



Behavioral Phenotype of Prematurity

The Perfect Storm of ‘Minor’ Morbidities

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Holland Bloorview

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HEALTH SCIENCES CENTRE

when it matters
MOST

Disclosure

I have no actual or potential conflict of interest in relation to this program.
I also assume responsibility for ensuring the scientific validity, objectivity,
and completeness of the content of my presentation.



"How is Kayli going to be class president if she won't disclose the contents of her lunchbox? How much chocolate is she hiding?"



Objectives

At the end of the session, you will be able to:

1. Review behavioural phenotype of prematurity
2. Review ethology of phenotype
3. Discuss gaps in current system for preterm infants
 - a. Community/school systems
 - b. Neonatal follow up

“Knowing that we can be loved exactly as we are gives us all the best opportunity for growing into the healthiest of people.”

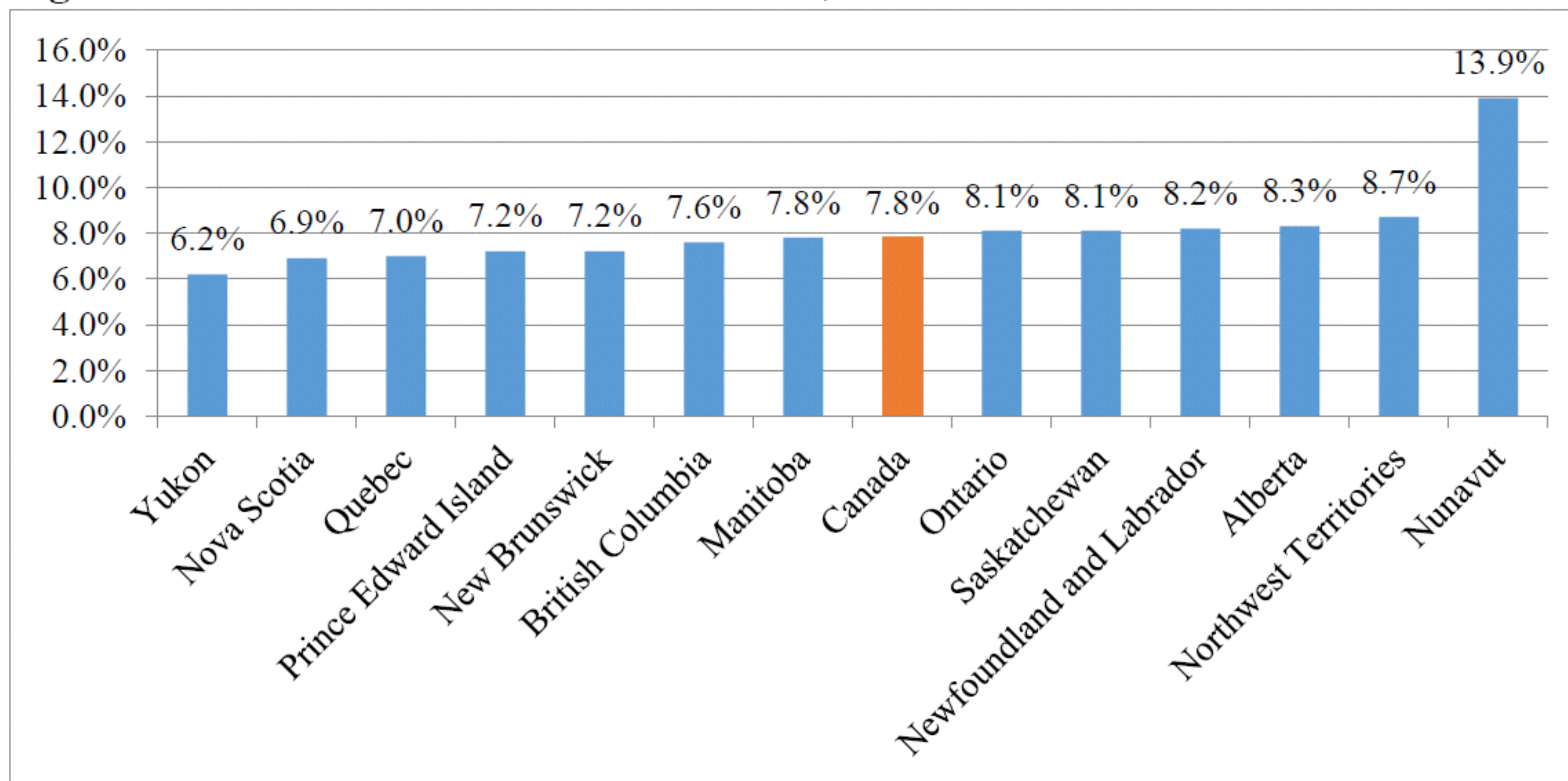


-Fred Rogers



Background

Figure 1: Rates of Preterm Birth in Canada, 2011/12¹⁰



Canadian Premature Babies Foundation –
Fondation pour Bébés Prématurés Canadiens



Born Too Soon

The Global Action Report on Preterm Birth

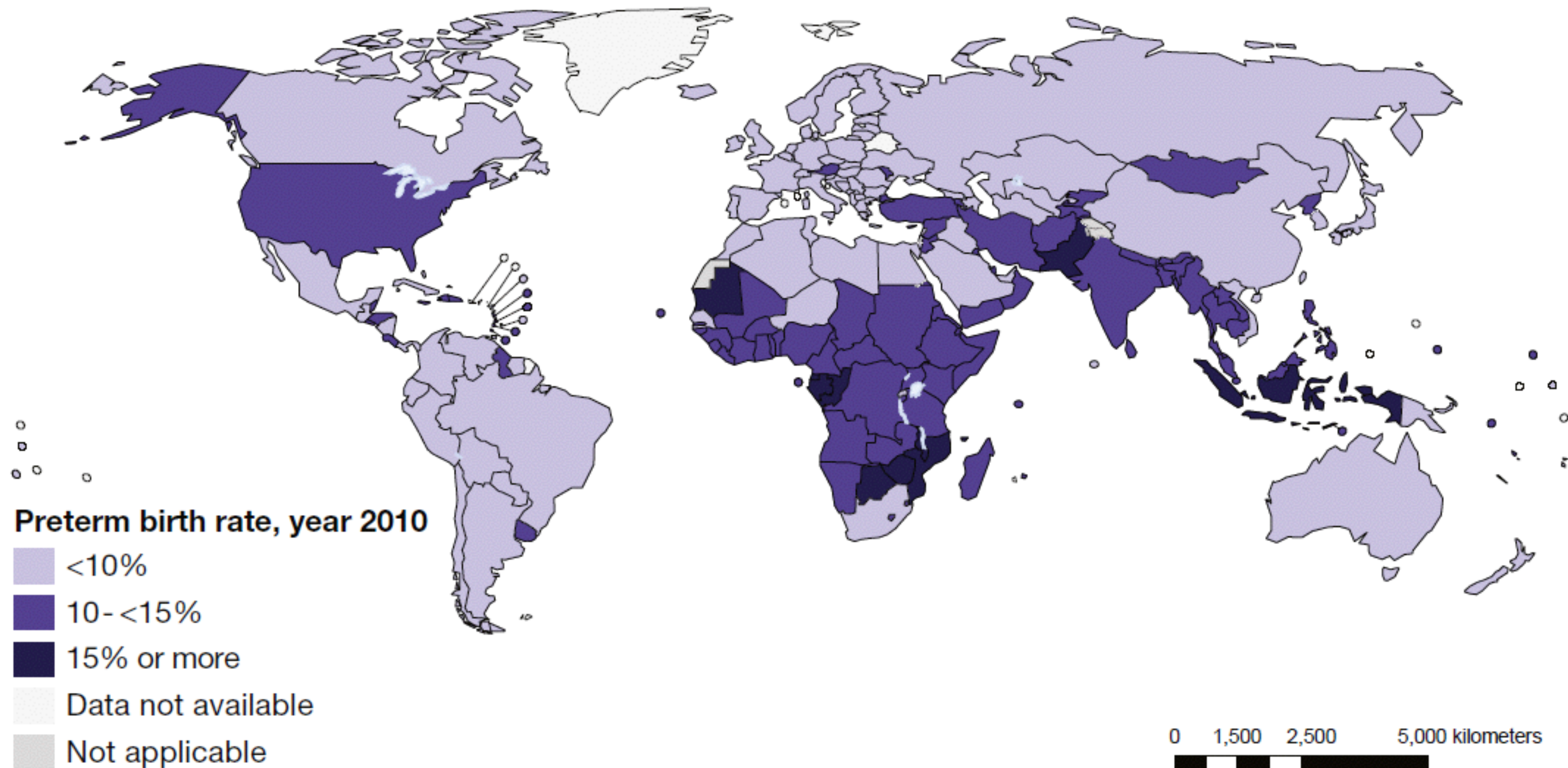
march of dimes

The Partnership
for Maternal, Newborn
& Child Health

Save the Children

World Health
Organization

Figure 2: Global burden of preterm birth in 2010

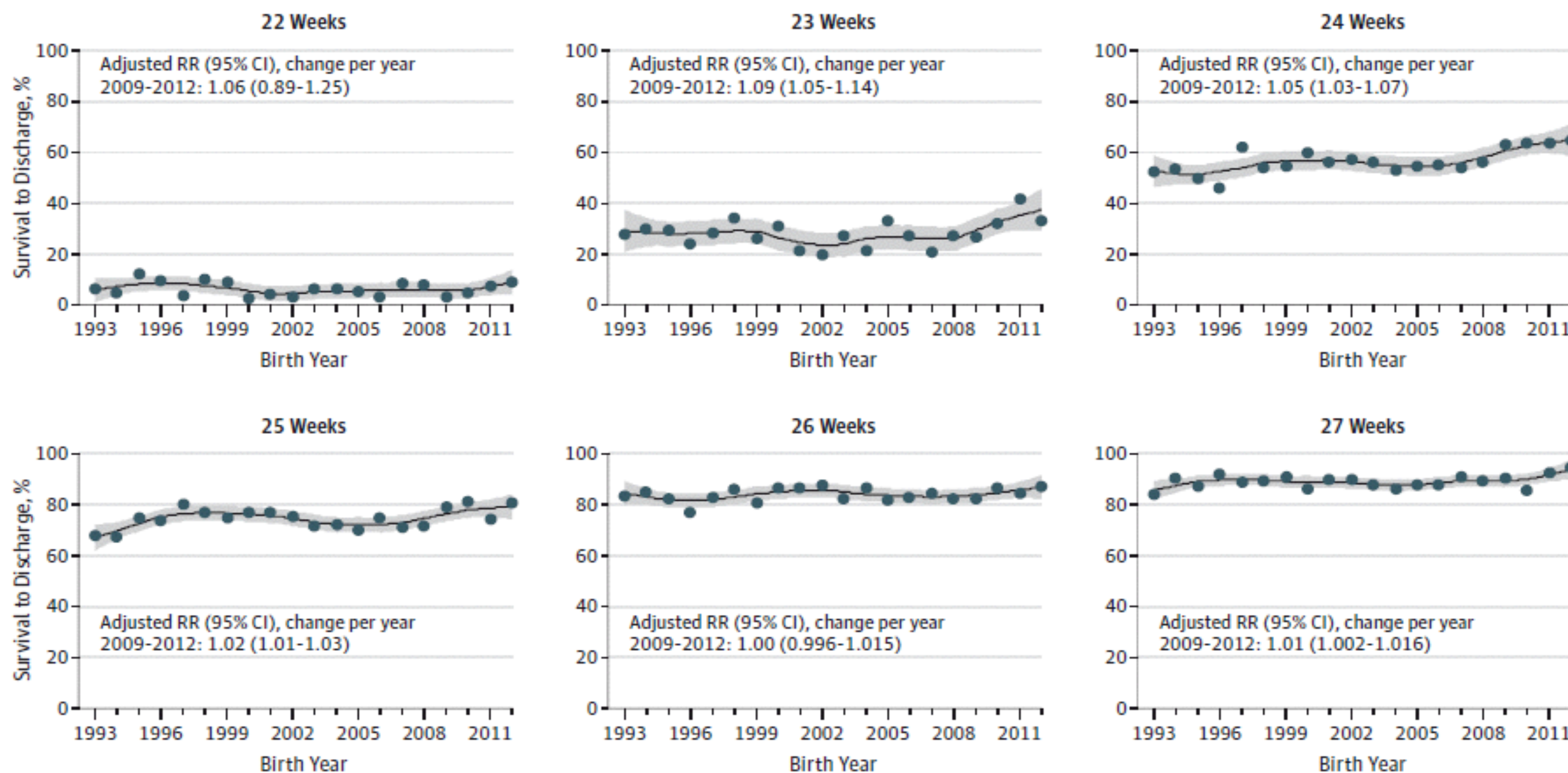


**11 countries with
preterm birth rates
over 15% by rank:**

| |
|----------------------|
| 1. Malawi |
| 2. Congo |
| 3. Comoros |
| 4. Zimbabwe |
| 5. Equatorial Guinea |
| 6. Mozambique |
| 7. Gabon |
| 8. Pakistan |
| 9. Indonesia |
| 10. Mauritania |
| 11. Botswana |

Background

Figure 3. Infant Survival to Discharge By Birth Year and Gestational Age



Age of viability decreasing

- 22 x/7 weeks versus 23 weeks versus 24 weeks

Rysavy MA, Lei L, Bell EF et al. Between-Hospital Variation in Treatment and Outcomes in Extremely Preterm Infants. NEJM 2015;327:1801-11

Neonatal Outcomes

Outcomes of prematurity fairly stable 6-25%

- Impairment defined by the presence of
- Cerebral palsy
- Vision impairment
- Hearing impairment
- Cognitive impairment



Magazine cover: http://sunnybrook.ca/uploads/1/_foundation/pubs/lr_sb_final_fall2015_aug21_acc.pdf

Synnes A, Luu TM, Moddemann D et al. Determinants of developmental outcomes in a very preterm Canadian cohort. *ADC Fetal Neonatal Ed.* 2017;102:F235-243.



Neonatal Outcomes

- 50-70% of children born very preterm will have difficulty with school performance
- Proposed factor = 'minor' morbidities
- 'Minor' morbidity because considered non-disabling in nature

Aylward GP. Neurodevelopmental Outcomes of Infants Born Prematurely. JDBP 2014;35:394-407



‘Minor’ Morbidities

Challenges with:

- Language comprehension and expression (Verbal and nonverbal communication)
- Learning (Spatial relationships)
- Impulse control, busy behaviour
- Organizational abilities
- Autism Spectrum Disorder (ASD)
- Social immaturity, Emotional lability
- Anxiety (separation anxiety)
- Motor coordination

Aylward GP. Neurodevelopmental Outcomes of Infants Born Prematurely. JDBP 2014;35:394-407

Church PT, Luther M, Asztalos E. The perfect storm: minor morbidities in the preterm survivor. Curr Pediatr Rev,2012; 8: 142-151.

Hutchinson EA, De Luca CR, Doyle, LW, Roberts G, Anderson PJ. Victorian Infant Collaborative Study Group. School-age Outcomes of Extremely Preterm or Extremely Low Birth Weight Children. Pediatrics. 2013;131(4):e1053.

Joseph RM, O’Shea TM, Allred EN, et al Neurocognitive and academic outcomes at age 10 years of extremely preterm newborns. Pediatrics 2016;137(4): e20154343.



Autism Spectrum Disorder

Deficits in social communication and social interaction

- Social emotional reciprocity
- Nonverbal communication
- Difficulty making, sustaining, or understanding relationships

Restricted repetitive patterns of behavior

- Stereotyped movement patterns
- Inflexible adherence to routines
- Fixated interests with abnormal intensity and focus

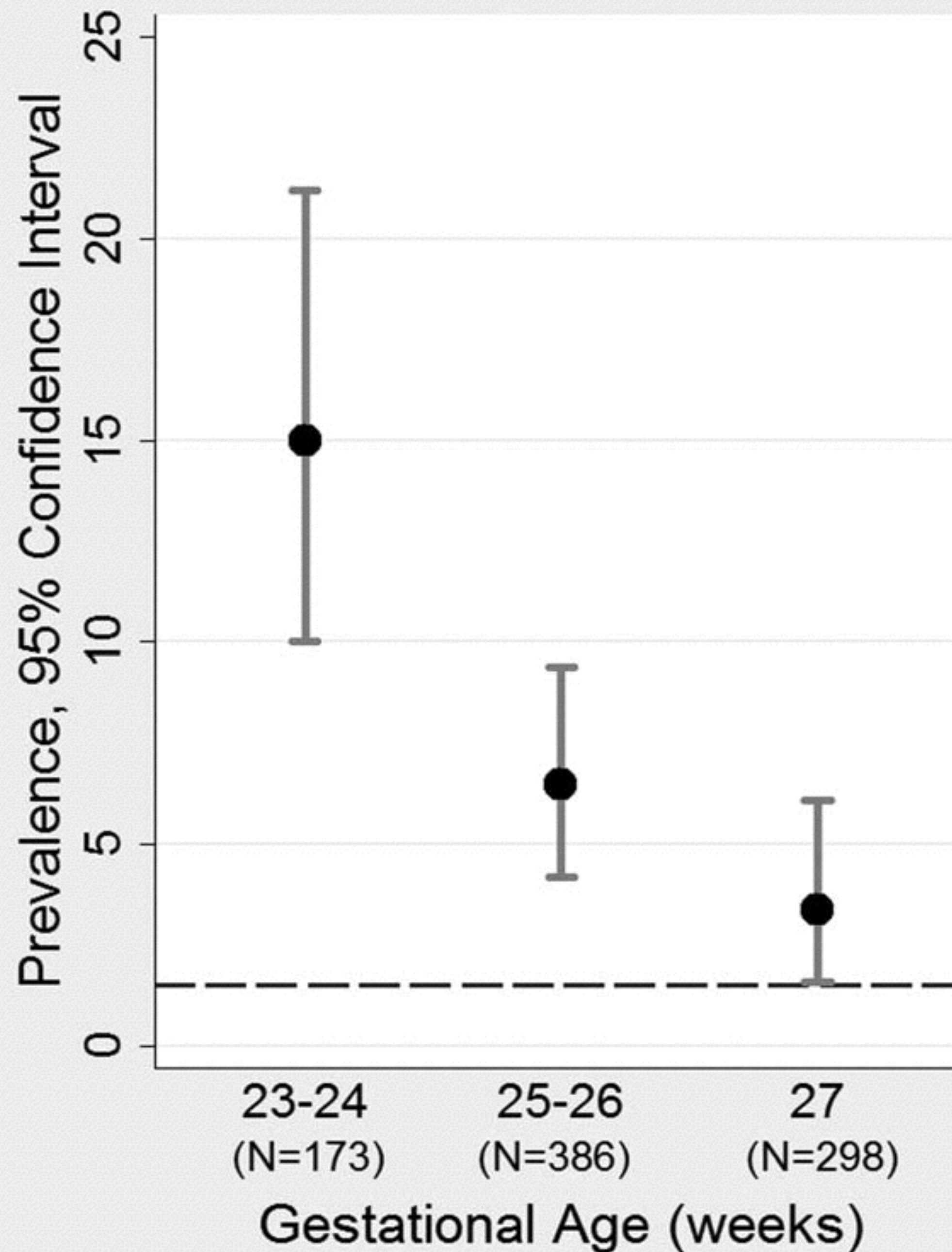
American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. Arlington, VA, American Psychiatric Association, 2013.



RESEARCH ARTICLE

Prevalence and Associated Features of Autism Spectrum Disorder in Extremely Low Gestational Age Newborns at Age 10 Years

Robert M. Joseph, Thomas M. O'Shea, Elizabeth N. Allred, Tim Heeren, Deborah Hirtz, Nigel Paneth, Alan Leviton, and Karl C. K. Kuban



Autism Spectrum Disorder

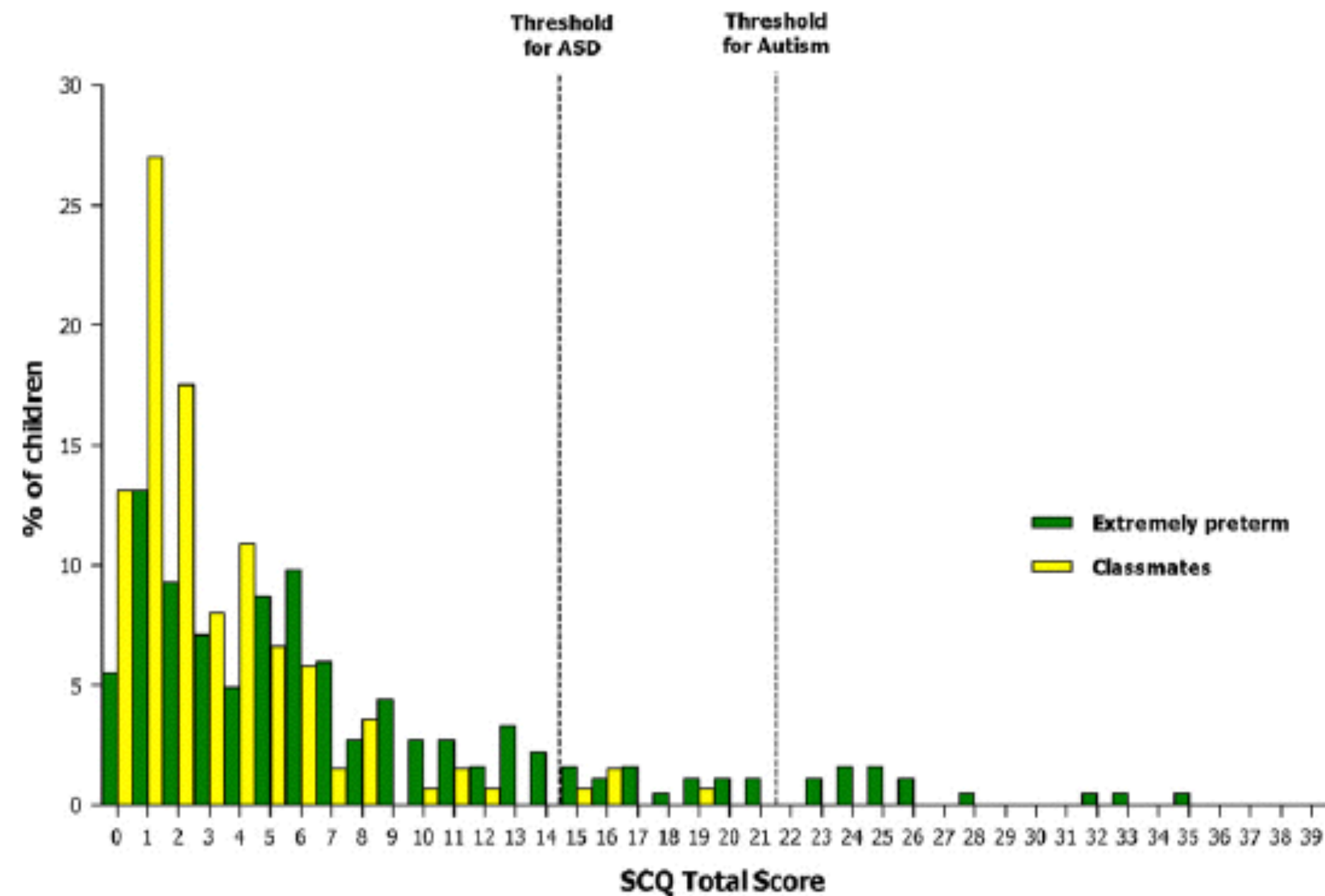
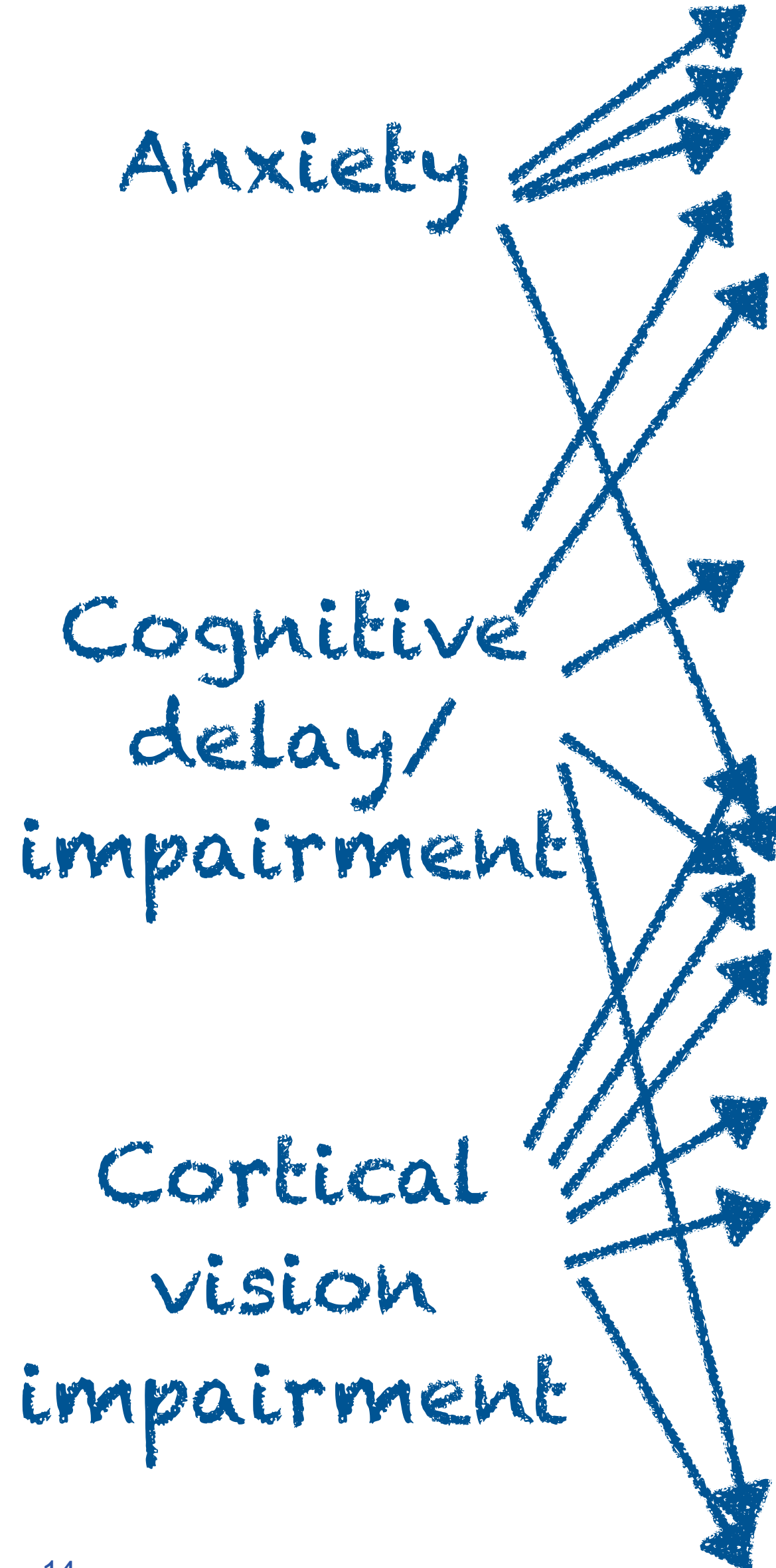


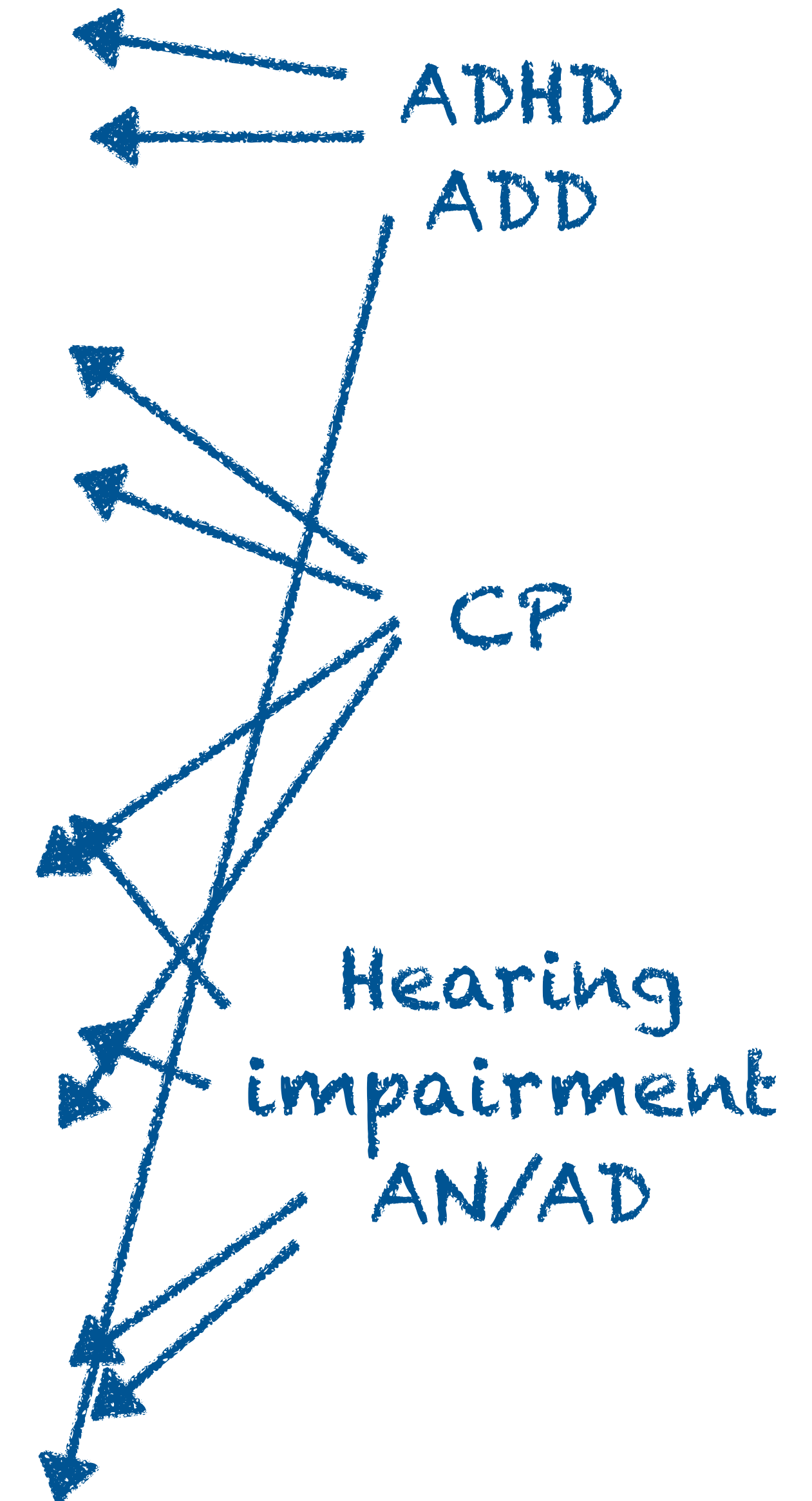
Figure. Frequency distribution showing proportion of children with each total SCQ score in the extremely preterm cohort (n = 183) and term-born classmates at 11 years of age (n = 137).

Johnson S, Hollis C, Kochhar P, Hennessey E, Wolke D, Marlow N. Autism Spectrum Disorders in Extremely Preterm Children. J Pediatrics 2010; 156: 525-531



M-CHAT Preterm

| M-CHAT (Modified Checklist for Autism in Toddlers) | | | |
|--|---|-----|----|
| Please fill out the following about how your child usually is. Please try to answer every question. If the behavior is rare (e.g., you've seen it once or twice), please answer as if the child does not do it. | | | |
| 1. | Does your child enjoy being swung, bounced on your knee, etc.? | Yes | No |
| 2. | Does your child take an interest in other children? | Yes | No |
| 3. | Does your child like climbing on things, such as up stairs? | Yes | No |
| 4. | Does your child enjoy playing peek-a-boo/hide-and-seek? | Yes | No |
| 5. | Does your child ever pretend, for example, to talk on the phone or take care of dolls, or pretend other things? | Yes | No |
| 6. | Does your child ever use his/her index finger to point, to ask for something? | Yes | No |
| 7. | Does your child ever use his/her index finger to point, to indicate interest in something? | Yes | No |
| 8. | Can your child play properly with small toys (e.g. cars or bricks) without just mouthing, fiddling, or dropping them? | Yes | No |
| 9. | Does your child ever bring objects over to you (parent) to show you something? | Yes | No |
| 10. | Does your child look you in the eye for more than a second or two? | Yes | No |
| 11. | Does your child ever seem oversensitive to noise? (e.g., plugging ears) | Yes | No |
| 12. | Does your child smile in response to your face or your smile? | Yes | No |
| 13. | Does your child imitate you? (e.g., you make a face-will your child imitate it?) | Yes | No |
| 14. | Does your child respond to his/her name when you call? | Yes | No |
| 15. | If you point at a toy across the room, does your child look at it? | Yes | No |
| 16. | Does your child walk? | Yes | No |
| 17. | Does your child look at things you are looking at? | Yes | No |
| 18. | Does your child make unusual finger movements near his/her face? | Yes | No |
| 19. | Does your child try to attract your attention to his/her own activity? | Yes | No |
| 20. | Have you ever wondered if your child is deaf? | Yes | No |
| 21. | Does your child understand what people say? | Yes | No |
| 22. | Does your child sometimes stare at nothing or wander with no purpose? | Yes | No |
| 23. | Does your child look at your face to check your reaction when faced with something unfamiliar? | Yes | No |





Neonatal Outcomes-Terminology

Spectrum in development from typical to atypical

- Normal
- Variant

- Problem
- Disorder

Wolraich ML, Felice ME, Drotar D, editors. The Classification of Child and Adolescent Mental Diagnoses in Primary Care. Diagnostic and Statistical Manual for Primary Care (DSM-PC) Child and Adolescent Version. Elk Grove Village, American Academy of Pediatrics; 1996.



Neonatal Outcomes

- Spectrum of outcomes possible
- Isolated 'minor' morbidity is rare
- Cluster of conditions more common
- Detection requires discrete assessments

Aylward GP. Neurodevelopmental Outcomes of Infants Born Prematurely. JDBP 2014;35:394-407



Neonatal Outcomes



Accardo PJ, Accardo JA, Capute AJ. A Neurodevelopmental Perspective on the Continuum of Developmental Disabilities. In: Accardo PJ, editor. Capute & Accardo's Neurodevelopmental Disabilities in Infancy and Childhood. 3rd Ed. Baltimore. Brooks Publishing; 2008.



Behavioral Phenotype

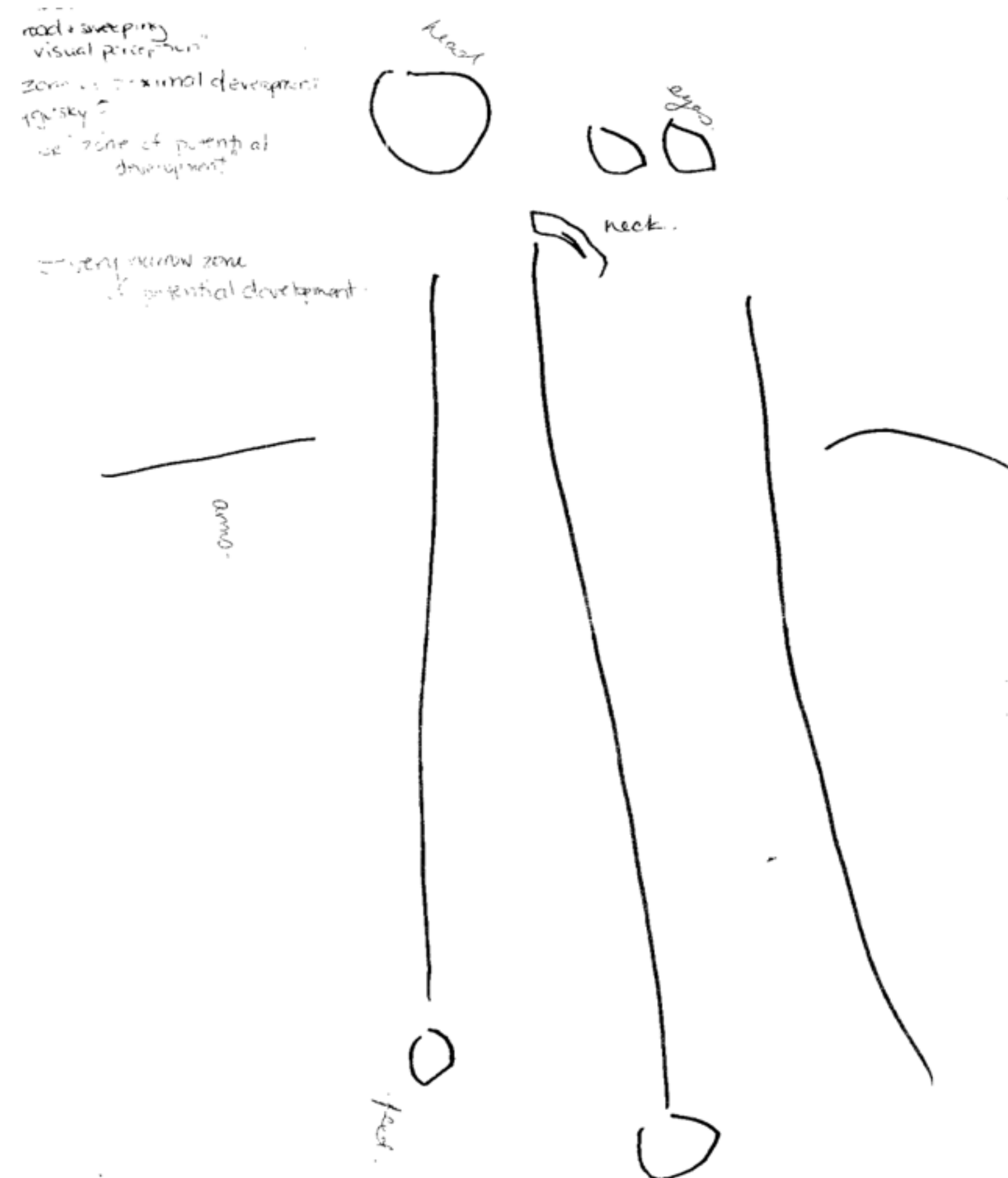
- Describes a constellation of behavioral, cognitive, motor, and social strengths & difficulties observed in a population with a common biological disorder
- Premature survivors have a phenotype
- Common biological disorder = alterations in brain development

Hodapp RM, Fidler DJ. Special Education and Genetics: Connections for the 21st Century. The J Spec Educ 1999; 33: 130-137.

Back SA, Miller SP. Brain Injury in Premature Neonates: A Primary Cerebral Dysmaturation Disorder? Ann Neurol 2014;75;469-86.

Church PT, Luther M, Asztalos E. The perfect storm: minor morbidities in the preterm survivor. Curr Pediatr Rev, 2012; 8: 142-151.

Behavioral Phenotype of Prematurity



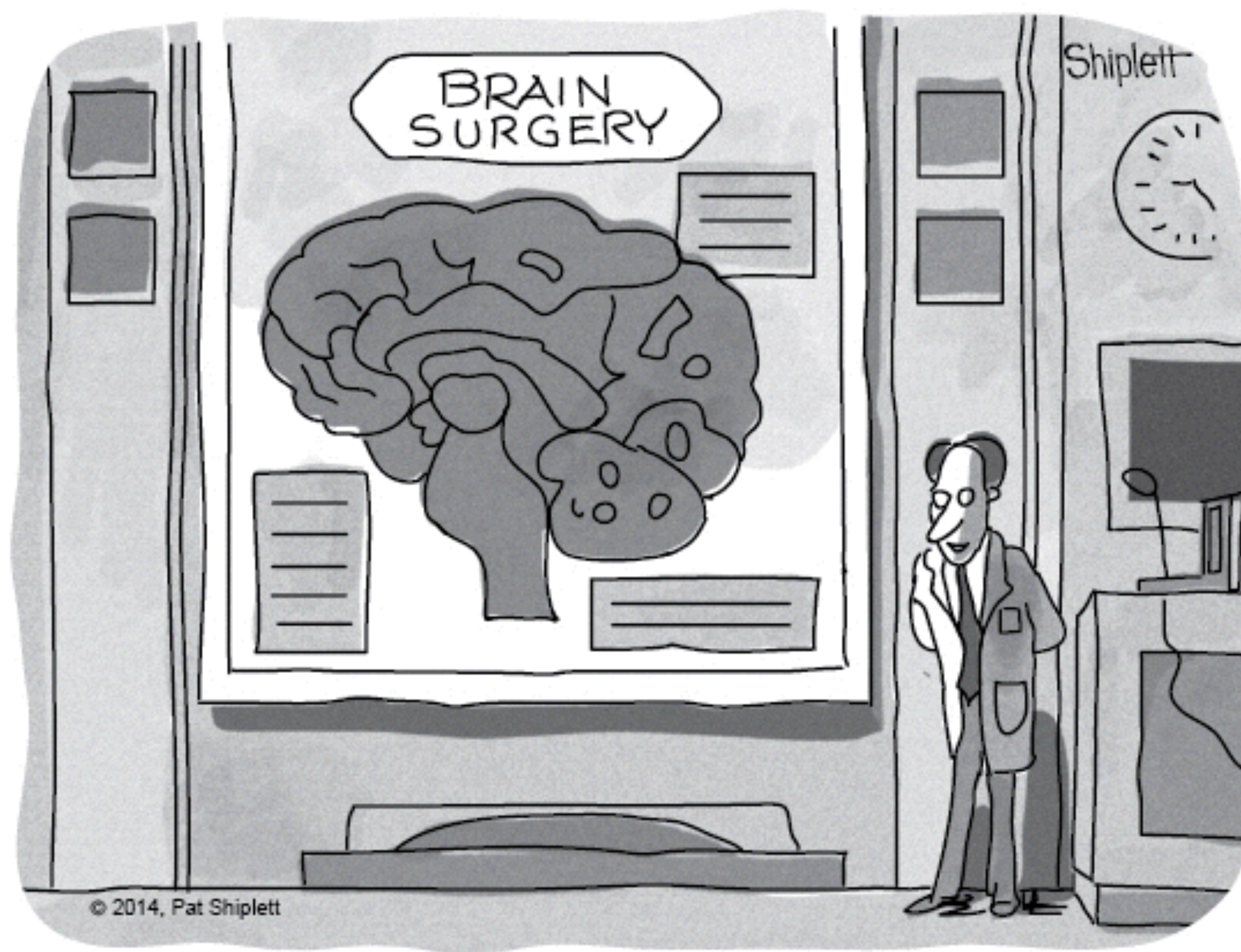
Behavioral Phenotype of Prematurity



Alex Libby: From Bully to the Bully Effect



<https://www.youtube.com/watch?v=gWl0kSG4FP0>



"This is not rocket science, people."



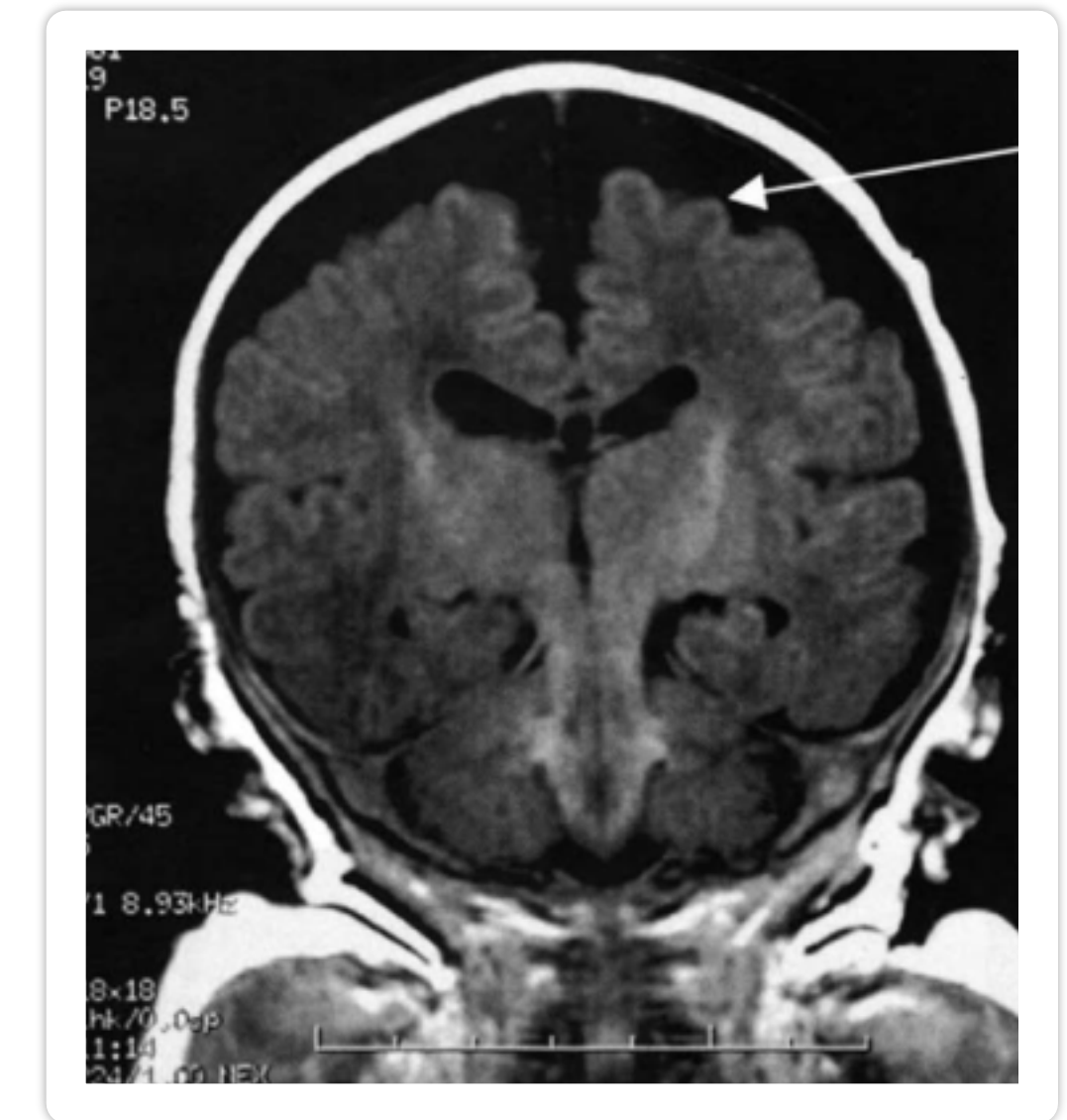
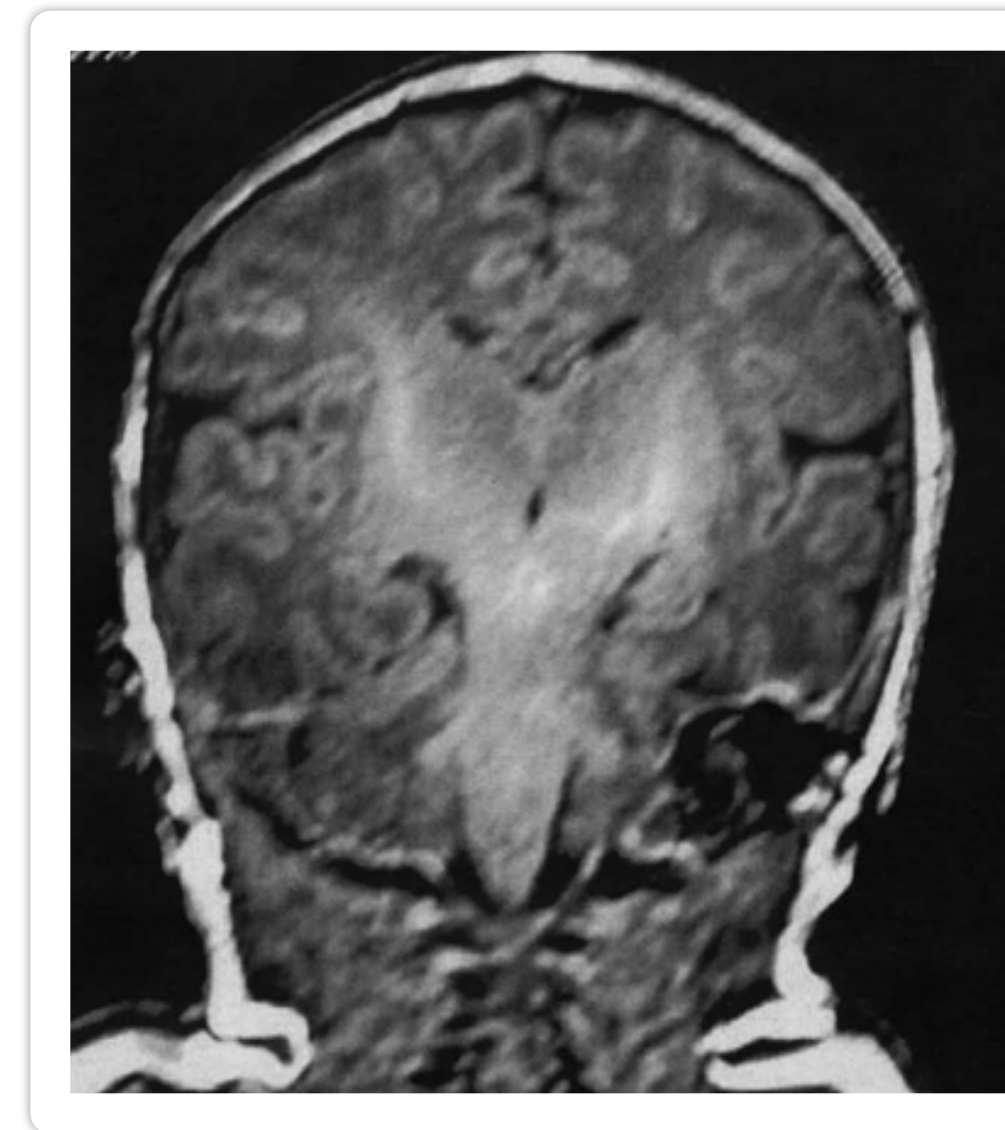
Etiology

Behavioral Phenotype of Prematurity

Dysmaturational:

- Gray matter architecture distorted
- White matter connectivity altered
- Cerebellum under-developed
- Sensory system disorganization

Secondary cortical dysplasia



Back SA, Miller SPM. Brain Injury in Premature Neonates: A Primary Cerebral Dysmaturational Disorder? Ann Neurol 2014;75:469-489

Volpe JJ. Brain injury in preterm infants: a complex amalgam of destructive and developmental disturbances. J Lancet 2009; 8: 110-124.

Alyward GP. Neurodevelopmental Outcomes of Infants Born Prematurely. J Dev Behav Pediatr 2005; 26: 427-440.

Inder TE, Wells SJ, Mogridge NB, Spencer C, Volpe JJ. Defining the Nature of the Cerebral Abnormalities in the Premature Infant: A Qualitative Magnetic Resonance Imaging Study. J Pediatr 2003; 143: 171-179.

Lickliter R. The Integrated Development of Sensory Development. Clin Perinatol 2011;38:591-603



Etiology

Behavioral Phenotype of Prematurity

Altered synaptogenesis

- Experience expectant versus experience dependent
- Similar experience with different effects
- Impact of pain and stress
- Plasticity can be good or bad

Kolb B, Gibb R. Brain Plasticity and Behaviour in the Developing Brain. J Can Acad Child Adolesc Psychiatry 2011; 20: 265-276.



Etiology

Behavioral Phenotype of Prematurity

Loss of controlled sensory exposure

Alterations to timing (too much too soon, too little too late)

- Impact perceptual organization

Loss of redundancy

- Impacts selective attention, perceptual organization, learning

Lickliter R. The Integrated Development of Sensory Development. Clin Perinatol 2011;38:591-603.



Etiology

Behavioral Phenotype of Prematurity

Wolke D, et al. *Arch Dis Child Fetal Neonatal Ed* 2013;**0**:F1–F6.

Heightened parental stress potentiates:

- Disrupted attachment
- Diminished parental capacity
- Goodness of Fit
- Vulnerable child syndrome

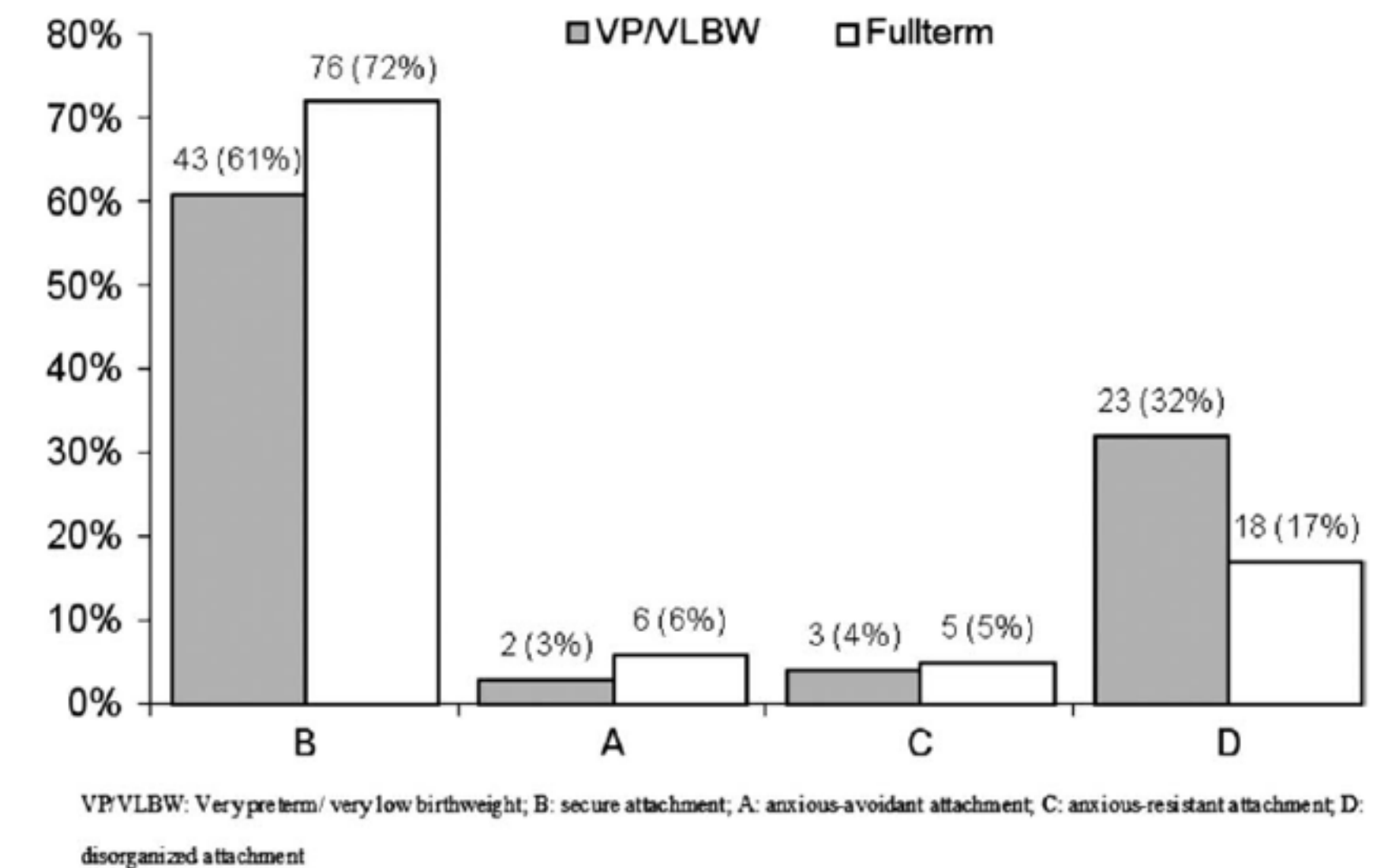


Figure 1 Distribution of A, B, C and D attachment classifications in very preterm/very low birthweight and full-term infants.

Treyvaud K, Anderson VA, Howard K, Bear M, Hunt RW, Doyle LW, et al. Parenting behavior is associated with the early neurobehavioral development of very preterm children. *Pediatrics* 2009; 123: 555-561.

Treyvaud K, Anderson VA, Lee KJ, Woodward LJ, Newnham C, Inder TE, et al. Parental mental health and early social-emotional development of children born very preterm. *J Pediatr Psychol* 2010; **35**: 768-777



Post-traumatic Symptomatology in Parents with Premature Infants: A Systematic Review of the Literature

Athanasios Karatzias, PhD¹, Zoë Chouliara, PhD², Fiona Maxton, PhD³, Yvonne Freer, PhD⁴, and Kevin Power, PhD⁵

Risk of psychological distress in parents of preterm children in the first year: evidence from the UK Millennium Cohort Study

Claire Carson, Maggie Redshaw, Ron Gray, Maria A Quigley

Prematurity, maternal posttraumatic stress and consequences on the mother–infant relationship[☆]

Margarita Forcada-Guex^a, Ayala Borghini^b, Blaise Pierrehumbert^b, François Ansermet^c, Carole Muller-Nix^{b,*}

STATE-OF-THE-ART

Screening parents of high-risk infants for emotional distress: rationale and recommendations

MT Hynan¹, KO Mounts² and DL Vanderbilt³



"The title of my science project is 'My Little Brother: Nature or Nurture.'"



Going home: Facilitating discharge of the preterm infant

Ann L Jefferies; Canadian Paediatric Society
Fetus and Newborn Committee
Paediatr Child Health 2014;19(1):31-36



ROYAL COLLEGE
OF PHYSICIANS AND SURGEONS OF CANADA
COLLÈGE ROYAL
DES MÉDECINS ET CHIRURGIENS DU CANADA

POLICY STATEMENT

Hospital Discharge of the High-Risk Neonate

Committee on Fetus and Newborn

American Academy
of Pediatrics



DEDICATED TO THE HEALTH OF ALL CHILDREN™

Organizational Principles to Guide and
Define the Child Health Care System and/or
Improve the Health of All Children



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High Rates of School Readiness Difficulties at 5 Years of Age in Very Preterm Infants Compared with Term Controls

Gehan Roberts, PhD,*†‡§ Jeremy Lim, BHLthSc (Hons),‡§ Lex W. Doyle, MD,*‡||
Peter J. Anderson, PhD*‡§

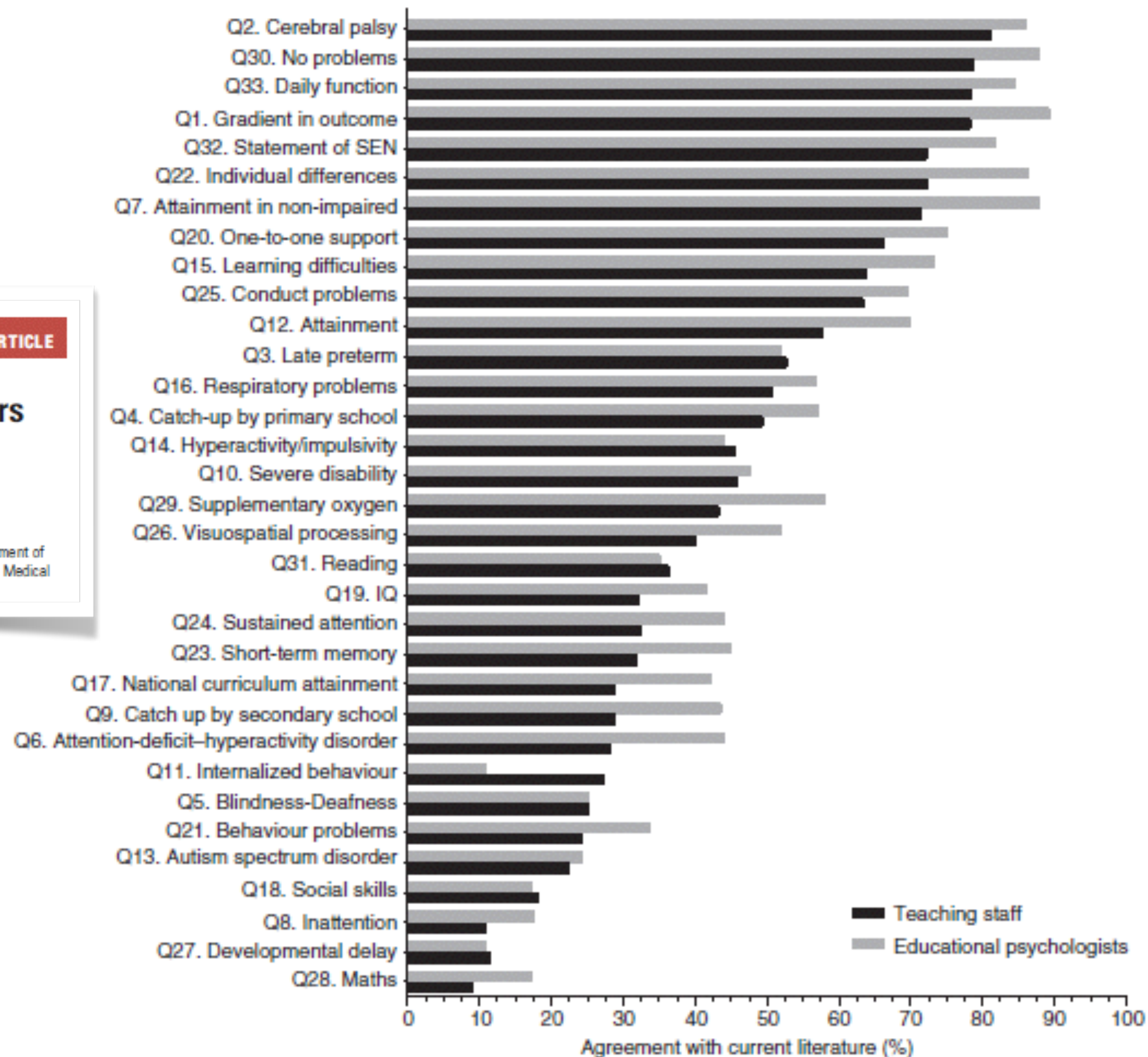
| School Readiness Domain | Individual Measures | VPT (N = 195) | Control (N = 70) | Mean Difference (95% CI) | <i>p</i> |
|---------------------------------|--|---------------|------------------|--------------------------|--------------------|
| Health and physical development | PEDS-QL score | 87.7 (16.0) | 95.4 (7.1) | −7.7 (−10.5 to −4.8) | <.001 ^a |
| | Movement-ABC percentile | 23.1 (23.1) | 44.5 (26.5) | −21.4 (−28.6 to −14.2) | <.001 ^a |
| | Visual-motor integration score | 94.4 (14.2) | 100.2 (15.5) | −5.8 (−9.8 to −1.8) | .005 ^a |
| Social-emotional skills | Total difficulties score, SDQ | 9.6 (5.7) | 7.1 (4.3) | 2.5 (1.2 to 3.8) | <.001 ^a |
| Approaches to learning | Global composite score, BRIEF-P | 54.6 (13.1) | 47.2 (10.6) | 7.4 (1.6 to 4.2) | <.001 ^a |
| | Digit recall, WMTB-C | 89.5 (15.5) | 101.3 (16.0) | −11.8 (−16.2 to −7.4) | <.001 |
| | Nonword recall, WMTB-C | 98.9 (19.4) | 109.3 (15.0) | −10.4 (−15.0 to 5.8) | <.001 ^a |
| Communication | Expressive language score, K-SEALS | 97.0 (13.8) | 105.8 (12.5) | −8.9 (−12.5 to −5.2) | <.001 |
| | Receptive language score, K-SEALS | 97.6 (13.0) | 107.2 (9.6) | −9.6 (−12.5 to −6.7) | <.001 ^a |
| Cognition and general knowledge | Number skills score, K-SEALS | 97.4 (12.6) | 104.5 (9.9) | −7.1 (−10.4 to −3.8) | <.001 |
| | Letter/word skills score, K-SEALS | 96.6 (16.5) | 107.0 (14.9) | −10.4 (−14.8 to −6.0) | <.001 |
| | Early academic composite score, K-SEALS | 96.9 (12.9) | 106.4 (10.9) | −9.5 (−12.9 to −6.0) | <.001 |
| | Nonverbal general ability score, K-BIT 2 | 96.1 (12.7) | 102.9 (10.1) | −6.7 (−10.1 to −3.4) | <.001 |



The long-term consequences of preterm birth: what do teachers know?

SAMANTHA JOHNSON¹ | CAMILLA GILMORE² | IAN GALLIMORE¹ | JULIA JAEKEL³ | DIETER WOLKE⁴

¹ Department of Health Sciences, University of Leicester, Leicester; ² Mathematics Education Centre, Loughborough University, Loughborough, UK. ³ Department of Developmental Psychology, Ruhr-University Bochum, Bochum, Germany. ⁴ Department of Psychology and Division of Mental Health and Wellbeing, Warwick Medical School, University of Warwick, Coventry, UK.





Knowledge of Educators

Educators (n=138) less knowledgeable about outcomes of prematurity

- 75% aware and/or knowledgeable about ADHD/ADD
- 62.5% aware and/or knowledgeable about learning disabilities
- 60.6% aware and/or knowledgeable about ASD
- **24.8%** aware and/or knowledgeable about developmental outcomes of prematurity

Factors that enhanced educators' knowledge

- Having experience with a child born preterm
- Having a child with an individualized education plan
- Additional educator qualifications

Church PT, Cavanagh A, Lee SK, Shah V. Academic Challenges for the Preterm Infant: Educators' Knowledge, Attitudes, and Perceptions of Identified Barriers. Prelim data.



Knowledge of Educators

What **did not enhance** educators' knowledge: being a parent of a preterm?

- 91.7% reported that medical history would help them teach more effectively
- No consistency on enrolment by due date vs. birthday; 1/3 disagree with enrolment by due date, 1/3 neutral, 1/3 agree
- 86.4 % of educators reported that they would benefit from additional education on preterm children



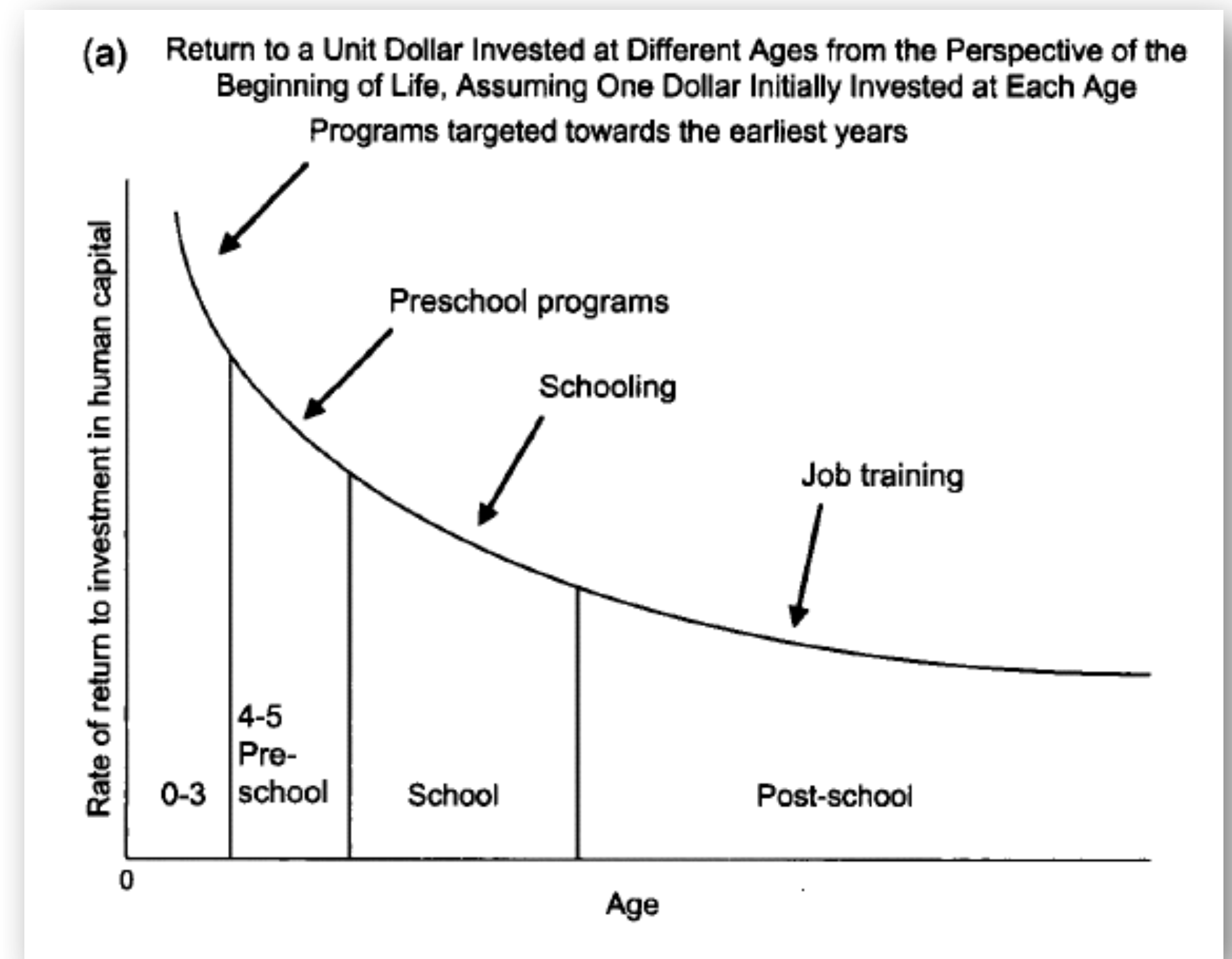
"It sort of makes you stop and think, doesn't it."

Concept of Plasticity

Dysmaturational infers that it is modifiable

- Nature through nurture
- Not nature vs nurture

SCHOOLS, SKILLS, AND SYNAPSES
Heckman, James J
Economic Inquiry; Jul 2008; 46, 3; ProQuest
pg. 289



National Research Council and Institute of Medicine. From Neurons to Neighborhoods: the Science of Early Childhood Development. Shonkoff JP, Phillips DA eds. Board on Children, Youth, and Families. Commission on Behavioral and Social Sciences and Education. Washington, DC: National Academy Press, 2000.

F-WORDS

FUTURE

FUN

FAMILY

FUNCTION

FRIENDS

FITNESS



Lessons from NIDCAP

NIDCAP approach based on 3 assumptions:

- Detailed observation of behavior provides basis for recommendations in how to minimize stress and optimize development
- Caregivers benefit from supportive education, as well as guidance and modeling in implementing recommendations
- Resultant changes lead to improved medical and neurobehavioral functioning

Als H. Newborn Individualized Development and Assessment Program (NIDCAP): New frontier for neonatal and perinatal medicine. J Neo Perinatal Med 2009; 2: 135-149.



SO HOW

DOES THIS TRANSLATE TO NEONATAL FOLLOW UP?



Lessons from NIDCAP

1. Detailed observation of behavior provides basis for recommendations in how to minimize stress and optimize development

Addition of Behavior Analyst to provide evidence-based approaches to behavioral issues

Use applied behaviour analysis

- Applied: real world
- Behaviour
- Analysis: demonstrate functional relationships

Baer DM, Wolf MM, Risley TR. Some current dimensions of applied behavior analysis. J Appl Behav Anal 1968; 1: 91–97.

Cooper JO, Heron, TE, Heward WL. Applied behavior analysis 2nd ed, 2007; Upper Saddle River, NJ: Pearson Prentice Hall.

Lessons from NIDCAP

2. Caregivers benefit from supportive education, as well as guidance and modeling in implementing recommendations

Shift to group based services:

- Triple P
- Incredible Years
- Transition to School session

Website/social media



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NEONATAL FOLLOW-UP CLINIC

Happy 3rd Birthday!

*"You have brains in your head. You have feet in your shoes.
You can steer yourself any direction you choose."
- Dr. Seuss*

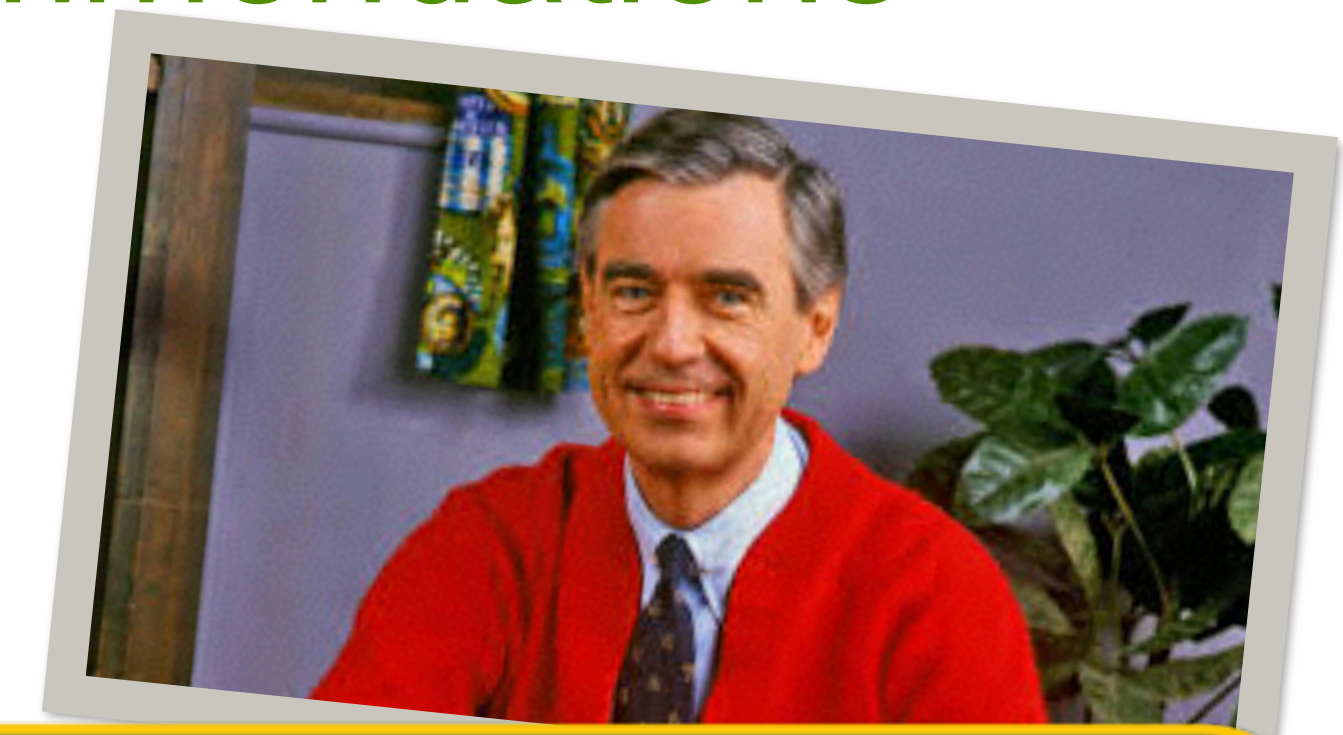
Look how far you've come!

Your child is three-years-old, and three is an exciting time! Many things are changing for your child as he or she gets a little bit older, and we hope all of your child's new skills fill you with joy.

We also understand that age three can bring new challenges to families, as your child develops his or her own strong opinions. The purpose of this newsletter is to share some tips to help your child find his or her way in this new world as an increasingly independent three-year-old!

A photograph of two adults and a young child sitting on the floor, playing with colorful toy blocks and a small house.

At three, the big and exciting next step for your child is the start of school next year. The tips on the following page will focus on preparing you and your child for that step.



a note on screen time



Spending lots of time on computers and tablets or watching TV can affect children's growth¹ and the development of learning,² communication,³ and emotional well-being.⁴ We encourage you to limit your child's exposure to a screen (TV, computer, tablet, phone) to less than 1 hour per day.⁷

When your child does watch a program, we recommend you watch too! This becomes a moment for you to teach and share. Programs such as Sesame Street and Mr. Rogers' Neighborhood are free on YouTube in short parts and offer quality educational programming.⁶


Sesame Street is great for teaching about early reading skills, numbers, colours, how to get along with your friends. Mr. Rogers' Neighborhood focuses on learning to be a good neighbor or friend, feelings, and how to control feelings.



Lessons from NIDCAP

3. Resultant changes lead to improved medical and neurobehavioral functioning

- Read!
 - Books are a wonderful way to build your child's knowledge and language. As you read, talk about the story with your child. You can do this in many different ways:
 - Encourage your child to point to pictures and name them.
 - Ask simple questions about the story, how the characters are feeling, what they are doing, and what is going to happen next.
 - Encourage your child to ask questions too!
 - Books can be expensive, but you can easily borrow books for free from a public library. Check with your local library about how to get a library card.





CHILD-BRIGHT
Network

- Feasibility of Acceptance Commitment Therapy in the NICU
- Impact on parental stress
- Pilot to start Fall 2017

Harris, R. Embracing your demons: An overview of acceptance and commitment therapy. *Psychotherapy in Australia*, 2006; 12: 2-8.

Hayes SC, Levin M, Plumb-Villardaga J, Vilatte JL, Pistorello J. Acceptance and commitment therapy and contextual behavioral science: Examining the progress of a distinctive model of behavioral and cognitive therapy. *Behav Ther*, 2013; 44: 180-198.

Powers MB, Vörding MBZS, Emmelkamp PMG. Acceptance and commitment therapy: A meta-analytic review. *Psychotherapy and Psychosomatics*. 2009;78:73–80.



IN SUMMARY . . .



- Behavioral Phenotype of Prematurity associated with increased difficulty functionally
- Gaps in resources exist
- Integration of Neonatology and Dev Peds essential to drive change in outcomes



"Stop fact-checking my story."



Acknowledgements

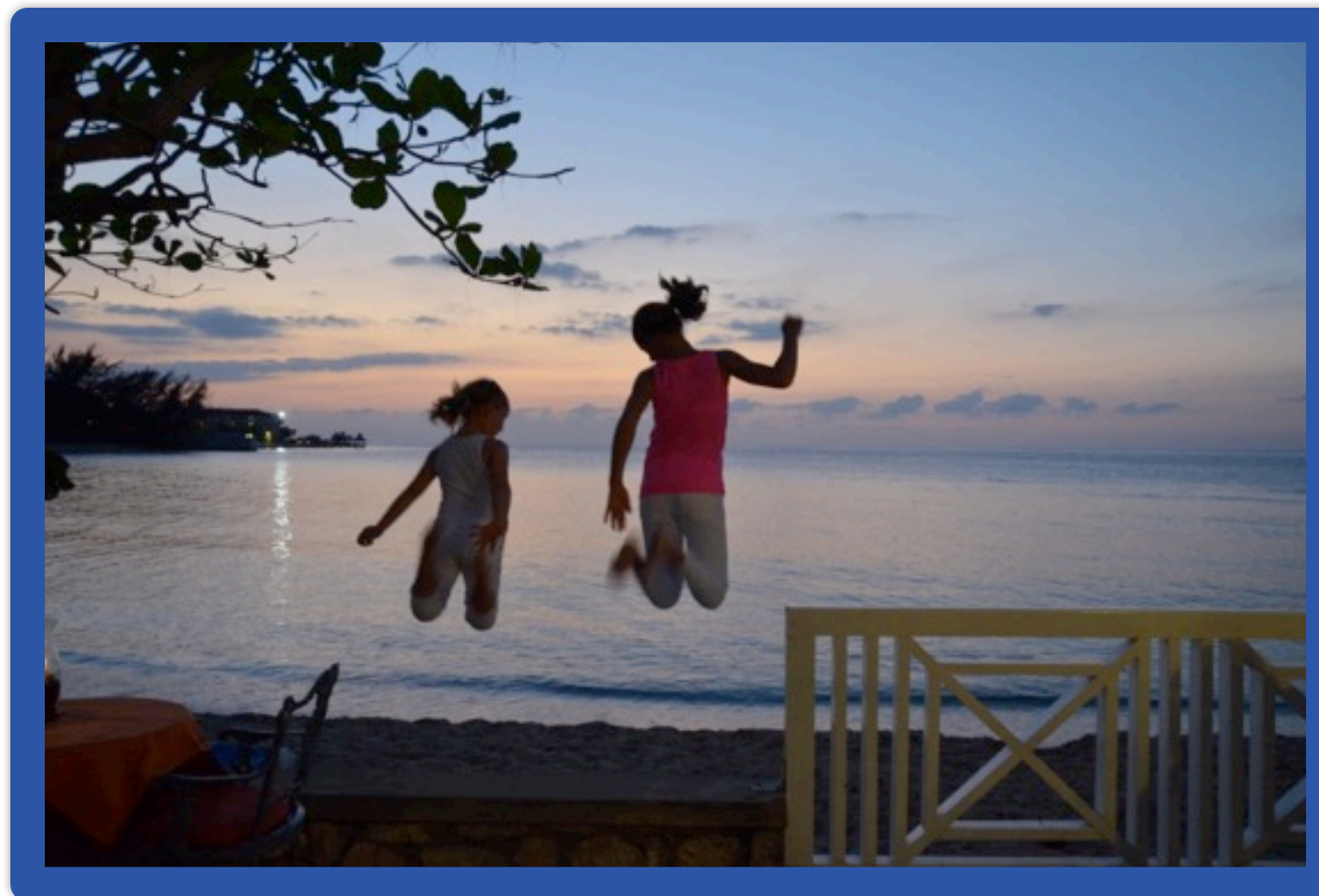
- Rudaina Banihani, MD, Neo-Dev Paeds
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- Patricia Maddalena, NP
- Rosanna Manarin, RN
- Lesley Barreira, Beh Anal
- Mallory Owen, OT
- Isabel Lam, OT/PT

- Michael Luther, PhD, Psyc
- Connie Taras-Gold, SLP
- Marion Deland, manager
- Ruth Kim, admin





QUESTIONS?



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