Pregnancy as a Window to Future Health

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Pregnancy as a Window to Future Health

- What is it?
- What do we know?
- Why does it matter?
- What can we do about it?

What is it?

- Adverse outcomes during pregnancy predict future health
- Maternal Health
- Offspring health

You've heard it before

- " My diabetes started with gestational diabetes"
- " I had preeclampsia and then it turned to chronic hypertension"
- My mom has diabetes but I have only had gestational"

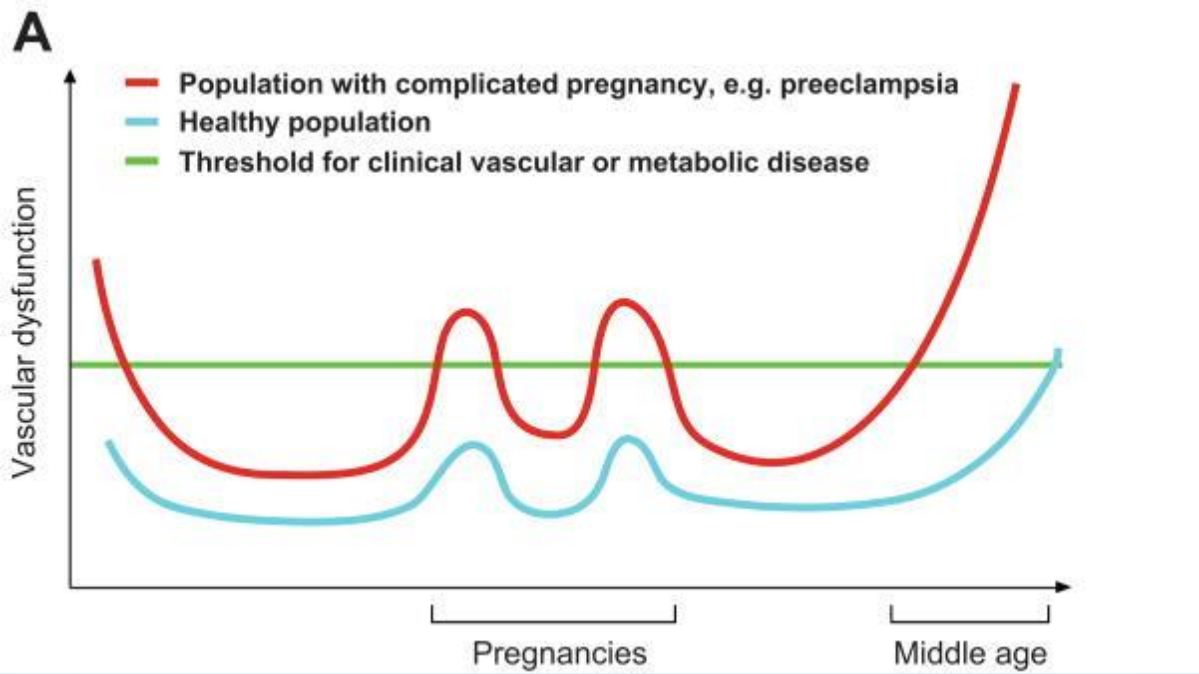

Pregnancy
Postpartum
Pre-pregnancy
LIPIDS

- J.K. a 32 Y.O. G2 P0010 who presented for care at 12 weeks. Self referred due to obstructive sleep apnea.
- She used CPAP and was counseled on risks
- She developed gestational diabetes and HELLP syndrome at 28 weeks

- What can we tell her?

Pregnancy as a Window to Future Cardiovascular Disease Risk

Pregnancy as a Cardiovascular Stress Test



Sattar N and Greer I, BMJ 2002;325:157–160

Ma l Syndromes

Maternal Placental Syndromes

- Preeclampsia
- Gestational hypertension
- Fetal growth restriction
- Abruption

Preeclampsia & Heart Disease

- Women with preeclampsia/eclampsia compared with low risk controls
- Followed for average 2 years
- Significant increase in preeclampsia in subsequent pregnancy
  - 46.8% versus 7.6%, $p < 0.0001$
  - Significant increase in development hypertension
    - 14.8% versus 5.6%, $p < 0.001$
  - Further increase among those with disease at <30 weeks gestation.

Sibai, B et al, Severe preeclampsia-eclampsia in young primigravid women; Subsequent pregnancy outcome and remote prognosis. AJOG 1986 155 (5)1011-1016

Preeclampsia & Preeclampsia & Heart Disease

- Retrospective cohort
- Scottish Morbidity Record system
- >129,000 women between 1981 and 1985.
- Risk of maternal ischemic heart disease admission or death over a 15-19 year follow up interval
  - Low birth weight- 2x
  - Preterm delivery -1.8x
  - Pre-eclampsia – 2x

Smith, GC et al. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study of 129 290 births *Lancet* 2001; **357:** 2002–06

Preeclampsia & Heart Disease

- Systematic review and meta analysis 2007
- 198,252 women with h/o preeclampsia
- 29, 495 episodes of CVD and cancer
- No increase in cancer risks
- Preeclamptic relative risk of
  - 3x HTN-3.70
  - 2x Ischemic HD
  - 1.8 x blood clots
  - 1.8x Stroke
  - 1.5 x Overall Death

Bellamy et al. Pre-eclampsia and risk of cardiovascular disease and cancer in later life: systematic review and meta-analysis British Medical Journal 2007;335:974.

Preeclampsia & CVD

- Prospective 15,065 first singleton births
- Women with gestational hypertension or Preeclampsia
  - Higher BMI, total cholesterol, LDL, triglycerides
  - Higher risk of future Diabetes
- Women with high blood pressure in more than one pregnancy
  - 10X more likely to require HTN medication

Obstet Gynecol. 2009 Nov;114(5):961-70

Hyperlipidemia & Preeclampsia

- Cholesterol and triglyceride in each trimester
  - 115 women with high blood pressure in pregnancy
  - 115 with normal blood pressure in pregnancy
- High triglycerides at 20 and 34 weeks among severe gestational hypertension, mild and severe preeclampsia over controls.
- No significant elevation in CHTN or mild GHTN

Gratacos et al. Variation in lipid levels during pregnancy in women with different types of hypertension. Acta obst gynecol scan 1996:75;896-901.

Preeclampsia and Hyperlipidemia

- Possible links
  - Impaired trophoblast invasion
  - Increased triglyceride associated with decreased prostacyclin release
  - Endothelial dysfunction due to elevated triglyceride levels

Charlton et al Cardiovascular risk, lipids and pregnancy: preeclampsia and the risk of later life cardiovascular disease. Heart Lung Circulation 2013

Placental Syndromes

- 2005 retrospective population-based cohort
- Identified women with placental syndromes
  - Preeclampsia, GHTN, IUFD, IUGR, Abruption
- Primary outcome composite of cardiovascular disease
- Database of >1million women
  - Excluded death prior to 24 months postpartum, age <14, living outside of study area
- 75,380 diagnosed with maternal placental syndrome
- Mean follow up 7.8 years

Ray et al. Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study
Lancet 2005 366: 1797-1803.

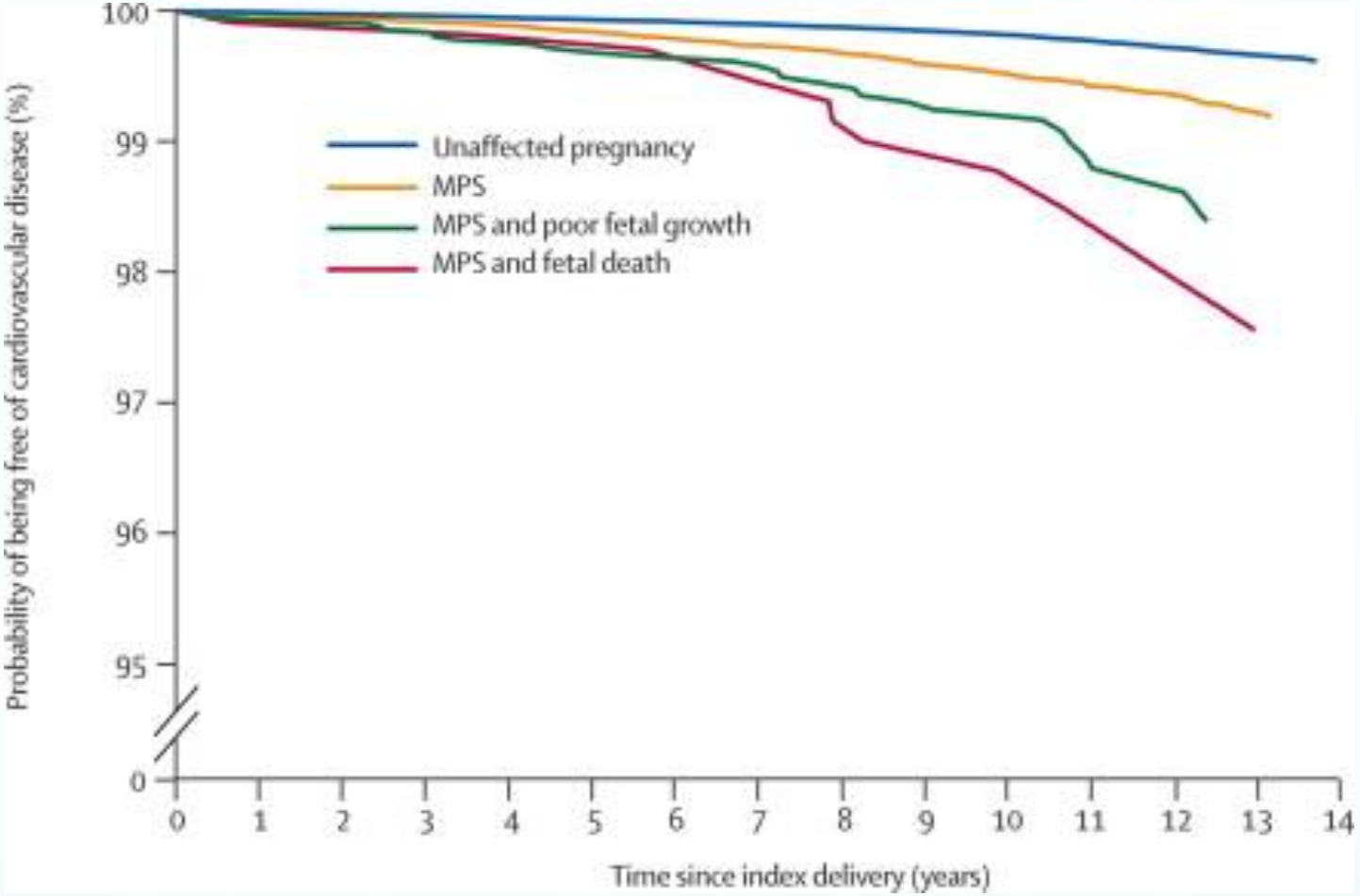


Figure 1 Risk of premature cardiovascular disease associated with a maternal placental syndrome (MPS) or an affected fetus, or both

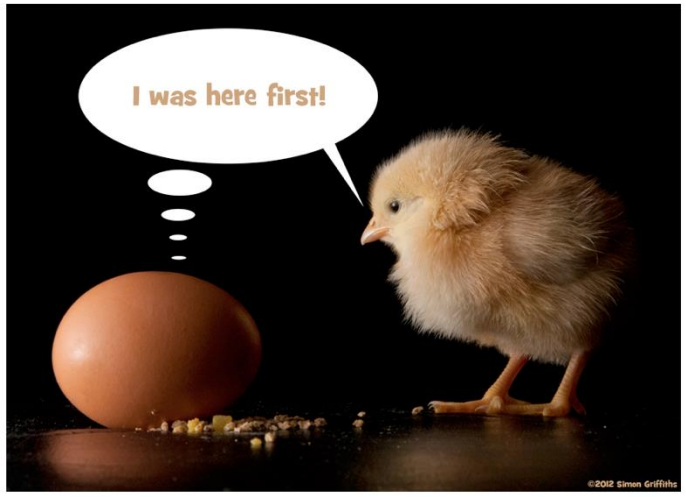
Joel G Ray , Marian J Vermeulen , Michael J Schull , Donald A Redelmeier

Cardiovascular health after maternal placental syndromes (CHAMPS): population-based retrospective cohort study

The Lancet, Volume 366, Issue 9499, 2005, 1797 - 1803
http://dx.doi.org/10.1016/S0140-6736(05)67726-4

Age Old Question.....

- Pregnancy unmasking underlying disease
- Preeclampsia and placental syndromes causing endothelial dysfunction and vascular damage in previously healthy women



Rich-Edwards et al. Breathing life into the lifecourse approach: Pregnancy history and cardiovascular disease in women. *Hypertension*. 2010 September ; 56(3): 331–334

Gestational Diabetes

Gestational Diabetes

- Affects 5% of pregnancies
- Failure to adequately compensate for gestational insulin resistance
- 30-50% lifetime risk of developing Diabetes Mellitus

[1]Rich-Edwards et al. Breathing life into the lifecourse approach: Pregnancy history and cardiovascular disease in women. *Hypertension*. 2010 September ; 56(3): 331–334
[2]Kauffman et al. Gestational diabetes diagnostic criteria: Long term maternal follow up. 1995 AJOG 172:621.

GDM and Risk of CVD

- 2008 Case control with median follow up of 11.5 years.
- 8,191 women with GDM vs. 81,262 controls
- HR of 1.71 for CVD events
- Predominately attributed to development of type 2 Diabetes Mellitus (adjust HR 1.13)

Shah et al. Increased Risk of Cardiovascular Disease in Young Women Following Gestational Diabetes Mellitus Diabetes Care 2008 31 (8)

Gestational Glucose Tolerance and CVD

- Retrospective population based cohort
- GDM (13,888); Abnormal GCT (71,831); No GTT (349,977)
- Median follow up 12.3years
- Primary outcome CVD
  - Coronary artery bypass, MI, Stroke, Endarterectomy, Coronary angioplasty.
- GDM-HR of 1.66 P <0.001
- Abnormal GCT- HR of 1.19 p=0.03

Retnakaran et al. Mild glucose intolerance in pregnancy and risk of cardiovascular disease: a population-based cohort. CMAJ 2009. 181(6-7).

Abnormal GCT and Metabolic Dysfunction

- Prospective observational trial
- Normal GCT (n=166), Abnormal GCT without GDM (n=93)
- 3 months postpartum
  - 75 gram OGTT
  - Physical exam
    - No difference in waist circumference or BMI
- Abnormal GCT
  - Decreased beta cell function
  - Poor insulin sensitivity
  - Greater incidence of prediabetes
    - 0·2% *vs.* 3·2%, $P = 0{\cdot}.04$)

Retnakaran et al. An abnormal screening glucose challenge test in pregnancy predicts postpartum metabolic dysfunction, even when the antepartum oral glucose tolerance test is normal. 2009 Clinical Endocrinology. 71 208·214.

What is Prediabetes?

Abnormal Glucose Testing

- 2011 Longitudinal cohort
- All received 1 hour GCT
  - if >140mg/dl then given 3 hour GTT
  - Diagnosed with GDM if 2 abnormal values on GTT
- Returned at 3 years postpartum
- 611 met criteria for analysis
- 16 with GDM, 21 with 1 abnormal value on GTT and 39 with all normal values on GTT

Stuebe et al. Gestational glucose tolerance and maternal metabolic profile at 3 years postpartum. Obstetrics and Gynecology. 2011: 111(5).

History of Preterm Birth and Cardiovascular Disease Risk

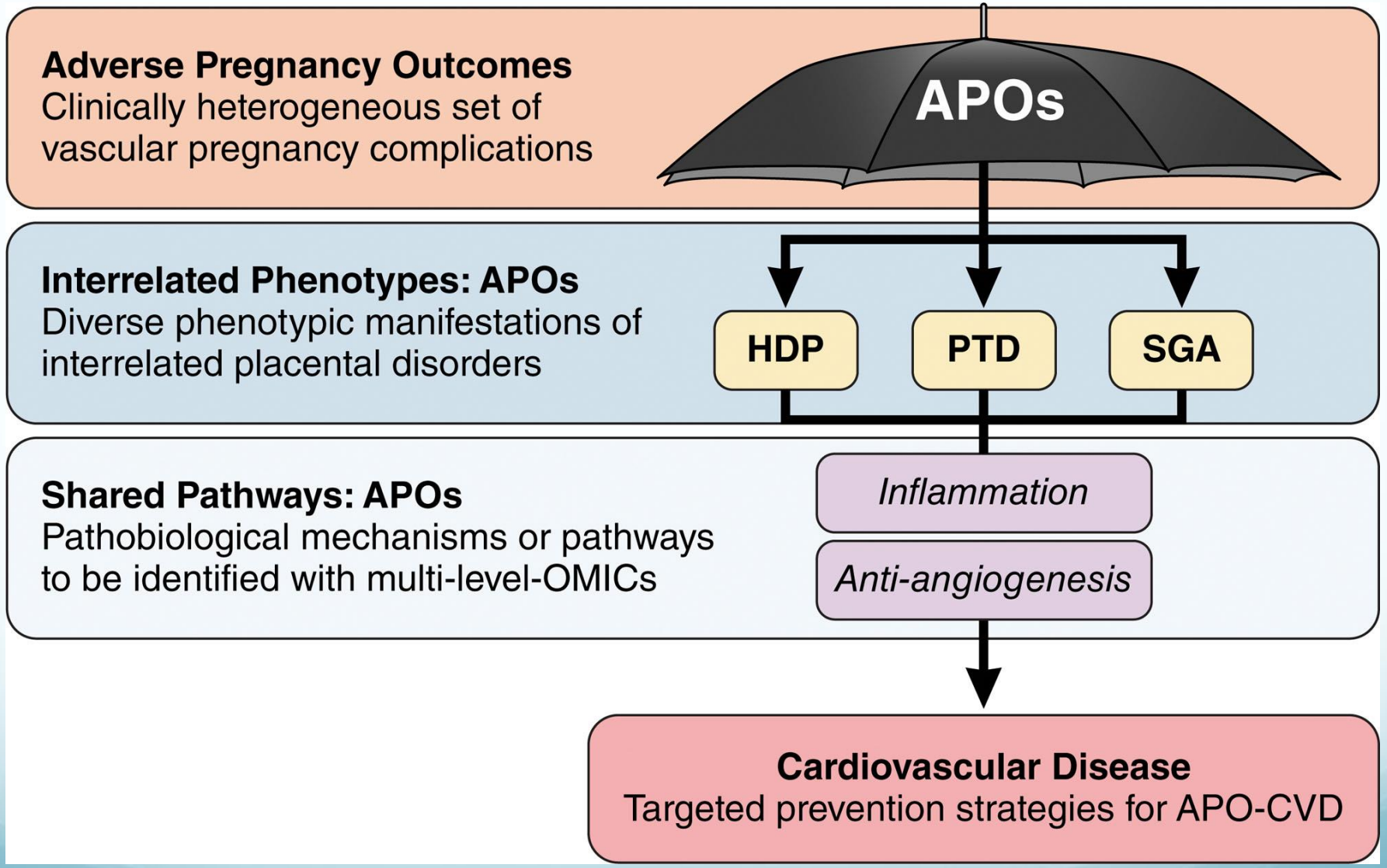
Preterm Birth

- Possible link between preterm birth and immune and inflammatory mediators of CVD
- AJOG 2014 Systematic Review preterm birth and heart disease risk
- 10 studies, consistent association between preterm birth and heart disease
  - 2x risk
  - Even after accounting for preeclampsia

Is it all obesity?

- 16,515 female participants (age 44.5-73.6 years) of the population-based Malmo¨ Diet and Cancer Study
- 1991 through 1996
- Grand multiparous women (5 children) had an increased risk of CV disease (hazard ratio, 1.60; 95% confidence interval, 1.20e2.14)
- Controlling for BMI and weight gain over time: hazard ratio, 1.38; 95% confidence interval, 1.02-1.87)
- Lactation: Risk elevated only in women who breastfed <4 months /child

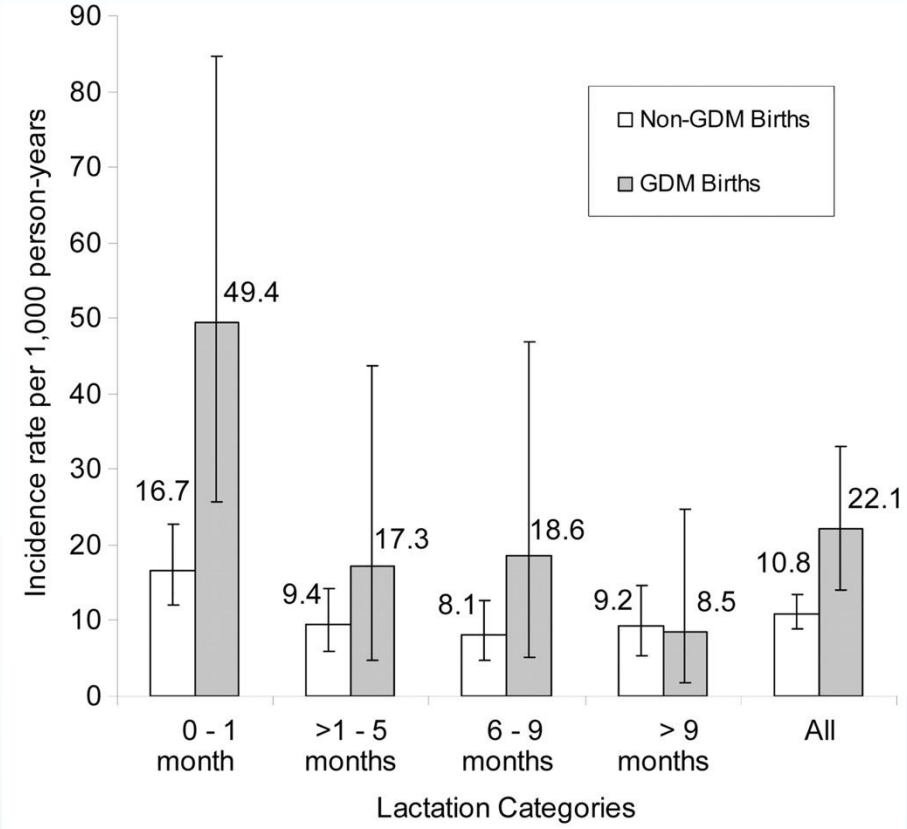
Klingberg et al. Am J Obstet Gynecol. 2017 Feb;216(2):172.e1-172.e


Adverse Pregnancy Outcomes
Clinically heterogeneous set of vascular pregnancy complications
APOs
Interrelated Phenotypes: APOs
Diverse phenotypic manifestations of interrelated placental disorders
HDP
PTD
SGA
Shared Pathways: APOs
Pathobiological mechanisms or pathways to be identified with multi-level-OMICs
Inflammation
Anti-angiogenesis
Cardiovascular Disease
Targeted prevention strategies for APO-CVD

Breastfeeding

- Lactation improves weight loss postpartum and risk of future metabolic disease
  - Lactogenesis resets pre-pregnancy physiology
- Metabolic disease associated with breastfeeding difficulties

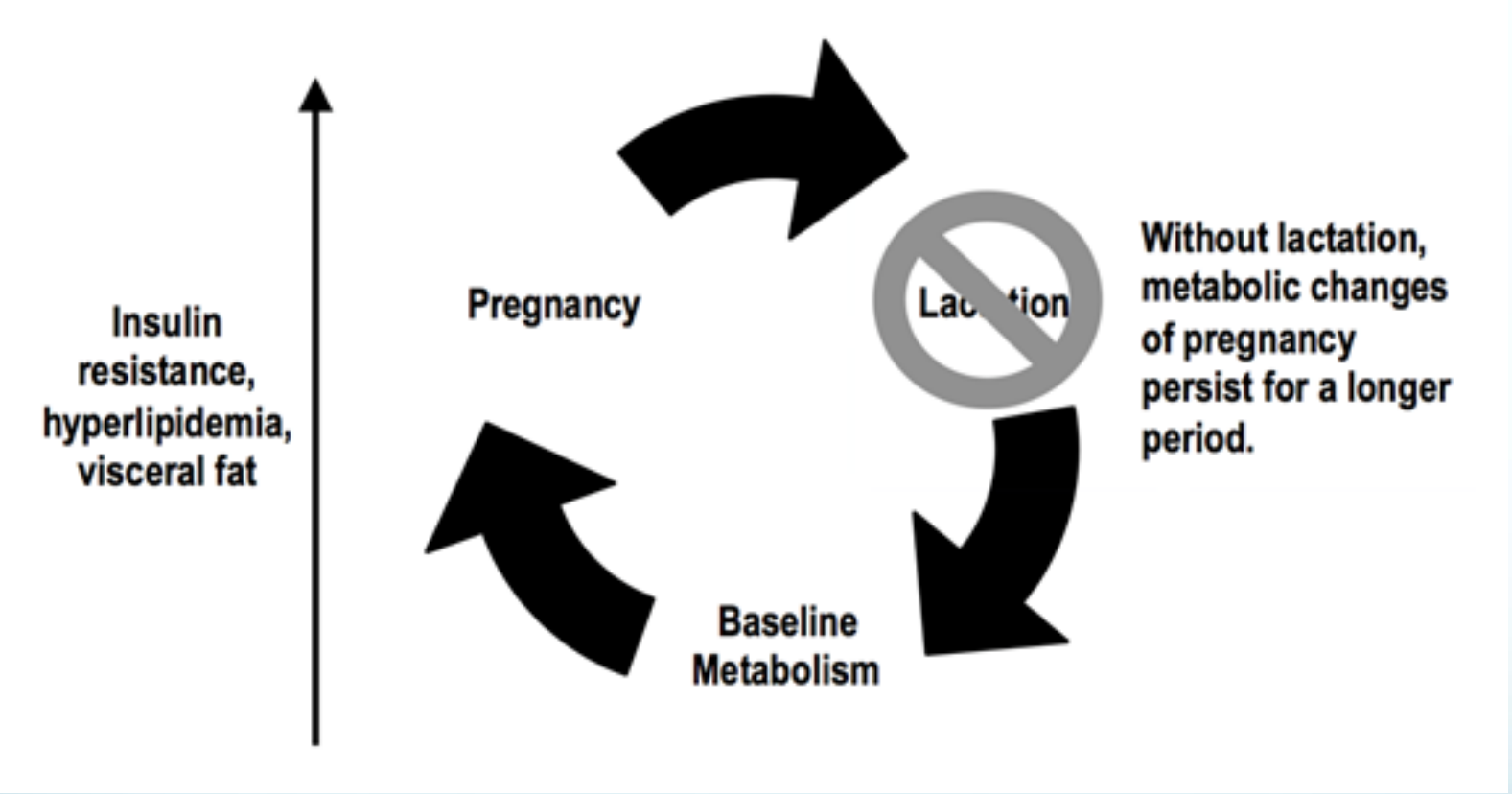
Crude incidence rates (95% CIs) of the metabolic syndrome during 20 years of follow-up for lactation categories by GDM status.



Metabolic Syndrome Case Participants by GDM Status:

Lactation Category:	0-1 month	>1-5 months	6-9 months	>9 months	All
Non-GDM, n	40	22	18	17	97
Person-years:	2,527	2,340	2,230	1,856	8,953
GDM, n	12	4	4	3	23
Person-years:	243	231	215	351	1,040

Gunderson E P et al. Diabetes 2010;59:495-504



Stuebe AM. Semin Perinatol. 2015 Jun;39(4):290-5

Breastfeeding

- Encourage mothers with adverse pregnancy outcomes to breastfeed
  - Decrease future CVD risk
  - May have increased difficulties over mothers without metabolic disease
- Breastfeeding difficulties may be risk factor for future metabolic disease

Back to J.K.

- Risk factors:
- Obesity
- GDM
- Preeclampsia
- Family history of stroke

- Opted to undergo a gastric bypass

Currently

- JK has a normal BMI
- Diabetes has resolved
- Normotensive
- Sleep Apnea resolved
- Desires another pregnancy

Why is knowing the risk important?

Chronic Disease

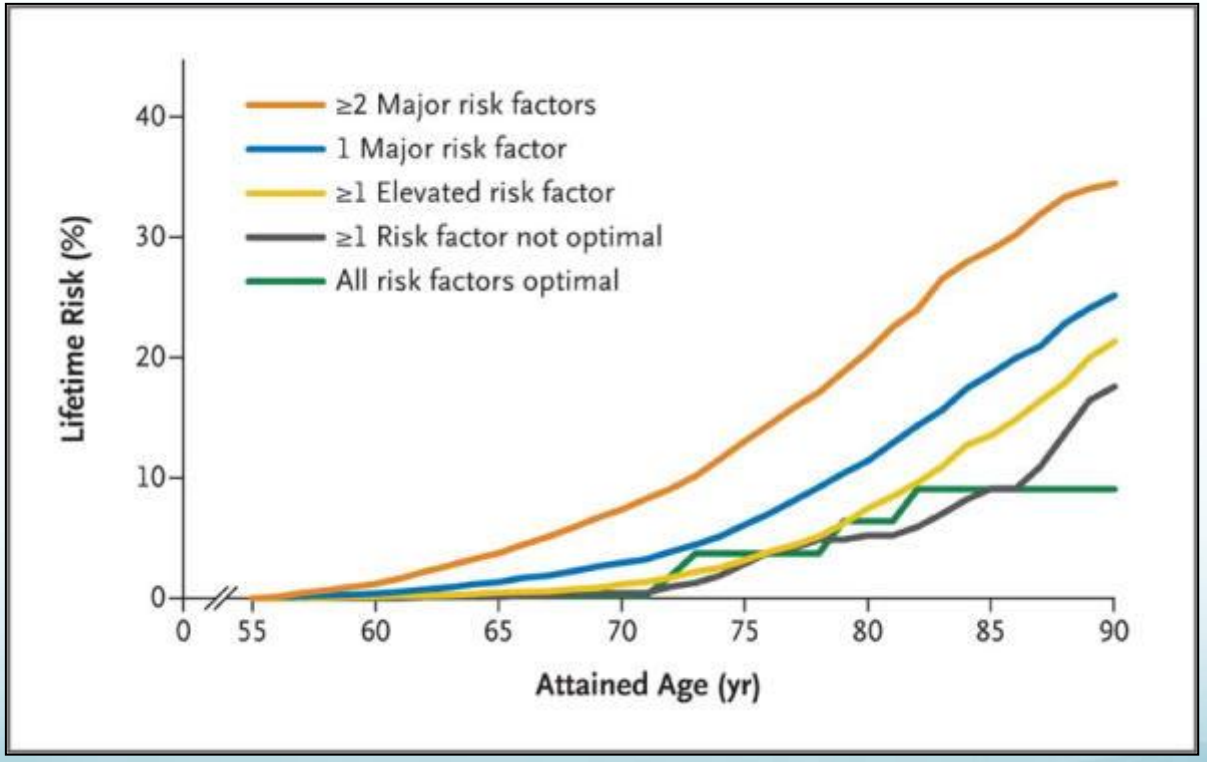
- 1 in every 2 adults suffers from a chronic disease.
- 2006 health care expenditure per person was approximately $7000
  - 75% to TREAT chronic disease
- At current rates 1/3 Americans born in 2000 will develop Diabetes in their lifetime
- Heart disease and stroke are the first and third leading cause of death in the United States

The Power of Prevention Chronic disease . . . The public health challenge of the 21st century. CDC 2009. http://www.cdc.gov/chronicdisease/pdf/2009-power-of-prevention.pdf

Heart Disease Risk Factor Calculation

Cardiovascular disease

- Even low burden of risk factors associated with significant increase in risk of cardiovascular death
- Prevention of risk factors can decrease mortality risk



[1]Berry, JD et al. Lifetime Risks of Cardiovascular Disease. NEJM 2012; 366: 321-9.

Change in Strategy

- Prevention involves
  - Health promotion
  - Early detection
    - Identifying and screening at risk populations
  - Management of existing disease

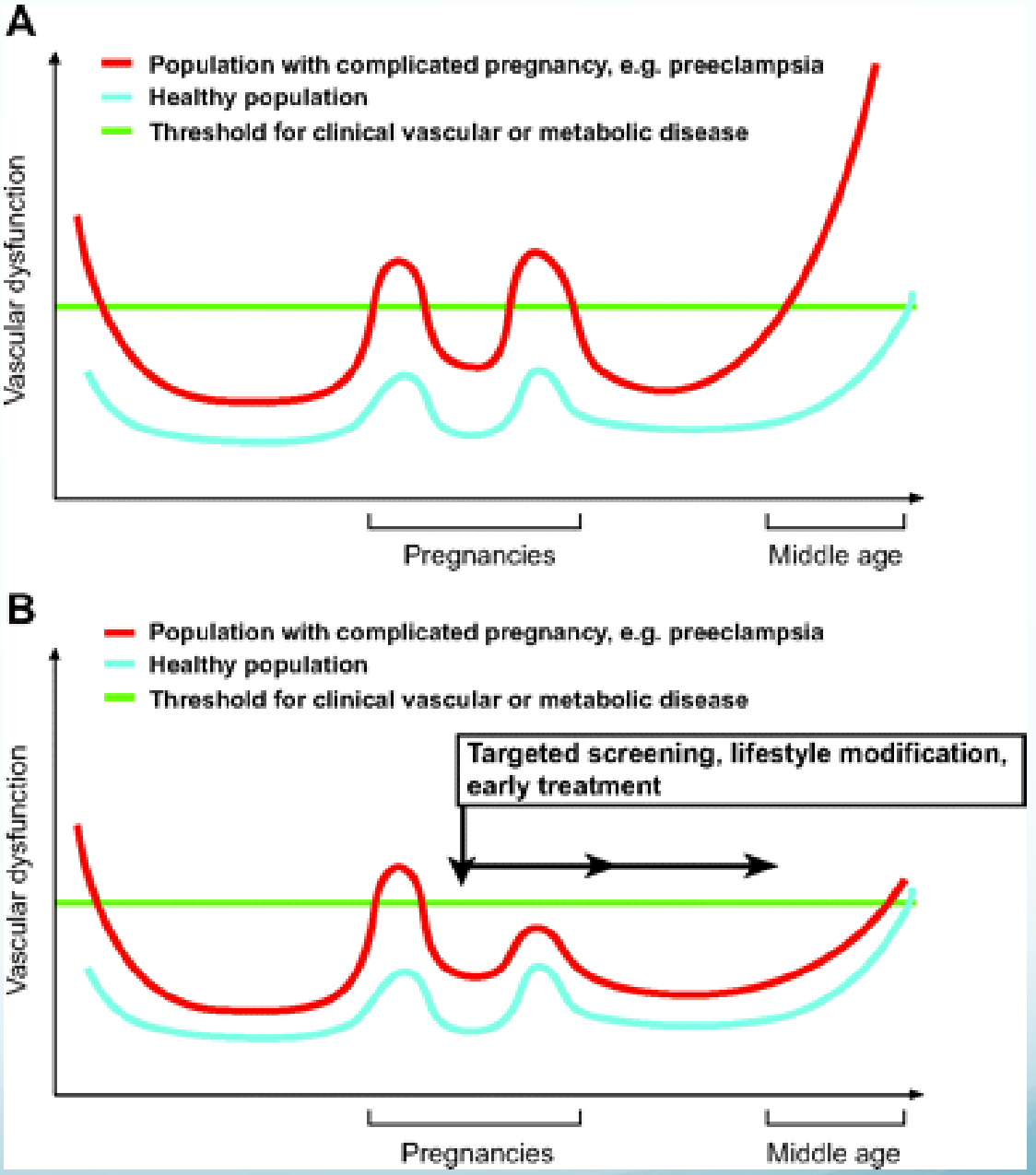
- 2/3 of Americans want a public prevention strategy
- 84% support public funding

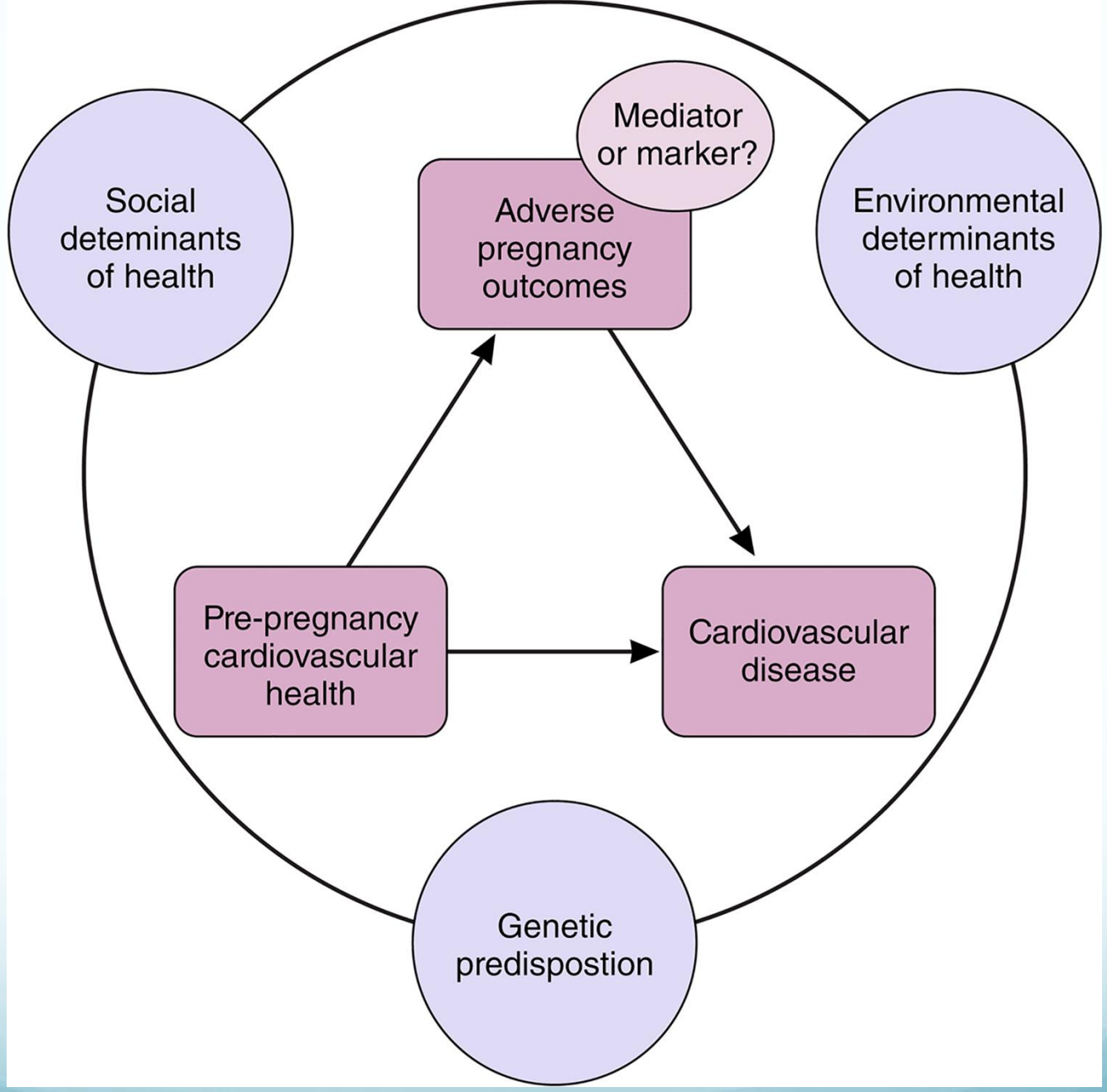
The Power of Prevention Chronic disease . . . The public health challenge of the 21st century. CDC 2009. http://www.cdc.gov/chronicdisease/pdf/2009-power-of-prevention.pdf

Women and Healthcare

- Access health care at three times
  - Infant
  - Pregnancy
  - Chronic disease
- Develop early detection methods
- Pregnancy as a window to Identify at risk populations

Prevention Goal




Social deteminants of health
Mediator or marker?
Adverse pregnancy outcomes
Environmental determinants of health
Pre-pregnancy cardiovascular health
Cardiovascular disease
Genetic predispostion

What Guidelines Do We Have?

Guidelines

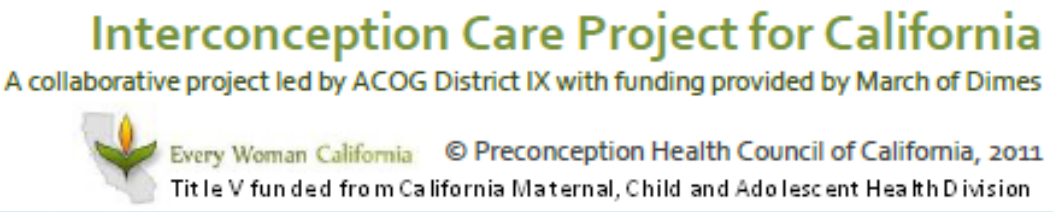
- American Heart Association
- American Diabetes Association
- American College of Obstetrics and Gynecology
- SMFM

How Do We Make It Happen?

- White Paper 2011-Saade and Smith
  - Stressed the importance of a policy change to allow for healthcare coverage at follow up visits
  - “...ensuring that physicians, patients and payers all understand that pregnancy can be a window to future health, and why this information is important will be essential. Collaboration between the professional societies, government and third party payers would shed more light on this issue and would go a long way to ensure better, more seamless care for women.”

Implementation

- Everywomancaliforinia.org
  - Interconception care project
  - Resources and recommendations to maximize postpartum care
  - http://everywomancalifornia.org/content_display.cfm?categoriesID=120&contentID=359

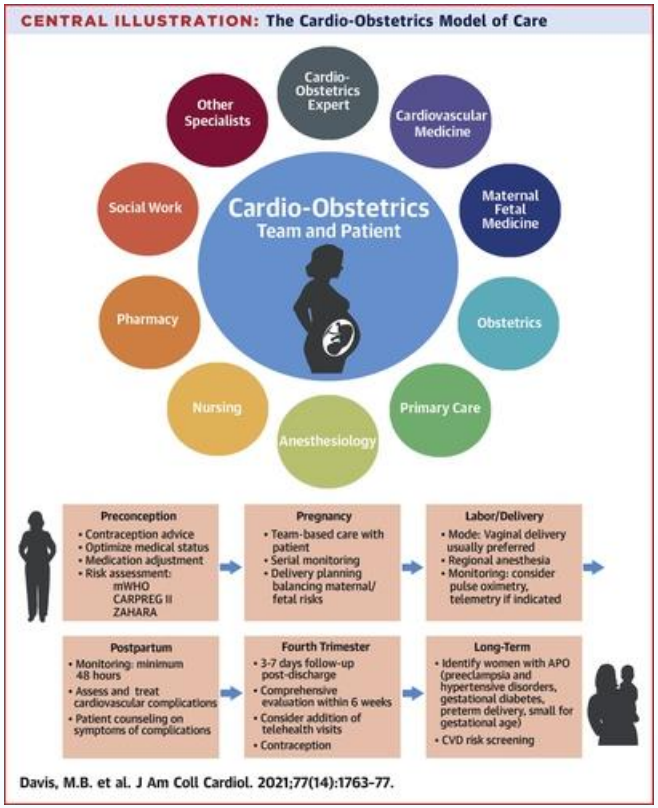


Implementation

- Graeme Smith's Maternal Child Health Clinic
  - APO invited to 6 month postpartum visit
  - Screen for CVD risk factors
  - Discuss prevention
  - Information given to primary physician
- The Mothers Program
  - Over half in first two years found to be at high lifetime CVD risk and/or have metabolic syndrome

SMFM Recommendations

- Pregnancy as a Window to Future Health Collaborative Workshop-February 4th 2014
  - Presentations from experts in the field
  - Discussion of methods for implementation
    - Timing of visits
    - Possibly link with pediatric visits
  - Need for policy changes
    - Improved insurance coverage
  - Educate and motivate patients



Melinda B. Davis et al. *JACC* 2021; 77:1763-1777.

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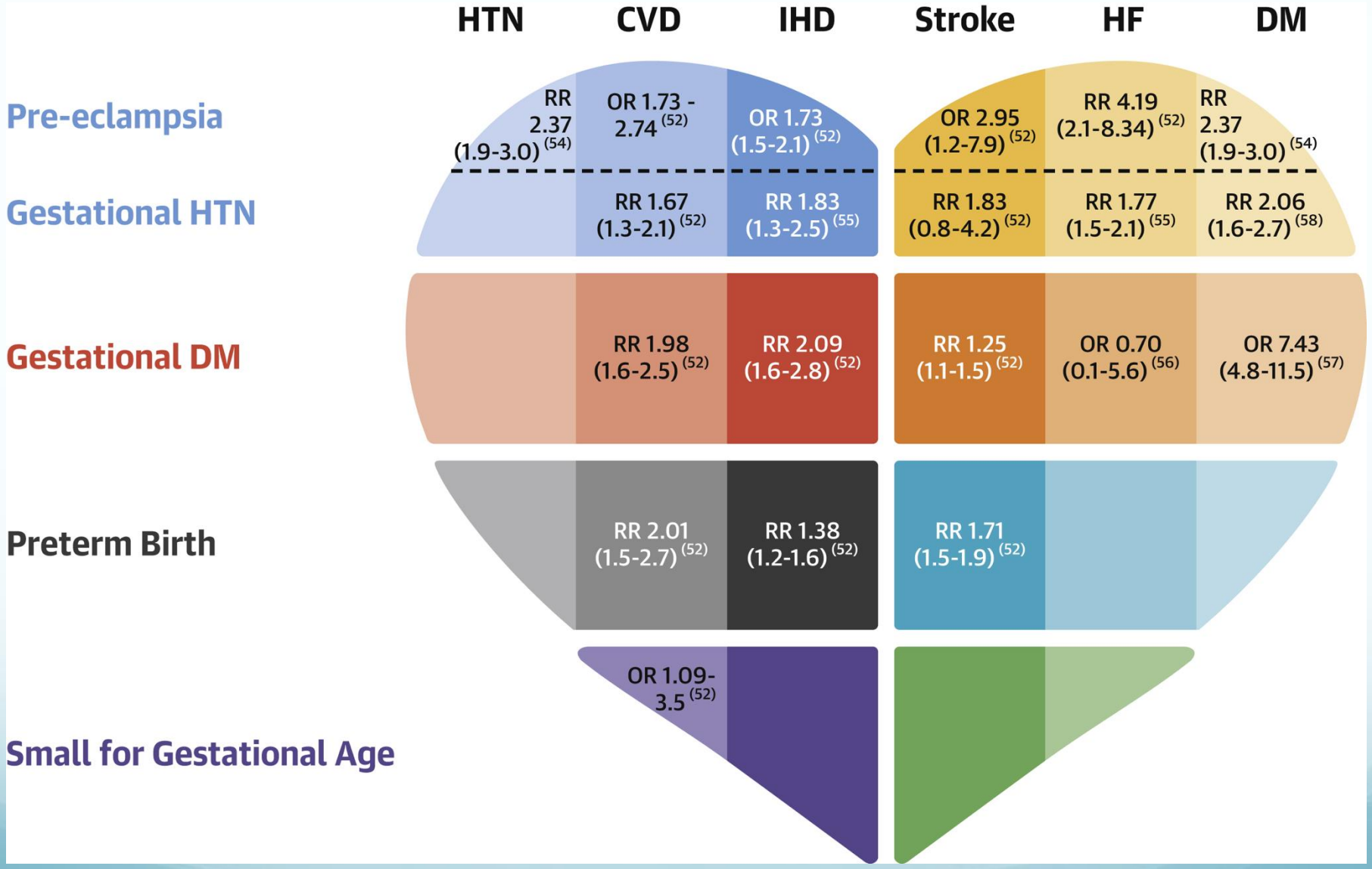
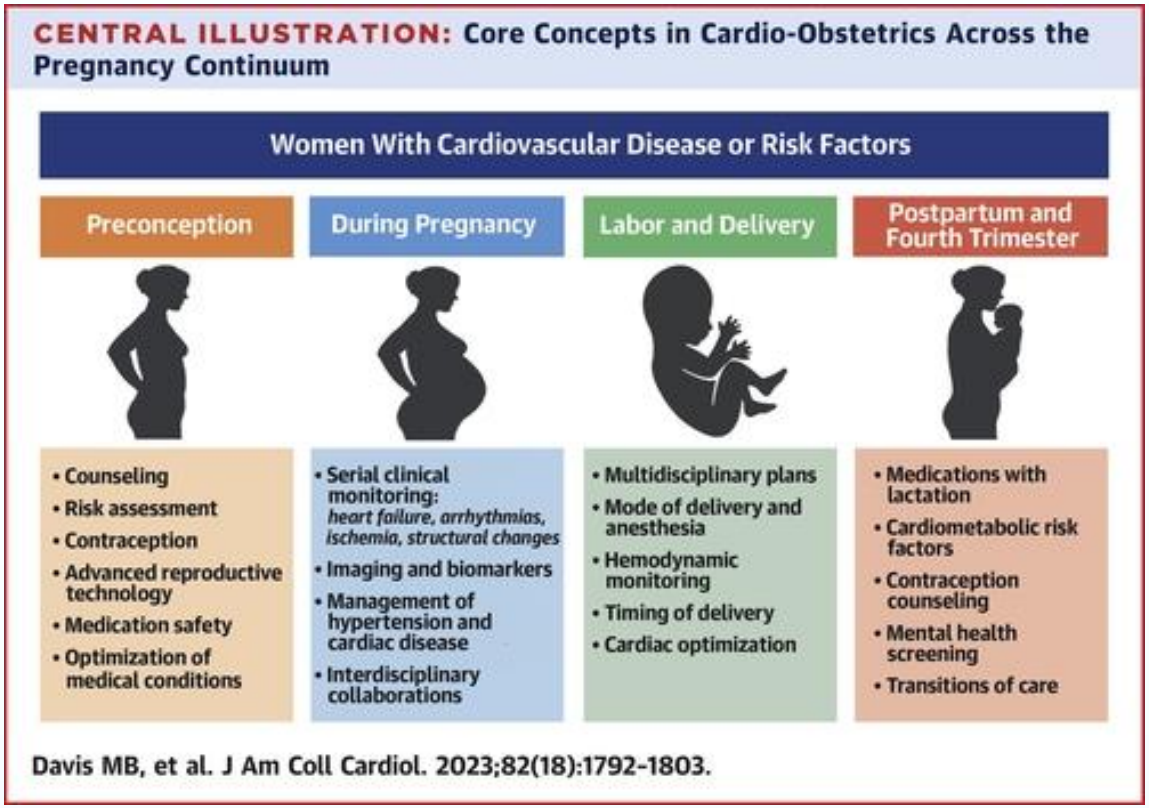

HTN
CVD
IHD
Stroke
HF
DM
Pre-eclampsia
RR 2.37 (1.9-3.0) (54)
OR 1.73 - 2.74 (52)
OR 1.73 (1.5-2.1) (52)
OR 2.95 (1.2-7.9) (52)
RR 4.19 (2.1-8.34) (52)
RR 2.37 (1.9-3.0) (54)
Gestational HTN
RR 1.67 (1.3-2.1) (52)
RR 1.83 (1.3-2.5) (55)
RR 1.83 (0.8-4.2) (52)
RR 1.77 (1.5-2.1) (55)
RR 2.06 (1.6-2.7) (58)
Gestational DM
RR 1.98 (1.6-2.5) (52)
RR 2.09 (1.6-2.8) (52)
RR 1.25 (1.1-1.5) (52)
OR 0.70 (0.1-5.6) (56)
OR 7.43 (4.8-11.5) (57)
Preterm Birth
RR 2.01 (1.5-2.7) (52)
RR 1.38 (1.2-1.6) (52)
RR 1.71 (1.5-1.9) (52)
Small for Gestational Age
OR 1.09-3.5 (52)



Melinda B. Davis et al. *JACC* 2023; 82:1792-1803.

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Thank You