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Delivery Room Resuscitation and Short-term Outcomes in Moderately Preterm Infants

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Abstract

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[*]List of additional members of the National Institute of Child Health and Human Development Neonatal Research Network is available at www.jpeds.com (Appendix) Portions of this study were presented at the ≪ ≫, ≪date≫, ≪city, state≫

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Objectives—To describe the frequency and extent of delivery room (DR) resuscitation and evaluate the association of DR resuscitation with neonatal outcomes in moderately preterm (MPT) infants.

Study design—This was an observational cohort study of MPT infants delivered at $29^{0/7}$ to $33^{6/7}$ weeks' gestational age (GA) enrolled in the Neonatal Research Network MPT registry. Infants were categorized into 5 groups based on the highest level of DR intervention: routine care, oxygen and/or continuous positive airway pressure (CPAP), bag and mask ventilation, endotracheal intubation, and cardiopulmonary resuscitation (CPR) including chest compressions and/or epinephrine use. The association of antepartum and intrapartum risk factors and discharge outcomes with the intensity of resuscitation was evaluated.

Results—Of 7,014 included infants, 1,684 (24.0%) received routine care and no additional resuscitation, 2,279 (32.5%) received oxygen or CPAP, 1,831 (26.1%) received bag and mask ventilation, 1,034 (14.7%) underwent endotracheal intubation, and 186 (2.7%) received CPR. Among the antepartum and intrapartum factors, increasing GA, any exposure to antenatal steroids (ANS) and prolonged rupture of membranes decreased the likelihood of receipt of all levels of resuscitation. Infants who were small for gestational age (SGA) had increased risk of DR resuscitation. Among the neonatal outcomes, respiratory support at 28 days, days to full oral feeds and length of stay were significantly associated with the intensity of DR resuscitation. Higher intensity of resuscitation was associated with increased risk of mortality.

Conclusion—The majority of MPT infants receive some level of DR resuscitation. Increased intensity of DR interventions was associated with prolonged respiratory and nutritional support, increased mortality and a longer length of stay.

Keywords

Resuscitation; Moderate Preterm; Delivery room; CPR; Endotracheal intubation; Oxygen

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Approximately 85% of infants delivered at term gestational age (GA) require no assistance in transitioning from the intrauterine to extrauterine environment after birth; only 5% require positive pressure ventilation and 0.1% require chest compressions and/or epinephrine (1). This transition is not as smooth for infants delivered prematurely. Finer et al reported that 6% of infants in the Vermont Oxford Network with birth weights between 501 to 1500 grams received cardiopulmonary resuscitation (CPR) that included chest compressions and/or administration of epinephrine in the delivery room (DR) (2). Compared with term infants, late and moderately preterm (MPT) infants delivered between 32 to 36 weeks of gestation are more likely to receive resuscitation at birth (3). Besides prematurity, there are other antepartum and intrapartum risk factors that can be associated with receipt of DR resuscitation in late and MPT neonates (4–6). Increasing intensity of DR resuscitation has been shown to predict risk of mortality and adverse neurodevelopmental outcome in extremely low birth weight and very low birth weight infants (7–9).

The Neonatal Resuscitation Program (NRP) guidelines published by the American Academy of Pediatrics recommend the presence of at least one qualified individual skilled in the initial steps of newborn care and positive pressure ventilation (PPV) at every birth; in the presence of risk factors, a qualified team with full resuscitation skills should be available (10).

However, the composition of the resuscitation team varies in different hospitals and comprises of personnel with varying expertise and experience. In small rural hospitals, it can be challenging to have a team prepared to provide neonatal resuscitation (11). Although MPT infants delivered between $29^{0/7}$ and $33^{6/7}$ weeks' GA constitute about 2.8% of all births in the United States (12), data are limited on the frequency and extent of DR resuscitation in this population. The antepartum risk factors associated with receipt of resuscitation in MPT infants remain unexplored. Identification of these factors could help clinical staff prepare better for MPT delivery with attendance of skilled personnel in the DR to provide prompt stabilization.

Data on neonatal outcomes following DR resuscitation are also scarce in the MPT population. Several investigators have reported increased risk of morbidity and mortality in extremely low birth weight and very low birth weight preterm infants who received CPR in the DR (13,14). The association of varying intensity of DR resuscitation and neonatal morbidities in the MPT infants remains unstudied.

In the current study, we describe the frequency and extent of DR resuscitation in infants enrolled in the MPT registry of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN), and examine the association between antepartum and intrapartum factors and the extent of DR resuscitation. We also evaluate the association of DR resuscitation with occurrence of neonatal morbidities prior to initial hospital discharge.

Methods

The study population included infants delivered between February 2012 and November 2013 at $29^{0/7}$ to $33^{6/7}$ weeks GA who were enrolled in the NRN MPT registry (15). Infants in whom a prenatal diagnosis caused a decision to withdraw or limit intensive care were excluded. Data were collected prospectively by trained research personnel using standard definitions. Maternal information included age and prenatal care, pregnancy complications including multiple births, insulin dependent diabetes, hypertension, prolonged rupture of membranes (>18 hours), clinical and histological chorioamnionitis, receipt of antenatal steroids (ANS) and magnesium sulfate, and mode of delivery. Neonatal information included sex, GA, birth weight and Apgar scores. Data on birth resuscitation included use of oxygen, continuous positive airway pressure (CPAP), bag and mask ventilation which included positive pressure ventilation with face mask and bag or T-piece resuscitator (Neopuff), endotracheal intubation, chest compressions and epinephrine.

Short-term outcomes were collected in the MPT registry at the time of discharge, transfer, death, or at 40 weeks' postmenstrual age (PMA), whichever occurred first. These included: respiratory distress syndrome (RDS) treated with surfactant therapy, respiratory support at 28 days of life including oxygen via nasal cannula, CPAP, non- invasive ventilation, or ventilatory support, presence and severity of intracranial hemorrhage based on Papile's classification (16) and cystic periventricular leukomalacia (cPVL) diagnosed after 28 days of age (among those who had cranial sonography), early- and late-onset sepsis defined by positive blood cultures at or before and after 72 hours of age, days to full oral feeds, and proven necrotizing enterocolitis (NEC) defined by modified Bell Stage ≥IIA (17). The study was approved by the IRB at each NRN center.

DR resuscitation was defined as receipt of any assistance after birth besides routine care that included providing warmth, drying and stimulation of the infant. Infants were divided into five groups according to the highest level of resuscitation they received: 1) routine care, 2) oxygen and/or CPAP, 3) bag and mask ventilation, 4) endotracheal intubation and 5) CPR including chest compressions and/or epinephrine use. This classification was based on the steps in the NRP algorithm and was similar to a previous study (1,7). Oxygen and CPAP were combined in one group as the indications for PPV using bag and mask are distinct.

Statistical Analyses

Maternal and neonatal characteristics and neonatal outcomes of infants in the five groups were compared using analysis of variance (ANOVA) for continuous variables and chi square test for categorical variables. A generalized logistic regression model was used to explore neonatal and maternal characteristics significantly associated with the five intensity levels of DR resuscitation. The significant maternal and neonatal baseline characteristics were included and the best model was selected using the Akaike Information Criterion (AIC) as a measure to balance model fit with model complexity. Multivariable logistic regression analysis was performed to assess the association between levels of resuscitation with selected morbidities after adjusting for center, GA, SGA status, any ANS, and multiple births - variables selected a priori due to their known association with outcomes among extremely preterm infants. Statistical analyses were conducted using SAS/STAT software, Version 9.4, Cary, North Carolina. A 2-sided *P* value less than 0.05 was considered to be statistically significant.

Results

A total of 7,057 infants across eighteen centers were enrolled in the MPT registry between February 2012 and November 2013. A prenatal decision to limit intensive care was made for 36 infants, and DR information was missing in 7 infants. Of 7,014 infants included in the analysis, 1,684 (24.0%) received routine care without additional resuscitation; 2,279 (32.5%) received oxygen or CPAP but not ventilation, intubation or CPR; 1,831 (26.1%) received bag and mask ventilation but not intubation or CPR; 1,034 (14.7%) received endotracheal intubation but not CPR; and 186 (2.7%) underwent CPR.

Maternal and neonatal characteristics are shown in Table 1. Lower birth weight and GA, SGA, lack of prenatal care, lack of ANS, use of antenatal magnesium therapy and Cesarean delivery were associated with a higher intensity of resuscitation. Maternal hypertension, prolonged rupture of membranes, and histologic chorioamnionitis were significantly associated with intensity of resuscitation. The proportion of singleton births was significantly higher (83.9% vs 71.6%) in the group that received CPR, compared with routine care. The final generalized logistic regression model exploring the relationship of maternal and neonatal characteristics with different levels of DR resuscitation included GA, SGA status, exposure to ANS and magnesium sulfate, multiple births, histologic chorioamnionitis, maternal hypertension, prolonged rupture of membranes (>18hours) and prenatal care (Table II). All estimates of odds ratios in Table 2 have no DR resuscitation as the reference group. Increasing GA, exposure to ANS and prolonged rupture of membranes decreased the likelihood of all levels of resuscitation. Multiple births were associated with lower risk of endotracheal intubation and CPR. SGA status and presence of prenatal care were associated with more frequent need for oxygen/CPAP, bag and mask ventilation and endotracheal intubation. Exposure to magnesium sulfate decreased the odds of endotracheal intubation and CPR. Maternal hypertension increased the need for oxygen/CPAP while histologic chorioamnionitis reduced the odds of oxygen/CPAP and intubation.

Short-term outcomes among MPT infants with different levels of resuscitation are noted in Table 3. Respiratory morbidities, including surfactant use and continued respiratory support at 28 days (ventilator, CPAP or oxygen) increased with increasing level of DR resuscitation. Although cranial ultrasound was obtained in only 58% of infants in our cohort, any grade of intraventricular hemorrhage and cPVL increased with increasing level of DR resuscitation. Similarly, rates of other neonatal morbidities including early- onset sepsis, late-onset sepsis, and NEC as well as days to full oral feeds, death before discharge, and length of stay among survivors progressively increased with level of resuscitation. Logistic regression analysis after adjusting for a priori selected covariates (center, GA, SGA, ANS and multiple births) showed longer length of stay among survivors, older postnatal age at full oral feeds and increased need for respiratory support at 28 days among infants who received any level of DR resuscitation (Table 4). Mortality was unchanged in the group that received oxygen/ CPAP, but increased significantly with higher levels of resuscitation. The adjusted risk of early-onset sepsis, late-onset sepsis and NEC did not increase with DR resuscitation. The odds of IVH and cPVL increased in the group who received CPR.

Discussion

In a large multicenter cohort of MPT infants born at $29^{0/7}$ to $33^{6/7}$ weeks GA, the majority (76%) received some level of resuscitation in the DR; with nearly 15% undergoing endotracheal intubation and 2.7% full CPR. The intensity of resuscitation decreased significantly for each advancing week of gestation. Prolonged rupture of membranes, and exposure to any ANS were associated with a reduced likelihood whereas SGA status and prenatal care were associated with increased likelihood of resuscitation levels other than CPR. Receipt of higher intensity of resuscitation after birth was associated with increased mortality, prolonged hospitalization and time to attain full feedings and higher likelihood of receipt of respiratory support at 28 days of age. CPR was associated with increased risk of intraventricular hemorrhage and cPVL among the MPT infants who had screening cranial sonograms.

MPT infants are a high risk group that accounts for utilization of a large proportion of neonatal intensive care Unit resources. Rates of DR resuscitation among late preterm infants, which range between 14–46% in different studies, are significantly lower than the rate in MPT infants, likely due to lower GA and antepartum factors predisposing to preterm delivery (3–4,18–20). In a study from Korea, almost 93% of infants between 29 to 32 weeks of GA received supplemental oxygen and 3% received CPR in the delivery room (21). These findings may reflect a difference in DR resuscitation practices in Korea compared with NRN centers. Boyle et al reported that 36.9% of infants delivered at 32–33 weeks received active resuscitation in the DR (3). However, their study did not include infants of 29–31 weeks GA. Our study confirmed that infants delivered at higher GA within the 29–33 week range had lower adjusted odds for resuscitation in the delivery room. Each increasing week of gestation decreased the risk of receiving resuscitation in the DR.

Prenatal care, defined in the data base as at least one prenatal visit prior to the delivery, was associated with increased receipt of oxygen, CPAP or bag and mask ventilation in our study. The reason for this association is unclear though we speculate that better prenatal care helped to identify higher risk women who subsequently delivered prematurely at tertiary centers.

There is limited literature evaluating the risk of DR resuscitation with maternal hypertension and SGA status in MPT infants. Aziz et al reported a 2-fold increase in respiratory support (positive pressure ventilation- endotracheal intubation) among moderate-high risk infants born to mothers with hypertension during pregnancy across all GAs (5). Similar associations have been reported between pregnancy induced hypertension and advanced resuscitation (endotracheal intubation and CPR) in infants greater than 34 weeks GA (6), and maternal hypertension and bag and mask ventilation in late preterm infants (4). Maternal hypertension was a significant risk factor among extremely low birth weight infants receiving CPR in the delivery room (8). In contrast, in the current study, maternal hypertension was independently associated with increased need for oxygen/CPAP alone. Magnesium sulfate was associated with reduced receipt of endotracheal intubation and CPR. We did not have available data on duration, dose or indications for its use. Magnesium may cause adverse events including diminished deep tendon reflexes and respiratory depression when used in the pregnant women (22). However, published reports do not show any association between magnesium sulfate exposure and level of delivery room resuscitation in the neonates (23,24). The association between SGA status and all levels of resuscitation except CPR in MPT infants in our study is consistent with previously reported data in late preterm infants (4,6,20). Maternal hypertension is an important risk factor for preterm delivery and SGA status, which could lead to emergency Cesarean section and use of antepartum magnesium sulfate (25). Due to the complex interaction between maternal hypertension, use of magnesium sulfate and SGA status, it is hard to dissociate the individual effects of each risk factor in this population.

The protective effect of ANS exposure has been shown in extremely low birth infants (7,8). We found that exposure to ANS confers an advantage in MPT infants as well. Prolonged rupture of membranes decreased the odds of resuscitation in our cohort whereas histologic chorioamnionitis was associated with reduced frequency of oxygen/CPAP and endotracheal intubation; the association did not retain significance for bag and mask ventilation or CPR. Histological chorioamnionitis has been associated with reduced incidence of respiratory distress syndrome in preterm neonates (26,27) which could lower the need for resuscitation. On the other hand, stress and an increased risk of sepsis may render these infants less vigorous at birth, accounting for the inconsistent associations noted. Multiple births, in our study, were associated with decreased risk for endotracheal intubation and CPR in the DR. There have been conflicting reports in the literature about the association of multiple births with DR resuscitation. Aziz et al reported that in infants less than 35 weeks GA, multiple births doubled the risk of receiving positive-pressure ventilation and/or endotracheal intubation in the DR; the association was not seen in infants >35 weeks gestation (5). Berazategui et al did not find an association between multiple births and advanced resuscitation in infants delivered at >34 weeks GA (6). The reason for this discrepancy is not clear. We speculate that increased surveillance in the antenatal and intrapartum period for multiple births might have contributed to our results.

There is a paucity of literature on the effects of neonatal resuscitation in MPT infants. We demonstrate that DR resuscitation in MPT infants was associated with adverse short-term outcomes, including increased receipt of respiratory support at 28 days of age, delayed attainment of oral feedings, and prolonged length of hospitalization after adjusting for GA, center, SGA, ANS and multiple births. It is intriguing that even with low rates of mortality overall, the need for bag and mask ventilation or higher levels of resuscitation in the DR was a predictor for mortality. CPR in the DR was associated with an increased risk of IVH and cPVL. Although we acknowledge that cranial ultrasound was only obtained in 58% of MPT infants enrolled in the registry, the increased risk of IVH and cPVL following DR CPR suggests the need for neurodevelopmental monitoring for sequelae, at least in this select group of MPT infants. DR resuscitation has been shown to be associated with adverse neonatal outcomes in other neonatal cohorts. In late preterm infants, higher intensity of resuscitation was associated with mortality, respiratory distress, pneumothorax, late-onset sepsis and length of stay (20). In a large cohort of extremely low birth infants from NRN centers, CPR in the DR was associated with increased risk of pneumothorax, BPD, grade 3–4 IVH, death by 12 hours and death or neurodevelopmental impairment among survivors at 18 months of corrected age (8). DeMauro et al reported higher rates of BPD and severe ROP in very low birth weight infants who received higher levels of resuscitation in the DR (7). Increased risks of death, neurological morbidity, ROP and BPD were observed with the use of chest compressions and/or epinephrine in infants less than 32 weeks by Shah et al (9). Finer et al described increased frequency of IVH in very low birth weight infants from Vermont Oxford Network database who received CPR in the DR (2).

Our study used prospectively collected data from large level 3–4 NICUs across the United States. Although there may be variation in the personnel and organization of DR practices, all the centers follow NRP guidelines published by the American Academy of Pediatrics, and standardized definitions were used for data collection. Although extremely preterm infants are electively intubated in the DR in some centers, MPT infants would be expected to be intubated only if they required PPV. Hence, we believe that endotracheal intubation and CPR in the DR can be reliable predictors of common NICU morbidities in MPT infants. The knowledge that a large proportion of MPT neonates receive resuscitation at birth and that the need for resuscitation can be predicted by antepartum factors is important information for planning appropriate resources and staffing in the DR.

We had limited information about the indications for Cesarean section as well as indications for and duration of resuscitation. The information about the dose and indication for use of magnesium sulfate was not collected, and we acknowledge that higher doses of magnesium sulfate could increase the intensity of resuscitation required in the DR. Whether resuscitation guidelines were consistently followed could not be determined. Some of the noted associations were inconsistent across intervention groups, which could be related to the different sample sizes of the groups. Another limitation of our study is the difference in certain practices, such as obtaining cranial ultrasounds in MPT infants across the centers, which reduced the denominators in some of our analyses.

In conclusion, our study suggests that a significant proportion of MPT infants receive some level of resuscitation in the DR. Increased awareness of need for DR intervention, with appropriate staffing and resources should be available in the centers delivering these infants. A higher intensity of resuscitation appears to be a harbinger of adverse neonatal outcomes in this population.

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Participating NRN sites collected data and transmitted it to RTI International, the data coordinating center (DCC) for the network, which stored, managed and analyzed the data for this study. On behalf of the NRN, Drs. Abhik Das (DCC Principal Investigator) and Shampa Saha (DCC Statistician) had full access to all of the data in the study, and with the NRN Center Principal Investigators, take responsibility for the integrity of the data and accuracy of the data analysis.

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APPENDIX

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RTI International (U10 HD36790) – Dennis Wallace, PhD; Kristin M. Zaterka-Baxter, RN BSN CCRP; Margaret Crawford, BS CCRP; Jenna Gabrio, BS CCRP; Sarah Kandefer, BS; Jeanette O'Donnell Auman, BS.

Stanford University and Lucile Packard Children's Hospital (U10 HD27880, UL1 TR93) – David K. Stevenson, MD; M. Bethany Ball, BS CCRC; Melinda S. Proud, RCP.

University of Alabama at Birmingham Health System and Children's Hospital of Alabama (U10 HD34216) – Namasivayam Ambalavanan, MD; Monica V. Collins, RN BSN MaEd; Shirley S. Cosby, RN BSN.

University of California - Los Angeles, Mattel Children's Hospital, Santa Monica Hospital, Los Robles Hospital and Medical Center, and Olive View Medical Center (U10 HD68270) – Uday Devaskar, MD; Meena Garg, MD; Teresa Chanlaw, MPH; Rachel Geller, RN BSN.

University of Iowa and Mercy Medical Center (U10 HD53109, UL1 TR442) – Tarah T. Colaizy, MD MPH; Dan L. Ellsbury, MD; Jane E. Brumbaugh, MD; Karen J. Johnson, RN BSN; Donia B. Campbell, RNC-NIC; Jacky R. Walker, RN.

University of New Mexico Health Sciences Center (U10 HD53089, UL1 TR41) – Kristi L. Watterberg, MD; Robin K. Ohls, MD; Conra Backstrom Lacy, RN; Sandy Sundquist Beauman, MSN,RNC-NIC; Carol Hartenberger, MPH, RN CCRC.

University of Pennsylvania, Hospital of the University of Pennsylvania, Pennsylvania Hospital, and Children's Hospital of Philadelphia (U10 HD68244) – Barbara Schmidt, MD; Haresh Kirpalani, MB MSc; Sara B. DeMauro, MD MSCE; Noah Cook, MD; Aasma S. Chaudhary, BS RRT; Soraya Abbasi, MD; Toni Mancini, RN BSN CCRC; Dara Cucinotta.

University of Rochester Medical Center, Golisano Children's Hospital, and the University of Buffalo Women's and Children's Hospital of Buffalo (U10 HD68263, UL1 TR42) – Satyan Lakshminrusimha, MD; Ronnie Guillet, MD PhD; Ann Marie Scorsone, MS; Julianne Hunn, BS; Rosemary Jensen; Holly I.M. Wadkins, MA; Stephanie Guilford, BS; Ashley Williams, M.S. Ed.

University of Texas Southwestern Medical Center at Dallas, Parkland Health & Hospital System, and Children's Medical Center Dallas (U10 HD40689) – Luc P. Brion, MD; Diana M. Vasil, RNC-NIC; Lijun Chen, PhD RN; Lizette E. Torres, RN.

University of Texas Health Science Center at Houston Medical School and Children's Memorial Hermann Hospital (U10 HD21373) – Kathleen A. Kennedy, MD MPH; Jon E. Tyson, MD MPH; Julie Arldt-McAlister, RN BSN; Carmen Garcia, RN CCRP; Karen Martin, RN; Georgia E. McDavid, RN; Sharon L. Wright, MT (ASCP).

Wayne State University, University of Michigan, Hutzel Women's Hospital, and Children's Hospital of Michigan (U10 HD21385) – Athina Pappas, MD; John Barks, MD; Rebecca Bara, RN BSN; Shelley Handel, AD; Diane F White, RT; Mary Christensen, RT; Stephanie A. Wiggins, MS.

Table 1

Maternal and Infant characteristics

Characteristics	Routine care N=1684	Oxygen/CPAP N=2279	Bag-mask ventilation N=1831	Endotracheal intubation N=1034	CPR N=186	P value (trend)
Birth weight, g mean (SD)	1855 (366)	1678 (433)	1636 (422)	1585 (449)	1679 (472)	<.0001
Gestational age, wk mean (SD)	32.21 (1.1)	31.4 (1.3)	31.3 (1.3)	30.8 (1.4)	31.0 (1.4)	<.0001
Small for gestation, %	248/1682 (14.7)	387/2279 (17.0)	338/1830 (18.5)	157/1033 (15.2)	21/185 (11.4)	0.0068
Maternal age, mean (SD)	28.5 (6.7)	28.7 (6.5)	28.2 (6.5)	28.1 (6.3)	27.5 (6.5)	0.0566
Gender: % male	877/1682 (52.1)	1172/2279 (51.4)	936/1830 (51.1)	567/1033 (54.9)	106/186 (57.0)	0.1945
Apgar score at 5 min < 5, %	2/1668 (0.12)	4/2275 (0.18)	50/1824 (2.7)	178/1025 (17.4)	108/177 (61.0)	<.0001
Major congenital malformations, %	72/1683 (4.3)	127/2278 (5.6)	134/1831 (7.3)	223/1033 (21.6)	35/186 (18.8)	<.0001
Prenatal care, %	1617/1683 (96.1)	2216/2276 (97.4)	1794/1828 (98.1)	994/1033 (96.2)	171/184 (92.9)	<.0001
Maternal hypertension, %	487/1682 (29.0)	838/2274 (36.9)	694/1826 (38.0)	296/1030 (28.7)	49/181 (27.1)	<.0001
Maternal diabetes (insulin dependent), %	105/1682 (6.2)	188/2275 (8.3)	148/1828 (8.1)	73/1029 (7.1)	9/181 (5.0)	0.0715
Chorioamnionitis, %	144/1673 (8.6)	143/2258 (6.3)	127/1820 (7.0)	70/1008 (6.9)	11/185 (6.0)	0.0849
Chorioamnionitis, histologic, %	399/1422 (28.1)	420/1910 (22.0)	415/1534 (27.1)	204/806 (25.3)	32/110 (29.1)	0.0005
Rupture of membranes >18 h, %	423/1581 (26.8)	400/2153 (18.6)	271/1712 (15.8)	146/953 (15.3)	19/170 (11.2)	<.0001
Cesarean delivery, %	735/1683 (43.7)	1489/2279 (65.3)	1273/1830 (69.6)	787/1034 (76.1)	154/186 (82.8)	<.0001
Antenatal steroids, %	1459/1668 (87.5)	1948/2261 (86.2)	1591/1819 (87.5)	833/1022 (81.5)	102/180 (56.7)	<.0001
Singleton, %	1205/1684 (71.6)	1512/2279 (66.3)	1311/1831 (71.6)	783/1034 (75.7)	156/186 (83.9)	<.0001
Antenatal magnesium sulfate, %	796/1659 (48.0)	1274/2239 (56.9)	1057/1796 (58.9)	506/993 (51.0)	58/176 (33.0)	<.0001

•Denominator for each variable is based on the availability of data

Table 2

Adjusted odds ratio of risk factors for levels of resuscitation*

	Oxygen/CPAP N = 2279	Bag-mask ventilation N = 1831	Endotracheal intubation N = 1034	CPR N = 186
Gestational age (per increasing week)	**0.55 (0.51–0.59)**	**0.52 (0.48–0.55)**	**0.37 (0.34–0.41)**	**0.41 (0.35–0.48)**
Small for gestation	**1.29 (1.05–1.59)**	**1.39 (1.12–1.73)**	**1.53 (1.17–2.00)**	0.99 (0.51–1.90)
Multiple births	1.18 (1.00–1.40)	0.95 (0.79–1.13)	**0.69 (0.55–0.86)**	**0.40 (0.22–0.73)**
Antenatal steroids	**0.69 (0.53–0.89)**	0.77 (0.58–1.01)	**0.56 (0.41–0.77)**	**0.20 (0.12–0.34)**
Magnesium sulfate	0.96 (0.81–1.14)	0.98 (0.82– 1.18)	**0.65 (0.52–0.81)**	**0.40 (0.24–0.67)**
Histologic chorioamnionitis	**0.81 (0.67–0.99)**	0.99 (0.82–1.22)	**0.72 (0.56–0.92)**	1.18 (0.70–1.99)
Maternal hypertension	**1.26 (1.05–1.50)**	1.18 (0.99–1.43)	0.84 (0.66–1.06)	1.27 (0.77–2.09)
Rupture of membranes > 18 h	**0.75 (0.61–0.91)**	**0.51 (0.41–0.63)**	**0.52 (0.40–0.68)**	**0.39 (0.20–0.75)**
Prenatal care	**1.72 (1.07–2.74)**	**3.23 (1.83–5.70)**	1.82 (1.00–3.28)	1.57 (0.52–4.75)

*Routine care in the DR is the reference level

Deviance goodness of fit test: P-value= 0.99

Table 3

Neonatal outcomes

Characteristics	Routine care N=1684	Oxygen/CPAP N=2279	Bag-mask ventilation N=1831	Endotracheal intubation N=1034	CPR N=186	P value (trend)
Surfactant use, %	82/1684 (4.9)	461/2279 (20.2)	447/1830 (24.4)	706/1034 (68.3)	129/185 (69.7)	<.0001
Respiratory support at 28 days, % Ventilator, CPAP, O_2	66/1611 (4.1)	261/2116 (12.3)	245/1753 (14.0)	332/944 (35.2)	54/145 (37.2)	<.0001
Ventilator at 28 days, %	8/1611 (0.5)	15/2116 (0.7)	28/1753 (1.6)	69/944 (7.3)	13/145 (9.0)	<.0001
CPAP at 28 days,	3/1611 (0.2)	16/2116 (0.8)	24/1753 (1.4)	40/944 (4.2)	2/145 (1.4)	<.0001
Oxygen at 28 days,	55/1611 (3.4)	230/2116 (10.9)	193/1753 (11.0)	223/944 (23.6)	39/145 (26.9)	<.0001
Any IVH, % Grades 1,2,3,4	93/657 (14.2)	135/1296 (10.4)	134/1124 (11.9)	137/800 (17.1)	37/144 (25.7)	<.0001
Cystic PVL after 28 days, %	2/213 (0.9)	15/639 (2.4)	16/614 (2.6)	19/484 (3.9)	9/69 (13.0)	<.0001
Early onset sepsis, %	10/1683 (0.59)	13/2279 (0.57)	13/1831 (0.71)	10/1031 (1.0)	5/185 (2.7)	0.0171
Late onset sepsis, %	33/1677 (2.0)	56/2272 (2.5)	64/1829 (3.5)	63/1030 (6.1)	5/183 (2.7)	<.0001
Days to full oral feeds (120 ml/kg/day) Mean (SD)	17.8 (11.7)	26.8 (20.7)	27.6 (15.0)	35.8 (17.4)	35.4 (17.3)	<.0001
Proven NEC, %	25/1684 (1.5)	47/2274 (2.1)	50/1829 (2.7)	40/1034 (3.9)	7/185 (3.8)	0.0008
Death before discharge, %	11/1684 (0.6)	22/2279 (1.0)	29/1831 (1.6)	74/1034 (7.2)	39/186 (21.0)	<.0001
Death among infants with major congenital malformations, %	5/72 (6.9)	9/127 (7.1)	13/134 (9.7)	51/223 (22.9)	23/35 (65.7)	<.0001
Length of stay (d), mean (SD) Min, Median, Max	24.9 (14.6) 1, 22, 213	34.0 (21.6) 1, 31, 395	35.8 (18.3) 2,33,214	43.7 (26.3) 1,44,434	37.2 (23.4) 1, 38, 83	<.0001

* Denominator for each variable is based on the availability of data

Table 4

Adjusted odds ratios (and 95% confidence intervals) of neonatal outcomes for levels of resuscitation*

Outcome	Oxygen/CPAP N = 2279	Bag-mask ventilation N = 1831	Endotracheal intubation N = 1034	CPR N = 186
Death	1.43 (0.68–2.99)	**2.63 (1.29–5.34)**	**12.73 (6.53–24.80)**	**48.02 (23.10– 99.83)**
Respiratory support at 28 days	**1.91 (1.41–2.57)**	**2.31 (1.71–3.13)**	**5.40 (3.97–7.35)**	**4.89 (3.02–7.89)**
Intraventricular hemorrhage	0.74 (0.55–1.0)	0.81 (0.60–1.10)	1.20 (0.89–1.64)	**1.75 (1.09–2.81)**
Cystic PVL after 28 days	2.45 (0.54–11.08)	3.19 (0.71–14.34)	4.06 (0.90–18.25)	**9.71 (1.89–49.82)**
Proven NEC	1.06 (0.63–1.77)	1.43 (0.86–2.38)	1.41(0.81–2.44)	1.64 (0.67–4.00)
Early sepsis	0.79 (0.32–1.91)	0.86 (0.35–2.14)	0.86 (0.32–2.30)	2.70 (0.82–8.92)
Late onset sepsis	0.77 (0.49–1.22)	1.00 (0.64–1.58)	1.29 (0.81–2.07)	0.76 (0.28–2.03)
Age at full oral feed (days)^	**2.98 (2.02–3.93)**	**2.99 (1.97–4.00)**	**6.72 (5.43–8.02)**	**6.28 (3.52–9.04)**
Length of stay (days)†^	**2.81 (1.71–3.91)**	**3.91 (2.75–5.08)**	**9.30 (7.88–10.73)**	**8.75 (5.81–11.68)**

*Routine care in the DR is the reference level. The covariates included in the regression are center, GA, SGA, ANS and multiple births.

†Average length of stay among survivors

^For continuous outcomes, an estimate of the difference between means and the 95% confidence interval of the estimate is reported