

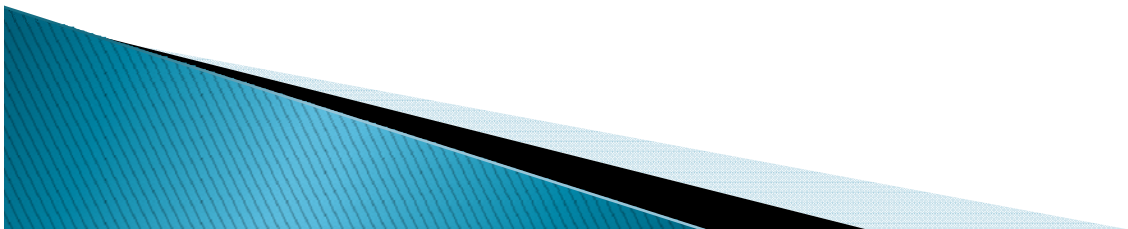
The Canadian Neonatal Follow-Up Network: Neurodevelopmental Outcomes at 18 Months Corrected Age

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University of British Columbia
Vancouver



Learning objectives

- ▶ Learn about the Canadian Neonatal Follow-Up Network
- ▶ Know the neurosensory outcomes at 18 months corrected age of children born very preterm in Canada
- ▶ Appreciate the risk factors for adverse outcome
- ▶ Understand the implications of different definitions of severe neurodevelopmental impairment



Canadian Neonatal Follow-Up Network



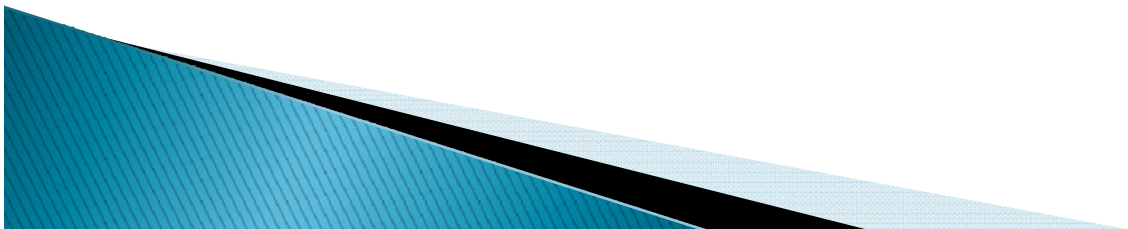
A network of health care professionals dedicated to improving the care of newborns and children at high risk of adverse outcome as a result of conditions requiring intensive medical care.

www.cnfun.ca

- ▶ CNFUN is a voluntary collaboration between Neonatal and Perinatal Follow-Up Programs in Canada
- ▶ Developed in liaison with the Canadian Neonatal Network in 2005
- ▶ Facilitates
 - Collaboration in research
 - Integrated data collection
 - Knowledge translation
 - Improvement of the quality of care and long-term outcomes of children seen in their programs.
- ▶ CNFUN Director: Dr. Anne Synnes

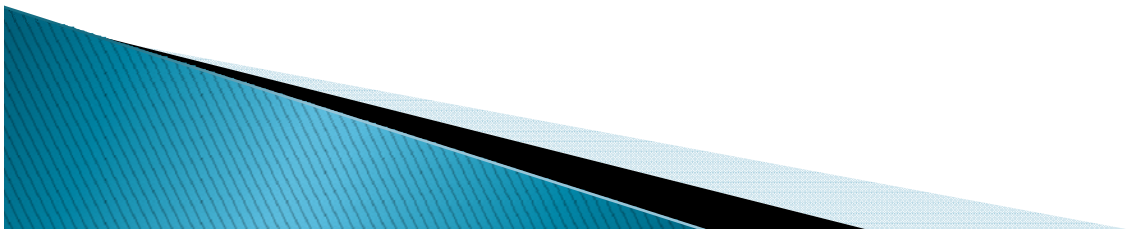
Background

- ▶ Despite improvement in survival of very preterm babies, about 50% of very preterm babies continue to experience one or more neurodevelopmental challenges.
- ▶ In the USA (NICHD), there are significant site variations in neurodevelopmental outcomes.



Research Questions

- ▶ What is the incidence of adverse neurodevelopmental outcomes of children born in Canada at < 29 weeks GA April 1, 2009-Sept 30, 2011?
- ▶ What are the determinants, including site, of neurodevelopmental outcome rates?

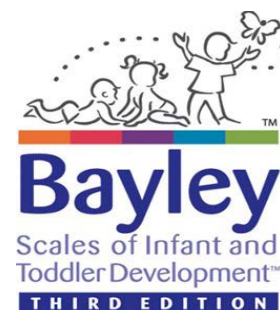





- ▶ 26 participating sites across Canada
 - Enrolled babies born April 1, 2009-Sept 30, 2011 at ≤ 28 wks GA
- ▶ Linked to Level-III NICUs (CNN)



- ▶ Details of CNFUN Assessments
- ▶ At 18 months corrected age:
 - Clinic visit
 - Sociodemographic information and post-NICU discharge health utilization
 - Growth and physical examination
 - CP and Gross Motor Function Classification System
 - Bayley Scales of Infant and Toddler Development (3rd edition)
- ▶ At 36 months corrected age:
 - Questionnaire mail out
 - Health Status Classification Pre-School (HSCS-PS)
 - Ages and Stages Questionnaire
 - Behaviour Rating Inventory of Executive Function-Preschool (BRIEF-P)



CNFUN Methods

- ▶ Developed database and manual (available at www.cnfun.ca)
 - ▶ Developed a certification program for Bayley-III testers
 - ▶ CNN collects neonatal data on all NICU admissions < 29 wks GA
 - ▶ NICUs notify local FU programs of eligible subjects and their unique identifier
 - ▶ CNFUN sites track patients and do 18 month in person assessment according to manual
 - ▶ De-identified data uploaded to MiCare coordinating site
 - ▶ CNFUN tracked follow-up rates and notified sites
 - ▶ Data verification and ascertaining data linkage
- 

Definitions of Adverse Neurodevelopmental Outcome

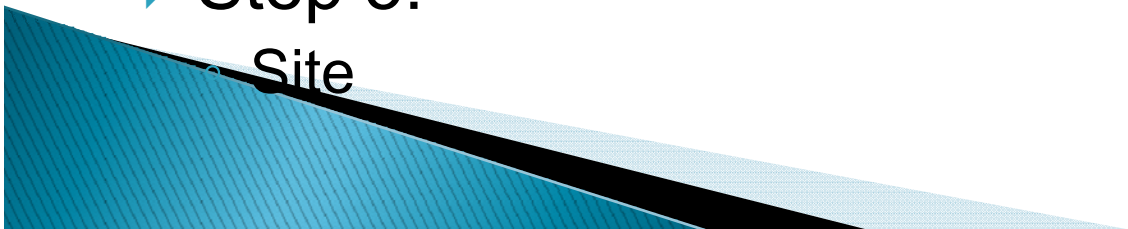
Impairments	Severe neurodevelopmental impairment = SNI (Any one or more of the following)*	Neurodevelopmental impairment =NDI (Any one or more of the following)#
Motor	CP with GMFCS III,IV or V	CP with GMFCS I or higher
	Bayley III Motor composite <70	Bayley III Motor composite <85
Cognitive	Bayley III Cognitive composite <70	Bayley III Cognitive composite <85
Language	Bayley III Language composite <70	Bayley III Language composite <85
Hearing	Hearing aid or cochlear implant	Sensorineural/mixed hearing loss
Vision	Bilateral visual impairment	Uni- or bilateral visual impairment

*Includes children who could not be tested using the Bayley-III but who had a Bayley-III General Adaptive Composite score < 70, or who were assessed to have a severe developmental delay

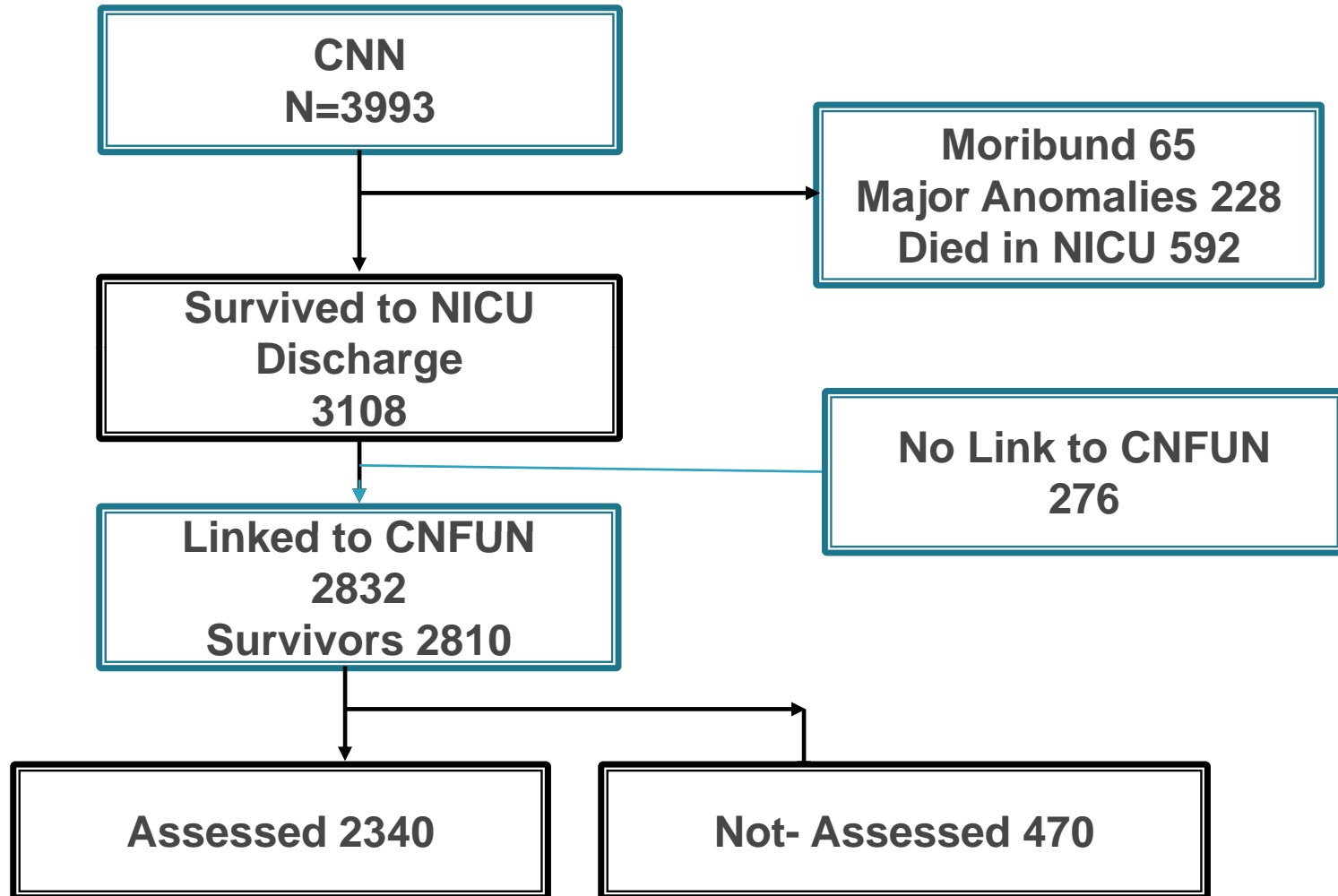
Children with a SNI or those who could not be tested using the Bayley-III but who had a Bayley-III General Adaptive Composite score < 85

Analyses

- ▶ Regression Analyses for SNI, NDI and SNI or death
- ▶ Step 1
 - Patient Characteristics and Pregnancy Complications
- ▶ Step 2:
 - SNAP-II
- ▶ Step 3:
 - NICU complications
- ▶ Step 4:
 - Severe brain injury
- ▶ Step 5:
 - Site



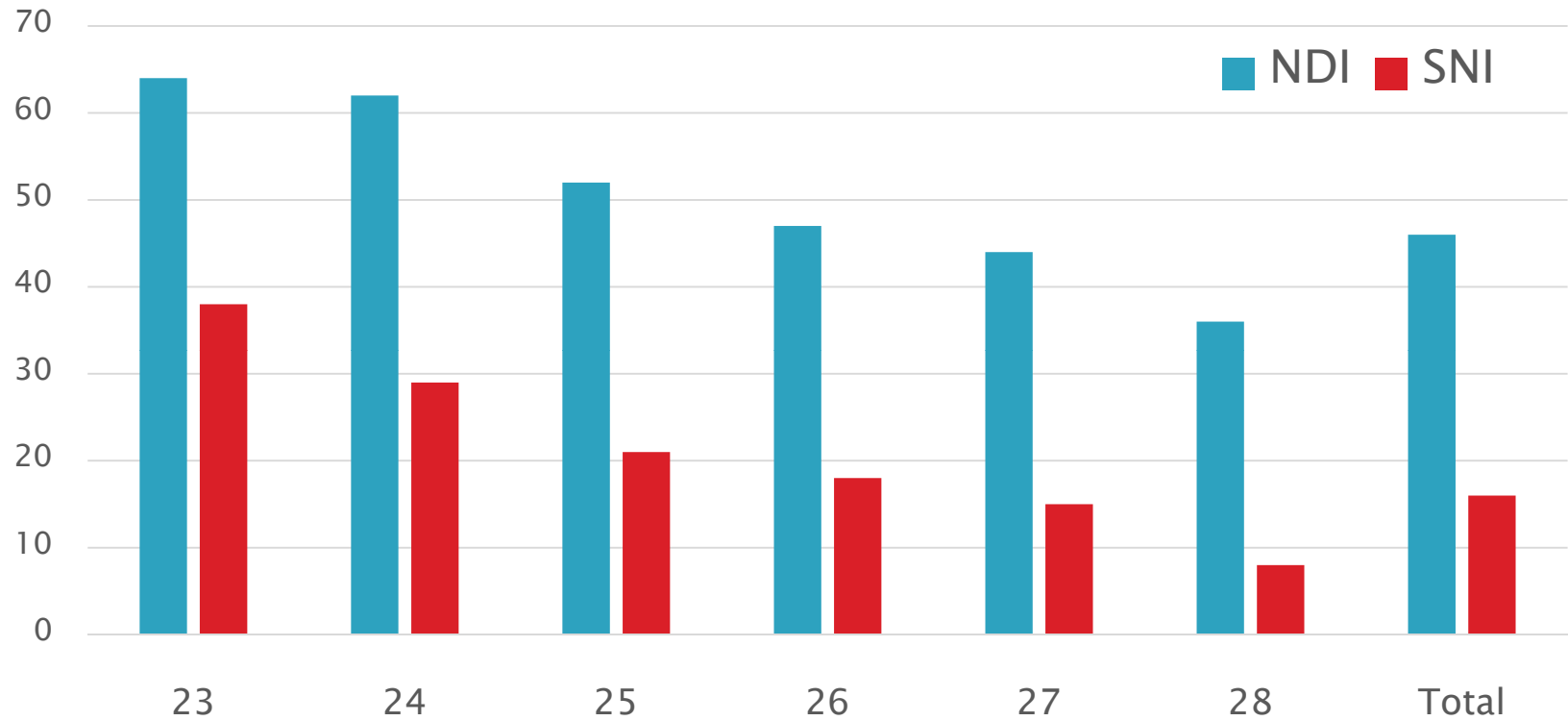
Flowchart



Comparison of Neonates Assessed and Those Lost to Follow-up

	Neonates with a neurodevelopmental assessment (n=2391)	Follow-up information not available (n=781)	P-value*
Median gestational age in weeks (IQR)	27 (25, 28)	27 (26, 28)	<0.01
Median birth weight in grams (IQR)	920 (770, 1100)	990 (800, 1160)	<0.01
Small for gestational age	171 (7.3)	48(6.5)	0.44
Male sex	1232 (52.7)	416 (55.9)	0.13
Chorioamnionitis	482 (25.1)	130 (23.4)	0.42
Maternal hypertension	391 (17.1)	110 (15.5)	0.34
Maternal diabetes mellitus	180 (8.0)	42 (6.0)	0.08
Any antenatal steroids	2063 (90.3)	599 (84.8)	<0.01
Rupture of membranes \geq 24 hours	482 (21.0)	120 (17.1)	0.02
Cesarean birth	1359 (58.3)	406 (55.3)	0.15
Twins or multiples	663 (28.3)	179 (24.1)	0.03
Apgar score at 5 minute (median, IQR)	7 (6, 8)	7 (6, 8)	0.05
SNAP-II score (median, IQR)	14 (9, 21)	9 (5, 16)	<0.01
Bronchopulmonary dysplasia	1043 (44.6)	257 (34.9)	<0.01
Early-onset sepsis	39(1.7)	9 (1.2)	0.38
Late-onset sepsis	656 (28.0)	180 (24.1)	0.04
Necrotizing enterocolitis	166 (7.1)	52 (7.1)	0.98
Retinopathy of prematurity >stage 3	276 (15.0)	53 (10.7)	0.01
Intraventricular hemorrhage grade 3 or 4 or periventricular leukomalacia	245 (10.8)	59 (8.8)	0.14
Periventricular leukomalacia	122 (5.6)	33 (5.3)	0.75

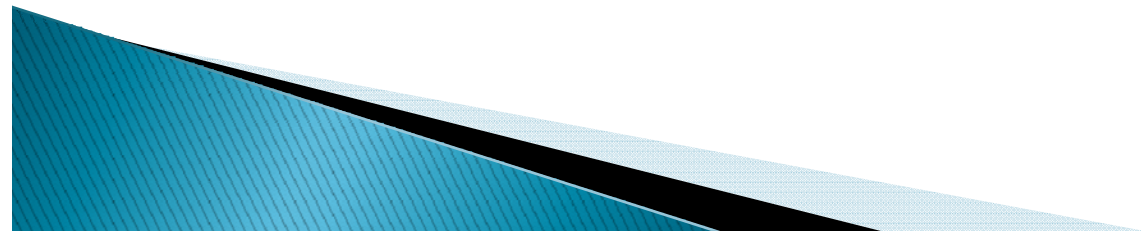
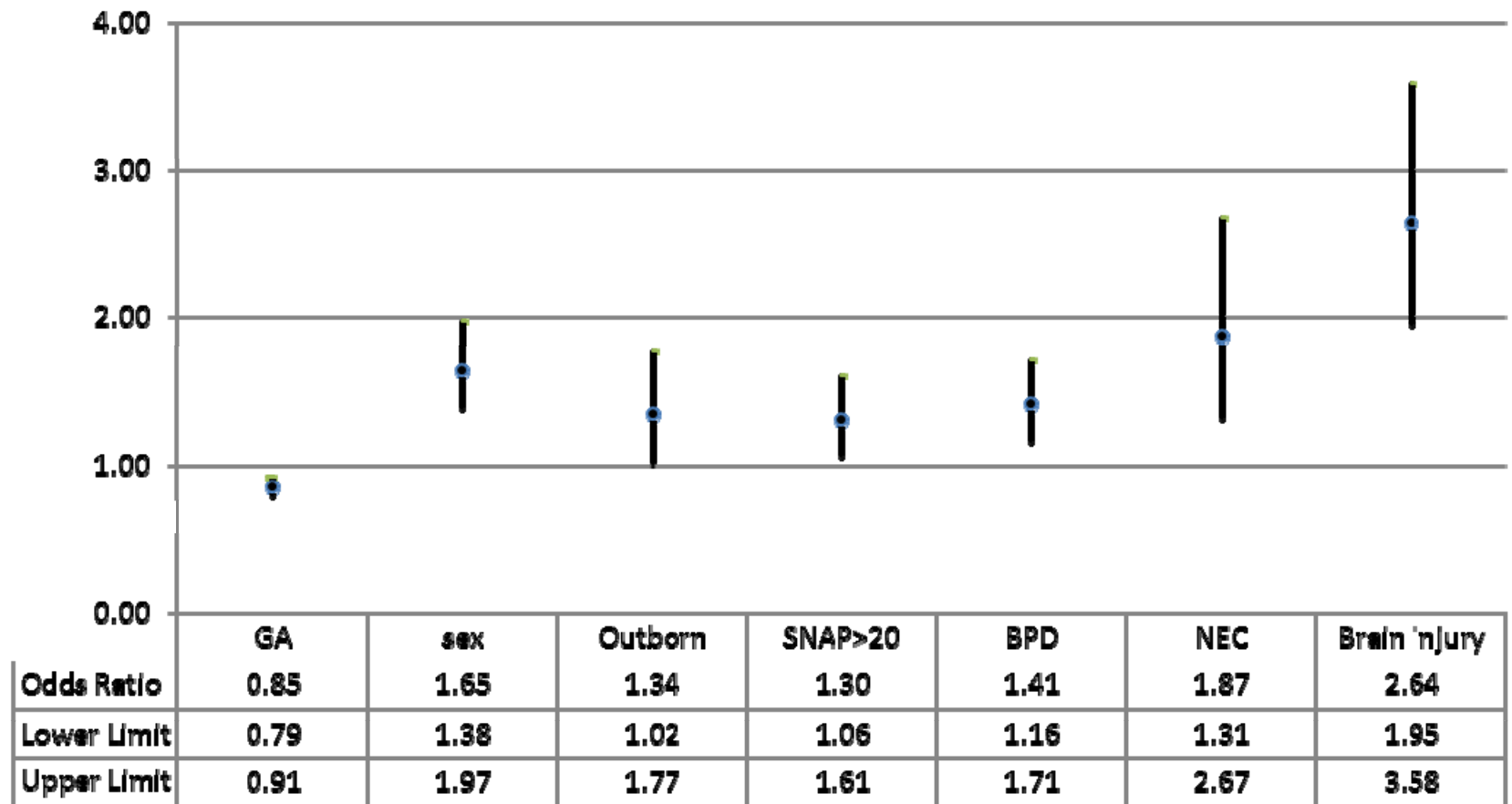
Composite Outcomes



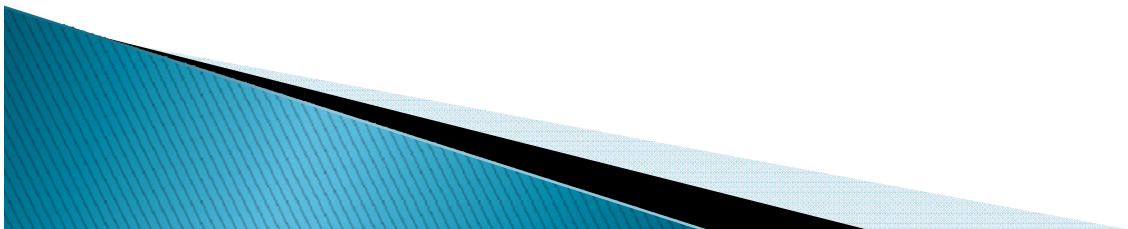
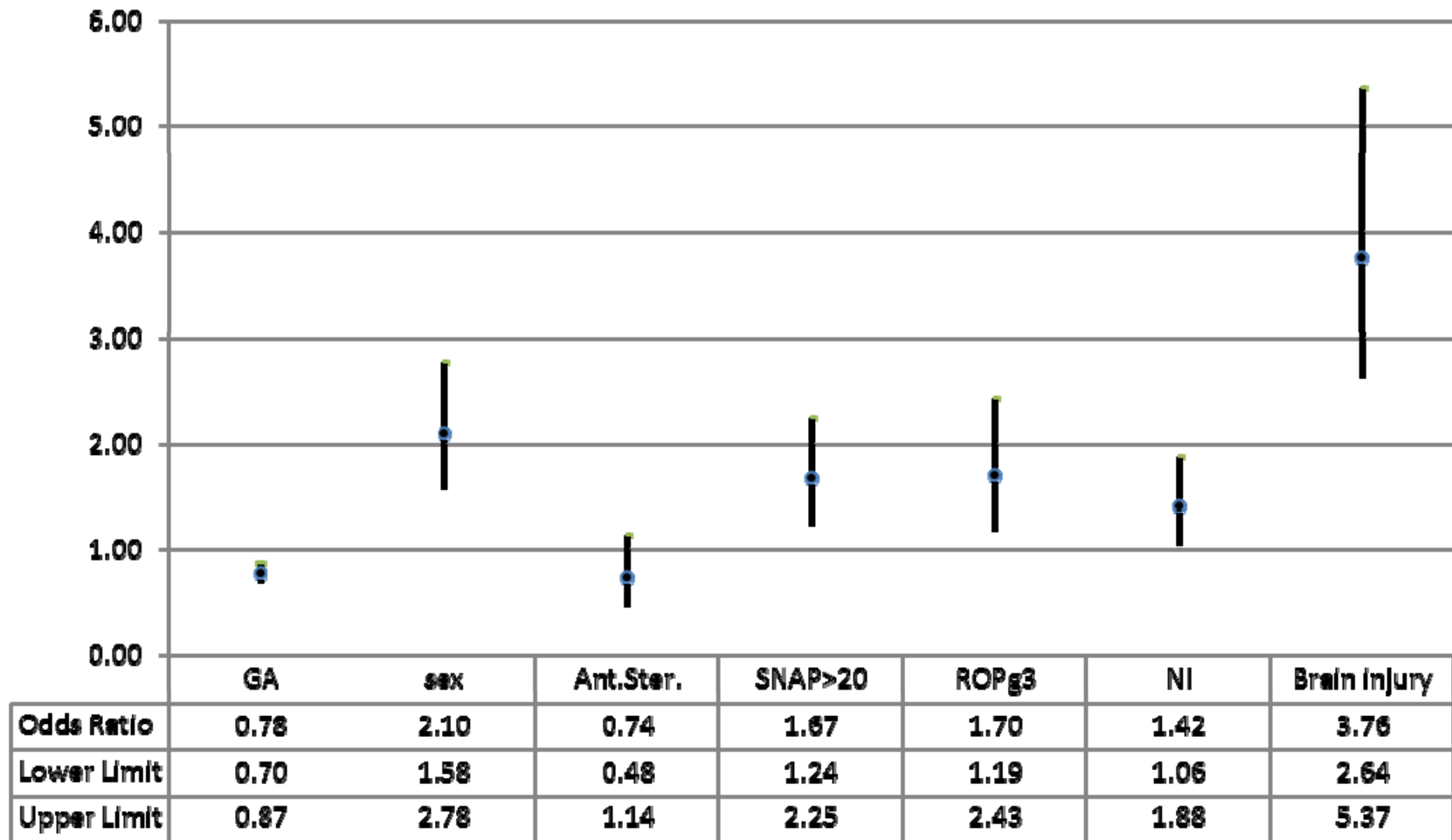
	ALL GA	Site Range	22-23 wks	24 wks	25 wks	26 wks	27 wks	28 wks
NDI	46%	15-100 %	63%	62%	52%	47%	44%	36%
SNI	16.5%	4-50%	37%	29%	21%	18%	15%	8%

	Entire cohort N (%)	Range (%) across sites*	≤ 23 wks GA (64)	24 Wks GA (187)	25 wks GA (395)	26 wks GA (505)	27 wks GA (607)	28 wks GA (633)
Cerebral palsy	146 (6.4)	1.4-28.6	8 (13.1)	22 (12.2)	32 (8.4)	32 (6.7)	23 (4)	29 (4.8)*
Bayley-III results								
Motor Composite								
Median (IQR)	94 (85, 100)		85 (73, 94)	88 (79, 97)	91 (82, 100)	94 (85, 100)	94 (88, 103)	97 (88, 103)
Score < 85	457 (21.5)	7.7-100	23 (46.0)	57 (33.7)	96 (26.8)	108 (24.0)	83 (15.7)	90 (15.8)*
Score < 70	140 (6.6)	1.9-22.2	9 (18.0)	21 (12.4)	31 (8.7)	34 (7.6)	23 (4.3)	22 (3.9)
Cognitive								
Median (IQR)	95 (90, 105)		90 (80, 95)	90 (80, 100)	95 (85, 105)	95 (85, 105)	95 (90, 105)	100 (90, 105)
Score < 85	321 (14.5)	3.7-32.1	19 (36.5)	44 (25.4)	63 (17.0)	80 (17.1)	75 (13.3)	40 (6.8)*
Score < 70	73 (3.3)	0.7-20.0		10 (5.8)	22 (6.0)	16 (3.4)	13 (2.3)	8 (1.4)
Language								
Median (IQR)	91 (79, 100)		83 (68, 94)	84 (74, 97)	89 (77, 100)	91 (79, 100)	91 (79, 103)	94 (83, 103)
Score <85	748 (34.9)	11.1-100	27 (54.0)	85 (50.0)	143 (39.2)	160 (35.1)	192 (35.5)	141 (25.1)*
Score < 70	229 (10.7)	2.9-39.6	14 (28.0)	32 (18.8)	53 (14.5)	51 (11.2)	54 (10.0)	25 (4.5)
Hearing								
Any hearing loss	182 (8.1)	2.0-33.3	9 (14.5)	19 (10.7)	45 (12.0)	30 (6.4)	37 (6.5)	42 (7.1)*
Hearing aid or cochlear implant	60 (2.6)	0.9-21.4	6 (9.5)	9 (4.9)	19 (5.0)	9 (1.9)	10 (1.7)	7 (1.2)
Vision								
Uni- or bilateral visual impairment	41 (1.9)	0.8-14.3	8 (14.3)	6 (3.5)	11 (3.0)	7 (1.5)	6 (1.1)*	
Bilateral visual impairment	35 (1.6)	0.8-14.3	7 (12.5)	6 (3.5)	10 (2.7)	5 (1.1)	5 (0.9)	

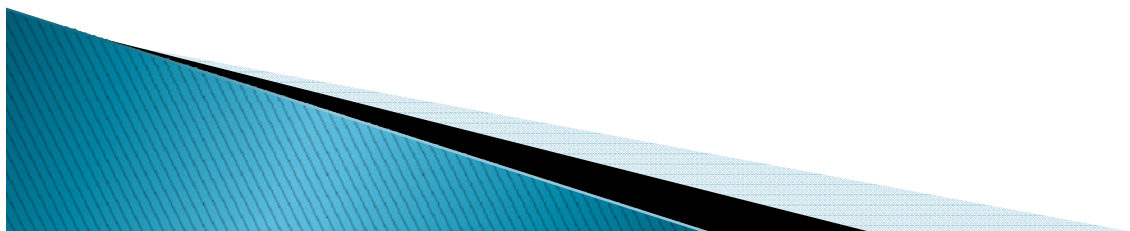
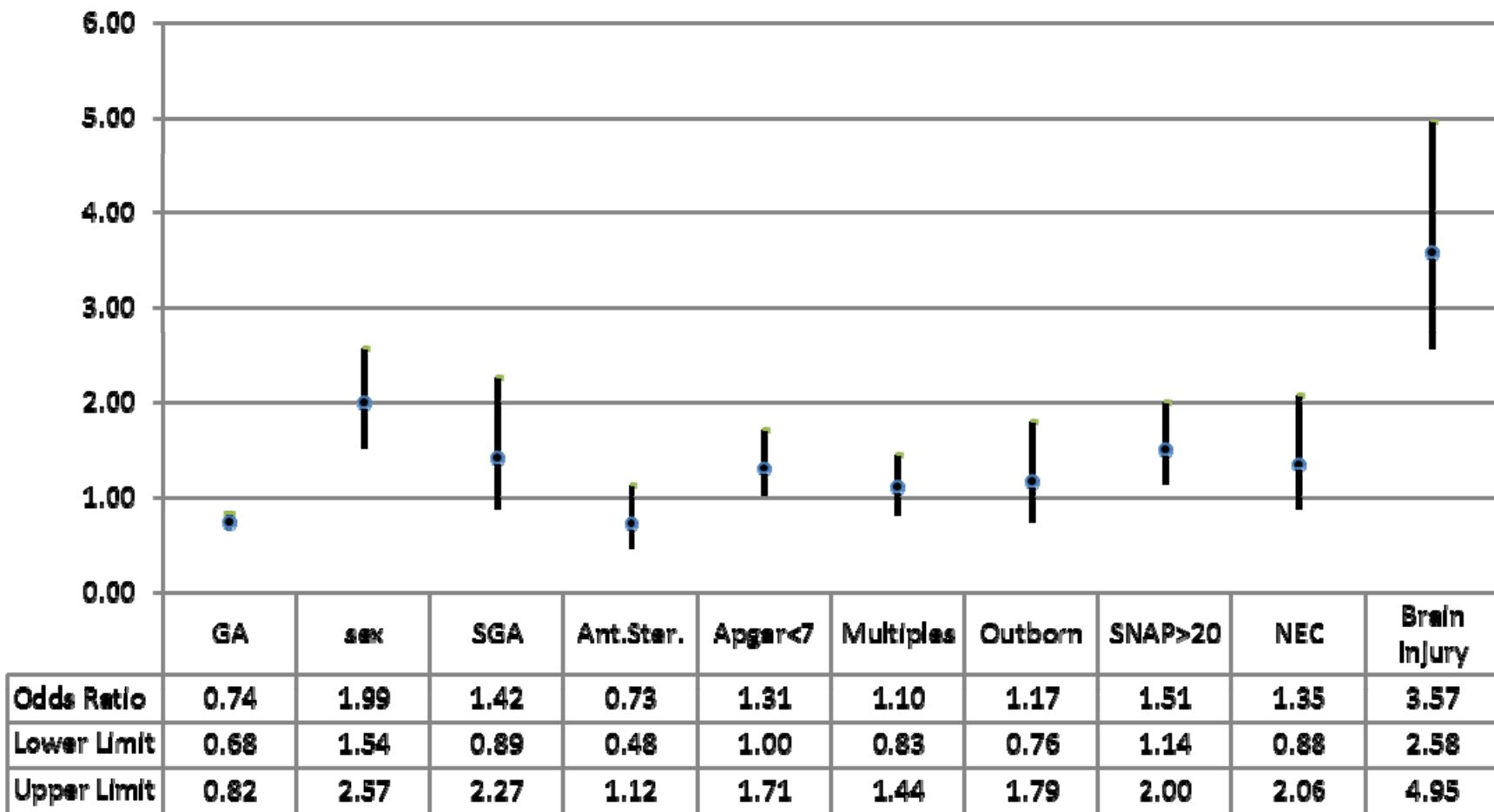
Neurodevelopmental Impairment



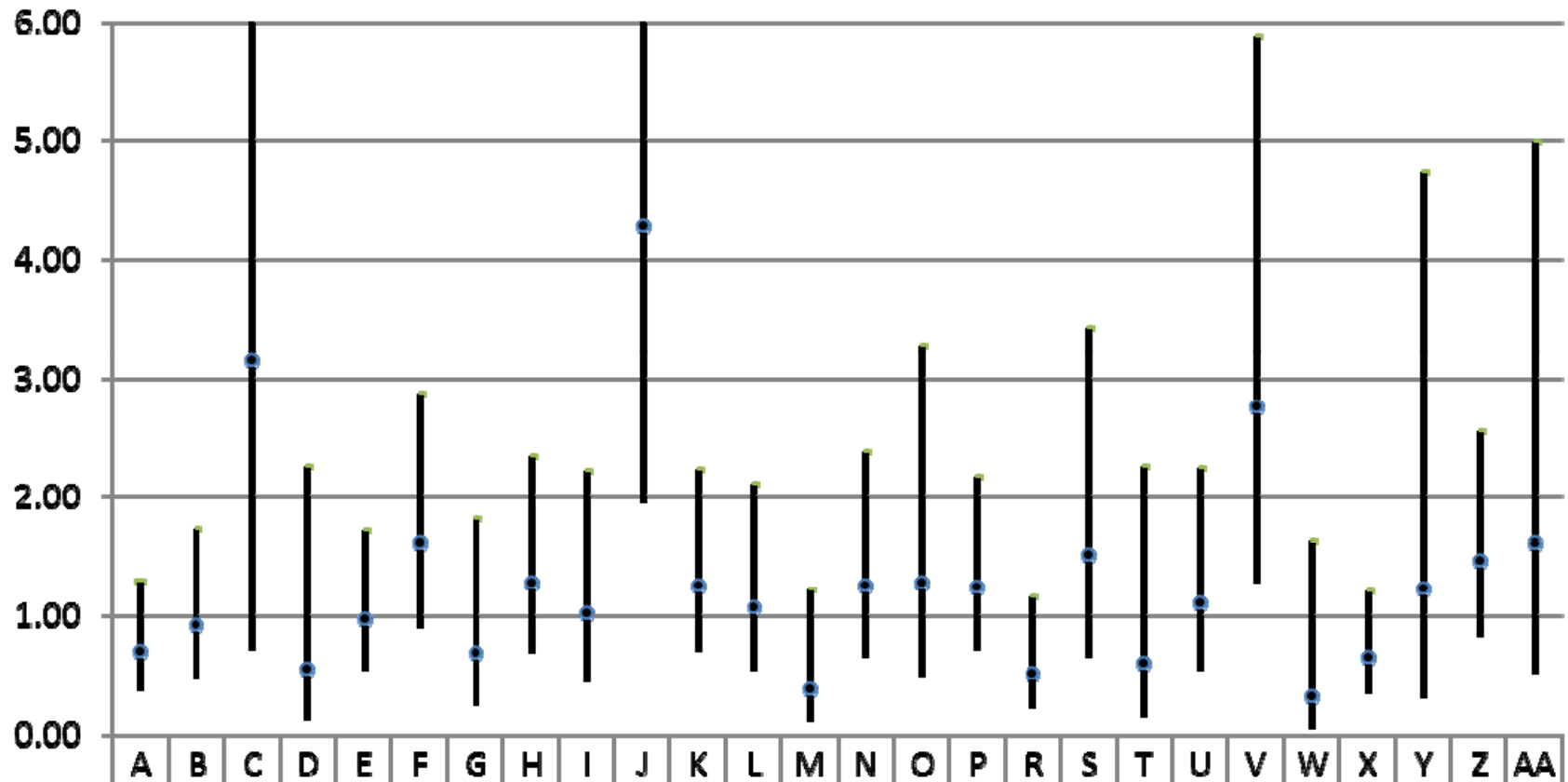
Severe Neurodevelopmental Impairment



Severe Neurodevelopmental Impairment or Death

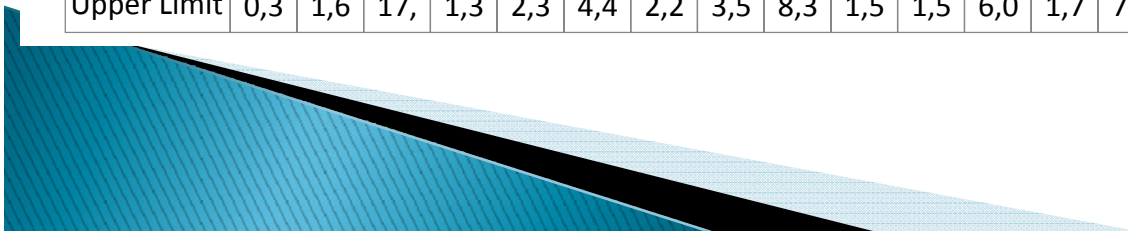
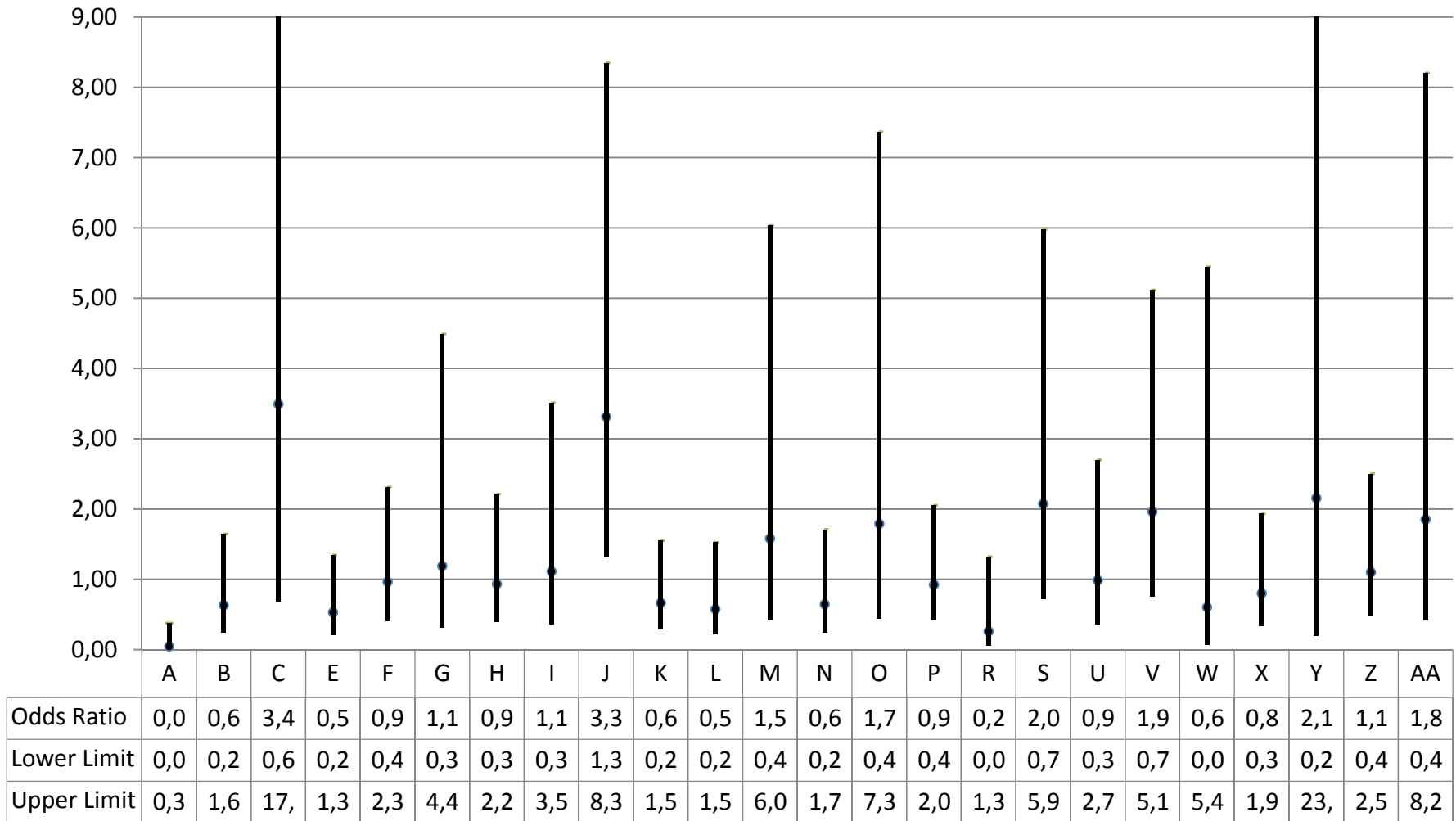


Neurodevelopmental Impairment

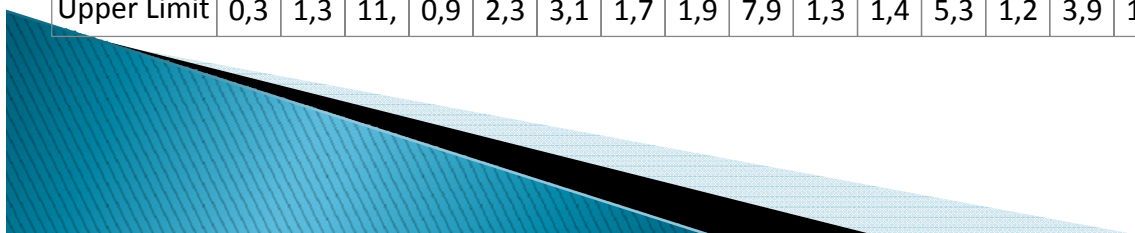
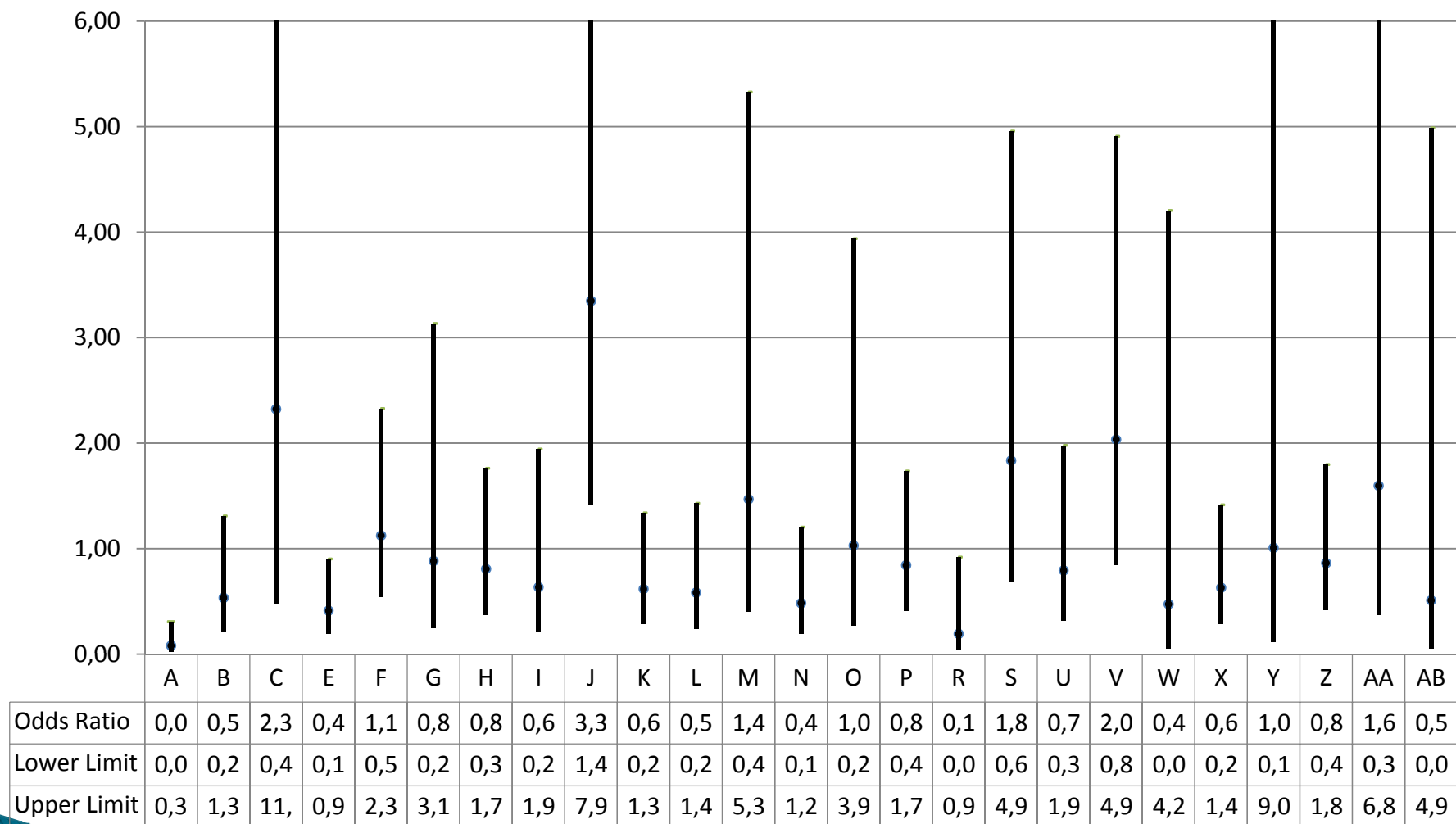


	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	R	S	T	U	V	W	X	Y	Z	AA
Odds Ratio	0.7	0.9	3.1	0.5	0.9	1.6	0.6	1.2	1.0	4.2	1.2	1.0	0.3	1.2	1.2	1.2	0.5	1.5	0.6	1.1	2.7	0.3	0.6	1.2	1.4	1.6
Lower Limit	0.3	0.5	0.7	0.1	0.5	0.9	0.2	0.7	0.4	1.9	0.7	0.5	0.1	0.6	0.5	0.7	0.2	0.6	0.1	0.5	1.3	0.0	0.3	0.3	0.8	0.5
Upper Limit	1.2	1.7	13.	2.2	1.7	2.8	1.8	2.3	2.2	9.3	2.2	2.1	1.2	2.3	3.2	2.1	1.1	3.4	2.2	2.2	5.8	1.6	1.2	4.7	2.5	4.9

Severe Neurodevelopmental Impairment

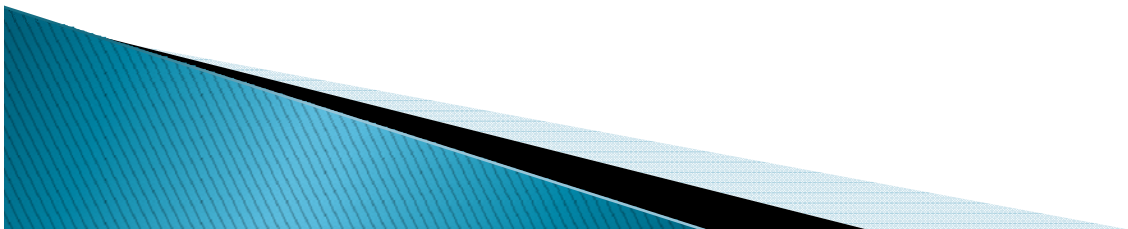


Severe Neurodevelopmental Impairment or Death



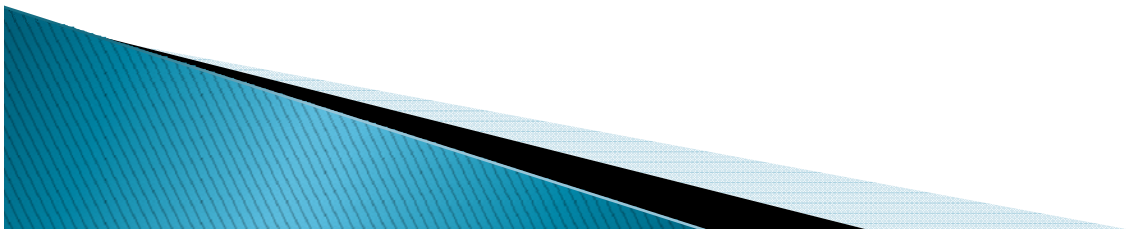
Comparison with the literature

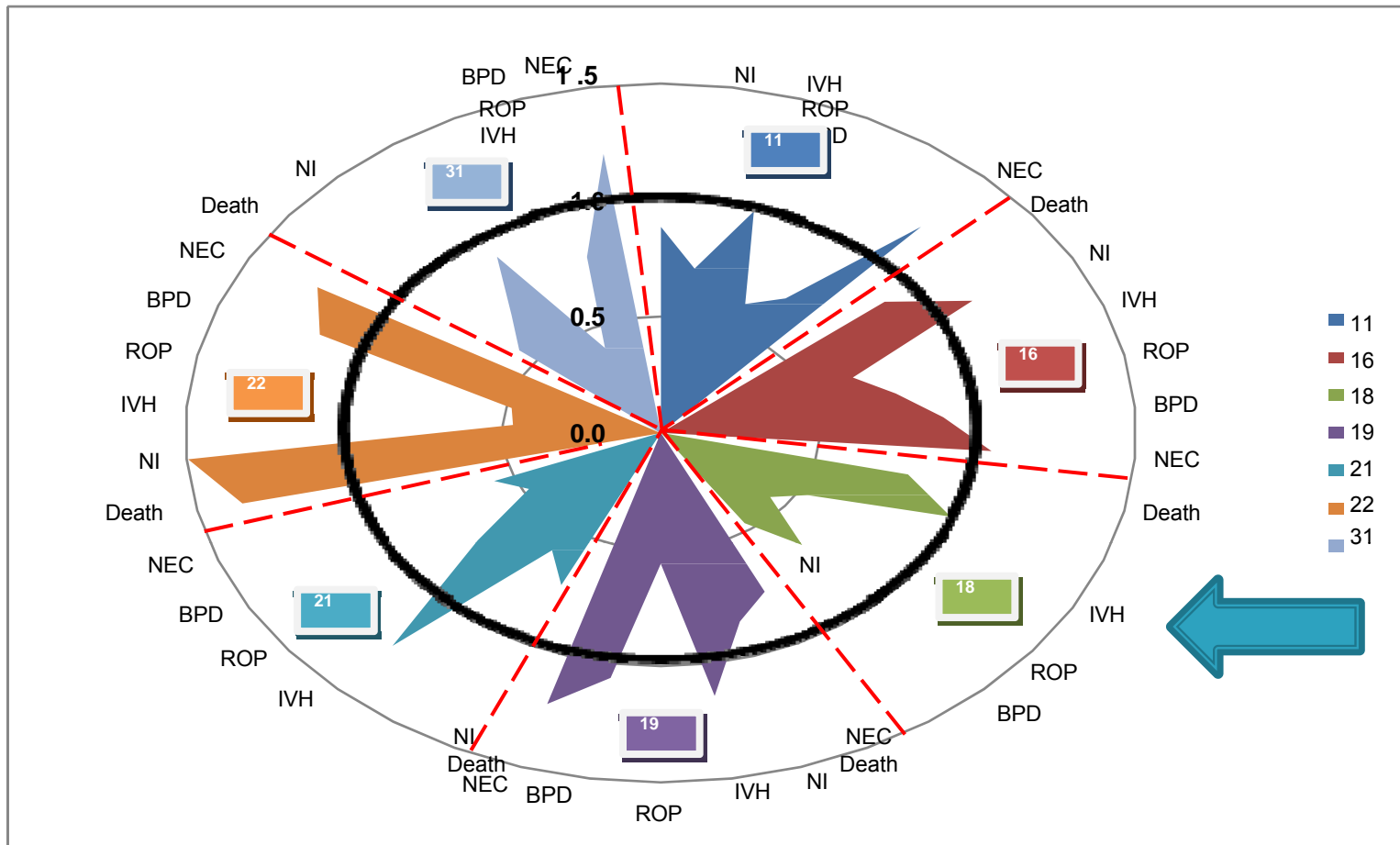
- EXPRESS Group (Sweden) 2004-2007 < 27 wks GA (Serenius 2013)
 - Cerebral Palsy 7%
 - Bayley III mean cognitive 94 vs 96.1 median 95
 - Bayley III mean language 98 vs 89.0 median 91
 - Bayley III mean motor 94 vs 91.8 median 94
- Australia < 28 wks / <1 kg, 2005 (Anderson Arch Pediatr Adolesc Med 2010)
 - Bayley III mean cognitive 96.9 vs 96.1
 - Bayley III mean language 94.2 vs 89.0
 - Bayley III mean motor 100.4 vs 91.8
- ELGAN Study group 2002-2004 < 28 wks GA (Kuban J Pediatr 2008)
 - Cerebral Palsy 11.4%



Conclusions

- ▶ 84% of survivors are free of severe impairment
- ▶ Statistically significant difference by GA
- ▶ Determinants of adverse outcome:
 - GA, sex, antenatal steroids, outborn, Apgar < 7
 - SNAP > 20
 - NICU morbidities (BPD, NEC, ROP, NI)
 - Severe brain injury
 - Site





Adjusted standardized ratios for mortality and morbidities

Site	Adjusted standardized ratio					
	Death	NI	IVH	ROP	BPD	NEC
11	0.9	0.7	1.0	0.6	0.7	1.2
16	0.9	1.1	0.7	0.8	0.9	1.0
18	0.8	1.0	0.5	0.4	0.7	0.5
19	0.8	0.8	1.1	0.6	1.1	1.2
21	0.7	0.6	1.2	0.7	0.5	0.6
22	1.4	1.5	0.5	0.5	1.2	1.3
31	0.6	0.7	0.9	0.4	0.8	1.2

The Effect of Neurodevelopmental Disability Definition on Incidence Rates Among Very Preterm Infants

MD Haslam, S Lisonkova, D Creighton, P Church, A Synnes, and CNFUN

▶ BACKGROUND

- Various criteria are used to define severe neurodevelopmental disability (SND) and the effect of definition is rarely reported.

▶ OBJECTIVES

- To examine the impact of differences in commonly used definitions of severe neurodevelopmental disability on the incidence rates and the associations with risk factors.



SND Definition	CP Severity*	Motor (Bayley-III)	Language (Bayley-III)	Cognitive (Bayley-III)	Hearing Impairment	SNI Incidence (%)	Rate Ratio (95% CI)
1	3-5	<70	<70	<70	Hearing aid or cochlear implant	16.2	3.33 (2.70, 4.10)
2	4-5	–	64	68	-	9.8	2.00 (1.60, 2.50)
3	4-5	<70	–	<70	Profound hearing loss (>90dBHL)	8.9	1.83 (1.46, 2.30)
4	4-5	≤55	≤55	≤55	–	6.0	1.23 (0.96, 1.58)
5	4-5	<55	<55	<55	Profound hearing loss (>90dBHL)	6.0	1.22 (0.96, 1.57)
6	3-5	–	<55	<55	Profound hearing loss (>90dBHL)	5.5	1.13 (0.88, 1.46)
7	4-5	-	<55	<55	-	4.9	Ref

*Using the Gross Motor Function Classification System

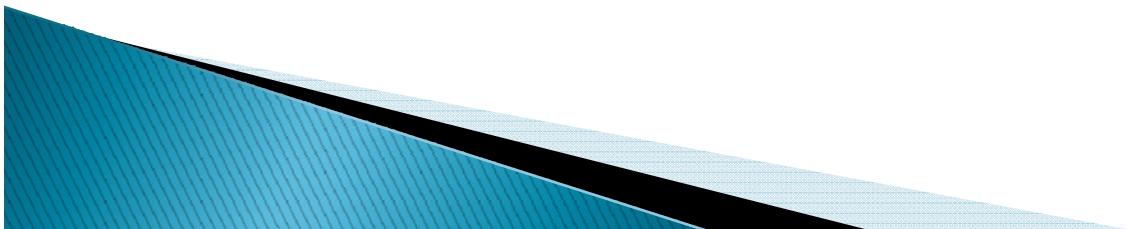
Note: Every definition also included a visual component (severely impaired if bilaterally blind)

Risk factor	Highest Incidence AOR (95% CI)	Lowest Incidence AOR (95% CI)
Ethnicity (First Nations)	3.22 (1.62, 6.42)	NS
Fetal drug exposure	3.00 (1.43, 6.29)	3.46 (1.21, 9.91)
Gestational age (weeks)	0.87 (0.78, 0.98)	NS
Sex (male)	1.83 (1.34, 2.49)	NS
SNAP-II >20	1.82 (1.33, 2.50)	2.05 (1.22, 3.44)
BPD	NS	3.00 (1.65, 5.43)
ROP≥ stage 3	1.80 (1.23, 2.64)	1.83 (1.05, 3.17)
Late onset sepsis	1.57 (1.15, 2.14)	1.81 (1.09, 3.01)
Injury (IVH≥grade 3 or PVL)	4.65 (3.22, 6.86)	4.81 (2.80, 8.27)

Importance of Definition

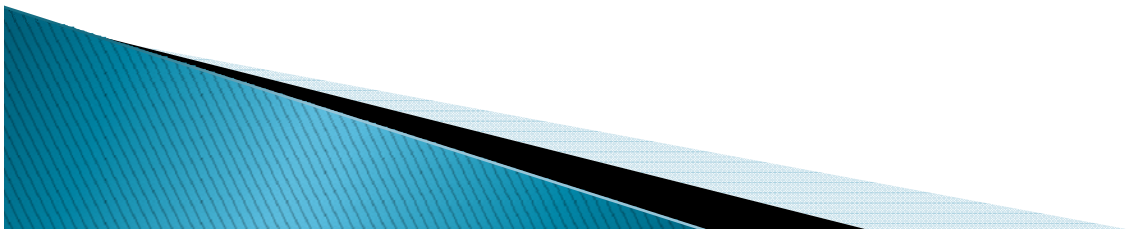
- ▶ Definition impacts incidence rate
- ▶ Definition impacts significant predictors
- ▶ Used for counselling and guidelines

But what outcomes are important for parents deciding on behalf of the child?



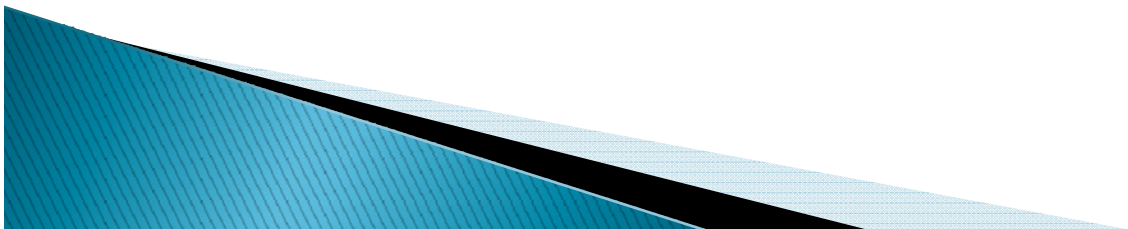
Examples of CNFUN projects

1. Neurodevelopmental outcomes of preterm infants treated with bevacizumab for severe retinopathy of prematurity (Luu et al)
2. Preterm children with suspected cerebral palsy at 18 months corrected age (Gillone et al)
3. Preterm Infant Journeys in a Canadian Regionalized Health Services Context (Ballantyne et al)
4. Short- and long-term outcomes of neonatal gram-negative sepsis in Canadian NICUs (Derynck et al)
5. The CNFUN Cohort of Children Born Preterm: Outcomes at Three Years



CNFUN Participating Sites

- ▶ **Dr. T. Pillay**, Victoria General Hospital; **Dr. A. Synnes**, BC Women's Hospital, **Dr. R. Sauvé**, Alberta Children's Hospital, Foothills Medical Centre; **Dr. A. Reichert**, Glenrose Rehabilitation Hospital; **Dr. J. Bodani**, Regina General Hospital; **Dr. K. Sankaran**, Royal University Hospital; **Dr. D. Moddemann**, Winnipeg Health Sciences Centre, St. Boniface General Hospital; **Dr. C. Nwaesei**, Windsor Regional Hospital; **Dr. K. Dow**, Kingston General Hospital; **Dr. D. Lee**, Children's Hospital London Health Sciences Centre; **Dr. L. Ly**, Hospital for Sick Children; **Dr. E. Kelly**, Mount Sinai Hospital; **Dr. S. el Helou**, Hamilton Health Sciences Centre; **Dr. P. Church**, Sunnybrook Health Sciences Centre; **Dr. E. Pelausa**, Jewish General Hospital; **Dr. P. Riley**, Montreal Children's Hospital, Royal Victoria Hospital; **Dr. F. Levebvre**, Hospital Sainte-Justine; **Dr. S. Belanger**, Centre Hospitalier Universitaire de Quebec; **Dr. R. Canning**, Moncton Hospital; **Dr. L. Monterrosa**, Saint John Regional Hospital; **Dr. H. Makary**, Dr. Everett Chalmers Hospital; **Dr. M. Vincer**, IWK Health Centre; **Dr. P. Murphy**, Charles Janeway Children's Health and Rehabilitation Centre.



Funding

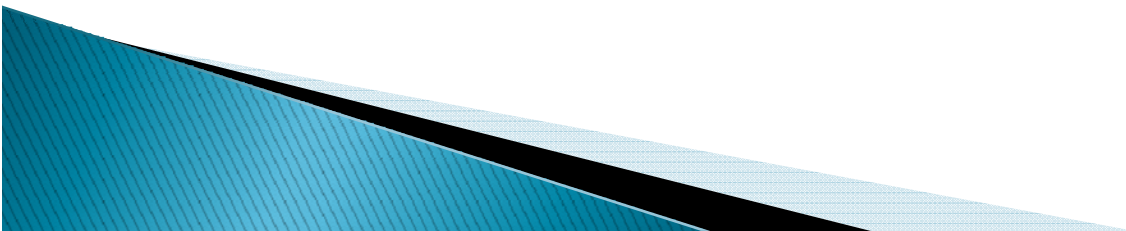
- ▶ CIHR Team in Maternal Infant Care



- ▶ Ontario Ministry of Health and Long-Term Care provided financial support to the CIHR MiCare Research Centre at Mount Sinai Hospital, Toronto, Ontario

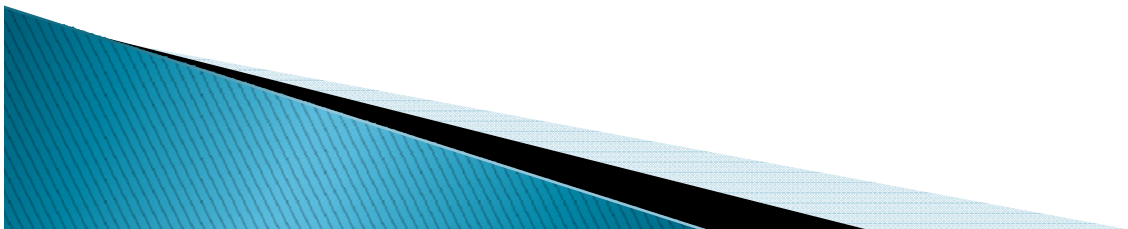


Questions?



Next Steps

- ▶ Complete and/ or publish > 20 projects
- ▶ Individual site outcomes over time periods
- ▶ Develop definitions that align with the WHO ICF-CY
- ▶ **PRETERM BIRTH TEAM GRANT** to improve developmental outcomes



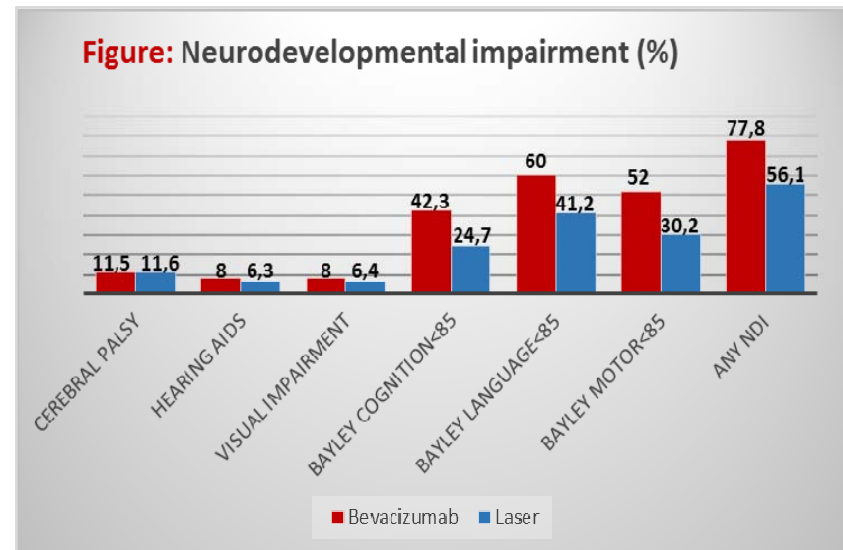


Neurodevelopmental outcomes of preterm infants treated with bevacizumab for severe retinopathy of prematurity

Morin J¹, Luu TM¹, Superstein R¹, Ospina LH¹, Lefebvre F¹, Simard M-N¹, Shah V², Shah PS² and Kelly EN²

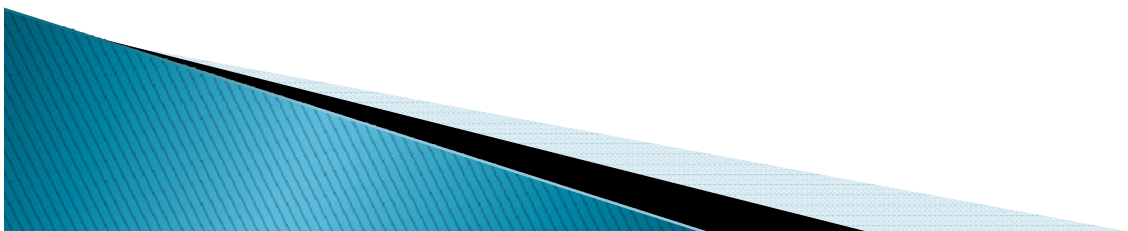
- To compare neurodevelopmental outcomes at 18-22 months of preterm infants treated with bevacizumab vs. laser.

	Bevacizumab N=27	Laser N=98
GA, mean (SD), wks	24.9 (1.5)	24.7 (1.3)
Birth weight, mean (SD), g	739 (172)	714 (140)
Male sex, n (%)	16 (59.3)	41 (41.8)
Maternal education, n (%)		
High school and less	9 (37.5)	27 (29.4)
Some college and above	15 (62.5)	65 (70.7)
SNAP-II score, median (IQR)	24 (19, 31)	19 (13, 28)
O2 at 36 weeks, n(%)	20 (74.1)	76 (77.6)
PDA ligation, n(%)	8 (29.6)	40 (40.8)
Culture-proven sepsis, n (%)	15 (55.6)	47 (48.0)
IVH, n(%)	12 (44.4)	46 (46.9)
ROP, n(%)		
Zone I, any stage	5 (19.2)	6 (6.7)
Zone II, stage 2-3 with plus disease	21 (80.8)	63 (70.0)
Stage 4-5	0 (0)	21 (23.3)
Neonatal hospitalization, mean (SD), days	139 (52)	128 (42)



Outcome	Unadjusted	Adjusted**
Neurodevelopmental impairment	2.74 (1.02, 7.37)	2.98 (0.99, 8.98)
Severe neurodevelopmental impairment	2.69 (1.13, 6.44)	2.61 (1.00, 6.83)
Bayley Cognition <85	2.23 (0.90, 5.58)	2.65 (0.92, 7.59)
Bayley Language <85	2.14 (0.86, 5.32)	1.84 (0.68, 4.96)
Bayley Motor <85	2.50 (1.01, 6.21)	2.30 (0.87, 6.08)

- Bevacizumab is associated with higher rates of neurodevelopmental impairment.
- Further investigations on the long-term safety of anti-VEGF treatment for ROP are warranted.

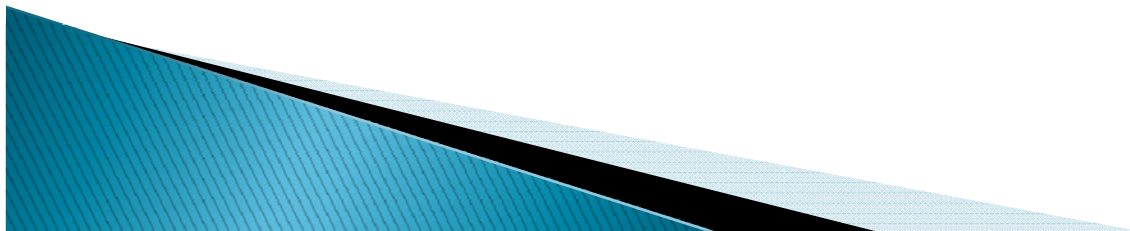
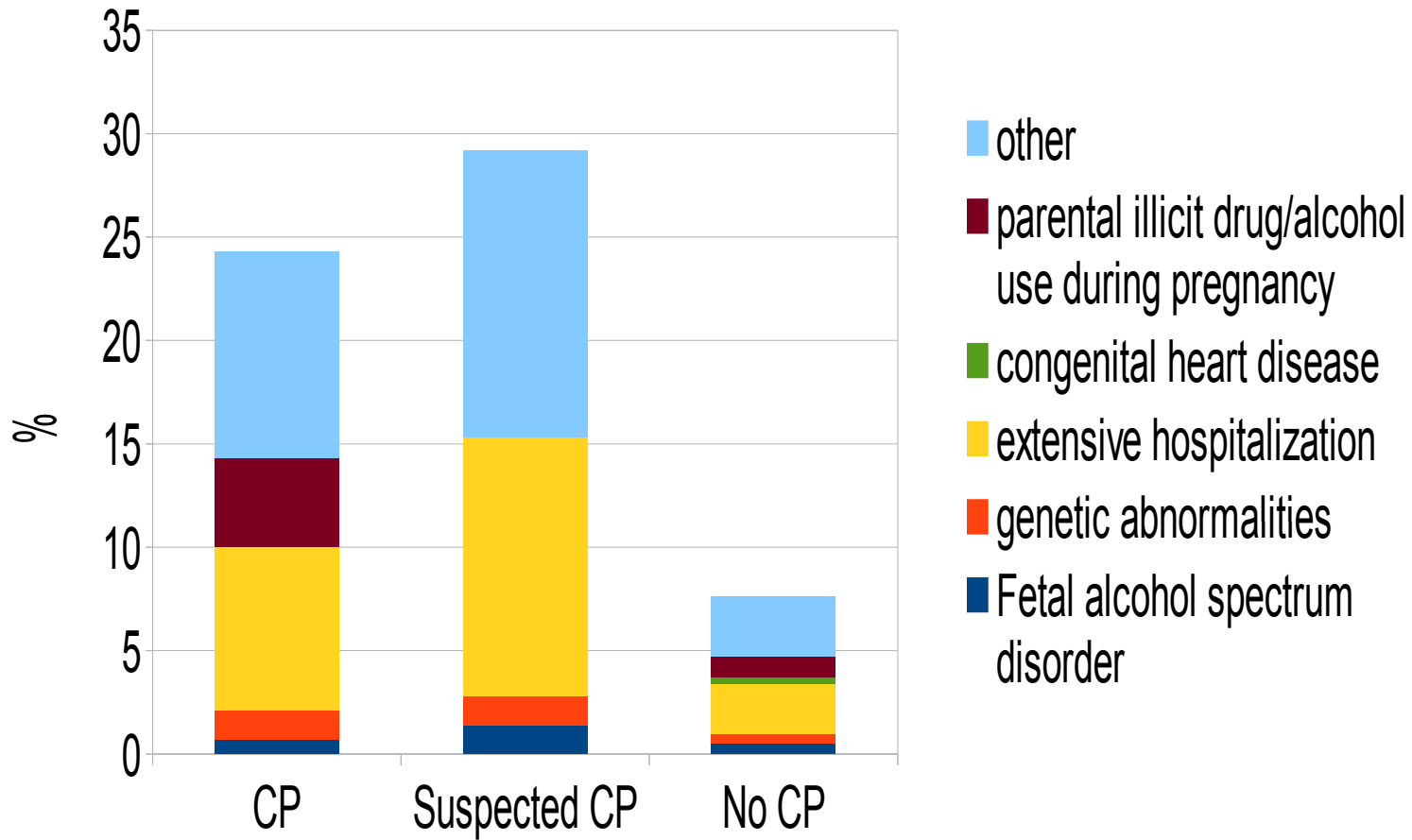


Preterm children with suspected cerebral palsy at 18 months corrected age in the Canadian Neonatal Follow-Up Network

J Gillone, A Synnes, A Majnemer, A Lodha, D Creighton, D Moddemann

	CP (6.8%)	Suspected CP (3.5%)	No CP (89.7%)	P value
GA (wks), median (IQR)	26 (25-27)	27 (25-27)	27 (25-28)	<0.01
BWT, mean (sd)	908 (223)	929 (205)	943 (224)	0.18
Age (mos), mean (sd)	18.6 (1.5)	19.0 (1.4)	18.7 (1.5)	0.22

Fig: Other diagnoses that may affect development



	CP	Suspected CP	No CP	P value
Bilateral visual problem, n (%)	20 (31.8)	1 (5.6)	14 (5.7)	<0.01
Hearing aid/cochlear implant, n (%)	21 (15.0)	3 (4.2)	27 (1.5)	<0.01
Bayley III cognitive, mean (sd)	80.5 (16.9)	90.4 (20.1)	97.1 (13.6)	<0/01
Bayley III language, mean (sd)	78 (17.9)	84.4 (18.6)	90.4 (16.7)	<0.01
Bayley III motor, mean (sd)	67 (15.1)	80.7 (17.9)	93.5 (12.9)	<0.01

36% with suspected CP would not be identified using conventional definitions of impairment

Suspected CP group had more rehospitalisations ($p < 0.01$) than those with or without CP





Preterm Infant Journeys in a Canadian Regionalized Health Services Context

Ballantyne M, Sauve R, Creighton D, Saigal S, Asztalos E, Couture E, Vincer M, Majnemer A, Synnes A

- In Canada, NICU and Neonatal Follow-Up are regionalized services
- To determine distances from home to NICU, home to NFU and infant factors affecting attendance rates at Canadian NFU programs for infants < 29 weeks gestation born in 2010

	CNFUN Attendees (n=1002)	CNFUN Non-attendees (n=252)	p value
<i>Distance Factors</i>			
Distance to NICU (kms), mean(sd)	99 (243)	128 (285)	0.18
Inter-NICU Transports, n (%)	170 (17)	43(17)	0.97
<i>Infant Factors</i>			
Gestational Age (wks), mean (sd)	26.4 (1.3)	26.7 (1.2)	0.01
SNAP-II score, median (IQR)	14 (8, 21)	9 (0, 14)	<0.01
Birth weight in grams, mean (sd)	945 (227)	1010 (246)	<0.01
BPD (36 weeks CA), n (%)	463(46)	81(33)	<0.01
ROP (grade 3 or 4) n (%)	118 (15)	13 (7)	0.01
NEC (surgical) n (%)	63 (6)	15 (6)	0.92
IVH (grade 3 or 4) n (%)	149 (15)	21 (10)	0.03

- Families of preterm infants, on average, travel considerable distances to access health services
- Attendance at NFU was associated with infant factors rather than travel distance.



Short- and long-term outcomes of neonatal gram-negative sepsis in Canadian NICUs

MR Derynck, MD¹, K Dow, MD¹, A Synnes, MD², PT Church, MD³, EN Kelly, MB, Bch^{4,5}, J Levenbach, PhD⁵, V Shah, MD^{4,5}

- Early-onset sepsis (<48 hours) and late-onset sepsis (>48 hours), affecting 1.5-2.2% and 24.4-31.7% of neonates in Canadian NICUs
- The prevalence of gram-negative sepsis (GNS) is increasing
- **To compare short- and long-term outcomes of neonates with early-onset and late-onset GNS to those without sepsis in Canadian NICUs**
- EOS is not associated with increased neonatal morbidities
- LOS is associated with an increased incidence of NEC OR 3.81 (2.14, 6.79)
- There is a difference in microbiological etiology of EOS and LOS

Adjusted odds ratios of neurodevelopmental outcomes at 18-21 months of age in relation to gram-negative sepsis

Outcome	EOS (<48 hours) N=29	LOS (>48 hours) N=171
Neurodevelopmental Impairment*	1.73 (0.69, 4.30)	1.02 (0.70, 1.49)
Severe Neurodevelopmental Impairment [†]	1.64 (0.72, 3.75)	1.05 (0.72, 1.53)

Diapositiva 39

- SDV1** Mount Sinai Hospital - also falls under University of Toronto so may be place that at the end?
Shah, Dr. Vibhuti; 09/04/2015
- SDV2** I have put the title in BOLD - IT STICKS OUT
YOU COULD DO THE SAME WITH THE NAMES AND AFFILIATIONS
Shah, Dr. Vibhuti; 09/04/2015
- SDV7** do we not provide baseline characteristics of the study population - did I miss it?
Shah, Dr. Vibhuti; 09/04/2015
- SDV8** should neonatal death be part of the exclusion criteria?

I do not remember how the data was analyzed
Shah, Dr. Vibhuti; 09/04/2015
- SDV9** word changed
Shah, Dr. Vibhuti; 09/04/2015
- SDV10** should it be 18-24 months??
Shah, Dr. Vibhuti; 09/04/2015
- SDV11** this is contradictory to what you say in introduction
gram negative sepsis is more common for E.coli .
Shah, Dr. Vibhuti; 09/04/2015
- SDV12** in the methodology you say 3 groups but no sepsis group is not shown

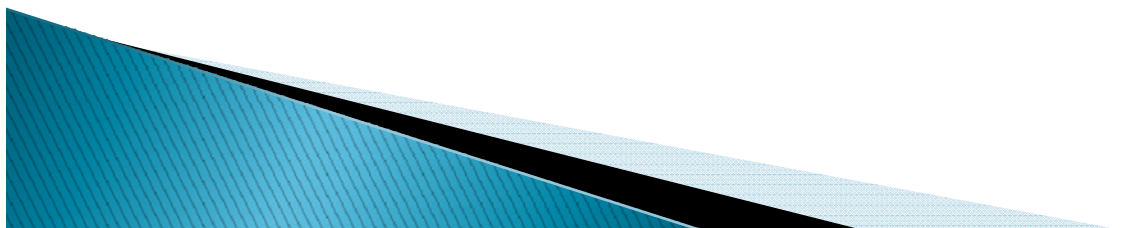
be clear in what you want to present and state the methods appropriately
Shah, Dr. Vibhuti; 09/04/2015
- SDV13** what specific associations you want to study?? be specific
Shah, Dr. Vibhuti; 09/04/2015
- SDV14** this is fine
Shah, Dr. Vibhuti; 09/04/2015

The Canadian Neonatal Follow-Up Network Cohort of Children Born Preterm: Outcomes at Three Years
 Alberta Girardi, PhD & Anne Synnes, MDCM

	Standard Mean (SD)	CNFUN Mean (SD)	Monitor Zone ¹	Below Cutoff ²
ASQ-3 Area				
Communication	51.88 (10.44)	48.10 (14.19)*	10.4%	14.0%
Gross Motor	54.68 (8.84)	48.76 (14.97)*	13.7%	18.5%
Fine Motor	47.07 (14.5)	41.73 (16.64)*	16.2%	12.3%
Problem Solving	51.97 (10.84)	47.68 (14.71)*	12.6%	17.7%
Personal-Social	52.82 (8.74)	49.05 (12.11)*	8.5%	14.6%

% Below Cut-off in One or More Areas of the ASQ-3 by Gestational Age

GA	22-23	24 wks	25 wks	26 wks	27 wks	28 wks
%	51.7	47.1	39.8	38.1	33.4	28.1

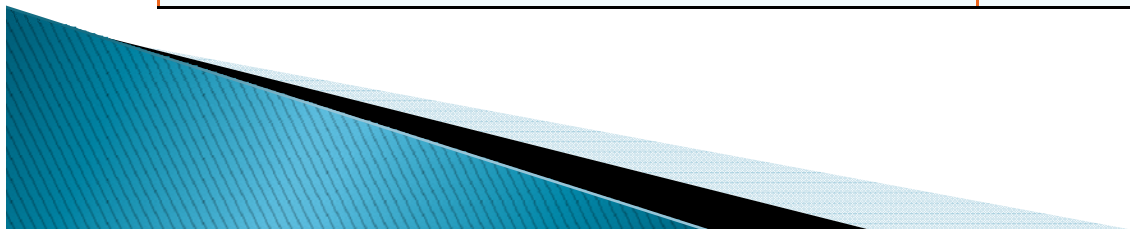


The Canadian Neonatal Follow-Up Network Cohort of Children Born Preterm: Outcomes at Three Years
 Alberta Girardi, PhD & Anne Synnes, MDCM

HSCS-PS Domain	% of CNFUN Sample with each HSCS-PS Score						Missing
	1	2	3	4	5	6	
1a. Seeing objects close	91.6	3.3	0.2	0.2	-	-	4.7
1b. Seeing object far away	84.4	4.2	0.6	0.3	-	-	10.5
2. Hearing (English version only)	89.8	1.3	2.3	0.5	0.4	0.1	5.7
3. Speaking	46.8	36.2	9.4	3.3	-	-	4.3
4. Getting Around	75.4	16.9	0.9	1.3	1.5	-	4.1
5. Using Hands and Fingers	87.9	5.8	1.5	0.7	-	-	4.1
6. Taking Care of Self	56.7	28.9	7.1	2.6	-	-	4.7
7. Feelings	93.5	1.7	0.2	-	-	-	4.6
8. Learning and Remembering	71.7	17.2	6.0	0.2	-	-	4.9
9. Thinking and Solving Problems	72.8	17.8	3.0	1.7	-	-	4.7
10. Pain and Discomfort	79.1	15.3	1.2	0.0	-	-	4.4
11. General Health	73.6	18.6	3.3	0.1	-	-	4.4
12. Behavior	80.3	3.1	1.6	0.4	-	-	4.6

The Canadian Neonatal Follow-Up Network Cohort of Children Born Preterm: Outcomes at Three Years
 Alberta Girardi, PhD & Anne Synnes, MDCM

	T-Score Mean (SD)	At or Above Cutoff ¹
BRIEF-P Domain		
Inhibit	51.0 (12.3)*	13.8%
Shift	48.6 (10.1)*	8.8%
Emotional Control	48.2 (10.3)*	8.3%
Working Memory	54.7 (13.5)*	23.0%
Plan/organize	49.7 (12.0)	10.2%
BRIEF-P Index Score		
Inhibitory Self-Control Index	49.8 (11.8)	13.0%
Flexibility Index	48.2 (10.5)*	8.1%
Emergent Metacognition Index	52.8 (13.5)*	18.9%
Global Executive Composite	50.8 (13.0)	14.7%



Inhaled steroid to prevent or treat bronchopulmonary dysplasia and neurodevelopmental outcomes.

Patterns and correlates of 'Health Resource Utilization' at 18 months CA.

The nature and incidence of major adverse neurodevelopmental outcomes at 18 months CA.

Preterm patient journeys – travels through the Canadian health care system.

Children with suspect cerebral palsy at 18–24 months CA.

Hypothermia in the extremely low GA infants: predictors and early neurodevelopmental outcomes.

Neurodevelopmental outcomes following intravitreal bevacizumab for retinopathy of prematurity.

Neurodevelopmental outcomes in infants born at the limits of viability.

Short- and long-term outcomes of infants with necrotizing enterocolitis: impact of laparotomy versus peritoneal drainage.

Developing a model to predict a positive neurodevelopmental outcome for the extremely preterm infant.


Bronchopulmonary dysplasia and long-term outcomes of very preterm infants.

Short- and long-term outcomes of neonatal gram-negative sepsis.

Early caffeine administration and long-term neurodevelopmental outcomes in infants born <29 weeks at 18–24 months CA.

Long-term neurodevelopmental outcomes following extensive cardiopulmonary resuscitation in the delivery room for infants born <29 weeks GA.

MgSO₄ administration for fetal neuroprotection.



The effect of 'Neurodevelopmental Impairment' definition on the incidence rates and prognosis among very preterm infants.

The effect of exposure to languages other than English in young children born preterm.

Sociodemographic characteristics of families of children born preterm.

Health and developmental outcomes of children born preterm, a 3-year CNFUN follow-up.

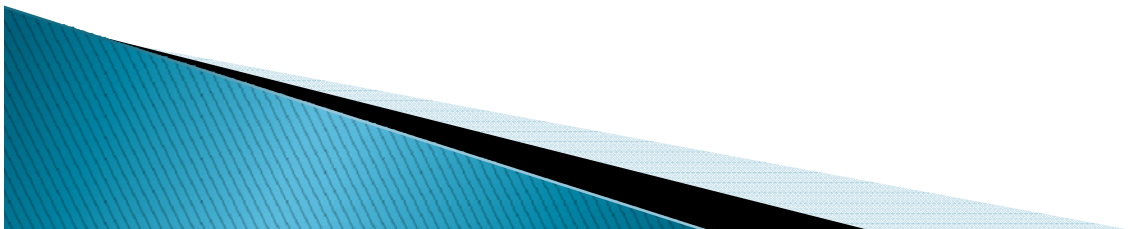
Neurodevelopmental outcome of infants with intraventricular hemorrhage (IVH).

Long-term neurodevelopmental outcomes of preterm infants who received room air, 100% oxygen, and intermediate oxygen during the start of delivery room resuscitation for infants born <29 weeks GA.

The neurodevelopmental outcomes of neonatal seizures in very preterm infants.

Long-term neurodevelopmental outcomes of extreme preterm infants treated with prophylactic indomethacin for prevention of intraventricular hemorrhage (IVH).

Maternal smoking and long-term neurodevelopmental outcomes in infants born <29 weeks GA.





The Canadian Neonatal Follow-Up Network (CNFUN) Cohort of Children

Born Preterm: Outcomes at Three Years
 Alberta Girardi, PhD & Anne Synnes, MDCM, on behalf of the
 Canadian Neonatal Follow-Up Network
 University of British Columbia



Background

- The Canadian Neonatal Follow-Up Network (CNFUN) is a collaboration of 26 neonatal and perinatal follow-up programs across Canada.
- A standardized assessment at 18 months corrected age and database of children born preterm at < 29 weeks gestation was implemented to evaluate their health, neurodevelopment and health resource use.
- 18 months can be too early to confirm neurodevelopmental status.
- Knowledge of long-term outcomes can assist parents in preparing for the challenges they may encounter through their children's development, and can identify areas of development that may benefit from early intervention.
- The aim of this study is to describe the function, neurodevelopment and executive function as assessed by questionnaire at 3 years corrected age in the same cohort.

Participants were caregivers of infants (n = 1376) born at less than 29 weeks gestational age between April 1, 2009 and September 30, 2011. Questionnaires were completed when the children were approximately 36 months of age, corrected for prematurity.

Sample Characteristics	
Infants	
Female	46.1%
Gestational age (med)	27 weeks
Weight (med)	910 grams
Caregivers	
Age (med)	31 years
Some college/university	69.2%
92.2%	
White	69.7%
86.1%	
Single caregiver	5.7%

Sociodemographic Questionnaire

Ages and Stages Questionnaire - 3rd Edition (ASQ-3)

- a comprehensive screening tool to identify developmental delays in young children

- lower scores indicate greater behavioral impairment
- Behavioral Inhibition of Executive Functioning - Preschool (BRIEF-P) - executive functioning is an umbrella term that describes cognitive processes involved in planning and organizing actions and emotions
- higher scores on the BRIEF-P indicate more difficulties with executive functioning

Health Status Classification System - Preschool (HSCS-PS)

- a multidimensional measure of overall health for use with preschool children
- items compare the child's functioning to other children of the same age, and assess the amount of assistance required to complete associated tasks
- higher scores indicate a greater need for assistance to function in that

Participating CNFUN Sites

Dr. A. A. BC Children's Hospital; Dr. T. Pillay, Victoria General Hospital; Dr. R. Sauvé, Alberta Children's Hospital, Foothills Medical Centre; Dr. A. Reichert, Glenora Rehabilitation Hospital; Dr. J. Bodani, Regina General Hospital; Dr. D. Modemann, Winnipeg Health Sciences Centre; St. Boniface General Hospital; Dr. C. Mussel, Windsor Regional Hospital; Dr. T. Daboval, Children's Hospital of Eastern Ontario; Dr. K. Dow, Hotel Dieu Hospital; Dr. D. Leo, Children's Hospital London Health Sciences Centre; Dr. E. Kelly, Mount Sinai Hospital; Dr. S. el Helou, Hamilton Health Sciences Centre; Dr. P. Church, Sunnybrook Health Sciences Centre; Dr. P. Riley, Montreal Children's Hospital, Royal Victoria Hospital; Dr. F. Ledford, Hôpital Sainte-Justine; Dr. C. Demers, Centre Hospitalier Universitaire de Sherbrooke; Dr. S. Belanger, Centre Hospitalier Universitaire de Québec; Dr. R. Canning, Moncton Hospital; Dr. L. Monterrosa, Saint John Regional Hospital; Dr. H. Makary, Dr. Everett Chalmers Hospital

Results

Developmental Outcomes (ASQ-3)

ASQ-3 Area	Mean (SD)	Standardized Mean (SD)	% Below	% Above
Communication	51.88 (10.44)	48.10 (14.19)*	10.4%	14.0%
Gross Motor	54.68 (8.84)	48.76 (14.97)*	13.7%	18.5%
Fine Motor	47.07 (14.5)	41.73 (16.64)*	16.2%	12.3%
Problem Solving	51.97 (10.84)	47.68 (14.71)*	12.6%	17.7%
Personal-Social	52.82 (8.74)	49.05 (12.11)*	8.5%	14.6%

* Mean score significantly different from standardization sample mean (p < .01)
 † Scores between 1.0 and 2.0 standard deviations below the standardization sample mean
 ‡ Scores less than 2.0 standard deviations below the standardization sample mean

% Below Cut-off in One or More Areas of the ASQ-3 by Gestational Age

Gestational Age	22-23 weeks	24 weeks	25 weeks	26 weeks	27 weeks	29 weeks
% Below Cut-off	51.7%	47.1%	39.8%	38.1%	33.4%	28.1%

Executive Functioning Outcomes (BRIEF-P)

BRIEF-P Domain	Mean (SD)	% Above
Inhibit	51.0 (12.3)*	13.8%
Shift	48.6 (10.1)*	8.8%
Emotional Control	48.2 (10.3)*	8.3%
Working Memory	54.7 (13.5)*	23.0%
Plan/organize	49.7 (12.0)	10.2%
BRIEF-P Index Score		
Inhibitory Self-Control Index	49.8 (11.8)	13.0%
Flexibility Index	48.2 (10.5)*	8.1%
Emergent Metacognition Index	52.8 (13.5)*	18.9%
Global Executive Composite	50.8 (13.0)	14.7%

* Mean T-score significantly different from standardization sample T-score of 50 (p < .01)
 † T-score ≥ 65 (at or greater than 1.5 standard deviations above the mean)

% At or Above Cut-off on the BRIEF-P Global Executive Composite by Gestational Age

Gestational Age	22-23 weeks	24 weeks	25 weeks	26 weeks	27 weeks	29 weeks
% Above Cut-off	21.0%	24.0%	15.8%	11.8%	13.9%	13.6%

Health Outcomes (HSCS-PS)

HSCS-PS Domain	% of CNFUN Sample with each HSCS-PS Score						Missing
	1	2	3	4	5	6	
1a. Seeing objects close	91.6	3.3	0.2	0.2	-	-	4.7
1b. Seeing object far away	84.4	4.2	0.6	0.3	-	-	10.5
2. Hearing (English version only)	89.8	1.3	2.3	0.5	0.4	0.1	5.7
3. Speaking	46.8	36.2	9.4	3.3	-	-	4.3
4. Getting Around	75.4	16.9	0.9	1.3	1.5	-	4.1
5. Using Hands and Fingers	87.9	5.8	1.5	0.7	-	-	4.1
6. Taking Care of Self	56.7	28.9	7.1	2.6	-	-	4.7
7. Feelings	93.5	1.7	0.2	-	-	-	4.6
8. Learning and Remembering	71.7	17.2	6.0	0.2	-	-	4.9
9. Thinking and Solving Problems	72.8	17.8	3.0	1.7	-	-	4.7
10. Pain and Discomfort	79.1	15.3	1.2	0.0	-	-	4.4
11. General Health	73.6	18.6	3.3	0.1	-	-	4.4
12. Behavior	80.3	3.1	1.6	0.4	-	-	4.6

Number of HSCS-PS Health Domains Affected (score of 3 or above in a domain)

Number of domains affected	Zero domains affected	1-2 domains affected	3 or more domains affected	Missing affected
% of CNFUN sample	72.6%	16.6%	7.0%	3.9%

Discussion / Implications

- Preterm children in Canada have lower scores in all developmental areas on the ASQ-3 and are more likely to need monitoring or intervention.
- Consistent with previous research, working memory is the domain of executive function most likely to be affected by prematurity (almost ¼ exceed the cutoff)
- Unexpectedly, the CNFUN cohort scored significantly lower in the inhibit and emotional control domains of executive functioning compared with norms.
- As gestational age (GA) decreased, a greater proportion of children exceeded clinical cutoffs on both the ASQ-3 and BRIEF-P, suggesting greater risk with decreasing GA
- The most frequently affected (score > 3) health domains on the HSCS-PS were speaking and self-care.

We acknowledge the CIHR team in Maternal-Infant Care (MiCare: CTP 87518) for providing organizational support to CNFUN and would like to thank the Ontario Ministry of Health and Long-Term Care for providing financial support to the CIHR MiCare Research Centre at Mount Sinai Hospital, Toronto, Ontario.