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Neonatal Outcomes of Moderately Preterm Infants Compared to Extremely Preterm Infants

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Abstract

BACKGROUND—Extremely preterm infants (EPT, <29 weeks' gestation) represent only 0.9% of births in the U.S., yet these infants are focus of most published research. Moderately preterm neonates (MPT, 29–$33^{6/7}$ weeks), are an understudied group of high-risk infants.

METHODS—Objective: To determine the neonatal outcomes of MPT across the gestational age spectrum, and to compare these to EPT. A prospective observational cohort was formed in 18 Level 3–4 NICUs in the *Eunice Kennedy Shriver* NICHD Neonatal Research Network. Participants included all MPT admitted to NICUs, and all EPT born at sites between January 2012 and November 2013. Antenatal characteristics, and neonatal morbidities were abstracted from records using pre-specified definitions by trained neonatal research nurses.

RESULTS—MPT infants experienced morbidities similar to, although at lower rates, than EPT infants. The main cause of mortality was congenital malformation, accounting for 43% of deaths. CNS injury occurred including intraventricular hemorrhage. Most MPT required respiratory support but sequelae such as bronchopulmonary dysplasia were rare. The primary contributors to hospitalization beyond 36 weeks' gestation were inability to achieve adequate oral intake and persistent apnea.

CONCLUSIONS—MPT experience morbidity and prolonged hospitalization. Such morbidity deserves focused research to improve therapeutic and prevention strategies.

Background

Extremely preterm infants (EPT, <29 weeks' gestation) represent only 0.9% of births in the U.S., yet these infants are the subject of the majority of published research studying newborns (1,2). Moderately preterm neonates (29–$33^{6/7}$ weeks), which constituted 2.8% of all births in the U.S. in 2013 and 22% of all preterm births, are an understudied group of high-risk infants (1). A medline search using the terms moderately preterm, preterm AND randomized trial found only one randomized trial in MPT – a surfactant trial in 1993 (3). Thus, the care of moderately preterm infants is extrapolated from studies of EPT or full term infants rather than from randomized trials specific to MPT. MPT infants are at risk for substantial short-term morbidity. Most published studies have focused on late preterm infants [34–36 weeks' gestational age] and some have included a subset of moderately preterm infants. These limited studies have shown higher rates of abnormal respiratory outcomes, cognitive functioning, school performance and behavior (4–8). Because of their large numbers (approximately 93,000 in 2013), morbidities experienced by moderately preterm neonates represent a substantial public health burden (7–8). Additional information about the morbidity in this group is needed from a contemporary cohort to inform the design of future interventional trials and improve the effectiveness of care. Thus, we performed a large prospective observational study of the outcomes in moderately preterm infants and evaluated those outcomes by gestational age. In addition, we compared outcomes of MPT

infants with those of extremely preterm infants enrolled in a longstanding registry of the NICHD Neonatal Research Network (NRN).

Methods

The NRN is a network of neonatal intensive care units (NICUs) at 18 academic centers in the United States and a data coordinating center, which was formed to conduct research to improve the care of high-risk infants. All infants between $29^{0/7}$ to $33^{6/7}$ weeks' gestational age born January 2012 through November 2013 and admitted within the first 72 hours of life were included in the Moderately Preterm Registry. The comparison group was comprised of infants enrolled in the NRN Registry of inborn infants of gestational age $22^{0/7}$ to $27^{6/7}$ weeks (extremely preterm, EPT) or birth weight 401 to 1000 grams who were born during the same months. Infants who were born alive, but died in the delivery room were also included. Trained research nurses using pre-specified definitions abstracted maternal demographic, pregnancy, delivery and infant data from birth to discharge, transfer, death, or 40 weeks' postmenstrual age (PMA), whichever occurred first. Detailed information on the EPT cohort by week of gestational age was published recently in JAMA (9). The Institutional Review Board at each center approved the registries.

Neonatal information included birth weight (BW), gestational age (GA), gender, race/ethnicity, mode of delivery, delivery room interventions, final status, and cause of death. Gestational age was determined as the best obstetric estimate by using ultrasonography and/or the date of the last menstrual period. Neonatal morbidities were recorded for infants surviving >12 hours, and included respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), modified Bell's Stage ≥IIA necrotizing enterocolitis (NEC) (10), any intracranial hemorrhage according to the criteria of Papile (11), severe intracranial hemorrhage (Grade III or IV), periventricular leukomalacia, retinopathy of prematurity (ROP) (12), bronchopulmonary dysplasia (BPD) defined as supplemental oxygen at 36 weeks' postmenstrual age (PMA), and early- and late-onset sepsis defined by positive blood cultures before or after 72 hours of age. Cranial sonograms and ROP exams were performed based on usual center practice. Outcomes collected at 36 weeks' PMA included the reason for continued hospitalization (continued respiratory support; persistent apnea and/or bradycardia – defined by local center practice; inadequate oral feedings defined by continued gavage feedings; other). Data collection continued until discharge or 40 weeks PMA, whichever occurred first. Only 16% of the cohort remained hospitalized at 40 weeks PMA.

The NRN has maintained a registry of the characteristics and outcomes of extremely preterm infants for over 20 years (9). We utilized this long standing registry to compare a cohort of MPT with a cohort of inborn EPT born during the same months. We further analyzed outcomes of MPT across the gestational age continuum. Statistical significance in this observational study was tested using the χ^2test for categorical variables and the Kruskall-Wallis Test for continuous variables. Comparisons were made by gestational age and contrasted with the frequency seen in EPT born during the same time period.

Results

Population and Pregnancy Characteristics

Seven thousand and fifty-seven moderately preterm (MPT) infants met study criteria. Of these, 6419 (91%) were inborn and 638 (9%) were outborn. During the same time period 4310 EPT were born at NRN sites. Maternal and infant characteristics are shown in Table 1. The average maternal age was 28.4±6.5 (mean ± SD) years. Most women were white (57%) and non-Hispanic (83.3%). Nearly half had completed high school and additional higher education (49.9%). Almost all attended at least one prenatal visit (97%). The majority of women were publicly insured (55.2%), with a small percentage uninsured (3.4%).

Multiple births were common among our MPT cohort (n=2059, 29.2%). Frequently observed pregnancy complications included hypertension (n=3172, 44.9%) and insulin-dependent diabetes (n= 527, 7.5%). Prolonged preterm rupture of the membranes occurred in 1267 (19.2%) and clinical chorioamnionitis was noted in 498 (7.1%). Overall, 85.3% of the cohort received antenatal steroids. Most mothers (68.5%) received antibiotics in the 72 hours prior to delivery, and 53.7% received magnesium sulfate. Four thousand four hundred and sixty-five (63.3%) of the infants were delivered by Cesarean section. The maternal characteristics of the MPT and EPT cohort were similar (Table 1). Notable exceptions are a higher rate of Black race and lower rates of private insurance in the EPT cohort. EPT infants were more likely to receive resuscitation in the delivery room and higher rates of all interventions including chest compressions.

Morbidity

Cardiorespiratory Outcomes

Respiratory illness was the most common morbidity noted (Table 2). With each one-week increase in gestational age, surfactant administration declined by approximately 10%. Fifty percent of infants born at 29 weeks received surfactant compared with only 12.8% of those born at 33 weeks. In contrast, 77.8% of EPT were treated with surfactant. At 28 days of life, 59.7% of infants born at 29 weeks no longer required any respiratory support; at 33 weeks, 95.4% were without respiratory support. In comparison, only 15% of EPT were off all respiratory support by 28 days of life. Bronchopulmonary dysplasia (based on oxygen use at 28 days of life) occurred in 16% of the MPT infants and 50% of the EPT. Patent ductus arteriosus (PDA) was diagnosed in only 754 MPT infants (10.7%) compared to 43% of the EPT infants. Most MPT diagnosed with PDA were not treated, but 150 (19.9% with PDA) were treated with indomethacin or ibuprofen and 34 (4.5% with PDA) with surgical ligation. In contrast, 60% of the EPT infants in whom PDA was diagnosed were treated.

Central Nervous System Outcomes

Overall 58% of MPT were screened with cranial ultrasound, compared with 97% of the EPT. The frequency with which an ultrasound was performed increased with decreasing gestational age. An intracranial hemorrhage was diagnosed in 13.3% of the MPT cohort and overall percentage did not vary across the gestational ages evaluated. However, with decreasing gestational age the severity of the ICH increased; 17.7% of 29 week MPT who

had a head ultrasound had a grade 3 or 4 ICH, while only 1.8% of 33 week infants screened had a grade 3 or 4 ICH. In contrast to the MPT, 26.9% of the EPT had an ICH. Almost 30% of MPT received a late imaging study, with 26.5% of these having an abnormal finding including ventriculomegaly, periventricular leukomalacia, and porencephalic cyst. Among MPT infants, the frequency of these findings did not vary by gestational age.

Retinopathy of prematurity of any degree was diagnosed in 8% of the MPT compared to 54% of the EPT. Severe retinopathy (defined as Stage 3 or worse) was diagnosed in 11% of the EPT, but in only 4 (0.17%) infants in the MPT cohort - all had Stage 3 disease and none needed treatment.

Nutrition and Infectious Outcomes

MPT infants took, on average, 10 days to regain their birth weight. While this figure varied significantly across the gestational age spectrum, the small differences are unlikely to be clinically meaningful. EPT infants regained their birth weight in a similar timeframe of 9.9 days. The first oral feed was offered to MPT infants at about 33 weeks' PMA, regardless of GA at birth, although the time to reach that benchmark varied by gestational age. Less mature infants took longer to achieve full enteral feeds (17 days at 29 weeks' GA), than more mature infants (9 days at 33 weeks' GA). The vast majority of both MPT and EPT infants were fed human milk (84% vs 99%), with less mature MPT more likely to receive human milk than more mature MPT (90% at 29 weeks vs 80.9% at 33 weeks, $p<0.001$).

As expected, necrotizing enterocolitis was diagnosed less frequently in MPT than in EPT (2.4% vs 8%), and was more likely to be treated with medical treatment only (1.7% vs 4%).

MPT infants experienced early onset sepsis at similar rates to EPT (0.7% vs 1.8%) with a predominance of gram positive organisms including Group B *Streptococcus* [33/52 (63%) infections]. No infants in either cohort were infected with *Listeria.* Late onset infection occurred less frequently in MPT than EPT infants (3.2% vs 19%).

Mortality and Hospital Course

Overall, 2.9% of the MPT cohort died compared to 24% of the EPT cohort. Deaths occurred early, with most MPT dying at 7–12 days of age. The primary cause of death was related to congenital malformation (43%) in the MPT and to RDS in EPT [Table 2]. While EPT remained in the hospital on average 99±46 days and usually were hospitalized past their due date, MPT were discharged at an earlier postmenstrual age with 38.1% discharged by 36 weeks PMA. The reason for MPT remaining in the hospital at 36 weeks included inadequate oral intake (69.8%), apnea or bradycardia (37.5%) and continued respiratory issues (16.7%). By 40 weeks PMA, 83.9% of MPT were discharged home with an average weight of 2.4 kg, while 58% of EPT were discharged home.

Discussion

Our cohort study contributes valuable information that will inform both clinicians and parents about the expected outcomes of these infants. The vast majority of neonatal clinical trials have focused on EPT. Yet, MPT infants experience many of the same risks for adverse

outcomes, albeit at lower rates than EPT infants. Given their much larger numbers in the population, MPT contribute substantial numbers of days in intensive care units and contribute significantly to the societal costs of neonatal intensive care and to the emotional toll on their families. The burden of disease born by MPT is substantial. For example, based on estimates from our study and national birth data, 12,447 MPT and 10,907 EPT suffered an IVH (1). This suggests that from an absolute number perspective MPT may contribute to the burden of disease more than the EPT cohort.

Research that focuses on the large group of MPT infants may generate novel ideas to support optimal growth and development and reduce the duration of hospitalization. Conditions associated with developmental immaturity, including apnea and bradycardia and inadequate oral feeding, were the predominant causes of continued hospitalization at 36 weeks. Across the MPT gestational age continuum, oral feedings were first introduced, on average, at 33 weeks' PMA. Approaches for assessing an infant's readiness for oral feeding vary (13). It is possible that a more standardized approach and earlier introduction of oral feeding may facilitate the development of this skill. Oral feeding of the MPT Infant is an area ripe for additional investigation. There are also differences in the approach to treatment of apnea of prematurity, including when to discontinue treatment with methylxanthines. After discontinuation of methylxanthines, most neonatologists in the U.S. continue hospitalization for an apnea-free period of observation of variable duration (14, 15). It is not known if discharge home on methylxanthines treatment would be a safe and effective method to reduce length of stay.

An often stated 'rule of thumb' is that families may expect a preterm infant to be discharged home by their estimated due date. However, in the MPT 38% were discharged home by 36 weeks' PMA, four weeks prior to their estimated due date, and 43%, were discharged home by 40 weeks. Infants with congenital malformation were overrepresented in the population remaining in hospital at 40 weeks' PMA.

Our study can be compared with an analysis of preterm morbidity led by Manuck and conducted in the NICHD Maternal Fetal Network as a study nested within a large observational study to develop quality measures for intrapartum obstetric care (Assessment of Perinatal Excellence; APEX) (16,17). Mothers who were at least 23 weeks of gestation and up to $35^{6/7}$ weeks of gestation with a live fetus on admission had data abstracted from the records during a 24 hour period of randomly selected days at 25 hospitals nationwide from 2008 to 2011; the main study included 115,502 women. In the nested study, infants with anomalies and multiple gestations were excluded, as were infants who died in the delivery room, and those >36 weeks. Once all exclusions were applied, the original sample of 118,422 infants was reduced to 8334 infants, of whom 1877 were MPT. Thus, a subset of the APEX population included MPT of similar gestational age (29–33 weeks) as our cohort. The outcomes evaluated were reported as Major Morbidity, as defined by pulmonary hypertension, intraventricular hemorrhage of Grade 3 or 4, hypoxic-ischemic encephalopathy, necrotizing enterocolitis Stage 2 or 3, or bronchopulmonary dysplasia. The rates of major morbidity increased with decreasing gestational age which parallels our data. The rate of major morbidity was 22.5% at 29 weeks and decreased to 4.2% at 33 weeks. Our study includes a larger sample size and a more robust slate of outcome variables.

Another recent cohort study, The Late and Moderately Preterm Birth Study (LAMBS) was conducted by Boyle and colleagues in the United Kingdom (18). This prospective, population -based study included outcomes for infants born at 32–36 weeks' gestation from a geographic area in Northern England in 2009–2010. The study included 1376 infants, of whom 1125 (99.5%) were discharged home. This cohort overlaps with our study at 32 and 33 weeks' gestation [n=132], but excluded infants with congenital anomalies. Their findings were similar to ours in that MPT had a gradient of increasing risk with decreasing gestation, including an increasing length of stay.

Our study has several strengths. The population was delivered at 18 Level 3–4 centers across the United States and includes both inborn and outborn infants, which contributes to the generalizability of the information. Another strength is that all data were collected by experienced research staff using standardized definitions, which were identical between the MPT and EPT cohorts. The large cohort allows us to present results by each week of GA, providing more precise information for counseling. One limitation is that information on the reason for preterm delivery was not uniformly collected for either inborn or outborn infants. Another possible concern is that the NRN population may not reflect similar populations of MPT that are not transferred to Level 3 centers. Ninety percent of the cohort in this population was born at the NRN center and only 10% were transferred after birth. We have previously compared the outcome of infants in NRN centers and in the Vermont Oxford Network of both academic and private practice Level 2 and Level 3 units, and found the infant population to be comparable (19). Thus, we believe that the findings in this study are generalizable to other US NICUs.

Conclusion

About 100,000 MPT infants are born in the U.S. each year but remain an understudied group. Because of the high numbers of MPT births in the U.S., morbidities in this group are an important public health concern. This study will inform the counseling of parents faced with the birth of a moderately preterm infant. MPT experience significant morbidity, as evidenced by the high rates of respiratory support and prolonged hospitalization. Such morbidity deserves focused research with an aim to develop novel therapeutic and prevention approaches.

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Appendix

AUTHOR CONTRIBUTIONS

Below we detail the contributions made by each author for this manuscript.

The MPR Subcommittee investigators have monthly conference calls during which protocol design and implementation issues are discussed, manuscripts are reviewed, and input obtained. The following authors have made significant contributions as determined by the Uniform Requirements for Manuscripts Submitted to Biomedical Journals:

- Michele C. Walsh, M.D., M.S. is the Lead Principal Investigator (PI) at Case Western Reserve University [CWRU] and the Chair of the Moderately Preterm Registry Protocol Subcommittee. She developed the study and managed protocol implementation. As the PI at CWRU, she oversaw enrollment at the site - which enrolled 302 infants in this study. Dr. Walsh drafted the manuscript and received input from the authors below as part of manuscript revision. Dr. Walsh had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
- Edward F. Bell, M.D. is the PI at the University of Iowa and a member of the Moderately Preterm Registry Protocol Subcommittee. He helped develop the study and manage protocol implementation. As the PI at the University of Iowa, he oversaw enrollment at the site - which enrolled 495 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Sarah Kandefer, B.S. served as the primary statistician for the study, and completed the statistical analyses for the paper. She developed the tables for the paper and provided critical revision to the manuscript and approved the final version of the manuscript.
- Waldemar A. Carlo, M.D. is the PI at the University of Alabama at Birmingham [UAB] and a member of the Moderately Preterm Registry Protocol Subcommittee. He helped develop the study and manage protocol implementation. As the PI at UAB, he oversaw enrollment at the site - which enrolled 537 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Carl T. D'Angio, M.D. is the PI at the University of Rochester and a member of the Moderately Preterm Registry Protocol Subcommittee. He helped develop the study and manage protocol implementation. As the PI at the University of Rochester, he oversaw enrollment at the site - which enrolled 617 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Abbot R. Laptook, M.D. is the PI at Brown University and a member of the Moderately Preterm Registry Protocol Subcommittee. He helped develop the study and manage protocol implementation. As the PI at Brown University, he

oversaw enrollment at the site - which enrolled 424 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.

- Pablo J. Sanchez, M.D. is the PI at Nationwide Children's Hospital and a member of the Moderately Preterm Registry Protocol Subcommittee. He helped develop the study and manage protocol implementation. As the PI at Nationwide Children's Hospital, he oversaw enrollment at the site - which enrolled 512 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Barbara J. Stoll, M.D. is the PI at Emory University and the Vice Chair of the Moderately Preterm Registry Protocol Subcommittee. She helped develop the study and manage protocol implementation. As the PI at Emory University, she oversaw enrollment at the site - which enrolled 335 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Seetha Shankaran, M.D. is the PI at Wayne State University and a member of the Moderately Preterm Registry Protocol Subcommittee. She helped develop the study and manage protocol implementation. As the PI at Wayne State University, she oversaw enrollment at the site - which enrolled 363 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Krisa P. Van Meurs, M.D. is the PI at Stanford University and a member of the Moderately Preterm Registry Protocol Subcommittee. She helped develop the study and manage protocol implementation. As the PI at Stanford University, she oversaw enrollment at the site - which enrolled 205 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Betty R. Vohr, M.D. is the Follow-up PI at Brown University and a member of the Moderately Preterm Registry Protocol Subcommittee. She helped develop and implement the study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Rosemary D. Higgins, M.D. served as the Program Scientist for the NICHD NRN and a member of the Moderately Preterm Registry Protocol Subcommittee. Dr. Higgins helped develop the protocol, oversaw recruitment, and assisted with data edits from the sites. She also provided critical revision to the manuscript and approved the final version of the manuscript.
- Abhik Das, Ph.D. is the PI for the NRN Data Coordinating Center and a member of the Moderately Preterm Registry Protocol Subcommittee. Dr. Das oversaw all aspects of the statistical analysis, provided critical revisions to the manuscript and approved the final version of the manuscript.
- Ellen C. Hale, B.S., R.N., C.C.R.C. is the Coordinator at Emory University and a member of the Moderately Preterm Registry Protocol Subcommittee. She helped

develop the study and manage protocol implementation. As the Coordinator at Emory University, she enrolled 335 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.

- Nancy S. Newman, R.N. is the Coordinator at CWRU and a member of the Moderately Preterm Registry Protocol Subcommittee. She helped develop the study and manage protocol implementation. As the Coordinator at CWRU, she enrolled 302 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Kurt Schibler, M.D. is the PI at Cincinnati Children's Medical Center [CCMC]. As the PI he oversaw enrollment at the site - which enrolled 683 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Barbara Schmidt, M.D. is the PI at the University of Pennsylvania. As the PI she oversaw enrollment at the site - which enrolled 511 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- C. Michael Cotten, M.D., M.H.S. is the PI at Duke University. As the PI he oversaw enrollment at the site - which enrolled 457 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Kathleen A. Kennedy, M.D., M.P.H. is the PI at the University of Texas Health Science Center at Houston. As the PI she oversaw enrollment at the site - which enrolled 456 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Brenda B. Poindexter, M.D., M.S. is the PI at Indiana University. As the PI she oversaw enrollment at the site - which enrolled 333 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- Kristi L. Watterberg, M.D. is the PI at the University of New Mexico. As the PI she oversaw enrollment at the site - which enrolled 242 infants in this study. She contributed critical revisions of the manuscript and approved the final manuscript for submission.
- William E. Truog, M.D. is the PI at Children's Mercy Hospital, Kansas City. As the PI he oversaw enrollment at the site - which enrolled 172 infants in this study. He contributed critical revisions of the manuscript and approved the final manuscript for submission.

DISCLOSURES

- No financial or other conflicts.

PRESENTATIONS

Portions of the material in this manuscript were presented at the Pediatric Academic Society Meeting, May 2014, Vancouver BC, CA.

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Table 1

Population Characteristics of Moderately Preterm and Extremely Preterm Infants

CHARACTERISTICS	*All MPT N=7057 (%)*	*EPT N=4310 (%)*	*p-value*
MATERNAL INFORMATION			
Maternal age (years; mean±SD)	28.4±6.5	28.1±6.3	0.038
Married (n, %)[1/]	3305 (46.9)	1896 (44.0)	0.003
Highest level of education[2/]: High school or less	2522 (50.1)	1611 (50.4)	0.739
More than high school	2512 (49.9)	1584 (49.6)	
Insurance status: Public or uninsured	4128 (58.6)	2607 (60.5)	0.019
Private	2821 (40.0)	1627 (37.8)	
Other/unknown	101 (1.4)	74 (1.7)	
Mother's ethnic category: Hispanic	1009 (14.3)	601 (14.0)	<.0001
Non-Hispanic or Latino	5871 (83.3)	3657 (84.9)	
Unknown	171 (2.4)	50 (1.2)	
Mother's race: Black	2232 (31.6)	1703(39.5)	<.0001
White	4025 (57.0)	2163 (50.2)	
Other	463 (6.6)	279 (6.5)	
Unknown	337 (4.8)	165 (3.8)	
PREGNANCY COMPLICATIONS			
Multiple birth	2059 (29.2)	1193 (27.7)	0.087
Prenatal care	6834 (97.0)	4140 (96.1)	0.012
Insulin-dependent diabetes during or before pregnancy	527 (7.5)	225 (5.2)	<.0001
Hypertension before pregnancy	799 (11.6)	544 (12.8)	0.059
Hypertension during pregnancy	2373 (33.7)	1255 (29.1)	<.0001
Clinical chorioamnionitis[2/]	498 (7.1)	522 (12.2)	<.0001
PROM (>18 hrs)[2/]	1267 (19.2)	760 (19.2)	0.969
Antenatal steroids	5963 (85.3)	3701 (86.0)	0.281
Antibiotics given in this admission[2/]	4951 (71.6)	3087 (72.0)	0.650
Magnesium given[2/]	3708 (53.7)	3011 (70.4)	<.0001
Delivery mode: Vaginal	2582 (36.6)	1449 (33.6)	<.0001
Cesarean section	4465 (63.3)	2855 (66.3)	
Unknown	8 (0.1)	5 (0.1)	
NEONATAL INFORMATION			
Birth weight, kg (mean±SD)	1695±422	839.0±251.6	<.0001
Male (n, %)	3682 (52.2)	2181 (50.7)	0.108
Resuscitation at delivery: Oxygen and/or bag/mask	5063 (71.8)	3948 (91.7)	<.0001
Ventilation (CPAP or intubation)	4292 (60.9)	3809 (88.5)	<.0001
Chest compressions	180 (2.6)	338 (7.9)	<.0001

[1/] Percentages calculated based on non-missing information.

[2/] More than 10% of data are missing for: maternal education (n=2,023 for MPR and n=1115 for GDB respectively), clinical chorioamnionitis (n=73 for MPR and n=14 for GDB), PROM (n=450 for MPR and n=353 for GDB), antibiotics given in this admission (n=140 for MPR and n=21 for GDB), antibiotics given in 72 hrs prior to delivery (n=155 for MPR and n=23 for GDB), magnesium (n=155 for MPR and n=31 for GDB), thermal wrap used (n=1,071 for MPR and n=433 for GDB), temperature at admission (n=768 for MPR and n=637 for GDB).

Table 2

Neonatal Outcomes for Moderately Preterm Infants by Gestational Age and Compared to Extremely Preterm Infants.

	GESTATIONAL AGE							
	29 N=815 (%)	***30 N=1066 (%)***	***31 N=1255 (%)***	***32 N=1712 (%)***	***33 N=2209 (%)***	***All MPT N=7057 (%)***	***EPT N=4310 (%)***	***p-value***
CARDIORESPIRATORY	410 (50.3)	414 (38.8)	376 (30.0)	351(20.5)	282 (12.8)	1833 (26.0)	3041 (77.8)	<.0001 *<.0001
Surfactant	778 (95.5)	1032 (96.8)	1230 (98.0)	1673 (97.7)	2156 (97.6)	6869 (97.3)	3523 (81.7)	0.0031 *<.0001
Infants alive at 28 days								<.0001 *<.0001
Respiratory support at 28 days:	456 (59.7)	740 (73.5)	1023 (85.5)	1469 (92.5)	1932 (95.4)	5620 (85.4)	549 (15.7)	
None	35 (4.58)	34 (3.38)	24 (2.01)	25 (1.57)	16 (0.79)	134 (2.04)	1329 (38.1)	
Ventilator	42 (5.50)	28 (2.78)	6 (0.50)	6 (0.38)	4 (0.20)	86 (1.31)	690 (19.8)	
CPAP	231 (30.2)	205 (20.4)	144 (12.0)	88 (5.54)	73 (3.60)	741 (11.3)	921 (26.4)	
Oxygen only	160 (19.7)	167 (15.7)	148 (11.8)	133 (7.78)	146 (6.62)	754 (10.7)	1637 (41.9)	<.0001 *<.0001
PDA diagnosed (n, %) [1/]								0.0005 *<.0001
PDA treatment:	100 (62.5)	114 (68.7)	113 (76.4)	113 (85.0)	126 (86.3)	566 (75.2)	636 (38.9)	
None	50 (31.3)	48 (28.9)	25 (16.9)	16 (12.0)	11 (7.53)	150 (19.9)	696 (42.5)	
Medical	10 (6.25)	4 (2.41)	8 (5.41)	3 (2.26)	9 (6.16)	34 (4.52)	92 (5.6)	
Surgery	0 (0)	0 (0)	2 (1.35)	1 (0.75)	0 (0)	3 (0.40)	213 (13.0)	
Both medical and surgical								
CENTRAL NERVOUS SYSTEM								
Head ultrasound first 28 days (n, %) [1/]	769 (94.4)	919 (86.5)	952 (76.2)	821 (48.9)	607 (28.2)	4068 (58.4)	3798 (97.14)	<.0001 *<.0001
Any grade intracranial hemorrhage	113 (14.8)	130 (14.3)	114 (12.1)	98 (12.0)	82 (13.7)	537 (13.3)	995 (26.93)	0.3250 *<.0001
Max grade intracranial hemorrhage								0.0047 *<.0001
Grade 1	72 (63.7)	85 (65.4)	82 (71.9)	85 (86.7)	58 (70.7)	382 (71.1)	334 (33.6)	

	GESTATIONAL AGE							
	29 N=815 (%)	***30 N=1066 (%)***	***31 N=1255 (%)***	***32 N=1712 (%)***	***33 N=2209 (%)***	***All MPT N=7057 (%)***	***EPT N=4310 (%)***	***p-value***
Grade 2	21 (18.6)	30 (23.1)	16 (14.0)	5 (5.10)	13 (15.9)	85 (15.8)	195 (19.6)	
Grade 3	8 (7.08)	11 (8.46)	4 (3.51)	4 (4.08)	5 (6.10)	32 (5.96)	210 (21.1)	
Grade 4	12 (10.6)	4 (3.08)	12 (10.5)	4 (4.08)	6 (7.32)	38 (7.08)	256 (25.7)	
Late imaging done	565 (70.8)	616 (59.4)	501 (40.8)	233 (14.2)	109 (5.21)	2024 (29.8)	3137 (80.39)	<.0001 *<.0001
Late image Abnormal	127 (22.5)	151 (24.5)	133 (26.5)	78 (33.6)	48 (44.0)	537 (26.5)	828 (26.40)	<.0001 *0.9103
Exam for ROP	691 (84.8)	770 (72.2)	521 (41.5)	299 (17.5)	116 (5.25)	2397 (34.0)	3364 (86.04)	<.0001 *<.0001
ROP Stage 3 or greater	2 (0.29)	1 (0.13)	1 (0.19)	0 (0)	0 (0)	4 (0.17)	372 (11.06)	<.0001 *<.0001
GASTROINTESTINAL AND NUTRITION OUTCOMES								
Days to regain weight (mean ± SD)	10.3±5.3	10.0±4.5	9.6±4.3	9.9±10.4	9.6±13.0	9.8±9.3	9.9±7.9	<.0001 *0.66
Fed human milk first 28 days	731(90.0)	952(89.6)	1065(85.1)	1381(80.9)	1784(80.9)	5913(84.0)	3431(96.5%)	<.0001 *<.0001
First oral feed, day (mean ± SD)[2/]	28.5±12.1	22.5±15.7	15.5±10.3	9.7±14.7	5.9±15.7	13.5±16.2	NA	<.0001
Full oral feed, day (mean ± SD)[2/]	45.6±13.2	38.0±12.5	29.4±12.3	22.2±16.7	15.1±14.7	26.0±17.7	NA	<.0001
NEC, any	37 (4.6)	40 (3.8)	28 (2.2)	33 (1.9)	31(1.4)	169 (2.4)	343 (8.8%)	<.0001 *<.0001
INFECTION AND HEMATOLOGY								
Early onset Infection (n, %)[1/]	10 (1.23)	17 (1.60)	10 (0.80)	6 (0.35)	9 (0.41)	52 (0.74)	71 (1.8%)	0.0004 *<.0001
Organism[2/]								0.762 0.116
Group B Strep	1 (10.0)	2 (11.8)	3 (30.0)	0 (0)	2 (22.2)	8 (15.4)	10 (14.1%)	
E. Coli	2 (20.0)	2 (11.8)	1 (10.0)	2 (33.3)	2 (22.2)	9 (17.3)	20 (23.6%)	
Other gram positive	3 (30.0)	11 (64.7)	4 (40.0)	4 (66.7)	3 (33.3)	25 (48.1)	19 (26.8%)	
Other gram negative	3 (30.0)	1 (5.88)	2 (20.0)	0 (0)	0 (0)	6 (11.5)	16 (22.5%)	
Other[3/]	1 (10.0)	1 (5.88)	0 (0)	0 (0)	2 (22.2)	4 (7.69)	6 (8.5%)	

	GESTATIONAL AGE							
	29 N=815 (%)	***30 N=1066 (%)***	***31 N=1255 (%)***	***32 N=1712 (%)***	***33 N=2209 (%)***	***All MPT N=7057 (%)***	***EPT N=4310 (%)***	***p-value***
Infant received antibiotics for ≥5 days	170 (20.9)	189 (17.7)	200 (16.0)	194 (11.3)	223 (10.1)	976 (13.8)	1465 (37.5)	<.0001 *<.0001
Late onset infection	67 (8.26)	49 (4.62)	39 (3.13)	31 (1.82)	35 (1.59)	221 (3.15)	741 (19.0)	<.0001 *<.0001
Phototherapy given	749 (91.9)	959 (90.0)	1070 (85.3)	1359 (79.4)	1515 (68.7)	5652 (80.1)	NA	<.0001
Phototherapy Days (mean, IQR)[4/]	5.0 (3.0,6.0)	4.9 (3.0,6.0)	4.4 (2.0,6.0)	4.0 (2.0,5.0)	3.8 (2.0,5.0)	4.3 (2.0,5.0)	NA	<.0001
Highest total serum bilirubin (mean, IQR)[4/]	8.3 (6.8,9.7)	8.7 (7.3,10.0)	9.1 (7.7,10.4)	9.6 (8.1,11.2)	9.9 (8.3,11.6)	9.3 (7.7,10.9)	6.8 (5.6, 7.8)	<.0001 *<.0001

1/ Percentages calculated based on non-missing information. All categories have less than 10% missing data. First p value compares the MPT gestational age distribution. Second p value with an * compares All MPT versus EPT.

2/ More than 10% of data are missing for: Days to regain weight (n=944 overall, 29 wks GA=76, 30 wks GA=90, 31wks GA=136, 32 wks GA=207, 33wk GA=435)

Full oral feeds (n=1,025 overall, 29 wks GA=157, 30 wks GA=182, 31wks GA=198, 32 wks GA=241, 33 wks GA=247). Date of first oral feed was not tracked in the EPT cohort