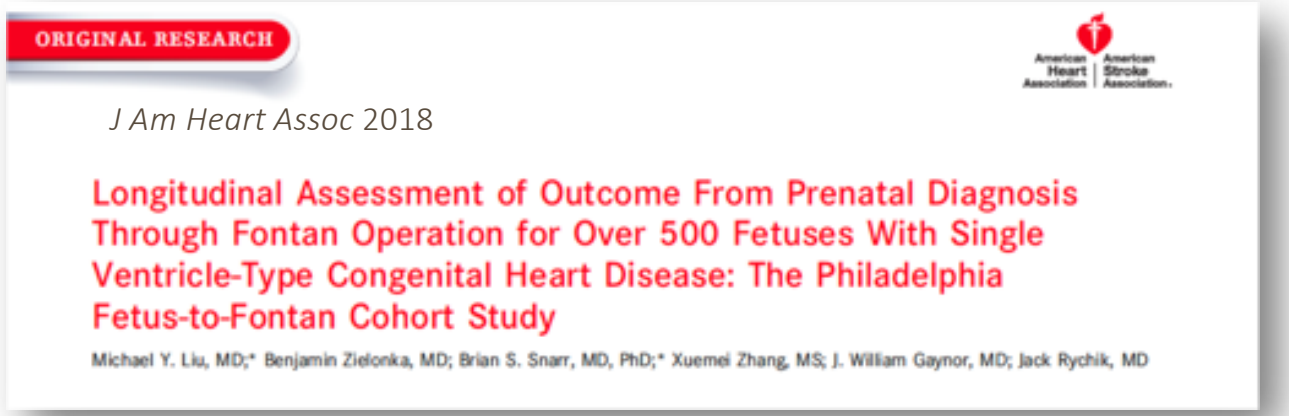
Prenatal Life with Single Ventricle: Is This A Golden Opportunity?

Jack Rychik. MD

Director, Fetal Heart Program

Children's Hospital of Philadelphia

The start of the single ventricle journey…


ORIGINAL RESEARCH

J Am Heart Assoc 2018

Longitudinal Assessment of Outcome From Prenatal Diagnosis Through Fontan Operation for Over 500 Fetuses With Single Ventricle-Type Congenital Heart Disease: The Philadelphia Fetus-to-Fontan Cohort Study

Michael Y. Liu, MD;* Benjamin Zielonka, MD; Brian S. Snarr, MD, PhD;* Xuemei Zhang, MS; J. William Gaynor, MD; Jack Rychik, MD

502

Prenatal Dx of SV

348

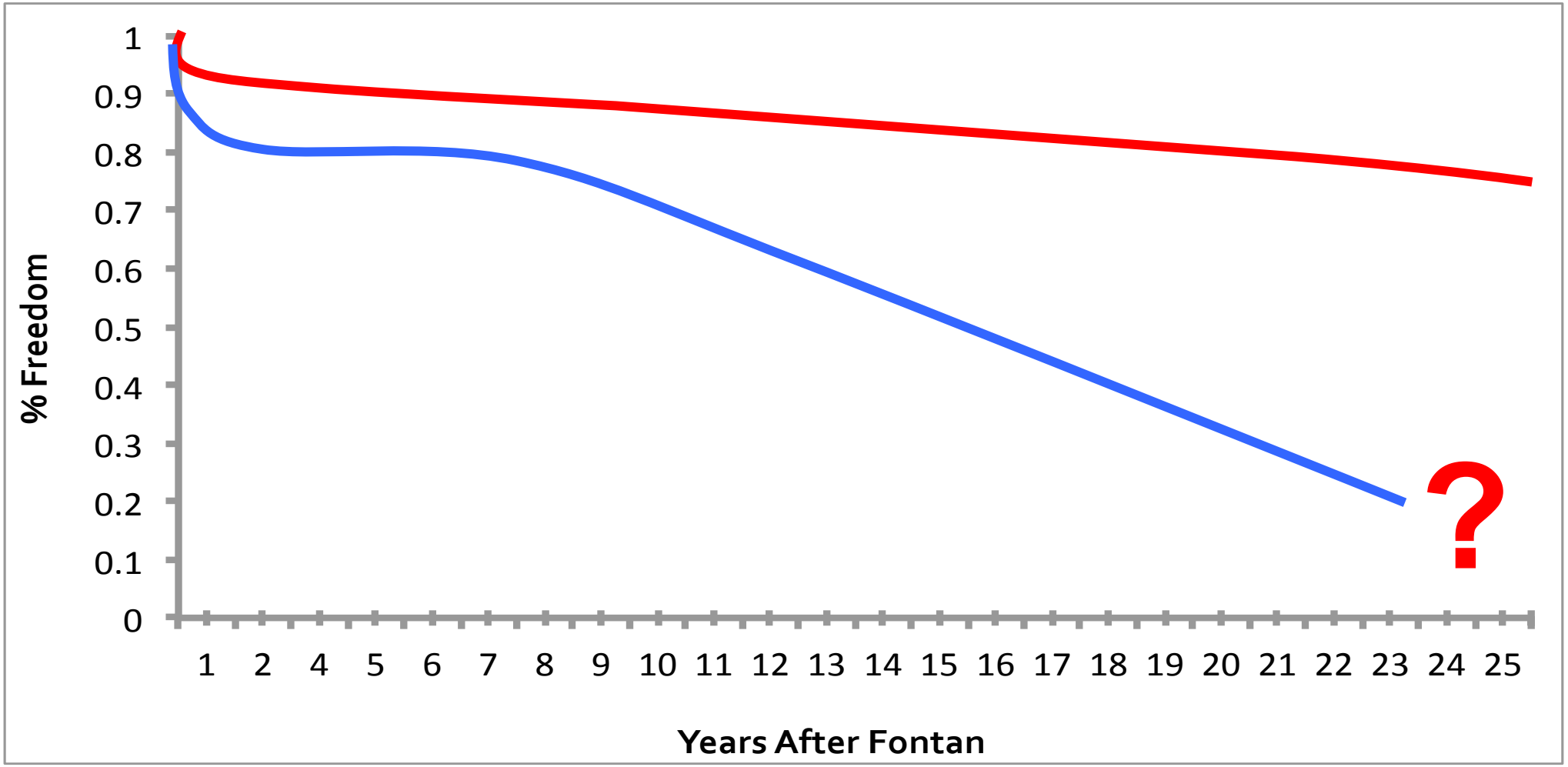
Survive to live-birth with ***intent-to-treat***

234

Survive 6 months post-Fontan

67% survival from fetal dx through Fontan

Freedom From *Mortality* and *Morbidity* After Fontan Operation



Ventricular Dysfunction

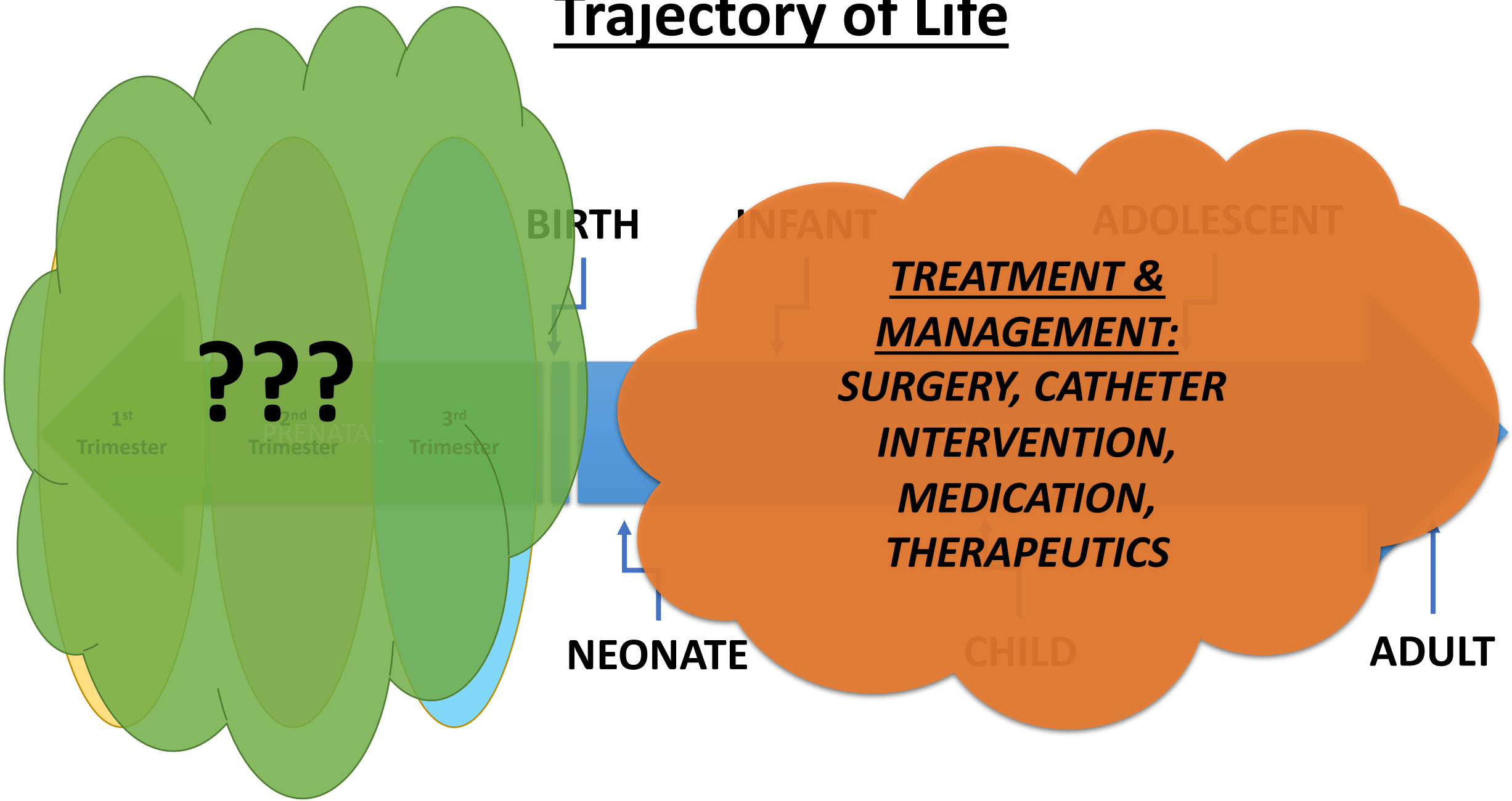
Neurodevelopmental Abnormalities

End-organ Dysfunctions (hepatic, lymphatic, coagulation, etc)

Poor Growth

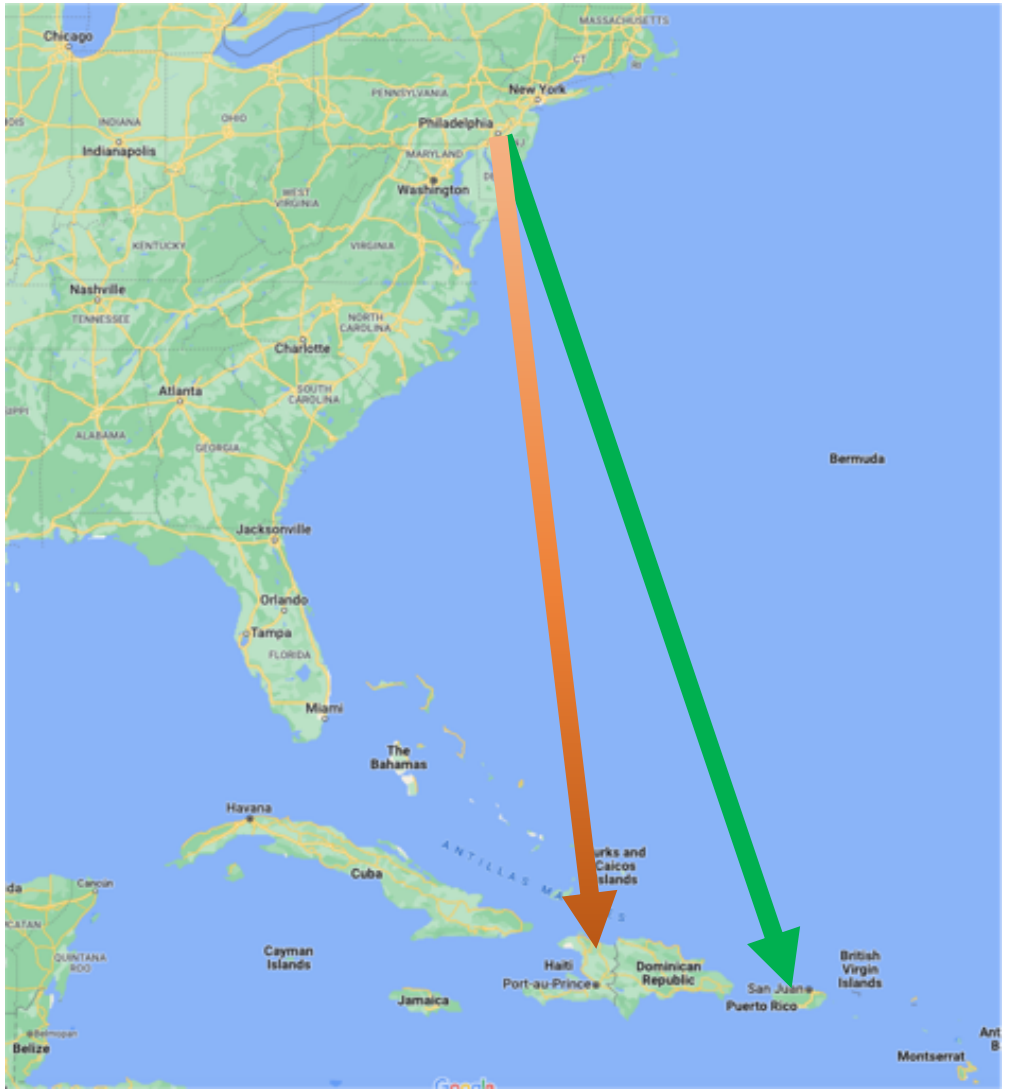
Behavioral & Psychological Challenges

Trajectory of Life

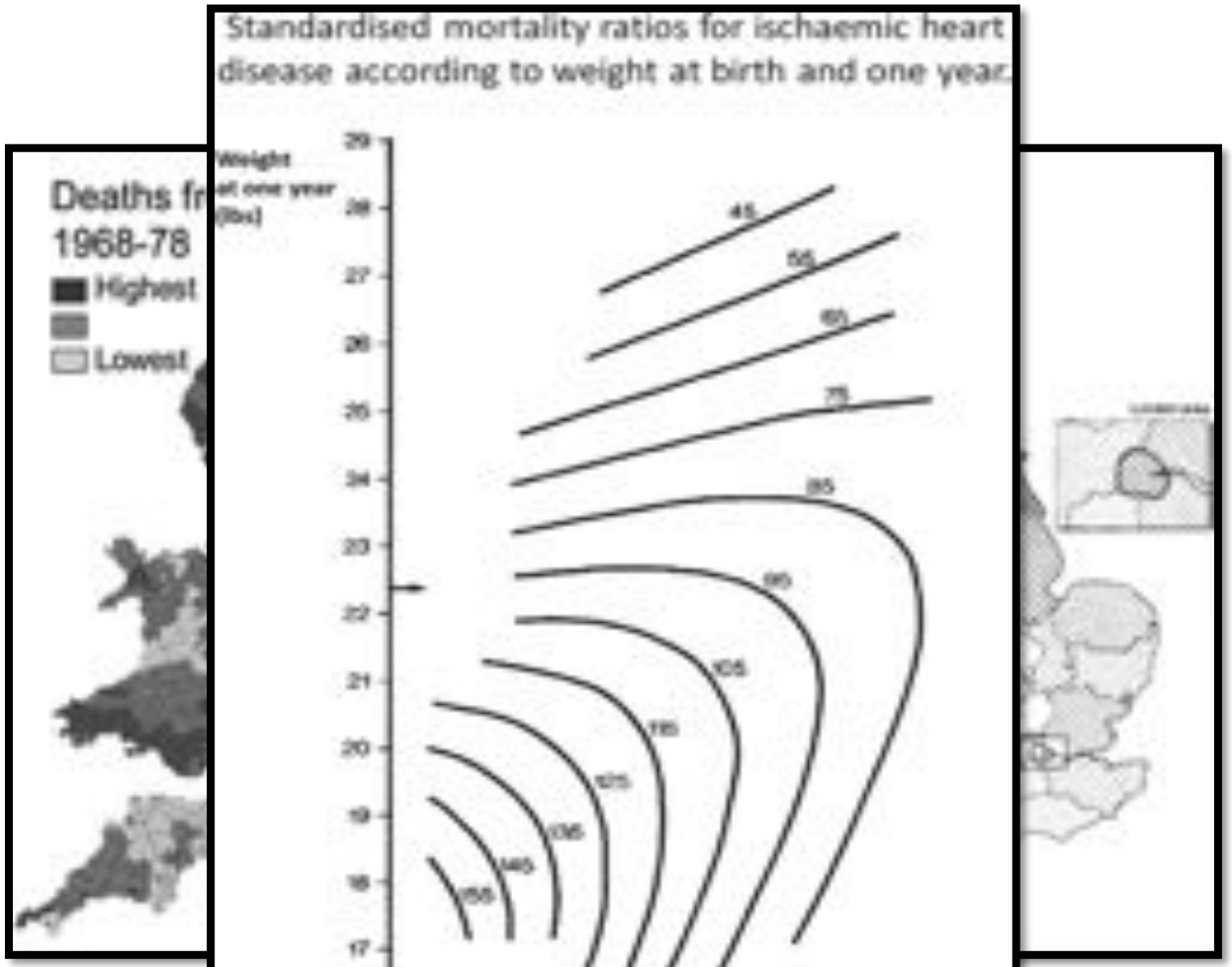


Treatment of CHD and *Trajectories*

- We currently intervene and “treat” newborns, infants, children and adults who are “fully formed” in order to manage CHD
- Are we ignoring “fetal plasticity” – a golden opportunity to impact change to a *greater degree* before birth than after birth
- Influencing the prenatal state may alter trajectory and provide for long-lasting changes that can profoundly alter outcomes



Fetal Programming – Barker Hypothesis



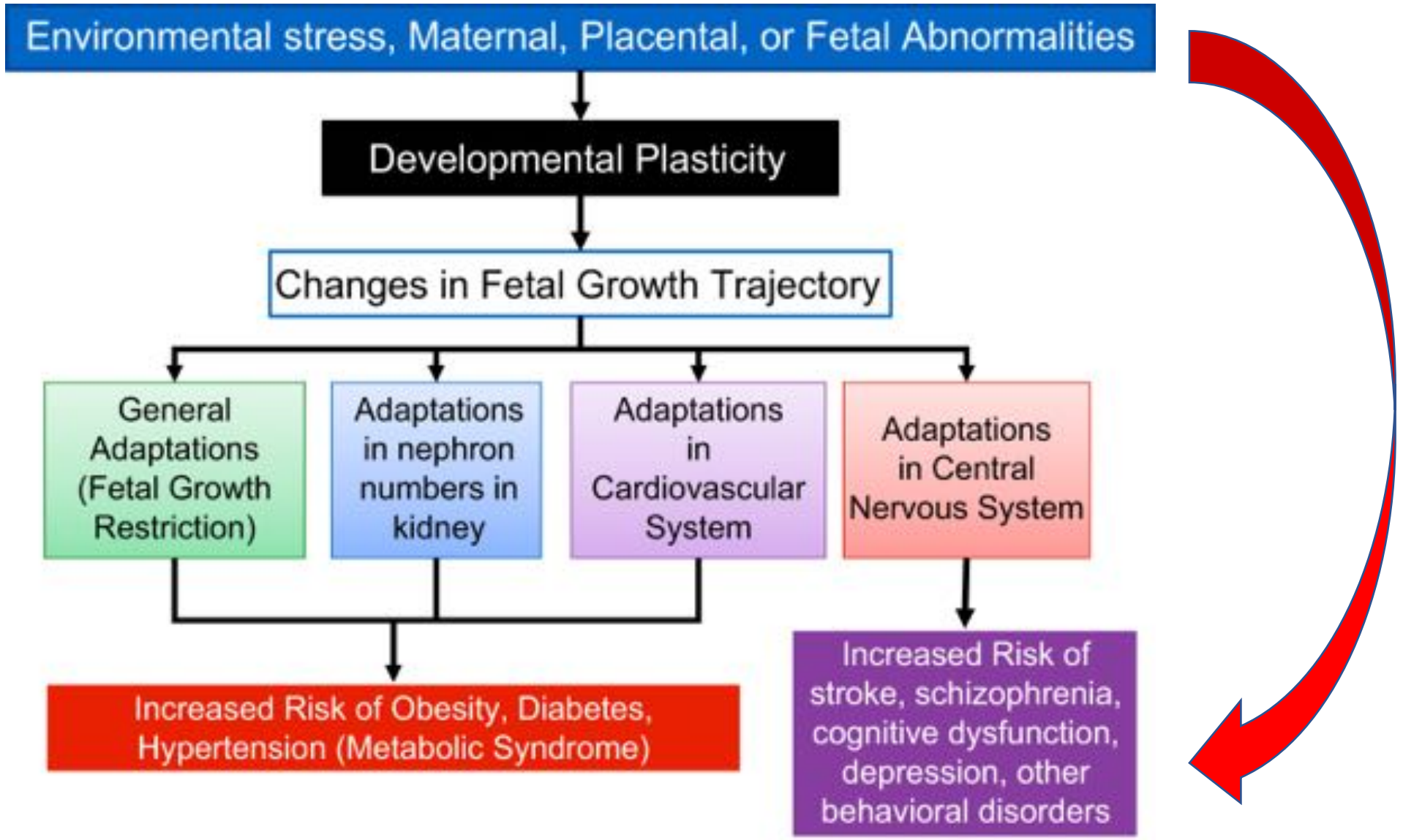
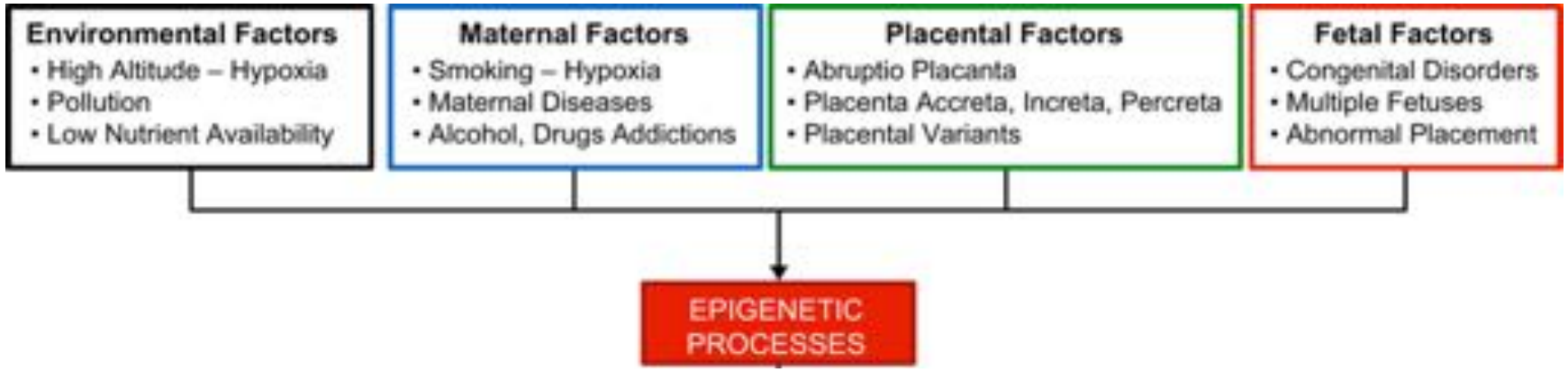


Illustration of the interplay of external factors on developmental plasticity and the downstream effects on general and system specific adaptations in the developing fetus. Also shown are the known disorders associated with such interactions.

***Physiol Rev* 2018**



***Physiol Rev* 2018**

12 week fetus with increased NT

6 year old HLHS with severe plastic bronchitis

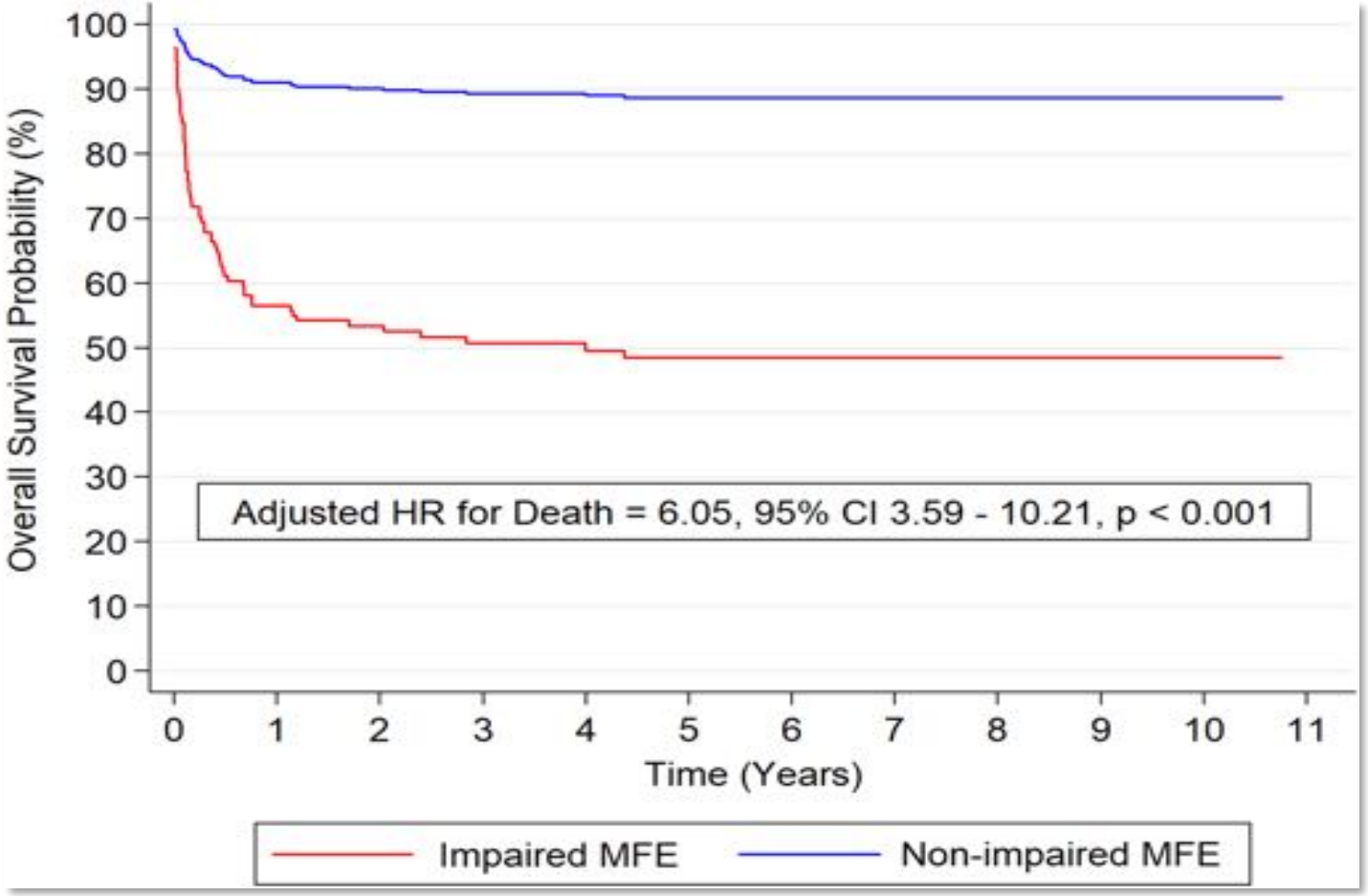
Impact of Maternal–Fetal Environment on Mortality in Children With Single Ventricle Heart Disease

Jill J. Savla, Mary E. Putt, Jing Huang, Samuel Parry, Julie S. Moldenhauer, Samantha Reilly, Olivia Youman, Jack Rychik, Laura Mercer-Rosa, J. William Gaynor and Steven M. Kawut

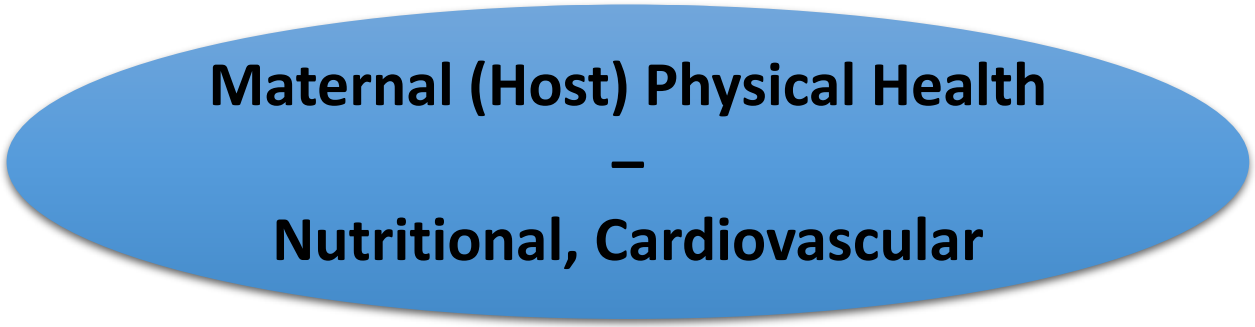
Originally published 11 Jan 2022 | https://doi.org/10.1161/JAHA.120.020299 | Journal of the American Heart Association. 2022;11:e020299

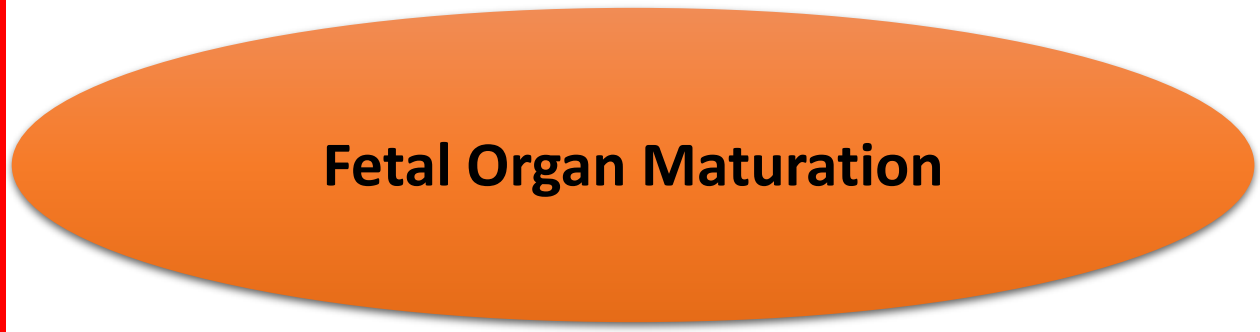
Altered Maternal-Fetal Environment (MFE):

- Maternal hypertension
- Preeclampsia
- Gestational diabetes
- Smoking during pregnancy



Possible Targets- Perhaps Modifiable?





THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

J Peds 2013

Maternal Psychological Stress after Prenatal Diagnosis of Congenital Heart Disease

Jack Rychik, MD[1,4], Denise D. Donaghue, RN, MSN[1], Suzanne Levy, PhD[2,5], Clara Fajardo, MS[2], Jill Combs, RN, MSN[1], Xuemei Zhang, MS[3], Anita Szwast, MD[1,4], and Guy S. Diamond, PhD[2,5]

- 58 mothers with prenatal dx of important CHD
- Initial evaluation at 2nd visit to FHP
- Tested at 3 time periods (26, 31, 34 wks)
- Battery of Self-Reported Psych tests
  - Beck Depression Inventory (Depression)
  - State-Trait Anxiety Inventory Scale (Anxiety
  - Impact of Events Scale (post-traumatic stre
  - Dyadic Adjustment Scale (marital satisfaction)
  - COPE Scale

Goals of Study:

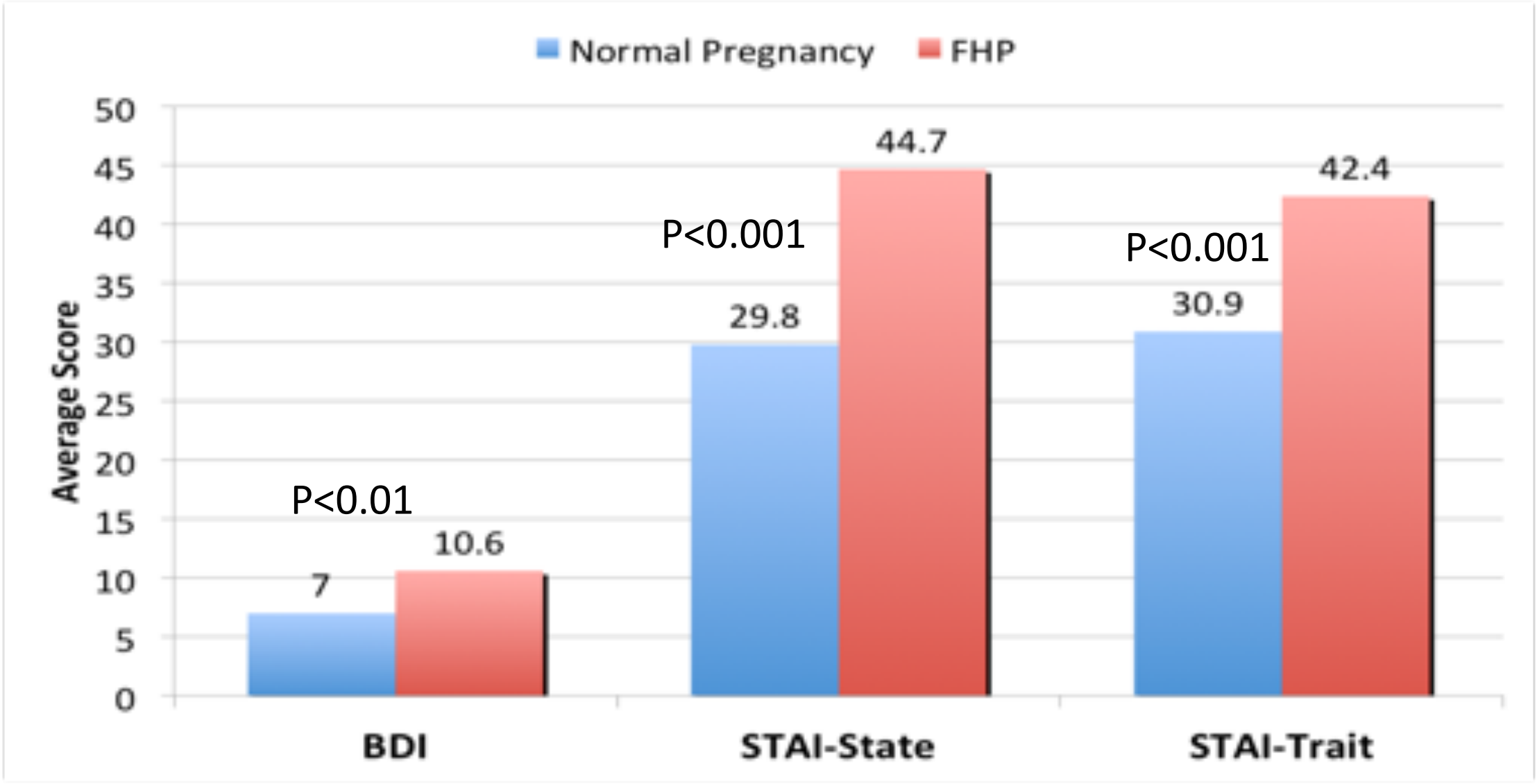
To identify and better understand potential variable modifiers to 3 stress domains:

1) Depression

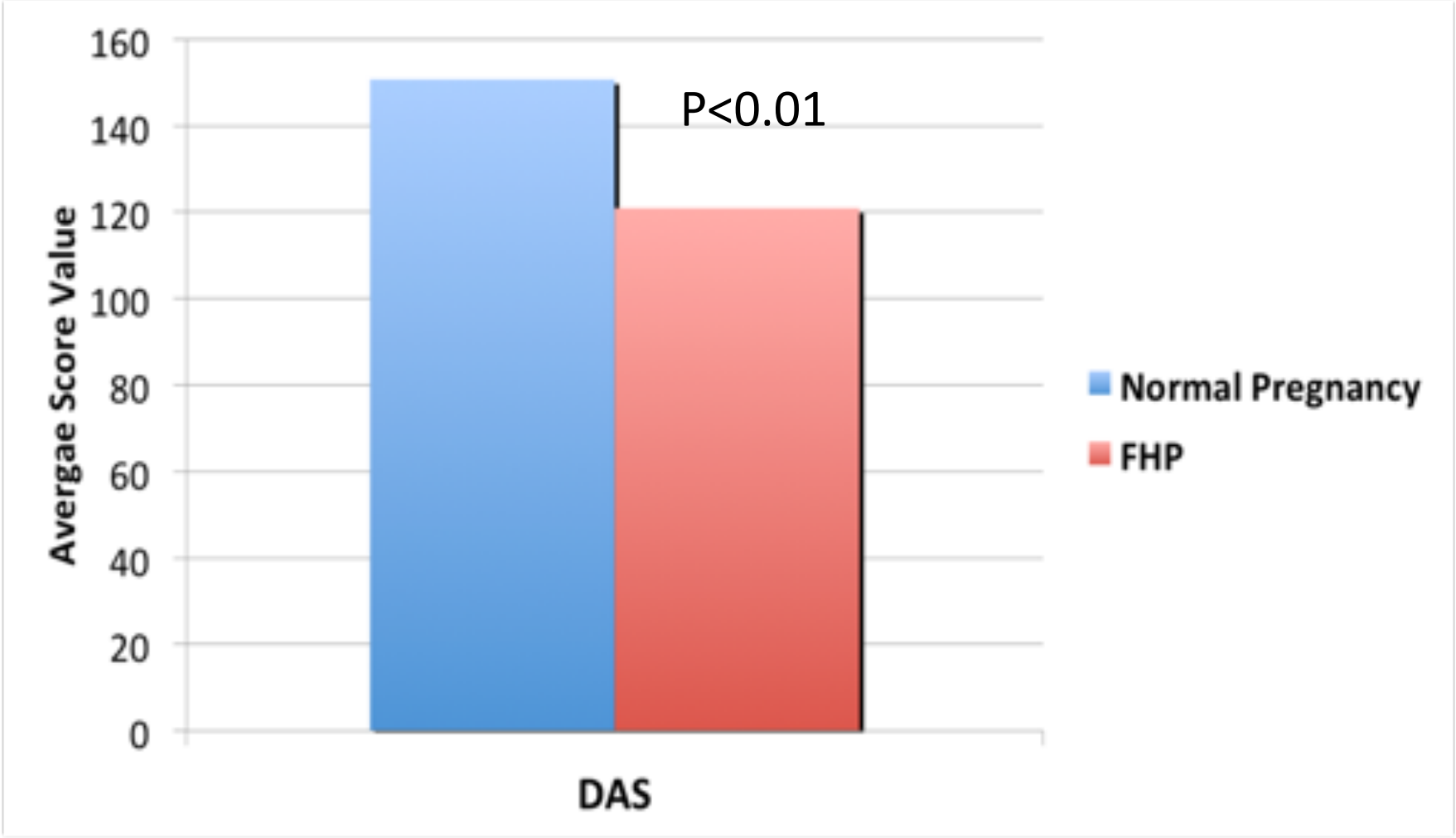
2) Anxiety

3) Traumatic stress

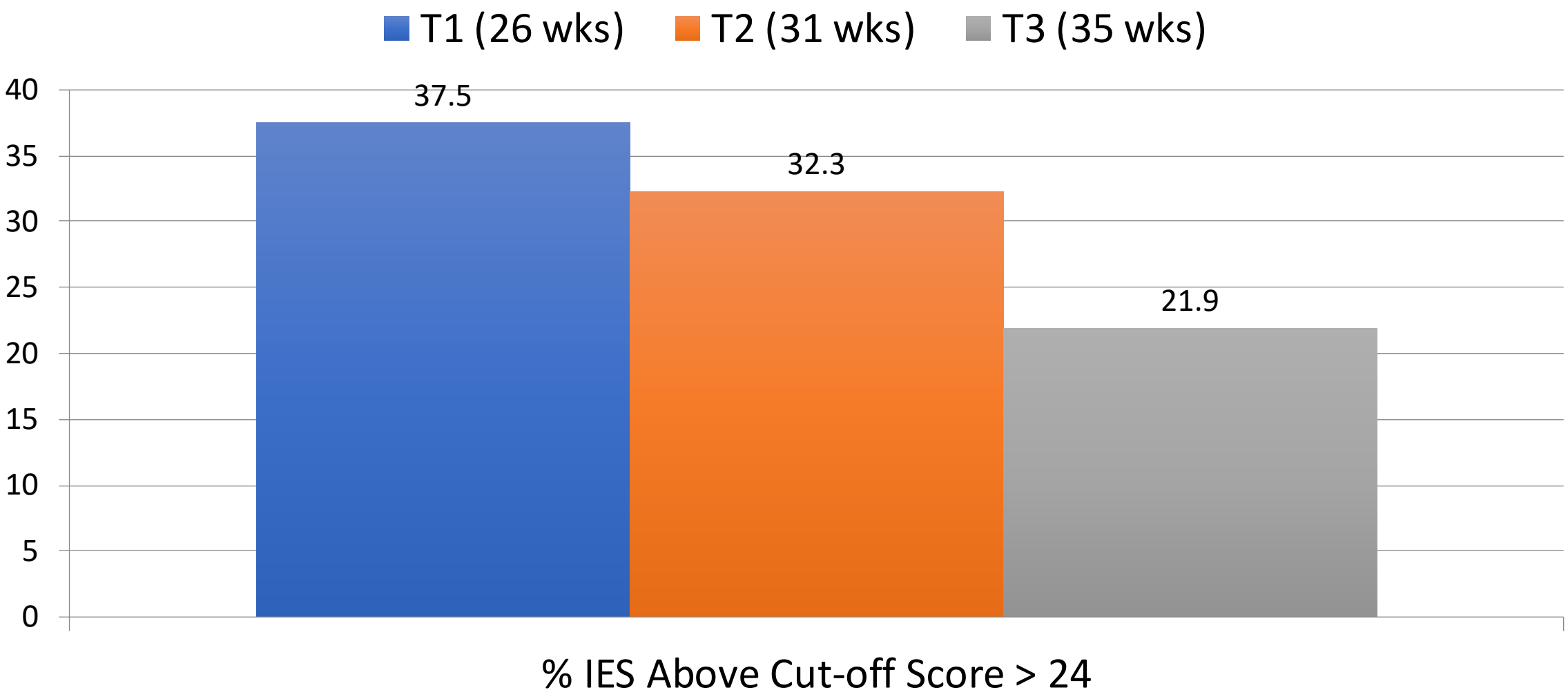
Scores of Maternal Distress



Dyadic Adjustment Scale

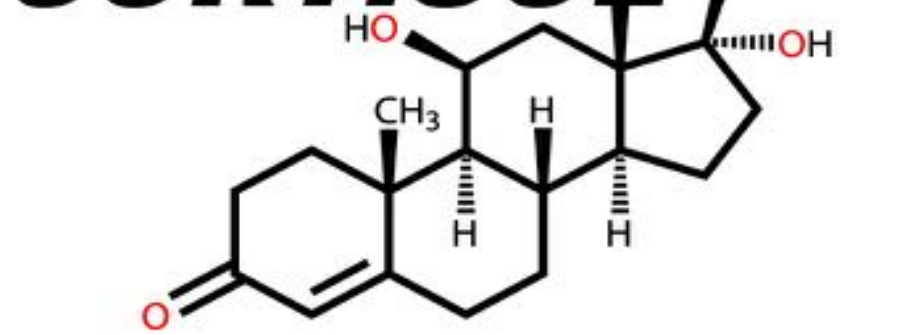


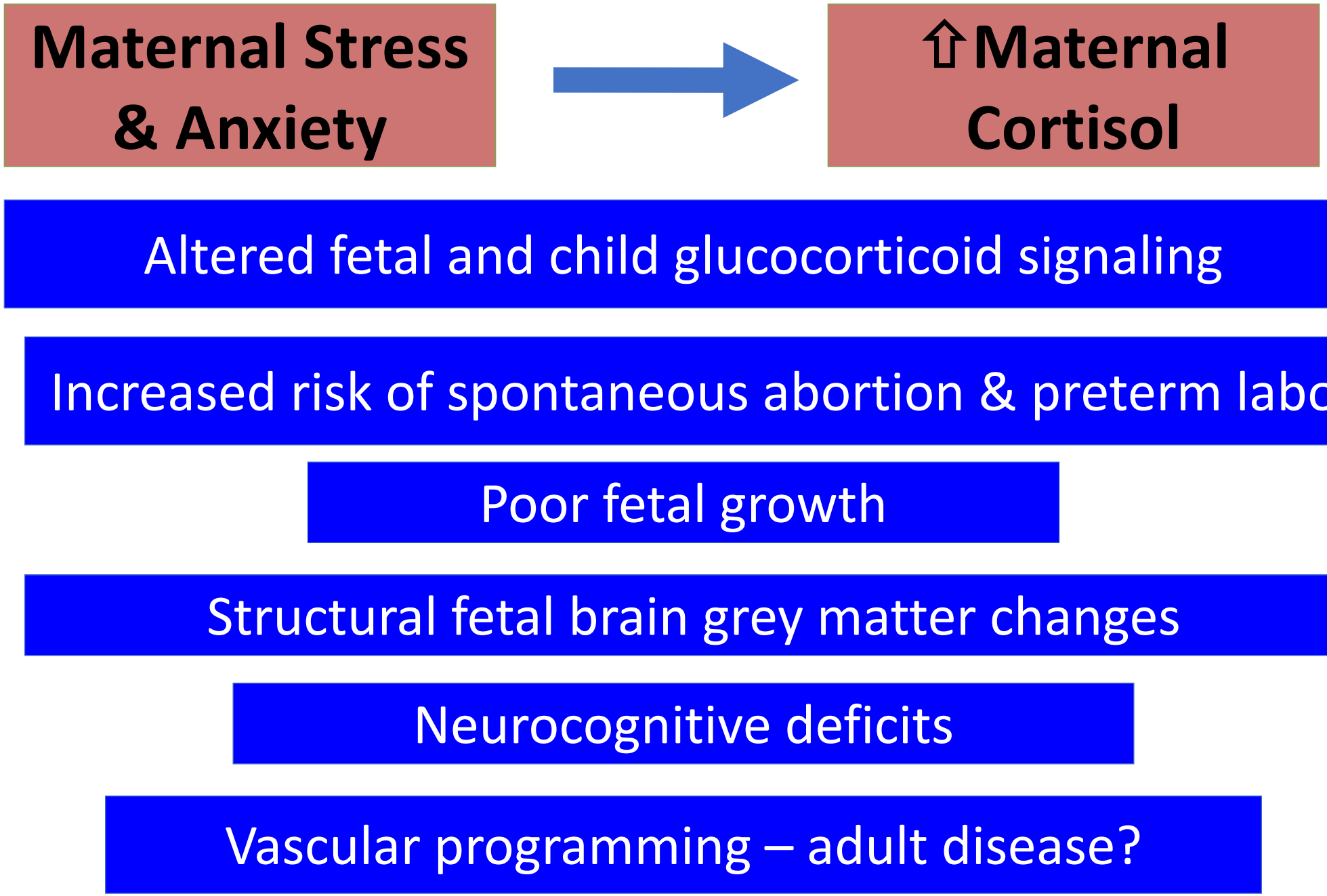
Effect of Serial Fetal Counseling



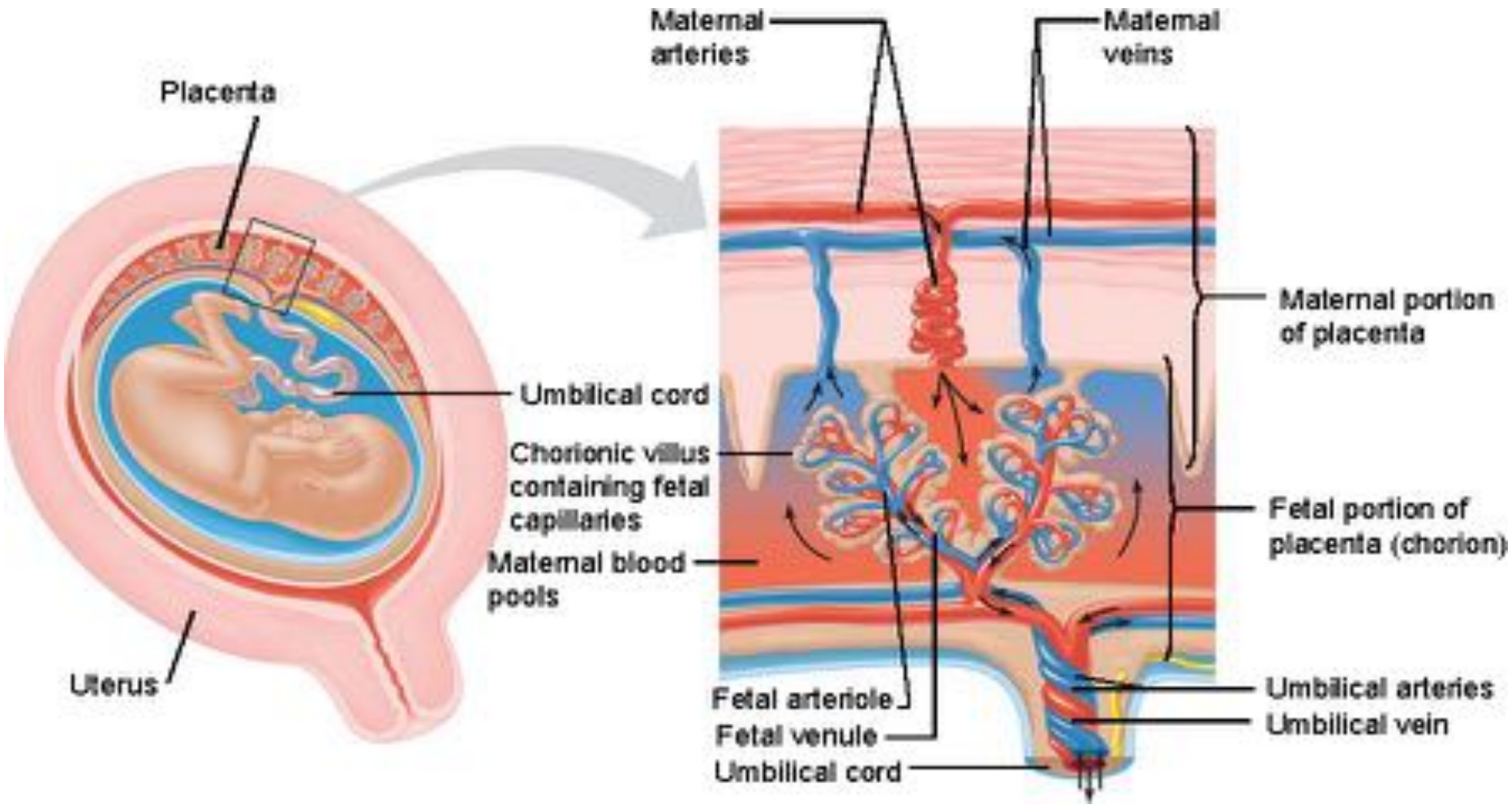
Impact of Prenatal Dx CHD on Maternal Psychological Stress

- 10% of mothers had ≥ mild depression
- 20% had clinically significant state anxiety
- 28% had traumatic stress scores indicating probable post-traumatic stress disorder
- Partner satisfaction scores lower than normal
- In order to improve maternal health and consequently fetal health, healthcare providers should look to promote an ***increase in relationship satisfaction*** and the coping skills of ***acceptance*** and ***positive reinterpretation and growth*** among women pregnant with a fetus diagnosed with CHD

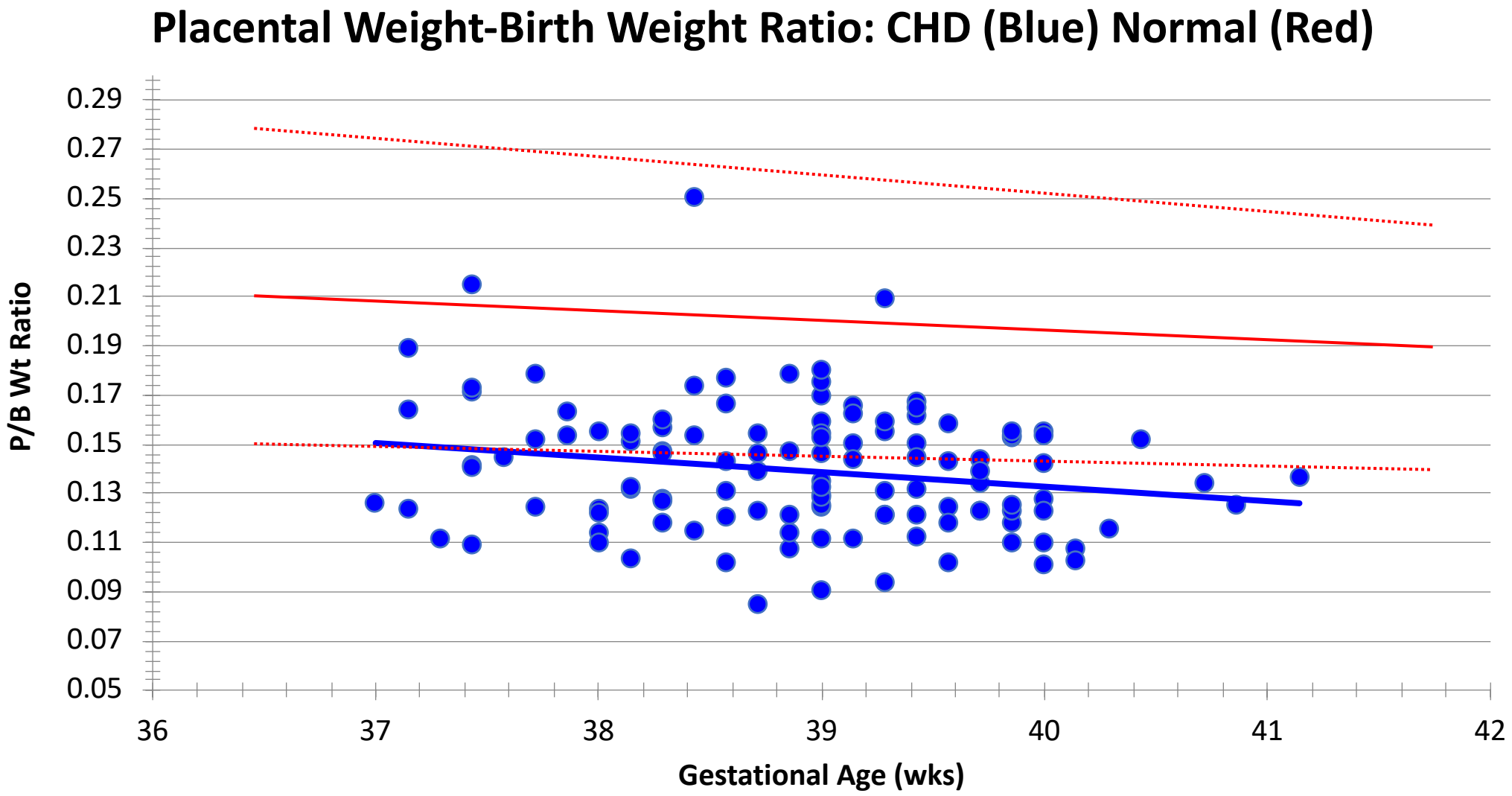

CORTISOL
O
OH
HO
OH
CH3
H
H
H
O


Maternal Stress & Anxiety
⇧Maternal Cortisol
Altered fetal and child glucocorticoid signaling
Increased risk of spontaneous abortion & preterm labor
Poor fetal growth
Structural fetal brain grey matter changes
Neurocognitive deficits
Vascular programming – adult disease?

Fetal cardiovascular development and placental vascular development occur at the same time!



What is the placenta like in our fetuses with CHD?

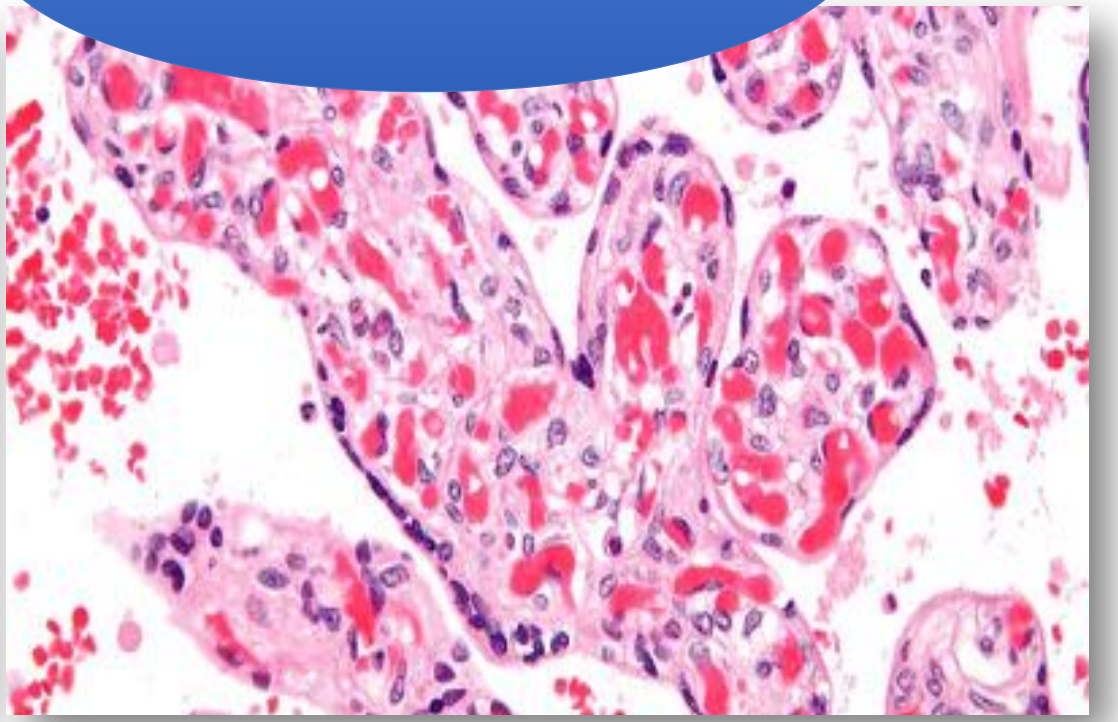


Pediatr Cardiol. 2018;39:1165-1171

What is the placenta like in our fetuses with CHD?

Thrombosis = 41%
Infarction = 20%

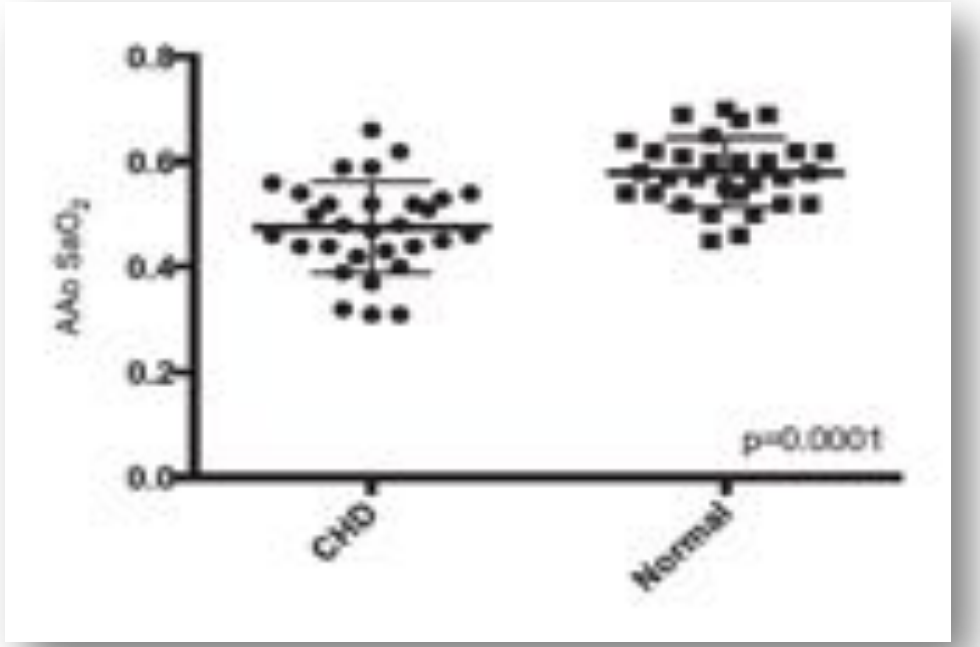
Chorangiosis = 20%



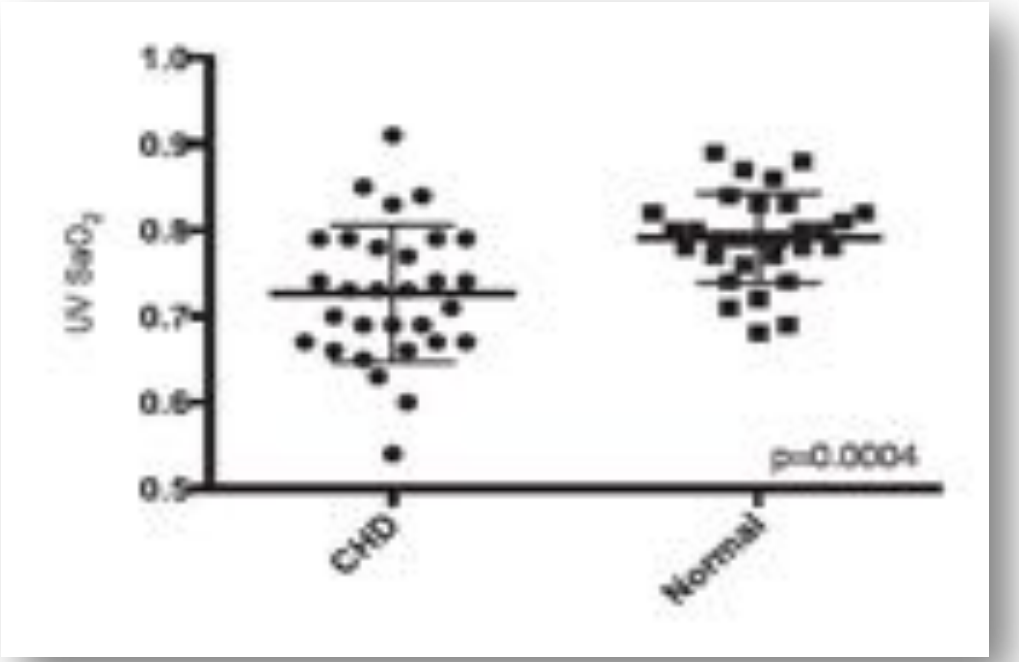
Pediatr Cardiol. 2018;39:1165-1171

Placental *Function* in CHD? *Fetal MRI Techniques*

Ascending Aorta Saturations Lower in Fetal CHD



Umbilical Vein Saturations Lower in Fetal CHD!



Sun et al Circulation. 2015;131:1313-1323

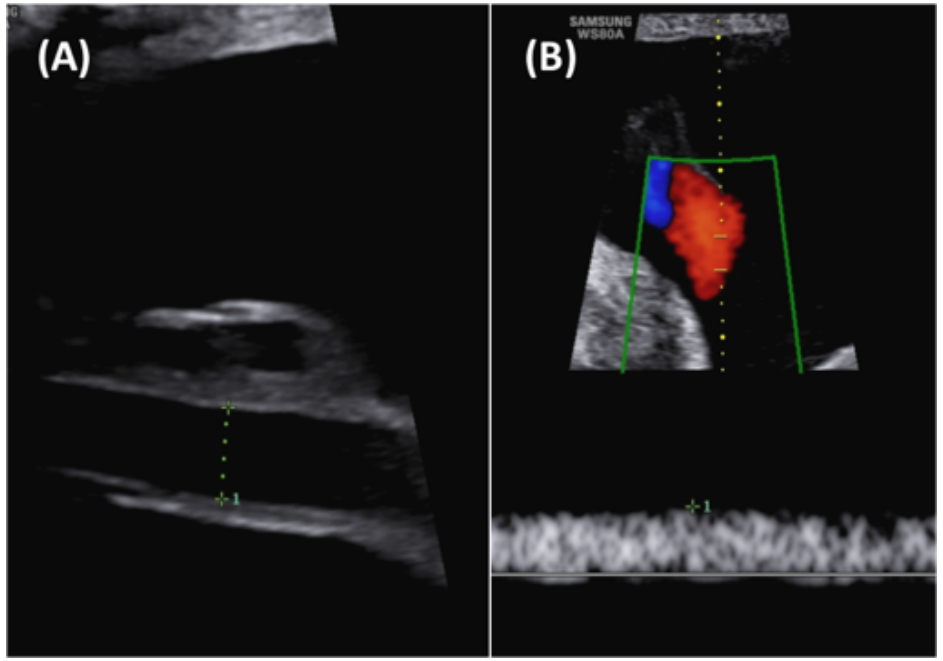
PRENATAL
DIAGNOSIS

ORIGINAL ARTICLE

Mid-gestational fetal placental blood flow is diminished in the fetus with congenital heart disease

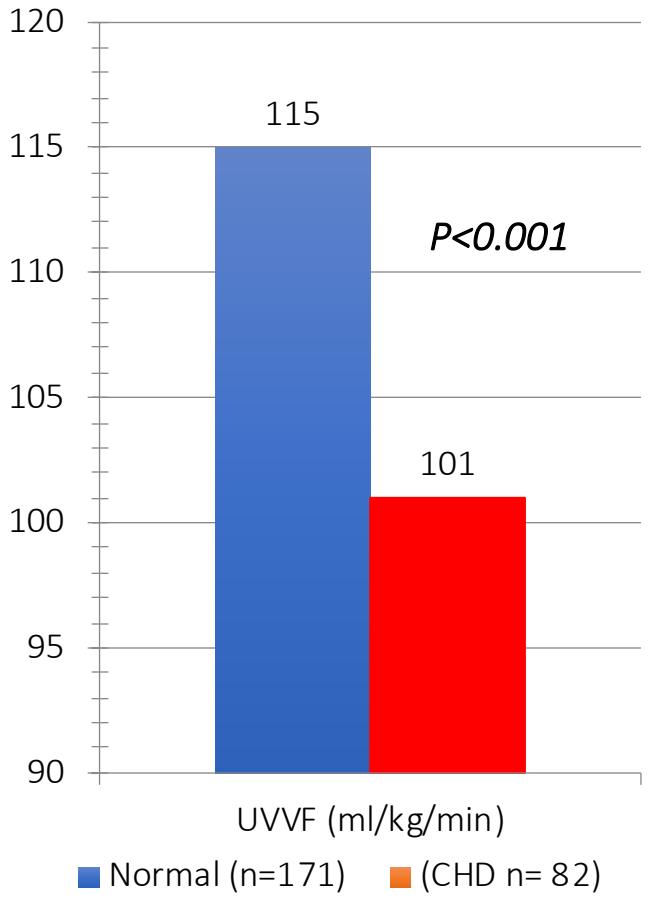
Deborah Y. Ho, Rebecca Josowitz, Hannah Katcoff, Heather M. Griffis, Zhiyun Tian, J. William Gaynor, Jack Rychik

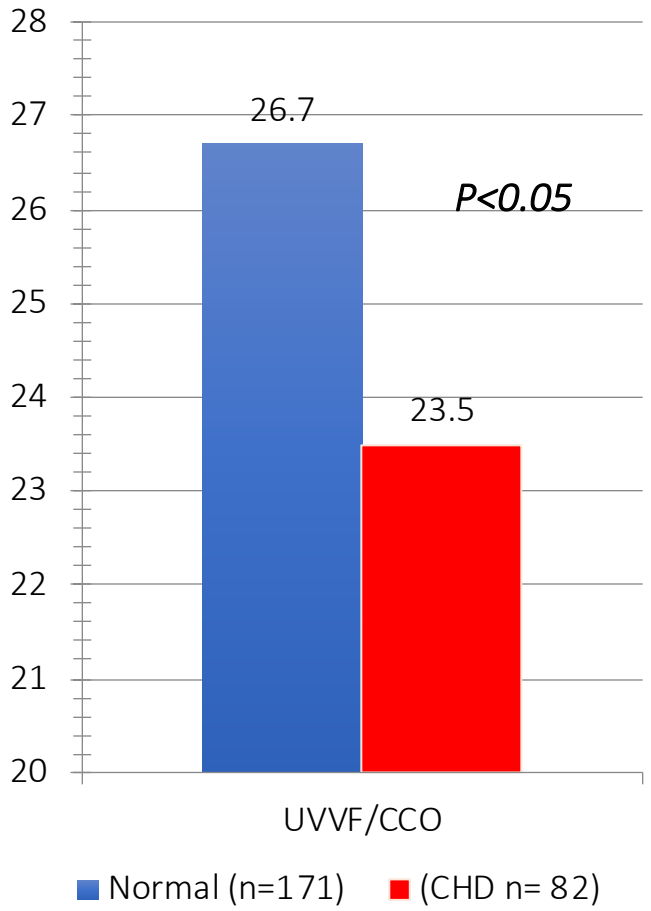
First published: 16 July 2020 | https://doi.org/10.1002/pd.5791



$$UVVF = \pi\left(\frac{D}{2}\right)^2\left(\frac{V_{max}}{2}\right)(60\ seconds)$$

Umbilical Venous Volume Flow





Ho et al. *Prenatal Diagnosis* 2020

JUM Journal of Ultrasound in Medicine

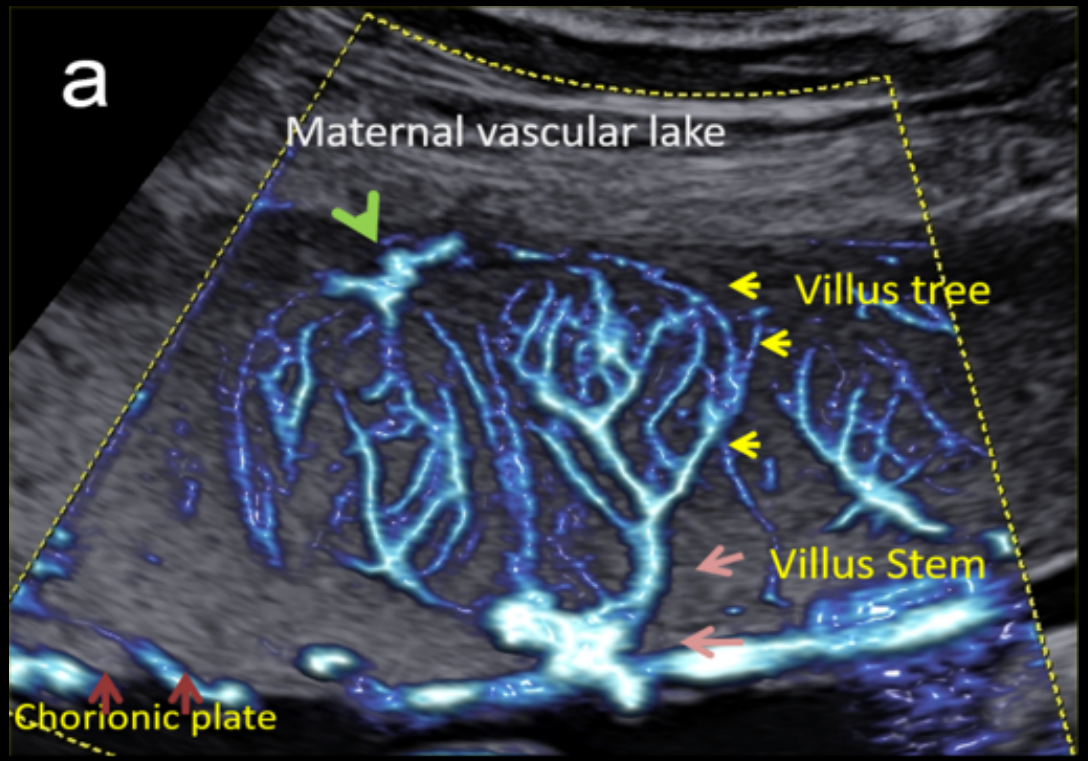
aium

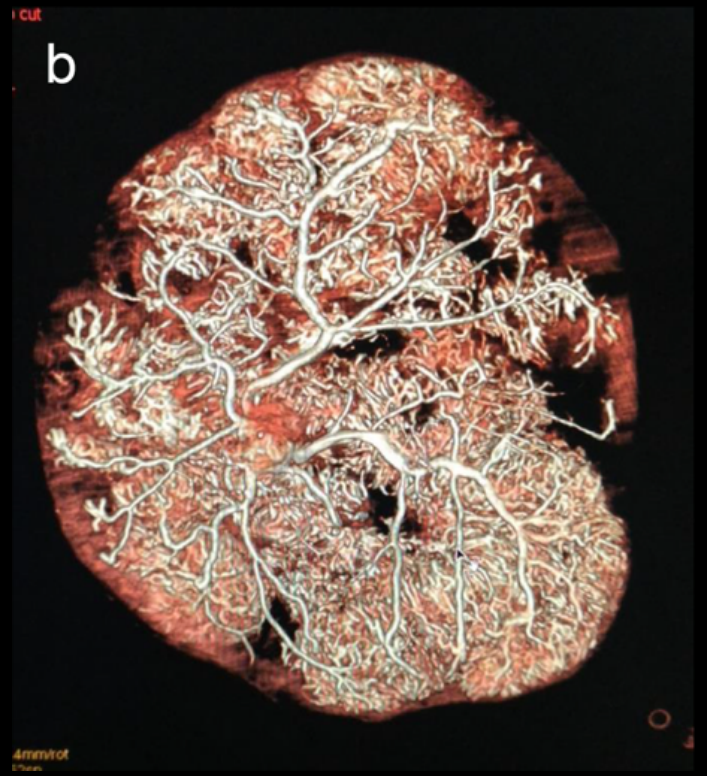
Original Research

Characterization of Placental Microvascular Architecture by MV-Flow Imaging in Normal and Fetal Growth–Restricted Pregnancies

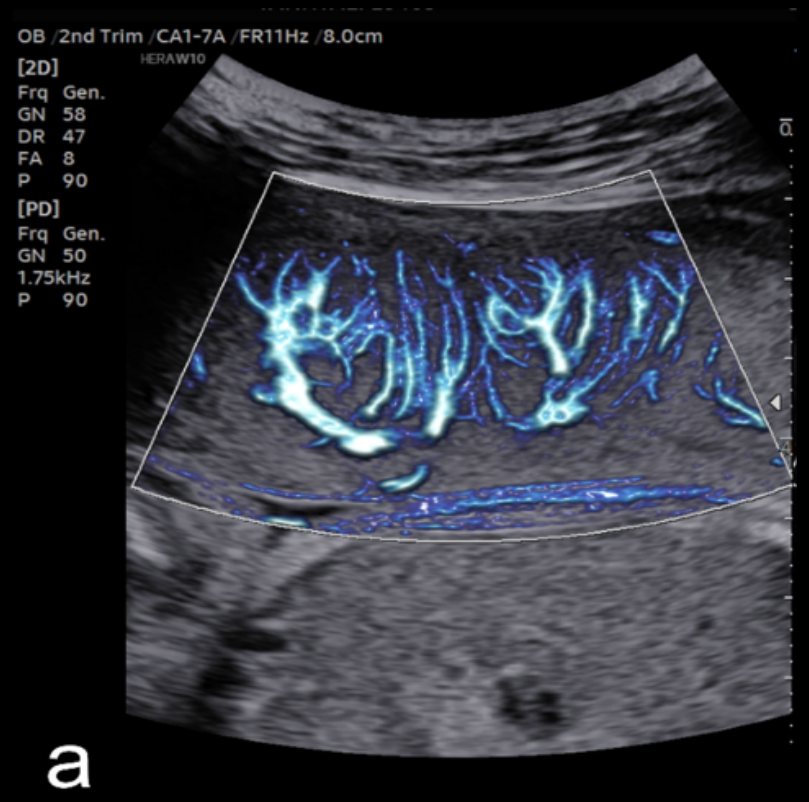
Xinlin Chen MD, Xia Wei MD, PhD, Sheng Zhao MD, PhD, Hui Huang PhD, Weiyun Wang MS, Junyu Qiu MD, Xiao Chen MD, Chen Cheng PhD, Zhiyun Tian MD, Jack Rychik MD

First published: 19 October 2020 | https://doi.org/10.1002/jum.15531

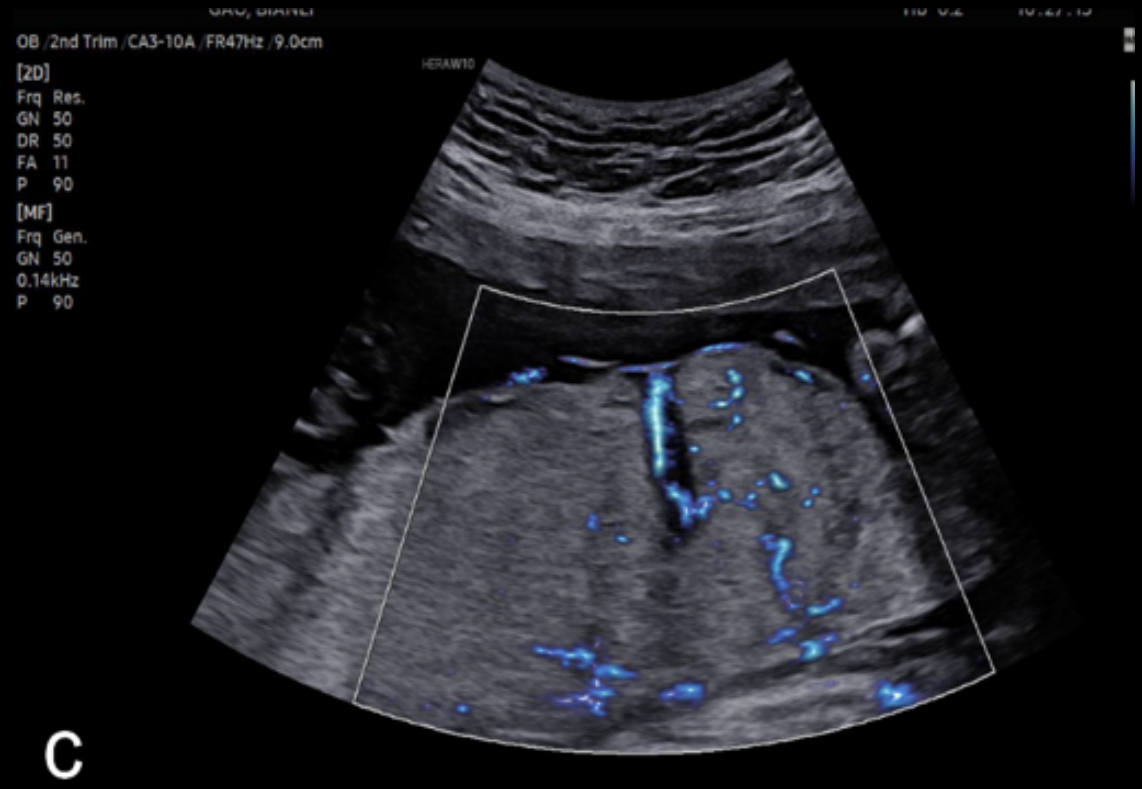




Placental Microvascular Assessment



Normal Placenta



CHD Placenta

Pediatric RESEARCH

www.nature.com/pr

REVIEW ARTICLE OPEN

Neuroplacentology in congenital heart disease: placental connections to neurodevelopmental outcomes

Rachel L. Leon[1], Imran N. Mir[1], Christina L. Herrera[2], Kavita Sharma[1], Catherine Y. Spong[2], Diane M. Twickler[2,3] and Lina F. Chalak[1]

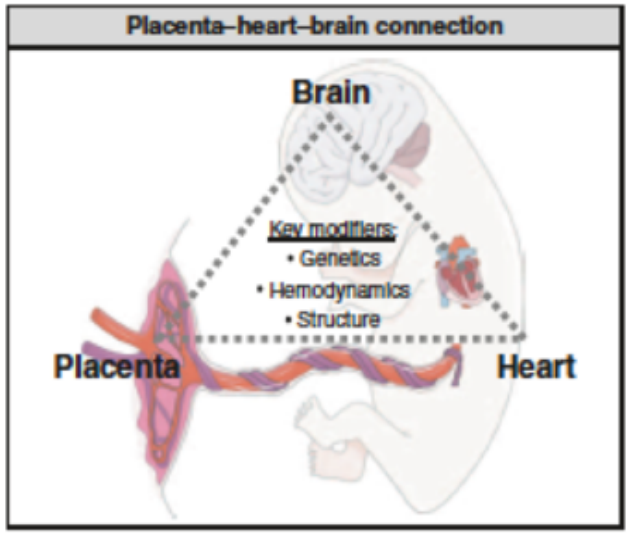
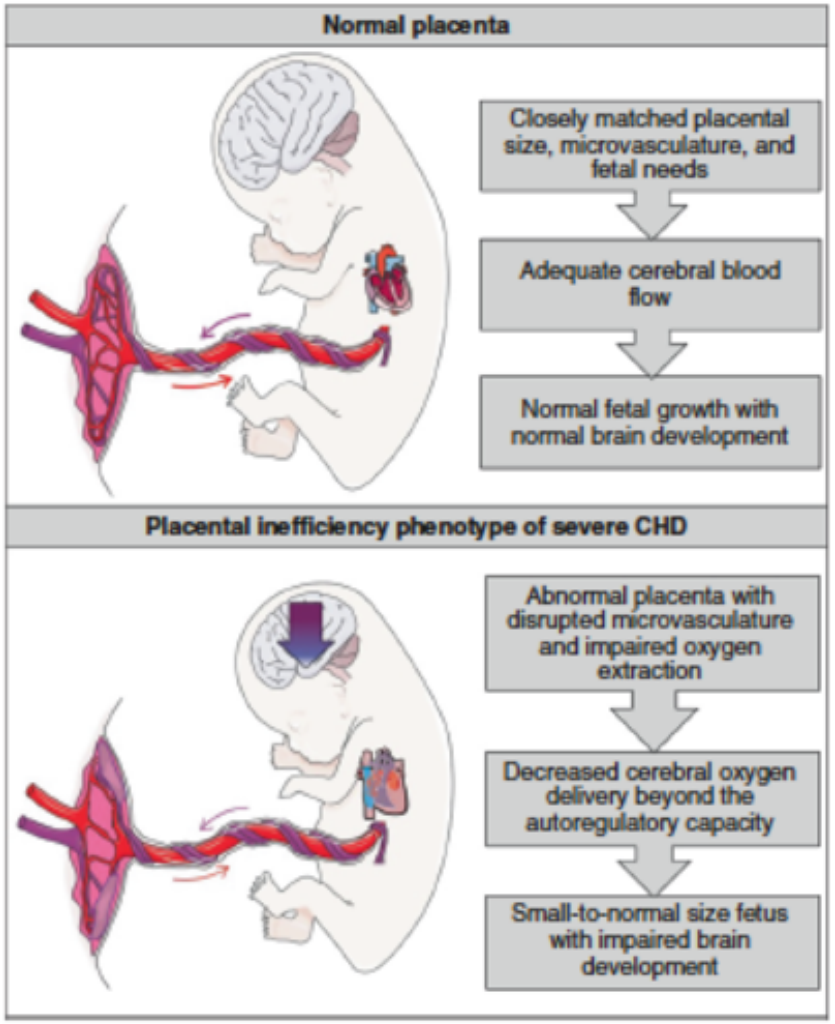


Fig. 2 The placenta–heart–brain connection is modified by genetic/epigenetic, hemodynamic, and structural/microstructural influences. These represent key areas for future investigations in the field of neuroplacentology in CHD.



Pediatric Research 2021

What should we be thinking about?

- Understand prenatal trajectories that predict specific outcomes:
  - Growth velocity - somatic
  - Growth velocity - head
  - Progression of Doppler vascular indices (UA, MCA, Uterine)
  - Improved characterization of placental health (form & function) new tools like UVVF, placental elastography, MRI placental imaging
- Associate with SV outcomes – many postnatal registries now in place: CNOC, FON, PC4, PAC3 – no systematic prenatal cataloguing currently in place! …*can't ignore event-filled period of life before birth to offer clues!*
- Outcome modification strategies?...change the substrate by taking advantage of fetal plasticity and prenatal programming