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Maternal Weight Gain During Pregnancy and Infant Illness

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Master of Public Health

Global Epidemiology

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

Maternal Weight Gain During Pregnancy and Infant Illness

By Olivia R. Sappenfield

Background: Maternal weight gain during pregnancy is a modifiable behavior that has been linked to adverse pregnancy outcomes. The association between maternal weight gain and adverse pregnancy outcomes is modified by pre-pregnancy body mass index (BMI) with women who gain weight within recommendations having better neonatal outcomes compared to women who gain weight outside recommendations across strata. The purpose of this study was to examine the association between maternal weight gain and infant illness.

Methods: Slovak mother and term infant pairs (n=1134) were recruited at delivery and followed until 16 months. Multiple logistic regression was used to evaluate the association between maternal weight gain based on the 2009 Institute of Medicine's recommendations and infant illness (0-16 months) including diarrhea, respiratory disease, otitis media, and illness requiring antibiotics.

Results: Underweight women gaining weight below recommendations had increased odds for all outcomes except otitis media (ever sick, adjusted odds ratio [aOR]: 1.45, 95% confidence interval [CI]: 0.40, 5.26) compared to normal weight women who gained within recommendations, though the results were imprecise. Among normal weight women, those gaining weight above recommendations had increased odds for all outcomes except otitis media compared to those gaining weight as recommended (ever sick, aOR: 1.19, 95% CI: 0.66, 2.17).

Discussion: Our findings suggest maternal weight gain during pregnancy may have effects in infancy for some outcomes. In particular, infants of underweight women who gain less weight and infants of normal weight women who gain more weight than recommended may be at risk for infant illness. Therefore, pregnant women should be advised to gain weight within recommendations.

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Table of Contents

Chapter I: Background

Maternal lifestyle has the potential to negatively affect infant health outcomes. Maternal weight gain during pregnancy in particular is important because it is a modifiable risk factor associated with preterm birth (<37 weeks gestation), low birth weight (LBW), small for gestational age (SGA), large for gestational age (LGA), and child obesity (1-6), and many of these outcomes are associated with poor infant health (7-13).

Maternal weight gain during pregnancy

The Institute of Medicine (IOM) constructed guidelines for maternal weight gain during pregnancy because studies showed women who gained too much or too little weight were at risk for adverse outcomes. The most studied adverse infant outcomes that are associated with weight gain during pregnancy are preterm birth, LBW, and size for gestational age.

Maternal weight gain during pregnancy measurement

To determine total weight gain during pregnancy, pre-pregnancy weight is subtracted from final weight at time of delivery. Many studies rely on self-reported pre-pregnancy weight to estimate true pre-pregnancy weight (2-4, 6, 14-16). Self-reported pre-pregnancy weight is subject to misclassification including deliberate underestimation. However, research has shown that the errors tend to be small and self-report is a relatively reliable measure of pre-pregnancy weight (17, 18). A second method of estimating true pre-pregnancy weight is measuring the woman's weight at her first antenatal visit (2, 19). In addition, studies used modeling to estimate pre-pregnancy weight from weight measured at first antenatal visit (2, 19). Using weight measured at

first antenatal visit is an imperfect measure because the woman is already pregnant, and therefore any measurement is not her true pre-pregnancy weight.

Two methods have frequently been used in the literature to obtain final pregnancy weight. The first uses the weight at the woman's last antenatal visit if the visit is within three weeks of delivery (4, 15, 19, 20). This method's biggest limitation is pregnant women continue to gain weight between their last antenatal visit and delivery. Therefore the reported maternal weight gain will likely be an underestimate. The second method obtains a woman's final pregnancy weight upon admission to the delivery ward (3, 14, 21). This method is more accurate than weight at last antenatal visit, but is potentially more difficult to obtain due to circumstances surrounding delivery. Additionally, this measure is difficult to compare across women because it is affected by length of pregnancy.

Once pre-pregnancy weight and final pregnancy weight are collected, gestational weight gain can be calculated. Most studies divide gestational weight gain into categories defined by the 2009 IOM (table 1.1) or the World Health Organization (WHO). Kleinman et al. compared four different methods to assess maternal weight gain, continuously throughout the pregnancy, linear weekly gain, categorically based on IOM categories, and area under the maternal weight gain curve and found that none of the methods was superior to the others (22). The researchers noted that results for the IOM categorization method accounted for pre-pregnancy body mass index (BMI) by definition.

Maternal weight gain during pregnancy

In studies that did not stratify on pre-pregnancy BMI, pregnant women with inadequate weight gain were more likely to deliver SGA and LBW infants compared to women who gained adequate weight, while pregnant women with excess weight gain were more likely to deliver LGA and macrosomic infants (5, 15, 23, 24). Stotland et al. found that the odds of delivering a SGA infant among women who gained weight below IOM recommendations were 1.66 (95% confidence interval [CI]: 1.44, 1.92) times the odds among women who gained weight within recommendations. Conversely women who gained weight above recommendations had decreased odds of SGA (aOR: 0.51, 95% CI: 0.44, 0.59) (15). The researchers found the opposite relations for odds of delivering a LGA infant.

While maternal weight gain has been associated with size at birth, no association was reported with infant outcomes such as child adiposity (5, 6, 20, 25). Branum et al. fit family fixed-effects models to account for unmeasured factors associated with the intrauterine environment, while assessing the association between maternal weight gain and child adiposity. They reported that the association between maternal weight gain during pregnancy and later child BMI was null (Inadequate weight gain, change in child BMI *z* score: 0.08, 95% CI: 0.00, 0.16; Excess weight gain, change in child BMI *z* score: 0.01, 95% CI: -0.13, 0.14) (20).

Compared to women who had a normal pre-pregnancy BMI, other BMI strata are more at risk for adverse neonatal outcomes (3, 6, 16, 25). Further, within strata of pre-pregnancy BMI, the effect of weight gain during pregnancy on neonatal outcomes varies. Underweight women who gain less than adequate weight are more at risk for poor

neonatal outcomes such as preterm, LBW, and SGA compared to underweight women who gain adequate weight (table 1.2) (2, 3, 5, 6). Cedergren found that women with a pre-pregnancy BMI less than 20 who gained less than 8 kg (16.6 lbs) were more than two times as likely to deliver SGA infants (aOR: 2.35, 95% CI 1.92, 2.88) and less than half as likely to deliver LGA infants (aOR: 0.43, 95% CI: 0.24, 0.75) compared to women with a pre-pregnancy BMI less than 20 who gained 8 to 16 kg (2). Whereas women with a pre-pregnancy BMI less than 20 who gained more than 16 kg were half as likely to deliver SGA infants (aOR: 0.50, 95% CI: 0.41, 0.61) and more likely to deliver LGA infants compared to women who gained 8 to 16 kg (aOR: 3.26, 95% CI: 2.76, 3.86). Savitz et al. reported similar results (6).

Normal weight women who do not gain weight within recommendations are also at risk for adverse infant health outcomes. Rode et al. reported that normal weight women who gained less weight than IOM recommendations were more than two times as likely to deliver a LBW infant compared to normal women who gained weight as recommended (aOR: 2.4, 95% CI: 1.5, 3.7). Cedergren observed similar results (2). In contrast, normal weight women who gained more weight than IOM recommendations were twice as likely to deliver a macrosomic infant (>4000 grams) compared to normal weight women who gained within recommendations (aOR: 1.9, 95% CI: 1.5, 2.5) (5). Researchers have also reported similar risk patterns for SGA and LGA among normal weight women (2, 6).

Among overweight and obese women, pregnant women who gain weight outside recommendations are at risk for poor neonatal outcomes. Crane et al. found that overweight women who gained weight above recommendations were 1.3 times (aOR: 1.30; 95% CI: 1.15, 1.47) more likely to deliver a macrosomic infant compared to

overweight women who gained weight within recommendations, and obese women who gained weight above recommendations were 1.2 times (aOR: 1.20 95% CI: 1.07, 1.34) more likely to deliver a macrosomic infant compared to obese women who gained weight within recommendations (4). Gaining less than adequate weight among overweight and obese women has been associated with decreased odds of delivering a macrosomic infant (aOR: 0.60; 95% CI: 0.40, 0.89) but an increased odds of delivering a LBW infant (aOR: 2.58; 95% CI: 1.16, 5.75) compared to overweight and obese women who gain adequate weight (4, 6).

The effect of maternal weight gain during pregnancy on neonatal outcomes is modified by pre-pregnancy BMI. However, within each strata, women who gain weight within recommendations are more likely to have better infant health outcomes than women who gain weight outside recommendations (26).

Infant Morbidity

Preterm, LBW, and SGA infants are at increased risk for infant death and serious morbidity including severe respiratory infections (7-11, 13, 27). In addition, both lower birth weight and earlier gestational age at birth are associated with increased risk of diarrheal-associated deaths (12). Infants who suffer acute and chronic infections are more likely to suffer severe morbidity and mortality (28-31). Diarrheal disease and respiratory disease are two leading causes of death among children under five (32-34). Additionally, respiratory infections are one of the leading causes of infant hospitalizations (35). Hospitalizations for diarrheal and respiratory diseases create an economic burden on the infant's family and community (35-37). Reducing an infant's risk of diarrheal or

respiratory disease can reduce the infant's risk for child and adult morbidity and decrease the economic impact of morbidity and hospitalizations on the community (35, 37, 38).

Diarrheal Disease

Studies have determined that diarrhea can cause stunting, malnutrition, and neurological problems particularly among infants in developing countries (30, 39, 40). Increased frequency of infection is associated with increased risk of severe morbidity. Parashar et al. found that the incidence of diarrhea was higher in developing countries, but the incidence of diarrhea due to rotavirus was similar in developed and developing countries (41). The researchers estimated that in industrialized settings, 1.7 million children under 5 require a visit to a healthcare facility for rotavirus-associated diarrhea with an estimated hospitalization incidence of 445 per 100,000 children. Rates of diarrhea are highest among infants aged six months to a year in both developing and developed countries (30, 38).

Factors associated with diarrheal infection include breastfeeding, birth weight, water quality, vitamin A supplementation, family income, maternal education, and maternal employment (12, 39, 42-47) (table 1.3).

Respiratory Disease

As stated previously, respiratory disease is one of the leading causes of mortality and hospitalization among children under five (32-34, 37). Black et al. found that pneumonia was one of the leading causes of death among neonates and children under five in Slovakia (48). Respiratory infection is not limited to pneumonia but includes rhinitis, laryngitis, acute respiratory infection (ARI), and bronchitis. Respiratory viruses are one of the most common causes of chronic obstructive pulmonary disease (COPD)

which is associated with ischemic heart disease (49). Bacterial infections and viral infections can exacerbate COPD contributing to child and adult morbidity (49, 50). Rhinovirus and respiratory syncytial virus have been linked to asthma development during childhood (28).

LBW infants are more at risk for developing asthmatic symptoms and respiratory infections than normal birth weight infants (51, 52) (table 1.4). Birth weight and weight gain during the first few years of life are also associated with adult lung function (28, 53). Other risk factors for respiratory infection include maternal race/ethnicity, marital status, child sex, maternal education, birth order, maternal age, and breastfeeding (44, 54).

Conclusion

Many studies have examined the association between maternal weight gain during pregnancy and neonatal outcomes such as LBW and size for gestational age, but few have examined its association with infant illness. The primary objective of this study is to evaluate whether maternal weight gain during pregnancy affects infant illness by analyzing data from a cohort of Slovak mother and infant pairs. Because prior studies reported that the effect of weight gain during pregnancy varied by pre-pregnancy BMI, this study will evaluate whether the association between infant illness outcomes and weight gain during pregnancy differ by pre-pregnancy BMI.

Table 1.1 2009 Institute of Medicine pregnancy weight gain recommendations

Pre-pregnancy BMI	BMI (WHO)	Total weight gain range (lbs)
Underweight	<18.5	28-40
Normal Weight	18.5-24.9	25-35
Overweight	25.0-29.9	15-25
Obese	≥30.0	11-20

Table 1.2. Studies evaluating the effect of maternal weight gain during pregnancy

Author(s) (year of publication)	Study Population	Place & Time	Study Design	Exposure	Outcome	Key Results
Crane J.M.G., et al. (2009)	Singleton births ≥20 weeks gestation	Newfoundland 2001-2007	Population-based cohort study	Maternal gestational weight gain, pre-pregnancy BMI	preterm birth (<34 and <37 weeks), birth weight, other neonatal outcomes	**mGWG[1] above recs vs. at recs:** normal BMI, macrosomia (aOR: 1.21; 95%CI: 1.10, 1.34) overweight, macrosomia (aOR: 1.30; 95%CI: 1.15, 1.47) obese, macrosomia (aOR: 1.20; 95%CI: 1.07, 1.34) **mGWG below recs vs. at recs:** normal BMI LBW (aOR: 2.49; 95%CI: 1.19, 5.23) overweight LBW (aOR: 3.06; 95%CI: 0.98, 9.49) overweight and obese LBW (aOR: 2.58; 95%CI: 1.16, 5.75) macrosomia (aOR: 0.60; 95%CI: 0.41,0.89)
Rode L., et al. (2007)	Singleton births ≥37 weeks gestation	Copenhagen 1996-1998	Hospital-based retrospective cohort	mGWG based on 1990 IOM recs.	birth weight (<3000g and ≥4000g =lower 10th and upper 20th percentile)	**Normal BMI women:** mGWG less than vs. within IOM recs: BW<3000g (aOR: 2.4; 95%CI: 1.5, 3.7) mGWG more than vs. within IOM recs: BW >4000g (aOR: 1.9; 95%CI: 1.5,2.5)

Cedergren M. (2006)	Singleton births ≥37 weeks gestation	Sweden 1994-2002	Prospective, population-based cohort	mGWG[a] category: <8kg (low weight gain) 8-16kg (normal weight gain) >16kg (high weight gain)	small and large for gestational age neonate	**mGWG <8kg vs. 8-16kg:** BMI <20: LGA (aOR: 0.43; 95%CI: 0.24, 0.75) SGA (aOR: 2.35; 95%CI: 1.92, 2.88) BMI 20-24.9: LGA (aOR: 0.53; 95%CI: 0.47, 0.61) SGA (aOR: 1.99; 95%CI: 1.77, 2.23) BMI 25-29.9: LGA (aOR: 0.48; 95%CI: 0.43, 0.53) SGA (aOR: 1.75; 95%CI: 1.48, 2.07) BMI 30-34.9: LGA (aOR: 0.66; 95%CI: 0.59, 0.75) SGA (aOR: 1.68; 95%CI: 1.26, 2.25) BMI ≥ 35kg: LGA (aOR: 0.54; 95%CI: 0.46, 0.63) SGA (aOR: 1.71; 95%CI: 1.03, 2.85) **mGWG >16kg vs. 8-16kg:** BMI <20: LGA (aOR: 3.26; 95%CI: 2.76-3.86) SGA (aOR: 0.50; 95%CI: 0.41-0.61) BMI 20-24.9: LGA (aOR: 2.73; 95%CI: 2.60, 2.88) SGA (aOR: 0.50; 95%CI: 0.45, 0.56) BMI 25-29.9: LGA (aOR: 2.14; 95%CI: 2.01, 2.28) SGA (aOR: 0.57; 95%CI: 0.47, 0.68) BMI 30-34.9: LGA (aOR: 2.24; 95%CI: 2.00, 2.51) SGA (aOR: 0.61; 95%CI: 0.40, 0.93) BMI ≥ 35kg: LGA (aOR: 1.54; 95%CI: 1.24-1.90) SGA (aOR: 0.50; 95%CI: 0.20, 1.24)

Stotland N.E., et al. (2006)	Singleton births ≥37 weeks gestation	California 1980-2001	Retrospective cohort	mGWG above, within, or below IOM recs.	neonatal outcomes, SGA, LGA, ICD-9 codes for neonatal outcomes	**mGWG below vs. at IOM recs:** SGA (aOR: 1.66, 95%CI: 1.44-1.92) LGA (aOR: 0.58, 95%CI: 0.47-0.72) **mGWG above vs. at IOM recs:** LGA (aOR: 1.98, 95%CI: 1.74-2.25) SGA (aOR: 0.51, 95%CI: 0.44-0.59)
Savitz D.A., et al. (2010)	Singleton births	New York City 1995-2003	Hospital-based retrospective cohort	categorical and continuous mGWG	preterm birth, SGA and LGA among term births, birth weight among term births	**Preterm birth:** Underweight women gaining 0-9 vs. 10-14kg (aOR: 1.5; 95%CI: 0.9, 2.6) Overweight women gaining 0-9 vs. 10-14kg (aOR: 1.7; 95%CI: 1.3, 2.3) **SGA (term births, 0-9kg vs. 10-14kg):** Underweight women (aOR: 1.5; 95%CI: 1.0, 2.3) Normal weight women (aOR: 1.5; 95%CI: 1.3, 1.7) Overweight women (aOR: 1.3; 95%CI: 1.1, 1.7) Obese women (aOR: 1.8; 95%CI: 1.3, 2.4) **SGA (term births, 15-19kg vs. 10-14kg):** Underweight women (aOR: 0.7; 95%CI: 0.5, 1.0) Normal weight women (aOR: 0.7; 95%CI: 0.6, 0.8) Overweight women (aOR: 0.6; 95%CI: 0.5, 0.8) Obese women (aOR: 0.9; 95%CI: 0.6, 1.4) **LGA (term births, 0-9kg vs. 10-14kg):** Underweight women (aOR: 0.4; 95%CI: 0.1, 1.8) Normal women (aOR: 0.7; 95%CI: 0.6, 0.9)

						Overweight women (aOR: 0.6; 95%CI: 0.5, 0.7) Obese women gaining (aOR: 0.7; 95%CI: 0.6, 0.9) **LGA (term births, 15-19kg vs. 10-14kg):** Underweight women (aOR: 1.6; 95%CI: 0.8, 3.2) Normal women (aOR: 1.5; 95%CI: 1.3, 1.7) Overweight women (aOR: 1.3; 95%CI: 1.1, 1.6) Obese women gaining (aOR: 1.5; 95%CI: 1.2, 1.9)
Theron G.B., et al. (1993)	Mothers with singleton pregnancies	Western Cape, South Africa	Hospital-based retrospective cohort	Average weight gain per week (kg)	SGA	**Weight gain (kg) per week, p<0.0005** ≤0.33: Not SGA 205(26.6%) SGA 84(36.1%) >0.33-0.45: Not SGA 184(23.9%) SGA 72(30.9%) >0.45-0.56: Not SGA 181(23.5%) SGA 35(15.0%) >0.56: Not SGA 200(26.0%) SGA 42(18.0%)

[1]mGWG= maternal weight gain during pregnancy

Table 1.3. Studies evaluating covariates associated with diarrheal disease

Author(s) (year of publication)	Study Population	Place & Time	Study Design	Exposure	Outcome	Key Results
Parashar U.D., et al. (1998)	Infants	USA 1991	Retrospective cohort	Birth weight	Mortality due to diarrhea	**Birth Weight (1500 to <2500g):** Maternal education (grade): ≤10 vs. ≥13 (aRR: 2.5, 95%CI: 1.3, 4.8) 11-12 vs. ≥13 (aRR: 1.9, 95%CI: 1.1, 3.3)
Costa-Fuchs S., et al. (2002)	Children 0-23 months	Brazil 1987-1988	Case-control	Maternal education, maternal employment	Diarrhea	**Prognosis of Diarrhea:** Maternal education: <8yrs vs. ≥8yrs. (aOR: 1.4, 95%CI: 0.7, 2.8) Maternal Employment: Yes vs. No (aOR: 0.6, 95%CI: 0.3, 0.9) **Dehydrating Diarrhea:** Maternal education: <8yrs vs. ≥8yrs. (aOR: 1.5, 95%CI: 0.8, 2.7) Maternal Employment: Yes vs. No (aOR: 1.1, 95%CI: 0.7, 1.7) **Mild Diarrhea:** Maternal education: <8yrs vs. ≥8yrs. (aOR: 1.5, 95%CI: 0.8, 2.6) Maternal Employment: Yes vs. No (aOR: 1.4, 95%CI: 0.9, 2.1)
Clemens J., et al. (1999)	Singleton birth neonates	Egypt 1995-1997	Prospective cohort	Breastfeeding: ever vs. never none, partial, exclusive early vs. late initiation	Diarrheal day	**Breastfeeding Initiation:** *At Birth* Early vs. late (IDR: 0.74, 95%CI: 0.56, 0.98) *1 year after birth* Early vs. late (IDR: 0.95, 95%CI: 0.70, 1.31) **Breastfeeding Exclusivity (vs. none):** Exclusive (IDR: 0.67, 95%CI: 0.47, 0.97) Partial (IDR: 0.72, 95%CI: 0.52, 1.01)
Arifeen S., et al. (2001)	Singleton births	Dhaka City, Bangladesh 1993-1995	Prospective cohort	Breastfeeding: None, partial, predominant, exclusive	Mortality due to ARI[1], Mortality due to diarrhea	**Overall Infant Mortality (vs. exclusive):** All Deaths: Predominant (aRR: 1.13, 95%CI: 0.65, 1.97) Partial+none (aRR: 2.23, 95%CI: 1.45, 3.44) ARI:

	Predominant (aRR: 0.91, 95%CI: 0.33, 2.56) Partial+none (aRR: 2.40, 95%CI: 1.14, 5.04)
Diarrhea:	
	Predominant (aRR: 2.22, 95%CI: 0.67, 7.37) Partial+none (aRR: 3.94, 95%CI: 1.47, 10.57)
Neonatal Mortality:	
All Deaths:	
	Predominant (aRR: 0.86, 95%CI: 0.20, 3.68) Partial+none (aRR: 1.17, 95%CI: 0.26, 5.30)
Postneonatal Mortality:	
All Deaths:	
	Predominant (aRR: 0.96, 95%CI: 0.49, 1.89) Partial+none (aRR: 2.30, 95%CI: 1.48, 3.59)
ARI:	
	Predominant (aRR: 0.77, 95%CI: 0.21, 2.85) Partial+none (aRR: 2.74, 95%CI: 1.27, 5.92)
Diarrhea:	
	Predominant (aRR: 1.82, 95%CI: 0.49, 6.79) Partial+none (aRR: 4.04, 95%CI: 1.50, 10.87)

[1]ARI= Acute Respiratory Infection

Table 1.4. Studies evaluating covariates associated with respiratory disease

Author(s) (year of publication)	Study Population	Place & Time	Study Design	Exposure	Outcome	Key Results
Quigley et al. (2007)	Singleton births ≥37 weeks gestation	United Kingdom 2000-2001	Prospective cohort	Breastfeeding	Hospitalization for diarrhea Hospitalization for lower respiratory tract infection (RTI)	**Exclusive vs. not breastfed:** Diarrhea (aOR: 0.37, 95%CI: 0.18, 0.78) Lower RTI (aOR: 0.66, 95%CI: 0.47, 0.92) **Partial vs. non breastfed:** Diarrhea (aOR: 0.63, 95%CI: 0.32, 1.25) Lower RTI (aOR: 0.69, 95%CI: 0.47, 1.00)
Shay et al. (1999)	Children <5 years	United States 1980-1996	Hospital-based retrospective cohort	Time, aggregate discharges by month	Bronchiolitis-associated hospitalizations	**Infant Male:** 1988-1990 vs. 1994-1996: (24.9 to 38.4 per 1000, p=0.01) **Infant Female:** 1988-1990 vs. 1994-1996: (15.1 to 24.4 per 1000, p=0.02) Males vs. Females (PR=1.6)
Singleton et al. (2009)	Singleton birth infants	United States 1999-2004	Retrospective cohort	Maternal risk factors	Lower RTI associated deaths	**Child Sex:** Male vs. Female: (aOR: 1.3, 95%CI: 1.2, 1.4) **Maternal Education (years):** <12 vs. ≥12: (aOR: 1.6, 95%CI: 1.5, 1.7) **Maternal Age (years, vs. ≥30):** <20: (aOR: 1.6, 95%CI: 1.4, 1.9) 20-24: (aOR: 1.4, 95%CI: 1.3, 1.6) 25-29: (aOR: 1.1, 95%CI: 1.0, 1.3) **Marital Status:** Married vs. unmarried: (aOR: 1.5, 95%CI: 1.4, 1.6) **Live-birth Order:** 2^{nd} or more vs. 1^{st}: (aOR: 1.6, 95%CI: 1.5, 1.7)

Boezen et al. (2002)	Mother and child pairs	Groningen, the Netherlands 1975-1978	Retrospective cohort	Perinatal factors	Current respiratory symptoms: Wheezing or whistling in last 12 mo., attack of shortness of breath, phlegm, dyspnea	**Severe RTI in First Year of Life:** Asthmatic symptoms: (aOR: 2.76, 95%CI: 1.51, 5.04) Cough: (aOR: 1.90, 95%CI: 1.08, 3.33) Pleghm: (aOR: 2.04, 95%CI: 1.13, 3.72) **Mother smoked during pregnancy:** Asthmatic symptoms: (aOR: 0.91, 95%CI: 0.54, 1.51) Cough: (aOR: 1.09, 95%CI: 0.71, 1.84) Pleghm: (aOR: 1.15, 95%CI: 0.72, 1.86) **Current smoker:** Asthmatic symptoms: (aOR: 1.70, 95%CI: 1.02, 2.84) Bronchitic symptoms: (aOR: 2.23, 95%CI: 1.50, 3.31) Cough: (aOR: 2.22, 95%CI: 1.46, 3.37) Pleghm: (aOR: 1.80, 95%CI: 1.12, 2.89)
Rahmanifar A., et al. (1996)	Singleton birth infants 0-6 months	Egypt 1982	Prospective cohort	Birth weight, vitamin supplementation, previous RTI in preceding months	RTI	Vitamin A (µg/d), Zinc, or Riboflavin (mg/d): -0.0020 ± 0.0013, p=0.15 Birth Weight: -1.07± 0.42, p=0.01 RTI (0-3 months): 0.272± 0.082, p=0.002

Chapter II: Manuscript

Introduction

Maternal weight gain during pregnancy is an important maternal behavior that can influence neonatal health outcomes (1-6). Weight gain during pregnancy is associated with adverse outcomes such as preterm births (<37 weeks gestation), low birth weight (<2500g) (LBW), small for gestational age (SGA), large for gestational age (LGA), and child obesity (1-6). Many of these outcomes are associated with poor infant health (7-13). However, there is little information on whether maternal weight gain during pregnancy has long term effects on infant health.

The Institute of Medicine (IOM) drafted guidelines in 2009 for maternal weight gain during pregnancy to reduce the risk of adverse maternal and perinatal outcomes. These guidelines differed across categories of pre-pregnancy body mass index (BMI). The literature indicates that women who gain weight outside pre-pregnancy BMI-specific recommendations are at increased risk for poor perinatal outcomes such as preterm birth, LBW, and size for gestational age compared to women who gain weight within recommendations (26). Specifically, pregnant women who gain less weight than recommended are more likely to deliver SGA and LBW infants compared to women who gain weight as recommended whereas those who gain more weight than recommended are more likely to deliver LGA and macrosomic infants (5, 15, 23, 24).

For some outcomes the effect of maternal weight gain on neonatal outcomes varies across BMI strata (15, 23). Within pre-pregnancy BMI strata, underweight women (<18.5 kg/m^2) with less than adequate weight gain are more likely to deliver an LBW, SGA, or preterm infant compared to underweight women who gain adequate weight (2-6,

23). Some research suggests that gaining more weight than recommended among underweight women may reduce the risk of adverse perinatal outcomes such as SGA (4, 5, 23).

Normal weight (18.5-24.9 kg/m^2) women who gain less weight than recommended are also at greater risk for delivering a SGA, LBW, or preterm infant compared to normal weight women who gain weight as recommended (2, 4-6). In addition, normal weight women who gain more weight than recommended are more likely to deliver a macrosomic infant (>4000 grams) compared to those who gain weight within recommendations (5).

In contrast, gaining more weight than recommended among overweight and obese (≥30 kg/m^2) women is associated with increased odds of having a preterm birth (5). In addition, overweight and obese women with less than adequate weight gain have increased odds of delivering a LBW infant but decreased odds of delivering a macrosomic infant compared to overweight and obese women who gain adequate weight (4, 6).

Preterm, LBW, and SGA infants are at increased risk for infant death and serious morbidity including respiratory infections and diarrheal disease (7-13), two of the leading causes of death among children under five (32-34). Additionally, respiratory infections are one of the leading causes of infant hospitalizations (35). Reducing an infant's risk of diarrheal or respiratory disease can reduce the infant's risk for child and adult morbidity and decrease the economic impact of morbidity and hospitalizations on the community (35-37).

Although numerous studies have evaluated the effect of maternal weight gain during pregnancy on neonatal outcomes little work has been done to evaluate whether maternal weight gain during pregnancy has longer term effects beyond pregnancy. The primary objective of this study is to examine whether maternal weight gain during pregnancy affects infant illness using data from a cohort of Slovak mother and infant pairs. Because prior studies suggest the effect of weight gain during pregnancy varies by pre-pregnancy BMI, we will assess weight gain during pregnancy stratified on pre-pregnancy BMI.

Methods

The original study recruited mother and infant pairs from the districts of Svidnik and Michalovce in Slovakia between 2002 and 2004. Mothers 18 years old or older were enrolled in the study at delivery by hospital staff trained in the study protocols. Women were recruited if they had fewer than four previous births, did not have serious pre-existing health conditions or complications during pregnancy, did not have an infant with severe birth defects, and had resided more than 5 years in their district. All study participants gave written informed consent. The final study population included 1134 mother and infant pairs. Infants were examined by a physician and mothers were interviewed after delivery and at 6, 16, and 45 months post-delivery. A detailed description of the study population and data collection procedures are described elsewhere (55, 56). This study was approved by the Institutional Review Boards at the University of California at Davis and the Slovak Medical University.

For this analysis mother and infant pairs were excluded if they were missing pre-pregnancy weight (n=82), maternal height (n=11), or had no reported weight at or after 36 weeks gestation (n=123). In addition preterm births were excluded (n=42) leaving 876 mother-infant pairs. Further exclusions were made as needed for specific analyses because of missing data. The final populations for the models for ever sick and diarrheal disease were 766, for respiratory disease was 757, for otitis media was 763, and for antibiotic use was 765.

Outcome

The outcome for this study was infant morbidity between 0 to 16 months. Morbidity outcomes were extracted from pediatric records and included frequency of any

infant illness, diarrheal disease, respiratory disease, otitis media, and antibiotic use. In addition, data were collected on frequency of colds (0, 1, or 2 or more times) from 0 to 16 months based on maternal report. All morbidity outcomes were dichotomized as ever vs. never having the outcome. The outcome "colds" was not considered for further analysis because the vast majority of children had a cold by 16 months (n=794).

Exposure

Maternal weight gain during pregnancy was categorized using the 2009 IOM weight gain recommendations (table 1.1). Maternal weight gain was defined using self-reported pre-pregnancy weight subtracted from last reported weight after 36 weeks gestation. Maternal weights during pregnancy were extracted from medical records. Self-reported pre-pregnancy weight was strongly correlated with measured pregnancy weight at 10 weeks (ρ=0.99, $p<0.0001$) among 205 women who had both measures suggesting self-reported pre-pregnancy weight was likely to be strongly correlated with actual pre-pregnancy weight. Last recorded maternal weight during pregnancy was compared to maternal weight at 38 weeks gestation to determine if classification of weight gain during pregnancy was affected by the length of the pregnancy. Final maternal weight measured during pregnancy was strongly correlated with maternal weight at 38 weeks gestation (ρ=0.98, $p<0.0001$) in a subset of 594 women who had both measures. Few women changed categories of weight gain during pregnancy depending on which weight was used (n=66). Therefore, weight gain during pregnancy was based on last recorded maternal pregnancy weight for analysis because it had the fewest missing values. Pre-pregnancy BMI was calculated using self-reported pre-pregnancy weight and maternal height extracted from medical records. All women were classified as below, at, or above

BMI-specific IOM recommendations. Due to small sample size overweight and obese women were combined for analysis after classification.

Covariates

Potential confounders were identified based on the literature and represented in a directed acyclic graph (DAG). The maternal questionnaire used for the delivery interview collected information on the mother's pregnancy, previous pregnancy history, lifestyle factors, and sociodemographic factors. Potential confounders based on maternal report included maternal age (18 to 24 years, 25 to 29 years, 30 to 44 years), maternal education (5^{th} grade or less, basic schooling, college without graduation, college or university), maternal employment (employed vs. unemployed), whether the mother took vitamins during pregnancy (yes or no), whether the mother smoked during pregnancy (yes or no), maternal ethnicity (Romani vs. non-Romani), whether the infant had at least one sibling in preschool (yes or no), and whether the mother ever breastfed her infant (yes or no). Child sex was determined from the birth certificate. Potential confounders based on maternal medical records included district (Michalovce vs. Svidnik), parity (none, one, two, three to five), and whether the woman attended prenatal care (yes or no). Breastfeeding and prenatal care were excluded from further analysis because almost all women had breastfed (97.1%) and attended prenatal care (99.0%).

Analysis

Descriptive analyses were conducted for weight gain during pregnancy stratified by pre-pregnancy BMI as well as for the infant illness outcomes. Potential confounders were identified through the literature and DAGs. Those covariates associated with both weight gain during pregnancy and infant illness outcomes were evaluated further.

Potential confounders included maternal education, maternal employment, maternal ethnicity, parity, vitamin supplementation during pregnancy, and smoking during pregnancy. In addition to the DAG, a change in estimate approach where the estimated effect of weight gain in different strata in a fully adjusted model was compared to the estimate in more parsimonious models was used in the final assessment of potential confounders. Maternal education and maternal ethnicity were important across all models and therefore included in the final models for all outcomes. SAS, version 9.3 (Cary, NC) was used to perform all analyses.

Results

Table 2.1 shows the descriptive characteristics of maternal and infant demographic variables. Of the 876 women, 216 (24.7%) gained weight below recommendations, 347 (39.6%) gained weight within recommendations, and 313 (35.7%) gained weight above recommendations. Women who gained weight as recommended were more likely to have no other children, to live in Michalovce district, and to take vitamins during pregnancy, and less likely to smoke during pregnancy and be Romani compared to women who gained weight outside recommendations. Underweight women who gained less weight than recommended were more likely to have less than a 5^{th} grade education compared to all other underweight women.

Infants who were ever sick were more likely to have mothers who were less educated, more likely to be unemployed, more likely to have other children, and more likely to live in Michalovce district (table 2.2). Infants who were ever diagnosed with a diarrheal disease, respiratory disease, or otitis media and infants who were ever given a course of antibiotics had a similar distribution as ever being sick (table 2.3-2.6).

Infants of underweight mothers who gained less weight than recommended had increased odds for all outcomes except otitis media compared to infants of normal weight mothers who gained weight as recommended, whereas infants of underweight mothers who gained more weight than recommended only had increased odds for diarrheal disease and otitis media, though the estimates were imprecise (table 2.7).

When compared to infants of underweight women who gained weight within recommendations, infants of underweight women who gained weight below recommendations were at increased odds of ever being sick (aOR: 1.64, 95% confidence

interval [CI]: 0.39, 6.88), having diarrheal disease (aOR: 1.45, 95% CI: 0.54, 3.89), having respiratory disease (aOR: 1.51, 95% CI: 0.36, 6.35), and using antibiotic (aOR: 1.41, 95% CI: 0.33, 6.01) but decreased odds of having otitis media (aOR: 0.56, 95% CI: 0.18, 1.79) compared to infants of underweight women who gained weight as recommended. While the infants of underweight women who gained more weight than recommended had decreased odds of ever being sick (aOR: 0.58, 95% CI: 0.13, 2.64), having diarrheal disease (aOR: 1.10, 95% CI: 0.31, 3.84), having respiratory disease (aOR: 0.66, 95% CI: 0.15, 2.93), having otitis media (aOR: 0.76, 95% CI: 0.18, 3.25), and using antibiotics (aOR: 0.67, 95% CI: 0.15, 2.96).

Infants of normal weight mothers who gained less weight than recommended had decreased odds of all outcomes except otitis media compared to infants of normal weight mothers who gained weight within recommendations, while infants of normal weight mothers who gained more weight than recommended had increased odds for all outcomes except otitis media

Infants of overweight and obese mothers regardless of weight gain were more likely to ever be sick or be diagnosed with respiratory disease compared to infants of normal weight mothers who gained weight as recommended. Compared to infants of normal weight women who gained weight as recommended, infants of overweight and obese women who gained weight as recommended had increased odds for all outcomes.

Discussion

Recent research recommends examining the effect of maternal weight gain during pregnancy on infant and childhood outcomes beyond neonatal outcomes and examining whether maternal weight gain above or below 2009 IOM recommendations contributes to infant complications (57). This study examined whether maternal weight gain outside of pre-pregnancy BMI-specific recommendations was associated with infant illness. This study's results provide some support for an association between weight gain outside recommendations during pregnancy and infant morbidity beyond perinatal outcomes, but the sample size strata were small so results were imprecise.

Infants of underweight women who gained less weight than recommended consistently had higher odds of adverse infant health outcomes other than otitis media compared with normal weight women who gained weight as recommended and compared with underweight women who gained weight as recommended. Unlike infants of underweight mothers who gained less weight than recommended, infants of underweight women who gained more weight than recommended did not consistently have higher odds of adverse infant health outcomes. The results for underweight women are similar to the pattern observed for perinatal outcomes such as preterm birth, LBW, and SGA, which may indicate these perinatal outcomes are intermediates between maternal weight gain and infant health. The potential association with infant illness up to 16 months is additional incentive for underweight women to gain weight within recommendations.

Among normal weight women, infants of mothers who gained more weight than recommended had increased odds of infant illness except for otitis media compared to infants of mothers who gained weight as recommended, whereas infants of mothers who

gained less weight than recommended had decreased odds. These results for normal weight women are not consistent with risk patterns observed for perinatal outcomes such as preterm birth, LBW, and SGA but are consistent with patterns observed for macrosomia (2, 4-6). This may indicate that for normal weight women maternal weight gain affects infant health by mechanisms other than through its effect on neonatal outcomes, although our estimates were imprecise.

Infants of overweight and obese women had consistently higher odds of ever being sick and ever being diagnosed with respiratory disease when compared to infants of normal weight women who gained weight within recommendations. In addition, infants of overweight and obese women who gained weight within recommendations had increased odds of all infant outcomes compared to infants of normal weight women who gained weight within recommendations. Overweight and obese women who gained weight outside recommendations had less consistent results though this may partially be attributable to sparser data within these strata. Studies suggest that overweight and obese women who gain excess weight are at increased risk for preterm birth (6, 60), and preterm infants are more at risk for respiratory disease which may suggest a mechanism by which maternal weight gain above recommendations in overweight and obese women may affect infant respiratory illness (7, 27).

The results for otitis media were inconsistent across pre-pregnancy BMI strata of weight gain during pregnancy, and they did not reflect the risk pattern observed for the other infant outcomes. This may partially be the result of sparse data within strata since only 176 infants were ever diagnosed with otitis media. It may also be that the risk of otitis media in infants is affected by different mechanisms than the other outcomes.

This study is one of the first to assess whether there is an association between weight gain during pregnancy and infant illness during the first 16 months after birth. Although this study used data from a large cohort, after exclusions, the stratified cell sizes were often too small to provide precise effect estimates. Weight gain during pregnancy was calculated using self-reported pre-pregnancy weight and final recorded weight during pregnancy. Weight gain during pregnancy based on these measures may not accurately reflect the mother's true weight gain during pregnancy which could lend to misclassification. However, self-reported pre-pregnancy weight and maternal weight at 10 weeks gestation were strongly correlated making extensive misclassification unlikely.

A strength of this study is that infant outcomes were exstracted from medical records and therefore are not subject to recall bias. However, a limitation of using medical records is that not all sick children are taken to see a medical provider which would underestimate the incidence of infant illnesses. This study did not examine an infant's frequency or severity of illness, although limiting the study to illnesses reported in the medical records may serve as a proxy for illness severity. Taking a course of antibiotics may also serve as a proxy for illness severity. Children who are sick more often or have more severe illness are more at risk for chronic morbidity. Future research should focus on examining the effect of weight gain outside recommendations during pregnancy on the frequency and severity of disease.

In conclusion, pregnant women who gain weight outside the 2009 weight gain recommendations are at greater risk for poor maternal and infant outcomes (26). This effect is modified by pre-pregnancy BMI. Unfortunately, once pregnant, women cannot change their pre-pregnancy BMI. However, women can change the amount of weight

they gain during pregnancy. The findings of this study suggest maternal weight gain during pregnancy may have effects in infancy for some outcomes. In particular, underweight women who gain less weight than recommended and normal weight women who gain more weight than recommended may be at risk for delivering infants with increased odds of infant illness. Therefore pregnant women should try to gain weight within current recommendations.

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Table 2.1. Characteristics of a cohort of Slovak, singleton, live births and their mothers by pre-pregnancy BMI-specific maternal weight gain during pregnancy, Slovak cohort 2002-2004 (N=876)

		Underweight Women (n=104)			Normal weight Women (n=605)			Overweight/Obese Women (n=167)		
		Below	At	Above	Below	At	Above	Below	At	Above
	N (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Maternal age, years										
18-24	350 (40.0)	17 (48.6)	12 (66.7)	23 (45.1)	72 (48.0)	86 (39.8)	92 (38.5)	9 (29.0)	20 (25.3)	19 (33.3)
25-29	328 (37.4)	13 (37.1)	4 (22.2)	24 (47.1)	49 (32.7)	79 (36.6)	94 (39.3)	9 (29.0)	34 (43.0)	22 (38.6)
30-44	198 (22.6)	5 (14.3)	2 (11.1)	4 (7.8)	29 (19.3)	51 (23.6)	53 (22.2)	13 (41.9)	25 (31.7)	16 (28.1)
Maternal education										
5th grade or less	124 (14.2)	14 (40.0)	1 (5.66)	7 (13.7)	31 (20.8)	20 (9.3)	32 (13.4)	4 (12.9)	3 (3.8)	12 (21.1)
Basic schooling	229 (26.2)	3 (8.6)	7 (38.9)	9 (17.7)	49 (32.9)	54 (25.0)	45 (18.8)	13 (41.9)	29 (36.7)	20 (35.1)
College without graduation	446 (51.0)	16 (45.7)	9 (50.0)	30 (58.8)	60 (40.3)	121 (56.0)	137 (57.3)	12 (38.7)	41 (51.9)	20 (35.1)
College or University	76 (8.7)	2 (5.7)	1 (5.6)	5 (9.8)	9 (6.0)	21 (9.7)	25 (10.5)	2 (6.5)	6 (7.6)	5 (8.8)
Missing	1	0	0	0	1	0	0	0	0	0
Maternal employment										
Employed	440 (50.8)	14 (40.0)	7 (41.2)	22 (43.1)	57 (38.5)	125 (58.4)	137 (58.3)	12 (38.7)	43 (54.4)	23 (41.1)
Unemployed	426 (49.2)	21 (60.0)	10 (58.8)	29 (56.9)	91 (61.5)	89 (41.6)	98 (41.7)	19 (61.3)	36 (45.6)	33 (58.9)
Missing		0	1	0	2	2	4	0	0	1
Maternal ethnicity										
Romani	125 (14.3)	16 (45.7)	1 (5.56)	5 (9.8)	32 (21.3)	20 (9.3)	27 (11.3)	5 (16.1)	6 (7.6)	13 (22.8)
non-Romani	751 (85.7)	19 (54.3)	17 (94.4)	46 (90.2)	118 (78.7)	196 (90.7)	212 (88.7)	26 (83.9)	73 (92.4)	44 (77.2)
Parity										
None	366 (41.8)	15 (42.9)	15 (83.3)	23 (45.1)	49 (32.7)	114 (52.8)	99 (41.4)	5 (16.1)	32 (40.5)	14 (24.6)
One	307 (35.1)	10 (28.6)	1 (5.6)	24 (47.1)	52 (34.7)	73 (33.8)	91 (38.1)	10 (32.3)	20 (25.3)	26 (45.6)
Two	140 (16.0)	7 (20.0)	2 (11.1)	4 (7.8)	31 (20.7)	21 (9.7)	37 (15.5)	9 (29.0)	20 (25.3)	9 (15.8)
Three to five	63 (7.2)	3 (8.57)	0 (0.0)	0 (0.0)	18 (12.0)	8 (3.7)	12 (5.0)	7 (22.6)	7 (8.9)	8 (14.0)
District										
Michalovce	619 (70.7)	27 (77.1)	17 (94.4)	45 (88.2)	93 (62.0)	157 (72.7)	166 (69.5)	22 (71.0)	60 (76.0)	32 (56.1)
Svidnik	257 (29.3)	8 (22.9)	1 (5.6)	66 (11.8)	57 (38.0)	59 (27.3)	73 (30.5)	9 (29.0)	19 (24.0)	25 (43.9)

Mother took vitamins during pregnancy										
Yes	568 (65.4)	17 (48.6)	14 (87.5)	35 (68.6)	85 (57.1)	166 (77.2)	154 (65.0)	17 (56.7)	53 (67.1)	27 (47.4)
No	301 (34.6)	18 (51.4)	2 (12.5)	16 (31.4)	64 (43.0)	49 (22.8)	83 (35.0)	13 (43.3)	26 (32.9)	30 (52.6)
Missing	7	0	2	0	1	1	2	1	0	0
Mother smoked during pregnancy										
Yes	103 (11.9)	10 (29.4)	2 (12.5)	8 (15.7)	24 (16.0)	15 (6.9)	26 (11.1)	4 (13.8)	5 (6.4)	9 (15.8)
No	763 (88.1)	24 (70.6)	14 (87.5)	43 (84.3)	126 (84.0)	201 (93.1)	209 (88.9)	25 (86.2)	73 (93.6)	48 (84.2)
Missing	10	1	2	0	0	0	4	2	1	0
Mother currently smokes										
Yes	149 (20.0)	12 (41.4)	5 (33.3)	13 (28.9)	25 (19.7)	39 (20.5)	33 (16.8)	3 (11.5)	12 (17.7)	7 (14.6)
No	596 (80.0)	17 (58.6)	10 (66.7)	32 (71.1)	102 (80.3)	151 (79.5)	164 (83.3)	23 (88.5)	56 (82.4)	41 (85.4)
Missing	131	6	3	6	23	26	42	5	11	9
Any sibling attended preschool										
Yes	312 (51.0)	11 (42.3)	4 (33.3)	14 (46.7)	59 (53.2)	67 (47.9)	81 (46.8)	16 (69.6)	36 (60.0)	24 (64.9)
No	300 (49.0)	15 (57.7)	8 (66.7)	16 (53.3)	52 (46.9)	73 (52.1)	92 (53.2)	7 (30.4)	24 (40.0)	13 (35.1)
Missing	264	9	6	21	39	76	66	8	19	20
Child sex										
Female	442 (50.0)	20 (57.1)	9 (50.0)	22 (43.1)	75 (50.0)	99 (45.8)	130 (54.4)	18 (58.1)	40 (50.6)	29 (50.9)
Male	434 (49.5)	15 (42.9)	9 (50.0)	29 (56.9)	75 (50.0)	117 (54.2)	109 (45.6)	13 (41.9)	39 (49.4)	29 (49.1)
Ever Sick										
Yes	671 (87.6)	27 (90.0)	12 (80.0)	39 (83.0)	115 (87.1)	170 (88.1)	176 (86.3)	25 (89.3)	62 (88.6)	45 (95.7)
No	95 (12.4)	3 (10.0)	3 (20.0)	8 (17.0)	17 (12.9)	23 (11.9)	28 (13.7)	3 (10.7)	8 (11.4)	2 (4.3)
Diarrheal Disease										
Yes	222 (29.0)	12 (40.0)	5 (33.3)	14 (29.8)	35 (26.5)	63 (32.6)	55 (27.0)	7 (25.0)	16 (22.9)	15 (31.9)
No	544 (71.0)	18 (60.0)	10 (66.7)	33 (70.2)	97 (73.5)	130 (67.4)	149 (73.0)	21 (75.0)	54 (77.1)	32 (68.1)
Respiratory Disease										
Yes	661 (86.4)	27 (90.0)	12 (80.0)	39 (83.0)	113 (85.6)	166 (86.0)	172 (84.7)	25 (89.3)	62 (88.6)	45 (95.7)
No	104 (13.6)	3 (10.0)	3 (20.0)	8 (17.0)	19 (14.4)	27 (14.0)	31 (15.3)	3 (10.7)	8 (11.4)	2 (4.3)
Otitis Media										
Yes	145 (19.0)	7 (24.1)	3 (20.0)	11 (23.4)	32 (24.2)	26 (13.5)	38 (18.8)	3 (10.7)	14 (20.0)	11 (23.4)
No	618 (80.0)	22 (75.9)	12 (80.0)	36 (76.6)	100 (75.8)	167 (86.5)	164 (81.2)	25 (89.3)	56 (80.0)	36 (76.6)
Antibiotic Use										
Yes	637 (84.2)	27 (90.0)	12 (80.0)	39 (83.0)	108 (83.1)	158 (83.2)	167 (83.1)	23 (82.1)	57 (82.6)	46 (97.9)
No	120 (15.9)	3 (10.0)	3 (20.0)	8 (17.0)	22 (16.9)	32 (16.8)	34 (16.9)	5 (17.9)	12 (17.4)	1 (2.1)

Table 2.2. Characteristics of a cohort of Slovak, singleton, live births and their mothers for ever sick by 16 months of age, Slovak cohort 2002-2004.

	Eligible Women		Never		Ever	
	N=874	%	n=108	%	n=766	%
Maternal age, years						
18-24	360	41.2	39	36.1	321	41.9
25-29	317	36.3	38	35.2	279	36.4
30-44	197	22.5	31	28.7	166	21.7
Maternal education						
5th grade or less	142	16.3	10	9.3	132	17.3
Basic schooling	226	26.0	17	15.7	209	27.4
College without graduation	432	49.6	62	57.4	370	48.5
College or University	71	8.2	19	17.6	52	6.8
Missing	3		0		3	
Maternal employment						
Employed	416	48.4	61	58.1	355	47.1
Unemployed	443	51.6	44	41.9	399	52.9
Missing	15		3		12	
Maternal ethnicity						
Romani	152	17.4	12	11.1	140	18.3
non-Romani	722	82.6	96	88.9	626	81.7
Parity						
None	348	39.8	58	53.7	290	37.9
One	304	34.8	24	22.2	280	36.6
Two	151	17.3	16	14.8	135	17.6
Three to five	71	8.1	10	9.3	61	8.0
District						
Michalovce	636	72.8	69	63.9	567	74.0
Svidnik	238	27.2	39	36.1	199	26.0
Mother took vitamins during pregnancy						
Yes	548	63.3	70	65.4	478	63.0
No	318	36.7	37	34.6	281	37.0
Missing	8		1		7	
Mother smoked during pregnancy						
Yes	114	13.2	14	13.2	100	13.2
No	749	86.8	92	86.8	657	86.8
Missing	11		2		9	
Mother currently smokes						
Yes	181	21.6	21	20.0	160	21.8
No	659	78.5	84	80.0	575	78.2
Missing	34		3		31	
Any sibling attended preschool						
Yes	351	54.8	31	41.3	320	56.5
No	290	45.2	44	58.7	246	43.5
Missing	233		33		200	
Child sex						
Female	433	49.5	59	54.6	374	48.8
Male	441	50.5	49	45.4	392	51.2

Table 2.3. Characteristics of a cohort of Slovak, singleton, live births and their mothers for diarrheal disease by 16 months of age, Slovak cohort 2002-2004.

	Eligible Women		Never		Ever	
	N=874	%	n=616	%	n=258	%
Maternal age, years						
18-24	360	41.2	233	37.8	127	49.2
25-29	317	36.3	230	37.3	87	33.7
30-44	197	22.5	153	24.8	44	17.1
Maternal education						
5th grade or less	142	16.3	87	14.2	55	21.5
Basic schooling	226	26.0	154	25.0	72	28.1
College without graduation	432	49.6	319	51.9	113	44.1
College or University	71	8.2	55	8.9	16	6.3
Missing	3		1		2	
Maternal employment						
Employed	416	48.4	304	50.2	112	44.3
Unemployed	443	51.6	302	49.8	141	55.7
Missing	15		10		5	
Maternal ethnicity						
Romani	152	17.4	99	16.1	53	20.5
non-Romani	722	82.6	517	83.9	205	79.5
Parity						
None	348	39.8	237	38.5	111	43.0
One	304	34.8	204	33.1	100	38.8
Two	151	17.3	116	18.8	35	13.6
Three to five	71	8.1	59	9.6	12	4.7
District						
Michalovce	636	72.8	433	70.3	203	78.7
Svidnik	238	27.2	183	29.7	55	21.3
Mother took vitamins during pregnancy						
Yes	548	63.3	385	62.9	163	64.2
No	318	36.7	227	37.1	91	35.8
Missing	8		4		4	
Mother smoked during pregnancy						
Yes	114	13.2	536	88.0	213	83.9
No	749	86.8	73	12.0	41	16.1
Missing	11		7		4	
Mother currently smokes						
Yes	181	21.6	116	19.7	65	25.9
No	659	78.5	473	80.3	186	74.1
Missing	34		27		7	
Any sibling attended preschool						
Yes	351	54.8	260	56.4	91	50.6
No	290	45.2	201	43.6	89	49.4
Missing						
Child sex						
Female	433	49.5	313	50.8	120	46.5
Male	441	50.5	303	49.2	138	53.5

Table 2.4. Characteristics of a cohort of Slovak, singleton, live births and their mothers for respiratory disease by 16 months of age, Slovak cohort 2002-2004.

	Eligible Women		Never		Ever	
	N=873	%	n=118	%	n=755	%
Maternal age, years						
18-24	360	41.2	43	36.4	317	42.0
25-29	316	36.2	43	36.4	273	36.2
30-44	197	22.6	32	27.1	165	21.9
Maternal education						
5th grade or less	142	16.3	10	8.5	132	17.6
Basic schooling	226	26.0	21	17.8	205	27.3
College without graduation	431	49.5	68	57.6	363	48.3
College or University	71	8.2	19	16.1	52	6.9
Missing						
Maternal employment						
Employed	416	48.5	63	54.8	353	47.5
Unemployed	442	51.5	52	45.2	390	52.5
Missing	15		3		12	
Maternal ethnicity						
Romani	152	17.4	12	10.2	140	18.5
non-Romani	721	82.6	106	89.8	615	81.5
Parity						
None	347	39.8	60	50.9	287	38.0
One	304	34.8	29	24.6	275	36.4
Two	151	17.3	18	15.3	133	17.6
Three to five	71	8.1	11	9.3	60	8.0
District						
Michalovce	635	72.7	76	64.4	559	74.0
Svidnik	238	27.3	42	35.6	196	26.0
Mother took vitamins during pregnancy						
Yes	547	63.2	77	65.8	470	62.8
No	318	36.8	40	34.2	278	37.2
Missing	8		1		7	
Mother smoked during pregnancy						
Yes	114	13.2	16	13.8	98	13.1
No	748	86.8	100	86.2	648	86.9
Missing	11		2		9	
Mother currently smokes						
Yes	181	21.6	23	20.0	158	21.8
No	658	78.4	92	80.0	566	78.2
Missing	34		3		31	
Any sibling attended preschool						
Yes	351	54.8	33	39.8	318	57.1
No	289	45.2	50	60.2	239	42.9
Missing	233		35		198	
Child sex						
Female	432	49.5	64	54.2	368	48.7
Male	441	50.5	54	45.8	387	51.3

Table 2.5. Characteristics of a cohort of Slovak, singleton, live births and their mothers for otitis media by 16 months of age, Slovak cohort 2002-2004.

	Eligible Women		Never		Ever	
	N=871	%	n=695	%	n=176	%
Maternal age, years						
18-24	359	41.2	274	39.4	85	48.3
25-29	315	36.2	248	35.7	67	38.1
30-44	197	22.6	173	24.9	24	13.6
Maternal education						
5th grade or less	142	16.4	87	12.6	55	31.4
Basic schooling	225	25.9	179	25.8	46	26.3
College without graduation	430	49.5	366	52.8	64	36.6
College or University	71	8.2	61	8.8	10	5.7
Missing	3		2		1	
Maternal employment						
Employed	415	48.5	345	50.5	70	40.5
Unemployed	441	51.5	338	49.5	103	59.5
Missing	15		12		3	
Maternal ethnicity						
Romani	151	17.3	92	13.2	59	33.5
non-Romani	720	82.7	603	86.8	117	66.5
Parity						
None	346	39.7	280	40.3	66	37.5
One	304	34.9	245	35.3	59	33.5
Two	150	17.2	114	16.4	36	20.5
Three to five	71	8.2	56	8.1	15	8.5
District						
Michalovce	633	72.7	500	71.9	133	75.6
Svidnik	238	27.3	195	28.1	43	24.4
Mother took vitamins during pregnancy						
Yes	547	63.4	448	65.0	99	56.9
No	316	36.6	241	35.0	75	43.1
Missing	8		6		2	
Mother smoked during pregnancy						
Yes	114	13.3	77	11.2	37	21.3
No	746	86.7	609	88.8	137	78.7
Missing	11		9		2	
Mother currently smokes						
Yes	181	21.6	141	21.1	40	23.7
No	656	78.4	527	78.9	129	76.3
Missing	29		27		2	
Any sibling attended preschool						
Yes	350	54.9	284	55.2	66	53.7
No	288	45.1	231	44.9	57	46.3
Missing	233		180		53	
Child sex						
Female	430	49.4	351	50.5	79	44.9
Male	441	50.6	344	49.5	97	55.1

Table 2.6. Characteristics of a cohort of Slovak, singleton, live births and their mothers for antibiotic use by 16 months of age, Slovak cohort 2002-2004.

	Eligible Women		Never		Ever	
	N=863	%	n=133	%	n=730	%
Maternal age, years						
18-24	358	41.5	48	36.1	310	42.5
25-29	309	35.8	50	37.6	259	35.5
30-44	196	22.7	35	26.3	161	22.1
Maternal education						
5th grade or less	140	16.3	9	6.8	131	18.0
Basic schooling	222	25.8	25	18.9	197	27.1
College without graduation	428	49.8	76	57.6	352	48.4
College or University	70	8.1	22	16.7	48	6.6
Missing	3		1		2	
Maternal employment						
Employed	412	48.5	74	56.9	338	47.0
Unemployed	437	51.5	56	43.1	381	53.0
Missing	14		3		11	
Maternal ethnicity						
Romani	149	17.3	11	8.3	138	18.9
non-Romani	714	82.7	122	91.7	592	81.1
Parity						
None	343	39.8	66	49.6	277	38.0
One	301	34.9	36	27.1	265	36.3
Two	151	17.5	20	15.0	131	18.0
Three to five	68	7.9	11	8.3	57	7.8
District						
Michalovce	626	72.5	87	65.4	539	73.8
Svidnik	237	27.5	46	34.6	191	26.2
Mother took vitamins during pregnancy						
Yes	541	63.3	90	68.2	451	62.4
No	314	36.7	42	31.8	272	37.6
Missing	8		1		7	
Mother smoked during pregnancy						
Yes	113	13.3	12	9.2	101	14.0
No	739	86.7	118	90.8	621	86.0
Missing	11		3		8	
Mother currently smokes						
Yes	178	21.5	22	16.9	156	22.3
No	652	78.6	108	83.1	544	77.7
Missing	33		3		30	
Any sibling attended preschool						
Yes	347	54.8	42	45.2	305	56.5
No	286	45.2	51	54.8	235	43.5
Missing	130		40		190	
Child sex						
Female	427	49.5	72	54.1	355	48.6
Male	436	50.5	61	45.9	375	51.4

Table 2.7. Association between pre-pregnancy BMI-specific maternal weight gain during pregnancy and infant morbidity adjusting for maternal education and maternal ethnicity, Slovak cohort 2002-2004 (N=766).[1]

		Ever Sick			Diarrheal Disease			Respiratory Disease[2]			Otitis Media[3]			Antibiotics[4]		
	n	aOR	95% CI		aOR	95% CI		aOR	95% CI		aOR	95% CI		aOR	95% CI	
Underweight:																
Below	30	1.25	0.34	4.52	1.67	0.74	3.78	1.36	0.38	4.91	0.82	0.30	2.22	1.45	0.40	5.26
At	15	0.79	0.33	1.90	1.14	0.56	2.31	0.90	0.38	2.14	1.47	0.67	3.21	1.02	0.43	2.42
Above	47	0.49	0.13	1.89	1.25	0.41	3.88	0.59	0.15	2.27	1.10	0.29	4.23	0.68	0.18	2.59
Normal weight:																
Below	132	0.86	0.44	1.67	0.89	0.54	1.47	0.88	0.47	1.65	1.16	0.66	2.02	0.85	0.46	1.58
At	193		Referent			Referent			Referent			Referent			Referent	
Above	204	1.19	0.66	2.17	1.34	0.87	2.07	1.13	0.64	1.98	0.70	0.40	1.21	1.05	0.61	1.79
Overweight/Obese:																
Below	28	1.11	0.31	4.02	0.87	0.34	2.17	1.31	0.37	4.70	0.45	0.13	1.63	0.84	0.29	2.42
At	70	3.17	0.72	14.03	1.19	0.59	2.39	3.63	0.83	15.92	1.08	0.48	2.40	8.76	1.15	66.54
Above	47	1.16	0.50	2.72	0.81	0.43	1.55	1.36	0.59	3.15	1.19	0.59	2.40	0.97	0.46	2.02

[1] Adjusted for maternal education and maternal ethnicity

[2] Respiratory Disease (n=757); Normal weight, above (n=203)

[3] Otitis Media (n=763); Underweight, below (n=29), Normal weight, above (n=202)

[4] Antibiotics (n=765); Normal weight, below (n=130), at (n=190), above (n=201)

Appendix

January 5, 2012

Olivia Sappenfield
Principal Investigator
Public Health

RE: Exemption of Human Subjects Research
IRB00054890
Gestational weight gain and infant morbidity

Dear Principal Investigator:

Thank you for submitting an application to the Emory IRB for the above-referenced project. Based on the information you have provided, we have determined on 1/5/2012 that although it is human subjects research, it is exempt from further IRB review and approval.

This determination is good indefinitely unless substantive revisions to the study design (e.g., population or type of data to be obtained) occur which alter our analysis. Please consult the Emory IRB for clarification in case of such a change. Exempt projects do not require continuing renewal applications.

This project meets the criteria for exemption under 45 CPR 46.101(b)(4). Specifically, you will collect and analyze personal health and demographic data collected from a sample of Slovakian mothers and their infants between 2002 and 2004.

- A waiver of all elements of informed consent has been granted for this study. Please

note that the Belmont Report principles apply to this research: respect for persons, beneficence, and justice. You should use the informed consent materials reviewed by the IRB unless a waiver of consent was granted. Similarly, if HIPAA applies to this project, you should use the HIPAA patient authorization and revocation materials reviewed by the IRB unless a waiver was granted. CITI certification is required of all personnel conducting this research.

Unanticipated problems involving risk to subjects or others or violations of the HIPAA Privacy Rule must be reported promptly to the Emory IRB and the sponsoring agency (if any).

In future correspondence about this matter, please refer to the study ID shown above. Thank you.

Sincerely,

Sam Roberts, CIP

Research Protocol Analyst
This letter has been digitally signed

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