |                              |
| N                       | 2948                              | 3877                 |                                 |                |                              |
| Mean (SD)               | 70.2 (28.6)                       | 74.2 (27.5)          | - 3.95* (- 5.29, - 2.62)        | < 0.0001       | 0.14                         |
| <b>SBP</b>              |                                   |                      |                                 |                |                              |
| N                       | 2866                              | 3781                 |                                 |                |                              |
| Mean (SD)               | 107.3 (11.8)                      | 108.6 (11.9)         | - 1.3* (- 1.97, - 0.81)         | < 0.0001       | 0.11                         |
| <b>DBP</b>              |                                   |                      |                                 |                |                              |
| N                       | 2867                              | 3781                 |                                 |                |                              |
| Mean (SD)               | 66.4 (9.5)                        | 67.2 (9.7)           | - 0.8* (- 1.26, - 0.33)         | 0.0009         | 0.08                         |
| <b>TC</b>               |                                   |                      |                                 |                |                              |
| N                       | 2792                              | 3644                 |                                 |                |                              |
| Mean (SD)               | 157.5 (27.8)                      | 157.8 (27.9)         | - 0.3 (- 1.71, 1.04)            | 0.6285         |                              |
| <b>LDL</b>              |                                   |                      |                                 |                |                              |
| N                       | 2788                              | 3639                 |                                 |                |                              |
| Mean (SD)               | 89.4 (24.6)                       | 89.3 (24.8)          | 0.1 (- 1.12, 1.31)              | 0.8868         |                              |
| <b>HDL</b>              |                                   |                      |                                 |                |                              |
| N                       | 2792                              | 3644                 |                                 |                |                              |
| Mean (SD)               | 51.0 (12.4)                       | 50.1 (12.5)          | 0.9* (0.33, 1.56)               | 0.0026         | 0.07                         |
| <b>Non-HDL</b>          |                                   |                      |                                 |                |                              |
| N                       | 2792                              | 3644                 |                                 |                |                              |
| Mean (SD)               | 106.4 (27.9)                      | 107.7 (28.5)         | - 1.3 (- 2.70, 0.11)            | 0.0705         |                              |
| <b>Log-TG</b>           |                                   |                      |                                 |                |                              |
| N                       | 2791                              | 3644                 |                                 |                |                              |
| Mean (SD)               | 4.35 (0.5)                        | 4.43 (0.5)           | - 0.08* (0.33, 1.56)            | < 0.0001       | - 0.16                       |



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*CVD* cardiovascular disease, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TC* total cholesterol, *LDL* low-density lipoprotein cholesterol, *HDL* high-density lipoprotein, *non-HDL* non-high-density lipoprotein cholesterol, *TG* triglycerides

\* Statistically significant test result (P = 0.05)

**Table 3** Results of the multiple regression analysis for the association between reported history of breastfeeding and CVD risk factors of Fifth-Grade WV Children born full-term using merged data from the Birth Score Project (1998–2003) and the CARDIAC Project (2010–2013)

| Risk factors | Model 1  |         |                   |                | Model 2  |         |                   |                         | Model 3  |         |                   |                         |
|--------------|--|---------|-------------------|----------------|--|---------|-------------------|-------------------------|--|---------|-------------------|-------------------------|
|              | Unstandardized regression coefficient (95% CI) | P-value | Standardized beta | R <sup>2</sup> | Unstandardized regression coefficient (95% CI) | P-value | Standardized beta | Adjusted R <sup>2</sup> | Unstandardized regression coefficient (95% CI) | P-value | Standardized beta | Adjusted R <sup>2</sup> |
| SBP          | -1.39 (-1.97 to -0.81)                         | <0.0001 | -0.06             | 0.0033         | -0.77 (-1.32 to -0.23)                         | 0.0052  | -0.032            | 0.1188                  | -0.43 (-0.98 to 0.13)                          | 0.1349  | -0.02             | 0.1311                  |
| DBP          | -0.79 (-1.26 to -0.33)                         | 0.0009  | -0.04             | 0.0017         | -0.44 (-0.89 to 0.02)                          | 0.06    | -0.022            | 0.0633                  |  |         |                   |                         |
| TC           | -0.34 (-1.71 to 1.04)                          | 0.6285  | -0.006            | 0.000          | -0.001 (-1.37 to 1.37)                         | 0.999   | -0.00001          | 0.0069                  |  |         |                   |                         |
| LDL          | 0.09 (-1.13 to 1.31)                           | 0.8868  | 0.002             | 0.000          | 0.62 (-0.59 to 1.83)                           | 0.3164  | 0.012             | 0.0231                  |  |         |                   |                         |
| HDL          | 0.95 (0.33 to 1.56)                            | 0.0026  | 0.04              | 0.001          | 0.28 (-0.29 to 0.86)                           | 0.335   | 0.011             | 0.1378                  |  |         |                   |                         |
| Non-HDL      | -1.29 (-2.68 to 0.11)                          | 0.0705  | -0.02             | 0.0005         | -0.28 (-1.64 to 1.07)                          | 0.6824  | -0.005            | 0.0611                  |  |         |                   |                         |
| Log TG       | -0.08 (-0.1 to -0.05)                          | <0.0001 | -0.07             | 0.0053         | -0.05 (-0.07 to -0.03)                         | <0.0001 | -0.048            | 0.1302                  | -0.04 (-0.06 to -0.01)                         | 0.008   | -0.03             | 0.1499                  |

Variables included in the model: Model 1: All the outcomes were regressed on breastfed variable (yes vs. no), Model 2: All the outcomes were regressed on breastfed variable and the child's BMI percentile in fifth grade. Model 3: All the outcomes were regressed on breastfed variable and the child's BMI percentile and additional covariates. Only covariates that were significant in the Spearman's correlation were used in the multiple regression analysis. Covariates included child's age, gender, race, infant birth weight in grams, maternal education status at birth (1–17 years of education), maternal health insurance status at time of delivery (non-Medicaid vs. Medicaid), family history of hypercholesterolemia (yes vs. no), number of previous pregnancies assessed at birth (1 vs. 0), maternal smoking status during pregnancy (yes vs. no), weight gain during pregnancy in lbs. Covariates that were not significant in the Spearman's correlation and were excluded: maternal age at birth of the index child, infant birth weight in grams, marital status of the mother at birth, number of prenatal care visits. Each non-significant covariate was deleted from the regression model one at a time. Variables retained in model for SBP: child's age, maternal education at birth, number of previous pregnancies, and family history of cholesterol

CVD cardiovascular disease, SBP systolic blood pressure, DBP diastolic blood pressure, TC total cholesterol, LDL low-density lipoprotein, HDL high-density lipoprotein cholesterol, TG triglycerides

**Table 4**

Results of the multiple regression analysis for all the variables in the model to predict triglyceride of fifth-grade WV children born full term using merged data from the Birth Score Project (1998–2003) and the CARDIAC Project (2010–2013)

|   | Full model                                      |                   |         |         | Covariate model         |   |                   |         |         |                         |
|---|---|-------------------|---------|---------|-------------------------|---|-------------------|---------|---------|-------------------------|
|   | Unstandardized regression coefficients (95% CI) | Standardized Beta | t Value | P-value | Adjusted R <sup>2</sup> | Unstandardized regression coefficients (95% CI) | Standardized beta | t Value | P-value | Adjusted R <sup>2</sup> |
| Intercept                                 | 3.31 (2.97 to 3.64)                             | 0.00              | 19.3    | <0.0001 | 0.1499                  | 3.17 (2.89–3.44)                                | 0                 | 22.56   | <0.0001 | 0.1486                  |
| Age (years)                               | 0.06 (0.04 to 0.09)                             | 0.06              | 4.4     | <0.0001 |                         | 0.072 (0.05 to 0.10)                            | 0.06              | 6.08    | <0.0001 |                         |
| Gender (male vs. female)                  | -0.11 (-0.14 to -0.08)                          | -0.10             | -8.24   | <0.0001 |                         | -0.11 (-0.13 to -0.09)                          | -0.11             | -10.48  | <0.0001 |                         |
| Race (White vs. others)                   | 0.14(0.09 to 0.19)                              | 0.07              | 5.3     | <0.0001 |                         | 0.12(0.08 to 0.17)                              | 0.06              | 5.58    | <0.0001 |                         |
| History of hypercholesterolemia           | 0.07 (0.04 to 0.10)                             | 0.06              | 5.04    | <0.0001 |                         | 0.07 (0.05 to 0.10)                             | 0.06              | 6.16    | <0.0001 |                         |
| Number of previous pregnancies ( 1 vs. 0) | -0.04 (-0.07 to -0.02)                          | -0.04             | -3.12   | 0.0018  |                         | -0.03 (-0.06 to -0.01)                          | -0.03             | -3.01   | 0.0026  |                         |
| Maternal education (Years)                | -0.010 (-0.017 to -0.004)                       | -0.04             | -3.16   | 0.0016  |                         | -0.008 (-0.014 to -0.004)                       | -0.04             | -3.43   | 0.0006  |                         |
| BMI percentile                            | 0.0065 (0.006-0.007)                            | 0.35              | 27.45   | <0.0001 |                         | 0.0065 (0.006-0.007)                            | 0.35              | 33.72   | <0.0001 |                         |
| Breastfed (yes vs. no)                    | -0.04 (-0.06 to -0.01)                          | -0.03             | -2.65   | 0.008   |                         |   |                   |         |         |                         |

Only covariates that were significant in the Spearman’s correlation were used in the multiple regression analysis. Covariates included child’s age, gender, race, infant birth weight in grams, maternal education status at birth (1–17 years of education), maternal health insurance status at time of delivery (non-Medicaid vs. Medicaid), family history of hypercholesterolemia (yes vs. no), number of previous pregnancies assessed at birth ( 1 vs. 0), maternal smoking status during pregnancy (yes vs. no), weight gain during pregnancy in lbs. Covariates that were not significant in the Spearman’s correlation and were excluded: maternal age at birth of the index child, infant birth weight in grams, marital status of the mother at birth, number of prenatal care visits. Each non-significant covariate was deleted from the regression model one at a time. These included infant birth weight in grams, family history of hypercholesterolemia (yes vs. no), number of previous pregnancies assessed at birth ( 1 vs. 0), maternal smoking status during pregnancy (yes vs. no), weight gain during pregnancy in lbs

WV-West Virginia, CI confidence interval, CVD cardiovascular disease, SBP systolic blood pressure, DBP diastolic blood pressure, TC total cholesterol, LDL low-density lipoprotein cholesterol, HDL high-density lipoprotein, non-HDL non-high-density lipoprotein cholesterol, TG triglycerides