

Are the long-term outcomes for extremely preterm children improving?

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Outline

- Long-term outcomes
- Outcome across different eras
- Parental mental health
- Interventions

Very Preterm Outcomes

Sensory

Sensory diff
Visual impair
Hearing impair

Very Preterm Outcomes

Sensory

Motor

Sensory diff
Visual impair
Hearing impair

Cerebral Palsy
DCD

Very Preterm Outcomes

Sensory

Motor

Cognitive

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Visual impair
Hearing impair

Cerebral Palsy
DCD

↓ IQ
↓ Language
↓ Info processing
↓ Attention
↓ Memory
↓ EF

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↓ Maths

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↑ Behav probs
↑ Anxiety
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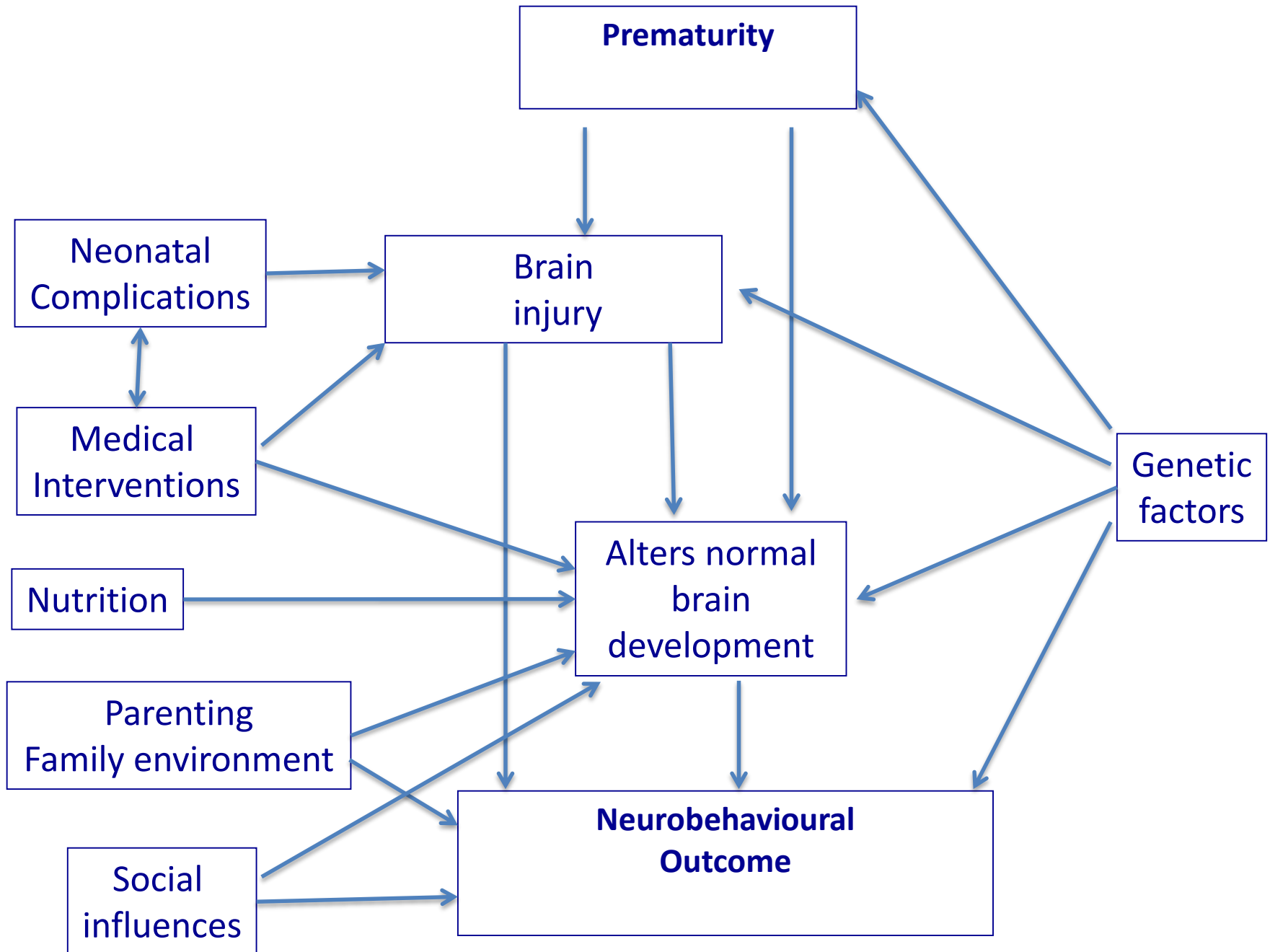
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Outcomes are variable



Are outcomes improving?

Victorian Infant Collaborative Study (VICS) Group

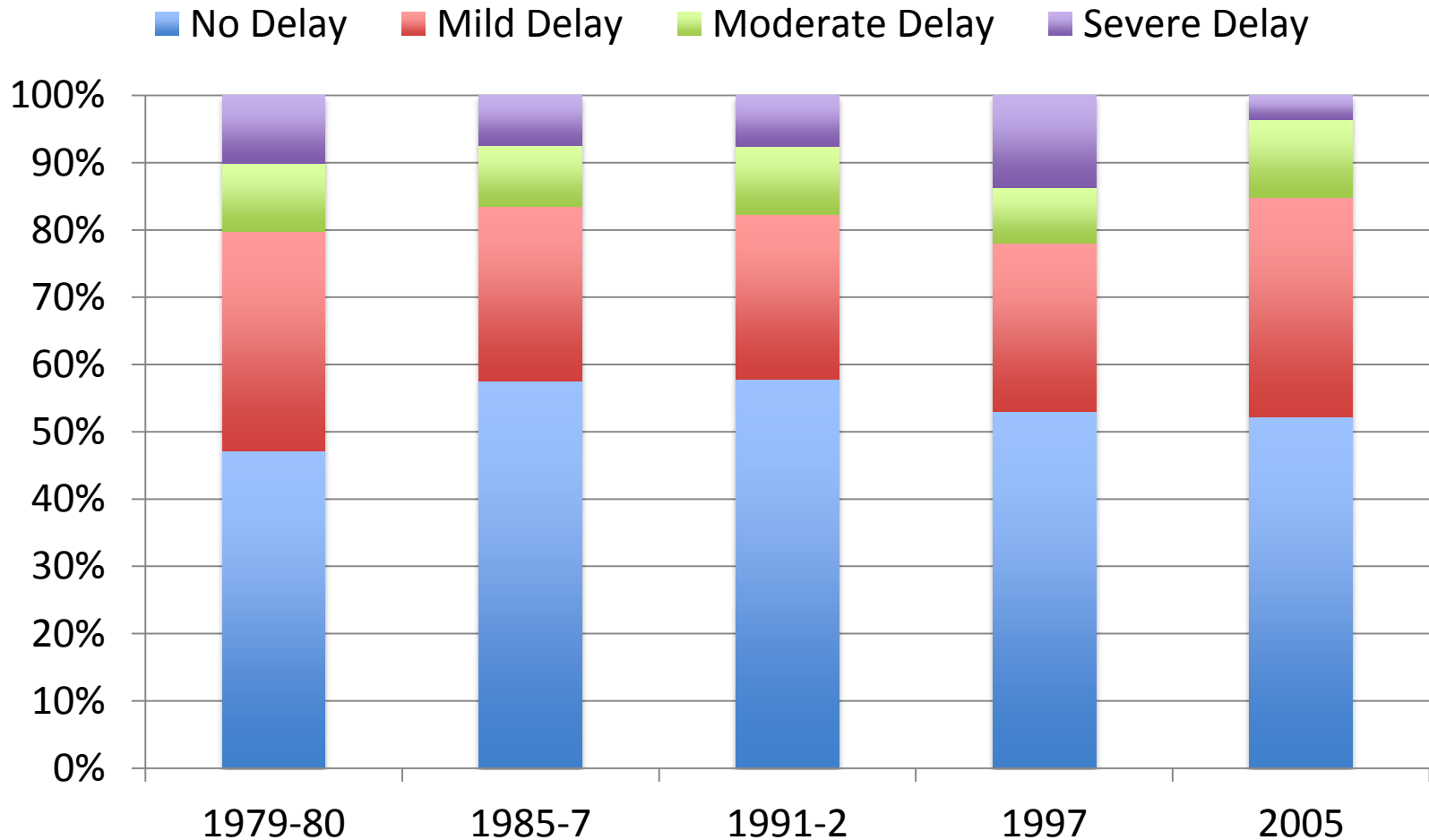


Jeanie Cheong, Peter Anderson, Alice Burnett, Catherine Callanan, Elizabeth Carse, Margaret P Charlton, Mary-Ann Davey, Noni Davis, Cinzia de Luca, Lex Doyle, Julianne Duff, Marie Hayes, Leah Hickey, Esther Hutchinson, Elaine Kelly, Marion McDonald, Gillian Opie, Gehan Roberts, Michael Stewart, Andrew Watkins, Amanda Williamson, Heather Woods.

Royal Women's Hospital, Mercy Hospital for Women, Monash Medical Centre, Royal Children's Hospital, Newborn Emergency Transport Service, Victorian Perinatal Data Collection Unit, Murdoch Childrens Research Institute, and University of Melbourne, Melbourne, Australia



Cognitive delay of ELBW infants at 2 years - Victoria



Objective

- To compare cognitive and academic outcomes in extremely preterm (EP: <28 weeks' GA) 8-year-olds born in Victoria, Australia in 1991-2, 1997, and 2005.

Geographic Cohorts

- All infants born <28 weeks' GA in state of Victoria, Australia
- Three eras
 - 1991 – 92
 - 1997
 - 2005
- Control groups
 - Term-born normal birth weight control infants
 - Matched for
 - expected date of birth
 - sex
 - mother's health insurance status
 - Country of birth (English the primary language or other)

8-year Assessments

- General Intelligence
 - 1991-92: Wechsler Intelligence Scale for Children, 3rd edition (WISC-III)
 - 1997: Wechsler Intelligence Scale for Children, 4th edition (WISC-IV)
 - 2005: Differential Ability Scales, 2nd edition (DAS-II)
- Academic Achievement (word reading, spelling, mathematics)
 - 1991-2: Wide Range Achievement Test, 3rd edition (WRAT-3)
 - 1997: Wide Range Achievement Test, 3rd edition (WRAT-3)
 - 2005: Wide Range Achievement Test, 4th edition (WRAT-4)
- All scales have a mean of 100 and SD 15
- Impairment based on control group distribution

EP Cohorts

	1991-92	1997	2005
Livebirths, n (%)	428	217	270
Survived to 8 years, n (% of livebirths)	225 (53)	151 (70)	170 (63)
Assessed at 8 years, n (%)	211 (94)	142 (94)	147 (86)
Corrected age at 8yr assessment, M (SD)	8.7 (0.3)	8.4 (0.5)	7.7 (0.4)

EP Cohorts

	1991-92 n=211	1997 n=142	2005 n=147
Outborn, n (%)	18 (9)	7 (5)	19 (13)
Antenatal corticosteroids, n (%)	150 (71)	126/140 (90)	125/146 (86)
Multiple birth, n (%)	70 (33)	29 (20)	35 (24)
GA at birth (weeks), M (SD)	25.8 (1.1)	25.6 (1.2)	25.8 (1.2)
Birthweight (grams), M (SD)	887 (175)	820 (173)	867 (193)
BW Z score, M (SD)	-0.27 (0.87)	-0.53 (0.79)	-0.31 (0.84)
Male, n (%)	105 (50)	79 (56)	72 (49)
Exogenous surfactant, n (%)	89 (42%)	120 (85%)	127 (86%)
Grade 3 or 4 IVH, n (%)	17 (8)	5 (4)	13 (9)
Cystic PVL, n (%)	15 (7)	5 (4)	5 (3)
Necrotizing enterocolitis, n (%)	15 (7)	8 (6)	16 (11)
Postnatal corticosteroids, n (%)	86 (41)	65 (46)	32/146 (22)
BPD, n (%)	98 (46)	59/141 (42)	84 (57)
Surgery in the newborn period, n (%)	59 (28)	44 (31)	46 (31)

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Control cohorts

	1991-92	1997	2005
Recruited at birth, n	265	199	219
Survived to 8 years, n	262	199	218
Assessed at 8 years, n (%)	224 (85)	169 (85)	189 (87)
Corrected age at 8yr assessment, M (SD)	8.9 (0.4)	8.5 (0.3)	7.7 (0.5)
Gestational age at birth (weeks), M (SD)	39.2 (1.4)	39.3 (1.1)	39.5 (1.3)
Birthweight (grams), M(SD)	3404 (440)	3505 (455)	3586 (488)
Birthweight z-score, M(SD)	0.00 (0.88)	0.15 (0.91)	0.25 (0.91)
Male, n (%)	104 (46)	91 (54)	85 (45)

Socio-demographics

EP Cohorts	1991-92	1997	2005
Mother's age – years, mean (SD)	28.5 (5.8)	29.8 (5.9)	30.5 (5.6)
Lower maternal education, n (%)	107/206 (52)	71 (50)	64/144 (44)
Lower social class, n (%)	69/206 (33)	37/131 (28)	53 (36)
Only English spoken at home, n (%)	167/208 (80)	111 (78)	124/146 (85)
Control Cohorts	1991-92	1997	2005
Mother's age – years, mean (SD)	29.5 (5.0)	30.8 (5.2)	32.7 (5.6)
Lower maternal education, n (%)	82/217 (38)	49/168 (29)	40/188 (21)
Lower social class, n (%)	44/220 (20)	25/161 (16)	22 (12)
Only English spoken at home, n (%)	190/220 (86)	143 (85)	160/188 (85)

Socio-demographics

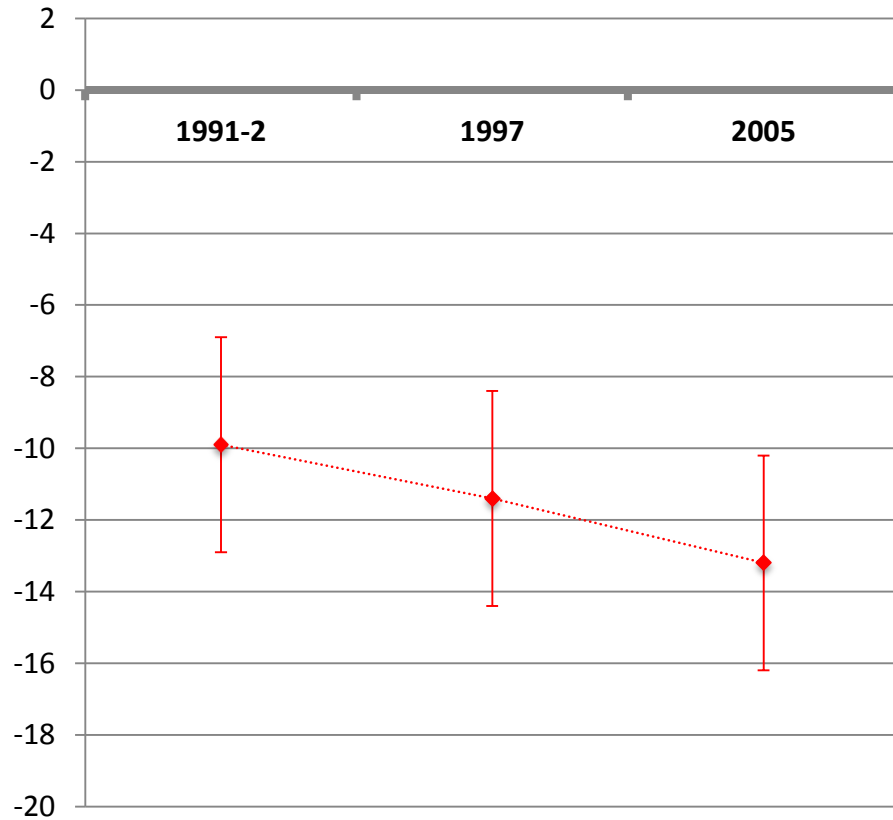
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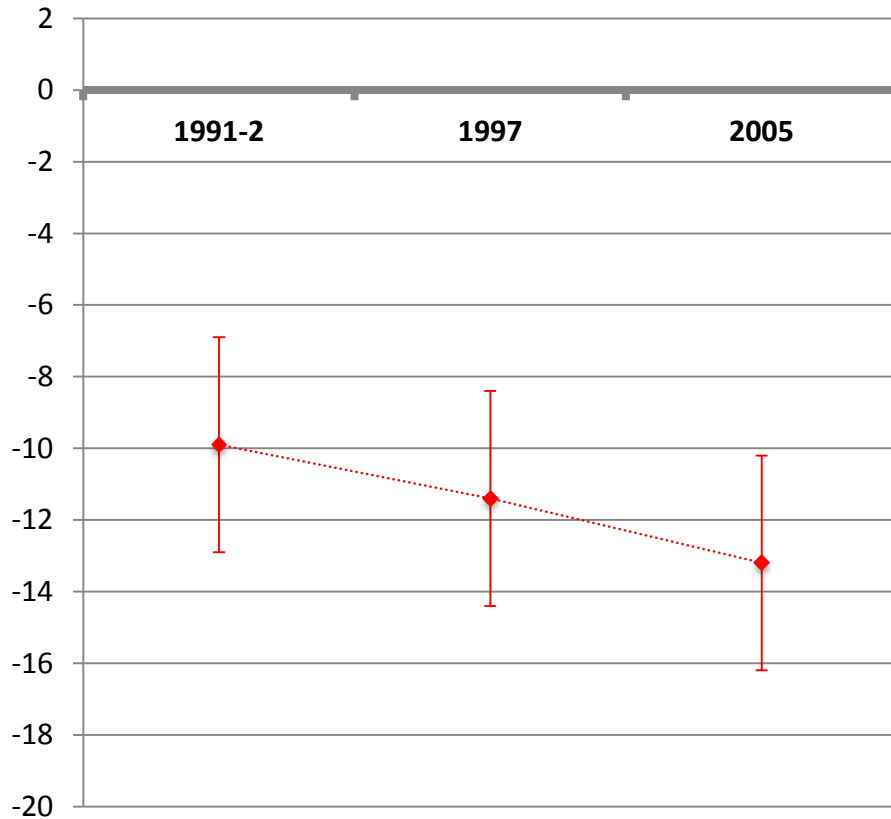
General Intelligence

Unadjusted Mean Differences

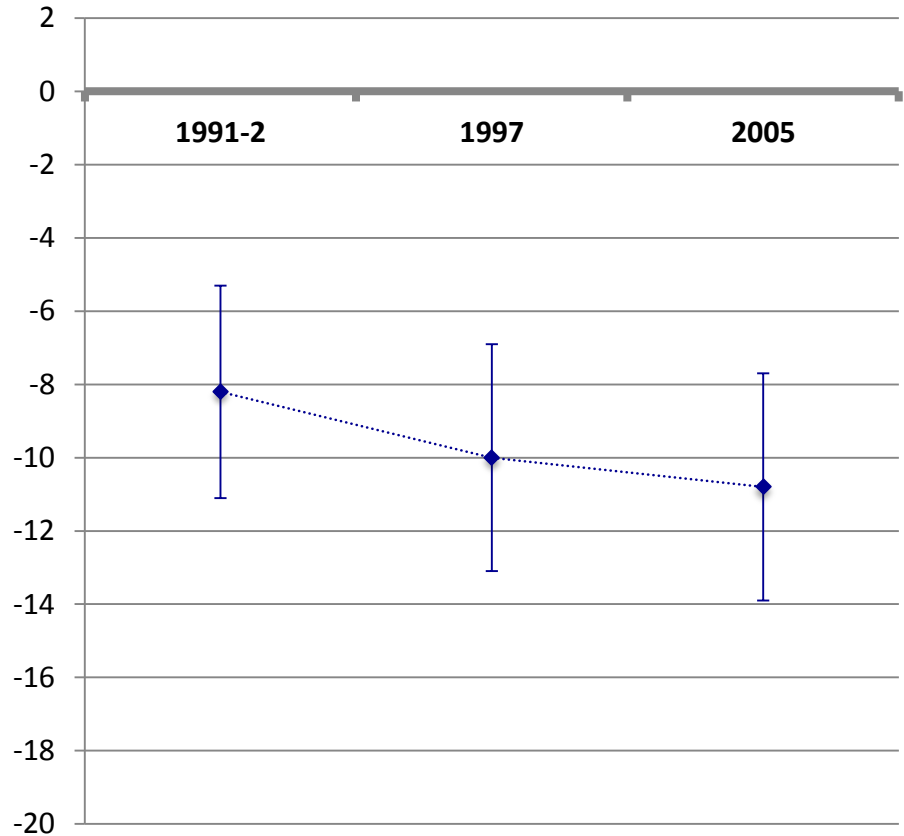


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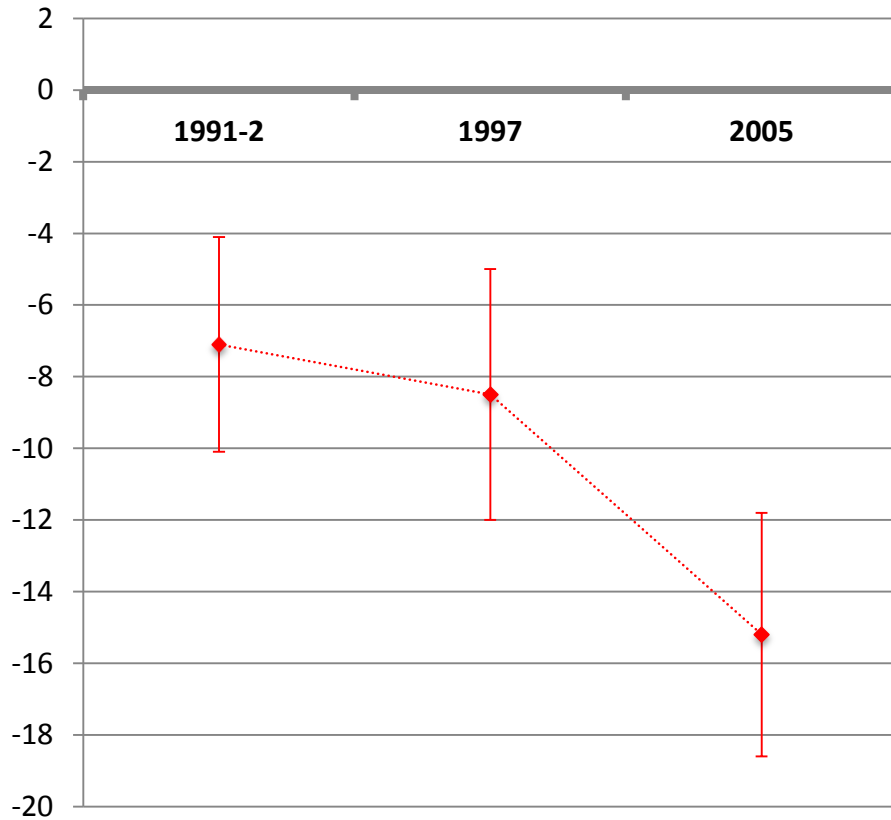
Adjusted Mean Differences



Adjusted for social demographic characteristics

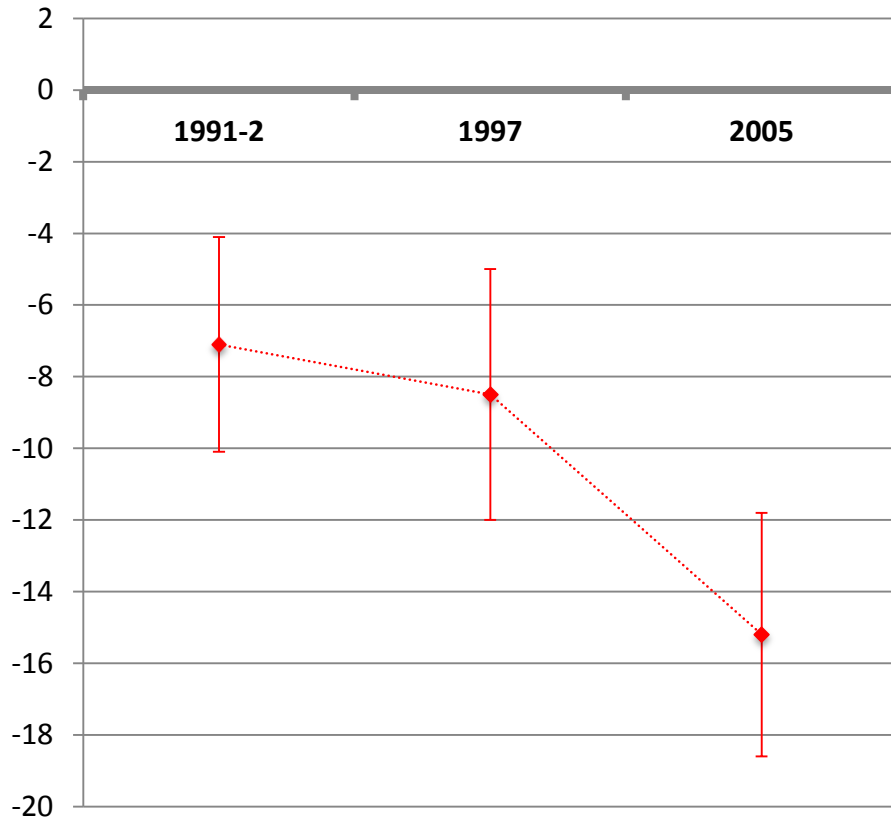
Reading

Unadjusted Mean Differences

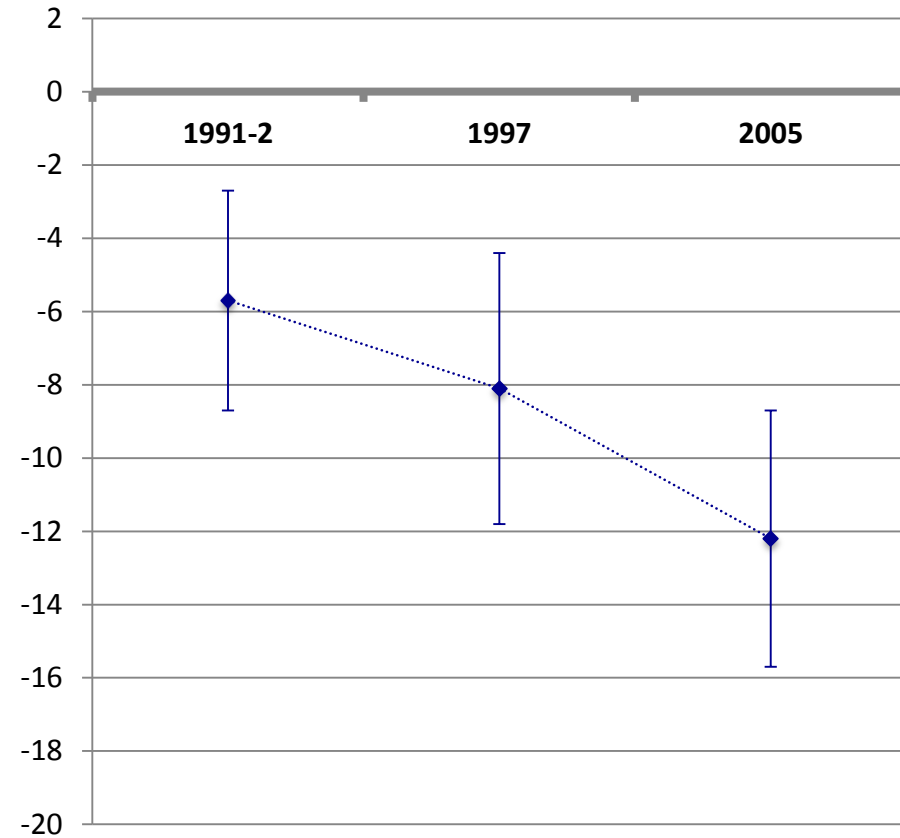


Reading

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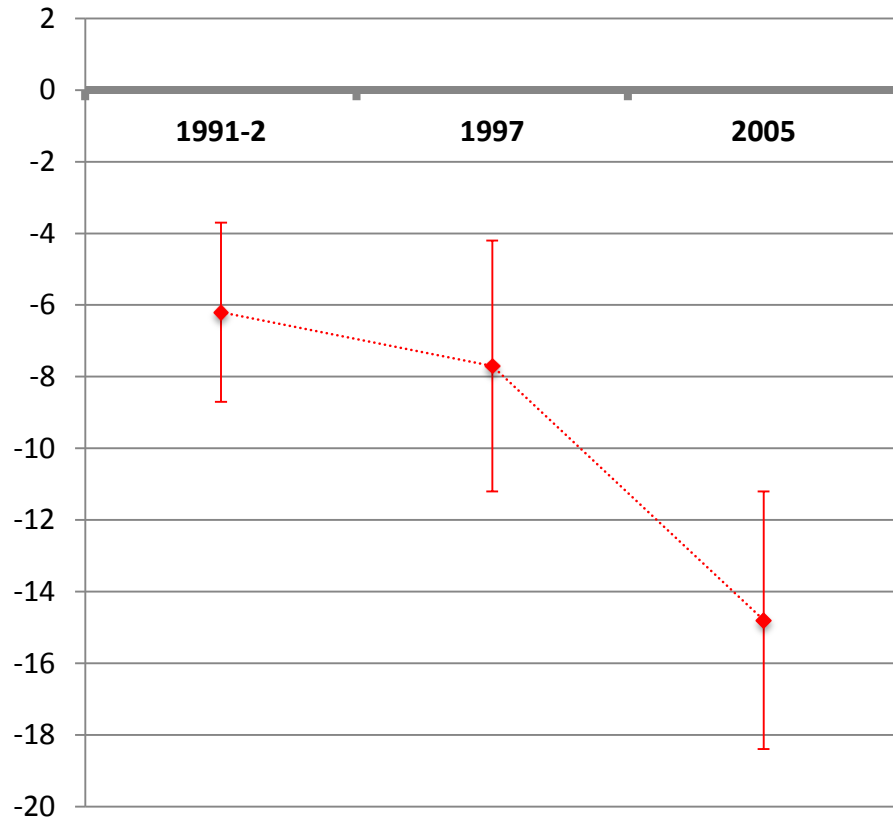
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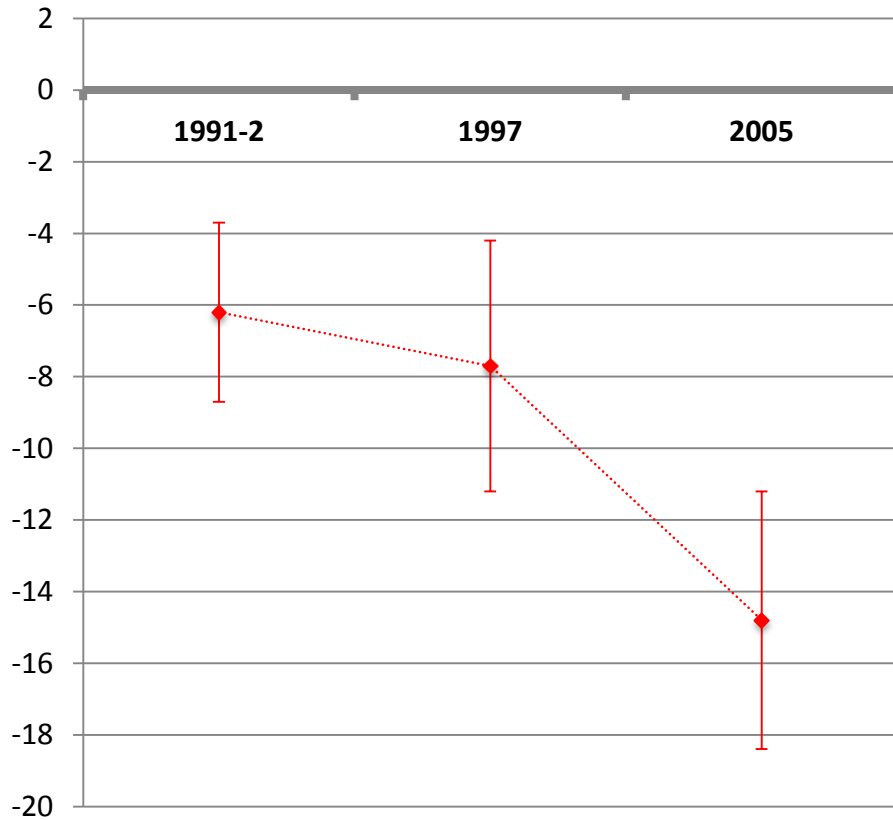
Spelling

Unadjusted Mean Differences

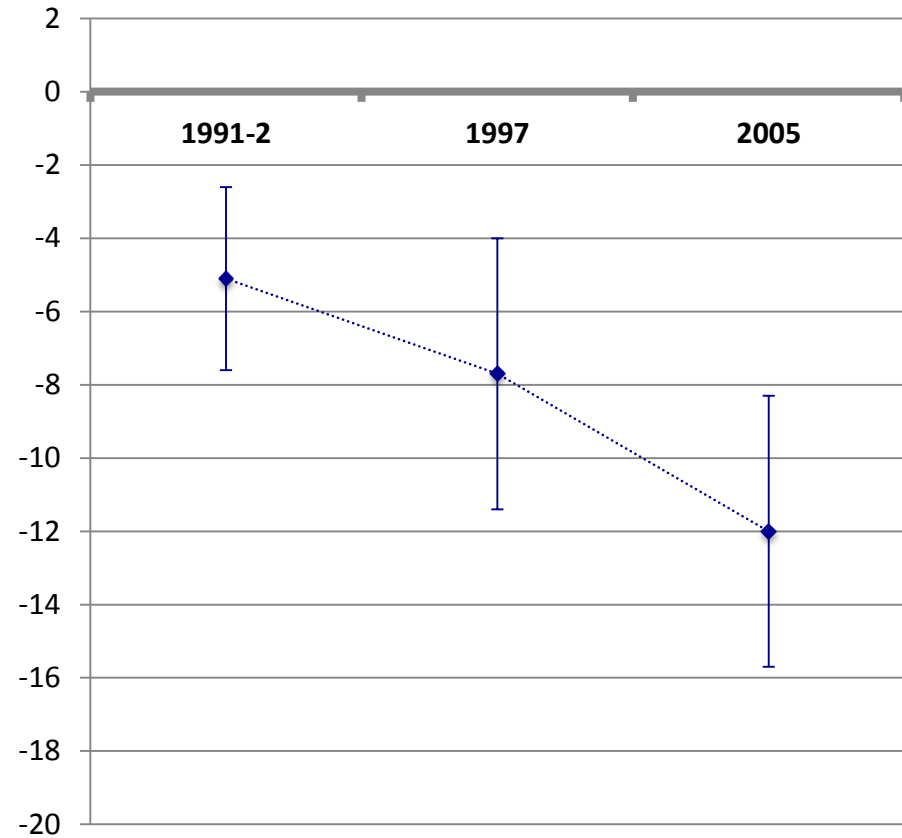


Spelling

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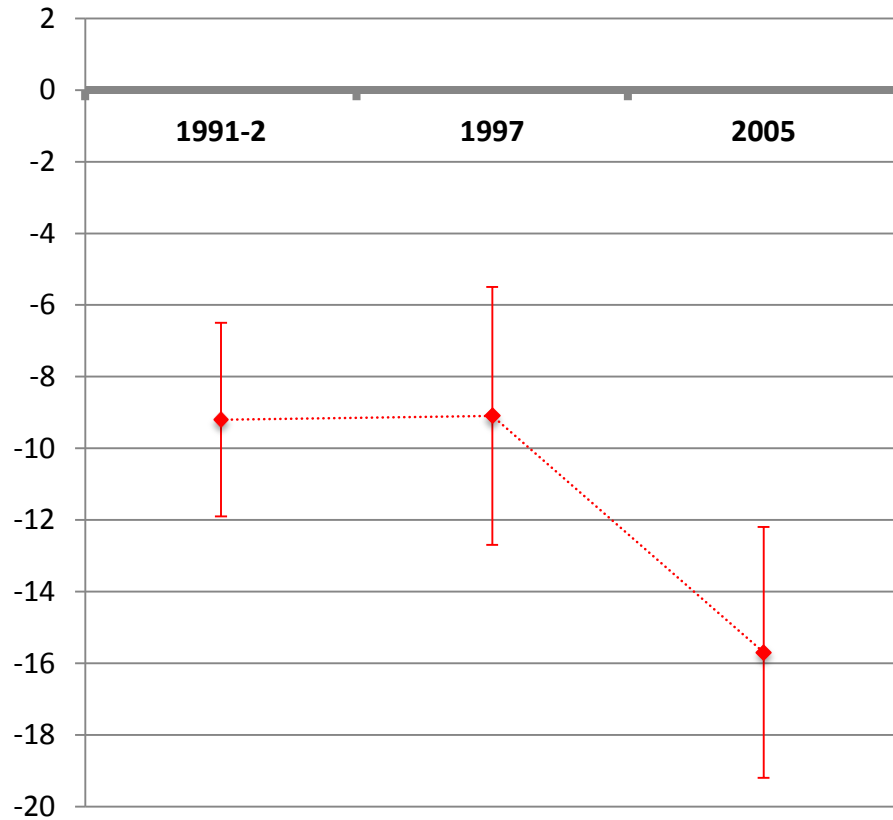
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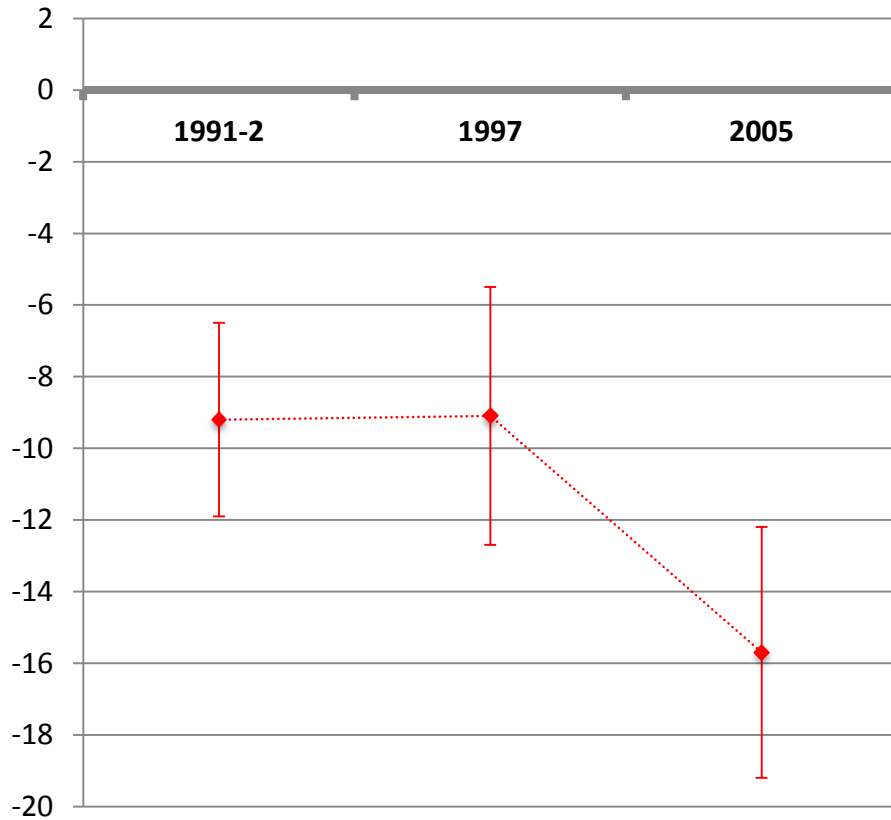
Mathematics

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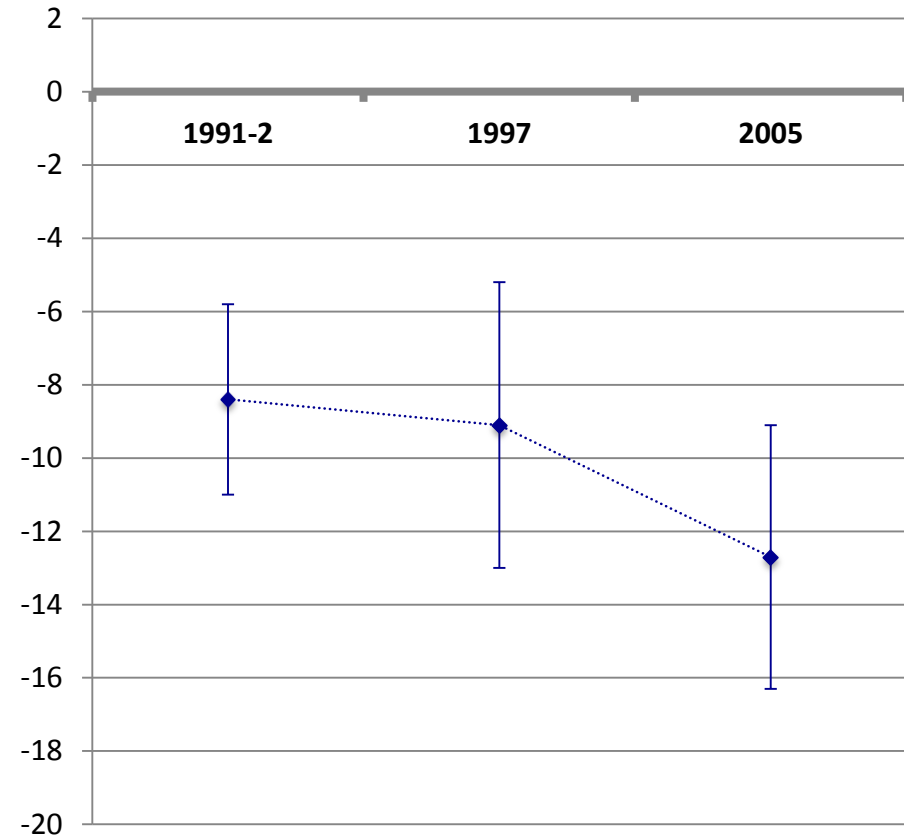


Mathematics

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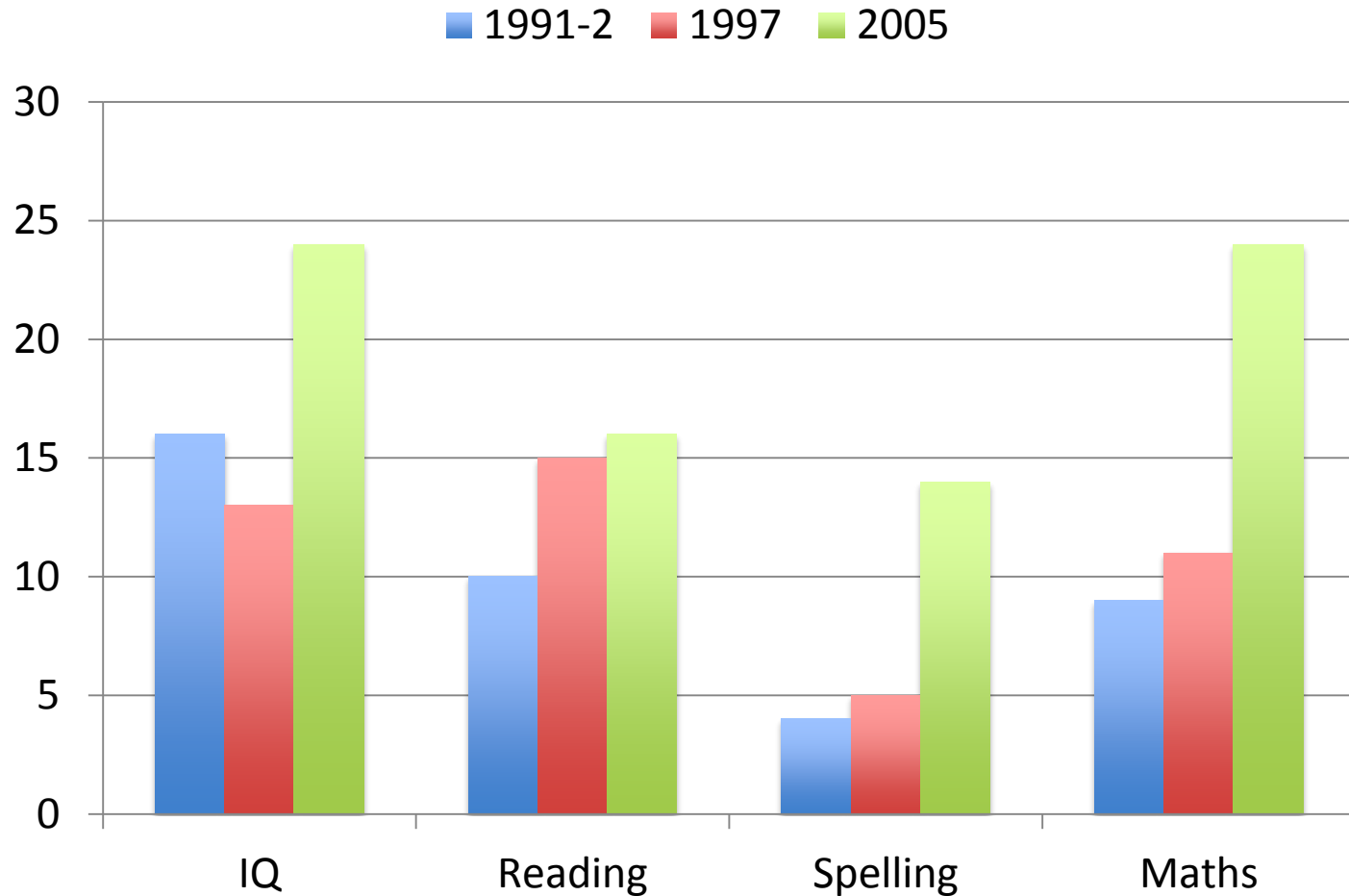


Adjusted Mean Differences



Adjusted for social demographic characteristics

Moderate-Severe Impairment (<-2SD)

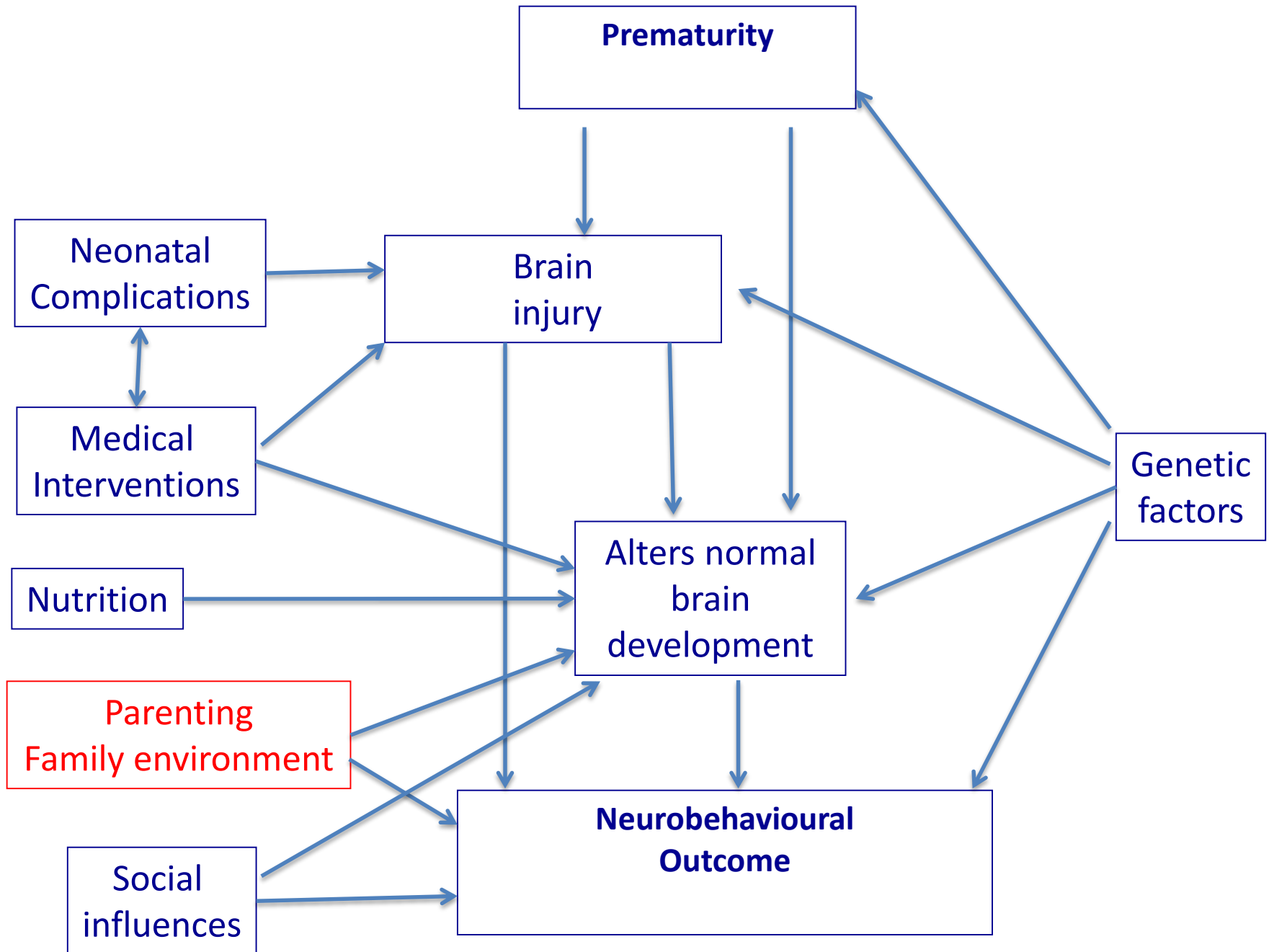


Summary

- School-aged cognitive and academic functioning have NOT improved during the post-surfactant era
- In contrast to 1991-2 cohort, 2005 cohort had greater rates of moderate-severe impairments
 - General intelligence
 - Reading
 - Spelling
 - Maths

Considerations

- 2005 cohort was assessed at an earlier age
 - Age at assessment included as a confounder
- 2005 control group was slightly more educated and of higher social class
 - Maternal education & social class included as confounders
- Different measures of general intelligence
 - Rate of impairment based on control distribution
 - Measure of academic achievement remained constant



Psychological Distress

Symptoms of:

- Anxiety
- Depression
- Acute stress and post-traumatic stress

VIBeS 2 study

- Longitudinal study including assessment of neurobehaviour, brain imaging and **parental mental health**
- Recruited 150 very preterm infants and 151 term born infants and their families between January 2011 and December 2013



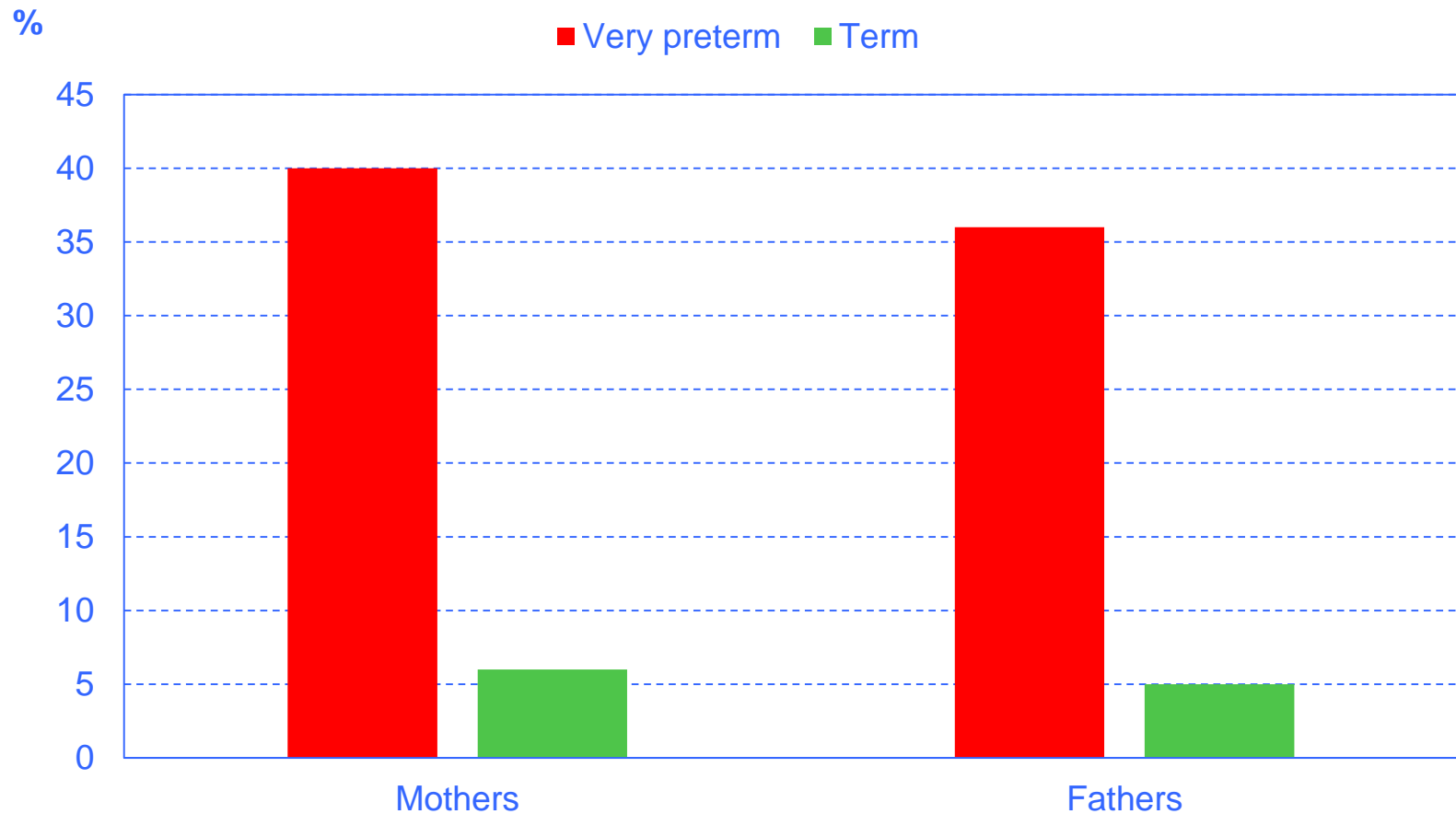
Assessment schedule

	28 w	30 w	32 w	34 w	36 w	38 w	40 w	3m	6m	12 m	18 m	24 m	36 m
Depression	√	√	√	√	√	√	√√	√√	√√	√√	√√	√√	√√
Anxiety	√	√	√	√	√	√	√√	√√	√√	√√	√√	√√	√√

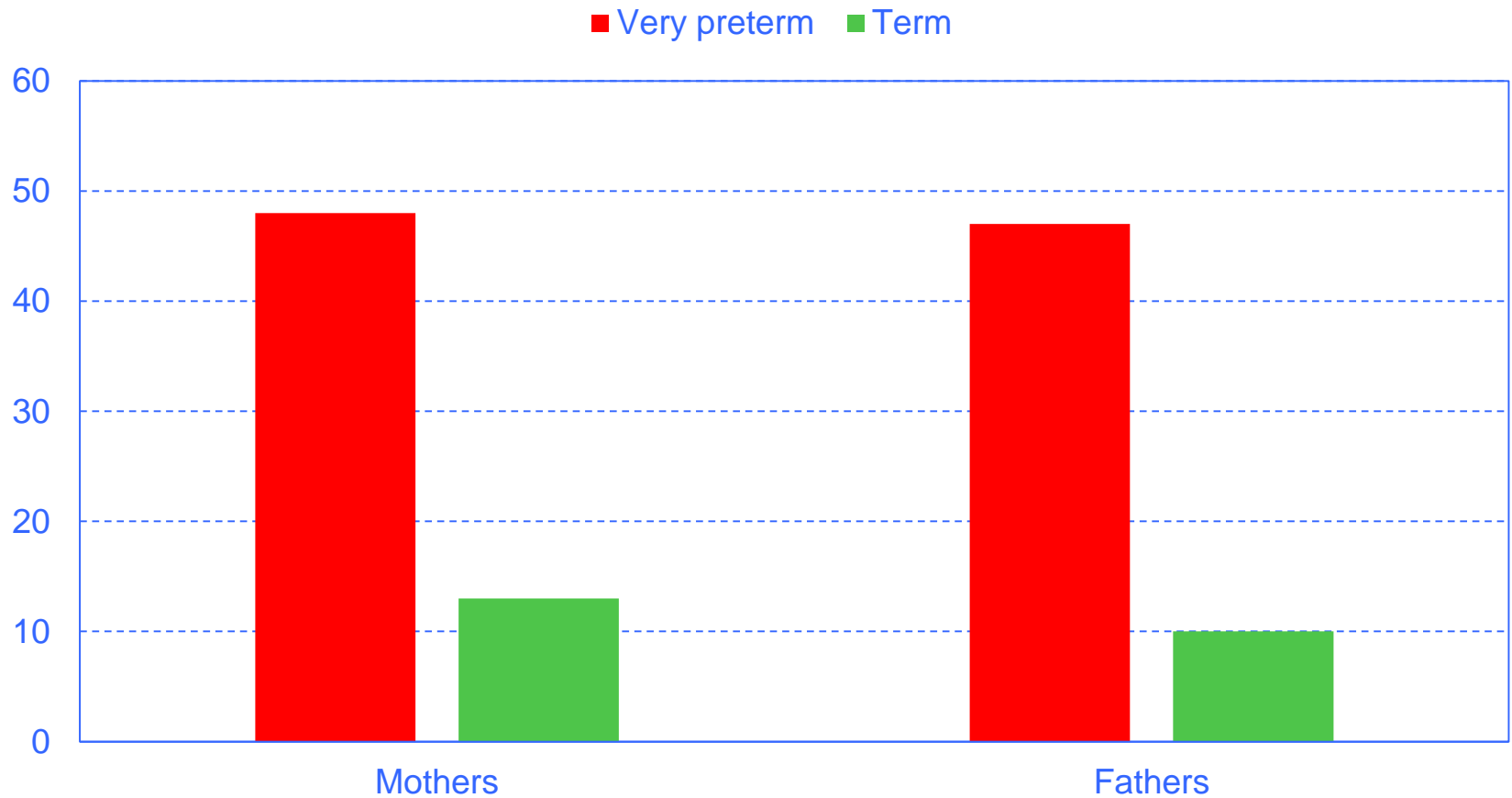
√ = VPT only, √√ = VPT and FT

All time points corrected for prematurity

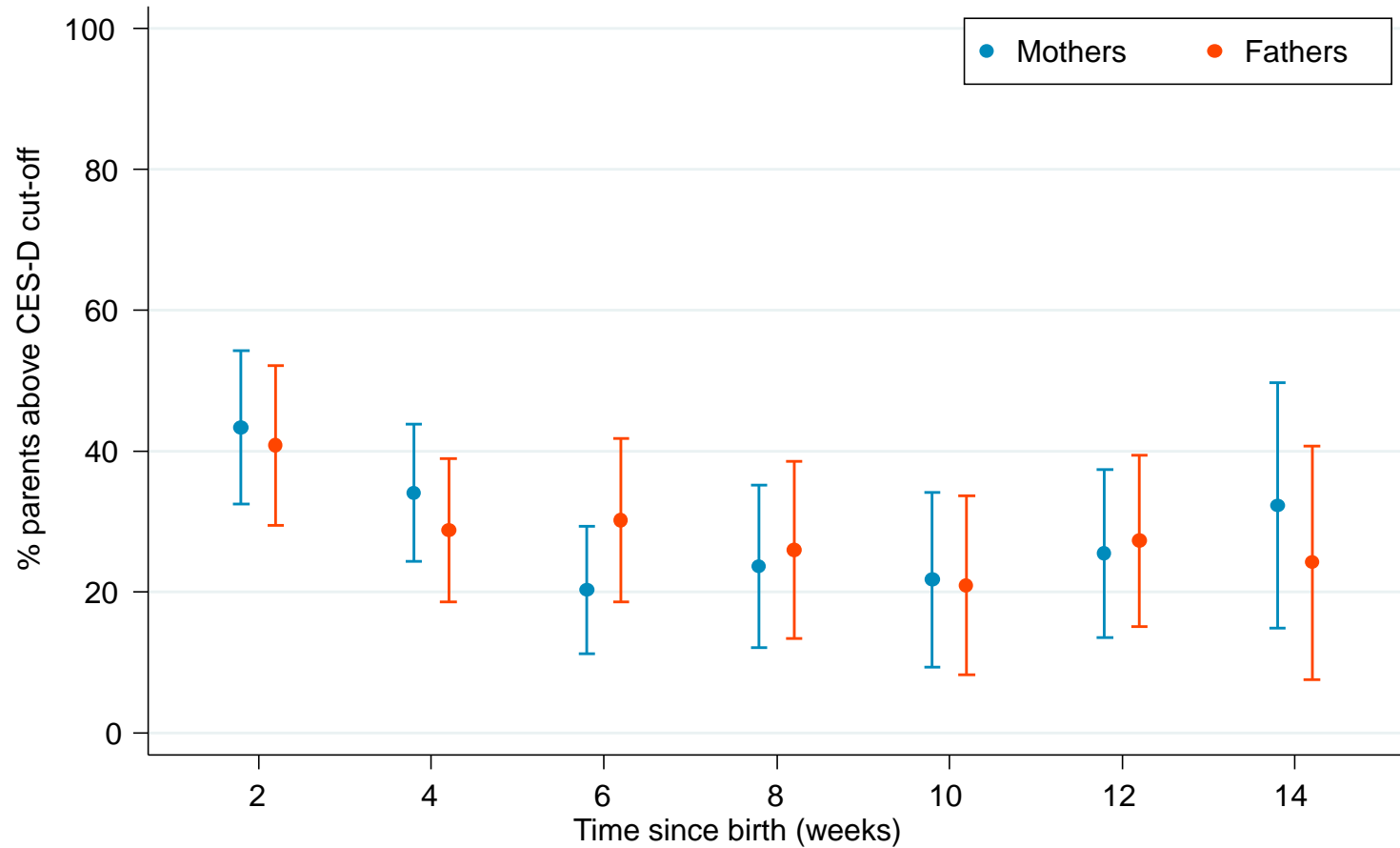
Elevated symptoms of depression 2-3 weeks after birth



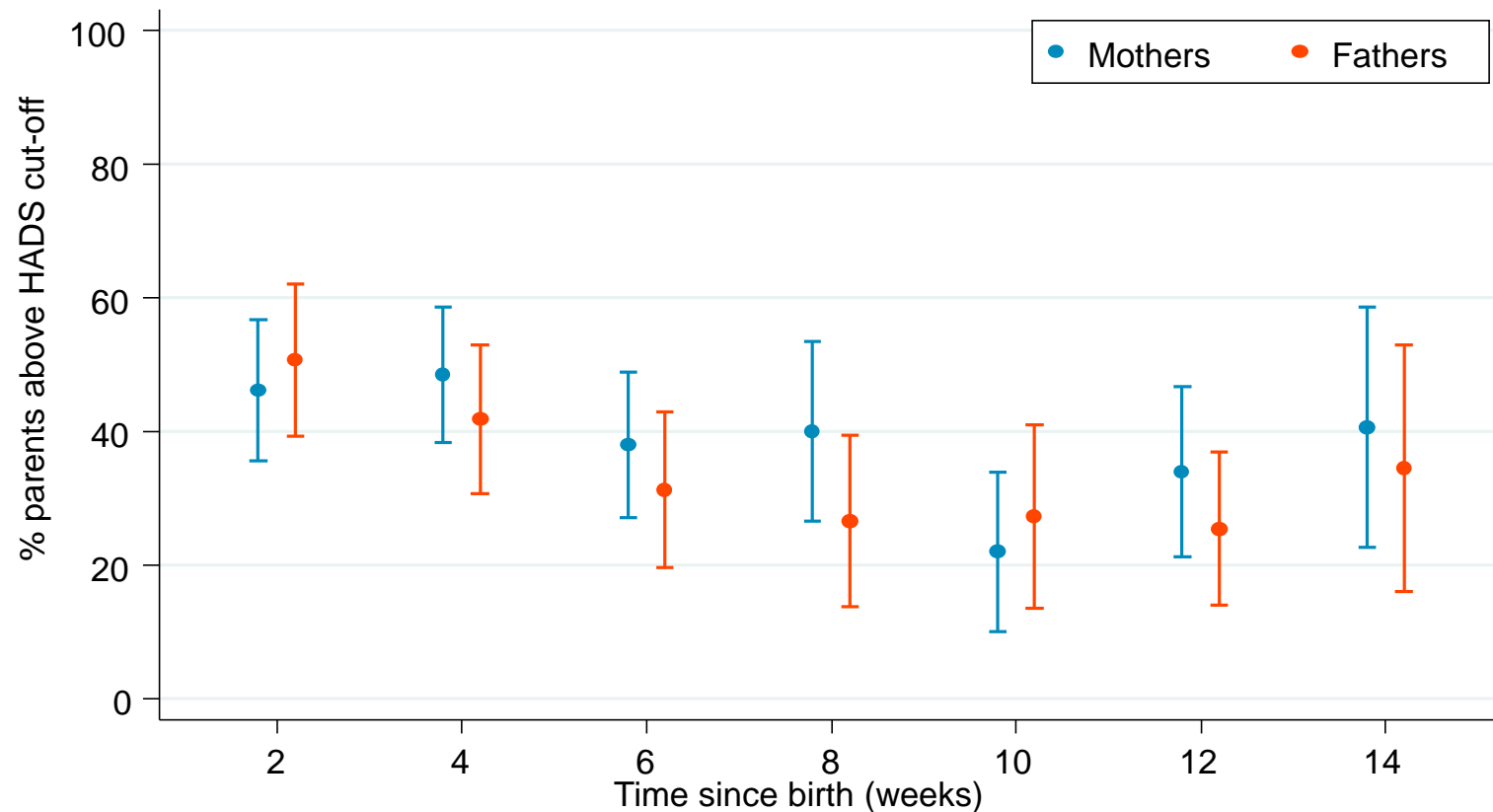
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Elevated symptoms of depression over time

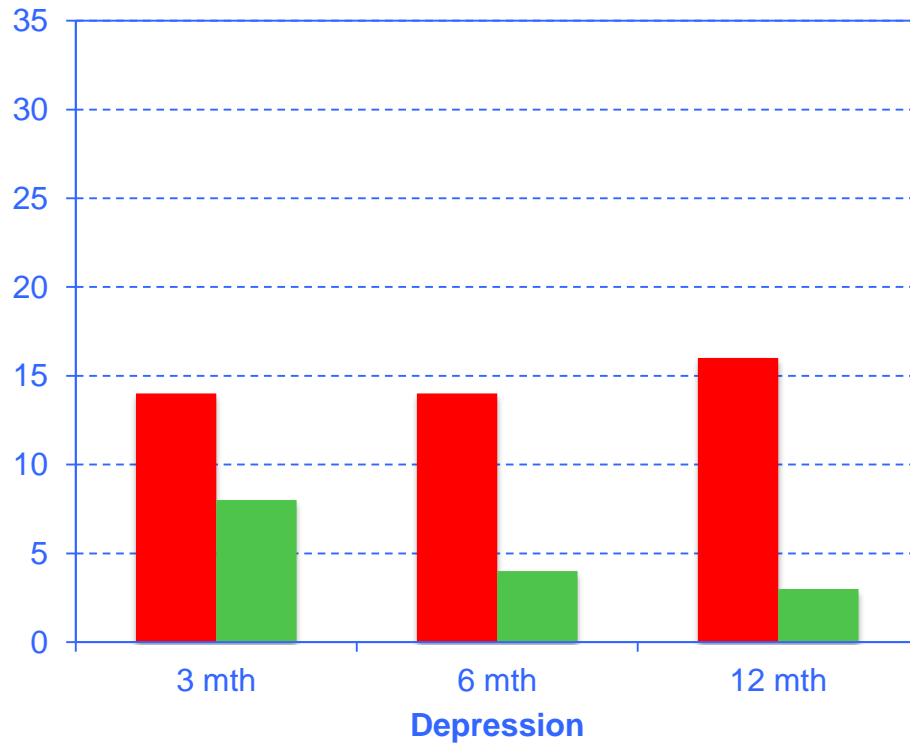


Elevated symptoms of anxiety over time

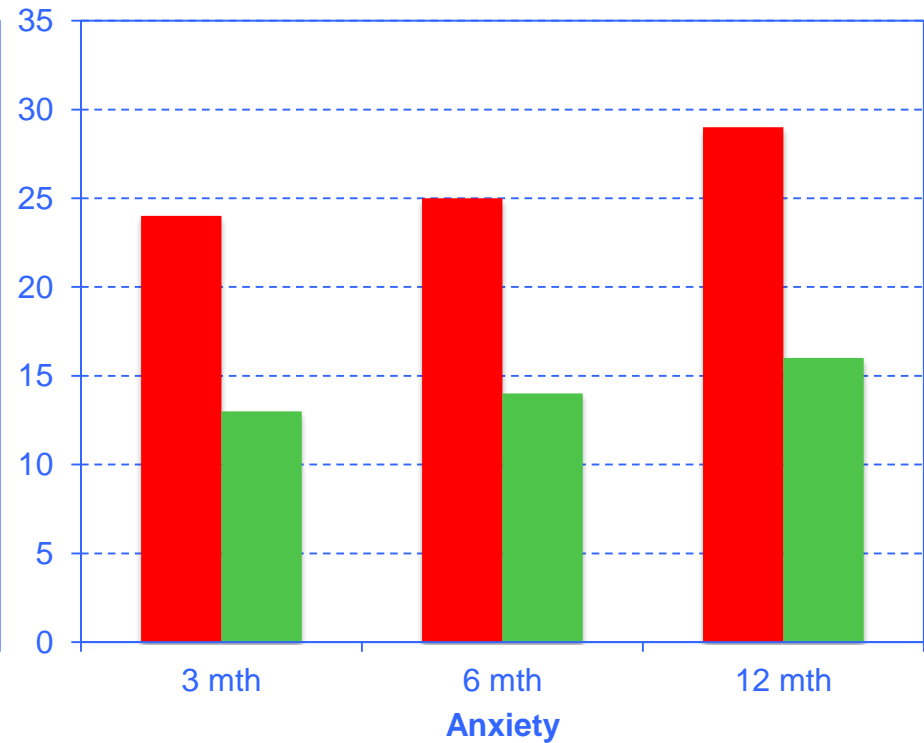


Maternal depression & anxiety – post discharge

■ Very Preterm ■ Term

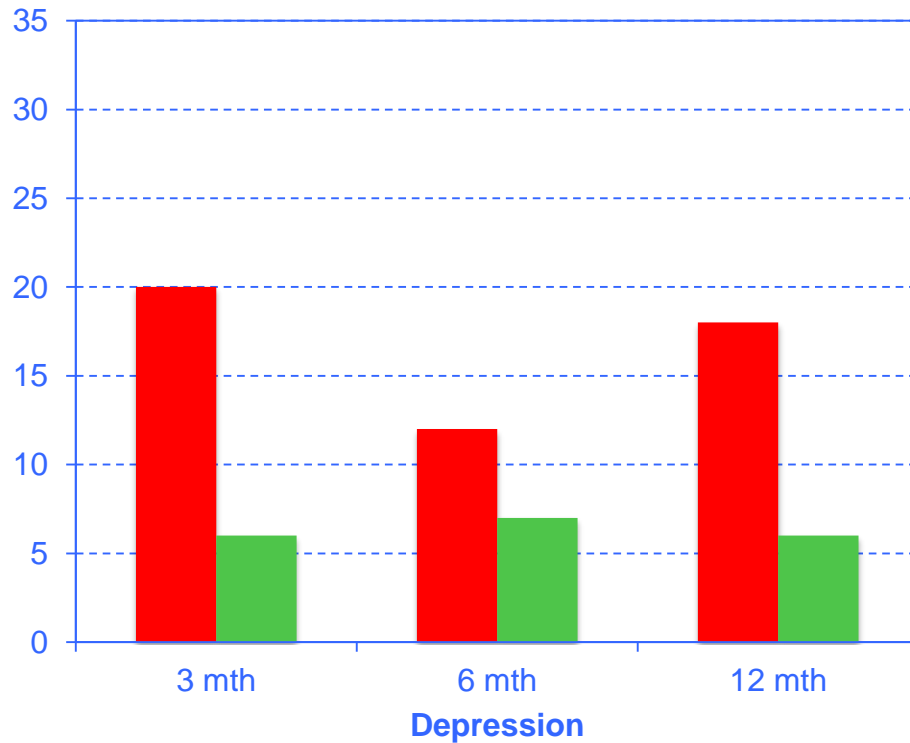


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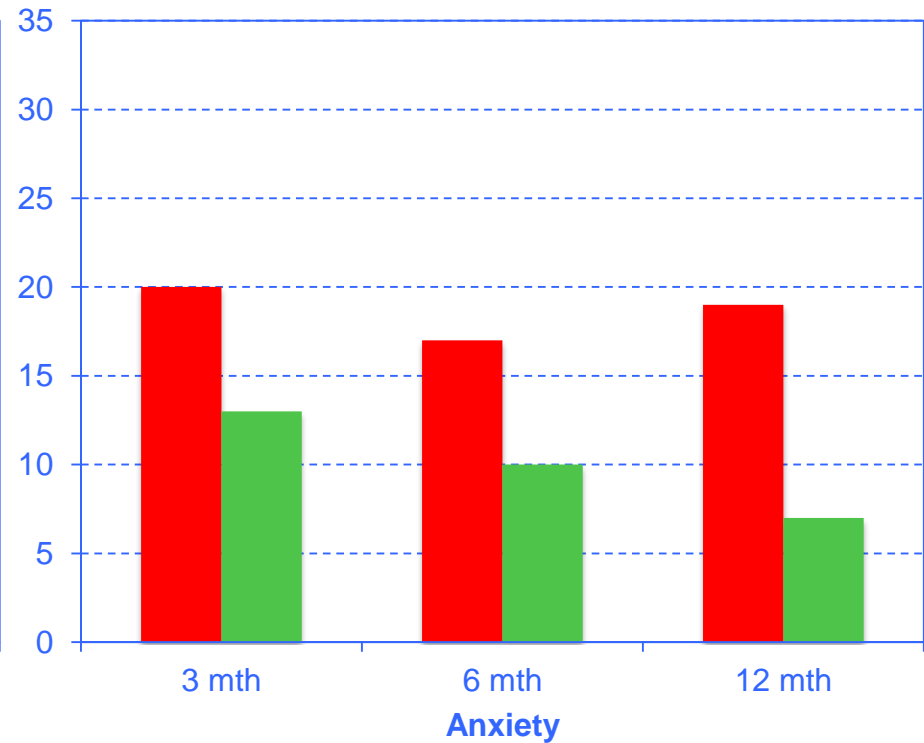


Paternal depression & anxiety – post discharge

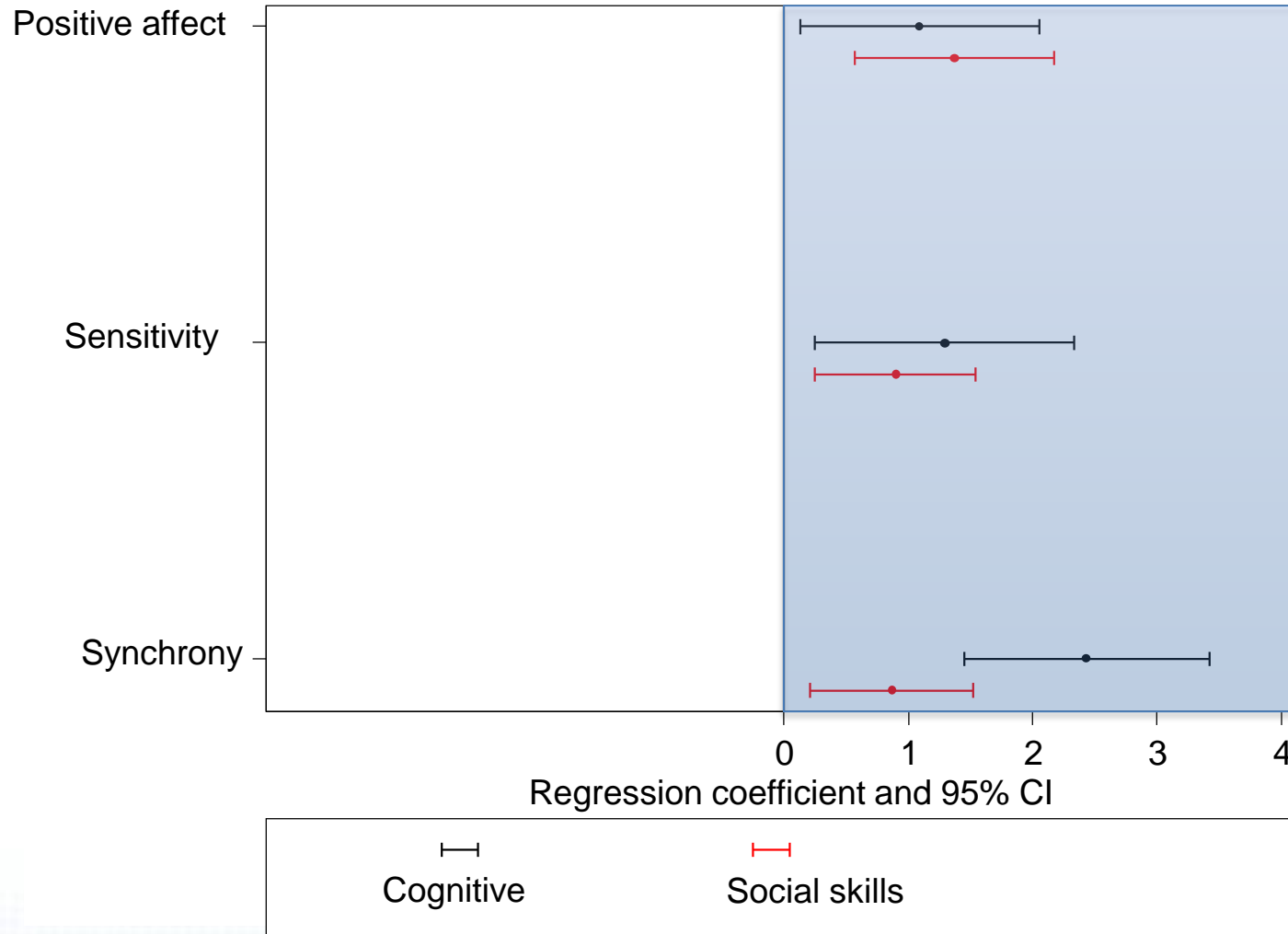
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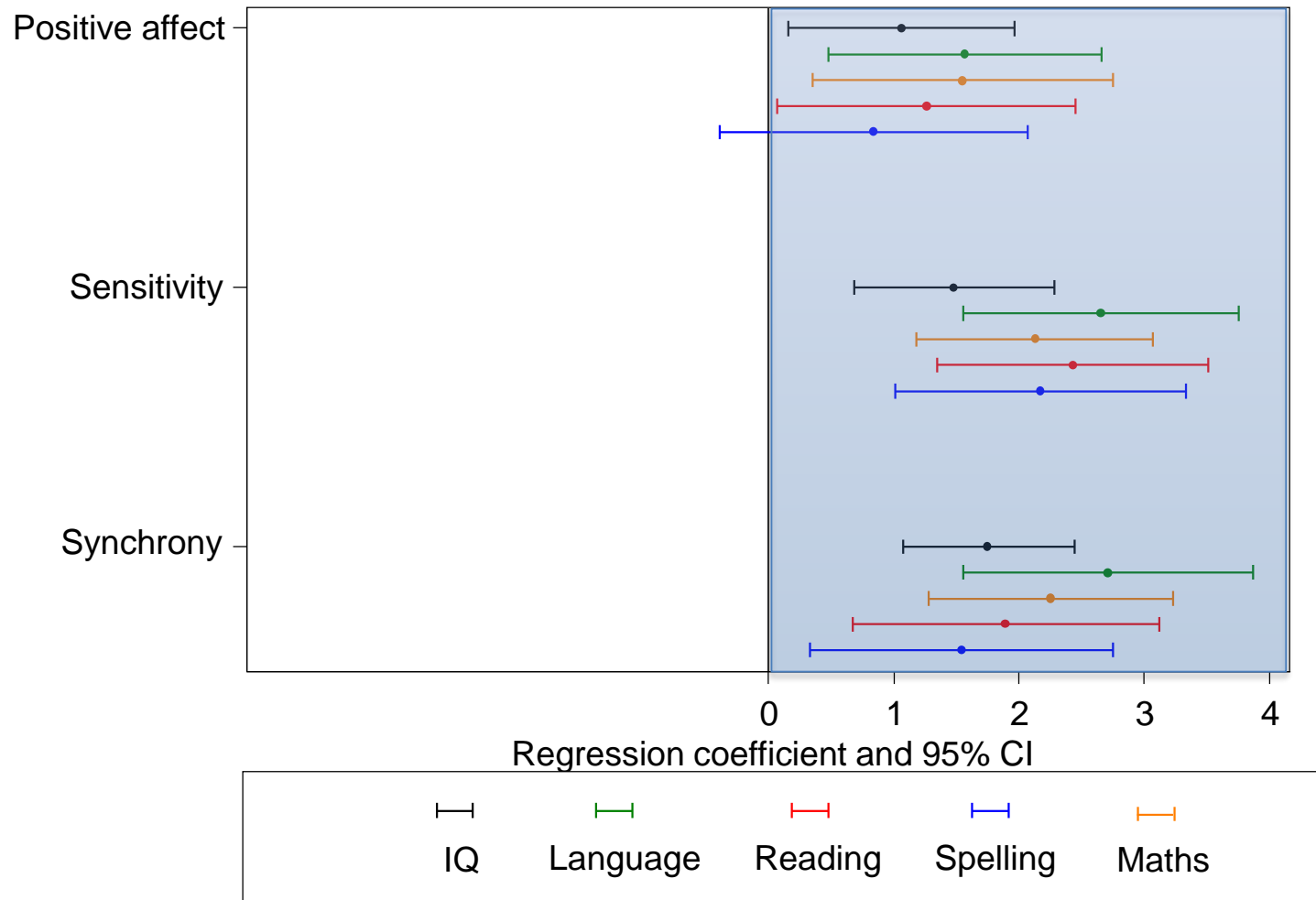


Parenting predicts 2 year outcomes



Treyvaud et al., 2009, Pediatrics

Parenting predicts 7 year outcomes



Treyvaud et al. (2016), Journal of Child Psychology & Psychiatry

Strategies for improving outcomes

Interventions

- Antenatal treatments (ie. Nutrition)
- Perinatal strategies (magnesium sulphate, steroids)
- Postnatal strategies (anti-inflammatory, antioxidants, nutrition, respiratory support)
- Developmental care
- Early intervention
- Secondary/tertiary intervention

Early developmental intervention programmes post-hospital discharge to prevent motor and cognitive impairments in preterm infants (Review)

Spittle A, Orton J, Anderson P, Boyd R, Doyle LW



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COLLABORATION®**

Results

	Mean Difference	n studies	n subjects
Cognitive – early child.	0.31	13	2147
Cognitive – pre-school	0.45	6	1276
Cognitive – school	0.25	4	1242
Motor - early child.	0.10	10	1745
Motor - pre-school	0.14	2	168
Motor - school	-0.34	1	49

VIBeS Plus

- Intervention developed for families with very preterm infants
- Aim: improve child development & parent mental health
- Intervention
 - Began after hospital discharge
 - Team (psychologist & physiotherapist) visit families in the home
 - 9 sessions over first 12 months of child's life
 - Focused on infant self-regulation, postural stability, co-ordination and strength, parent-infant relationship, parent mental health, family support and relationships
- RCT of 120 children born <30 weeks and their families
- Followed up at 2, 4 and 7 years (corrected age)

Results

- Parents in the intervention group:
 - Fewer depression and anxiety symptoms
 - 2, 4 & 7 years
- Children in the intervention group:
 - Fewer emotional and behavioural problems at age 2 and 4 years
 - Mean 0.27 SD improvement in cognitive development at two years' corrected age
 - No significant cognitive benefits at 7 years

Spittle et al. (2010), Pediatrics, 126, e171-178

Spencer-Smith et al. (2012), Pediatrics, 130, 1-8

Spittle et al (in press), Pediatrics

e-prem program

- Based on our effective home-visiting program “VIBeS Plus”
- Online information modules and videos + telephone counselling/coaching
- Currently piloting program
- RCT started late 2014



Take home messages

- Very preterm children are at-risk of a spectrum of developmental issues
 - Inter-individual variability
- The long-term outcomes do NOT seem to be improving
- Mothers & fathers are highly distress
 - Persisting effects
 - Influences parenting and child outcomes
- Early intervention is effective

The VIBeS Family



Paediatrics

Terrie Inder
Lex Doyle
Rod Hunt
Jeanie Cheong
Gehan Roberts
Jennifer Walsh
Noni Davis
Julianne Duff

Nursing

Merilyn Bear
Emma McInnes
Kate Callanan
Marion McDonald
Brenda Argus
Bernice Mills

Psychology

Peter Anderson
Karli Treyvaud
Megan Spencer-Smith
Leona Pascoe
Carly Molloy
Natalie Reidy
Shannon Scratch
Alexandra Ure
Carmel Ferretti
Anastasiya Suetin
Carmen Pace
Cristina Omizzolo
Sacha Stokes
Cody Potter
Andrea McInnes
Michelle Wilson-Ching
Alice Burnett
Andrea Grehan
Loeka Van Bijnen

Neuro-imaging

Deanne Thompson
Jeffrey Neil
Chris Smyser
David Van Essen
Jim Alexopoulos
Yuning Zhang
Meredith Estep
Michael Kean
Marc Seal
Zohra Ahmadzai
Lillian Gabra Fam
Linda Chan
Dolly Thai
Claire Kelly
Wai Yen Loh

Neuroscience

Sandra Rees

Physiotherapy

Alicia Spittle
Lucy Lorefice
Katy de Valle
Jane Orton
Ros Boyd
Leesa Allinson

Occupational Therapy

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