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Maternal Age, Multiple Birth and Extremely Low Birth Weight Infants

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Abstract

Objectives—To compare the rates of adverse neurodevelopmental outcome or death at 18 to 22 months among extremely low birth weight (ELBW) infants born to mothers ≥ 40 years to the corresponding rates among infants of younger mothers.

Study Design—Prospective evaluation of ELBW infants to quantify the relative risks of maternal age and multiple birth for death or adverse neurodevelopmental outcome.

Results—The sample consisted of 14,671 live ELBW births divided into maternal age groups: <20 ; 20–29; 30–39; and ≥ 40 years. Of infants born to mothers ≥ 40 years, 20% were multiples. Mothers ≥ 40 years had high rates of obstetrical interventions and medical morbidities compared to mothers < 40 years. ELBW live births of mothers ≥ 40 years were 22 % more likely to survive and had a 13% decreased risk of neurodevelopmental impairment or death compared to mothers < 20 . Multiple birth, however, was associated with a 10 % greater risk of neurodevelopmental impairment or death.

Conclusion—Although mothers ≥ 40 years had high pregnancy related morbidities, we found no overall increased risk of the composite outcome of death or NDI. Multiple birth, however, was a predictor of all adverse outcomes examined, regardless of maternal age.

Keywords

outcomes; neurodevelopmental impairment; death

National statistics show that birth rates for women 40–44 years of age continued to increase in 2005 and 2006 to a rate of 9.4 per 1000.[1–3] Delayed childbearing has been attributed to prolonged education, commitment to profession, delayed marriage and other personal reasons. [4] Problems associated with older childbearing include hypertension, diabetes, cardiovascular disease, preterm labor, fetal malformations, and fetal death.[5–11] Older women are at increased risk for spontaneously occurring multiple gestation, and multiple gestation associated with infertility treatments and assisted reproductive technology (ART).[12–15] The current trend for older child-bearing has been associated with an increase in multiple births and extremely-low-birth-weight (ELBW, < 1000 grams) infants.[10–15] Between 1980 and 1999,

the overall U.S. multiple birth rate increased 59%. [1] Multiples accounted for 3.4% of all births in 2005. [3] Between January 1995 and December 2003, 26% of live births < 1500 grams at NICHD Neonatal Research Network Centers were multiples. [16] Although a downward trend in the proportion of higher-order multiples was observed in 2005 in the United States, the twin birth rate remained unchanged at 32.2 per 1000 births in 2004 and 2005. [1,3] Older mothers however, are more likely to have higher education, be married, have private health insurance, and higher family income, all factors which provide a more optimal environment and are associated with more favorable outcomes for children. [17–19] Our prior studies of ELBW outcomes have shown that higher maternal education, private health insurance, and white race were independently associated with higher Bayley mental developmental index (MDI) scores and lower rates of neurodevelopmental impairment (NDI) at 18 months. [17–20] The associations of older maternal child-bearing age (≥ 40 years) of ELBW infants with maternal morbidities, neonatal morbidities, multiple birth, neonatal death and neurodevelopmental outcomes are unknown.

The purpose of this study was to compare the rates of multiple gestations, neonatal morbidity, death, NDI and the composite outcome of NDI or death at 18 to 22 months corrected age among ELBW infants born to mothers ≥ 40 years to the corresponding rates among ELBW infants born to mothers < 40 years. We hypothesized that, within a large cohort of ELBW infants, maternal age ≥ 40 yrs would be associated with increased rates of multiple birth, increased maternal and neonatal morbidity and increased NDI or death. We also hypothesized that outcomes at 18 to 22 months CA would be related to maternal socioeconomic status.

Methods

Maternal and neonatal characteristics and morbidities were collected prospectively by trained research personnel to 120 days or day of discharge. [18] The following definitions were used: early-onset sepsis was defined as a positive blood cultures ≤ 72 hours, late-onset sepsis was positive blood cultures >72 hours, preterm premature rupture of membranes (PPROM) was ROM >18 hours prior to delivery, and maternal hypertension was systolic blood pressure >140 mm Hg or a diastolic blood pressure >90 mm Hg on at least 2 occasions prior to or during the pregnancy. The study definition of resuscitation was the presence of any of the following in the delivery room: supplemental oxygen ($Fi O_2 > 0.21$), hand ventilation with a bag and mask, continuous positive airway pressure, intubation, chest compressions, and epinephrine.

Infants were evaluated at 18–22 months CA corrected age using the standard Neonatal Research Network follow-up protocol. [18] The follow-up assessment included interim medical history, maternal demographic information including marital status, race, number of years of education, and type of health insurance, and child developmental, neurological, and physical assessments. The neurologic examination, based on the Amiel Tison [21] assessment, was performed by certified examiners who had been trained to reliability. Cerebral palsy (CP) was defined as a non-progressive central nervous system disorder characterized by abnormal muscle tone in at least one extremity and abnormal control of movement and posture. [18] CP was classified as “moderate” if the child could sit independently or with support, but an assistive device was required for ambulation, and “severe” if the child was unable to sit or walk even with support. The Bayley Scales of Infant Development II [22] Mental and Motor Scales were administered by certified examiners trained to reliability. Bayley scores of 100 ± 15 represent the mean ± 1 standard deviation (SD). A score <70 (2 standard deviations below the mean) was interpreted as evidence of developmental delay.

An interim history, including information on hearing and vision status, were obtained. [18] Hearing impairment was defined as need of amplification for both ears. A history of post-discharge eye assessments was obtained and a standard eye exam was completed. Blindness

was defined as corrected vision less than 20–200 in both eyes. NDI was defined as the presence of any of the following: moderate to severe CP, MDI < 70, PDI < 70, blind in both eyes and bilateral amplification for hearing loss.

Statistical analyses were completed by RTI International. Mothers and infants were divided into groups based on maternal age, < 20, 20–29, 30–39 and ≥ 40 years. Proportions and means were calculated. Chi-square test was used to test for significant differences in the prevalence of the maternal and neonatal characteristics and in the death rates across the age groups. One-way ANOVA was used to determine differences in the mean values of characteristics and outcomes. Multiple comparison procedures for pair-wise comparisons developed by Zar [23] and Dunnett [24] were used to further identify differences between mothers ≥ 40 years and the younger age groups. These procedures adjust the statistical tests of significance for simultaneous tests between any two age groups.

In order to assess independent associations with the infant neurodevelopmental outcomes (Bayley MDI < 70, Bayley PDI < 70, moderate to severe CP and NDI), regression modeling analyses were conducted. Factors examined were maternal characteristics present at birth and known to be associated with study outcomes and included mothers age group, multiple birth, primiparity, type of health insurance, and educational level. Additional socioeconomic variables could not be entered since they were not available on the infants who died. Because the focus of this study was the assessment of the relationship of maternal characteristics on infant outcome, adjustments were made only for maternal characteristics. Generalized linear regression models with a Poisson error distribution were used to derive relative risk estimates. The study centers were specified as a clustering factor in the models and the generalized estimation equations (GEE) method was used to take into account the within-center correlations.

In addition to the main effects of these predictors, the interaction terms of maternal age group with multiple birth, Medicaid status, educational level and primiparity were tested for statistical significance. Relative risk estimates were then derived from parsimonious models that included predictors and interaction terms with statistically significant effects. The study was approved by each center's Institutional Review Board.

Results

Table 1 shows the maternal characteristics of the 13, 441 mothers whose live born ELBW infants were cared for at one of the NICHD Neonatal Network centers from January 1, 1995 to December 30, 2003. Compared to mothers < 20 and 20–29 years, mothers ≥ 40 years were more likely to be White, married, and have higher education and private health insurance than were mothers < 20 years. They were less likely to be primiparous and more likely to be delivered by C-section than all other maternal age groups. They received more prenatal care than mothers < 20 and were more likely to have received antenatal steroids than mothers < 20 and 20–29 years. Maternal morbidity rates were higher among the mothers ≥ 40 years; they were more likely to have hypertension than other maternal age groups, more PPROM than mothers < 20 years and more diabetes than mothers ≤ 29 years.

Table 2 shows the neonatal characteristics and morbidities of the 14,671 ELBW live births by maternal age group. There were no significant differences in gestational age, birth weight, or gender among groups. ELBW infants born to mothers ≥ 40 years were less likely to be singletons compared to infants born to mothers < 20 and more likely to be singletons than infants compared to mothers 30–39 years. Infants of mothers ≥ 40 years were less likely to have an Apgar score < 4 at 5 minutes and more likely to receive some resuscitation at birth than all other study groups. They were more likely to be SGA than infants of mothers < 20 and 20–

29 years. Although, the infants of mothers ≥ 40 years were less likely to have IVH 3–4 than infants of mothers < 20 years, and were less likely to die prior to discharge than infants of mothers < 20 years and 20–29 years, there were no differences in the rates of sepsis, PVL, proven NEC and oxygen at 36 weeks. Infants of mothers ≥ 40 years were less likely to die prior to discharge than infants of mothers ≤ 29 years. Singletons born to mothers ≥ 40 years were less likely to die prior to discharge than singletons born to mothers < 20 years. Although the death rate for multiples of mothers ≥ 40 years was the lowest, it did not differ significantly from infants in younger age groups. The death rate, however, was significantly higher for multiples than singletons prior to discharge, $p < 0.003$, whereas there was no difference after discharge, $p = 0.67$. (data not shown in table)

A comparison of infants with complete follow-up assessments with those lost or with incomplete follow-up revealed no differences among maternal age groups in rates of multiples, marital status, or education level. Infants followed were more likely to have a lower birth weight (790 ± 135 grams versus 800 ± 137 grams, $p < 0.006$) and were less likely to be SGA (17.4% versus 20.8%, $p < 0.001$) compared to those lost.

Outcomes at 18 to 22 months CA are shown in Table 3. Follow up rate was highest for infants of mothers ≥ 40 years. There were no significant differences among the study groups in Bayley MDI or PDI scores, rates of bilateral blindness, hearing loss requiring amplification, moderate to severe CP or NDI. Death by the 18–22 month follow-up evaluation was lowest among mothers ≥ 40 years and was significantly lower than among infants born to mothers < 20 and 20–29 years. The rate of the composite outcome of NDI or death was lowest among infants of mothers ≥ 40 years and was significantly lower for infants of mothers ≥ 40 years compared to infants of mothers < 20 .

Table 4 shows the relative risk estimates and their 95% confidence intervals for the study outcomes derived from the estimated regression models. No independent effects of maternal age ≥ 40 years on NDI were identified. Maternal age ≥ 40 years was associated with a 22% decreased risk of death and a 13% decreased risk of NDI or death compared to mothers < 20 years. After adjusting for health insurance, maternal education, primiparity, and maternal age, multiple birth was associated with more than a 20% increase of low Bayley scores, moderate to severe CP, and NDI, a 12 % increased risk of death and a 10% increased risk of death or NDI. Medicaid insurance was associated with a 35 to 59% increased risk of low Bayley scores a 45% increased risk of moderate to severe CP and a 44% increased risk of NDI. The effects of high school education or less were more modest; a 13% increased risk of low MDI and a 7% increased risk of NDI and a 20% decreased risk of moderate to severe CP. In contrast, primiparity was associated with 23% decreased risk of moderate to severe CP and a 4% decreased risk of NDI or death.

In addition, interaction effects of maternal age groups with multiple birth, Medicaid insurance and primiparity were tested in the regression models (not shown in table). Although there were no significant interaction effects with multiple birth, significant interaction effects with Medicaid insurance or primiparity were observed. The effects of maternal age group on low Bayley MDI scores and NDI were dependent on Medicaid insurance. Infants of mothers ≥ 40 years on Medicaid were at the significantly increased risk of low Bayley MDI scores compared to infants of mothers on Medicaid < 20 (1.34 ;1.10–1.63), 20–29, (1.28 ;1.08–1.53), and 30–39 years (1.31 ;1.05–1.64). This was not true among infants of mothers who were not on Medicaid. Similarly, infants of primiparous mothers ≥ 40 years were at significantly increased risk of low Bayley PDI scores compared to primiparous mothers < 20 (1.90;1.32–2.75), 20–29 (1.85;1.25–2.73) and 30–39 years (1.73;1.17 to 2.56), and at increased risk of NDI compared to infants of primiparous mothers < 20 years. (1.49; 1.05–2.12).

Discussion

Our hypothesis that mothers ≥ 40 years would have higher rates of multiple births among ELBW infants was not confirmed. Although mother's ≥ 40 years had significantly more triplets compared to mothers < 20 years, they did not differ from the other study groups in the rate of twin delivery.

Mothers ≥ 40 years did however, have increased rates of pregnancy related morbidities including diabetes, hypertension and PPRM; the rate of diabetes was 9 times greater for mothers ≥ 40 years compared to mothers < 20 years and 3 times higher than mothers 20–29 years. The rates of hypertension/preeclampsia were 31% to 54% higher for mothers ≥ 40 years compared to mothers < 40 years, and the rate of PPRM was 28% higher compared to mothers < 20 years. These findings of increased maternal morbidities for mothers ≥ 40 years are consistent with the reports of maternal population based studies. [4–10] Neonatal mortality rates pre- and post-discharge were lowest among infants of mothers ≥ 40 years. Although others have shown higher rates of fetal loss among neonates of older mothers,[11] fetal outcomes and ART information were not available for our cohort. A recent large population-based study in Israel, however, found no differences in mortality among VLBW infants conceived by ART compared to controls.[25]

Our findings suggest that more favorable pregnancy care of older mothers may contribute to better outcomes among ELBW infants. Increasing maternal age was associated with higher rates of antenatal steroids, prenatal care and C-section delivery. Data showing an increased rate of obstetrical interventions with increasing maternal age[26] have previously been reported.

Maternal age group was associated with few significant differences in infant outcomes tested. The infants of mothers ≥ 40 years were less likely to have a low Apgar score at 5 minutes than all other study groups and were more likely to have resuscitation efforts than all three other study groups. Infants of mothers ≥ 40 years were more likely to be SGA than infants of mother < 30 years and less likely to have a grade 3–4 IVH than infants of mothers < 20 years. The SGA rate ranged from 15.9% for the mothers < 20 years to 18.5% for mothers ≥ 40 years. The rate of SGA has been shown in population- based studies to increase with increasing maternal age. [4–10] An increased rate of SGA infants is not surprising, considering the increased rates of hypertension, diabetes, and multiple gestation among older mothers.[10–12]

Our hypothesis that ELBW infants born to mothers ≥ 40 years were at increased risk of adverse NDI was not supported, and maternal age ≥ 40 years was, in fact, associated with a decreased risk of death or death and NDI compared to mothers < 20 years. However, the relationship between age and NDI was complex and we documented an interaction between the effects of maternal age ≥ 40 years with primiparity on neurodevelopmental outcomes. Although there was no independent effect of primiparity on NDI, infants of primiparous mothers ≥ 40 years were at increased risk of NDI compared to mothers < 20 years, with a similar trend compared to mothers 20–29 and 30–39 years. In addition, infants of primiparous mothers ≥ 40 years were at increased risk of a Bayley PDI < 70 compared to infants of primiparous mothers in all 3 younger age groups. Others have shown that nulliparous pregnancies of older women are associated with increased maternal complications.[27] We believe this is the first time an association between maternal age ≥ 40 years, primiparity, and adverse child outcomes has been identified. Although only 13% of the mothers ≥ 40 years were primiparous compared to 64% of mothers < 20 , primiparous mothers ≥ 40 years may have additional medical problems that contribute to the adverse pregnancy and child outcomes. In the regression models for death or the composite outcome of death or NDI, maternal age effects were identified and infants of mothers ≥ 40 years had both decreased rates of death and death or NDI compared to infants of

mothers < 20 years. Most of the variance in the models was accounted for by death and infants of mothers ≥ 40 years had the lowest death rates. Also, in the regression for the composite outcome of NDI or death, primiparity was associated with a 4% decreased risk of NDI or death. These findings support the concept that a complex interaction of multiple maternal biologic and environmental factors contributes to child outcome.

Although mothers ≥ 40 years had a higher incidence of maternal pregnancy related morbidities that may increase the risk of adverse outcome, they also had higher rates of characteristics associated with more optimal outcomes including higher education level and private health insurance.[28] Mothers ≥ 40 years were also more likely to receive prenatal care than mothers < 20, receive antenatal steroids than mothers < 30 and be delivered by C-section than mothers < 40. In addition, their infants were more likely to be resuscitated and less likely to have a low Apgar at 5 minutes than all other study groups.

We hypothesized that our outcomes would be mediated by SES. In fact, Medicaid insurance and $\leq$ high school education were both independently associated with adverse outcomes. We sought to pursue this further by examining interactions with maternal age with health insurance. It is of interest that the interaction of private insurance with maternal age did not significantly lower the risk of adverse outcome, whereas the interaction of Medicaid insurance and age ≥ 40 years significantly increased the risk of low Bayley MDI compared to infants of mothers in all the other age groups. This suggests that there may be additional barriers to medical care and intervention services for offspring of mothers ≥ 40 years who are on Medicaid.

Multiple birth, however, was independently associated with higher rates of MDI < 70, PDI < 70, moderate to severe CP, NDI, and the combined outcome of NDI and death. Delayed childbearing in conjunction with use of ART procedures has contributed to increased rates of preterm birth and multiple birth.[1,3] Although we did not have data on ART or ovulatory stimulation, we assume that the majority of the multiple gestations were secondary to ART or ovulatory stimulation. There were no significant interactions between maternal age and multiple birth and the increased independent risk of multiple birth for death or NDI applied to all age groups.

Limitations of our study are that we did not include births greater than 1000 g birth weight, the study was not population based, and we did not have information on maternal use of ART.

Conclusion

Despite the fact that mothers ≥ 40 years had high pregnancy related morbidities, there were no independent effects of maternal age on NDI, with the exception of primiparous mothers ≥ 40 years. Furthermore, ELBW infants of mothers ≥ 40 years had a decreased rate of death and the combined outcome of death or NDI compared to ELBW infants of mothers < 20 years. Multiple birth, however, was a powerful predictor of adverse outcomes across all ages. Guidance to mothers of all ages regarding the potential risks of multiple birth on adverse outcomes is recommended.

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Abbreviations

ART	assisted reproductive technology
CP	cerebral palsy
ELBW	Extremely-low-birth-weight
NDI	Neurodevelopmental impairment
MDI	Bayley II Mental developmental index
PDI	Psychomotor developmental index
PPROM	preterm premature rupture of membranes

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APPENDIX I

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University of California – San Diego Medical Center and Sharp Mary Birch Hospital for Women (U10 HD40461) – Neil N. Finer, MD; Maynard R. Rasmussen, MD; Yvonne E. Vaucher, MD MPH; Kathy Arnell, RN; Clarence Demetrio, RN; Martha G. Fuller, RN MSN;

Chris Henderson, RCP CRTT; Wade Rich, BSHS RRT; Rene Barbieri-Welge; Ayala Ben-Tall; Elaine Ito; Meghan Lukasik; Deborah Pontillo; Donna Posin, OTR/L MPA; Cheryl Runyan; James Wilkes.

University of Cincinnati University Hospital, Cincinnati Children's Hospital Medical Center, and Good Samaritan Hospital (GCRC M01 RR8084, U10 HD27853) – Edward F. Donovan, MD; Jean Steichen, MD; Kurt Schibler, MD; Kathleen Bridges, MD; John Fridriksson, MD; Barb Alexander, RN; Cathy Grisby, BSN CCRC; Teresa L. Gratton, PA; Marcia Mersmann, RN; Holly Mincey, RN BSN; Jody Shively, RN.

University of Miami Holtz Children's Hospital (GCRC M01 RR16587, U10 HD21397) – Shahnaz Duara, MD; Charles R. Bauer, MD; Sylvia Hiriart-Fajardo, MD; Ruth Everett-Thomas, RN MSN; Mary Allison, RN; Carmel Azemar, MSW; Maria Calejo, MS; Alexis N. Diaz, BA; Silvia M. Frade Eguaras, MA; Yamiley C. Gideon, BA; Wendy Griffin, RN; Rafael Guzman, MSW; Kasey Hamlin-Smith, PhD; Elizabeth Jacque, RN; Lisa Jean-Gilles, BA; Ann Londono; Elaine O. Mathews, RN; Alexandra Stroerger.

University of New Mexico Health Sciences Center (GCRC M01 RR997, U10 HD27881) – Lu-Ann Papile, MD; Conra Backstrom Lacy, RN; Jean Lowe, PhD, Ginny Laadt, PhD OTR, Debra V. Long, BSN.

University of Rochester Golisano Children's Hospital at Strong (GCRC M01 RR44, U10 HD40521) – Dale L. Phelps, MD; Ronnie Guillet, MD PhD; Gary J. Myers, MD; Carl T. D'Angio, MD; Linda J. Reubens, RN CCRC; Diane Hust, RN PNP; Rosemary L. Jensen; Erica Burnell, RN; Julie Babish Johnson, MSW; Cassandra A. Horihan, MS; Emily Kushner, MS; Joan Merzbach, MSW; Gina Rowan, RN; Kelley Yost, PhD; Lauren Zwetsch, PPN; Kristina Mossgraber.

University of Tennessee (U10 HD21415) – Sheldon B. Korones, MD; Henrietta S. Bada, MD; Kim Yolton, PhD; Tina Hudson, RN BSN.

University of Texas Southwestern Medical Center at Dallas Parkland Health & Hospital System and Children's Medical Center Dallas (GCRC M01 RR633, U10 HD40689) – Abbot R. Laptook, MD; Charles R. Rosenfeld, MD; Walid A. Salhab, MD; R. Sue Broyles, MD; Roy J. Heyne, MD; Ricardo D. Uauy, MD PhD; Susie Madison, RN; Jackie F. Hickman, RN; Gaynelle Hensley, RN; Nancy A. Miller, RN; Janet S. Morgan, RN; Sally Adams, PNP; Cathy Boatman, MS CIMI; Cristin Dooley, MS; Alicia Guzman; Elizabeth Heyne, PA; Cristine Lupino, MS; Linda Madden, PNP.

University of Texas Health Science Center at Houston Medical School, Children's Memorial Hermann Hospital, and Lyndon Baines Johnson General Hospital/Harris County Hospital District (U10 HD21373) – Kathleen A. Kennedy, MD MPH; Brenda H. Morris, MD; Pamela J. Bradt, MD MPH; Patricia W. Evans, MD; Terri Major-Kincade, MD MPH; Laura L. Whitely, MD; Esther G. Akpa, RN BSN; Magda Cedillo; Patty A. Cluff, RN; Anna E. Lis, RN BSN; Georgia E. McDavid, RN; Claudia Y. Franco, RN BSN MSN NNP; Nora I. Alaniz, BS; Susan Dieterich, PhD; Stacey Reddoch, BA; Patti L. Tate, RCP.

Wake Forest University Baptist Medical Center, Forsyth Medical Center, and Brenner Children's Hospital (GCRC M01 RR7122, U10 HD40498) – T. Michael O'Shea, MD MPH; Robert G. Dillard, MD; Lisa K. Washburn, MD; Nancy J. Peters, RN CCRP; Barbara G. Jackson, RN BSN; Debbie Allred, MA; Korinne Chiu, MA; Don Goldstein, PhD; Raquel Halfond, MA; Cherie Heller, MD MPH; Gail Hounshell, PhD; Melissa Morris, MA; Carol Peterson, MA; Ellen Waldrep, MS.

Wayne State University Hutzel Women's Hospital and Children's Hospital of Michigan (U10 HD21385) – Seetha Shankaran, MD; Yvette Johnson MD MPH; Athina Pappas, MD; Rebecca Bara, RN BSN; Geraldine Muran, RN BSN; Deborah Kennedy, RN BSN; Laura Goldston, MA.

Yale University Yale-New Haven Children's Hospital (GCRC M01 RR6022, U10 HD27871) – Richard A. Ehrenkranz, MD; Ian Gross, MD; Michael D. Kaplan, MD; Linda Mayes, MD; Patricia Gettner, RN; Monica Konstantino, RN BSN; Elaine Romano, RN MSN; Pat Cervone, RN; Nancy Close, PhD.

Table 1

Characteristics of Mothers by Maternal Age Group

Maternal Age Group		<20 years	20-29 years	30-39 years	≥40 years	Total
Mothers	N	2301	6495	4266	379	13441
Race/ethnicity						
Black	1228*	53.4%	3018*	1559	150	5955*
White	677*	29.4%	2315	1879	148	5019*
Hispanic	356	15.5%	978	601	61	1996
Other	38*	1.7%	169	214	19	440*
Education						
≤high school	1660*	87.7%	2298*	1097	101	4656*
≥some college	162*	12.3%	1603*	1584	151	3500*
Married	235*	10.3%	2641	2800	262	5938*
Medicaid insurance						
	1220*	89.8%	2767*	1246	120	5353*
Primiparity						
	1461*	63.5%	1887*	849*	50	4247*
Prenatal care						
≥1 visit	2002*	87.2%	6008	3985	349	12344*
Antenatal steroids	1425*	62.1%	4514*	3035	291	9265*
C-section	1044*	45.5%	3319*	2456*	247	7066*
PPROM						
	414*	18.8%	1598	1210	94	3316*
Hypertension	400*	17.4%	1401*	1099*	143	3043*
Diabetes	15*	0.7%	138*	193	24	370*

* Significant difference at 0.05 across age categories if marked in column "total" otherwise versus 40 years

Table 2

Neonatal Characteristics of ELBW Infants by Maternal Age Group

Characteristic	Maternal Age					Total
	<20 years	20–29 years	30–39 years	≥40 years		
Infants	2429	7111	4726	405	2.8%	14671
Gestation (wks)	25±2.3	25.5±2.3	25.6±2.4	26±2.3		25.5±2.3
Birth weight (g)	738.3±154	734.9±158	738±160	745.5±153		736.7±158
Male	1272	3514	2384	193	47.7%	7363
Births						
Singletons	2072*	5474	3431*	323	79.8%	11300*
Twins	349	1371	988	67	16.5%	2775
Triplets	8*	266	306	15	3.7%	595*
Apgar 1 min <4	1173*	3279	2074	168	41.8%	6694*
Apgar 5 min <4	515*	1435*	876*	53	13.2%	2879*
Resuscitation	2217*	6464*	4262*	385	95.1%	13328*
SGA	347*	1107*	847	86	21.2%	2387*
Early Sepsis	32	108	130	13	3.5%	283*
Late sepsis	794	2315	1379	147	39.9%	4635*

Characteristic	Maternal Age					Total
	<20 years	20–29 years	30–39 years	≥40 years		
IVH 3–4	431*	1048	655	52	2186*	18.0%
PVL	103	317	203	15	638	5.7%
Proven NEC	208	684	378	41	1311*	10.4%
O ₂ @ 36 wks	747	2332	1602	140	4821	48.4%
Death						
<discharge	934*	2461*	1507	114	5016*	34.2%
<discharge singletons	785*	1846	1071	90	3792*	33.6%
<discharge multiples	149	615	436	24	1224*	36.3%
>discharge	44	116	38	6	204	2.5%

* Significant difference at 0.05 across age categories if marked in column "Total" or from "≥40 years otherwise"

Table 3

Neurodevelopmental Outcomes and Death by Maternal Age Group

Characteristic	Maternal Age					
	<20	20–29	30–39	≥40 years	Total	
Eligible follow-up	1494	4646	3216	290	9646	100.0%
Seen in follow-up	1246	3859	2752	259	8116	84.1%
Mean Bayley MDI	77.6±17	78.1±18	80.8±19	79.3±19	78.9±18	
MDI <70	379	1150	706	81	2316*	31.3%
Mean Bayley PDI	83.2±19	82.6±19	82.9±18	82.2±18	82.8±19	
PDI <70	248	781	519	55	1603	21.9%
Blind	5	40	26	1	72	0.9%
Deaf	16	70	52	1	139	1.8%
Moderate/severe CP	97	281	197	15	590	7.4%
NDI	447	1371	896	94	2808*	38.1%
Death by 18m	978*	2577*	1545	120	5220*	39.1%
NDI or death	1425*	3948	2441	214	8028*	63.7%
Rehospitalized	698*	1939	1240	122	3999*	49.6%

* Significant differences at .05 across age categories if marked in column "Total" or otherwise versus ≤40 years

Table 4
Regression modeling estimates of relative risk and 95% confidence interval for study outcomes

Characteristics	MDI<70	PDI<70	Mod/severe CP	NDI	Death	NDI or death
Multiple birth yes versus no	1.25 1.16–1.35	1.23 1.13–1.33	1.26 1.09–1.47	1.22 1.14–1.30	1.12 1.07–1.18	1.10 1.07–1.13
Medicaid yes versus no	1.59 1.43–1.76	1.35 1.19–1.53	1.45 1.15–1.83	1.44 1.35–1.54	NA	NA
≤High school versus ≥college	1.13 1.04–1.22	1.00 0.92–1.09	0.80 0.70–0.92	1.07 1.01–1.12	NA	NA
Primiparity yes versus no	0.97 0.90–1.04	0.98 0.87–1.09	0.77 0.61–0.97	0.98 0.92–1.03	0.98 0.93–1.04	0.96 0.93–0.99
Age category						
≥ 40 years vs. < 20 years	1.19 0.98–1.45	1.13 0.88–1.43	0.71 0.42–1.18	1.11 0.96–1.30	0.78 0.68–0.89	0.87 0.77–0.97
≥ 40 years vs. 20–29 years	1.14 0.94–1.37	1.10 0.86–1.40	0.85 0.55–1.30	1.08 0.92–1.27	0.87 0.75–1.01	0.93 0.83–1.04
≥ 40 years vs. 30–39 years	1.19 0.96–1.48	1.11 0.84–1.48	0.81 0.49–1.34	1.10 0.92–1.31	0.94 0.82–1.07	1.00 0.89–1.11

NA= data not available for infants who died