FUTURE OF PEDIATRICS TALKS!

A VIRTUAL SUMMER SERIES

Pediatric Health Network

Children's National

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- No unapproved or investigational use of any drugs, commercial products or devices

Adre du Plessis, MBChB

Prenatal Pediatrics
Building a Bridge for Children from High-Risk Pregnancies

Adre J. du Plessis, MBChB
Director, The Prenatal Pediatrics Institute
Chief, Division of Prenatal and Transitional Pediatrics
Children's National Hospital
Washington DC

FUTURE OF PEDIATRICS

Objectives

This presentation will provide the pediatrician with an enhanced understanding of:

1. developmental plasticity and its role in the long-term outcome of the high-risk fetus;
2. the expanding role of the pediatrician in the prenatal and postnatal care of the high-risk fetus; and
3. the unmet challenges for detection, surveillance and long-term monitoring of the offspring of high-risk pregnancies.

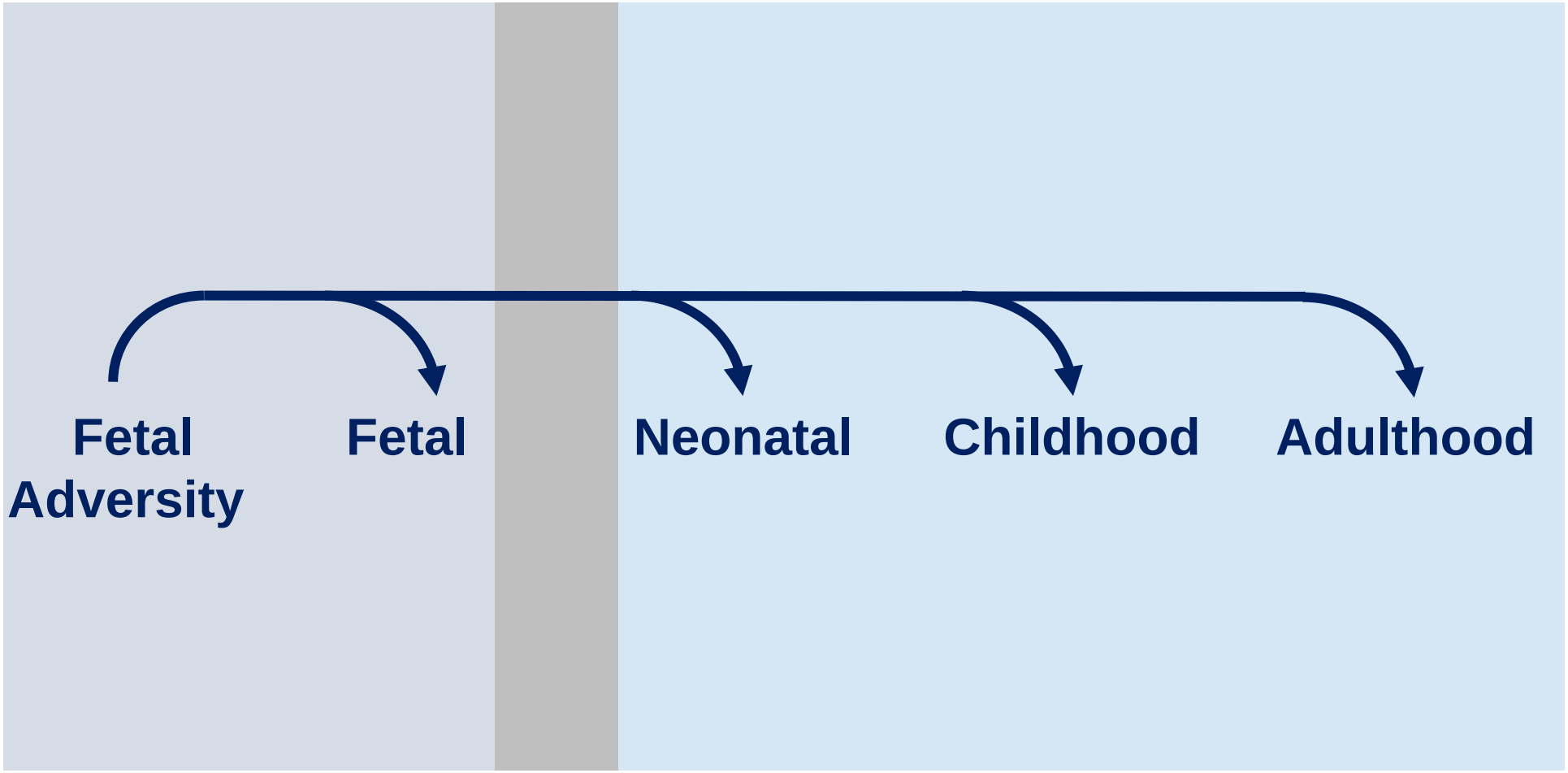
What is the role of the pediatrician in fetal care?

Pediatricians are increasingly involved in fetal care for several major reasons

- **During pregnancy**
  - Pediatric *subspecialists* increasingly involved
    - Counseling families
    - Planning to manage hazardous transition
- 50 years experience with 'the ex-utero fetus' – prematurity and NICU care
- Advancing fetal diagnostics

- **After birth**
  - Care of fetal anomalies and their complications
  - Prenatal origins of later chronic disorders

Consequences of Fetal Adversity: Timing of Manifestations



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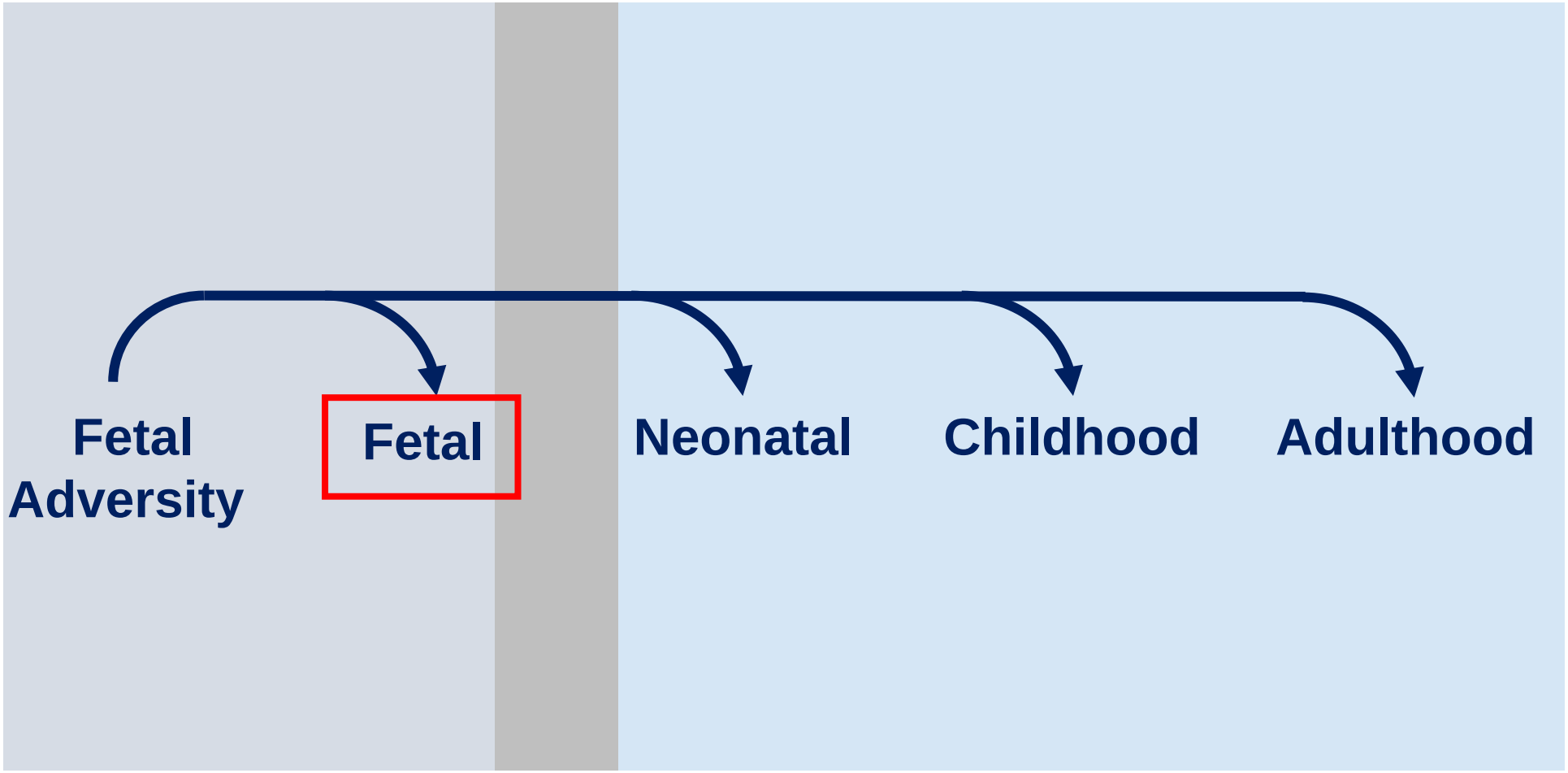

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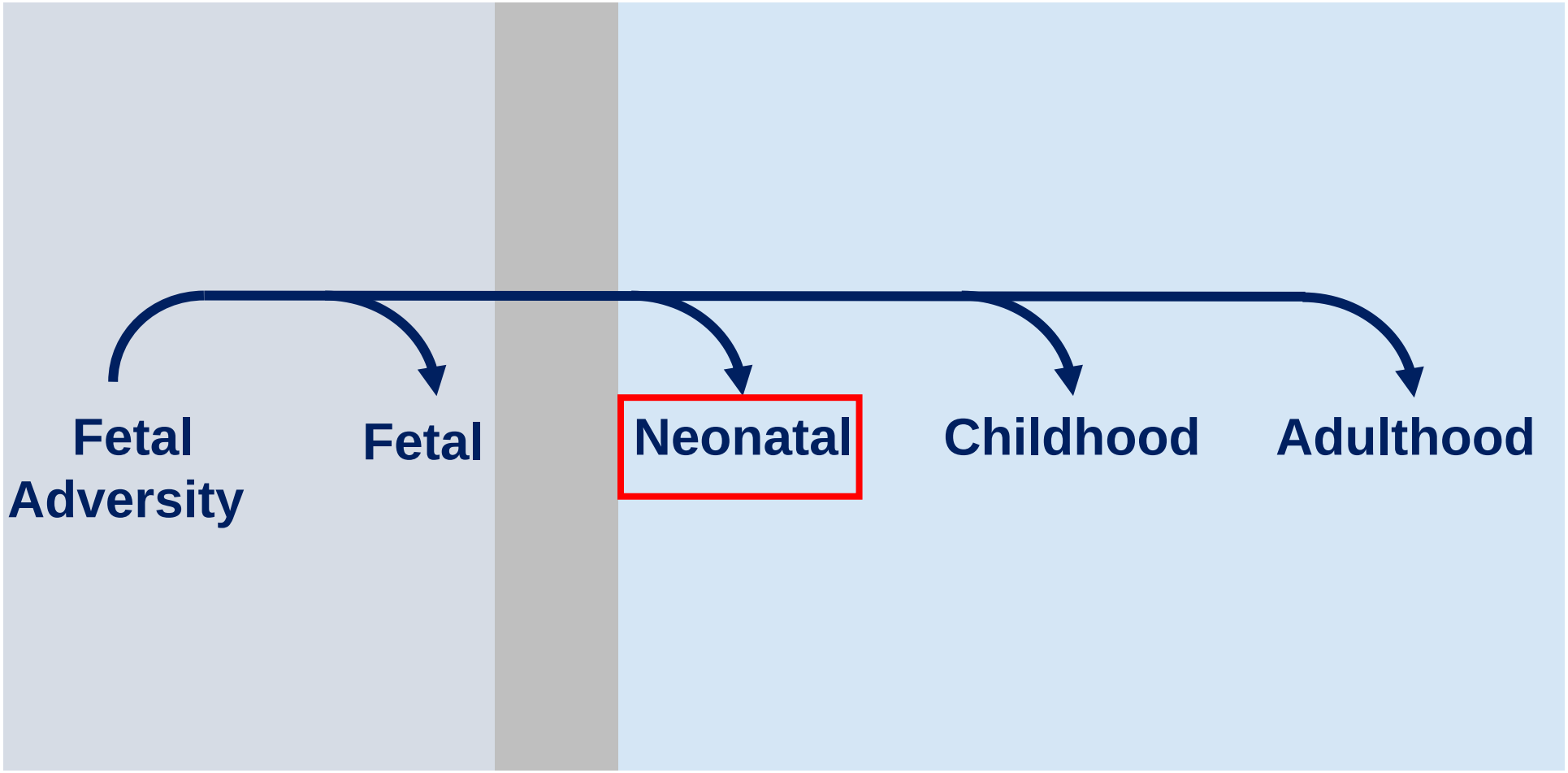

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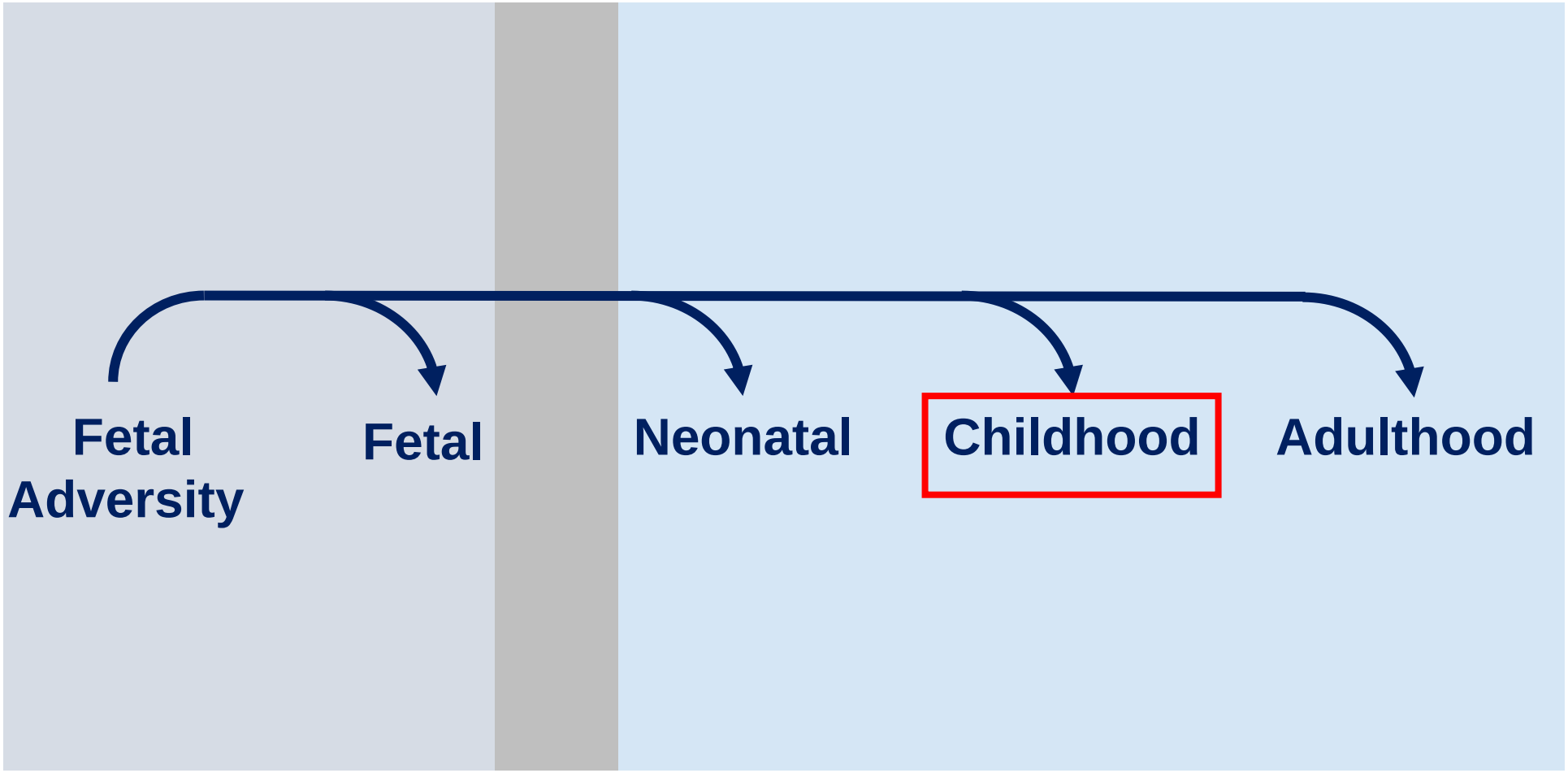
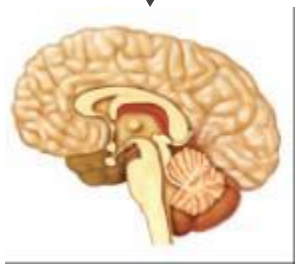


Environmental Influences on the Genome

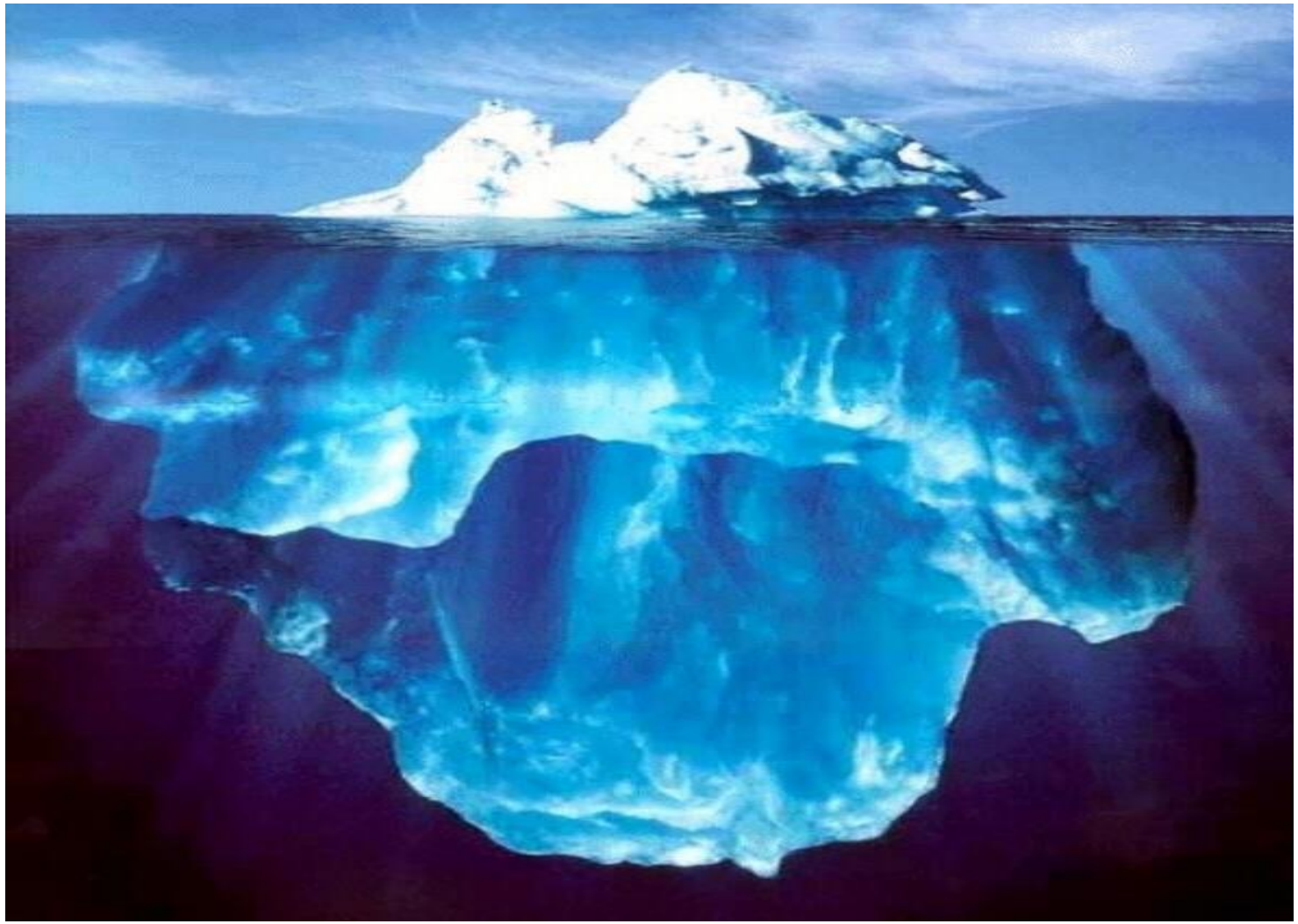
Single Genotype

Environmental influences ----------> *Epigenetic modification*



Range of Phenotypes

Identifying Fetal-Onset Conditions in Utero

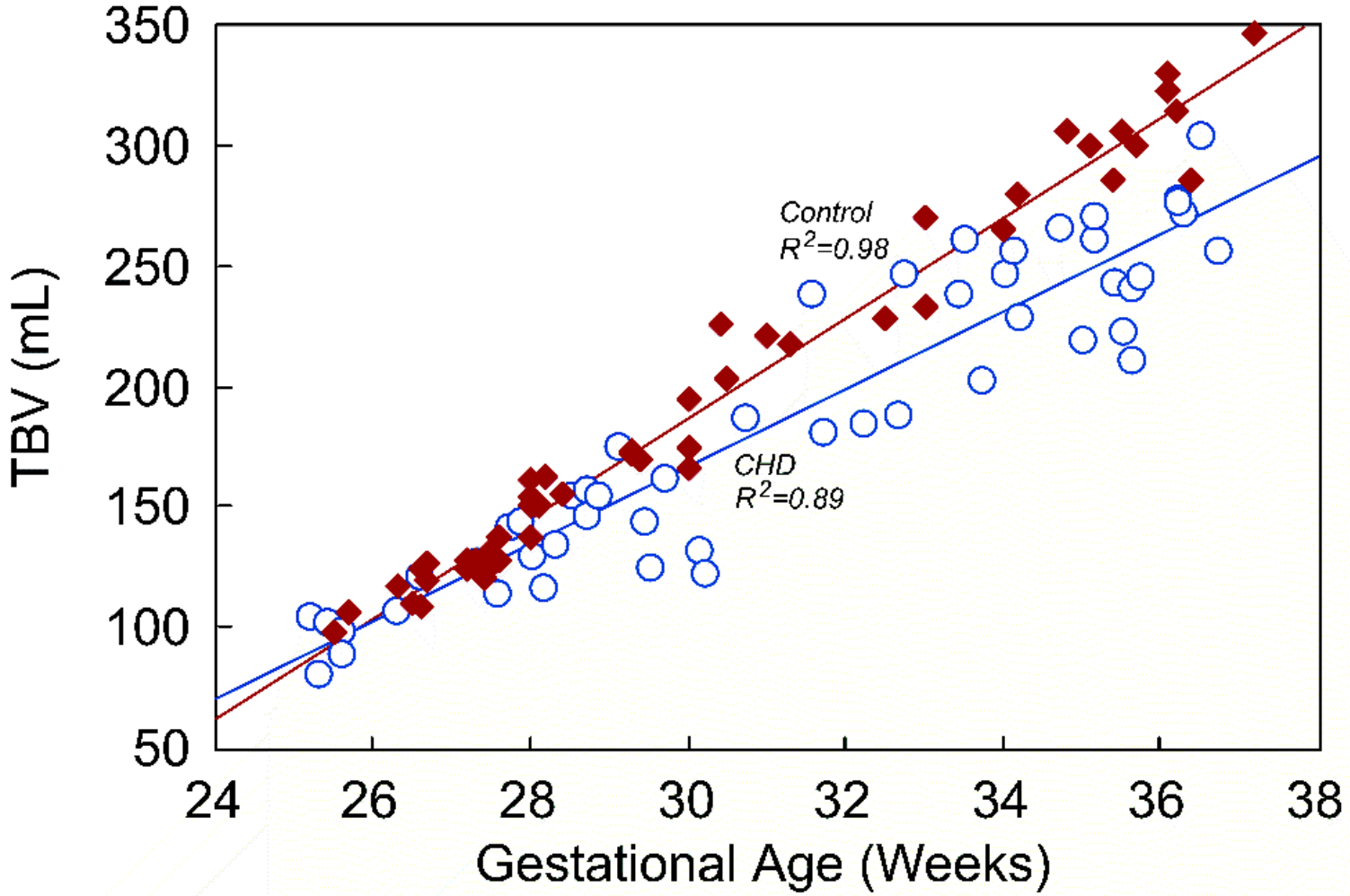


Currently we identify only the tip of the iceberg!

Congenital anomalies may have important developmental effects

The fetus is not a lesion!

Fetus Brain Growth with Congenital Heart Disease



Developmental Plasticity

- Characteristics of developmental plasticity (DP)
  - Nature of the response depends on the nature of the environmental cue
  - There are critical windows of plasticity in different organ systems
  - Duration of developmental plasticity is time-limited: operates longer for processes associated with growth and metabolism (e.g., the brain)

- Some environmental influences are clearly pathological and result in developmental disruption and teratogenesis – with no adaptive advantage – rather than channeling development

Fetal Origins of Lifespan Health Risk (Barker Hypothesis)

Dutch Famine ("Winterhonger) 1944-1945

- The fetus adopts anticipator physiology
- Plasticity – two-edged sword

The growth-restricted fetus

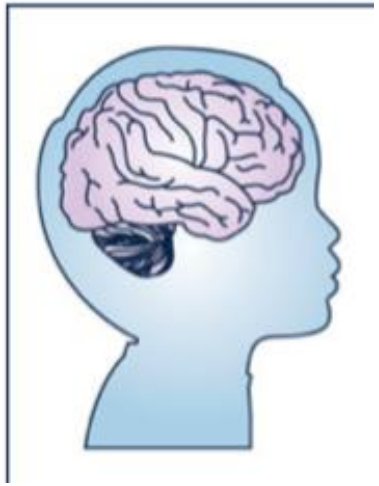
Fetal Growth Restriction

- Fetus not meeting its genetically destined growth potential
- Placental insufficiency is the leading cause
- BW <10th percentile for gestational age (Kingdom & Smith, 2000)

PLUS

- Evidence of placental insufficiency (decreased umbilical artery Doppler flow) (Figueras & Gratacos, 2014)
- Between 3 – 15% pregnancies in the developed world
- Up to 6-old greater in low-income countries
- Global incidence of ~30 million/year (de Onis et al. 1998; Bernstein et al. 2000; Lackman et al. 2001; Fang, 2005; Chauhan & Magann, 2006; Figueras & Gratacos, 2014)

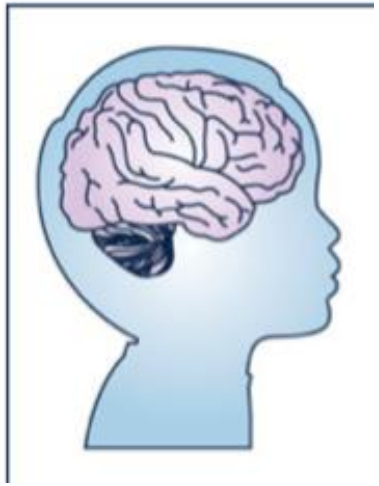
Brain Development in Fetal Grown Restriction



Structural Deficits

- Reduced head circumference
- Reduced total and grey matter volume
- Reduced hippocampal and cerebellar volume
- Reduced total cell number
- Reduced myelin content/ delayed myelination
- Thin cortex with altered gyrification
- Reduced connectivity

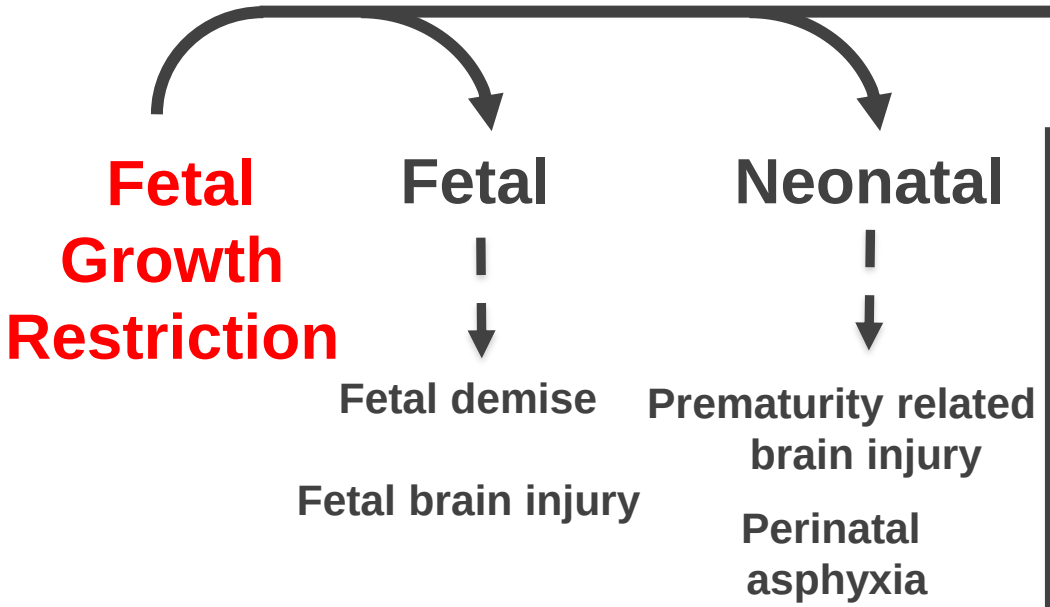
Brain Development in Fetal Grown Restriction



Functional Deficits

- Motor
  - Impaired gross, fine, and visuomotor skills
  - Cerebral palsy
- Cognition and learning
  - Decreased IQ/impaired executive function
  - Memory (esp. verbal) impairment
- Behavior
  - Social interaction deficits/Autistic spectrum disorders
  - Attentional deficits/Hyperactivity
  - Anxiety, irritability, and depression

Fetal Growth Restriction: Consequences and Timing of Manifestation



Infancy, Childhood, Adulthood

- Obesity
- Diabetes
- Hypertension
- Dyslipidemias
- Heart disease
- Stroke
- Attentional disorders
- Developmental delay
- Behavioral dysfunction
- Autism
- Mood disorders
- Schizophrenia

Mental health disorders are now recognized as the most common complication of pregnancy

Maternal stress and depression may have profound effects on fetal development

Prenatal Stress Questionnaires

Healthy Pregnant Volunteers (n=90)

- Prenatal Stress/Anxiety
  - 27% tested positive for stress/anxiety
- Edinburgh Postnatal Depression Scale
  - 8% tested positive for depression

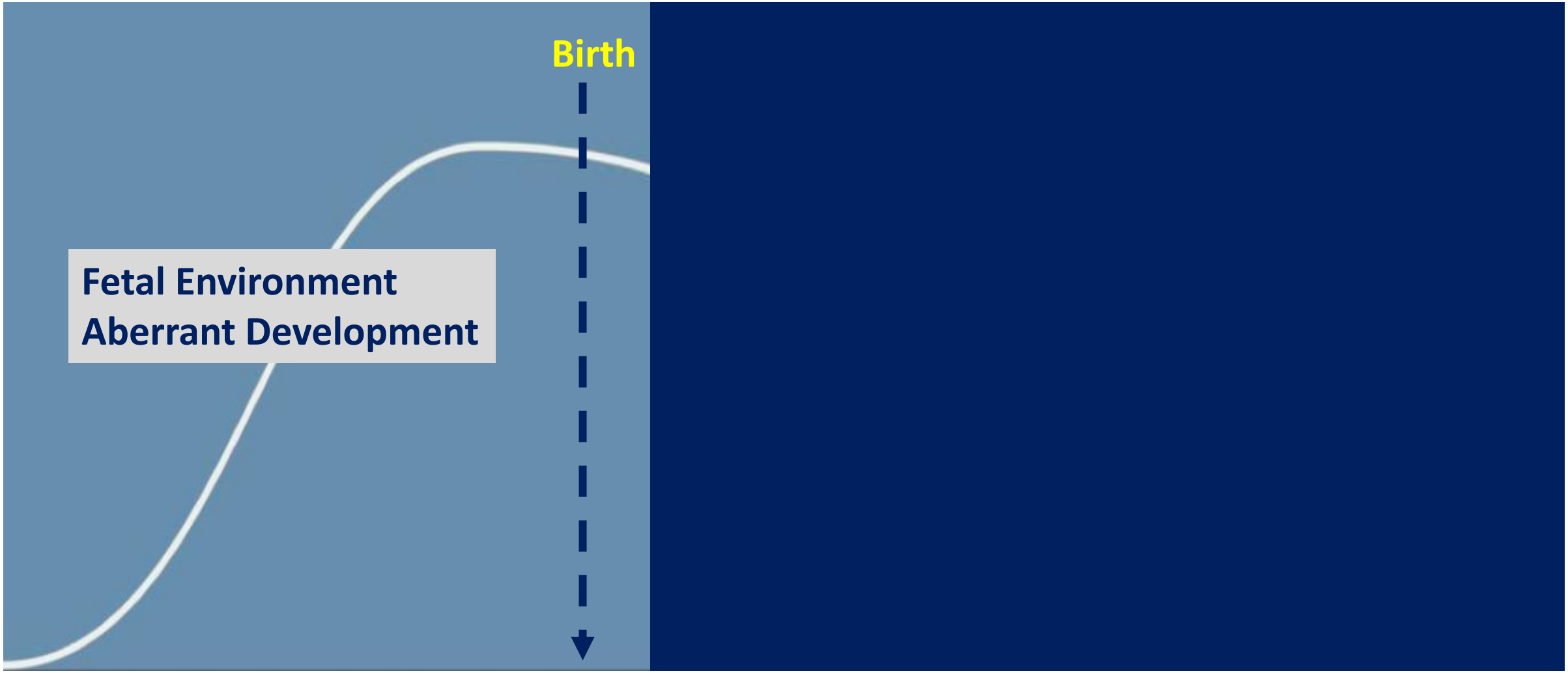
Limperopoulos et al. 2019

Fetal Brain Growth and Maternal Psychological Distress

Fetal Brain 3-D Measures	Female		Male	
	STRESS	DEPRESSION	STRESS	DEPRESSION
	P Value	P Value	P Value	P Value
Total Brain	**0.02**	--	0.83	--
Cerebrum	**0.01**	--	0.80	--
Cerebellum	0.14	**0.02**	0.46	0.81
Brainstem	--	0.79	--	**0.03**
Hippocampus	--	**0.03**	--	0.76

Limperopoulos et al. 2019

Brain Plasticity



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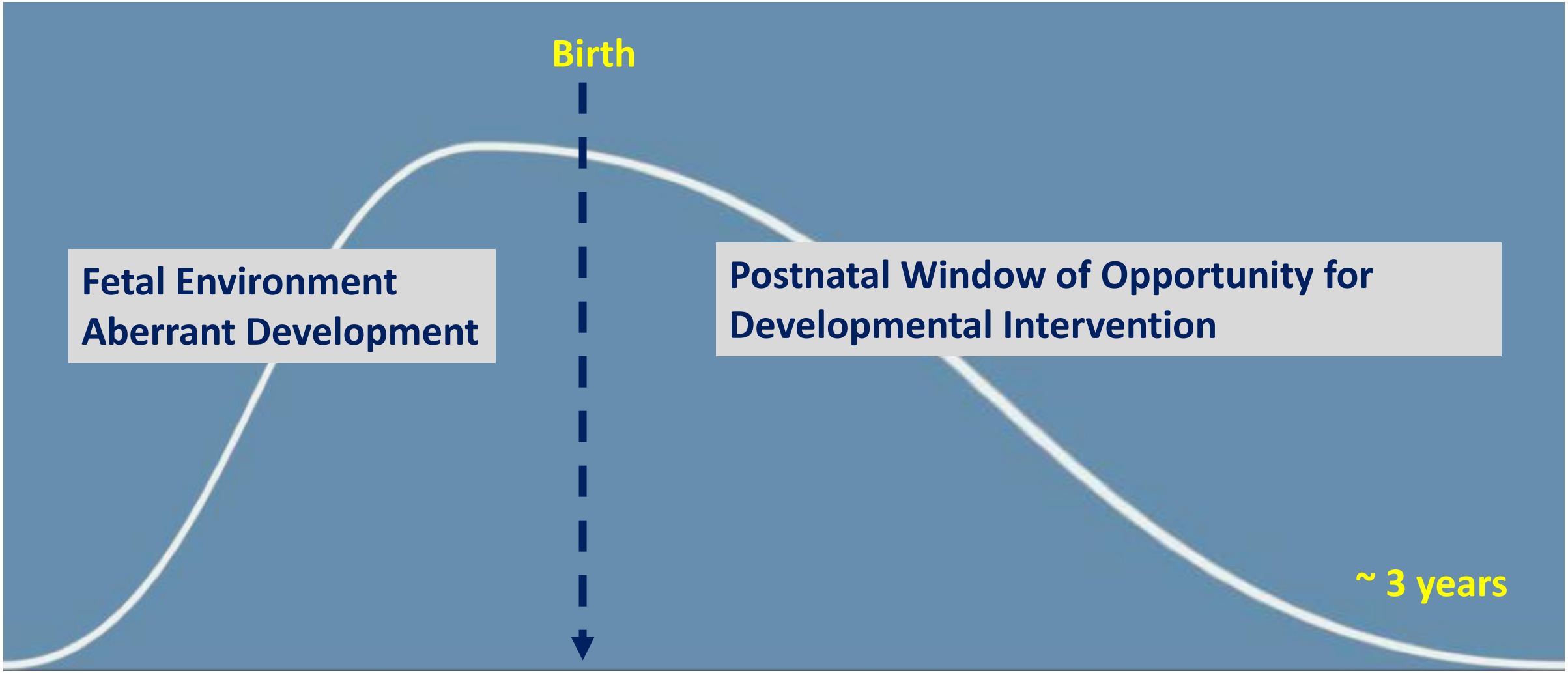
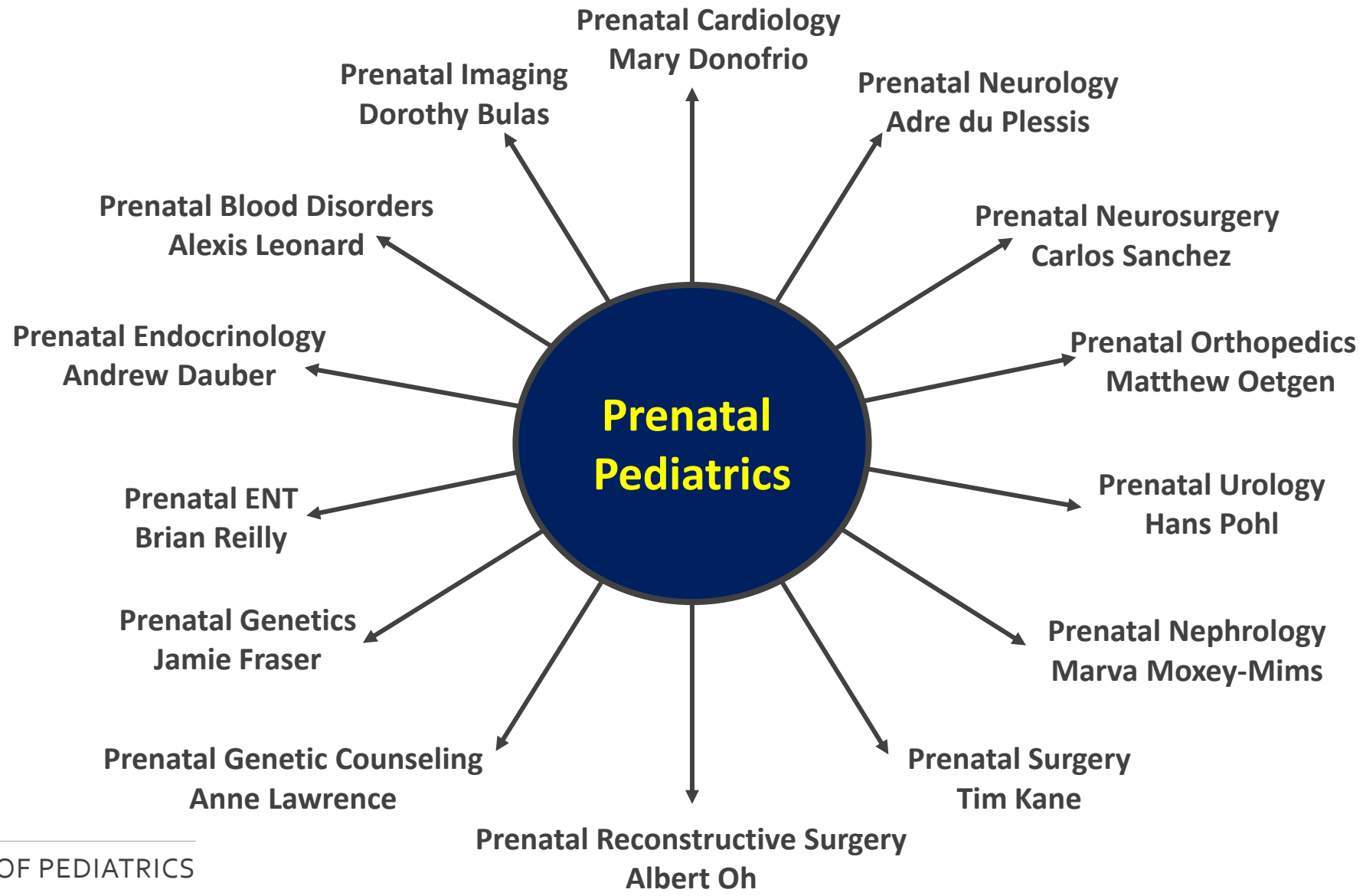
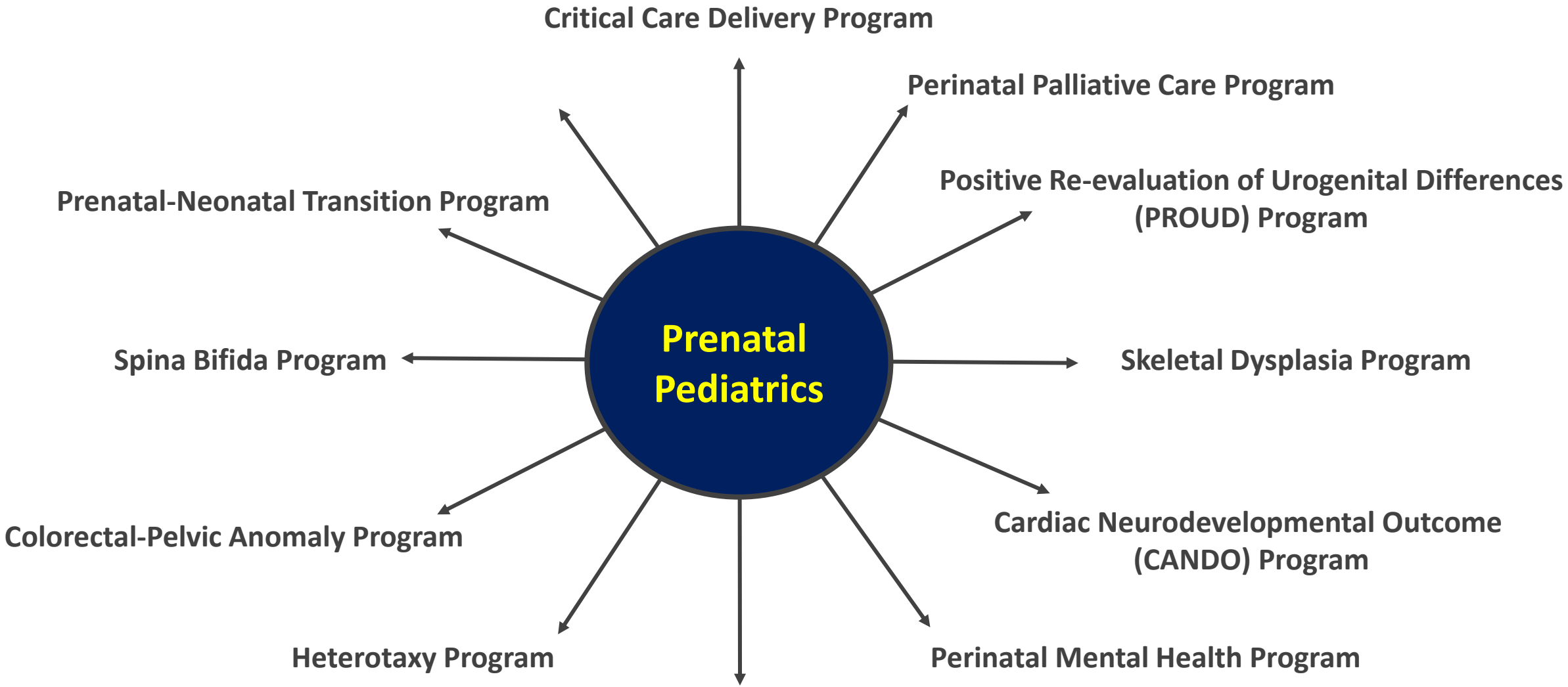


The Prenatal Pediatrics Institute at Children's National

Prenatal Pediatrics – Subspecialty Program Directors



Multidisciplinary Programs supporting Prenatal Pediatrics



Summary

The current and future state of Prenatal Pediatrics

- The focus should expand beyond anatomic malformations
- Major obstetric complications (placental failure; pre-eclampsia; infection; diabetes, maternal stress/depression, substance abuse; many others) pose significant risk to the infant, child, and adult, potentially across the lifespan
- The focus on the whole fetus not only ‘abnormalities in pictures’
- There is an urgent need for improved communication, referral, and monitoring of the high-risk fetus before and after birth

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Contact:
Phone 202-476-7409
Fax 202-476-5897

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