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Long-term outcome of preterm infants into Adulthood

Professor **Dieter Wolke** (Ph.D; Dr rer nat h.c.; C.Psychol; AFBPsS)
University of Warwick, Department of Psychology

D.Wolke@warwick.ac.uk
www.dieterwolke.com

Small Beginnings

Ben 2013



Preterm Birth

- Immaturity Organ Development
- Complications/Insult



Impact

Immediate

- Parents
- PTSD

Longterm?

Longterm

- Preterm Phenotype



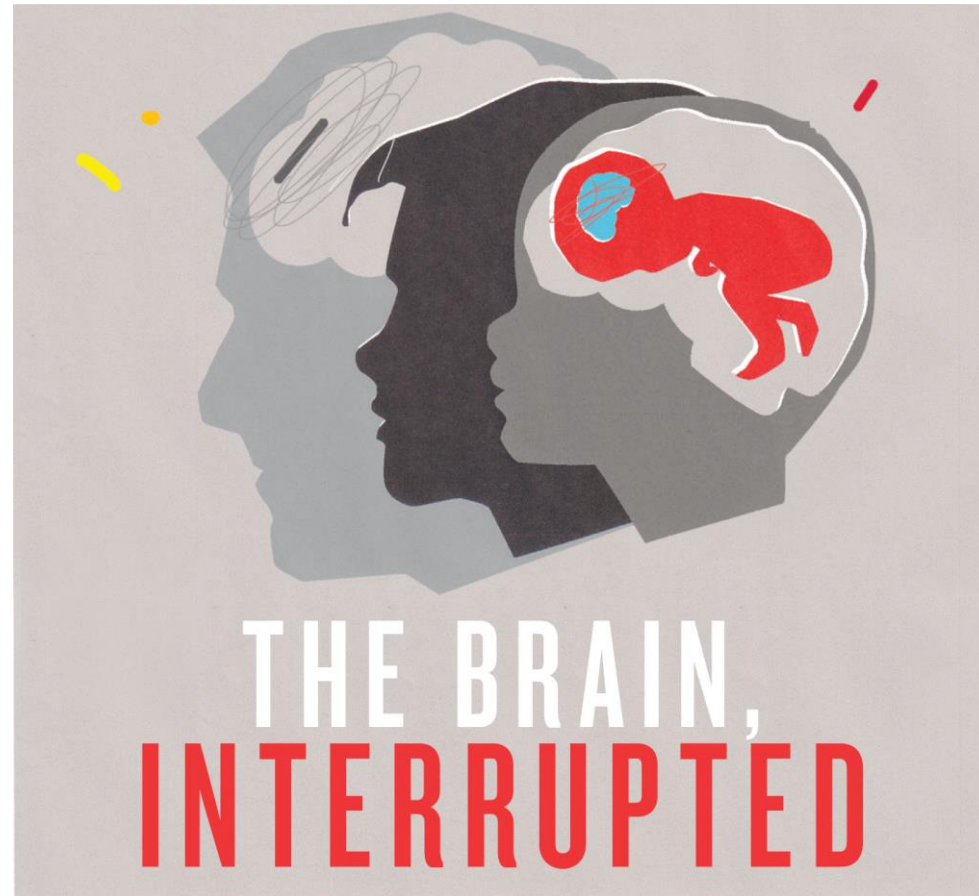
Forever premature

As more babies born early enter adulthood, the lifelong effects are finally becoming clear, finds Linda Geddes

| NewScientist | 20 February 2016

Babies are increasingly surviving premature birth — but researchers are only beginning to understand the lasting consequences for their mental development.

BY ALISON ABBOTT



Overview: Focus on Adulthood

Questions:

CHILDREN

1. Do VP outgrow their problems? Which?
2. What new problems arise?
3. Effects of the environment and parenting?

PARENTS

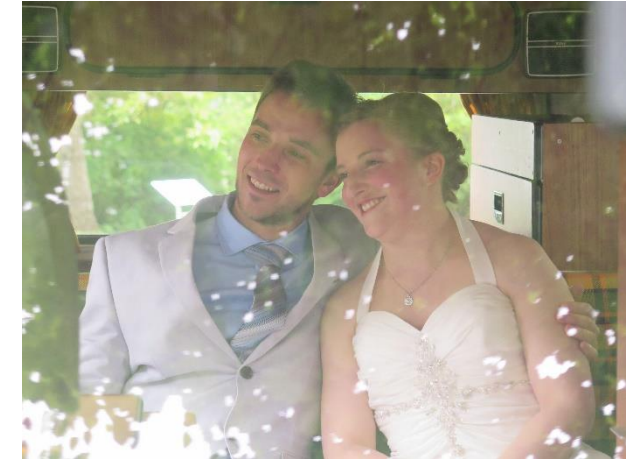
- Quality of Life: Will it be ok in the End?



From Birth to Adulthood - Melanie



26 weeks
30 cm
750 g





<http://recap-preterm.eu/>

Cohorts

- Bavarian Longitudinal Study

<32 weeks or < 1500g, born 1985/86



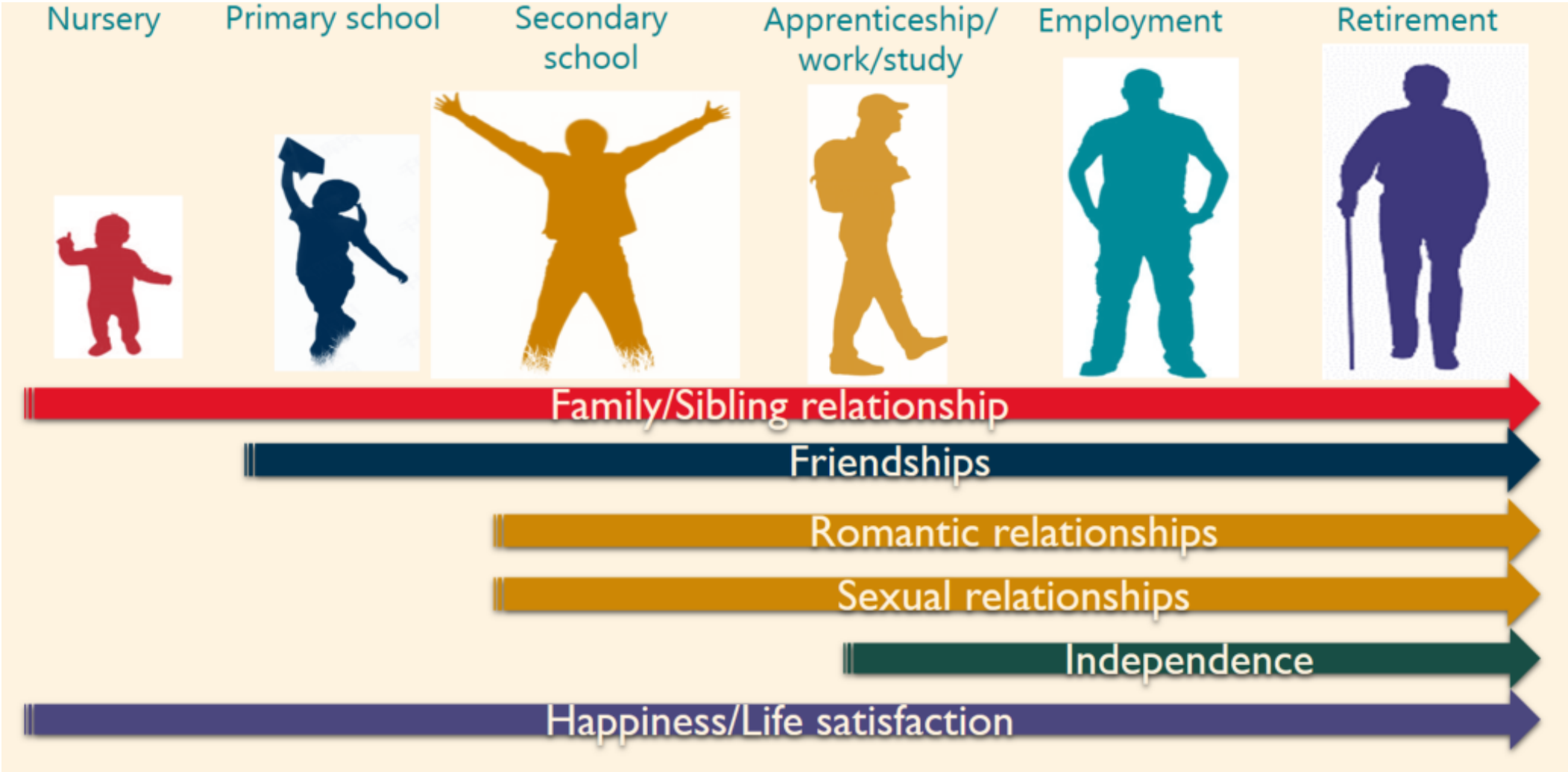
- EPICure Study



<26 weeks gestation, born 1995

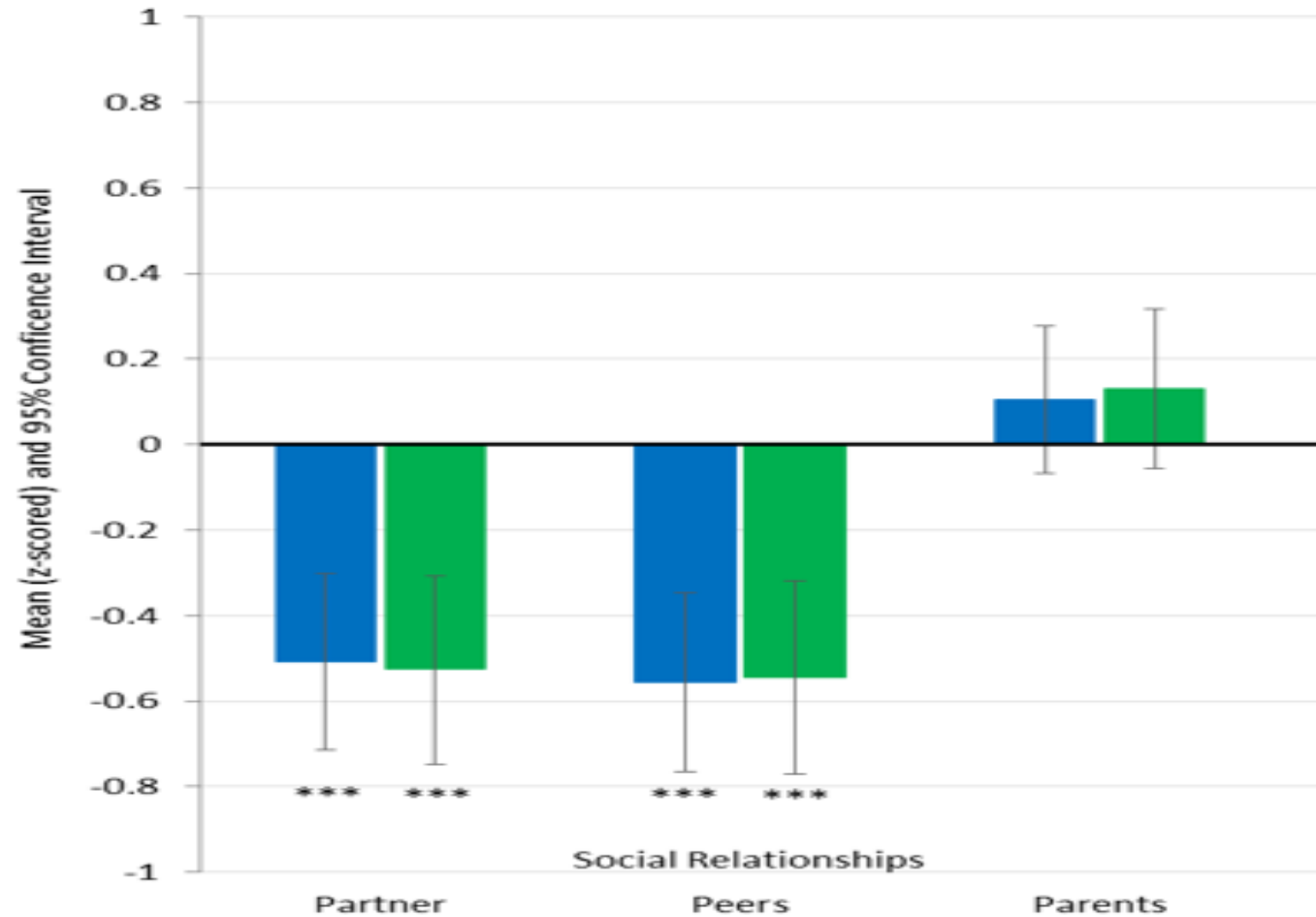


Life Course Tasks





Adulthood: Parents, Peers and Partnering



In blue unadjusted differences, in green differences adjusted for SES, sex, multiple birth, marital status at birth and participant's age.

Social Relationships: Sex & Romance



Reaching Life Course Goals: Social *



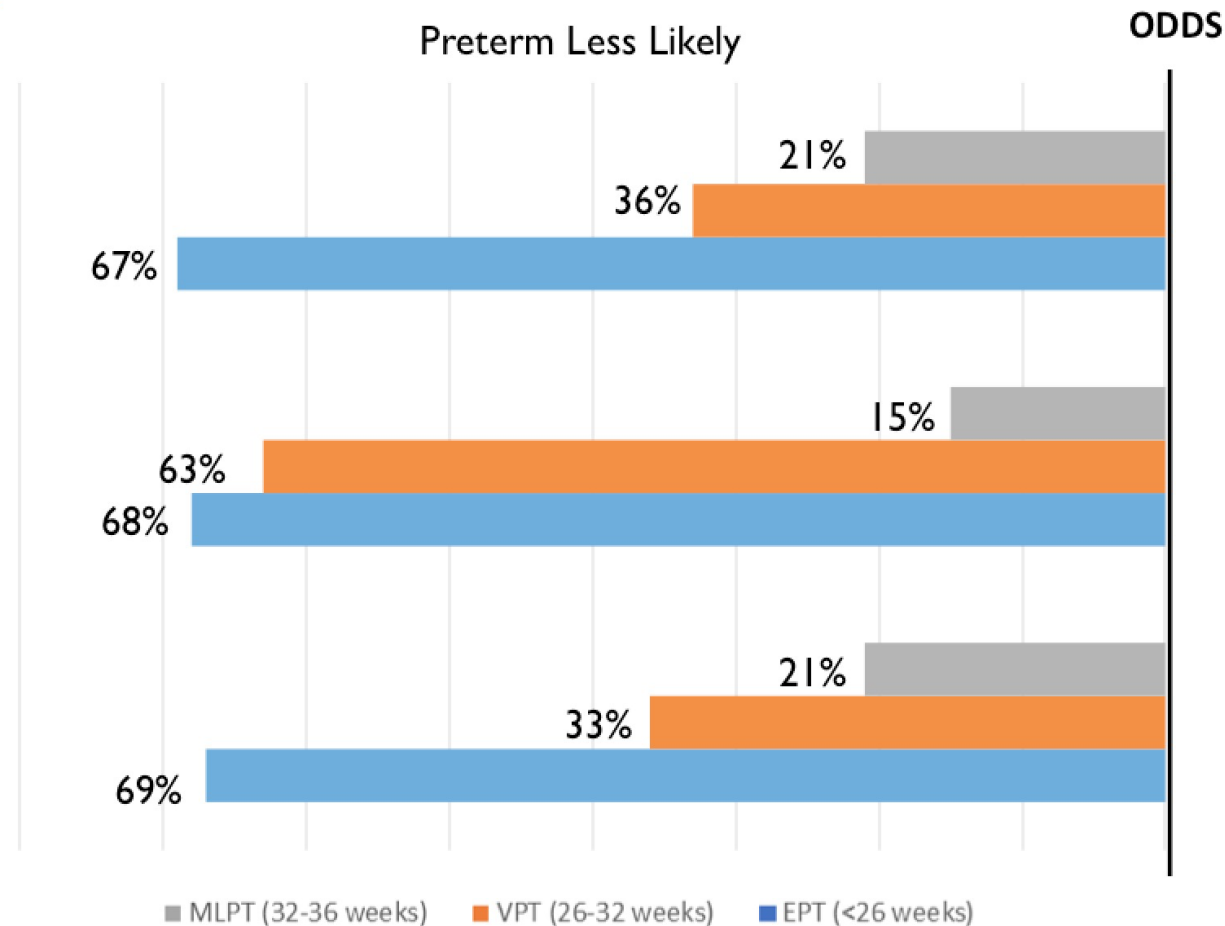
Romantic Partnership



Sexual Intercourse



Parenthood



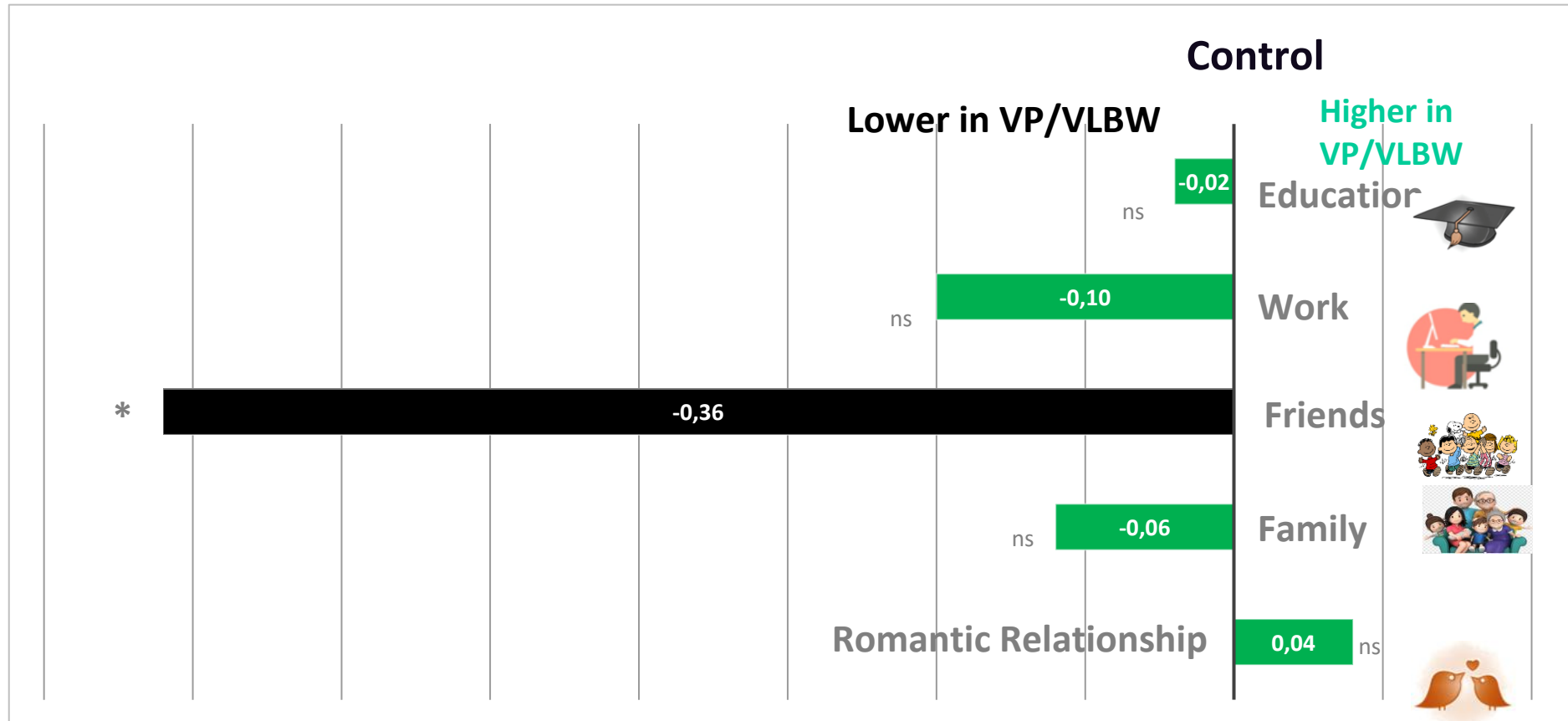
Romance, Sexual Experience and Children (IPD)

VP adults have **less often experienced**:

- ▶ **Ever** sexual intercourse and if, then later
- ▶ **Ever** had a longer romantic relations (especially *male* VP)
- ▶ **Less likely** to have children of their own (especially *male* VP/VLBW)
- ▶ Those with disability are least likely to make these experiences



Social Relationships: Adult Friends



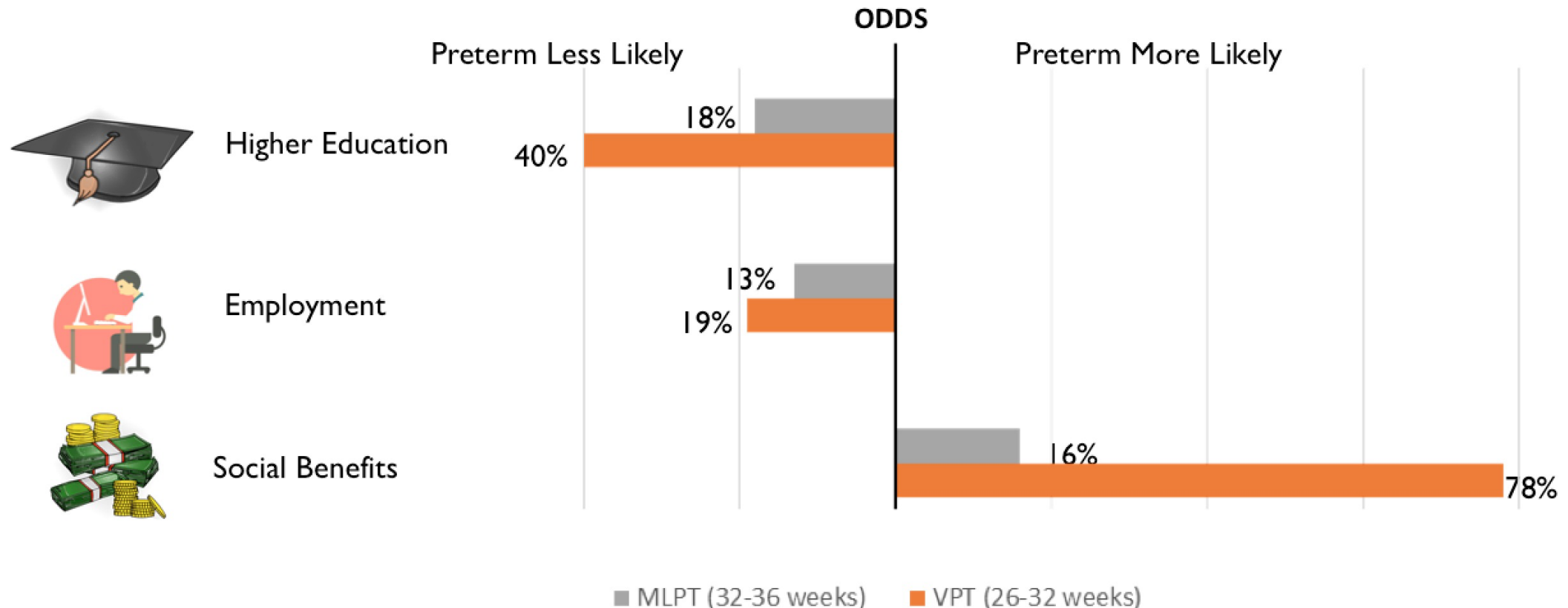
Fewer friends; lower friendship relationship

Ni, Y., Mendonça, M., Baumann, N., Eves, R., Kajantie, E., Hovi, P., . . . Wolke, D. (2021). Social Functioning in Adults Born Very Preterm: Individual Participant Meta-analysis. *Pediatrics*, e2021051986. doi:10.1542/peds.2021-051986



Independence and Wealth

Reaching Life Course Goals: Wealth*



Bilgin, A., Mendonca, M., & Wolke, D. (2018). Preterm Birth/Low Birth Weight and Markers Reflective of Wealth in Adulthood: A Meta-analysis. *Pediatrics*. doi:10.1542/peds.2017-3625. (RECAP Preterm, funded by the European Union's Horizon 2020 research and innovation programme)



Quality of Life



EPIcure 

BLS 

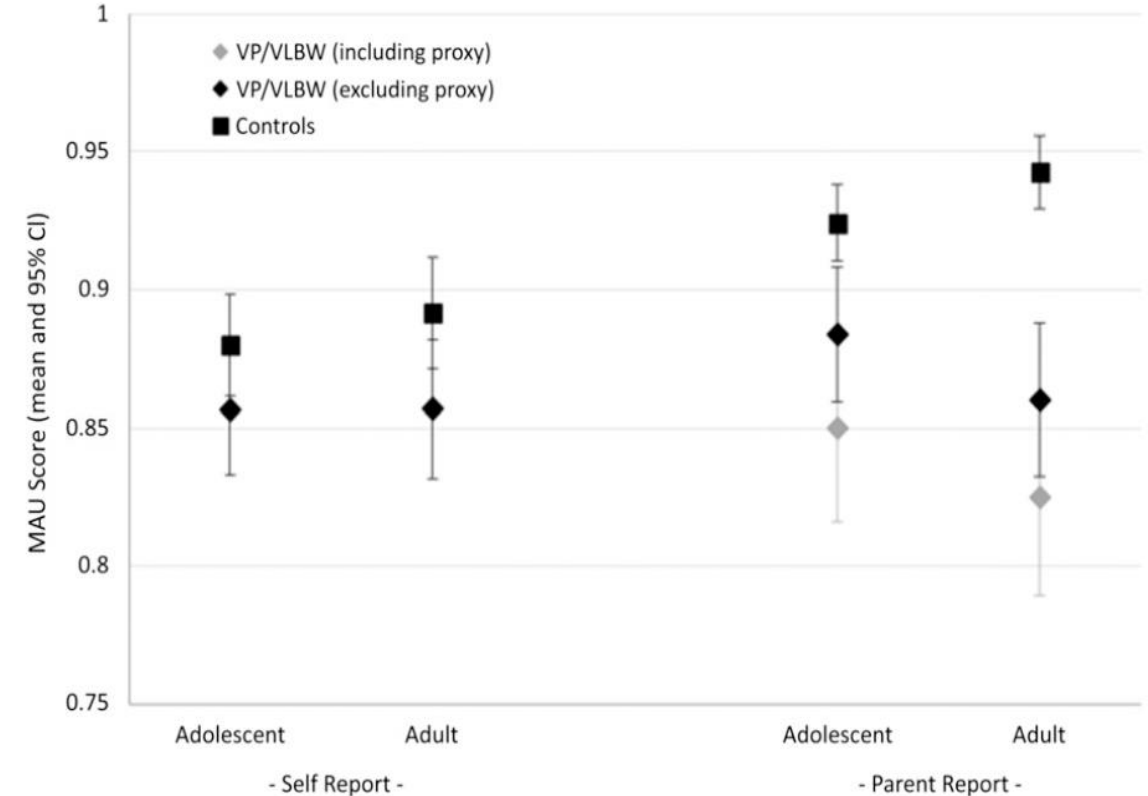
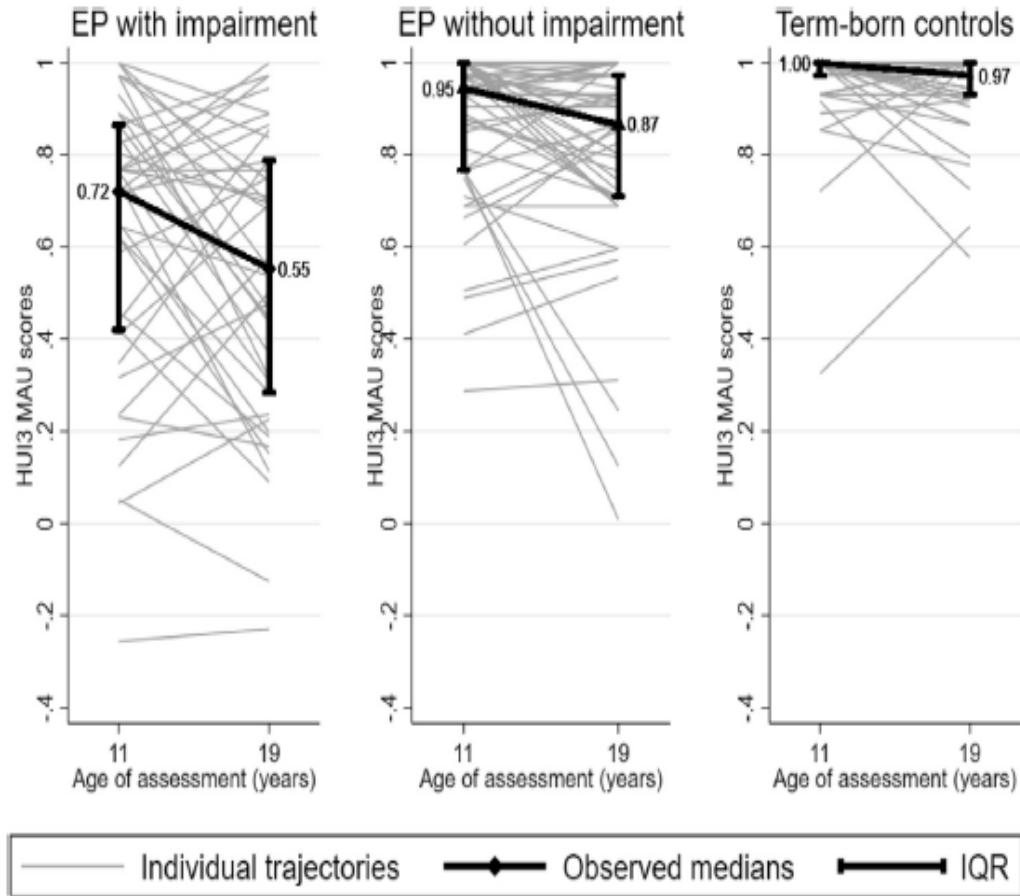


FIGURE 2

Self- and parent-reported HRQL MAU scores from adolescence to adulthood.

Health-Related Quality of Life Into Adulthood After Very Preterm Birth

Nicole Baumann, BSc,^a Peter Bartmann, MD, Dr rer nat,^b Dieter Wolke, PhD, Dr rer nat hc^{a,c}

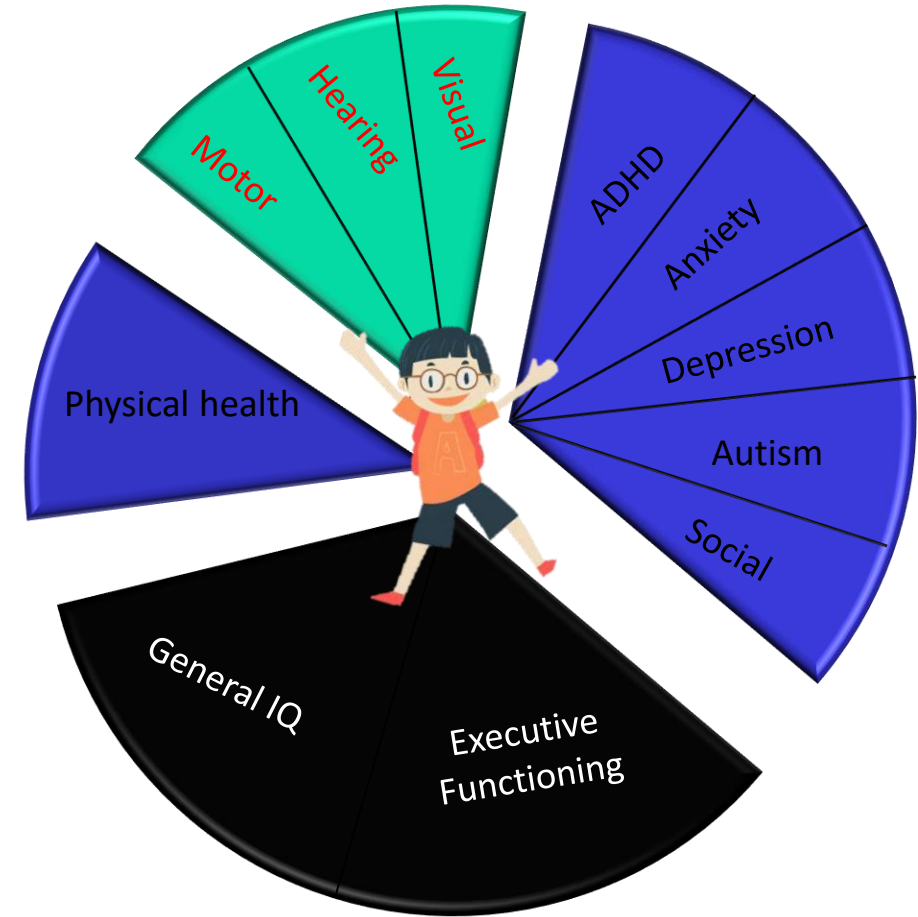
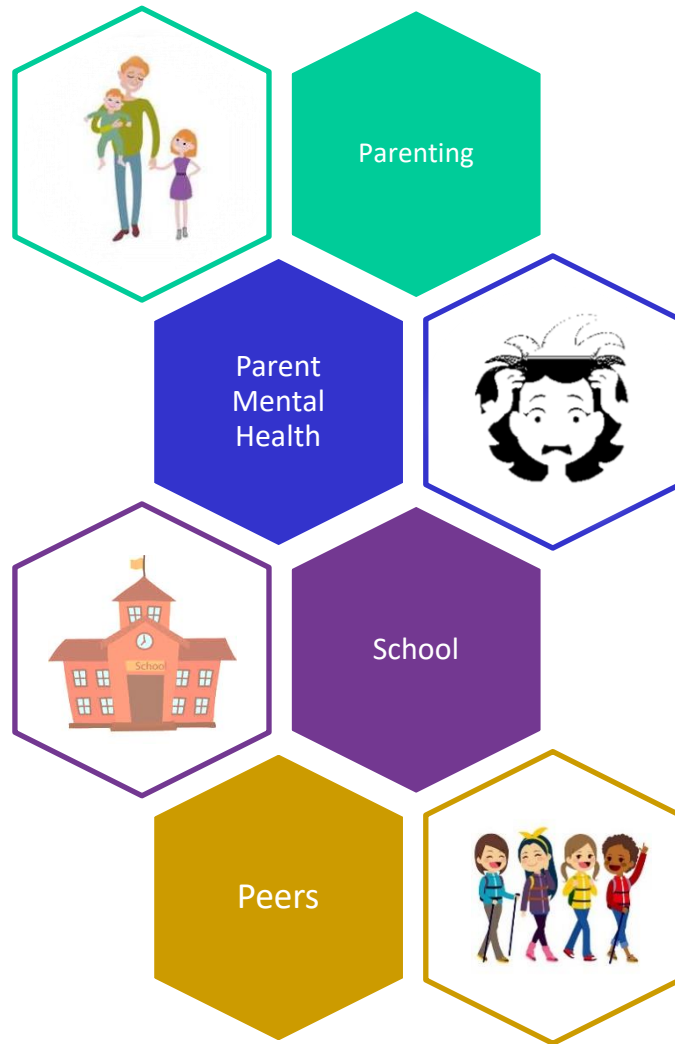
Pediatrics. 2016;137(4):e20153148

WHAT THIS STUDY ADDS: Those born very preterm perceive their HRQL as lower than their parents and as poorer than term born controls in adolescence and adulthood. Lower HRQL is related to lower economic functioning and poorer social relationships with peers and partners.

The Quality of Life reduces with age



Childhood Functioning and reaching Life Course Goals*



*Johnson, S., & Wolke, D. (2017). Prematurity and low birthweight. In B. Hopkins, E. Geangu, & S. Linkenauer (Eds.), *The Cambridge Encyclopedia of Child Development* (2 ed., pp. 705-716). Cambridge: Cambridge University Press.

Adult Outcomes

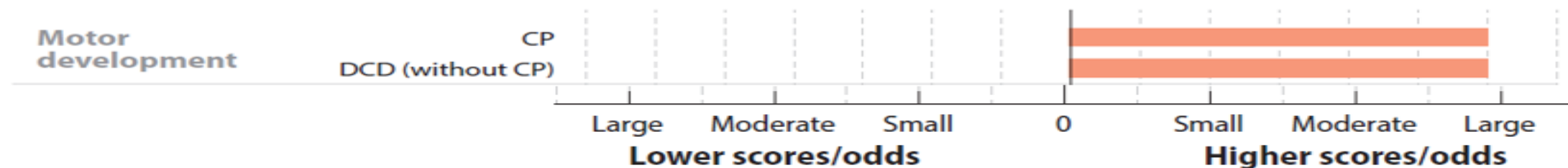
Annual Review of Developmental Psychology

The Life Course Consequences of Very Preterm Birth

<https://doi.org/10.1146/annurev-devpsych-121318-084804>

Dieter Wolke,^{1,2} Samantha Johnson,³
and Marina Mendonça¹

Motor

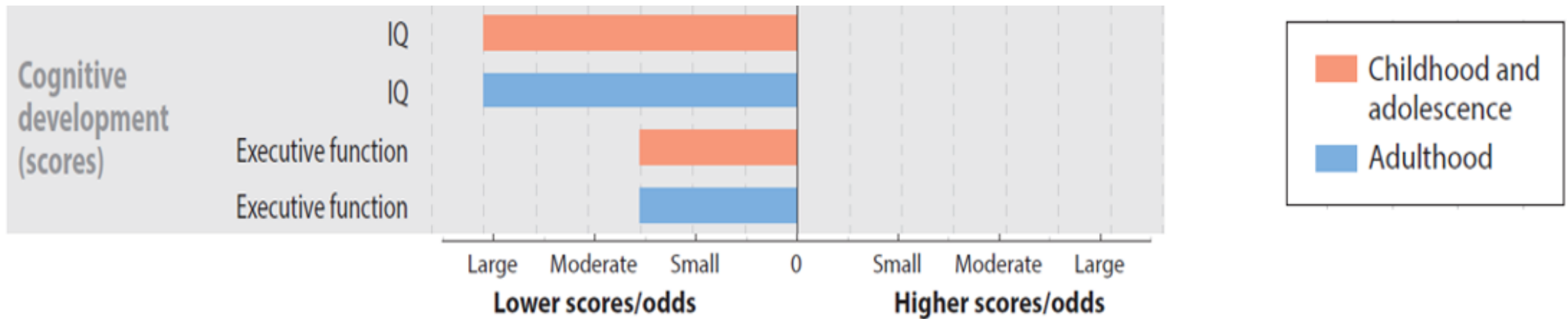


	Very Preterm/VLBW	Extremely Preterm/ELBW
Cerebral Palsy (CP)	3-5%	7-11%
Developmental Coordination disorder (DCD)	10-20%**	13-26%*

Into Adulthood: Severe Motor Problems (CP) persist; DCD show low stability

Adult: Cognitive Outcomes

<https://doi.org/10.1146/annurev-devpsych-121318-084804>



Association of Very Preterm Birth or Very Low Birth Weight With Intelligence in Adulthood

An Individual Participant Data Meta-analysis

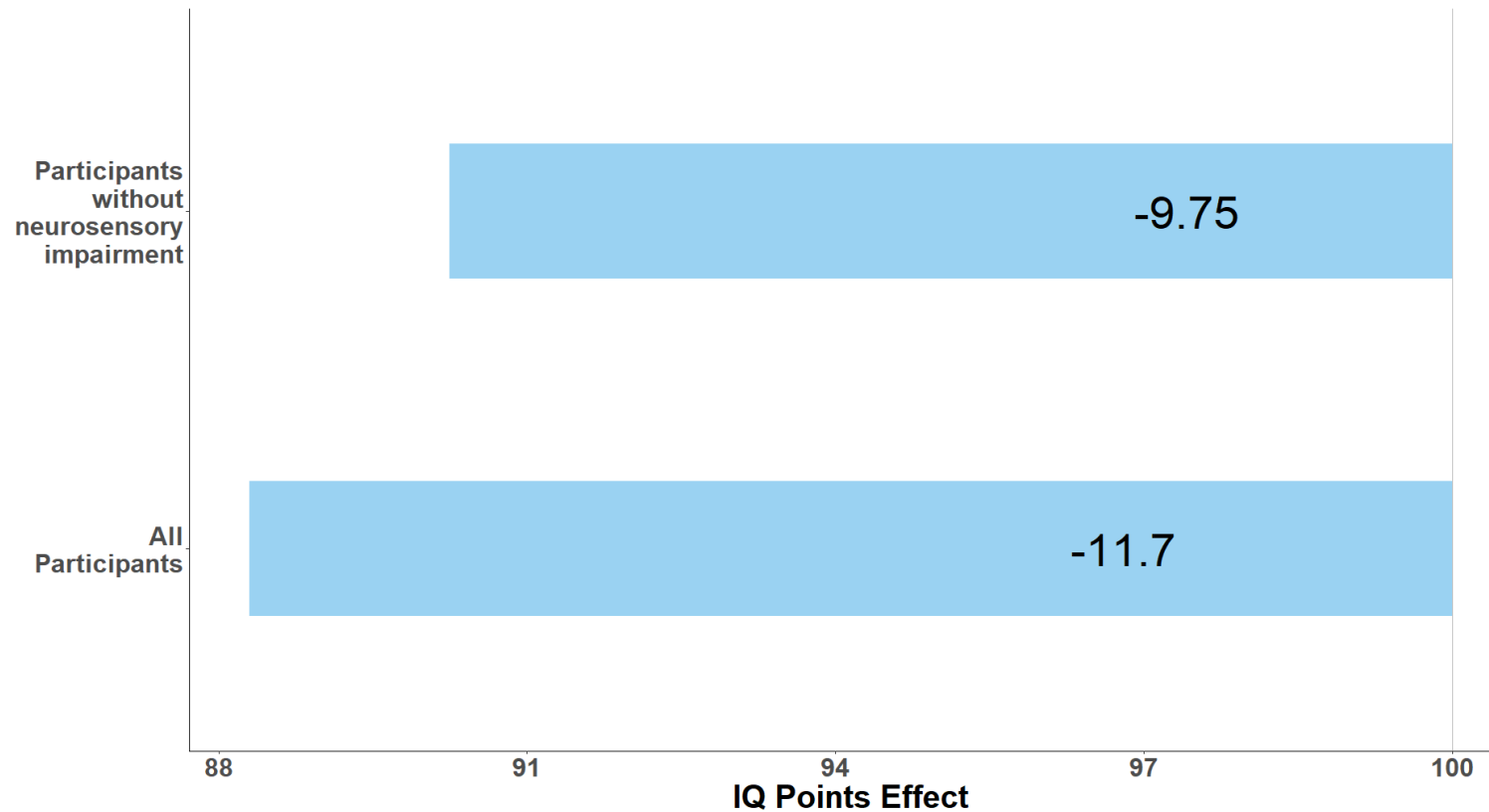
Published 28 May 2021



Robert Eves, MSc; Marina Mendonça, PhD; Nicole Baumann, BSc; Yanyan Ni, PhD; Brian A. Darlow, MD; John Horwood, MSc; Lianne J. Woodward, PhD; Lex W. Doyle, MD; Jeanie Cheong, MD; Peter J. Anderson, PhD; Peter Bartmann, MD, PhD; Neil Marlow, DM; Samantha Johnson, PhD; Eero Kajantie, DMedSc; Petteri Hovi, MD, PhD; Chiara Nosarti, PhD; Marit S. Indredavik, MD, PhD; Kari-Anne I. Evensen, PhD; Katri Räikkönen, PhD; Kati Heinonen, PhD; Jennifer Zeitlin, DSc; Dieter Wolke, PhD, Dr rer nat hc



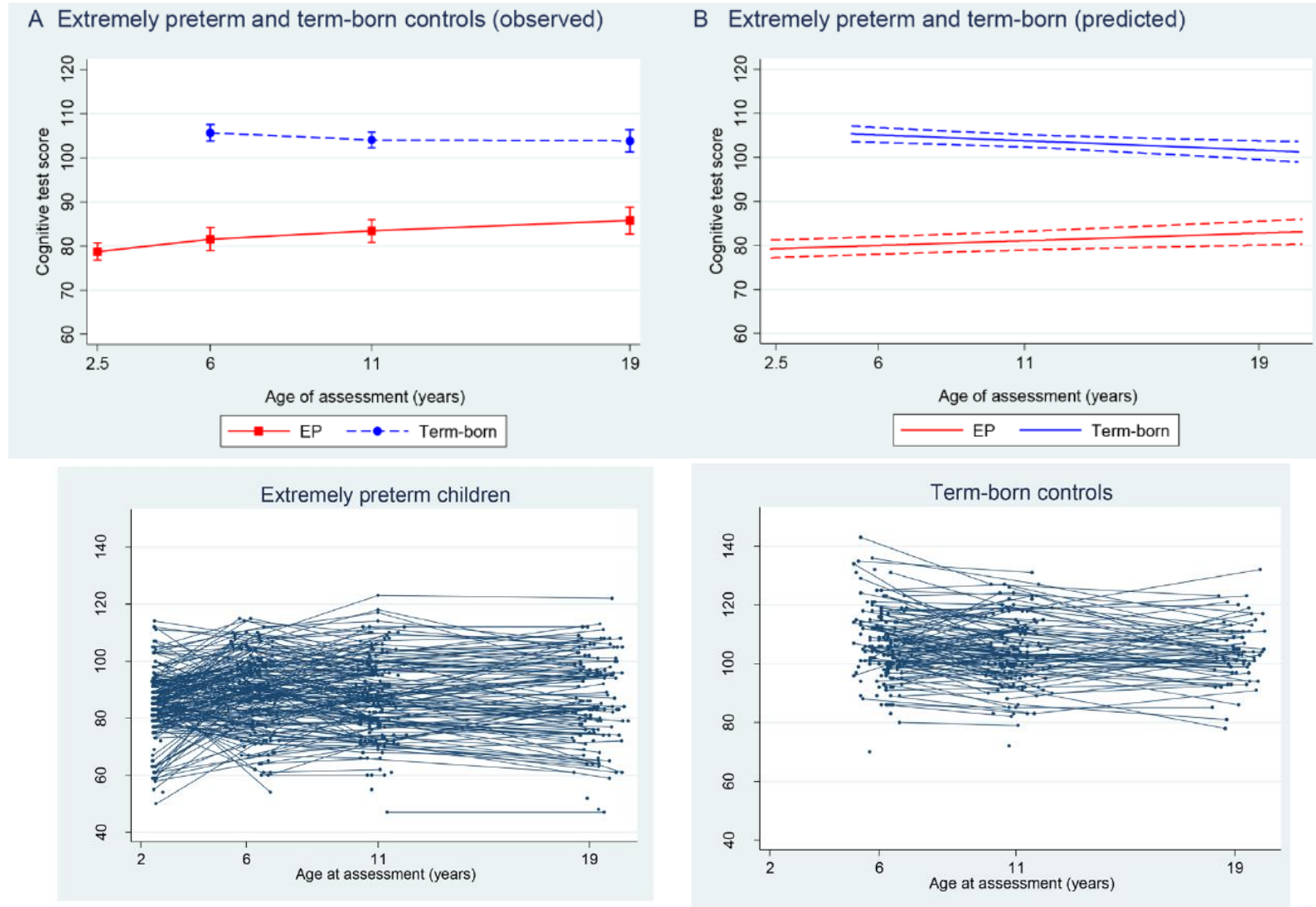
8 cohorts from 7 countries





Epicure: IQ from 2.5 to 19 years of age

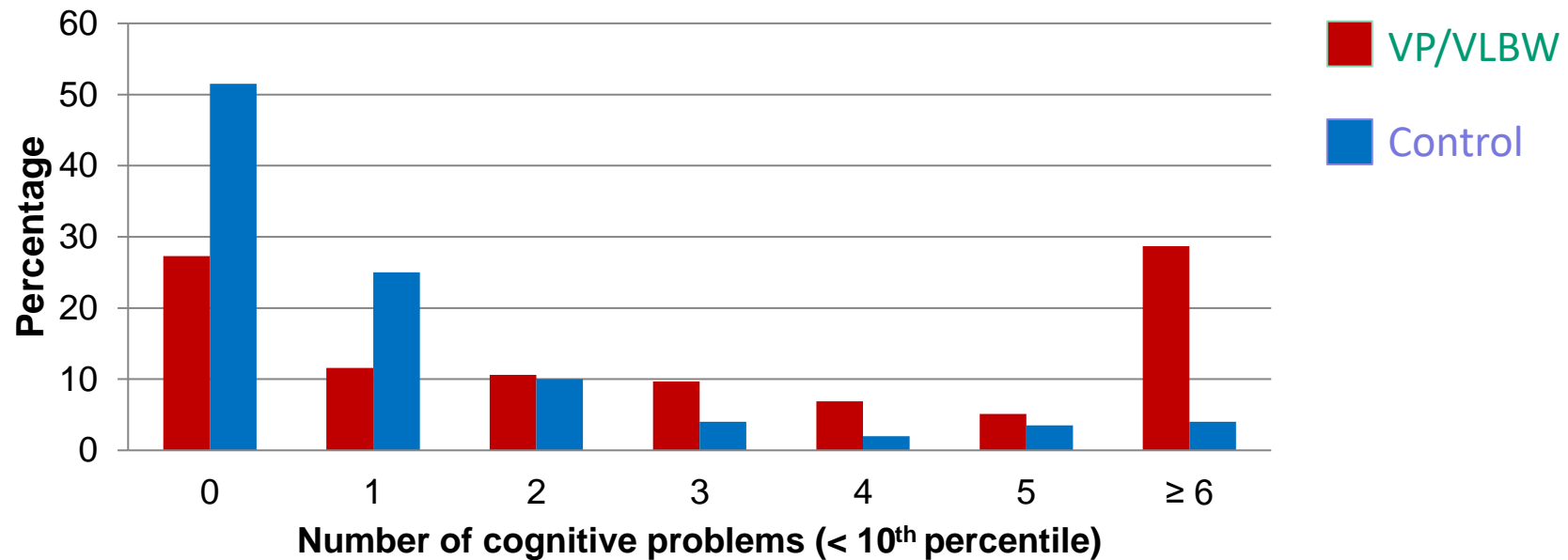
Impaired cognitive function persist from infancy to adulthood in EP





VP/VLBW adults have more often multiple cognitive deficits not specific EF! **YES**

Fig.2. Relative frequency of multiple cognitive problems of VP/VLBW adults in comparison to their full-term counterparts.

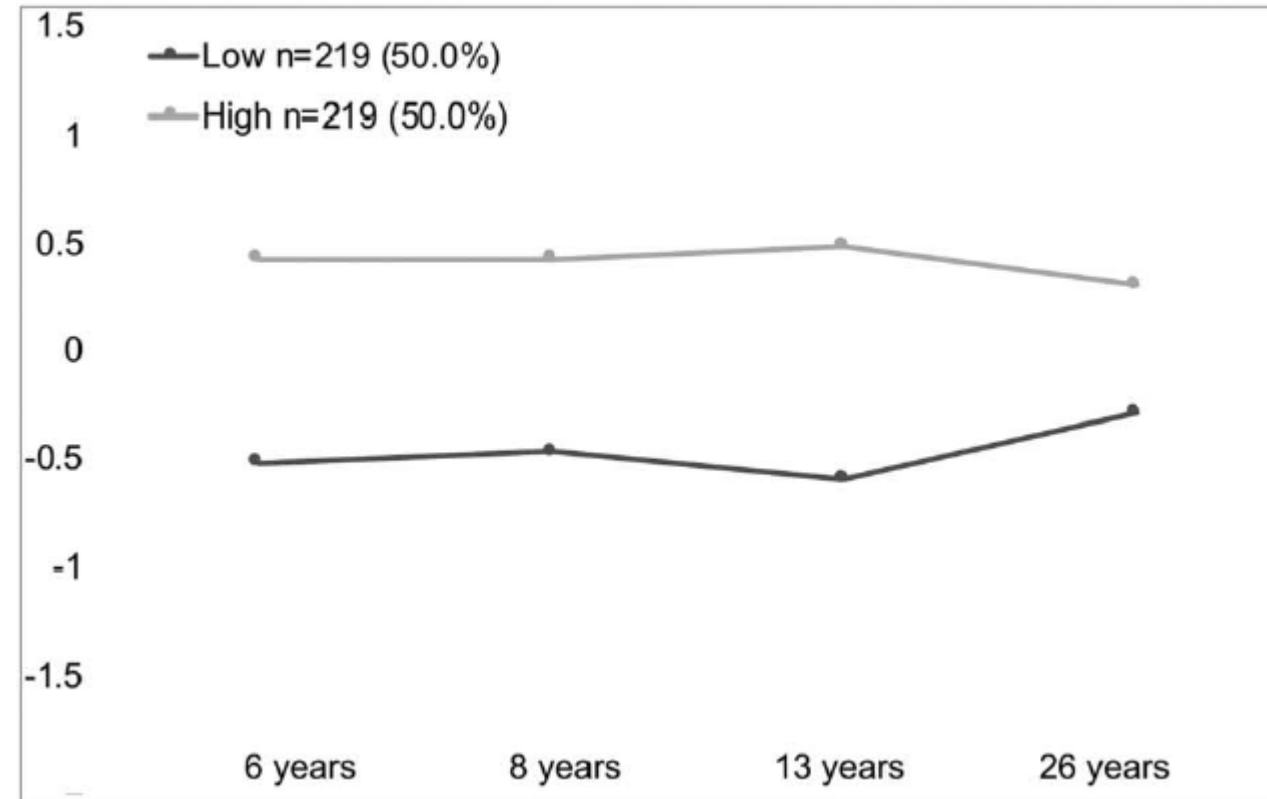


Note. The number of cognitive outcome measures (out of 10) with a score below the 10th percentile of control distribution were counted in weighted, population representative control and VP/VLBW samples.

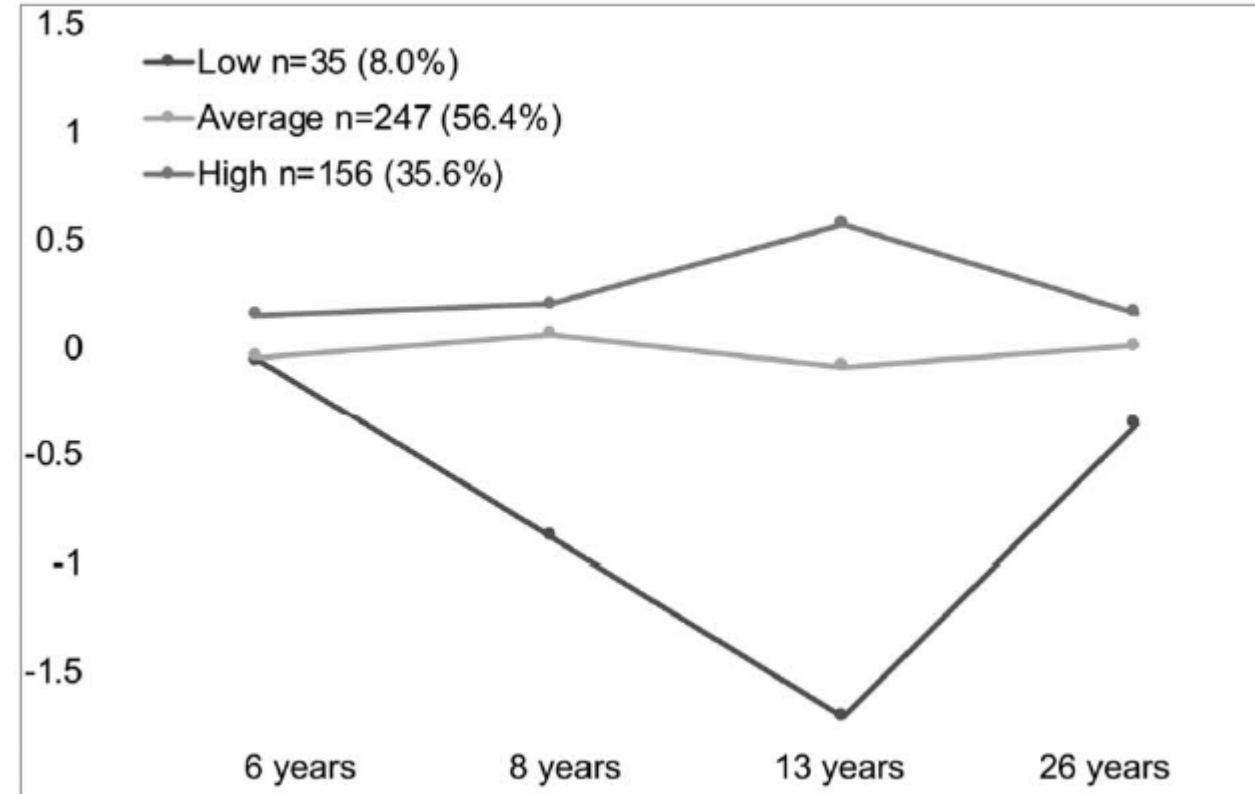
Peer trajectories: IQ several impacts



B Peer problems trajectories



C Friendships trajectories



Not VP/VLBW but **IQ in childhood** predicts trajectories: Higher IQ-score more friends, less peer problems

Summary Cognition

VP/VLBW adults

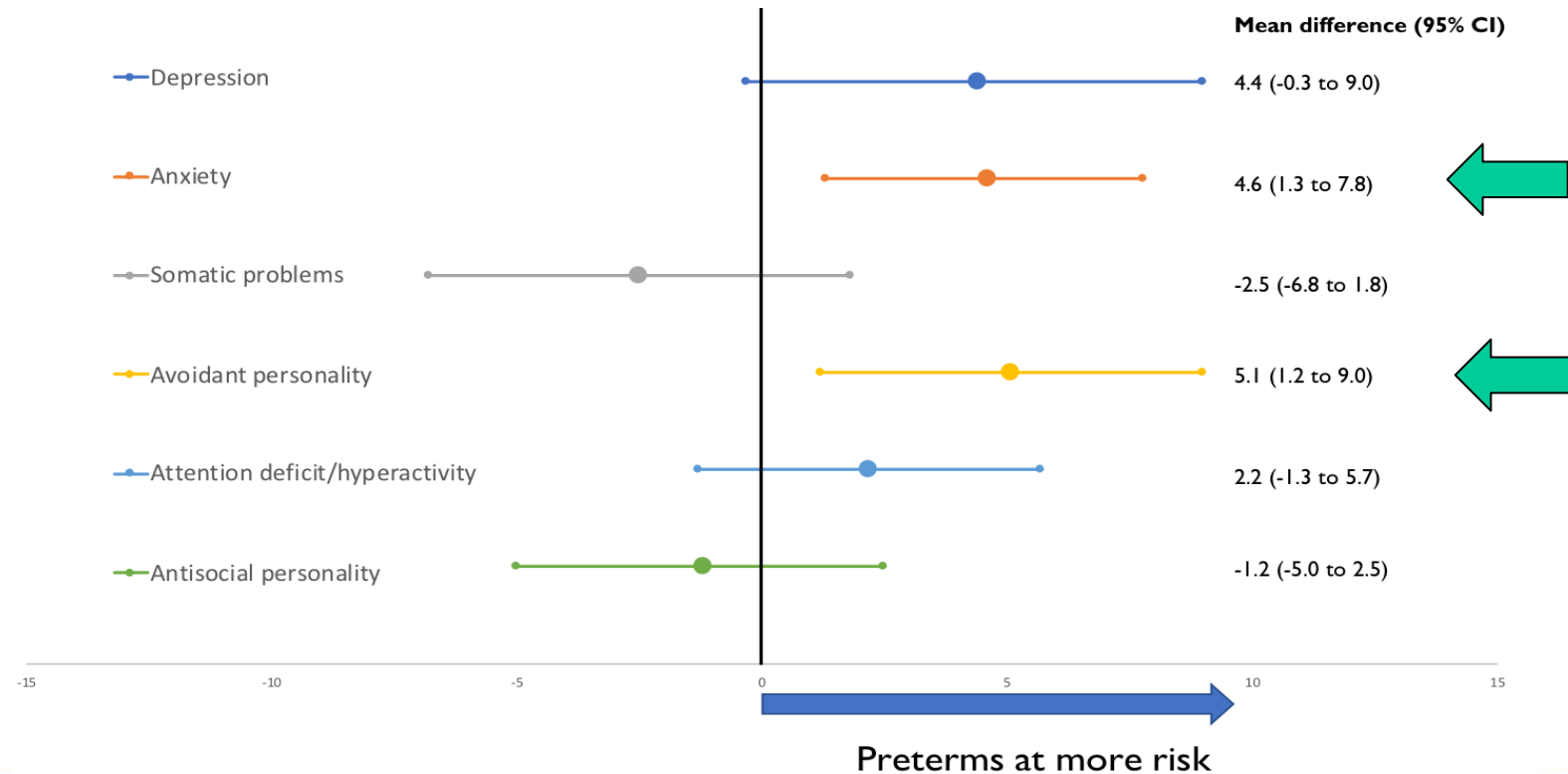
1. Perform **poorer** in all aspects of IQ and EF, on average.
2. Have more often **multiple cognitive deficits** rather than specific EF deficits
3. IQ affects a wide range of areas of life course functioning – from schooling to peer relationships
4. At **age 2 years** adult IQ deficits **can be predicted** in VP/EP children





Mental Health

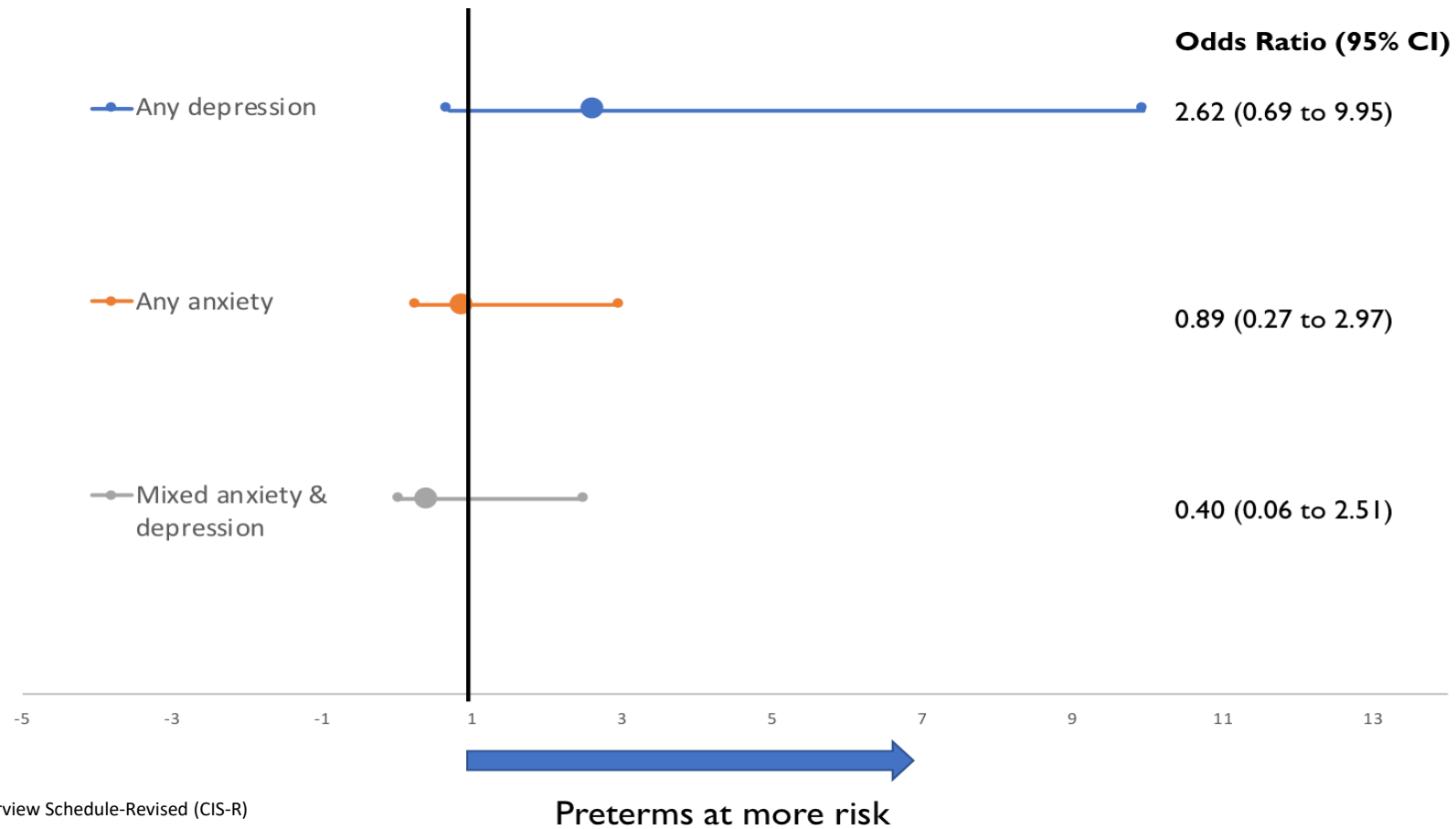
EPIcure @ 19: DSM-oriented Scales (self-report)



Johnson, S., O'Reilly, H., Ni, Y., Wolke, D., & Marlow, N. (in press). Psychiatric symptoms and disorders in extremely preterm young adults at 19 years of age and longitudinal findings from middle childhood. *Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP)*.




EPIcure @ 19: Primary CIS-R* Diagnosis



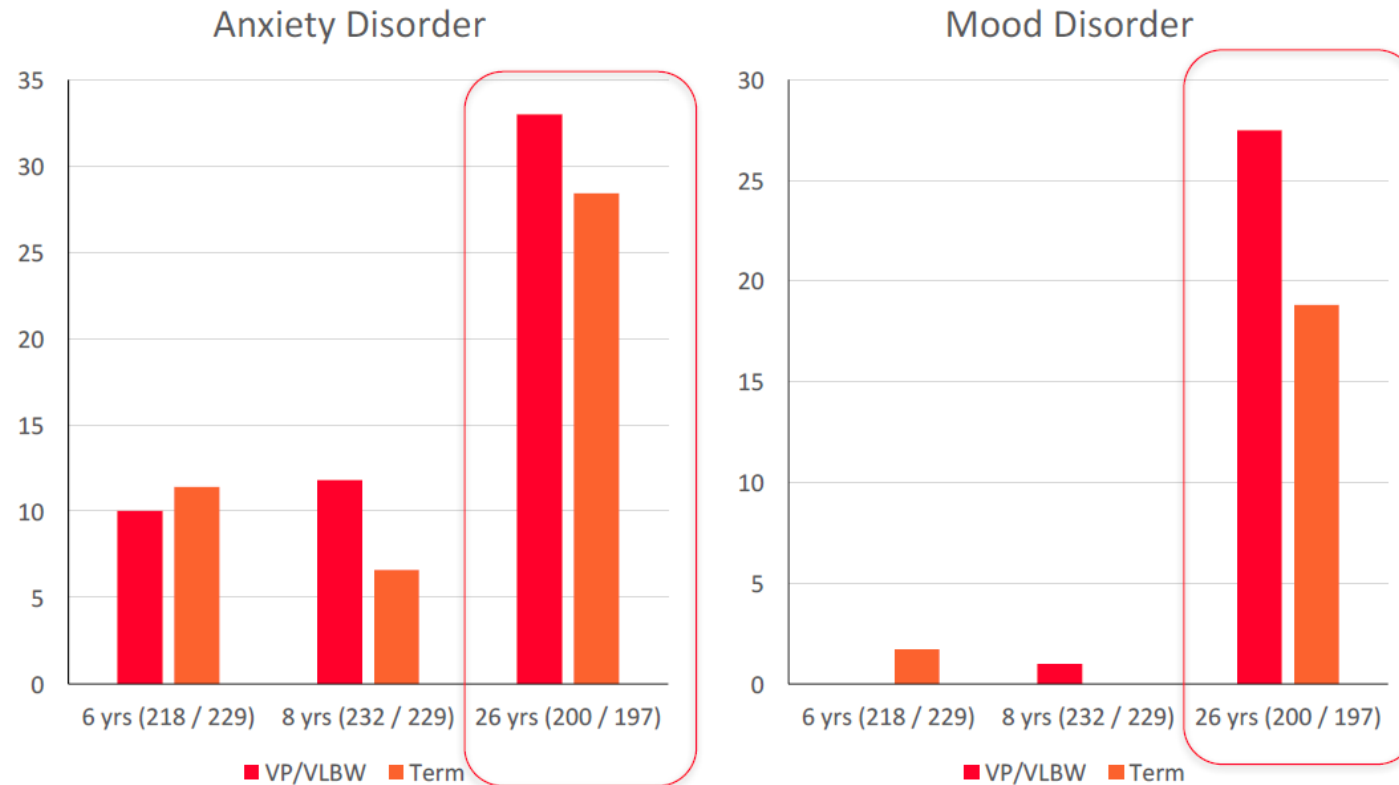
Johnson, S., O'Reilly, H., Ni, Y., Wolke, D., & Marlow, N. (in press). Psychiatric symptoms and disorders in extremely preterm young adults at 19 years of age and longitudinal findings from middle childhood. *Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP)*.



Mood and anxiety disorders in very preterm/very low-birth weight individuals from 6 to 26 years

Julia Jaekel,^{1,2}  Nicole Baumann,² Peter Bartmann,³ and Dieter Wolke²

¹Department of Child and Family Studies, University of Tennessee Knoxville, Knoxville, TN, USA; ²Department of Psychology, University of Warwick, Coventry, UK; ³Institute of Neonatology, University Hospital Bonn, Bonn, Germany

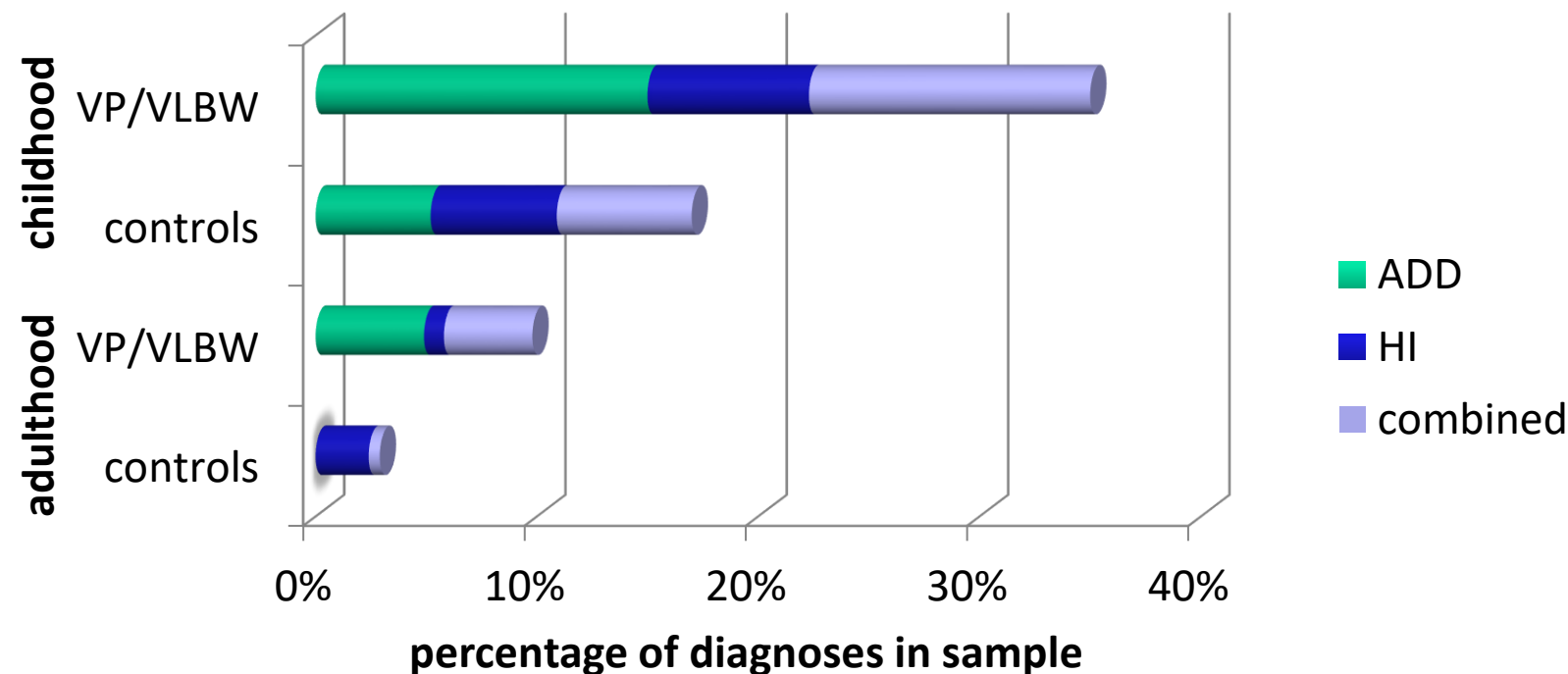




Attention problems in very preterm children from childhood to adulthood: the Bavarian Longitudinal Study

Linda D. Breeman,¹ Julia Jaekel,^{1,2} Nicole Baumann,¹ Peter Bartmann,³ and Dieter Wolke^{1,4}

ADHD diagnoses





Contents lists available at [ScienceDirect](#)

EClinicalMedicine

journal homepage: www.elsevier.com/locate/eclinm

Psychiatric disorders in individuals born very preterm / very low-birth weight: An individual participant data (IPD) meta-analysis

Peter J Anderson, PhD^{a,b,*}, Debora Marques de Miranda, MD^c,
Maicon Rodrigues Albuquerque, PhD^c, Marit Sæbø Indredavik, PhD^d,
Kari Anne I. Evensen, PhD^{d,e,f}, Ryan Van Lieshout, MD^g, Saroj Saigal, MD^h,
H. Gerry Taylor, PhDⁱ, Katri Raikonen, PhD^j, Eero Kajantie, DMedSc^{d,k,l,m},
Neil Marlow, DMⁿ, Samantha Johnson, PhD^o, Lianne J. Woodward, PhD^p,
Nicola Austin, DM^q, Chiara Nosarti, PhD^{r,s}, Julia Jaekel, PhD^{t,u}, Dieter Wolke, PhD^u,
Jeanie LY Cheong, MD^{b,v,w}, Alice Burnett, PhD^{b,v}, Karli Treyvaud, PhD^{b,x},
Katherine J Lee, PhD^{b,y}, Lex W Doyle, MD^{b,v,w}

Published December 2021

- ▶ IPD of 10 cohort studies
- ▶ Psychiatric diagnoses in adulthood

Added value of this study

This individual participant data meta-analysis suggests that individuals born VP/VLBW might have higher odds of meeting criteria for Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, and Anxiety Disorder than term/NBW controls.

Summary Mental Health

- Continued increased risk of ADHD and ASD symptoms
- Small increased risk for overall anxiety after VP/VLBW birth once carefully controlled for multiple comparisons
- Avoidant Personality (anxious social interactions/withdrawn)

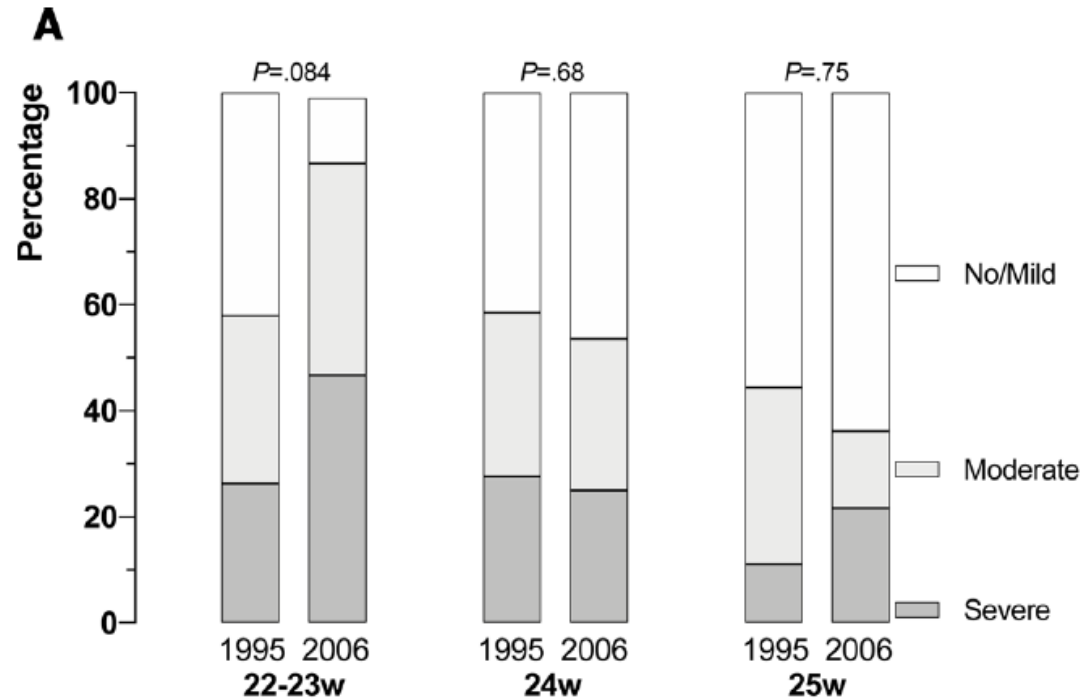




Is everything better now? Survival: YES; Outcome: NO

No change in neurodevelopment at 11 years after extremely preterm birth

Neil Marlow ^{ID},¹ Yanyan Ni,^{1,2} Rebecca Lancaster,³ Emmi Suonpera,¹ Marialivia Bernardi,¹ Amanda Fahy,¹ Jennifer Larsen,³ Jayne Trickett,³ John R Hurst,⁴ Joan Morris,⁵ Dieter Wolke ^{ID},⁶ Samantha Johnson³



Impairment, motor or IQ – no improvement

Reduced health-related quality of life in children born extremely preterm in 2006 compared with 1995: the EPICure Studies

Yanyan Ni ^{ID},^{1,2} Samantha Johnson,³ Neil Marlow ^{ID},¹ Dieter Wolke ^{ID}^{2,4}

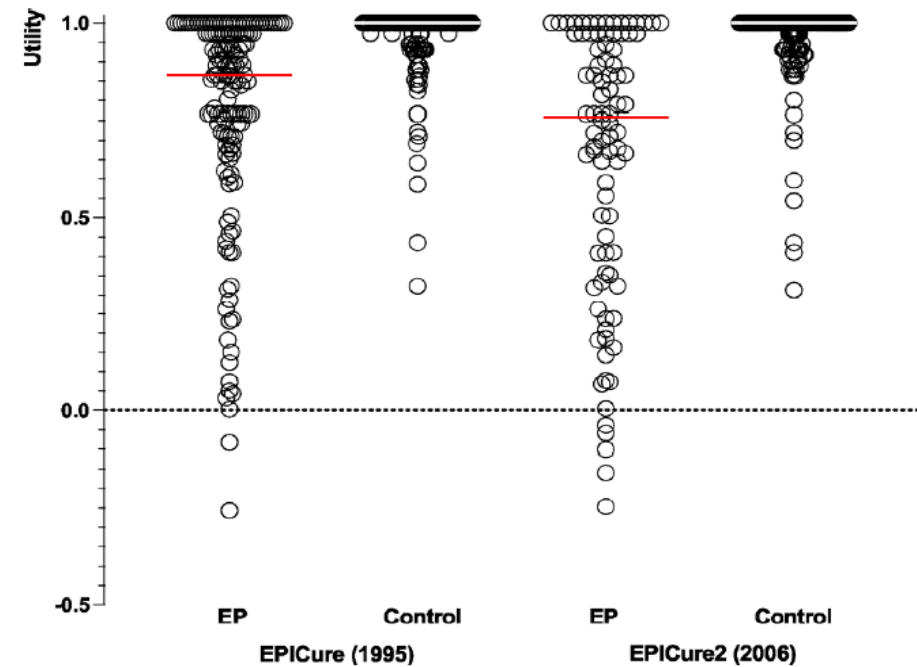
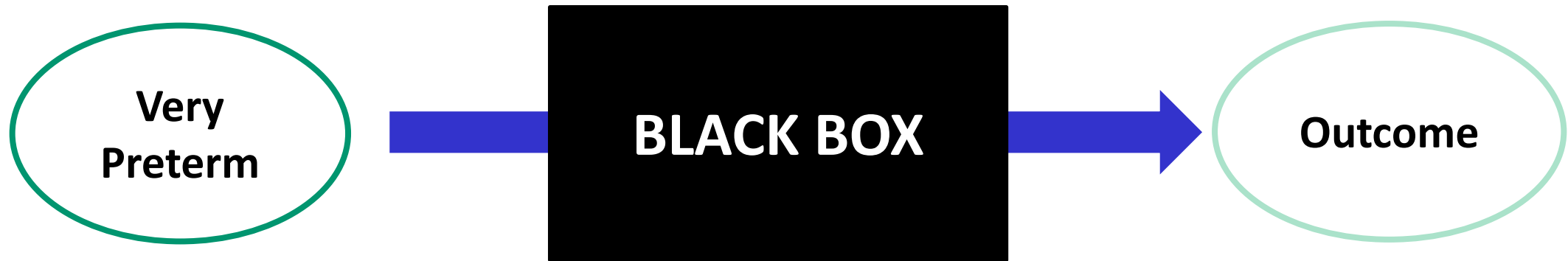


Figure 1 Distribution of the HUI3 utility scores for children born <26 weeks of gestation in England and term-born controls. EP, extremely preterm; HUI, Health Utilities Index.

Current Research: VP and Outcome



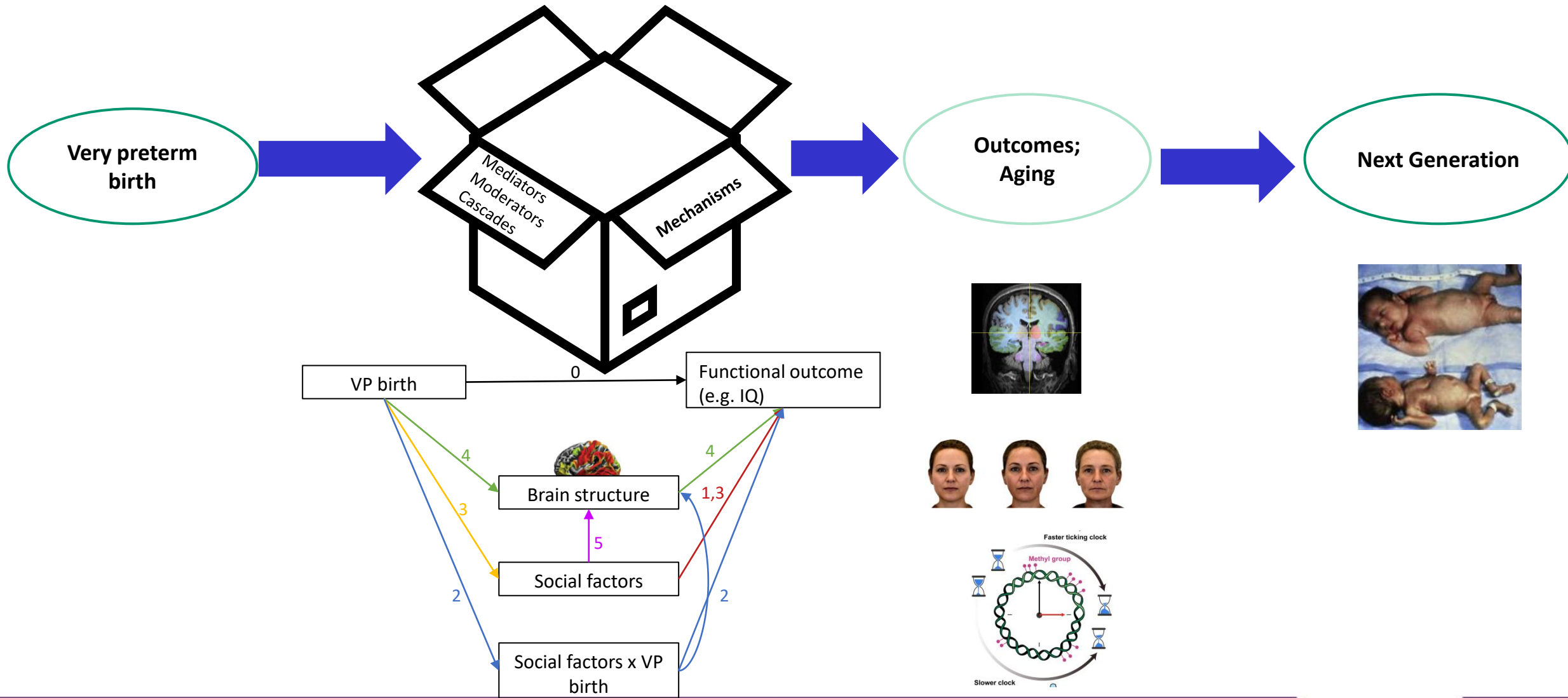
It is:

- Negative experience
- Requires adaptation
- Deviation from expectable environment

In areas of:

- Disease
- Disability
- Mental Health

Our Approach



New €2.8m project will seek insights into aging from pre-term births

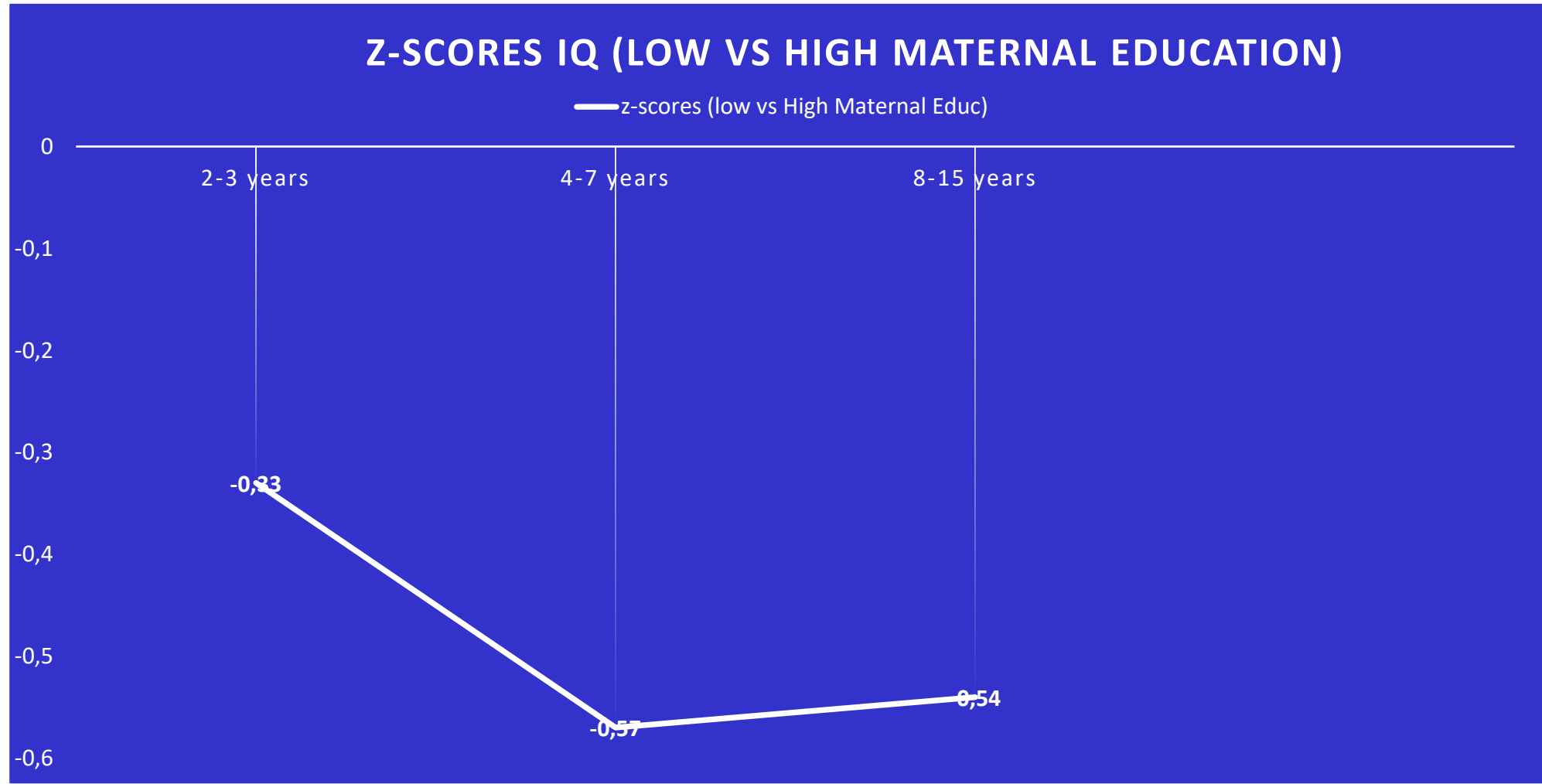
- University of Warwick research to investigate whether many age-related conditions are determined for us before we are born
- Project received funding from European Research Council of 2,803,123 euros

ERC Advanced Grant
(April, 26, 2022)



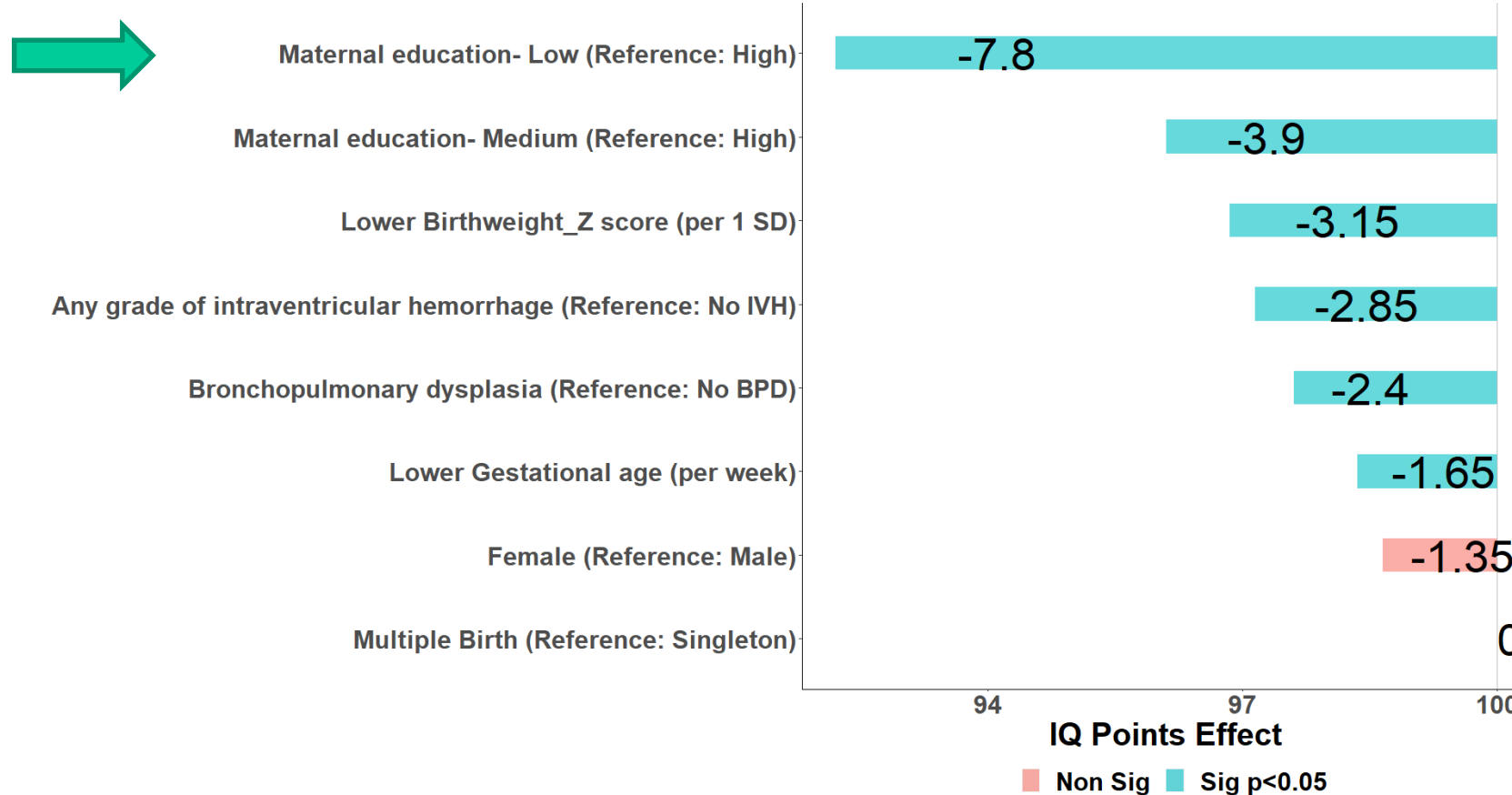
The PRETERM-LIFECOURSE project, led by Professor Dieter Wolke, will study whether age related function, disease and the time we may die is already determined in the womb and at birth. To test whether the speed of development is altered and has trade-offs such as early ageing, they will study babies born very preterm (more than 8 weeks early) who the team have followed from birth and have now reached middle age.

Family of Origin: Maternal Education – IQ – Child Age



Sentenac, M., Benhammou, V., Aden, U., Ancel, P.-Y., Bakker, L. A., Bakoy, H., . . . Zeitlin, J. (2021). Maternal education and cognitive development in 15 European very-preterm birth cohorts from the RECAP Preterm platform. *INTERNATIONAL JOURNAL OF EPIDEMIOLOGY*. doi:10.1093/ije/dyab170

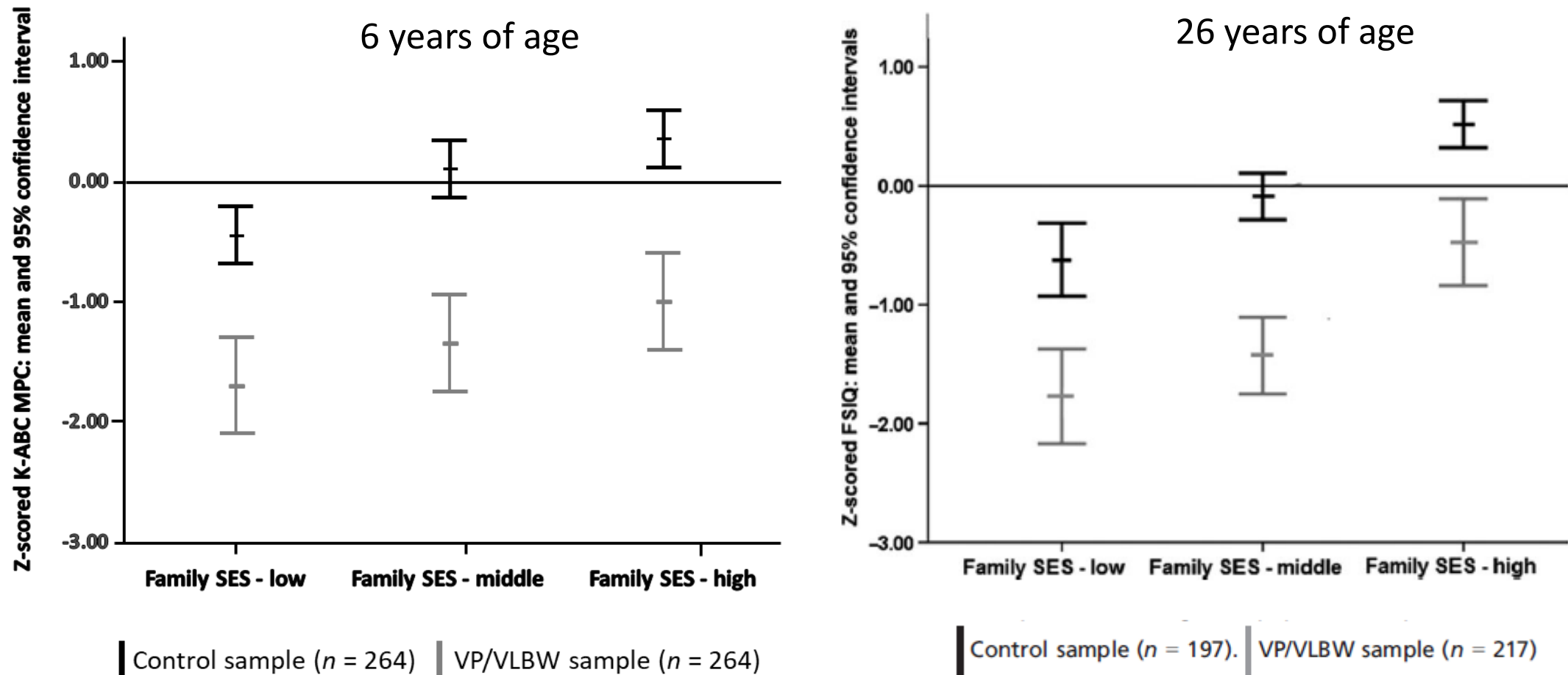
Association of Individual Level Factors with Adult IQ in VP/VLBW



Term Born Controls:
Mean 100, SD 15

Full Scale IQ-scores according to family SES at 6 years and at 26 years of age in VP/VLBW and Full-term Controls (BLS)

Main Effect

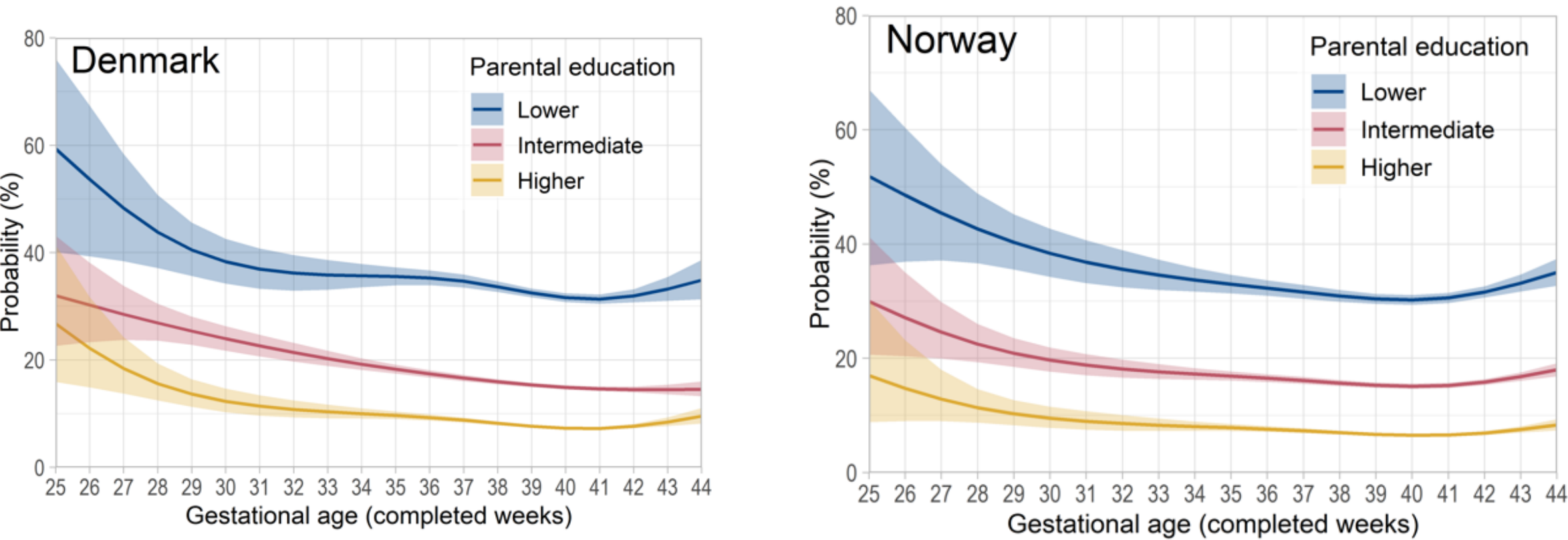


© Dieter Wolke

Parental Education: Offspring Educational Attainment at 25 years

Probability of Low Educational Attainment: Gestation and Family of Origin

Main Effect



Parenting at 6 years: Educational attainment at 13 years

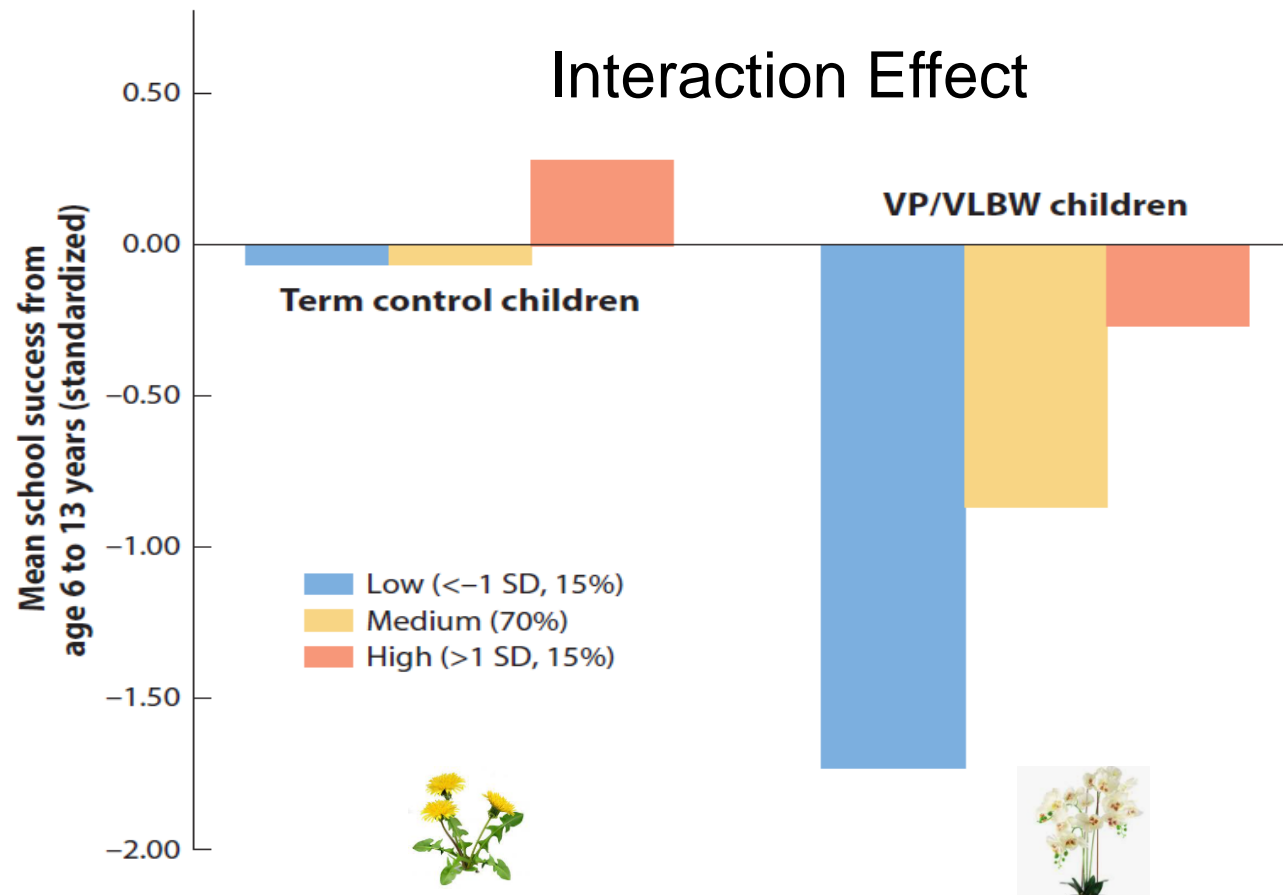


Figure 2

Effect of sensitive parenting (low, medium, or high) at 6 years of age on school success at 13 years of age. Variation by very preterm (VP)/very low birthweight (VLBW) versus term-born status. Abbreviation: SD, standard deviation. Adapted with permission from Wolke et al. (2013).

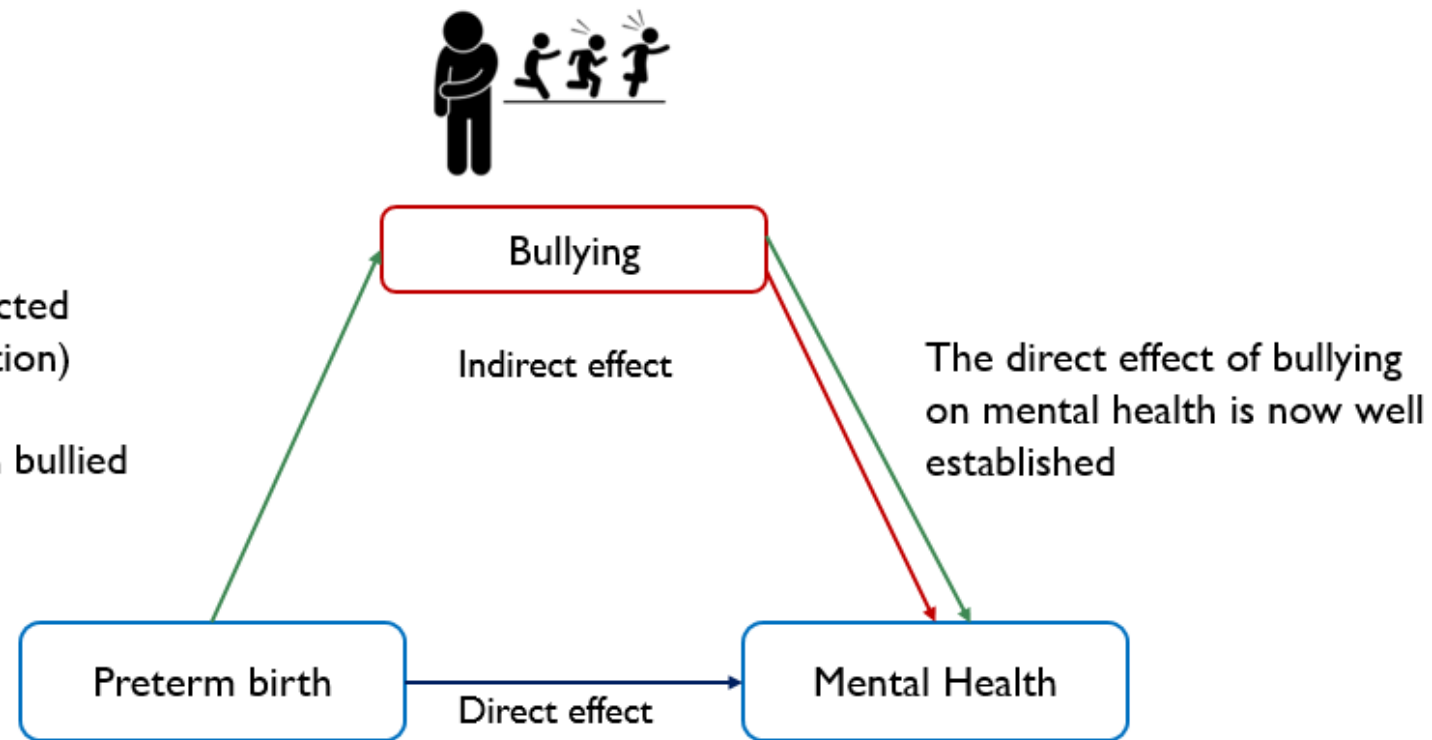


Mental Health: Mechanism Victimisation

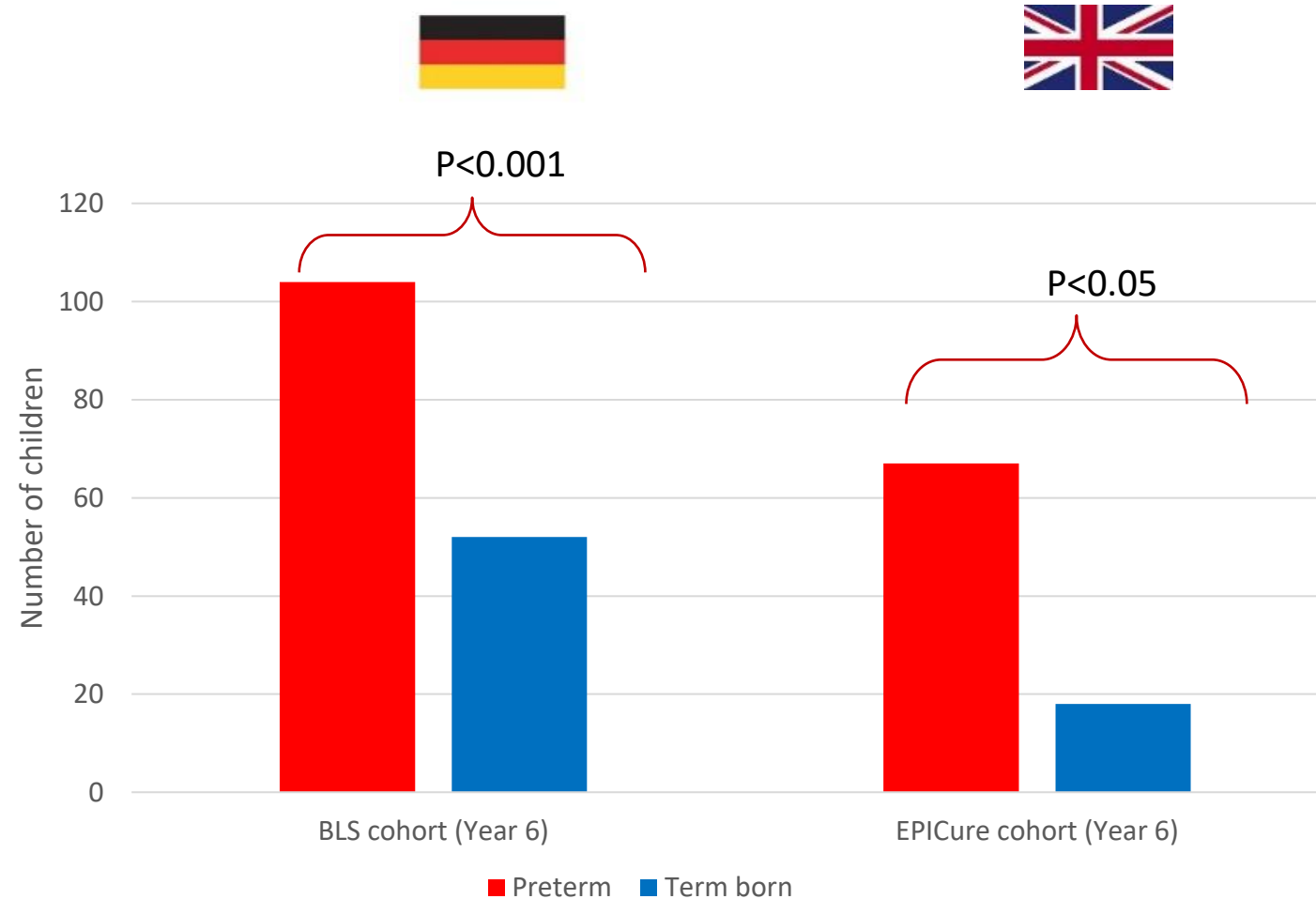
Mediation Model: Prematurity, Trauma and Mental Health

Mediation

- VP/VLBW more affected by bullying (moderation)
- They are more often bullied (mediation)



Frequency of being bullied in preterm children



Wolke, D., Baumann, N., Strauss, V., Johnson, S., & Marlow, N. (2015). Bullying of preterm children and emotional problems at school age: Cross-culturally invariant effects. *The Journal of Pediatrics*, 166(6), 1417–1422. <https://doi.org/10.1016/j.jpeds.2015.02.055>

Bullying and emotional problems



Table III. Regressions of prematurity and being bullied at 1 or 2 time points on emotional problem scores in year 6/7 of schooling

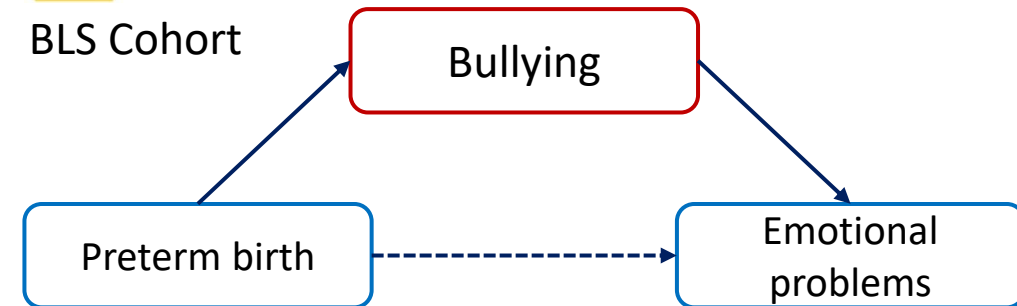
Predictors	Model 1 (unadjusted), main effects, B (95% CI)	Model 2 (adjusted*), effects, B (95% CI)
BLS cohort		
VP/VLBW	0.48 (0.15-0.81) [†]	0.25 (−0.06 to 0.57)
Being bullied at 1 time point	0.68 (0.32-1.04) [‡]	0.26 (−0.08 to 0.60)
Being bullied at 2 time points	1.46 (0.94-1.97) [‡]	0.78 (0.28-1.27) [†]
EPICure cohort		
EP	0.91 (0.39-1.42) [†]	0.73 (0.22-1.24) [†]
Being bullied at 1 time point	1.37 (0.80-1.95) [‡]	1.33 (0.60-1.67) [‡]
Being bullied at 2 time points	2.43 (1.68-3.18) [‡]	1.55 (0.79-2.30) [‡]

[†] $P < .01$.

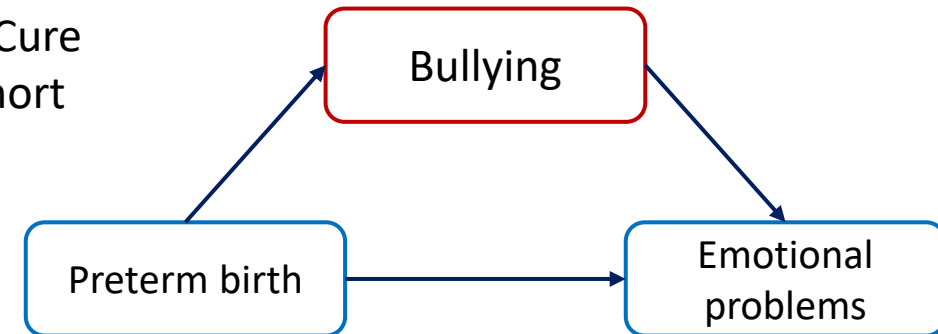
[‡] $P < .001$.



BLS Cohort



EPICure
Cohort



Wolke, D., Baumann, N., Strauss, V., Johnson, S., & Marlow, N. (2015). Bullying of preterm children and emotional problems at school age: Cross-culturally invariant effects. *The Journal of Pediatrics*, 166(6), 1417–1422. <https://doi.org/10.1016/j.jpeds.2015.02.055>

Summary: Peer Bullying



Preterm born children
have more psychiatric
problems



Bullying increases
risk of psychiatric
problems



Preterm born
children are bullied
more often



Bullying mediates the
relationship between
preterm birth and
psychiatric outcomes

Social Neuro-protection

**Social Influences/
Social Neuroprotection**



Very preterm birth



BLACK BOX



Lifespan Outcome

Core Assessments

44

- Family of Origin
 - *Parental Education*
 - or Socio-economic status
- *Parenting* measure – *Best observed – sensitivity*;
 - or Parenting style reported
- Need to assess *Peer Relationships*

Parenting and peer measures are completely missing but needed



What About Quality of Life (QoL) For Parents?



Very Preterm Birth and Parents' Quality of Life 27 Years Later

Dieter Wolke, PhD, Dr rer nat hc,^{a,b} Nicole Baumann, BSc,^b Barbara Busch, MD,^c Peter Bartmann, MD, Dr rer nat^c



Parents Quality of Life when their Children's are Adults: What predicts it?

► What is the Quality of Life?

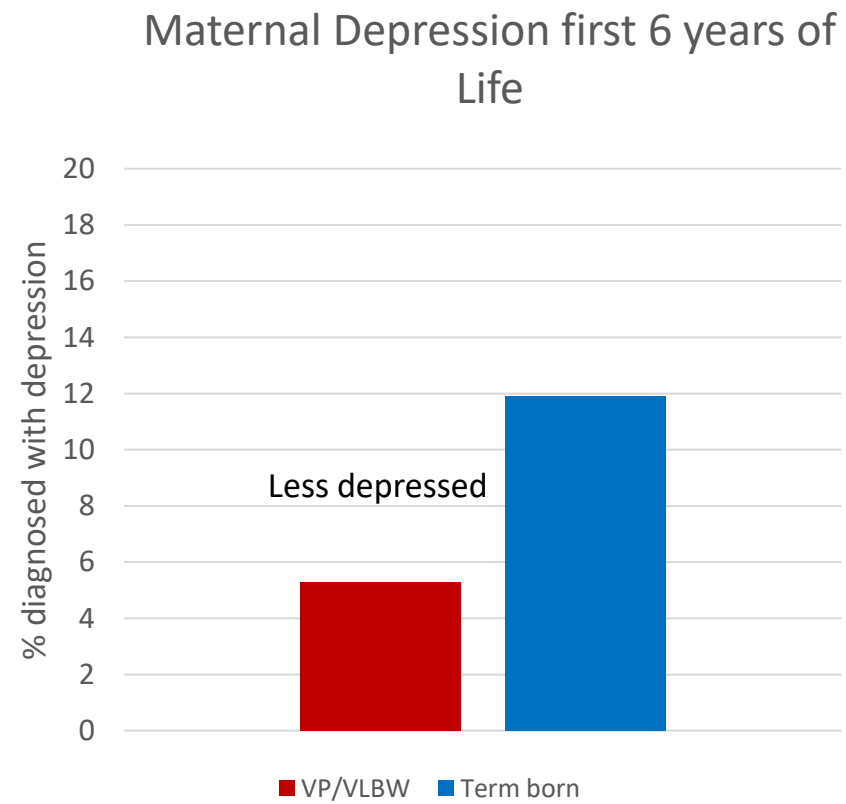
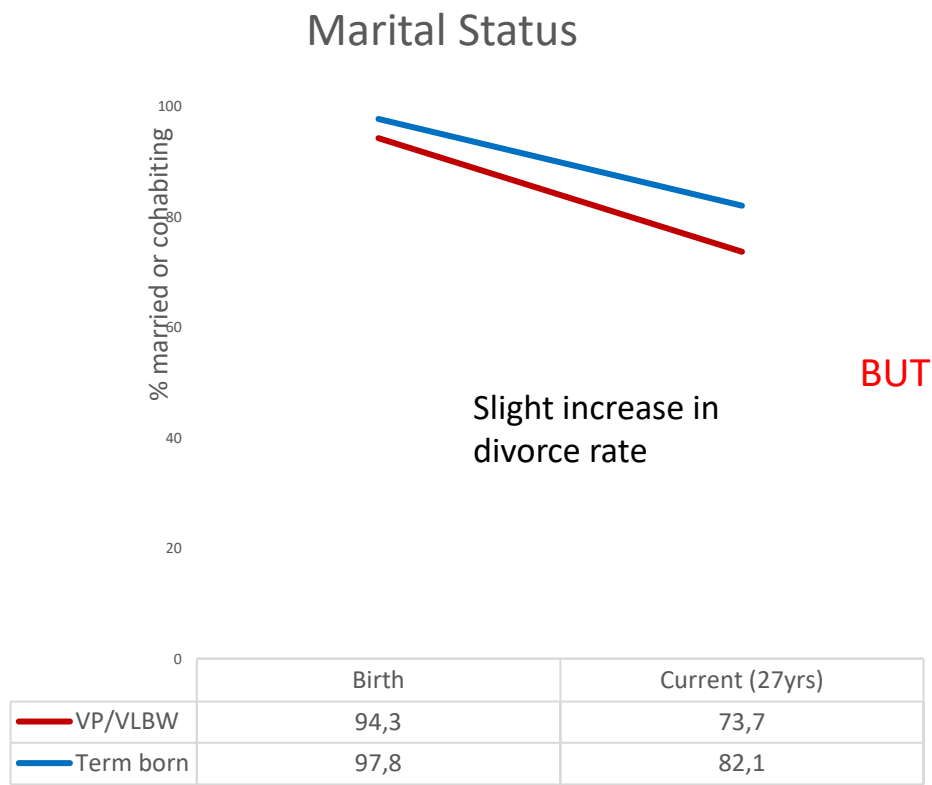
World Health Organization Quality of Life assessment
Global score of quality of life and general health
Physical health
Psychological health
Social relationships
Environment
Life satisfaction (global score)

► What in Children's childhood functioning predicts Quality of Life of Parents?

VP and VLBW versus term
Any disability
Mental health
Academic achievement
Parent–child relationship
Peer relationship



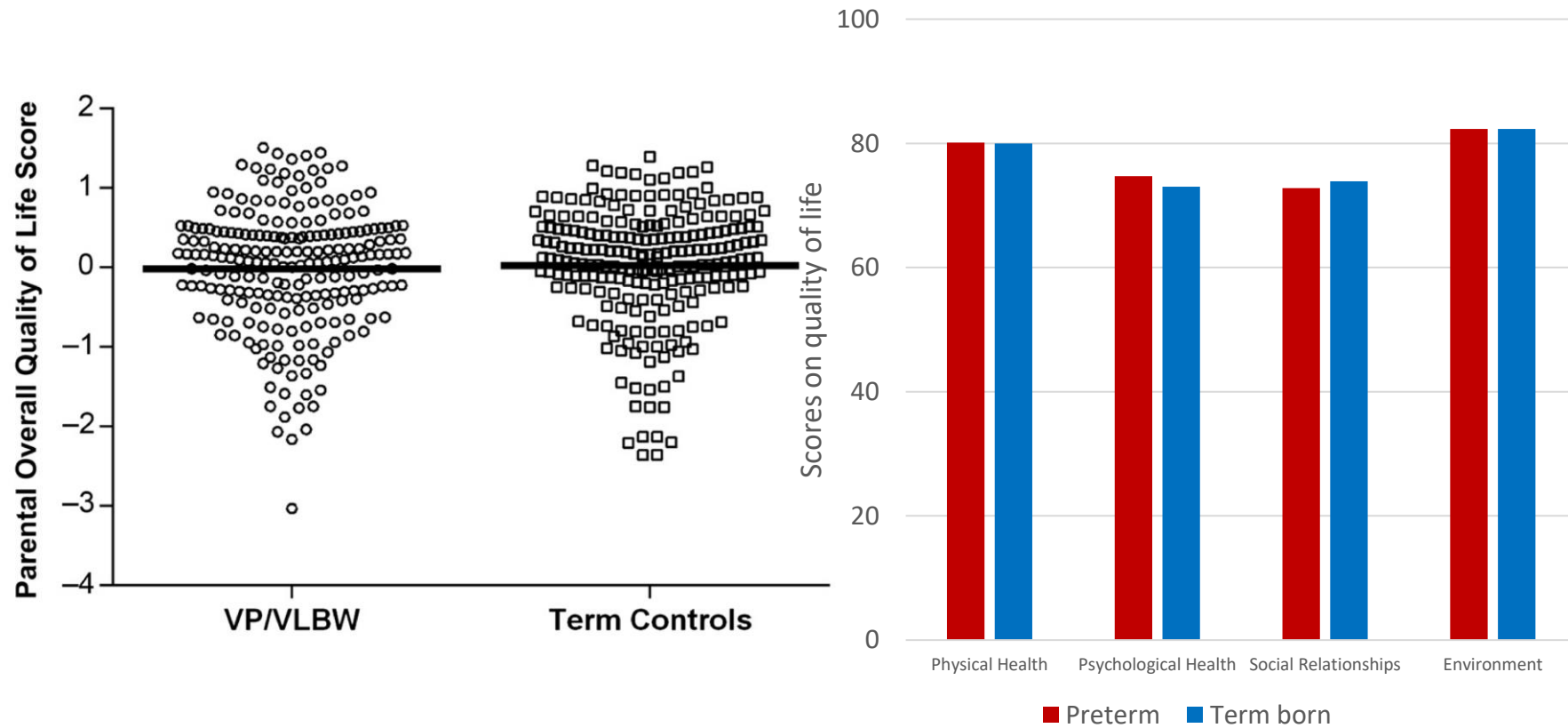
Make it or Break it!



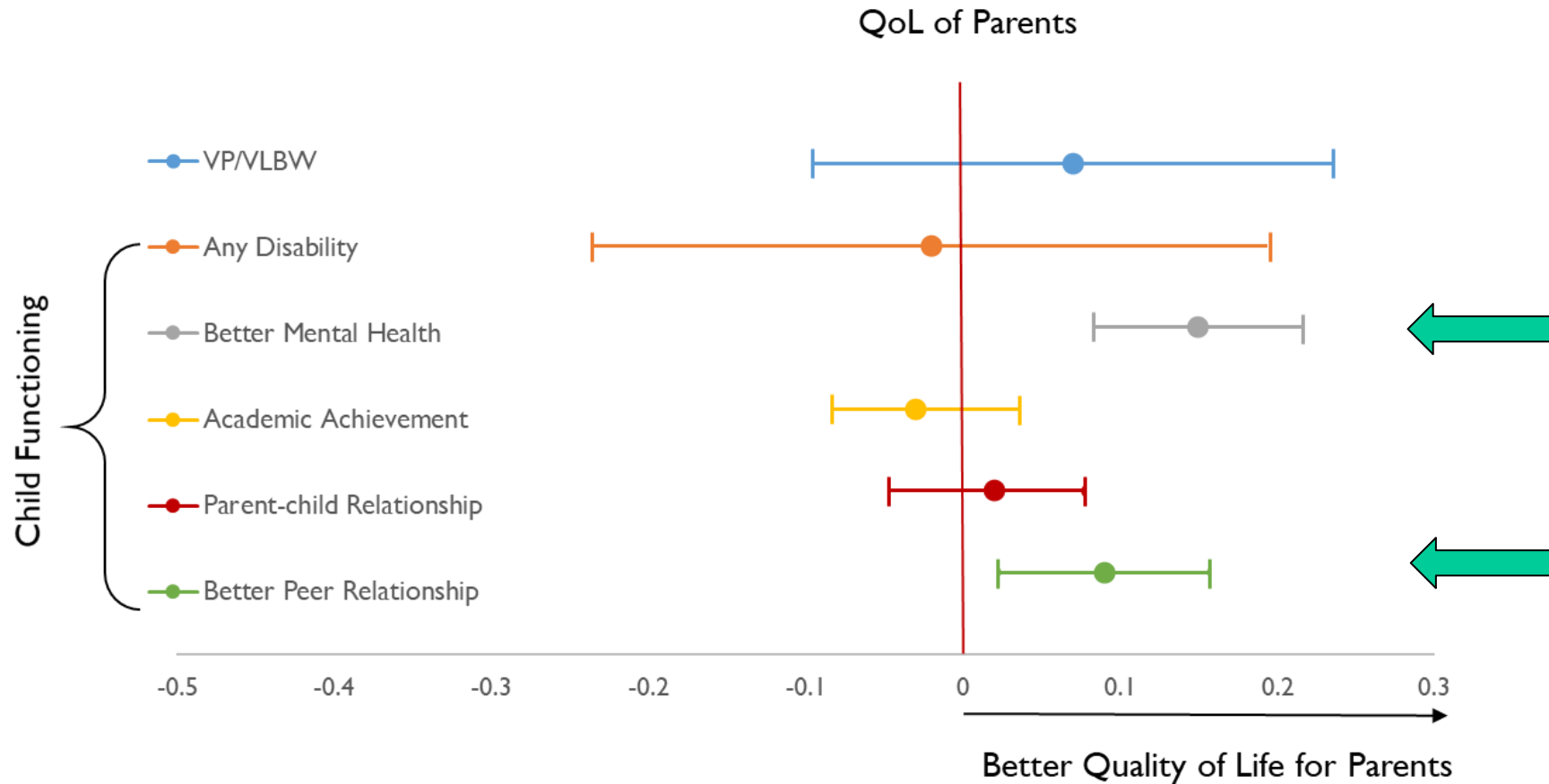


Parents' QoL 27 Years Later

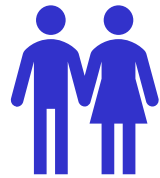
No Difference



Child Functioning and Parents' QoL



What really matters for Parents' Quality of Life



Resilience

Quality of life of parents of preterm born children no different from parents of term born children



Children's mental health and peer relationships predicted parents' quality of life more than a decade later

If their kids are **happy** and have **friends** in childhood – parents are more satisfied in adulthood



Although preterm born children more often experienced disability, it did not reduce quality of life of parents

Conclusions

NEONATALLY

- Create a more family centred neonatal unit
- Try for gentle safe treatment



AFTER DISCHARGE

- Preterms are more sensitive to adverse environment (more vulnerable)
- Support optimal parenting
- Focus on social integration and social skills – prevent bullying
- Parent and Teacher Training on Needs of Preterm children (Preschool, early school age)



**Social
Neuro-
protection**

Chairs of the TEG



*Professor Dieter Wolke,
UK/Germany*



*Dr Aleid van
Wassenae-Leemhuis,
The Netherlands*



Comprehensive Review

Annual Review of Developmental Psychology

The Life Course Consequences of Very Preterm Birth

Dieter Wolke,^{1,2} Samantha Johnson,³
and Marina Mendonça¹

2019, Vol 1, 69-92 DOI: [10.1146/annurev-devpsych-121318-084804](https://doi.org/10.1146/annurev-devpsych-121318-084804)



Questions?

