

NICHD

NEONATAL RESEARCH NETWORK



Survival, major morbidities, and neurodevelopmental impairment in extremely preterm, small for gestational age infants

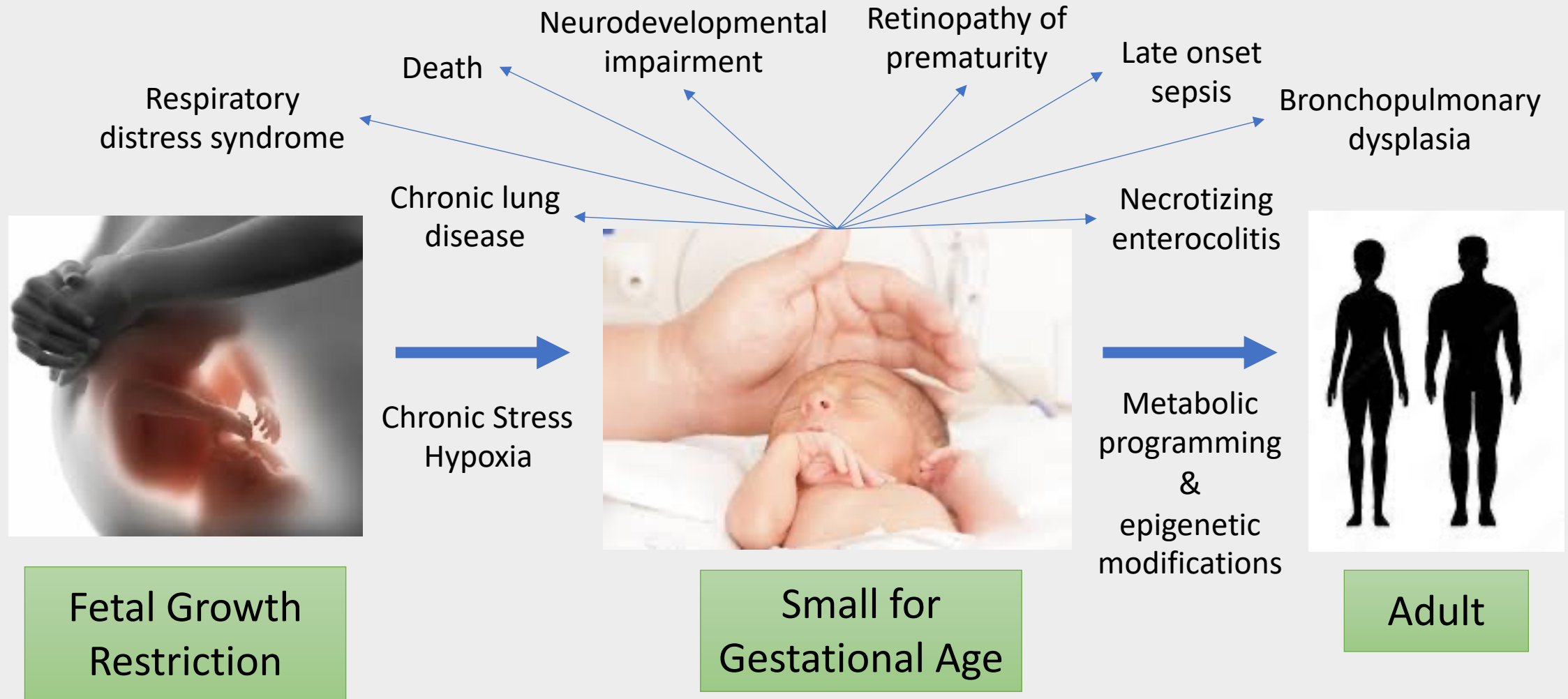
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Disclosures

- Speaker: Kathleen Minor, MD
- Dr. Kathleen Minor has no financial relationships to disclose or Conflicts of Interest to resolve. Any real or apparent conflicts of interest related to the content of this presentation have been resolved.
- This presentation will not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

Background



Prior Data: Preterm SGA Outcomes

- Prior NRN publication compared SGA to AGA infants <27 weeks gestation between 2006-2008.

Neonatal Outcomes	aOR	95% Confidence Interval
Death or NDI	3.91	2.91-5.25
Death or NDI (early deaths excluded)	3.63	2.68-4.92
Bayley III cognitive score <70	2.08	1.12-3.85
Bayley III cognitive score <80	2.38	1.49-3.81
Moderate or severe cerebral palsy	2.55	1.69-3.86
Blindness (<20/200 vision bilaterally)	10.9	2.15-55.5

- Updated and expanded analysis warranted due to changing practice patterns and outcomes

Objective and Hypothesis

Objective: Determine **survival to hospital discharge** in extremely preterm **SGA** (birthweight <10th percentile) versus **AGA** infants cared for in the NICHD NRN from 2012-2020.

Hypothesis: Among infants born 23^{0/7} to 26^{6/7} weeks' gestation, SGA infants will have a lower rate of survival to discharge compared to non-SGA infants.

Study Design

Secondary analysis of a prospective cohort from NICHD NRN centers

Eligibility

- Born 23^{0/7} to 26^{6/7} weeks' gestation
- Between July 1, 2012 and
 - December 31, 2020 (in-hospital outcomes)
 - December 31, 2018 (outcomes assessed at 2 years of age)
- Liveborn
- No major congenital anomalies or genetic disorders/syndromes



Exposure

- **SGA:** birthweight <10th percentile based on **Olsen Growth Curves**



Control

- **AGA:** birthweight \geq 10th percentile based on **Olsen Growth Curves**

Outcomes

Primary Outcome

Survival to discharge

Secondary Outcomes
(Composite outcomes and their components)

Survival to discharge
without **major morbidity**

Survival to two years
without **neurodevelopmental impairment**

Outcomes

Primary Outcome

Survival to discharge

Secondary Outcomes
(Composite outcomes and their components)

Survival to discharge
without **major morbidity**

Survival to two years
without **NDI**

Defining terms

Major Morbidity

- BPD, grade 2-3
- IVH, grade 3-4
- NEC, proven
- cPVL
- LOS, culture proven
- ROP, \geq stage 3

Neurodevelopmental Impairment

Mild or None

- All** of the following:
- Bayley-III cognitive composite score **and** motor composite score of ≥ 85
 - GMFCS, level 0 or 1

Moderate

- Any** of the following:
- Bayley-III cognitive composite score **or** motor composite score: 70-84
 - GMFCS, level 2 or 3

Severe

- Any** of the following:
- Bayley-III cognitive composite score **or** motor composite score <70
 - GMFCS, level 4 or 5
 - Bilateral blindness
 - Bilateral severe functional hearing impairment

Analysis

Outcomes were stratified descriptively by completed weeks gestation and year of birth

Generalized linear mixed models were fit to assess the association of SGA with the outcomes of interest

- Model adjusted for:
 - Center (random effect)
 - Sex
 - Antenatal steroids
 - Magnesium sulfate
 - Maternal hypertension
 - Multiple gestation
 - Gestational age

Cohort

Liveborn Infants between July 1, 2012 and December 31, 2020 at 23^{0/7} to 26^{6/7} weeks gestation
n = 8869

Exclusions:
n = 489 congenital anomaly
n = 14 missing birthweight

In hospital outcomes

SGA
n = 1331

AGA
n = 7035

2 year follow up data

Two-year follow-up data available
(born prior to January 1, 2019)
n = 988

Two-year follow-up data available
(born prior to January 1, 2019)
n = 5352

Results: Maternal and Neonatal Demographics

Notable differences in baseline demographics among SGA compared to AGA infants included:



Maternal characteristics:

- ↑ Hypertension
- ↑ Cesarean delivery
- ↓ Antepartum bleeding
- ↓ Chorioamnionitis
- ↓ Antenatal antibiotics
- ↓ Rupture of membranes >18 hours



Neonatal characteristics:

- ↑ 5-min Apgar <5
- ↑ Nitric oxide use
- ↑ Treatment for hypotension <24 hours of life
- ↑ Decision to limit intensive care after birth or after 120 days

Results: In-Hospital Outcomes

Outcome	SGA	AGA
	(N = 1331)	(N = 7035)
Primary Outcome		
Survival to discharge	56%	78%
Secondary In-Hospital Outcomes		
Survival to discharge without major morbidity	12%	28%
Major morbidity prior to discharge among survivors	79%	64%
BPD, Grade 2-3	61%	37%
IVH, Grade 3-4	12%	17%
Proven nec	12%	10%
Surgery resulting in short gut	2%	1%
cPVL	5%	6%
LOS, culture positive	29%	24%
ROP, Stage \geq 3	32%	19%

Results: Outcomes at 2 Years

Secondary Follow-up Outcomes	SGA	AGA
	(N = 988)	(N = 5352)
Survival to two-year follow-up	54%	77%
Survival to two-year follow-up without severe NDI	34%	57%
Severe NDI among survivors	31%	22%
Survival to two-year follow-up without moderate-severe NDI	17%	36%
Moderate-severe NDI among survivors	66%	51%
NDI categories among survivors		
Normal/mild	34%	49%
Moderate	35%	29%
Severe/profound	31%	22%
Rehospitalization since discharge	59%	49%

Results: Multivariable Analysis

Outcome	aOR ^c	95% CI
Survival to discharge	0.29	0.25-0.33
Survival to discharge without major morbidity	0.29	0.24-0.36
Major morbidity prior to discharge among survivors ^a	2.51	2.04-3.10
Survival to two-year follow-up	0.28	0.23-0.33
Survival to two-year follow-up without severe neurodevelopmental impairment	0.33	0.27-0.39
Severe neurodevelopmental impairment among survivors ^b	1.76	1.37-2.26
Survival to two-year follow-up without moderate-severe neurodevelopmental impairment	0.32	0.26-0.40
Moderate-severe neurodevelopmental impairment among survivors ^b	2.05	1.61-2.60

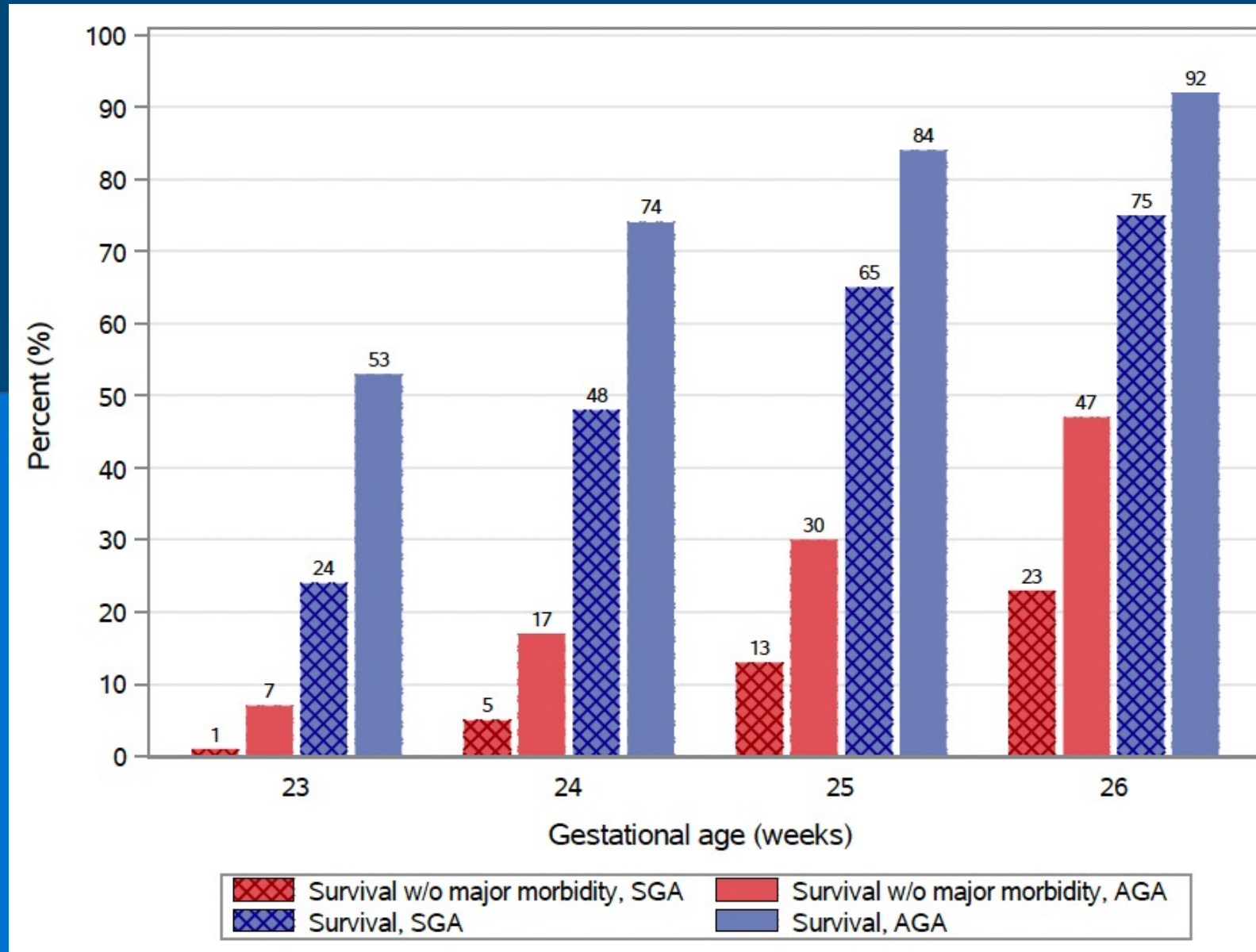
All associations with P<0.0001

^a Restricted to reflect survivors to discharge.

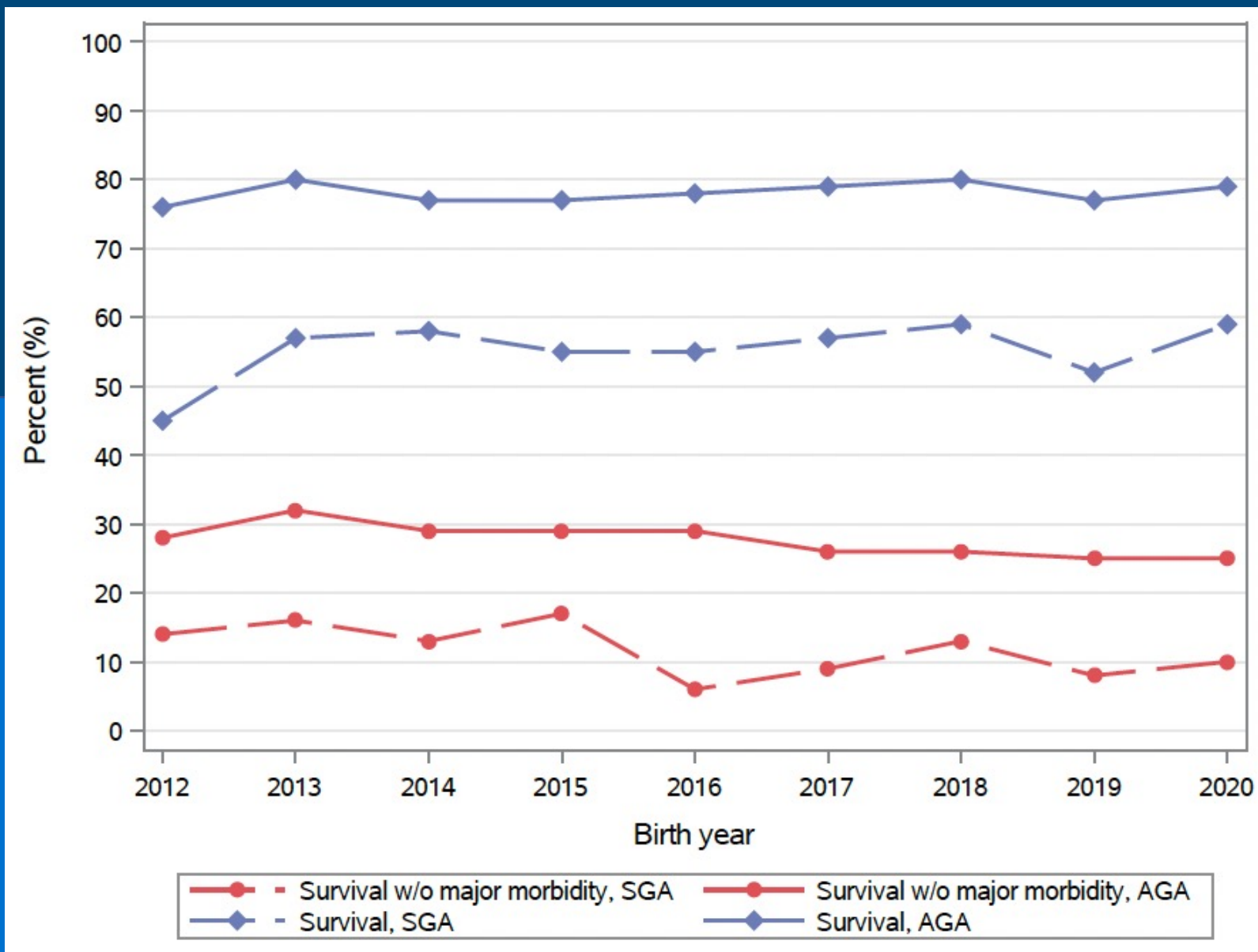
^b Two-year follow-up assessment restricted to window of 14-30 months corrected age.

^c Model adjusted for center (random effect), sex, antenatal steroids, magnesium sulfate, maternal hypertension, multiple gestation, and gestational age.

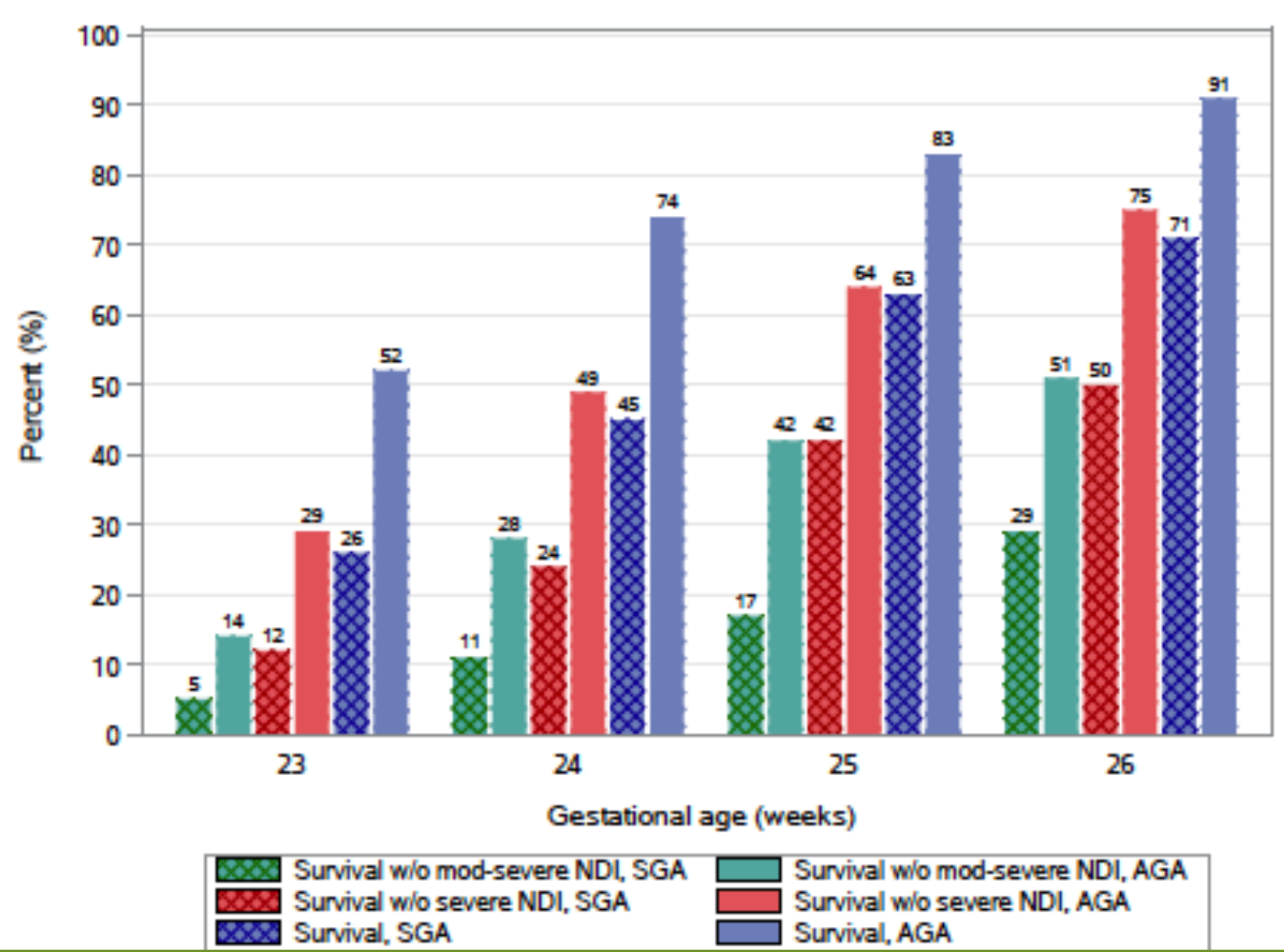
In-hospital outcomes of SGA and AGA infants for gestational ages 23 to 26 completed weeks



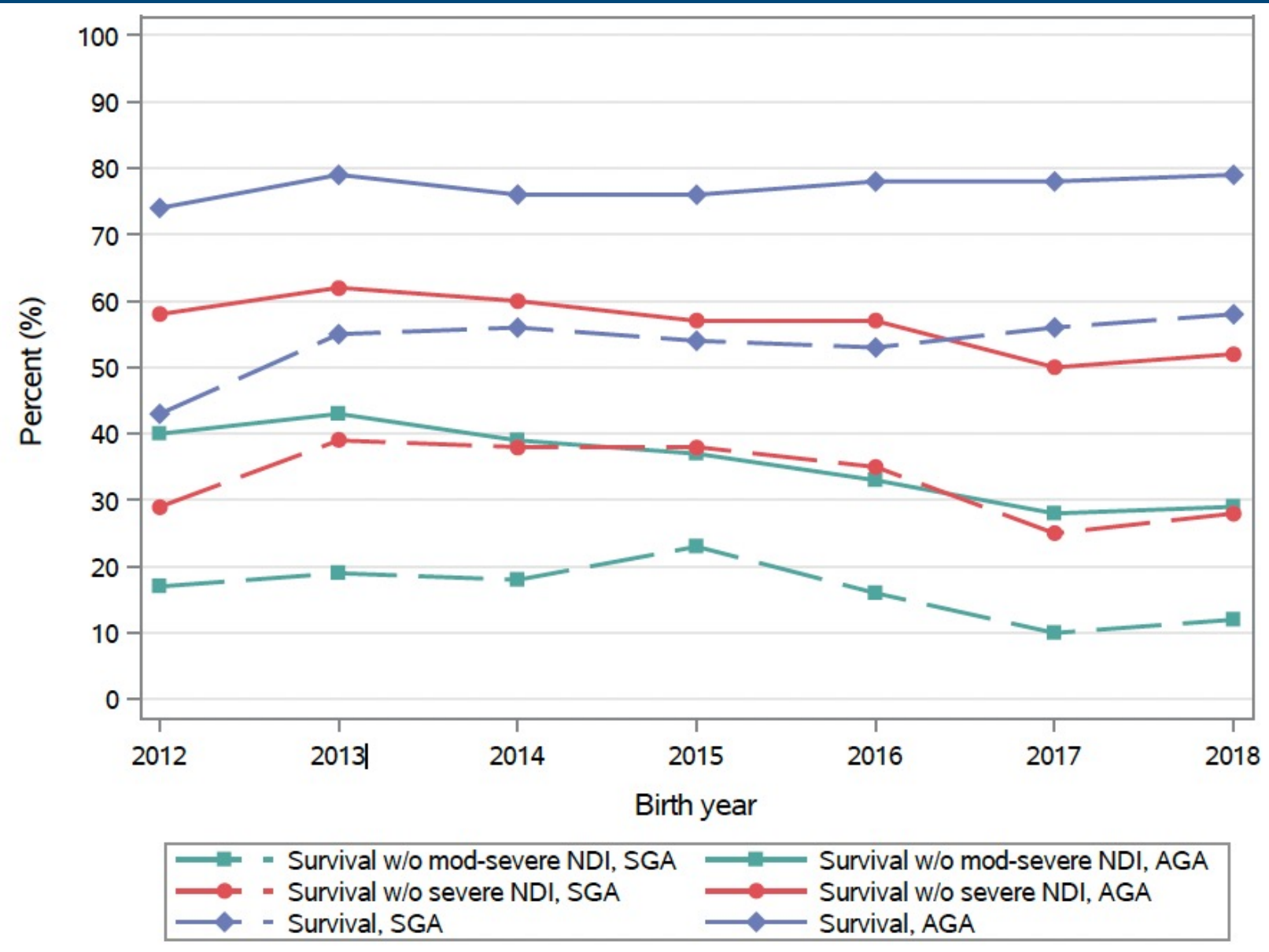
In-hospital outcomes of SGA and AGA infants from birth years 2012 to 2020



Two-year follow-up outcomes of SGA and AGA infants for gestational ages 23 to 26 completed weeks



Two-year follow-up outcomes of SGA and AGA infants from birth years 2012 to 2018



Conclusions

Extremely preterm SGA infants, compared to similar AGA infants, experience:

- ↓ Adjusted odds of survival to discharge
- ↓ Adjusted odds of survival free of major morbidity
- ↓ Adjusted odds of survival to two-year follow up
- ↓ Adjusted odds of survival to two-year follow-up without severe or moderate to severe NDI

These associations are maintained across gestational ages and birth years.

Future Directions

Evaluate 22 weeks' gestation, as resuscitation and interventions are being offered at this gestation with shared decision making.

Elucidate additional risk stratification of outcomes:

- Severity of growth restriction
- Symmetric versus asymmetric growth restriction

Characterize disparities in interventions and outcomes.

Neonatal Research Network Centers (2016-2023)

- Brown University
- Case Western Reserve University
- Cincinnati Children's Medical Center
- Duke University
- Emory University
- Nationwide Children's Hospital, Ohio State University
- RTI International
- Stanford University
- University of Alabama at Birmingham
- University of Iowa
- University of New Mexico
- University of Pennsylvania
- University of Rochester
- University of Texas Southwestern
- University of Texas Health Science Center at Houston
- University of Utah

Neonatal Research Network Centers (2011-2016)

- Brown University
- Case Western Reserve University
- Children's Mercy Hospitals and Clinics, University of Missouri-Kansas City
- Cincinnati Children's Medical Center
- Duke University
- Emory University
- Indiana University
- Nationwide Children's Hospital, Ohio State University
- RTI International
- Stanford University
- University of Alabama at Birmingham
- University of California – Los Angeles
- University of Iowa
- University of New Mexico
- University of Pennsylvania
- University of Rochester
- University of Texas Southwestern
- University of Texas Health Science Center at Houston
- Wayne State University

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Thank You, Questions?



NRN Presentations



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Background

ANALYSIS

Strengths/Limitations

RESULTS

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Background

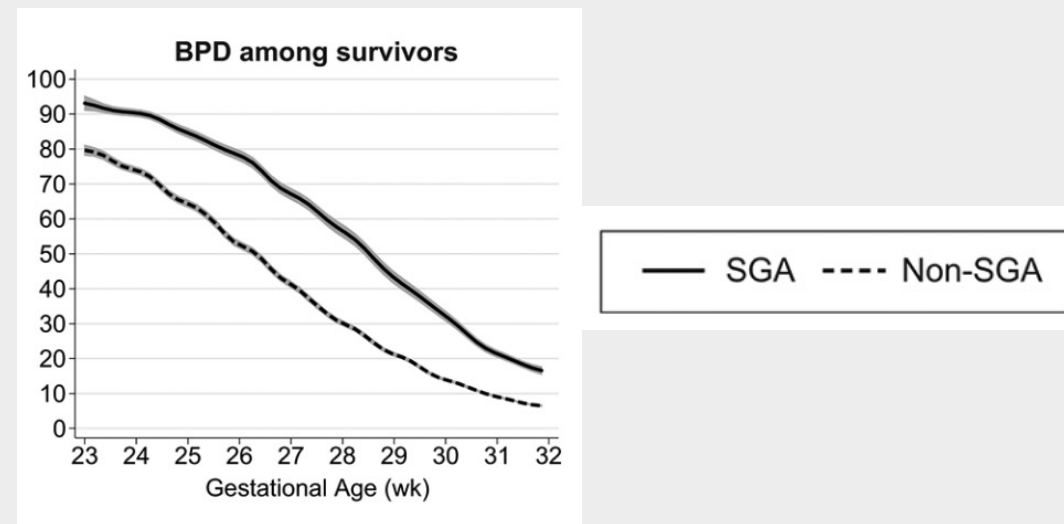
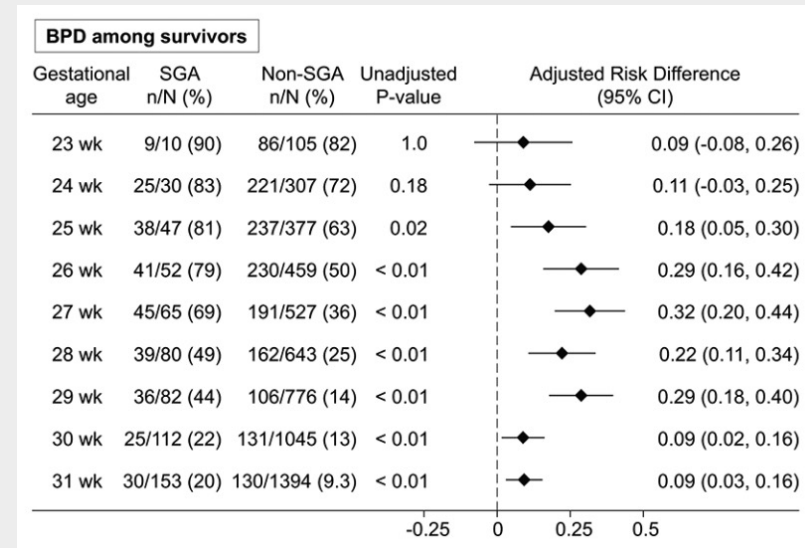


Preterm SGA: Outcomes

- Canadian Network 2003-2008: sub-analysis of neonates ≤ 26 weeks' gestation, SGA compared to non-SGA neonates (Qiu, 2012):
 - Increased risk of death in the NICU (32.7% vs 24.5%, $p < 0.05$)
 - Decreased survival free of major morbidity (12.2% vs 19%, $p < 0.05$)
- Retrospective NICHD NRN cohort, neonates born < 27 weeks' gestation, 2006-2008, SGA compared to non-SGA neonates (De Jesus 2013):
 - Increased risk of death or neurodevelopmental impairment (aOR 3.91; 95% CI 2.91-5.25, $P < .001$)
- Population-based cohort in Canada from 2002-2015 in neonates born from 23-31 weeks. Severe SGA ($< 5^{\text{th}}$ percentile) compared to non-SGA (Ray et al 2017)
 - Increased rate of death < 28 days after birth
- VON, 2006-2014, 22-29 wks' gestation, SGA infants:
 - Increased mortality, respiratory distress, necrotizing enterocolitis, late onset sepsis, severe retinopathy or prematurity and chronic lung disease (degree dependent on GA and steroids)
- Retrospective study, 2010-2016 of neonates < 32 wks, Optum Neonatal Database, < 32 wks (Jensen 2019)
 - SGA neonates were at increased risk for bronchopulmonary dysplasia, retinopathy of prematurity,
 - Risk adjusted probability of mortality, BPD and death or major morbidity among SGA infants was similar to non-SGA infants that were 2-3 weeks less mature
- Academic center, Germany from 2005-2017 compared SGA to non-SGA for all neonates born with $BW \leq 750g$
 - Retinopathy of prematurity (OR 2.87, 95% CI 1.14-7.23) and need for home monitoring (OR 2.38, 95% CI 1.05-5.41)

Preterm SGA: Outcomes

- Adjusted risk difference between SGA and non-SGA infants peaked at 27 weeks gestation for BPD among survivors (greatest from 26 to 28⁶ weeks)
- Risk adjusted probability of BPD among SGA infants is similar to that of non-SGA infants born 2-3 weeks less mature
- Sheep data: Growth restriction hinders surfactant production and postnatal growth of terminal, gas exchanging airways



NRN Generic Database

- Established in 1986 by the NICHD, part of the NIH, as a means to conduct multi-center clinical trials and observational studies in neonatal medicine
- Collaboration of NICUs from academic medical centers across the US
- Level III/IV NICUs that admit inborn and outborn infants

Why utilize this database:

- Granularity of both short-and longer-term outcome data available with patient centered outcomes beyond survival
- The incidence of extreme prematurity and SGA is low, this necessitates a large population with adequate statistical power to detect clinically important differences
- Diverse population

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ANALYSIS



Definitions

Bronchopulmonary Dysplasia (BPD)	<p>Define BPD severity based on mode of respiratory support at 36 weeks' postmenstrual age, regardless of supplemental O2 use.</p> <ul style="list-style-type: none">- No support: No BPD- Grade 1: $NC \leq 2L/min$- Grade 2: $NC > 2L/min$ or Non-invasive positive airway pressure- Grade 3: Invasive mechanical ventilation <p>Jensen et al (2019)</p>
Intraventricular Hemorrhage (IVH)	<p>Based on cranial sonogram with most severe findings performed within 28 days after birth.</p> <ul style="list-style-type: none">- Grade I: subependymal hemorrhage- Grade II: IVH without ventricular dilation- Grade III: IVH with ventricular dilation- Grade IV: IVH with parenchymal hemorrhage <p>Papile et al (1978)</p>
Necrotizing Enterocolitis (Nec)	<p>Proven with or without surgery or by autopsy</p>
Cystic Periventricular Leukomalacia (cPVL)	<p>Based on cranial ultrasound findings at 28 days or 36 weeks postmenstrual age</p>
Late Onset Sepsis, culture proven (LOS)	<p>Sepsis occurring ≥ 72 hours of life with positive blood culture and appropriate therapy for 5 or more days or intent to treat if death occurred within 5 days.</p> <p>Meningitis occurring ≥ 72 hours of life with positive CSF culture and appropriate therapy for 7 or more days or intent to treat if death occurred within 7 days</p>
Retinopathy of Prematurity (ROP)	<p>Stage 1: Demarcation line</p> <p>Stage 2: Ridge</p> <p>Stage 3: Extraretinal fibrovascular proliferation</p> <p>Stage 4: Retinal detachment</p>

Covariates

- Covariates known to affect outcomes were selected a priori and included: center (random effect), sex, antenatal steroids, magnesium sulfate, maternal hypertension, multiple gestation, gestational age

De Jesus, <i>J Pediatr</i> , 2013	Jensen et al, <i>Arch Dis Child Fetal Neonatal Ed</i> , 2019	Bell et al, <i>JAMA</i> , 2022
Center (random effects) Sex Multiple gestations Gestational age Antenatal corticosteroid use Hypertension Education	Sex Multiple gestation Pre-eclampsia/eclampsia Antenatal steroids Diabetes Gestational hypertension Cesarean birth ROM ≥ 18 hours Initiation of prenatal care in the 1st tri Race Insurance status	Center (fixed effect) Sex Multiple gestation Gestational age SGA Maternal race/ethnicity Education

	Alexander	Aris	Olsen	Fenton	Intergrowth-21st
Population	Single live births from the NCHS US Live Birth File Birth years: 1991	Singleton live births from the National Vital Statistics System of NCHS Birth years: 2017	Infants in the Pediatrix Medical Group from 248 hospitals in 33 states Birth years: 1998-2006	Systematic review and meta-analysis using data from 6 large population-based surveys from the US, Canada, Australia, Germany, Italy, Scotland. Birth years: 1991-2007	International multicenter, multiethnic, population-based project in 8 urban study sites in Brazil, Italy, Oman, India, Kenya, China, Oxford UK, Seattle WA. Birth year: 2009-2014
N used to develop chart	3,134,879 single live births No information on how many births were 22-28 weeks GA.	3,285,552 singleton infants 61,106 were born at 22-33 weeks. No information on how many of those were born at 22-28 weeks.	257,855 singleton infants without congenital anomalies or other factors thought to impact growth who survived to discharge. (Curves created using n=130,111; validated in n=127,744) 8618 infants born 23-28 weeks GA. 22 weeks: n=0; 23 weeks: n=286; 24 weeks: n=889	3,986,456 infants for birth weight; 173,612 infants for head circumference; 151,527 for length. Merged with WHO longitudinal measurements from 882 infants. 22 weeks: n=816; 23 weeks n=1682; 24 weeks n=3012. 22-week data are from German, Australian and Canadian sources	Newborn Cross-Sectional Study to develop sex and GA standards at birth (33+ w): 20,486 singleton live born infants with no major complications, no evidence of fetal growth restriction (FGR) on ultrasound, born to mothers without FGR risk factors who had a reliable estimate of GA. Very Preterm size at birth reference: 408 neonates (214 boys, 194 girls).
GA	20-44 weeks	22-42 weeks	23-41 weeks	22-40 weeks (interpolation used to join the WHO Growth Standard at 50 weeks)	Newborn: 33-42 weeks Very Preterm: 24-32 weeks
GA measurement	Completed weeks based on the LMP date	Completed weeks by obstetric estimate of gestation at delivery	Completed weeks by neonatologist best estimate using obstetric history, obstetric exams, prenatal ultrasound, and postnatal physical exam	German study reported weeks and days; all others completed weeks. Charts produced from meta-analysis show measurements by actual age (completed weeks and days).	GA weeks and days estimated by ultrasound ≤24 weeks. If estimated based on ultrasound >24 weeks, only considered reliable if difference between U/S estimate and LMP estimate was ≤7 days.

Pros of Olsen Growth Curves

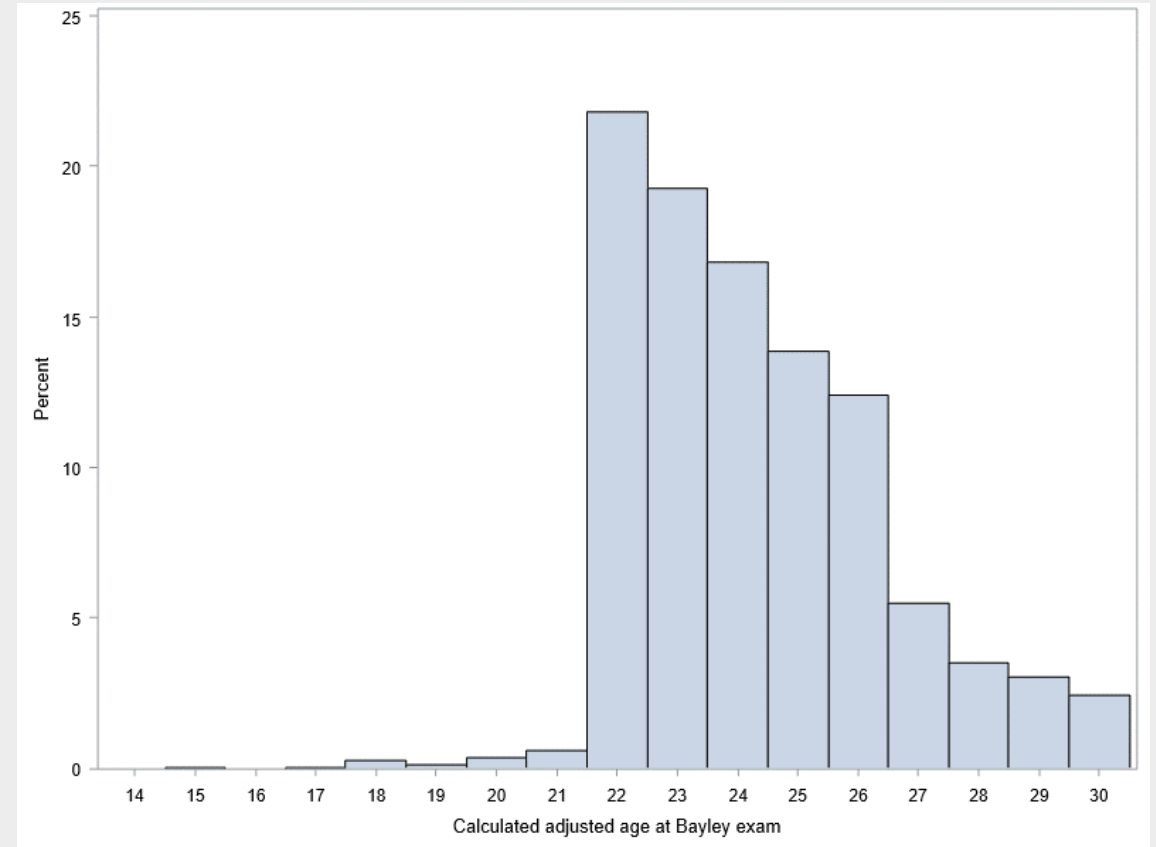
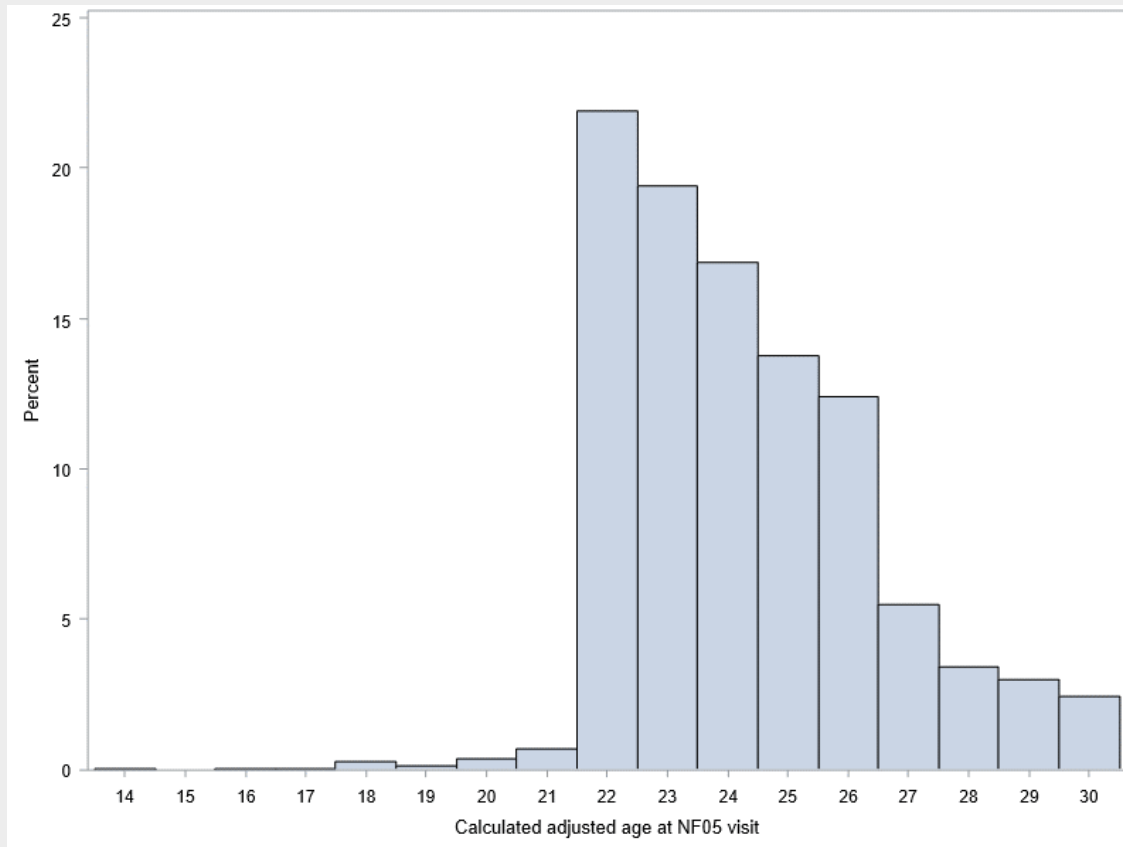
- **Contemporary**
- Large sample with race distribution similar to US births from a large number of hospitals across the US
- Multiple percentiles by sex for BW, length, HC (**can determine symmetric vs. asymmetric**)
- Z scores (and exact percentiles) can be calculated easily with LMS parameters provided

Cons of Olsen Growth Curves

- No percentiles for GA 20-22 wks
- Percentiles for GA 23-28 wks based on only 8618 infants
- NICU admissions only—sample may not represent all infants, especially at older GA

Follow Up Ages

- We included NDI follow-up data if it was assessed between **14 and 30 months corrected age**
- **98%** of participants had equal follow up assessments (NF05 and Bayley)
 - Of these 1% fell below 22 months and 14% were >26 months
- **84%** had both follow-up assessments within the 22-26 month window



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RESULTS



Results: Maternal Demographics

Characteristic	SGA (N = 1331)	AGA (N = 7035)
Hypertension		
None	538/1330 (40%)	5696/7024 (81%)
Pregnancy-induced	411/1330 (31%)	510/7024 (7%)
Chronic	354/1330 (27%)	752/7024 (11%)
Unknown etiology	27/1330 (2%)	66/7024 (1%)
Antepartum bleeding	185/1330 (14%)	1750/7030 (25%)
Chorioamnionitis		
None	979/1328 (74%)	2798/7012 (40%)
Clinical	21/1328 (2%)	206/7012 (3%)
Histological	328/1328 (25%)	4008/7012 (57%)
Antenatal antibiotics within 72 hours	917/1326 (69%)	5495/6983 (79%)
Rupture of membranes > 18 hours	204/1305 (16%)	2048/6819 (30%)
Antenatal steroids	1221/1328 (92%)	6249/7022 (89%)
Complete course	965/1219 (79%)	4504/6230 (72%)
Magnesium sulfate	1111/1327 (84%)	5621/6985 (80%)
Multiple birth	284/1331 (21%)	1842/7035 (26%)
Mode of delivery		
Vaginal vertex	200/1331 (15%)	2294/7035 (33%)
Vaginal breech	72/1331 (5%)	383/7035 (5%)
Cesarean section	1058/1331 (79%)	4348/7035 (62%)
Unknown	1/1331 (0%)	10/7035 (0%)
Diagnosis that influenced decision to limit care	9/1331 (1%)	15/7035 (0%)

Abbreviations: AGA = appropriate for gestational age; n = number in category; N = sample size; SGA = small for gestational age

Results: Neonatal Demographics

Characteristic	SGA	AGA
	(N = 1331)	(N = 7035)
Outborn	12/1331 (1%)	225/7035 (3%)
Male sex	679/1331 (51%)	3615/7035 (51%)
5-minute Apgar score < 5	505/1320 (38%)	1875/6981 (27%)
Gestational age		
23	270/1331 (20%)	1278/7035 (18%)
24	314/1331 (24%)	1706/7035 (24%)
25	360/1331 (27%)	1915/7035 (27%)
26	387/1331 (29%)	2136/7035 (30%)
Received surfactant	1157/1331 (87%)	6122/7035 (87%)
Steroids for BPD/CLD	391/1106 (35%)	1763/6354 (28%)
Nitric oxide	254/1161 (22%)	802/6670 (12%)
Treatment for hypotension < 24 hours of life	451/1161 (39%)	1922/6672 (29%)
Seizures	41/1160 (4%)	190/6669 (3%)
Treatment withdrawn with intent to limit care		
Intubation/ventilation	251/1161 (22%)	802/6672 (12%)
Nutrition/hydration	119/1161 (10%)	398/6671 (6%)
Medication	148/1161 (13%)	437/6671 (7%)
Treatment withdrawn with intent to limit care after 120 days		
Intubation/ventilation	24/526 (5%)	48/2162 (2%)
Nutrition/hydration	6/526 (1%)	17/2162 (1%)
Medication	10/526 (2%)	26/2162 (1%)
Proven infection	46/687 (6.7%)	291/3862 (7.5%)

Characteristics of infants in whom decision make to limit intensive care after birth or after 120 days

	AGA (n=872) n (%)	SGA (n=281) n (%)	Total (n=1139) n (%)
Died	860	279	1139
Survived	12 (1.4)	2 (0.7)	14 (1.2)
Gestational age (weeks)			
- 23	309 (35)	71 (26)	380 (33)
- 24	371 (31)	89 (32)	360 (31)
- 25	188 (21)	68 (24)	256 (22)
- 26	104 (12)	53 (20)	157 (14)
Mean birth weight (grams, [SD])	697 (135)	479 (79)	

Results: Secondary outcomes for survivors to two years corrected age according to small for gestational age versus appropriate for gestational age designation from birth years 2012 to 2018

Outcome	SGA (N = 445)	AGA (N = 3317)
Bayley-III Cognitive Composite Score		
n, mean (sd)	438, 79.6 (15.9)	3276, 85.2 (15.5)
n, median (IQR)	438, 80 (20)	3276, 85 (20)
<70	106/438 (24%)	472/3276 (14%)
70-84	128/438 (29%)	826/3276 (25%)
≥85	204/438 (47%)	1978/3276 (60%)
Bayley-III Language Composite Score		
n, mean (sd)	426, 75.5 (17.2)	3204, 81.3 (17.8)
n, median (IQR)	426, 77 (27)	3204, 83 (26)
<70	146/426 (34%)	829/3204 (26%)
70-84	130/426 (31%)	885/3204 (28%)
≥85	150/426 (35%)	1490/3204 (47%)
Bayley-III Motor Composite Score		
n, mean (sd)	432, 78.8 (17.9)	3198, 84.7 (16.3)
n, median (IQR)	432, 82 (23.5)	3198, 88 (18)
<70	109/432 (25%)	511/3198 (16%)
70-84	131/432 (30%)	769/3198 (24%)
≥85	192/432 (44%)	1918/3198 (60%)
Cerebral palsy		
None	340/445 (76%)	2694/3314 (81%)
Mild	51/445 (11%)	360/3314 (11%)
Moderate	25/445 (6%)	168/3314 (5%)
Severe	29/445 (7%)	92/3314 (3%)
Gross Motor Function		
Normal	259/443 (58%)	2319/3308 (70%)
Possible or definite Level 1	108/443 (24%)	674/3308 (20%)
Level 2 or 3	47/443 (11%)	226/3308 (7%)
Level 4 or 5	29/443 (7%)	89/3308 (3%)
Vision		
Normal in both eyes	346/445 (78%)	2864/3314 (86%)
Corrective lenses/abnormality, no blindness	88/445 (20%)	409/3314 (12%)
Blind in one eye		7/3314 (0%)
Blind in both eyes	11/445 (2%)	34/3314 (1%)
Functional hearing impairment	16/443 (4%)	85/3262 (3%)
Hearing aid or cochlear implant	13/442 (3%)	79/3248 (2%)
Oral Motor Skills		
Independently feeds self	303/445 (68%)	2768/3312 (84%)
Dependent oral feeding	38/445 (9%)	251/3312 (8%)
Limited oral feeding	74/445 (17%)	224/3312 (7%)
No oral feeding	30/445 (7%)	69/3312 (2%)

Results: In-Hospital Outcomes

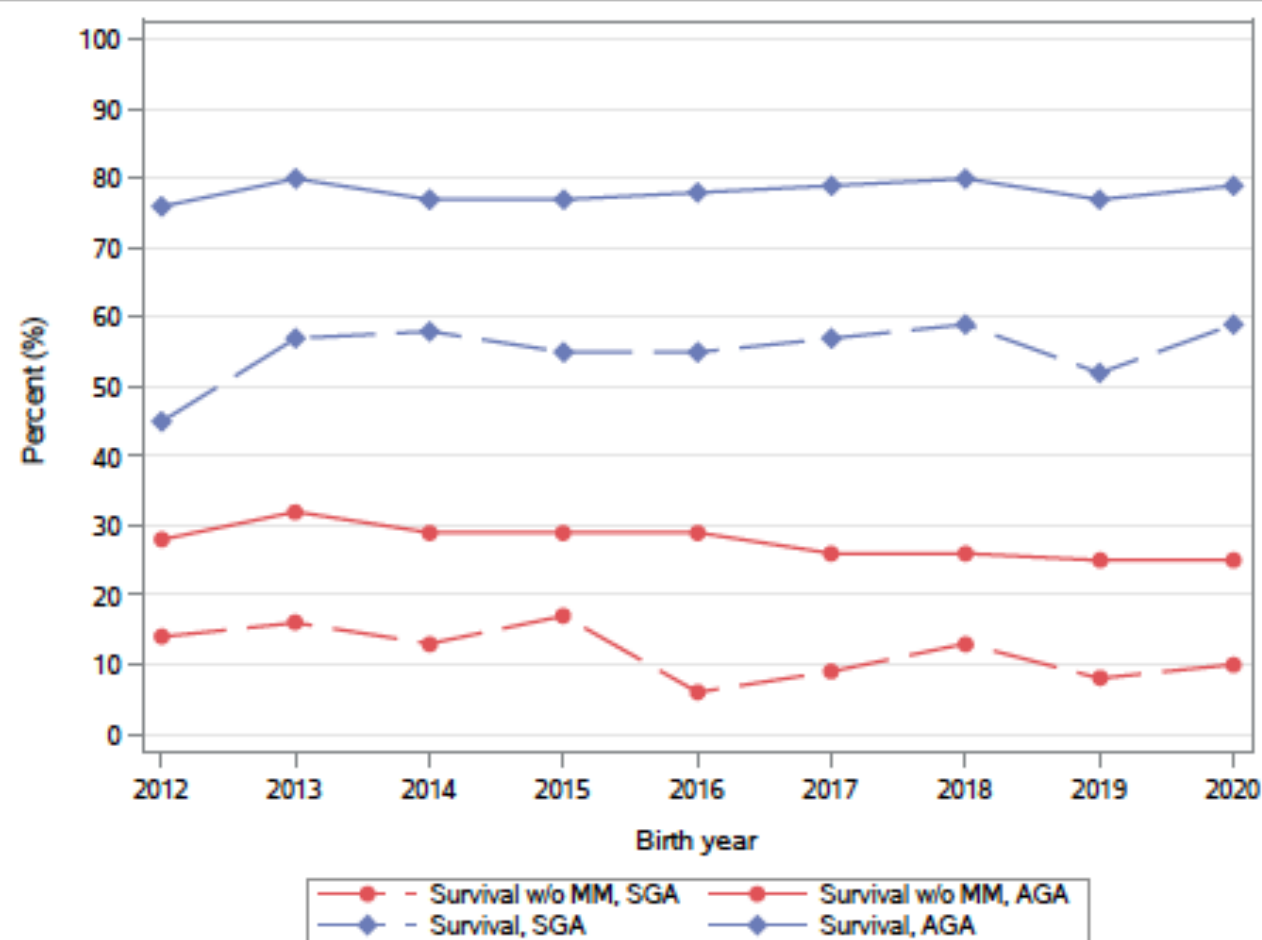
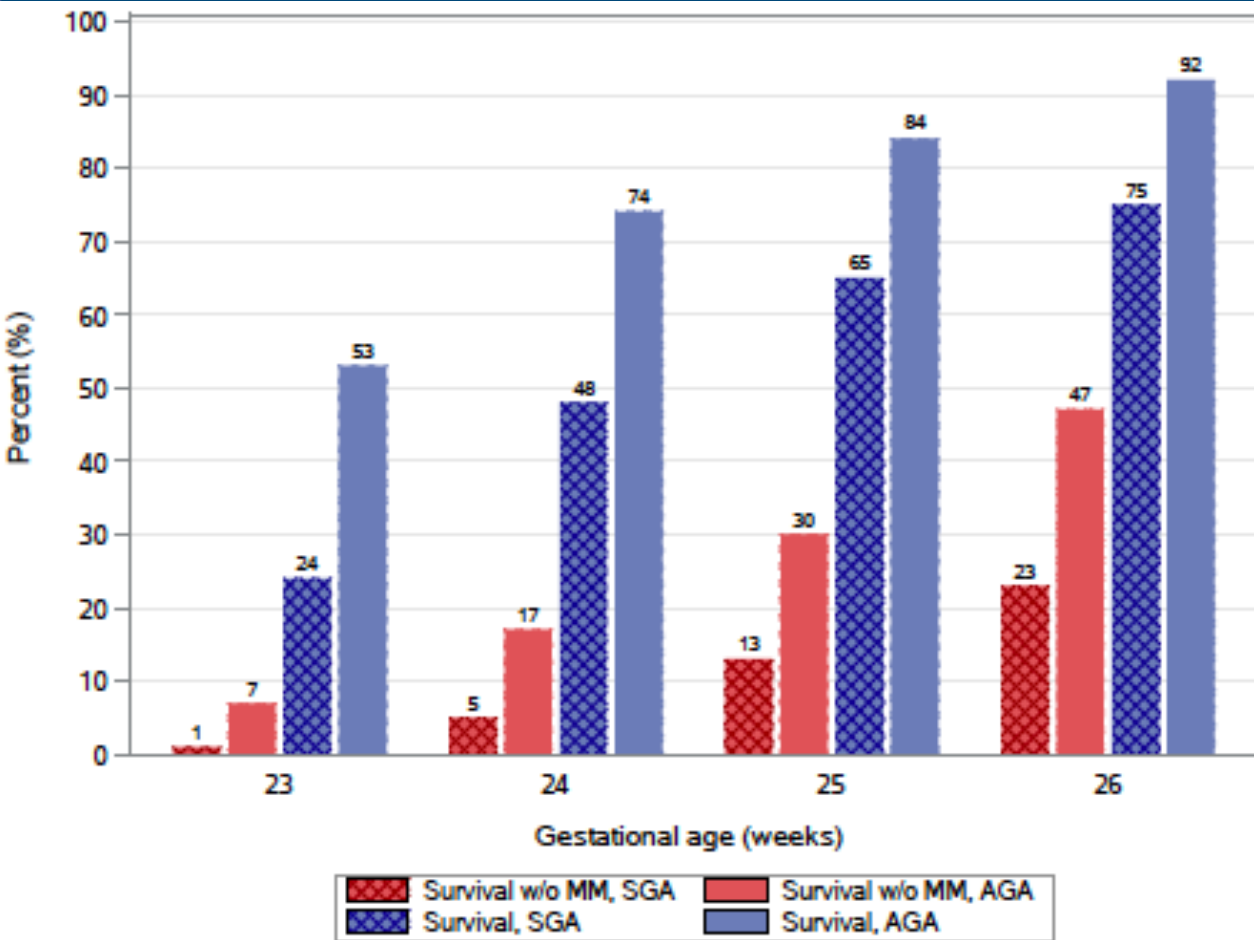
Outcome	SGA	AGA
	(N = 1331)	(N = 7035)
Primary Outcome		
Survival to discharge	740/1328 (56%)	5494/7022 (78%)
Secondary In-Hospital Outcomes		
Survival to discharge without major morbidity	153/1315 (12%)	1912/6896 (28%)
Major morbidity prior to discharge among survivors	571/724 (79%)	3444/5356 (64%)
Bronchopulmonary dysplasia, Grade 2-3	442/722 (61%)	1982/5332 (37%)
Intraventricular hemorrhage, Grade 3-4	85/739 (12%)	908/5472 (17%)
Proven necrotizing enterocolitis	87/739 (12%)	527/5490 (10%)
Surgery resulting in short gut	13/740 (2%)	66/5493 (1%)
Periventricular leukomalacia	39/740 (5%)	326/5485 (6%)
Late-onset sepsis, culture positive	217/740 (29%)	1300/5494 (24%)
Retinopathy of prematurity, Stage \geq 3	232/734 (32%)	1052/5440 (19%)

Results: Outcomes at 2 years

Secondary Follow-up Outcomes	SGA	AGA
	(N = 988)	(N = 5352)
Survival to two-year follow-up	536/988 (54%)	4131/5339 (77%)
Survival to two-year follow-up without severe NDI	300/886 (34%)	2489/4380 (57%)
Severe NDI among survivors	134/434 (31%)	683/3172 (22%)
Survival to two-year follow-up without moderate-severe NDI	148/886 (17%)	1559/4380 (36%)
Moderate-severe NDI among survivors	286/434 (66%)	1613/3172 (51%)
NDI categories among survivors		
Normal/mild	148/434 (34%)	1559/3172 (49%)
Moderate	152/434 (35%)	930/3172 (29%)
Severe/profound	134/434 (31%)	683/3172 (22%)
Rehospitalization since discharge	262/445 (59%)	1618/3312 (49%)

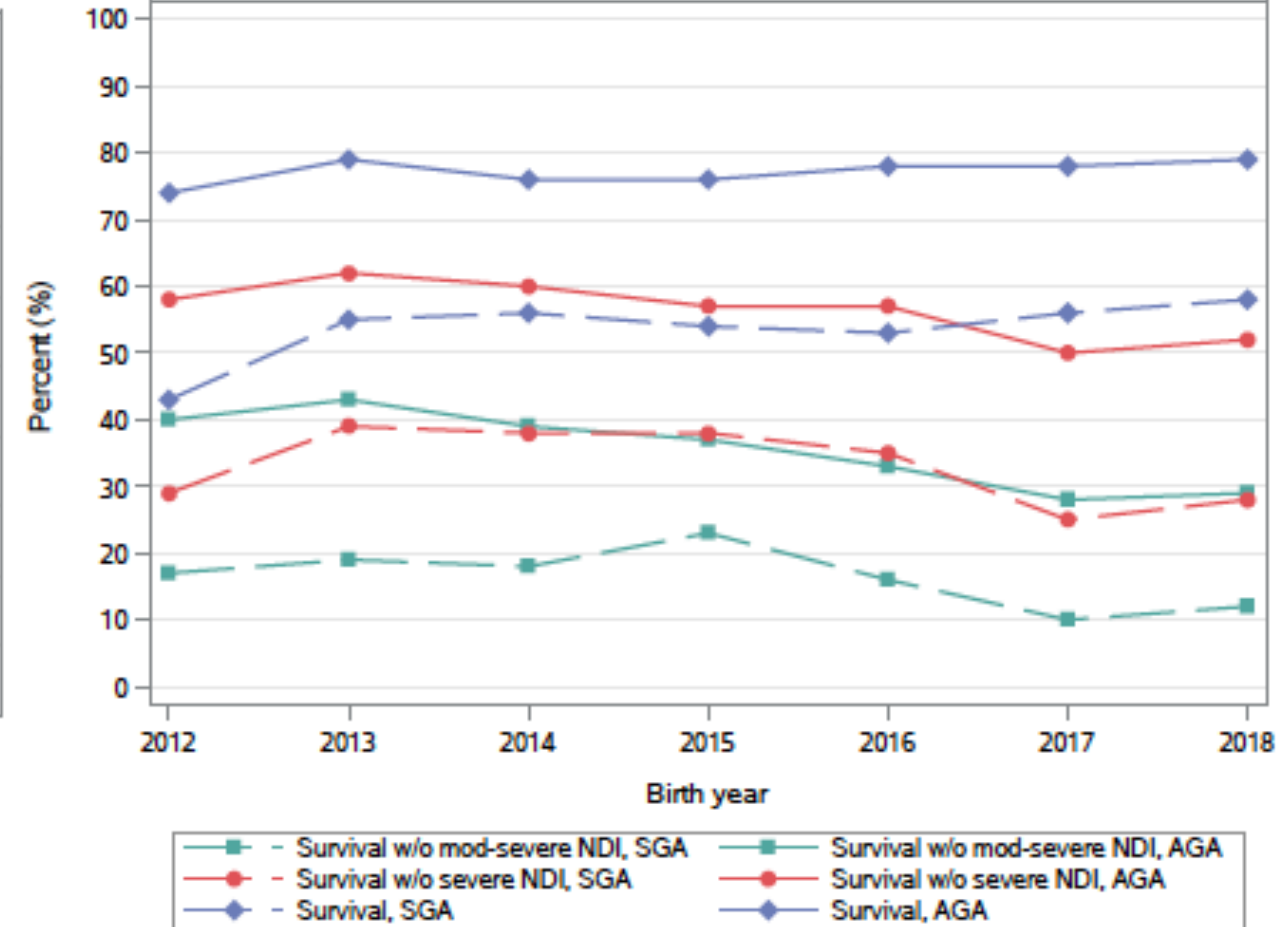
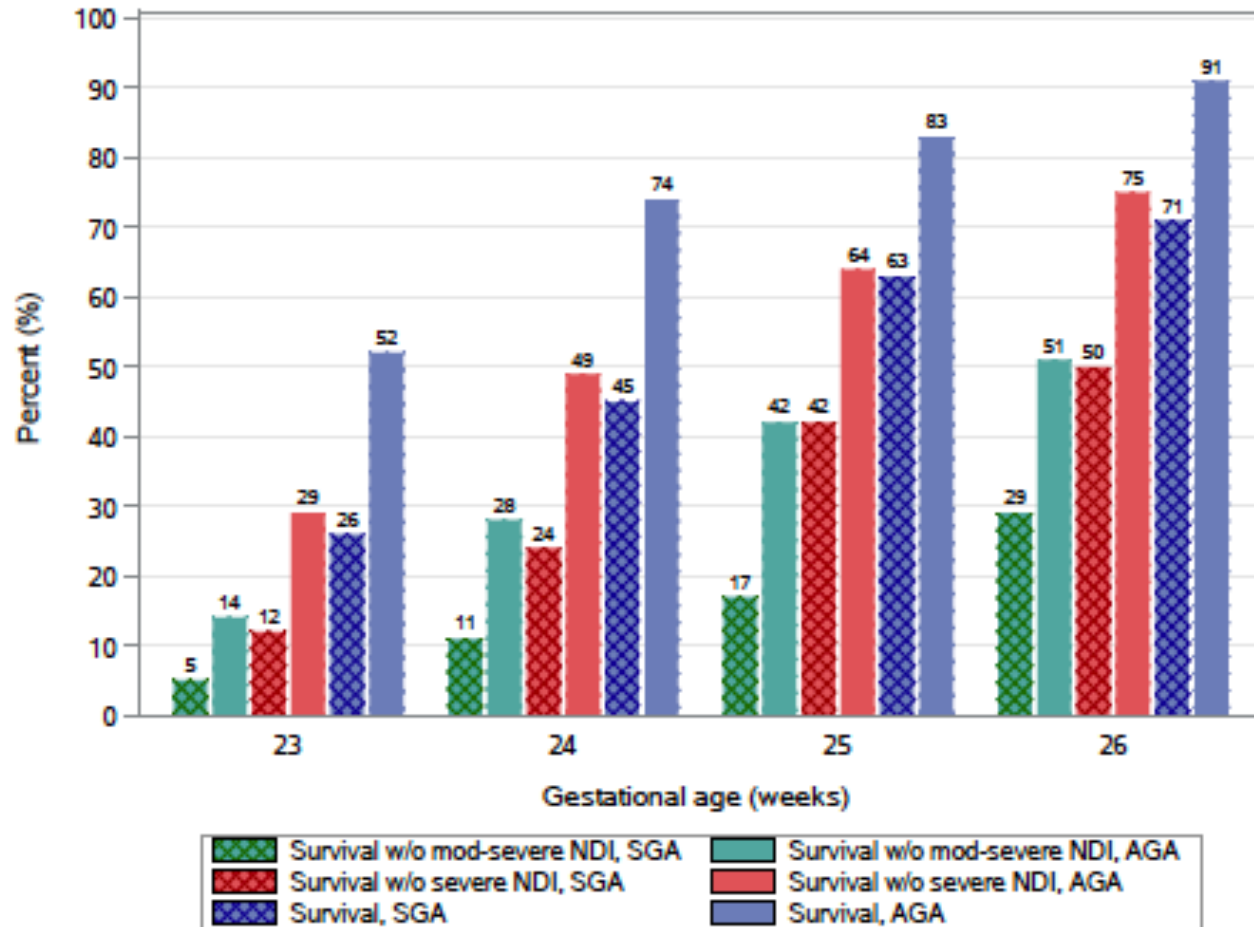
In-hospital outcomes of SGA and AGA infants for gestational ages 23 to 26 completed weeks

In-hospital outcomes of SGA and AGA infants from birth years 2012 to 2020



Two-year follow-up outcomes of SGA and AGA infants for gestational ages 23 to 26 completed weeks

Two-year follow-up outcomes of SGA and AGA infants from birth years 2012 to 2018



NICHHD

NEONATAL RESEARCH NETWORK



Strengths/Limitations



Strengths

- Large, diverse population provides definitive answers for short and long term outcomes in small for gestational age infants
- Family centered, clinically relevant outcomes, beyond survival.
- High quality data source with ability to ascertain the outcome for rare exposures

Limitations

- Heterogeneity in etiologies associated with small for gestational age, some of which may impact outcomes
- Academic centers: selection bias may limit generalizability
- Lack of standardized growth curves to analyze those at 22 weeks gestation
- Smaller numbers available at earlier gestational ages
- Multiple birth years included, over which obstetric and NICU practices have shifted

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