



Stanford
M E D I C I N E

Outcomes of infants born extraordinarily preterm

FDA Pediatric Advisory Committee
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Overview

- Survival and in-hospital morbidities
 - Eunice Kennedy Shriver NICHD Neonatal Research Network
- 2-year neurodevelopmental and functional outcomes
 - Eunice Kennedy Shriver NICHD Neonatal Research Network
- School age outcomes
 - Victoria Infant Collaborative Study Group (VICS)
 - Extremely Preterm Infants in Sweden Study (EXPRESS 1)

NICHD Neonatal Research Network

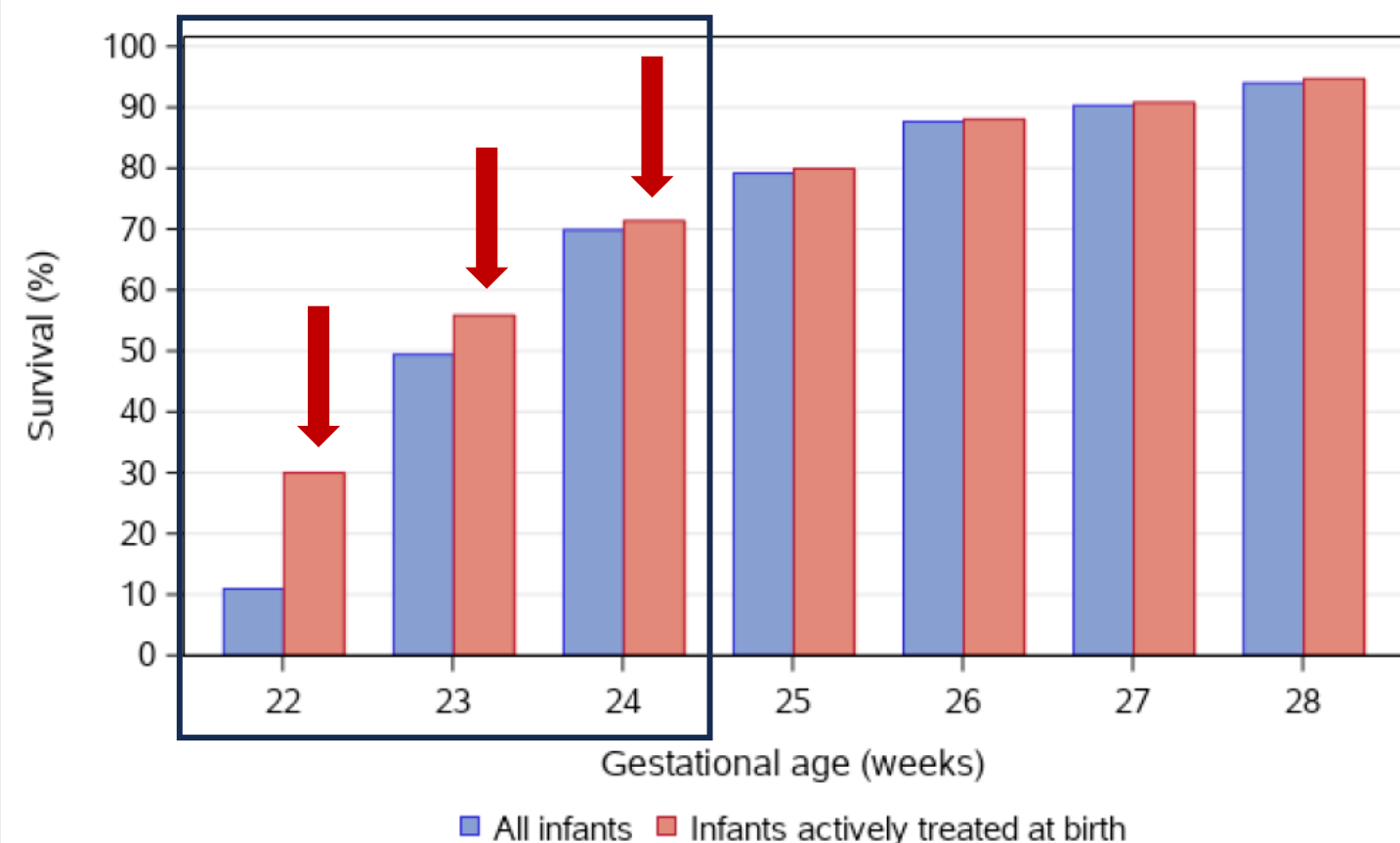
- **Generic Database** → delivery to discharge
 - Infants born weighing 401 g to 1000 g and/or born **between 22 + 0/7 and 28 + 6/7 weeks' gestation** at NRN hospitals.
- **Follow Up Study** → 22-26 months corrected age
 - Enrolled in GDB and **born at less than 27+0/7 weeks' gestation** or in NRN clinical trial.



Mortality, In-Hospital Morbidity, Care Practices, and 2-Year Outcomes for Extremely Preterm Infants in the US, 2013-2018

Born 2013-18 → NICU outcomes
Born 2013-16 → 2-year outcomes

Survival to discharge or 1 year if still hospitalized



No./total (%), by gestational age, in weeks

2013-2018

22

23

24

All infants

No.

550

1083

1398

Infants actively treated at birth^d

No.

201

958

1369



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In-hospital morbidities among infants surviving > 12 hours

Variables ^a	No./total (%), by gestational age in weeks ^b		
	2013-2018		
	22 (n = 159)	23 (n = 856)	24 (n = 1298)
Cranial sonogram within 28 d	136/159 (85.5)	819/855 (95.8)	1251/1298 (96.4)
Intracranial hemorrhage grade III or IV ^k	52/136 (38.2)	298/819 (36.4)	308/1251 (24.6)
NEC stage ≥IIA ^l	19/159 (11.9)	130/854 (15.2)	150/1298 (11.6)
Surgery for NEC	12/159 (7.5)	78/854 (9.1)	82/1298 (6.3)
Length of hospitalization, median (IQR), d			
All patients	26 (7-142) [n = 159]	121 (18-156) [n = 856]	115 (82-148) [n = 1298]
Surviving infants only	156 (135-217) [n = 60]	143 (122-175) [n = 535]	127 (108-156) [n = 972]

	22	23	24
Infants surviving to 36 wk postmenstrual age ^m	64	559	1015
Evaluation for BPD			
Oxygen use at 36 wk ⁿ	50/64 (78.1)	470/557 (84.4)	769/1009 (76.2)
Mode of support at 36 wk ^o			
No BPD	6/64 (9.4)	46/553 (8.3)	145/984 (14.7)
Grade 1	9/64 (14.1)	198/553 (35.8)	358/984 (36.4)
Grade 2	36/64 (56.3)	209/553 (37.8)	316/984 (32.1)
Grade 3	13/64 (20.3)	100/553 (18.1)	165/984 (16.8)



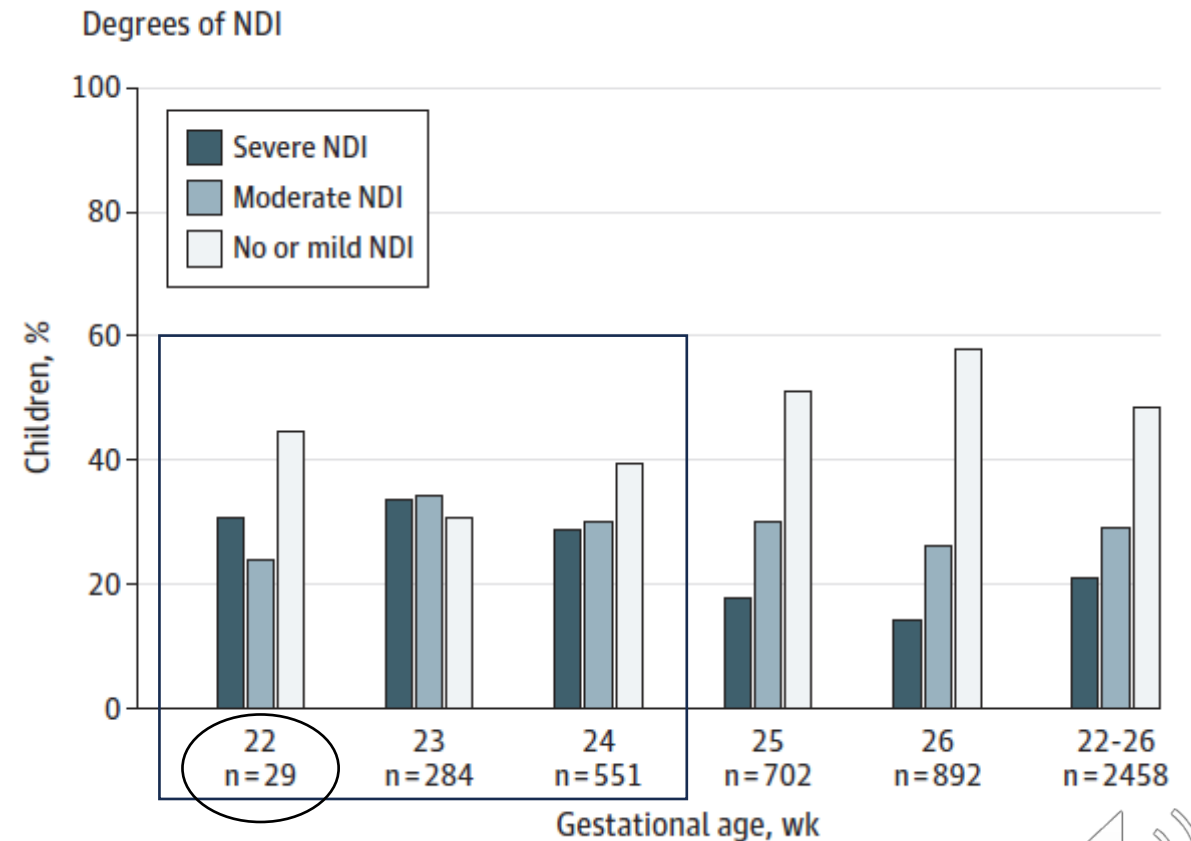
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Neurodevelopmental outcomes at 22-26 months corrected age

Neurodevelopmental impairment = “NDI”

- Composite outcome combining criteria and cut points from *several domains* including motor, cognitive/developmental, neurosensory.
- **Severe NDI** was defined as Bayley-III cognitive or motor composite score <70; or GMFCS level 4 or 5; or bilateral blindness or bilateral deafness.

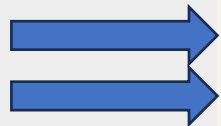


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Functional and resource needs at 22-26 months corrected age

Variables	No./total (%), by gestational age in weeks ^a		
	22 (n = 31)	23 (n = 292)	24 (n = 567)
Medical history and functional outcomes			
Had a hospitalization after discharge	20/31 (64.5)	171/290 (59.0)	311/567 (54.9)
No. of hospitalizations, median (IQR)	3 (2-4)	2 (1-3)	2 (1-3)
Oral motor skills			
Independently feeds self	20/31 (64.5)	208/290 (71.7)	436/567 (76.9)
Dependent oral feeding	5/31 (16.1)	30/290 (10.3)	50/567 (8.8)
Limited oral feeding	5/31 (16.1)	38/290 (13.1)	59/567 (10.4)
No oral feeding	1/31 (3.2)	14/290 (4.8)	22/567 (3.9)



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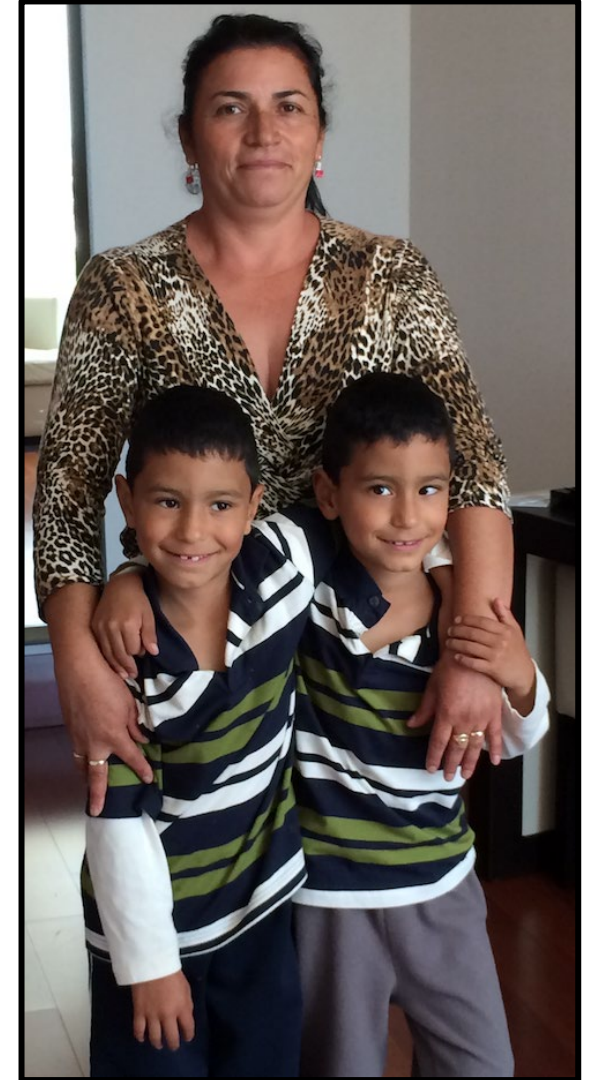
Variables	No./total (%), by gestational age in weeks ^a		
	22 (n = 31)	23 (n = 292)	24 (n = 567)
Current medical equipment			
Oxygen	3/31 (9.7)	33/290 (11.4)	33/567 (5.8)
Ventilator or continuous positive airway pressure	0/31 (0.0)	9/290 (3.1)	10/567 (1.8)
Gastrostomy or other tube feeding	6/31 (19.4)	52/290 (17.9)	81/567 (14.3)
Tracheostomy	1/31 (3.2)	19/290 (6.6)	29/567 (5.1)
Mobility aids/supportive equipment			
Adapted stroller or wheelchair	1/31 (3.2)	16/290 (5.5)	24/566 (4.2)
Braces/orthotics	7/31 (22.6)	60/290 (20.7)	88/566 (15.5)
Walker	4/31 (12.9)	24/290 (8.3)	23/566 (4.1)
Stander	1/31 (3.2)	10/290 (3.4)	14/566 (2.5)
Corner chair or other adaptive seat	1/31 (3.2)	9/290 (3.1)	7/566 (1.2)
Any (≥1) of above	10/31 (32.3)	77/290 (26.6)	103/566 (18.2)
Multiple (≥2) of above	3/31 (9.7)	32/290 (11.0)	32/566 (5.7)



School Age Follow-Up (and beyond) for < 24 weeks' EGA

Challenges

- Lag time for cohorts → birth year to follow through.
- Changes in approach to care over time → may not be reflective of contemporary birth cohort.
- Relatively few children born 22 or 23 weeks' EGA currently represented.



Changes in long-term prognosis with increasing postnatal survival and the occurrence of postnatal morbidities in extremely preterm infants offered intensive care: a prospective observational study

Lancet Child Adolesc Health 2018

*Jeanie L Y Cheong, Katherine J Lee, Rosemarie A Boland, Alicia J Spittle, Gillian F Opie, Alice C Burnett, Leah M Hickey, Gehan Roberts, Peter J Anderson, Lex W Doyle, for the Victorian Infant Collaborative Study Group**

Outcomes at 8 years for children born 22+0 through 27+6 weeks GA across 3 cohorts in Victoria

Australia:

- 1991–92
- 1997
- 2005



VICS: Outcomes at 8 years by GA – 3 birth cohorts (1991-92, 1997, 2005)

Mutually exclusive outcomes by EGA and total

	N	Death	Major disability	No major disability	Not assessed
22 weeks	7	5 (71%)	1 (14%)	0 (0%)	1 (14%)
23 weeks	44	23 (52%)	6 (14%)	14 (32%)	1 (2%)
24 weeks	99	44 (44%)	11 (11%)	41 (41%)	3 (3%)
25 weeks	179	57 (32%)	22 (12%)	94 (53%)	6 (3%)
26 weeks	205	41 (20%)	27 (13%)	126 (61%)	11 (5%)
27 weeks	217	35 (16%)	19 (9%)	138 (64%)	25 (12%)
Total	751	205 (27%)	86 (11%)	413 (55%)	47 (6%)

Data are n (%). Gestational ages are in completed weeks.

Table 3: Outcomes at 8 years by gestational age at birth

Major disability among survivors

23 weeks – 29%

24 weeks – 20%

25 weeks – 18%

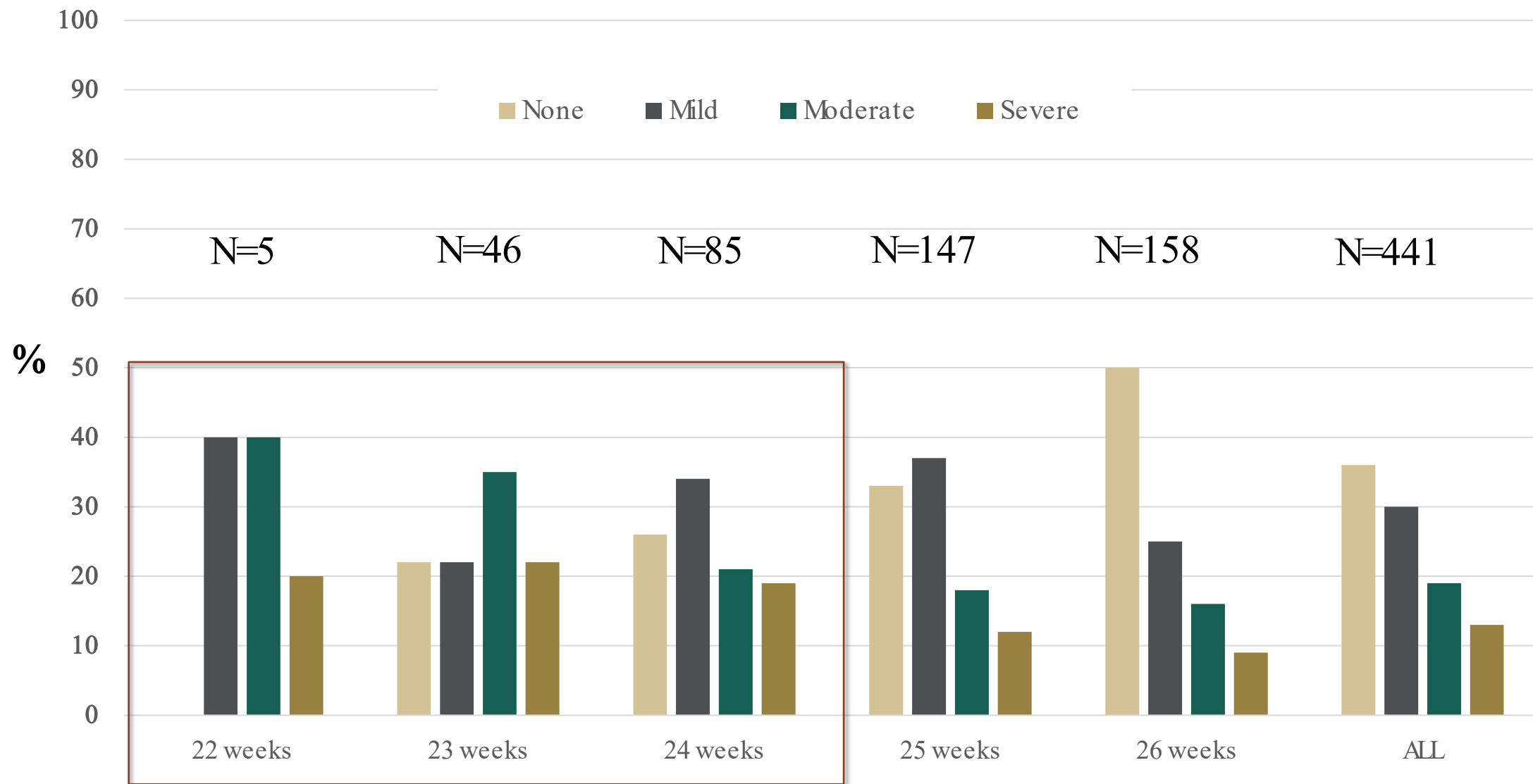
26 weeks – 17%

27 weeks – 10%



Neurodevelopmental Disability at 6.5 years

EXPRESS-1 cohort (birth years 2004-2007)



Predicting school age from toddlerhood??

Importance of longer-term outcomes

Table 5. Change in Classification of Overall Disability From 2.5 to 6.5 Years for Children Born Extremely Preterm and Assessed at Both Ages^a

Disability at 2.5 y Corrected Age	Disability at 6.5 y, No. (%) of Children				Total No.
	None	Mild	Moderate	Severe	
None	108 (58.4)	52 (28.1)	19 (10.3)	6 (3.2)	185
Mild	36 (27.1)	48 (36.1)	42 (31.6)	7 (5.3)	133
Moderate	12 (16.9)	27 (38.0)	17 (24.3)	14 (20.0)	70
Severe	1 (2.2)	4 (8.9)	11 (24.4)	29 (64.4)	45
Total	157 (36.3)	131 (30.3)	89 (20.6)	56 (12.9)	433

Only 47% remained in the same category →

- 21% moved to a better category, 32% moved to a worse category.



Importance of longer-term outcomes



