Intention to Treat: Obstetrical Management at the Threshold of Viability

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Condensation:

Use of obstetrical interventions in the periviable period is more likely when parents desire active resuscitation and increases odds of survival to discharge from the NICU.

Short title:

Obstetrical Management at the Threshold of Viability

AJOG at a Glance:

- A. This study was conducted to review the use of obstetrical interventions in multiple academic centers in the U.S. in deliveries prior to 25 weeks gestation, and to assess the odds of survival based on their usage.
- B. Interventions were more likely to be used when resuscitation was desired. Increased survival was noted when pharmacologic interventions were bundled for deliveries occurring at 23 and 24 weeks gestation.
- C. This study provides data on use of obstetrical interventions for management of pregnancies with threatened delivery prior to 25 weeks, including 22 week management, when interventions are more controversial.

ABSTRACT

Key words: Extremely preterm infants, obstetric interventions at viability, periviability

Background: Despite medical advances in the care of extremely preterm neonates, and growing acceptance of resuscitation at 23 and even 22 weeks' gestation, controversy remains concerning use of antepartum obstetrical interventions intended to improve outcomes in the setting of anticipated extremely preterm birth. In the absence of demonstrated benefit prior to 23 weeks, and with uncertain benefit at 23 weeks, prior obstetric committee opinions have advised against their use at these gestational ages.

Objectives:

- To review the use of obstetrical interventions at the threshold of viability based on neonatal resuscitation plan
- To review the odds of survival to NICU discharge based on use of obstetrical interventions while adjusting for neonatal factors

Study Design:

This retrospective study of 6 study centers reviewed pregnant patients admitted between 22 0/7 and 24 6/7 weeks facing delivery from 2011 to 2015. Patients with known anomalies or missing data were excluded. Records were reviewed for demographics, resuscitation plan, and obstetrical interventions. Mode of delivery, delivery room care, and final infant dispositions were recorded. Multiple gestations were included as one pregnancy in regard to the use of obstetrical interventions and were excluded from survival analysis.

Results:

478 mothers met inclusion criteria. When resuscitation was planned, mothers were more likely to receive all conventional obstetrical interventions (antenatal steroids, magnesium sulfate for neuroprotection, tocolytics, and *Group Beta Streptococcus* prophylaxis) regardless of gestational age at admission and were more likely to be delivered by cesarean section ($p < 0.05$). Analyzed as a group, when antenatal steroids, magnesium sulfate, tocolytics and GBS prophylaxis were administered, the odds of survival to NICU discharge increased for newborns born at 22 weeks (OR 11.33, CI 1.405-91.4) and 23 weeks gestation (OR 15.5, CI 3.747-64.11) ($p < 0.05$). In singletons, the odds of survival to NICU discharge was not improved by cesarean delivery versus vaginal delivery even after adjusting for use of additional interventions, weight, gender and gestational age (OR 1.0, CI 0.59-1.8, $p = 0.912$).

Conclusion:

In this study, when postnatal resuscitation was planned at 22 and 23 weeks gestation, women were more likely to receive antenatal steroids, magnesium sulfate, and antibiotics; provision of this bundle imparted survival benefit at 23 weeks but could not be demonstrated at 22 weeks due to small sample size. These findings support of

1 neonate-oriented obstetric interventions in the setting of delivery at 23 weeks when
2 resuscitation is planned, and further exploration of optimal obstetric care when
3 resuscitation of infants born at 22 weeks is anticipated.
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1 Introduction

2 Periviable deliveries, occurring between approximately 20 0/7 weeks to 25 6/7
3 weeks, account for less than 1% of all births, but in some studies, up to 40% of all infant
4 deaths [1-3]. While higher rates of neonatal active treatment have been shown to
5 increase survival at the lowest gestational ages, obstetric interventions for these
6 extremely premature infants have shown negligible improvement in survival rates and
7 neurodevelopmental impairment [4] and clear guidelines for management are lacking
8 [2, 4, 5]. Even without clear guidelines, some centers continue to push the boundaries
9 for interventions in these extremely premature infants.

10 Common obstetrical interventions used for both prolongation of pregnancy and
11 improvement of neonatal outcomes include antenatal steroids, tocolytics, magnesium
12 sulfate for neuroprotection, antibiotics for *Group Beta Streptococcus* (GBS) prophylaxis,
13 and cesarean delivery [6]. While the benefits of antenatal steroids have been
14 documented, substantial uncertainty surrounds the benefit of the remainder of
15 interventions for improving outcomes for extremely preterm infants, creating a
16 potential disconnect between evidence-based obstetric recommendations and neonatal
17 practice [1-4]. Some new studies also suggest benefits of antenatal steroids alone at
18 these extremely early gestational ages with benefits seen following a full course of
19 steroids as early as 22 weeks [7]. Therefore, the goal of this study was to evaluate the
20 use of these interventions for pregnancies with threatened delivery between 22 0/7 to
21 24 6/7 weeks gestational age based on plans for resuscitation following delivery, and to
22 determine the impact of these interventions on infant survival. Although these

1 interventions are not recommended, they are nonetheless utilized. We sought to
2 understand the utilization of pharmacologic interventions for women based on their
3 gestational-week of admission and neonatal consequences related to utilizing these
4 interventions. We propose that while these interventions are not recommended at
5 earlier gestational ages, they are nonetheless utilized, especially when resuscitation is
6 planned for these early neonates.

7

8 **Materials and Methods**

9 We conducted a multi-center retrospective study consisting of INDEED
10 (Investigating Neonatal Decisions for Extremely Early Deliveries) study group centers
11 with data collected from January 1, 2011 to December 31, 2015. The primary aim of the
12 INDEED study group was to understand conditions around decisions for active delivery
13 room treatment for those pregnancies deliveries between 22 0/7 to 24 6/7 weeks
14 gestational age. All participating hospitals were part of tertiary academic medical
15 referral centers providing tertiary high-risk obstetric and neonatal care to high-risk
16 obstetric patients. The Institutional Review Board reviewed and approved waiver of
17 consent for this study at each individual site. A grant from North Shore University
18 Health System supported use of the REDCap database [8].

19 *Study Population*

20 Both obstetrical and neonatal databases were reviewed for patients presenting
21 between 22 0/7 to 24 6/7 weeks gestational age with a living fetus with threatened
22 preterm delivery and delivering before 25 weeks; those who remained pregnant beyond

1 this periviable period were excluded. Women were excluded from the study if their
2 fetus had a known major congenital or genetic anomaly. Women were analyzed by
3 interventions received, regardless of singleton or multiple gestation to gauge rates of
4 interventions or condition at delivery.

5 *Study Institutions*

6 Study institutions were located across the central regions of the United States.
7 Resuscitation plans based on individual centers have previously been published by Dalia
8 et al noting varying levels of resuscitation for all gestational age groups except those at
9 24 weeks. At 25 weeks gestational age, all interventions were provided for infants
10 including resuscitation. During this review period, at two centers, options offered for
11 newborn care at 22 completed weeks reportedly varied by neonatologists. Three had
12 agreed-upon approaches by neonatology, and one had a written policy; of these
13 centers, two offered only comfort care and two recommended comfort care but would
14 provide resuscitation per parent request. Obstetric care for planned neonatal
15 resuscitation was not standardized. The six centers were analyzed as having higher and
16 lower resuscitation rates, based on significantly different rates of resuscitation at 22 and
17 23 completed weeks [9].

19 *Data Collection*

20 Records were reviewed for maternal demographic and medical information, plan
21 of care for resuscitation through neonatal and/or obstetrical documentation and use of
22 obstetric interventions and neonatal characteristics. Interventions reviewed include:

1 antenatal steroids (at least one dose prior to delivery), magnesium sulfate for
2 neuroprotection, tocolytics (indomethacin, nifedipine, terbutaline or magnesium for
3 tocolysis), antibiotics for GBS prophylaxis, and mode of delivery. For cesarean section,
4 documented indications included fetal distress, fetal malpresentation, maternal well-
5 being, a combination of the above, or unknown. Primary outcome of death vs. survival
6 to NICU discharge of newborn was reported per each pregnancy.

7 Delivery room care was reviewed from both obstetrical and neonatal
8 documentation. Gender, gestational age at delivery, and delivery weight (in grams)
9 were collected as covariates. Documentation of delivery room resuscitation plan,
10 (initiation of comfort care or neonatal resuscitation) was reviewed. Neonatal condition
11 at delivery and death or survival to NICU discharge home were noted. Infants
12 transferred to another center were not counted as having confirmed survival to NICU
13 discharge, as their ultimate disposition was unknown.

14 *Statistical Analysis*

15 Descriptive statistics were calculated for the overall population and also for each
16 gestational week at 22, 23 and 24 weeks. Summary statistics describing maternal
17 characteristics compared to interventions used, stratified by the completed weeks
18 gestation on presentation. Groups were analyzed using independent t-tests for
19 continuous variables and chi-squared tests for categorical variables. Generalized linear
20 models were created to note differences between intervention and non-intervention
21 groups for antenatal steroids, magnesium sulfate, and GBS prophylaxis. Generalized
22 linear mixed models were generated for differences between intervention and control

groups and included a random effect for the institution to account for the effect of different sites involved in the study.

Effects of obstetric interventions on survival to NICU discharge adjusted for neonatal characteristics were analyzed in step-wise manner. All newborns delivered between 22 and 24 completed weeks gestation for whom resuscitation was planned were analyzed first as one group, then by each gestational week. Multivariable logistic regression analyses evaluated effects of pharmacologic obstetric interventions, adjusting for neonatal characteristics, on survival to NICU discharge. Specifically, in our overall survival model for all 412 newborns with planned resuscitation, the effects on survival to discharge of the following variables were examined: receipt of any antenatal steroids, magnesium for neuroprotection, tocolytics, antibiotics for GBS prophylaxis and delivery by cesarean section, adjusting for neonatal factors known to influence survival: singleton status, sex, gestational age at delivery, and birthweight in grams. We subsequently modeled the effect of each pharmacologic intervention on survival to NICU discharge, controlling for neonatal factors. Post-hoc analyses to further examine findings at 24 weeks are explained in that section. Statistical analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC) and SigmaStat 4.0 (Systat Software Inc., San Jose, CA). P-values <0.05 were considered significant.

Results

478 pregnant women met inclusion criteria after 8 were excluded for fetuses with anomalies and 10 were excluded for missing medical records despite identification

1 in a database. Approximately one-third of these patients were nulliparous, with an
2 average maternal age of 27.3 years. Gestational age at mother's admission ranged from
3 22 0/7 to 24 6/7 weeks, with mean and standard deviation 23 3/7 + 6 days. Gestational
4 age at delivery (of twin A if multiple gestation) also ranged from). There were 398
5 singleton pregnancies with the remaining 80 comprised of twins (n=74 mothers) and
6 higher order multiples (n=8 mothers).

7 *Frequency of Obstetric Interventions by gestational age at admission*

8 Baseline characteristics of women and receipt of obstetrical interventions are
9 shown in Table 1. To understand the progression of care for women admitted at these
10 early ages, we report here interventions received based on the gestational age at which
11 women were first admitted. (In contrast, information on prevalence of interventions
12 based on week of delivery are found in Table 2.) For the cohort, and for every
13 gestational age group by week a plan for resuscitation was the most consistent factor
14 associated with increased likelihood for receiving obstetric interventions. Maternal age,
15 parity, and marital status did not appear to impact provision of these interventions.
16 Estimated fetal weight was unknown prior to delivery for 27% (129 of 478) of women.
17 A higher mean birthweight was also noted for those infants whose mothers received
18 antenatal steroids, magnesium sulfate, and tocolytics.

19 Women admitted at 22 weeks gestation

20 143 pregnant women were admitted between 22 0/6 and 22 6/7; 33% (n=47)
21 received at least one dose of steroids, 27% (n=38) received magnesium sulfate, 24%
22 (n=34) received antibiotics for GBS prophylaxis, and 18% (n=26) received tocolytics prior

to delivery. Among those admitted at 22wks, 48% had a plan for resuscitation, and infants were delivered at 22 weeks (n=95), 23 weeks (n=33), and 24 weeks (n=15). Women planning neonatal resuscitation were more likely to receive steroids ($p<0.05$), magnesium sulfate ($p<0.05$), and GBS prophylaxis ($p<0.05$), but not tocolytics compared to those women not planning on neonatal resuscitation. Most (90%) of 22 week deliveries occurred vaginally. Cesarean section was performed in 20% (14 of 69) of cases in which neonatal resuscitation was planned and never when no resuscitation was planned (Table 1). The majority of these cases (12 of 14) were in the case of multiple gestations with the indication for singleton deliveries including malpresentation and maternal well-being.

Women admitted at 23 weeks gestation

197 pregnant women were admitted between 23 0/7 and 23 6/7; 72% (n=142) received at least one dose of steroids, 60% (n=118) received magnesium sulfate, 42% (n=84) received antibiotics for GBS prophylaxis, and 34% (n=68) received tocolytics prior to delivery, with planned resuscitation for 82% of infants. Among those admitted at 23 weeks, 117 delivered at 23 weeks and 80 delivered at 24 weeks. Women planning neonatal resuscitation were significantly more likely to receive all four interventions. Sixty-one percent of these pregnancies were delivered vaginally (n=117) with an increase in cesarean sections when neonatal resuscitation was planned (n=75 planned resuscitation, n=3 no resuscitation planned). Singleton deliveries accounted for 35% of cesarean deliveries with the most common indication being malpresentation (10 of 26).

Women admitted at 24 weeks gestation

138 women were admitted between 24 0/7 and 24 6/7; 81% (n=112) received at least one dose of steroids, 77% (n=106) received magnesium sulfate, 44% (n=61) received antibiotics for GBS prophylaxis, and 33% (n=46) received tocolytics prior to delivery, with planned resuscitation for 96% of infants. All patients planning resuscitation received steroids. Thirty-eight percent of pregnancies presenting at 24 weeks were delivered vaginally (n=42). Singleton deliveries accounted for 75% of cesarean deliveries with the most common indication being malpresentation (43 of 120). All patients included delivered prior to 25 weeks gestational age.

Impact of pharmacologic obstetrical interventions on confirmed survival to NICU discharge

Neonatal resuscitation was planned for 304 of the 397 mothers' newborns: 48%, 82%, and 96% at 22 weeks, 23 weeks, and 24 weeks gestational age, respectively. Receipt of maternal obstetric interventions and neonatal characteristics and outcomes for the 412 newborns with planned resuscitation are found in Table 2. Four-hundred twelve newborns had resuscitation planned; all but 13 (3%) were liveborn and admitted to the NICU. Because the ultimate dispositions for 13 NICU patients transferred outside facilities were not known, the confirmed survival to discharge home from the NICU for the entire group of newborns with resuscitation planned was admitted to the NICU was 45% (187 of 412).

For the entire group of 412 newborns with planned resuscitation, in the model analyzing survival as a function of maternal receipt of the 5 obstetric interventions (steroids, magnesium, tocolytics, GBS prophylaxis, cesarean delivery) and four neonatal

1 factors (gestational age, birthweight by week-specific study population quartiles, sex,
2 and singleton status), three variables—steroids, gestational age, and birthweight—were
3 significant. Amongst newborns with planned resuscitation, odds of confirmed survival
4 to NICU discharge were 2.6 times higher for those whose mothers received antenatal
5 steroids (CI: 1.3-5.6, $p=0.011$), after adjusting for the two other factors significant in the
6 model—gestational age and birthweight.

7 In models analyzing the effect each medicinal intervention had on odds of
8 survival while adjusting for the neonatal variables (age, sex, singleton, birthweight),
9 again, only steroids were found to be significantly associated with survival to discharge
10 (OR 2.7, CI: 1.5-4.9, $p=0.002$).

11 Newborns delivered 22 0/7 to 22 6/7 weeks

12 At 22 weeks, 36 of 40 newborns with planned resuscitation were liveborn, and
13 condition of one was not known; 3 newborns were confirmed as surviving to discharge
14 home. The outcomes in relation to exposures to maternal receipt of perinatal
15 medications are reported in Figure 1. At 22 weeks, interventions did not result in
16 significant differences in survival to home discharge, but sample size was small.

17 Newborns delivered 23 0/7 to 23 6/7 weeks

18 One-hundred twenty-two newborns delivered at 23 weeks had resuscitation planned;
19 116 (95%) were liveborn; 42 (34%) survived to discharge home from NICU, and one baby
20 was transferred to an outside facility. As shown in Figure 1, for these newborns, the
21 following interventions were associated with increased odds of confirmed survival to
22 home from the NICU: antenatal steroids (OR 5.2, CI 1.8-14.6, $p=0.002$), magnesium (OR

4.3, CI 1.8-10.1, $p=0.001$, and bundle of receiving steroids, magnesium, GBS prophylaxis and tocolytics (OR 3.2, CI 1.2-8.7, $p=0.037$).

Newborns delivered 24 0/7 to 24 6/7 weeks

Two-hundred fifty newborns delivered at 24 weeks had resuscitation planned; 247 of these (99%) were liveborn. Fifty-seven percent (142 newborns of 250) survived to discharge home from NICU, and 11 were transferred to an outside facility. As seen in Figure 1, maternal receipt of obstetric interventions did not affect likelihood of survival to discharge home. Because these findings differed dramatically from those found for newborns delivered at 23 weeks, post hoc analyses were performed. The sample size of 250 newborns allowed performance of multivariable analyses of calculating odds of survival with each intervention while adjusting for neonatal factors of gestational age, birthweight and, sex, and singleton status. Birthweight was the only significant factor in these analyses. More specifically, birthweight lower than the lowest week-specific study group quartile was associated with lower odds of survival. However, as seen in Figure 2, the 24-week study population birthweight quartiles were markedly higher than even age-specific Fenton percentiles (average of male and female) [10], while those of the 23-week study population were closer to the Fenton percentiles. This may partially explain the dominance of birthweight on odds of survival to NICU discharge at 24 weeks while pharmacologic interventions were significantly associated with higher survival odds at 23 weeks.

Comment

1 Principal findings of this study

2 In this study, we sought to review the utilization of pharmacologic obstetric
3 interventions and short-term neonatal survival across six academic centers. We found
4 that when resuscitation was planned, mothers were more likely to receive all
5 pharmacological interventions regardless of gestational age at admission. They were
6 also more likely to be delivered by cesarean section.

7 Our findings suggest that, at these centers, obstetric practice is aligned with
8 published obstetric practice guidelines at 24 weeks gestational age, but not at 22 and 23
9 weeks [2]. While there is no clear evidence in current literature to support antenatal
10 steroids, magnesium sulfate, antibiotics, and cesarean delivery at 22 and 23 weeks, we
11 found some of these patients did receive these interventions, particularly antenatal
12 steroids; not surprisingly, provision of some of these interventions - antenatal steroids,
13 magnesium sulfate, antibiotics for GBS, and cesarean delivery - was associated with a
14 plan for neonatal resuscitation.

15 Newborns with planned resuscitation whose mothers received antenatal
16 steroids had increased chances of survival to discharge home from the NICU in logistic
17 regression models for the group as a whole and at 23 weeks. Unfortunately, our small
18 sample size of 40 newborns delivered at 22 weeks precluded examining this group
19 separately. We did not identify survival benefit associated with provision of
20 pharmacologic interventions at 24 weeks; we speculate that the unusual weight
21 distribution in this group of neonates may have overshadowed the influence of these
22 interventions on survival to NICU discharge.

1 Results

2 Overall, our study findings are consistent with previous work demonstrating benefit of
3 admission of antenatal steroids at earlier gestational ages. Mori et al. of Japan noted
4 improved survival when antenatal steroids were used at 22 and 23 weeks [11]. Similar
5 findings were noted by Hayes et al in the US when antenatal steroids were given at 23
6 weeks gestational age [12]. Study designs, however, have been small and
7 retrospective and questions of equipoise may limit randomized controlled trials, leaving
8 obstetricians with a lack of high-quality evidence or consensus on management. There
9 has also been controversy around the best mode of delivery for these extremely
10 premature infants, largely over concerns for increased maternal morbidities. Previous
11 studies have shown little benefit to cesarean delivery over vaginal delivery prior to 24
12 weeks gestational age, though many physicians continue to offer cesarean delivery prior
13 to this point [6, 13-16] . In our population, while cesarean delivery occurred in about
14 half of deliveries overall, this had no significant effect on survival outcomes in the model
15 examining all possible obstetric interventions and neonatal factors for newborns with
16 planned resuscitation; closer examination of the impact of cesarean delivery is
17 warranted as the aims of this study did not delve into the indications for cesarean
18 deliveries.

19 Clinical Implications

20 As the care of extremely premature neonates becomes more advanced, we
21 anticipated that while not recommended, use of these obstetrical interventions during
22 this early gestational ages would continue based on the parents desire for neonatal

1 resuscitation. We recognize that while these results may not coincide with the most
2 recent joint committee recommendations, these results may be used for future
3 guidelines and discussion between both obstetricians and neonatologists for
4 management.

5 While our findings demonstrate rates of interventions correlating to planned
6 neonatal resuscitation at 22 weeks, our small cohort did not reveal statistically
7 significant improvement in survival to NICU discharge. Our review of recent studies
8 reporting survival rate at this gestational week (See Supplemental Table 1) reveals
9 vast differences in reported survival rates. However, ours is the only study to our
10 knowledge that reviews receipt of multiple interventions prior to delivery and
11 impact on neonatal survival. We believe this adds to the discussion among
12 obstetricians and neonatologists to review best practices among these extremely
13 premature infants.

14

15 Research Implications

16 As we continue to review both this data and current literature, there are several
17 questions regarding best practice management for these periviable deliveries. In the
18 obstetric world, the role of cesarean section at these early gestational ages remains
19 controversial prior to 24 weeks gestational ages. While full review of indications of
20 delivery and outcome associations was beyond the scope of this analysis, it continues to
21 warrant further research. We have also noticed differences among resuscitation

1 counseling and recognize this as an important area for further study.

2 Strengths and Limitations

3 While periviable deliveries make up a low percentage of preterm births, this
4 study was able to include a large subset of deliveries across multiple perinatal centers.
5 This robust group of data adds to current knowledge on management of these births
6 and addresses both aspects of obstetric and neonatology management during the
7 antepartum period. We recognize limitations of our study. Data were collected
8 retrospectively from all study centers; prospective study might minimize missing data
9 and more clarity about perinatal decision-making and neonatal outcome. Finally, new
10 data and recommendations on management released by prominent pediatric and
11 obstetric organizations during this time period may have led to changes in physician
12 practices since the years of our study [2, 6].

13 Conclusions

14 Despite its limitations, this study contributes findings from nearly 500 women
15 delivering in the periviable period to continue the discussion among obstetric and
16 neonatal providers for best practices for treating mothers presenting in these extremely
17 early gestational ages. While we do not offer a consensus for management at 22 and 23
18 weeks gestational age, the disconnect between existing guidelines and obstetric
19 practice in this large cohort emphasizes the complexity of perinatal medical decision
20 making for women at risk for extremely preterm delivery, particularly those desiring
21 resuscitation for their infants after birth. If neonatal resuscitation is offered and
22 planned, it is logical to offer interventions with potential to improve neonatal outcomes;

1 our findings suggest a discomfort among obstetric providers to forego potentially
2 beneficial interventions, even in the absence of strong evidence to support their use.
3 The demonstration of survival benefit for infants at 23 weeks when their mothers
4 received these interventions supports continued close examination of existing
5 guidelines; small numbers of infants born and resuscitated at 22 weeks continues to
6 complicate evidence-based perinatal decision making when deliver at this gestational
7 age is anticipated.

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Tables and Figures:

Table 1: Characteristics and Receipt of Obstetric Interventions of 478 pregnant women

*Significant at <0.05 level

**Significant at <0.01 level

Table 2: Newborns with planned resuscitation: Clinical characteristics, perinatal interventions and outcomes by delivery week

*Reflects use estimated fetal weight within one week of birth when birthweight unknown, n=7; missing weights (birth or delivery-week estimated fetal weight data), n=17

**Unknown condition at birth, but did not survive to NICU admission

Figure 1: Use of interventions and survival based on gestational age at delivery

*p<0.05

Figure 2: Distribution of birthweights of 412 newborns with planned resuscitation

*F refers to Fenton curve percentiles (mean of female/male)

Supplemental Table 1: Studies since 2015 including 22 week liveborn newborns, perinatal management, and survival

Table I: Characteristics and Receipt of Obstetric Interventions of 478 pregnant women overall and by gestational age in weeks

Overall (N = 478)										
	Antenatal Steroids			Magnesium sulfate			Tocolytics			
	Yes	No		Yes	No		Yes	No		
Mother's age	27.7 (6.4)	27.0 (6.0)		27.0 (6.1)	27.6 (6.3)		26.6 (6.2)	27.5 (6.1)	27.3 (6.2)	27.2 (6.2)
Birthweight	419.0 (240.8)	290.5 (196.1)	**	412.8 (242.0)	330.7 (216.5)	**	459.9 (231.3)	342.2 (228.5)	381.8 (247.5)	382.4 (228.1)
Parity										
Nulliparous	(51.33%)	89 (50.28%)		139 (53.05%)	104 (48.37%)		78 (55.71%)	165 (48.96%)	92 (51.69%)	151 (50.50%)
Multiparous	146 (48.67%)	88 (49.72%)		123 (46.95%)	111 (51.63%)		62 (44.29%)	172 (51.04%)	86 (48.31%)	148 (49.50%)
Race/Ethnicity										
Caucasian	104 (34.67%)	46 (26.44%)		87 (33.46%)	63 (29.44%)		52 (37.41%)	98 (29.25%)	53 (29.78%)	97 (32.77%)
African American	171 (57%)	107 (61.49%)		151 (58.08%)	127 (59.35%)		81 (58.27%)	197 (58.81%)	108 (60.67%)	170 (57.43%)
Other	25 (8.33%)	21 (12.07%)		22 (8.46%)	24 (11.21%)		6 (4.32%)	40 (11.94%)	17 (9.55%)	29 (9.80%)
Marital Status										
Single	204 (67.77%)	121 (68.36%)		176 (67.18%)	149 (68.98%)		91 (65%)	234 (69.23%)	116 (64.8%)	209 (69.90%)
Married	97 (32.23%)	56 (31.64%)		86 (32.82%)	67 (31.02%)		49 (35%)	104 (30.77%)	63 (35.2%)	90 (30.10%)
Insurance			*							
Medicaid	178 (59.53%)	106 (60.92%)		151 (58.08%)	133 (62.44%)		75 (53.96%)	209 (62.57%)	101 (57.06%)	183 (61.82%)
Private	106 (35.45%)	49 (28.16%)		95 (36.54%)	60 (28.17%)		58 (41.73%)	97 (29.04%)	65 (36.72%)	90 (30.41%)
None	15 (5.02%)	19 (10.92%)		14(5.38%)	20 (9.39%)		6 (4.32%)	28 (8.38%)	11 (6.21%)	23 (7.77%)
Desired resuscitation?			**			**			**	**
Yes	281 (93.67%)	84 (48.55%)		244 (93.13%)	121 (57.35%)		123 (87.86%)	242 (72.67%)	166 (93.26%)	199 (67.46%)
No	19 (6.33%)	89 (51.45%)		18 (6.9%)	90 (42.65%)		17 (12.14%)	91 (27.33%)	12 (6.74%)	96 (32.54%)
22 Weeks (N = 143)										
	Antenatal Steroids			Magnesium sulfate			Tocolytics			
	Yes	No		Yes	No		Yes	No		
Mother's age	28.9 (5.3)	27.2 (6.1)		27.8 (5.4)	27.7 (6.1)		29.3 (6.4)	27.4 (5.6)	29.4 (5.7)	27.2 (5.9)
Birthweight	349.7 (214.1)	256.8 (198.9)	*	348.5 (217.7)	267.1 (200.4)		388.3 (209.6)	270.1 (203.3)	257.7 (208.3)	317.9 (209.5)
Parity										
Nulliparous	24 (52.17%)	55 (57.29%)		23 (60.53%)	56 (53.85%)		13 (50%)	66 (56.9%)	14 (42.42%)	65 (59.63%)
Multiparous	22 (47.83%)	41 (42.71%)		15 (39.47%)	48 (46.15%)		13 (50%)	50 (43.10%)	19 (57.58%)	44 (40.37%)
Race/Ethnicity										
Caucasian	19 (40.43%)	22 (23.16%)		16 (42.11%)	25 (24.04%)		13 (50%)	28 (24.14%)	13 (38.24%)	28 (25.93%)
African American	23 (48.94%)	63 (66.32%)		18 (47.37%)	68 (65.38%)		12 (46.15%)	74 (63.79%)	18 (52.94%)	68 (62.96%)
Other	5 (10.64%)	10 (10.53%)		4 (10.53%)	11 (10.58%)		1 (3.85%)	14 (12.07%)	3 (8.82%)	12 (11.11%)
Marital Status			*						*	*
Single	24 (51.06%)	69 (71.88%)		21 (55.26%)	72 (68.57%)		12 (46.15%)	81 (69.23%)	16 (47.06%)	77 (70.64%)
Married	23 (48.94%)	27 (28.13%)		17 (44.74%)	33 (31.43%)		14 (53.85%)	36 (30.77%)	18 (52.94%)	32 (29.36%)

Insurance				*		**					
<i>Medicaid</i>	22 (46.81%)	56 (60.22%)		17 (44.74%)	61 (59.8%)	6 (23.08%)	72 (63.16%)	15 (45.45%)	63 (58.88%)	71 (56.35%)	7 (50%)
<i>Private</i>	20 (42.55%)	24 (25.81%)		18 (47.37%)	26 (25.49%)	18 (69.23%)	26 (22.81%)	14 (42.42%)	30 (28.04%)	37 (29.37%)	7 (50%)
<i>None</i>	5 (10.64%)	13 (13.98%)		3 (7.89%)	15 (14.71%)	2 (7.69%)	16 (14.04%)	4 (12.12%)	14 (13.08%)	18 (14.29%)	0
Desire for resuscitation?		**			**				**		**
<i>Yes</i>	38 (82.61%)	31 (33.33%)		31 (81.58%)	38 (37.62%)	16 (61.54%)	53 (46.9%)	24 (72.73%)	45 (42.45%)	55 (44%)	14 (100%)
<i>No</i>	8 (17.39%)	62 (66.67%)		7 (18.42%)	63 (62.38%)	10 (38.46%)	60 (53.10%)	9 (27.27%)	61 (57.55%)	70 (56%)	0

23 Weeks (N = 197)

	Antenatal Steroids			Magnesium sulfate			Tocolytics			GBS PPX			Mode of delivery	
	Yes	No		Yes	No		Yes	No		Yes	No		Vaginal	Cesarean
Mother's age	26.9 (6.3)	27.8 (6.7)		26.7 (6.3)	27.7 (6.5)		25.6 (6.1)	27.9 (6.4)		27.0 (6.6)	27.2 (6.2)		27.2 (6.2)	26.9 (6.7%)
Birthweight	411.9 (244.3)	339.3 (179.8)	*	409.6 (246.4)	367.5 (203.4)		462.4 (233.9)	348.1 (220.2)	**	391.7 (242.2)	396.4 (225.5)		399.5 (220.6)	391.5 (248.8%)
Parity														
<i>Nulliparous</i>	76 (53.52%)	23 (41.82%)		65 (55.08%)	34 (43.04%)		40 (58.82%)	59 (45.74%)		47 (55.95%)	52 (46.02%)		57 (48.31%)	42 (53.85%)
<i>Multiparous</i>	66 (46.48%)	32 (58.18%)		53 (44.92%)	45 (56.96%)		28 (41.18%)	70 (54.26%)		37 (44.05%)	61 (53.98%)		61 (51.69%)	36 (46.15%)
Race/Ethnicity														
<i>Caucasian</i>	48 (33.8%)	19 (35.9%)		37 (31.62%)	30 (38.46%)		23 (34.33%)	44 (34.38%)		24 (28.57%)	43 (38.74%)		43 (36.75%)	23 (29.87%)
<i>African American</i>	84 (59.15%)	28 (52.83%)		72 (61.54%)	40 (51.28%)		41 (61.19%)	71 (55.47%)		55 (65.48%)	57 (51.35%)		62 (52.99%)	50 (64.94%)
<i>Other</i>	10 (7.04%)	6 (11.32%)		8 (6.84%)	8 (10.26%)		3 (4.48%)	13 (10.16%)		5 (5.95%)	11 (9.91%)		12 (10.26%)	4 (5.19%)
Marital Status														
<i>Single</i>	102 (71.83%)	35 (63.6%)		85 (72.03%)	52 (65.82%)		46 (67.65%)	91 (70.54%)		60 (71.43%)	77 (68.14%)		82 (69.49%)	55 (70.51%)
<i>Married</i>	40 (28.17%)	20 (36.4%)		33 (27.97%)	27 (34.18%)		22 (32.35%)	38 (29.46%)		24 (28.57%)	36 (31.86%)		36 (30.51%)	23 (29.49%)
Insurance														
<i>Medicaid</i>	92 (65.25%)	33 (60.00%)		78 (66.67%)	47 (59.49%)		45 (67.16%)	80 (62.02%)		54 (64.29%)	71 (63.39%)		71 (60.17%)	54 (70.13%)
<i>Private</i>	46 (32.62%)	17 (30.91%)		36 (30.77%)	27 (34.18%)		21 (31.34%)	42 (32.56%)		26 (30.95%)	37 (33.04%)		41 (34.75%)	21 (27.27%)
<i>None</i>	3 (2.13%)	5 (9.09%)		3 (2.56%)	5 (6.33%)		1 (1.49%)	7 (5.43%)		4 (4.76%)	4 (3.57%)		6 (5.08%)	2 (2.6%)
Desire for resuscitation?		**			**			*			**			**
<i>Yes</i>	131 (92.25%)	31 (57.41%)		110 (93.22%)	52 (66.67%)		62 (91.18%)	100 (78.13%)		82 (97.62%)	80 (71.43%)		86 (73.5%)	75 (96.15%)
<i>No</i>	11 (7.75%)	23 (42.59%)		8 (6.78%)	26 (33.33%)		6 (8.82%)	28 (21.88%)		2 (2.38%)	32 (28.57%)		31 (26.5%)	3 (3.85%)

24 Weeks (N = 138)

	Antenatal Steroids			Magnesium sulfate			Tocolytics			GBS PPX			Mode of delivery	
	Yes	No		Yes	No		Yes	No		Yes	No		Vaginal	Cesarean
Mother's age	26.3 (5.8)	29.8 (6.9)	*	27.0 (6.1)	26.8 (6.3)		26.6 (5.9)	27.2 (6.3)		26.6 (5.6)	27.3 (6.5)		26.1 (5.4)	27.5 (6.5)
Birthweight	460.4 (241.9)	285 (217.0)	*	444.0 (243.6)	422.8 (256.3)		502.3 (235.3)	409.4 (245.0)		448.2 (253.2)	433.7 (239.4)		436.9 (247.1)	442.4 (245.2)
Parity														
<i>Nulliparous</i>	54 (48.21%)	11 (42.31%)		51 (48.11%)	14 (43.75%)		25 (54.35%)	40 (43.48%)		31 (50.82%)	34 (44.16%)		29 (55.77%)	36 (41.86%)
<i>Multiparous</i>	58 (51.79%)	15 (57.69%)		55 (51.89%)	18 (56.25%)		21 (45.65%)	52 (56.52%)		30 (49.18%)	43 (55.84%)		23 (44.23%)	50 (58.14%)
Race/Ethnicity														
<i>Caucasian</i>	37 (33.33%)	5 (19.23%)		34 (32.38%)	8 (25.00%)		16 (34.78%)	26 (28.57%)		16 (26.67%)	26 (33.77%)		14 (27.45%)	28 (32.56%)
<i>African American</i>	64 (57.66%)	16 (61.54%)		61 (58.10%)	19 (59.38%)		28 (60.87%)	52 (57.14%)		35 (58.33%)	45 (58.44%)		32 (62.75%)	48 (55.81%)

<i>Other</i>	10 (9.01%)	5 (19.23%)	10 (9.52%)	5 (15.63%)	2 (4.35%)	13 (14.29%)	9 (15.00%)	6 (7.79%)	5 (9.80%)	10 (11.63%)
Marital Status										
<i>Single</i>	78 (69.64%)	17 (65.38%)	70 (66.04%)	25 (78.13%)	33 (71.74%)	62 (67.39%)	40 (65.57%)	55 (71.43%)	39 (75.00%)	56 (65.12%)
<i>Married</i>	34 (30.36%)	9 (34.62%)	36 (33.96%)	7 (21.88%)	13 (28.26%)	30 (32.61%)	21 (34.43%)	22 (28.57%)	13 (25.00%)	30 (34.88%)
Insurance				*						
<i>Medicaid</i>	64 (57.66%)	17 (65.38%)	56 (53.33%)	25 (78.13%)	24 (52.17%)	57 (62.64%)	32 (53.33%)	49 (63.64%)	30 (58.82%)	51 (59.30%)
<i>Private</i>	40 (36.04%)	8 (30.77%)	41 (39.05%)	7 (21.88%)	19 (41.30%)	29 (31.87%)	25 (41.67%)	23 (29.87%)	18 (35.23%)	30 (34.88%)
<i>None</i>	7 (6.31%)	1 (3.85%)	8 (7.62%)	0	3 (6.52%)	5 (5.49%)	3 (5.00%)	5 (6.49%)	3 (5.88%)	5 (5.81%)
Desire for resuscitation?		**								
<i>Yes</i>	112 (100%)	22 (84.62%)	103 (97.17%)	31 (96.88%)	45 (97.83%)	89 (96.74%)	60 (98.36%)	74 (96.10%)	49 (94.23%)	85 (98.84%)
<i>No</i>	0	4 (15.38%)	3 (2.83%)	1 (3.13%)	1 (2.17%)	3 (3.26%)	1 (1.64%)	3 (3.90%)	3 (5.77%)	1 (1.16%)

*Significant at <0.05 level.

**Significant at <0.01 level.

Table 2: 412 newborns with planned resuscitation: clinical characteristics, perinatal interventions and outcomes by delivery week

	22 0/7 - 22 6/7 n=40	23 0/7 - 23 6/7 n=122	24 0/7 - 24 6/7 n=250	All gestational ages n=412
Perinatal interventions n (%) or mean $\pm$ SD (range)				
Antenatal steroids (partial or complete course)	14 of 40 (35%)	84 of 122 (69%)	220 of 250 (88%)	318 of 412 (77%)
Gestational weeks at OB admission	22.4 $\pm$ 0.3 (22.0-22.8)	23.2 $\pm$ 0.3 (22.1-23.9)	23.9 $\pm$ 0.6 (22.0-24.9)	23.6 $\pm$ 0.7 (22.0-24.9)
Age at receipt, weeks	22.3 $\pm$ 0.5 (21.0-22.9)	23.3 $\pm$ 0.4 (21.7-23.9)	24.0 $\pm$ 0.5 (22.6-24.9)	23.8 $\pm$ 0.6 (21.0-24.9)
Hours between last steroid dose and delivery (of Baby A)	40.9 $\pm$ 48 (1.4-164)	33.7 $\pm$ 44(0.33-249)	73.1 $\pm$ 71 (0-280)	61.3 $\pm$ 66 (0-280)
Magnesium for neuroprotection	11 of 40 (28%)	70 of 122 (57%)	197 of 250 (79%)	278 of 412 (68%)
Tocolytics	6 of 40 (15%)	39 of 122 (32%)	98 of 246 (40%)	143 of 408 (35%)
Cesarean delivery	2 of 40 (5%)	38 of 120 (32%)	160 of 250 (64%)	200 of 410 (49%)
Neonatal characteristics				
Gestational weeks at OB admission	22.4 $\pm$ 0.3 (22.0-22.8)	23.2 $\pm$ 0.3 (22.1-23.9)	23.9 $\pm$ 0.6 (22.0-24.9)	23.6 $\pm$ 0.7 (22.0-24.9)
Gestational weeks at delivery	22.5 $\pm$ 0.3 (22.0-22.9)	23.5 $\pm$ 0.3 (23.0-23.9)	24.4 $\pm$ 0.3 (24.0-24.9)	24.0 $\pm$ 0.7 (22.0-24.9)
Birthweight, g mean $\pm$ SD (range)* 25%ile, 75%ile	497 $\pm$ 64 (295-502) 457, 547	574 $\pm$ 95 (310-880) 505,640	660 $\pm$ 115 (280-1060) 590, 730	619 $\pm$ 119 (280-1060) 540, 691
Singleton delivery	26 of 40 (65%)	89 of 122 (73%)	193 of 250 (77%)	308 of 412 (75%)
Male sex	24 of 40 (60%)	65 of 122 (53%)	130 of 250 (52%)	219 of 412 (53%)
Neonatal outcomes				
Liveborn	36 of 39 (92%)**	116 of 122 (95%)	247 of 250 (99%)	399 of 411 (97%)
Survival to NICU discharge	3 of 39 (8%)	42 of 121 (35%)	142 of 239 (59%)	187 of 399 (47%)
Survival to NICU discharge or transfer to other facility	4 of 40 (10%)	43 of 122 (35%)	153 of 250 (61%)	200 of 412 (49%)
Liveborn baby surviving to discharge home from NICU	3 of 35 (9%)	42 of 115 (37%)	142 of 247 (58%)	187 of 399 (47%)
Liveborn baby discharged home or transferred from NICU	4 of 36 (11%)	43 of 116 (37%)	153 of 247 (62%)	200 of 399 (50%)

*Reflects use estimated fetal weight within one week of birth when birthweight unknown, n=7; missing weights (birth or delivery-week estimated fetal weight data), n=17

**Unknown condition at birth, but did not survive to NICU admission

Newborns
born at
22 weeks
(n=40)

Newborns
born at
23 weeks
(n=122)

□ Survived to home
discharge from NICU

■ Died or transferred to
outside facility

* p<0.05

Newborns
born at
24 weeks
(n=150)

Journal Pre-proof

Distribution of birthweights of 412 newborns with planned resuscitation

T Caps 10th and 90th percentiles study newborns
 Boxes 75th and 25th percentiles
 --- Mean
 Median
 + 5th and 95th percentiles
 *F Fenton curve percentiles (mean of female/male)