Pregnancy and Reproductive Risk Enhancing Factors for Women

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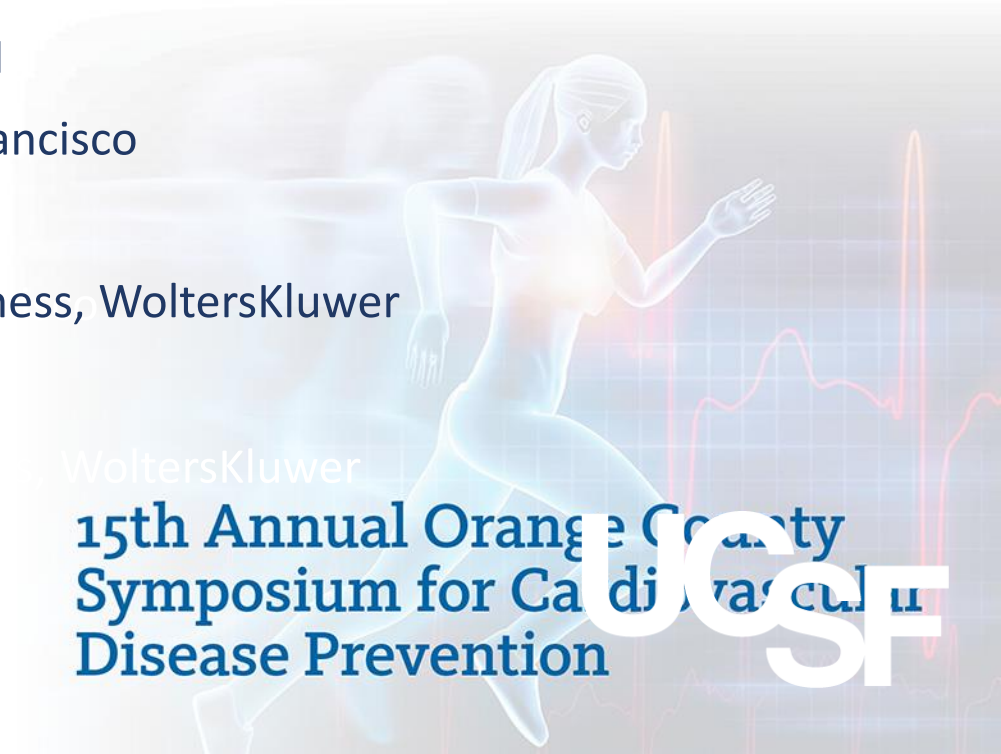
Deputy Editor, UpToDate, Clinical Effectiveness, WoltersKluwer



Goals of Talk

- Evidence in the context of a woman's lifespan
- Implications for CVD risk stratification
- Opportunities to improve CVD prevention

APOs across the life-course in women

in utero, childhood ***Teen*** ***Pre-Conception*** ***Pregnancy*** ***Post-Pregnancy*** ***Menopause*** ***Older ages/ post menopause***

APOs across the life-course in women

in utero, childhood
- Epigenetic Δ
- Congenital heart disease
- Cardiometabolic risk

Teen
- Early age at 1st birth
- ↑ APO risk

Pre-Conception
- CVD risk factors predict APOs

Pregnancy
- APOs increase CVD risk factors/ CVD

Post-Pregnancy

Menopause

Older ages/ post menopause

- Lifestyle/ CVD RF modification/ intensive f/u & monitoring

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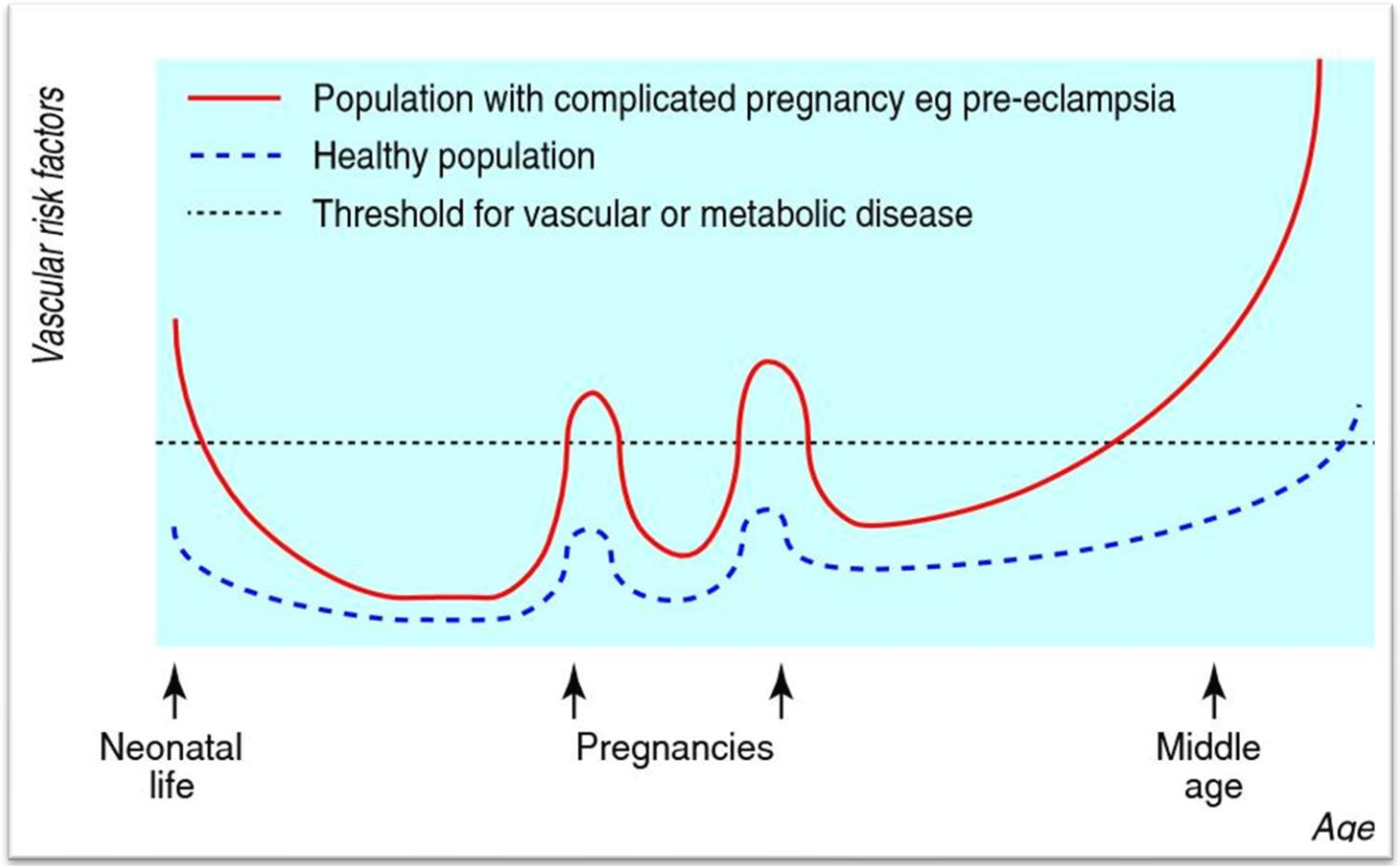
Background: Pregnancy as a Cardiometabolic "Stress Test"

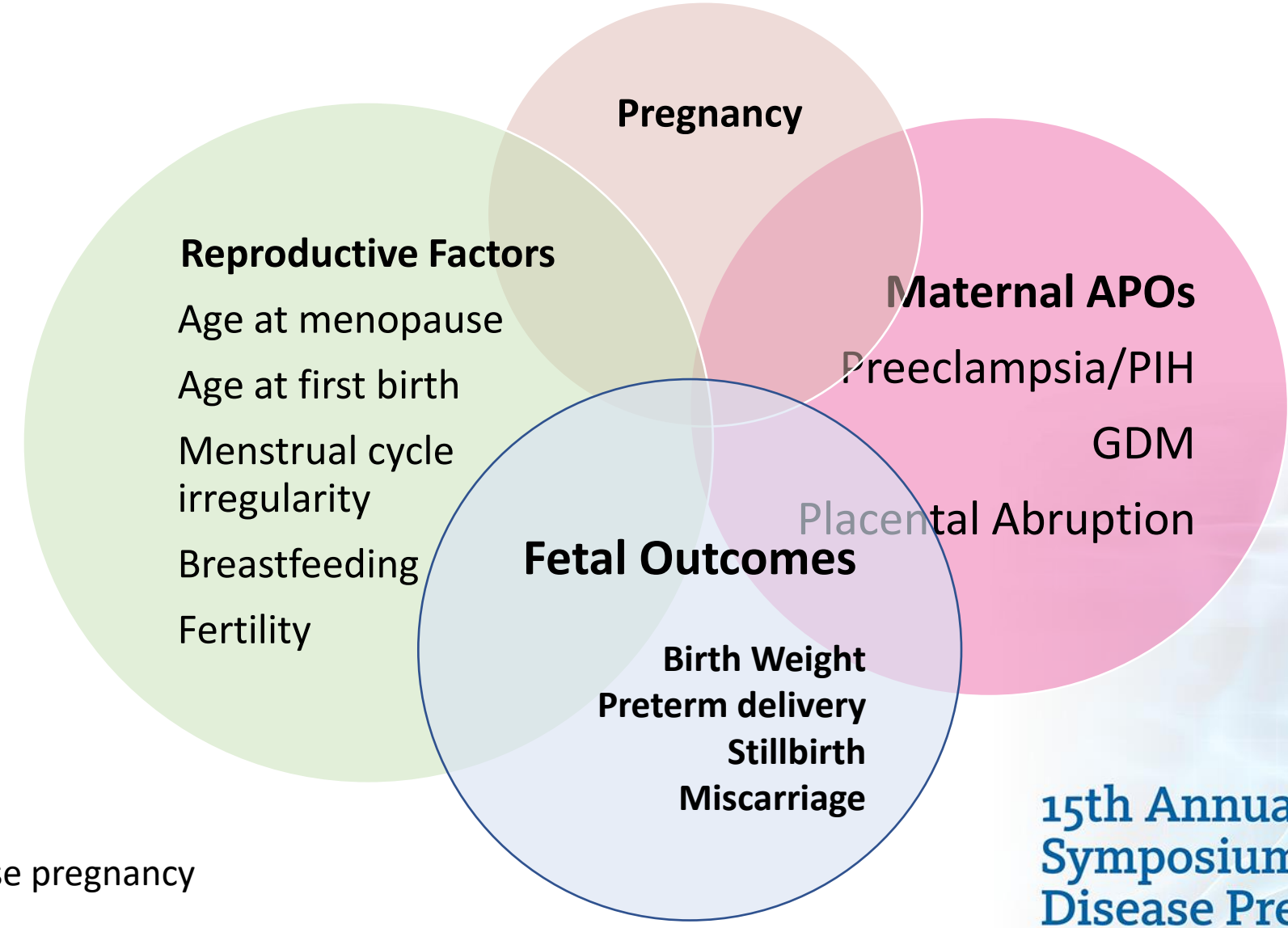


Physiologic Changes in "Normal Pregnancy"

- Vascular function
- Inflammation
- Hemostasis
- Insulin Resistance
- Cholesterol metabolism
- Adiposity

Sattar N and Greer I , BMJ 2002

Background : Reproductive and Pregnancy Factors & CVD: Mother and Child



APO= adverse pregnancy outcome

Table 2. APOs and Associations With Mortality and CVD Outcomes (Table view)

Pregnancy outcome/reproductive risk factors	Outcome association	Strength of Evidence*
Hypertensive disorders of pregnancy (preeclampsia, gestational hypertension)	↑ Atherosclerotic CVD (including coronary heart disease, peripheral vascular disease, and ischemic stroke)	A
	↑ Hemorrhagic stroke	B
	↑ Heart failure	B
GD	↑ Atherosclerotic CVD	A
Preterm delivery	↑ Atherosclerotic CVD	A
SGA	↑ Atherosclerotic CVD	A
Large for gestational age	↑ Atherosclerotic CVD	B
Placental abruption	↑ Atherosclerotic CVD	A
Miscarriages/stillbirths	↑ Atherosclerotic CVD	A

APO indicates adverse pregnancy outcome; CVD, cardiovascular disease; GD, gestational diabetes; and SGA, small for gestational age.
See Supplemental Table 1 for specific studies and references.
* Strength of Evidence A indicates multiple consistent cohort studies, meta-analyses of such studies, or both. Strength of Evidence B indicates fewer available studies or inconsistencies in the evidence.

American Heart Association Pregnancy and CVD statement 2021

Infancy: APOs and effects on fetal development, infancy

- Epigenetic changes
- Offspring cardiometabolic changes
- Congenital heart disease

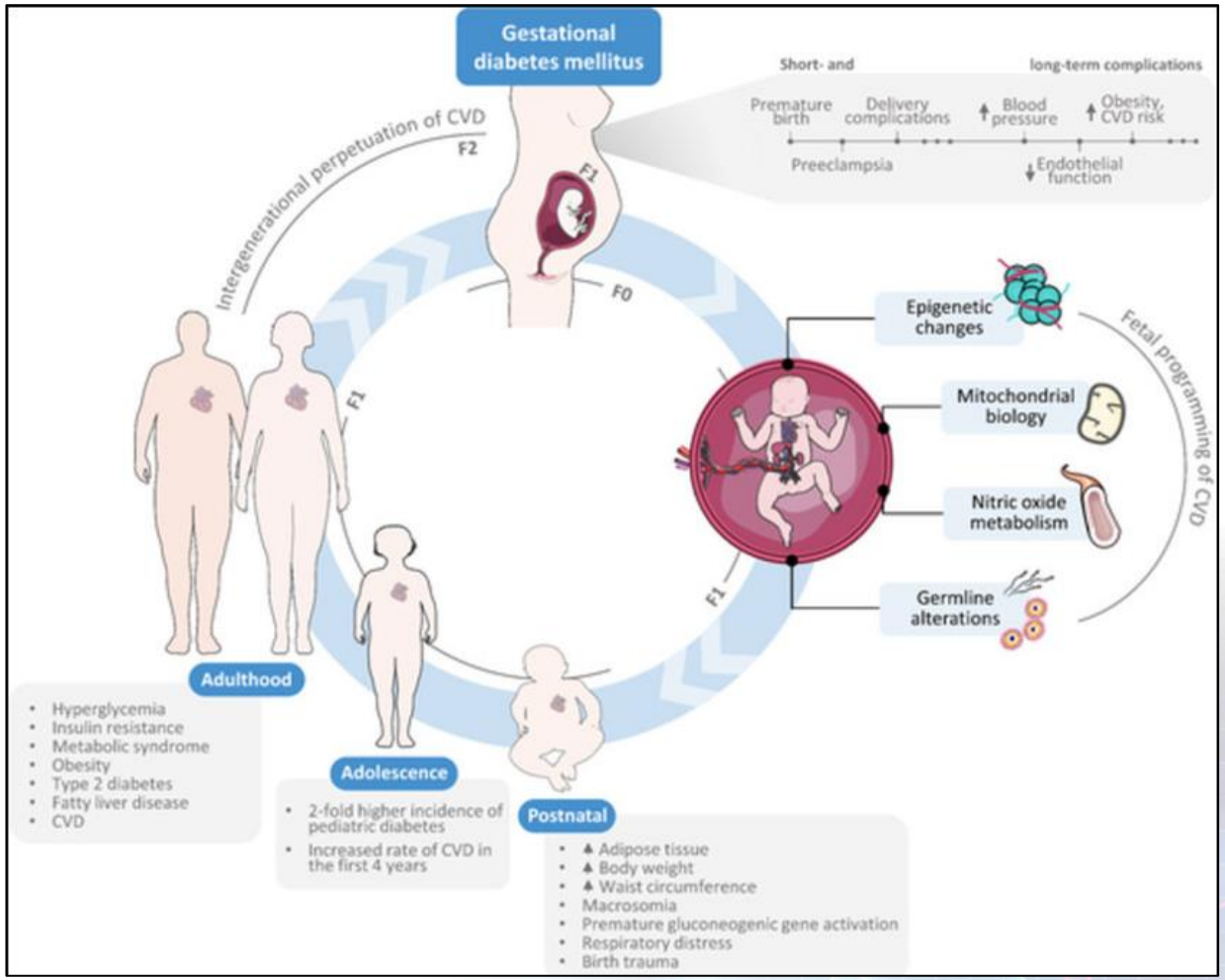
Intergenerational transmission of gestational diabetes (GDM) to offspring health

In-utero effects
- Epigenetic changes
- Mitochondrial biology
- Germline alterations
- 5X risk of congenital heart disease

Postnatal changes
- Macrosomia
- Adipose tissue
- Birthweight

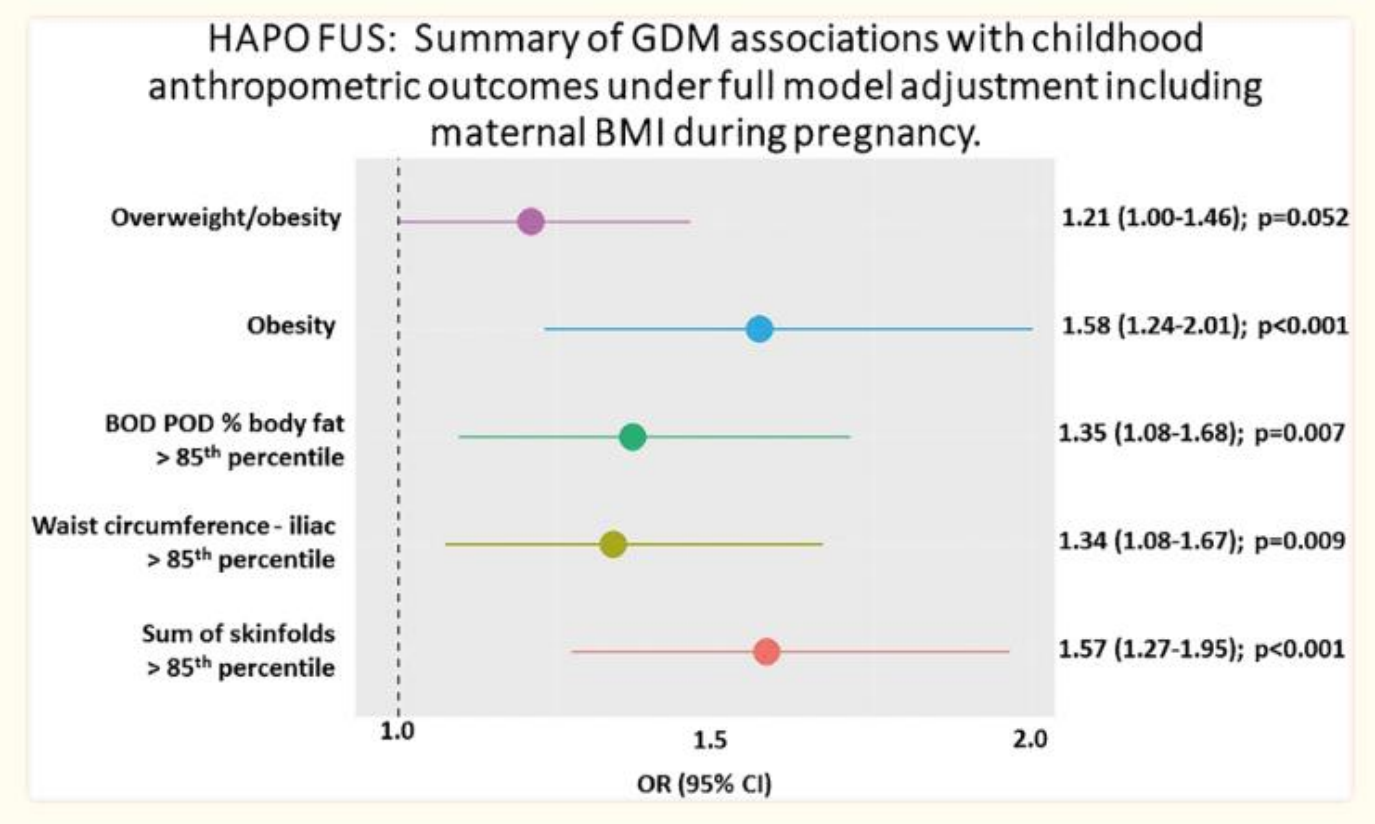
Childhood
- 2 fold increase in Type II DM

Increased risk of GDM in next gen



Tocantins et al, WIRE 2022

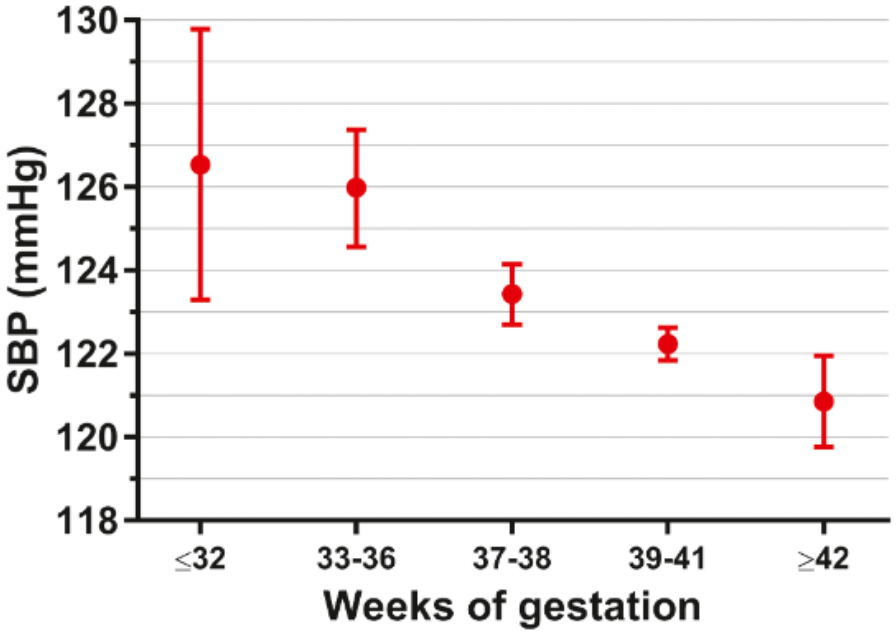
GDM and increased offspring cardiometabolic risk at age 11: HAPO follow up study

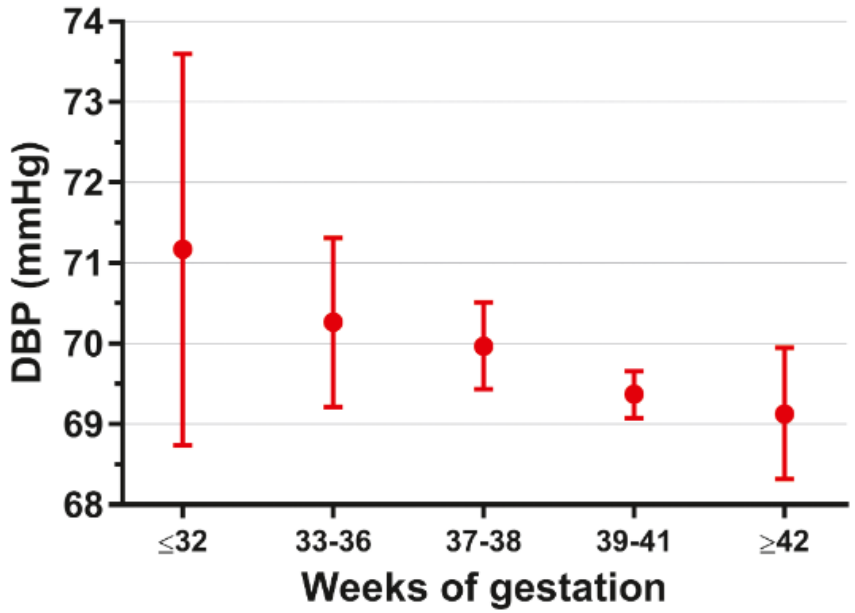


HAPO=hyperglycemia and adverse pregnancy outcomes

Bianco et al, 2019 Current Diabetes Reports

Shorter gestational age, preterm birth and increased blood pressure in 5300 Swedish women (mean age 19 y)





Skudder-Hill et al, JAHA 2019

Adolescent and teenage CVD risk factors: early age at first birth

Women's Health Initiative

- AFB <20 yrs and incident coronary heart disease 1.42 (1.29-1.46) (referent = age at first birth > 25 yrs)

International Mobility in Aging Study (Canada, Albania, Colombia, and Brazil)

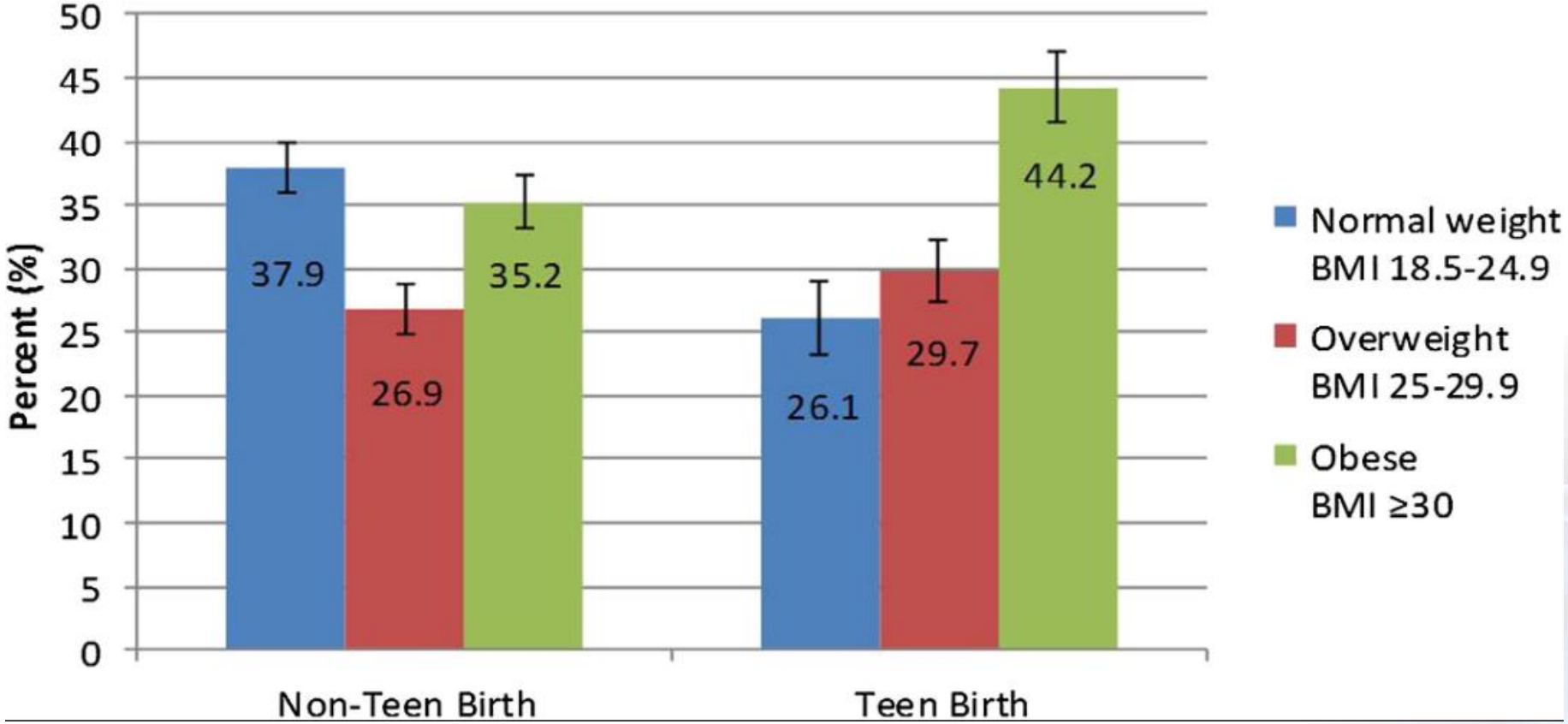
- Highest mean Framingham Risk Score (FRS) for younger AFB (p< 0.001)

• AFB –	< 20	20-24	25-29	30-34	> 35
• FRS –	23.2	20.8	16.3	17.7	14.3

Age at first birth -AFB
Framingham risk score - FRS

Parikh NI et al Circulation, 2016, Rosendaal NTA et al JAHA 2017,

Adiposity categories according to teen birth status at age 20-59 yrs, NHANES



Chang et al, AJOG 2013

Mechanisms of increased adiposity in teenage mothers

- Greater gestational weight gain and greater postpartum weight retention than adult mothers.
- After 28 weeks' gestation, growing adolescents continue to accrue fat rather than mobilize fat stores like nongrowing adolescents and adults.
- Despite sufficient weight gain, young still-growing women appeared not to mobilize fat reserves late in pregnancy to enhance fetal growth, apparently reserving them instead for their own continued development → small babies

Chang et al, AJOG 2013, Scholl et al, AJCN 1994

Adolescent, teen pregnancies and CVD-related APOs

- Increased risks of:
  - preterm delivery
  - low birth weight
  - ecclampsia

Childbearing years

1. Prepregnancy CVD risk factors are associated with APO's Common soil, similar CV biologic pathways

2. Pregnancy may accelerate CVD risk factors in women

3. Postpartum period can be leveraged for CVD risk factor modification

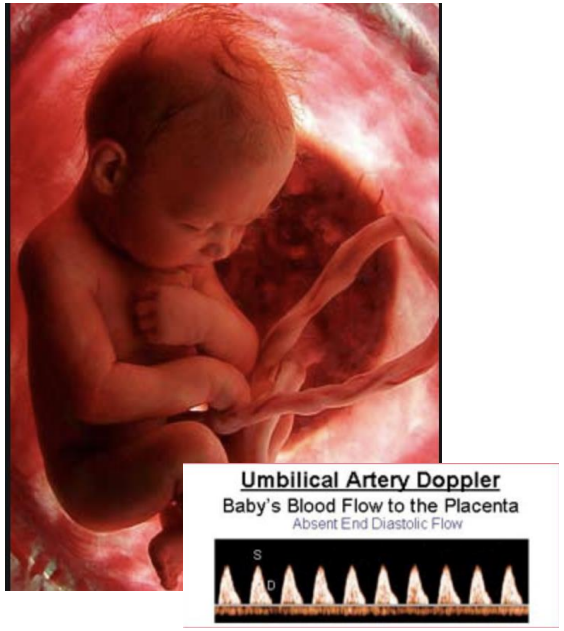
Gestational weight gain and APOs

- Among women in obese weight categories less than recommended weight gain was associated with less:
  - Preeclampsia
  - Large for gestational age
  - C-section
- Higher than average weight gain association with HDP (OR, 1.79 [95% CI, 1.61–1.99])
- Higher gestational weight gain (OR per 1-SD higher gestational weight gain, 1.14 [95% CI, 1.10–1.18]) associated with higher risks of gestational diabetes.

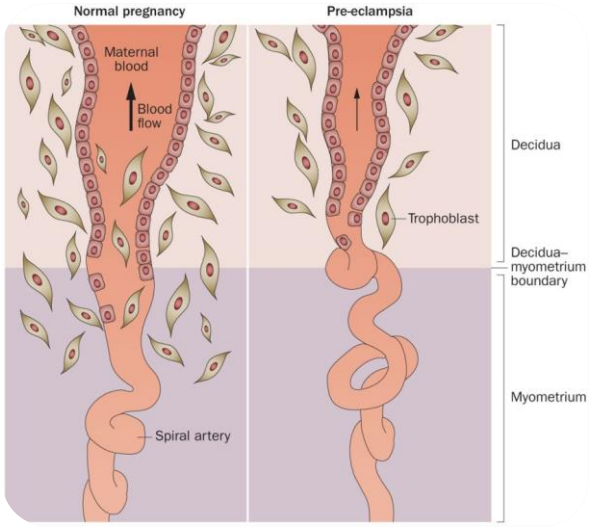
Mustafa et al AJOG 2022
Santos et al 2019 BJOG 2019

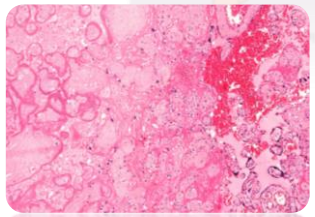
Hypertension in pregnancy as a maternal-fetal vascular disease

Fetal growth restriction

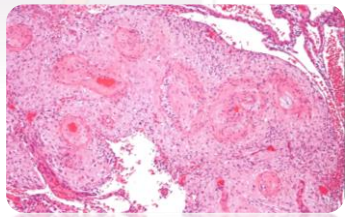


Placental
maternal-fetal interface





Placental infarct



Decidual artery
medial hypertrophy

Maternal Factors:

Hypertension, BMI, stress, diet, exercise, family history, genetics

Paternal Factors:

Preeclampsia in his mom, obesity,
Fetal paternal HLA-G variants , changed paternity

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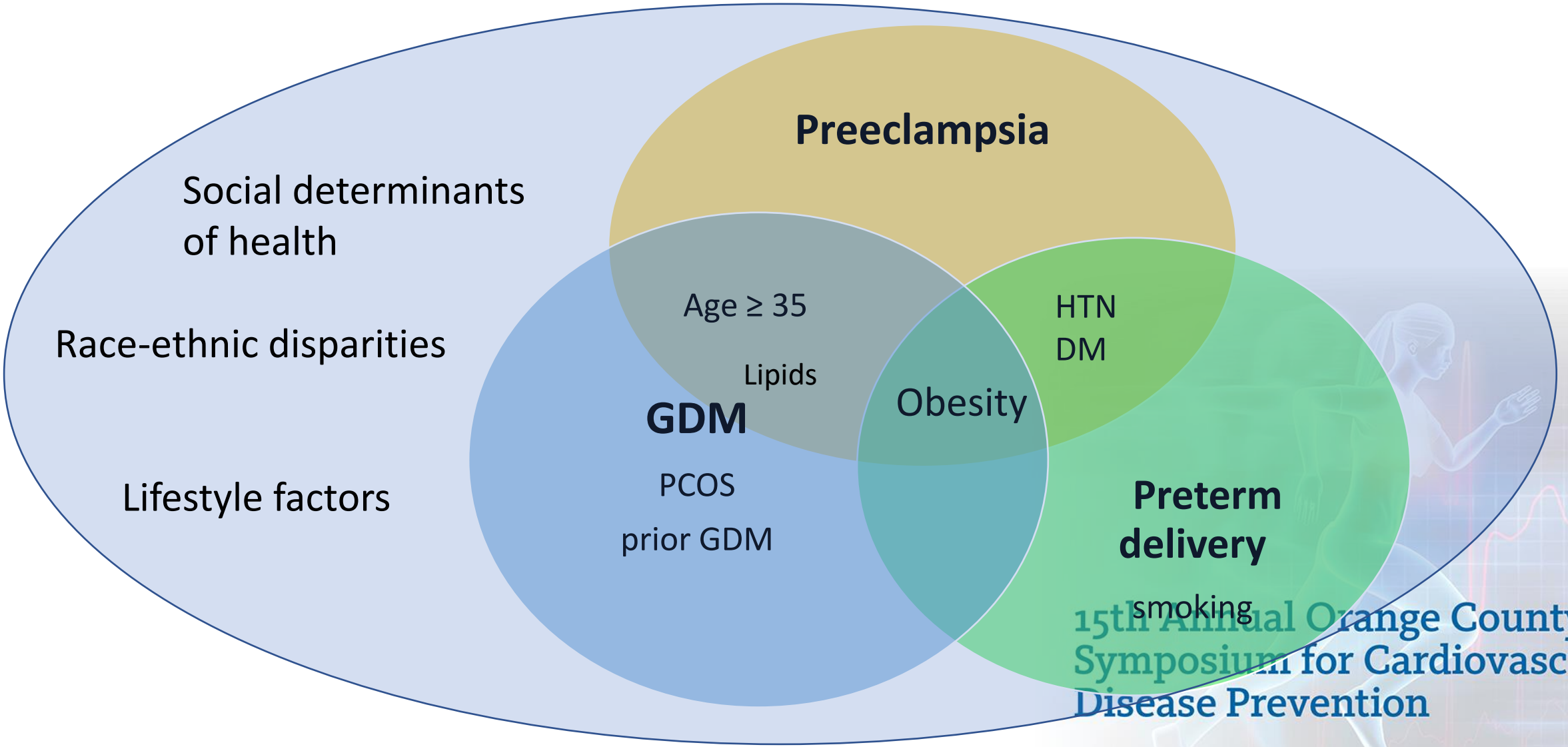
Doppler from Mt. Sinai hospital website
Galaviz-Hernandez C et al, Front Phys

Prepregnancy CVD risk factors predict incident APOs



Maternal CVD risk factors and preterm birth in CA: A case control study of 868 women

Early pregnancy CVD risk factors predict preterm birth:

- Hypertension
- Diabetes
- Higher total and LDL cholesterol

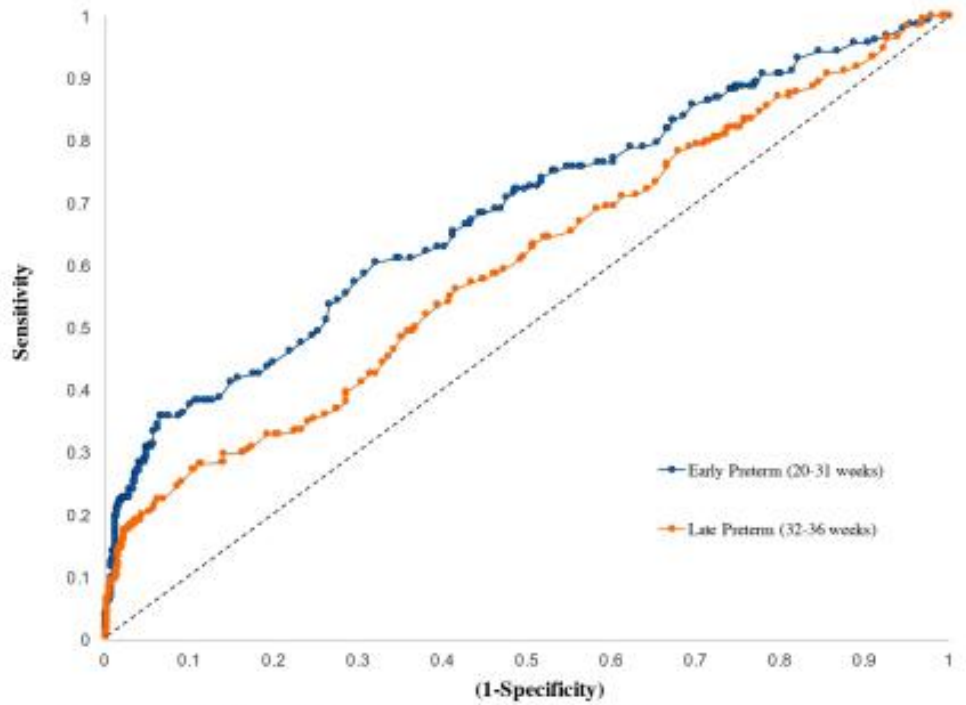


Figure 1 ROC curve for late and early preterm birth. ROC curves based on significant multivariate models of cardiovascular disease risk for late and early preterm birth, with C statistics of 0.601 and 0.686, respectively. ROC, receiver operating characteristic.

Rohlfing et al, BMJ Open 2019

Prevention of APOs and CVD in pregnancy

- Preeclampsia- low dose aspirin

- Lipid lowering: July 2021, the US FDA requested the removal of contraindication to statin use in women who are pregnant or contemplating pregnancy

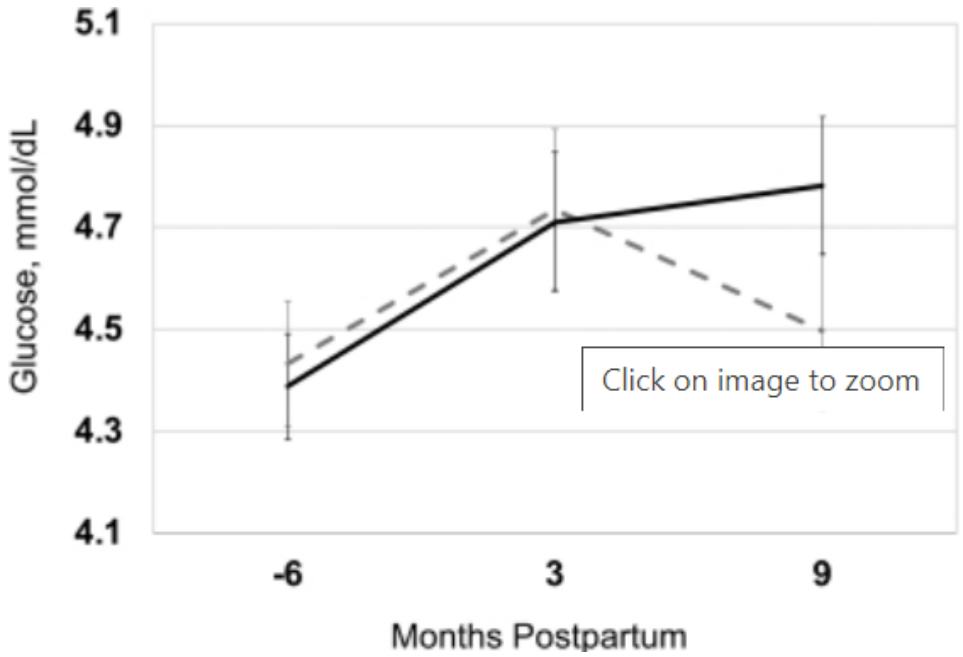
  - Meta-analysis of 9 studies→ similar rates of stillbirth, induced abortion, higher rate of spontaneous abortion.
  - In 469 statin exposed pregnant women → Increased risk of preterm birth and low birth weight.
  - Uses: Familial hypercholesterolemia, severely elevated LDL-C, prior ASCVD when benefits outweigh risks

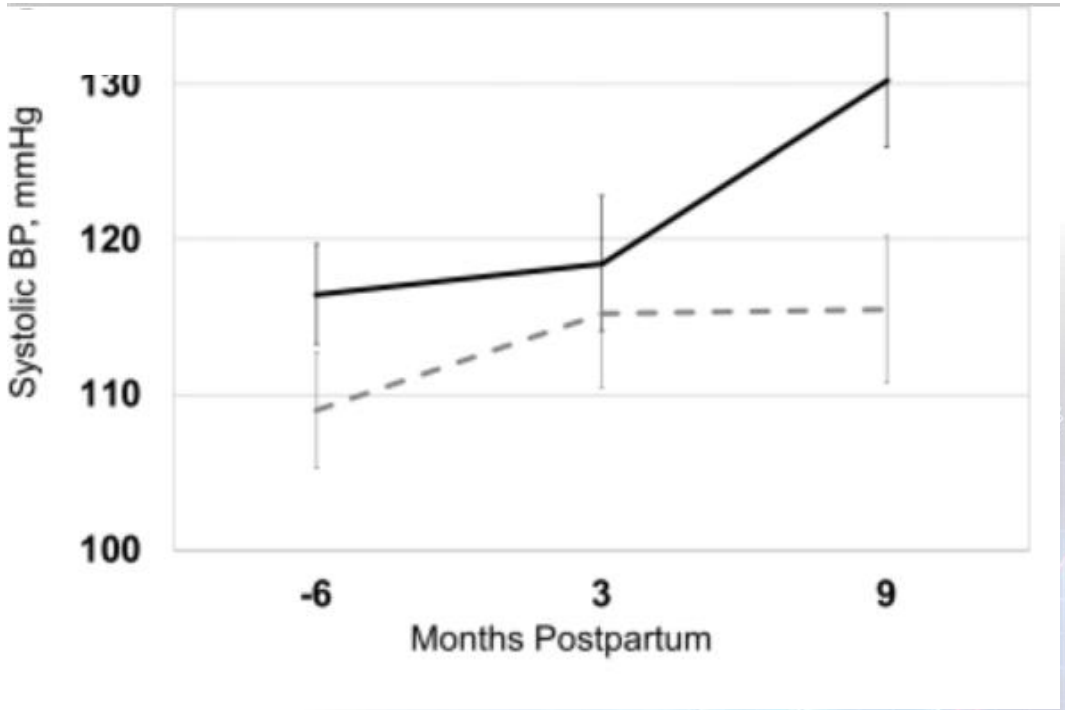
Risk factors for preeclampsia

One or more high risk factor:	Two or more moderate risk factors:
High blood pressure before pregnancy (chronic hypertension)	First pregnancy
High blood pressure or pre-eclampsia in a previous pregnancy	Age 40 or older
Diabetes	BMI >35
Chronic kidney problems	Twins or triplets
Autoimmune problems such as Systemic Lupus Erythematosus (SLE)	Your last pregnancy more than 10 years ago
	A family history of pre-eclampsia

Pre-pregnancy Risk Factors, APO's, Post Pregnancy Risk Factors→ Where does CVD risk originate? Chicken or Egg?

Increased peripartum glucose and systolic BP trajectories in APO's vs uncomplicated pregnancy: 110 low income women in the MAMAS study





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Parikh et al J Womens Health 2020

APO's and CVD Risk Factors

Table 3. Summary of Studies of APOs and CVD Risk Factors: Results From Meta-Analyses and Individual Studies

	Elevated blood pressure/hypertension	Diabetes (or hyperglycemia)	Dyslipidemia
Hypertensive disorders of pregnancy	M+*	M+†‡	M+§
GD mellitus	+[47_48]	M+‖	+[49_50,51]
Preterm delivery	+[39,48,52–54_51,55]	+[39,55_51]	+[39,55_51,53,56]
SGA	+[48,53_55]	+[55]	–[53]
Pregnancy loss	+[44,57,58]	+[58]	+[58_44]

APO indicates adverse pregnancy outcomes; CVD, cardiovascular disease; GD, gestational diabetes; M, meta-analysis; SGA, small for gestational age; +, positive association; and –, negative association.
Meta-analyses results:

* Preeclampsia and hypertension,[59] 32 studies (relative risk, 3.13 [95% CI, 2.51–3.89]).

† Preeclampsia and type 2 diabetes,[60] 10 studies (relative risk, 2.25 [95% CI, 1.73–2.90]).

‡ Gestational hypertension and type 2 diabetes,[60] 7 studies (relative risk, 1.56 [95% CI, 1.21–2.01]).

§ Hypertensive disorders of pregnancy and dyslipidemia[61]: 0.13 mmol/L (95% CI, 0.05–0.21) for triglycerides (10 studies), 0.22 mmol/L (95% CI, 0.11–0.33) for total cholesterol (11 studies), −0.11 mmol/L (95% CI, −0.18 to −0.04) for high-density lipoprotein cholesterol (10 studies), and 0.21 mmol/L (95% CI, 0.10–0.32) for low-density lipoprotein cholesterol (9 studies).

‖ GD and type 2 diabetes,[62] 20 studies (relative risk, 9.51 [95% CI, 7.14–12.67]; $P<0.001$]).

AHA Pregnancy and CVD Statement 2021

Severity of hypertensive disorder of pregnancy and later CVD risk in women

Gestational HTN

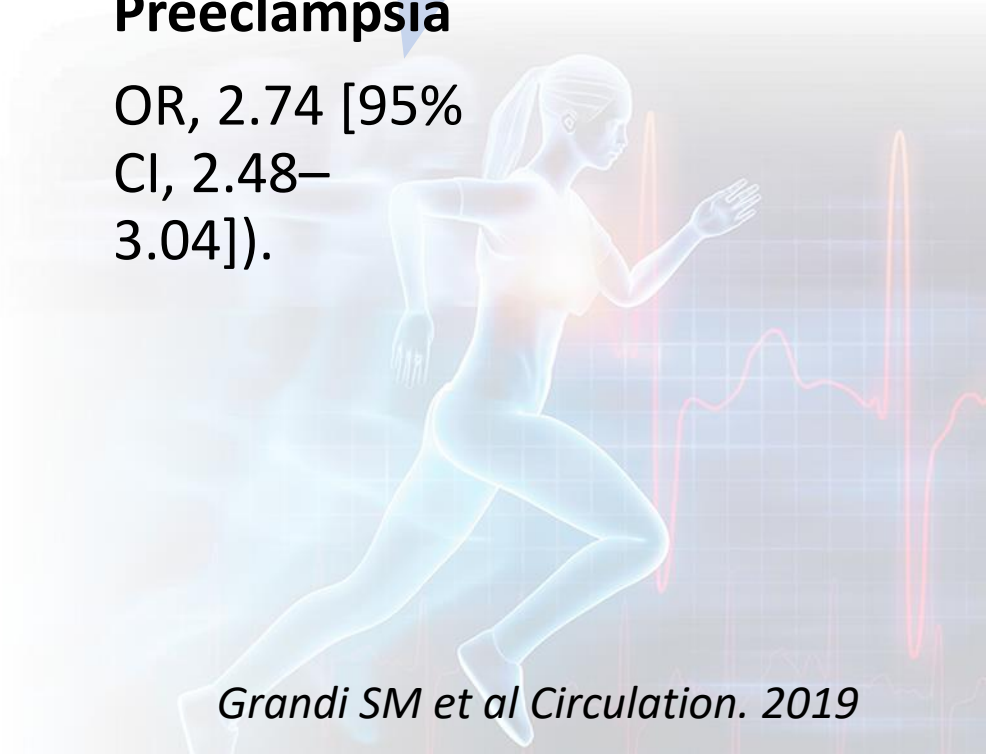
OR 1.67 [95% CI, 1.28–2.19

Moderate Preeclampsia

OR, 2.24 [95% CI, 1.74–1.93])

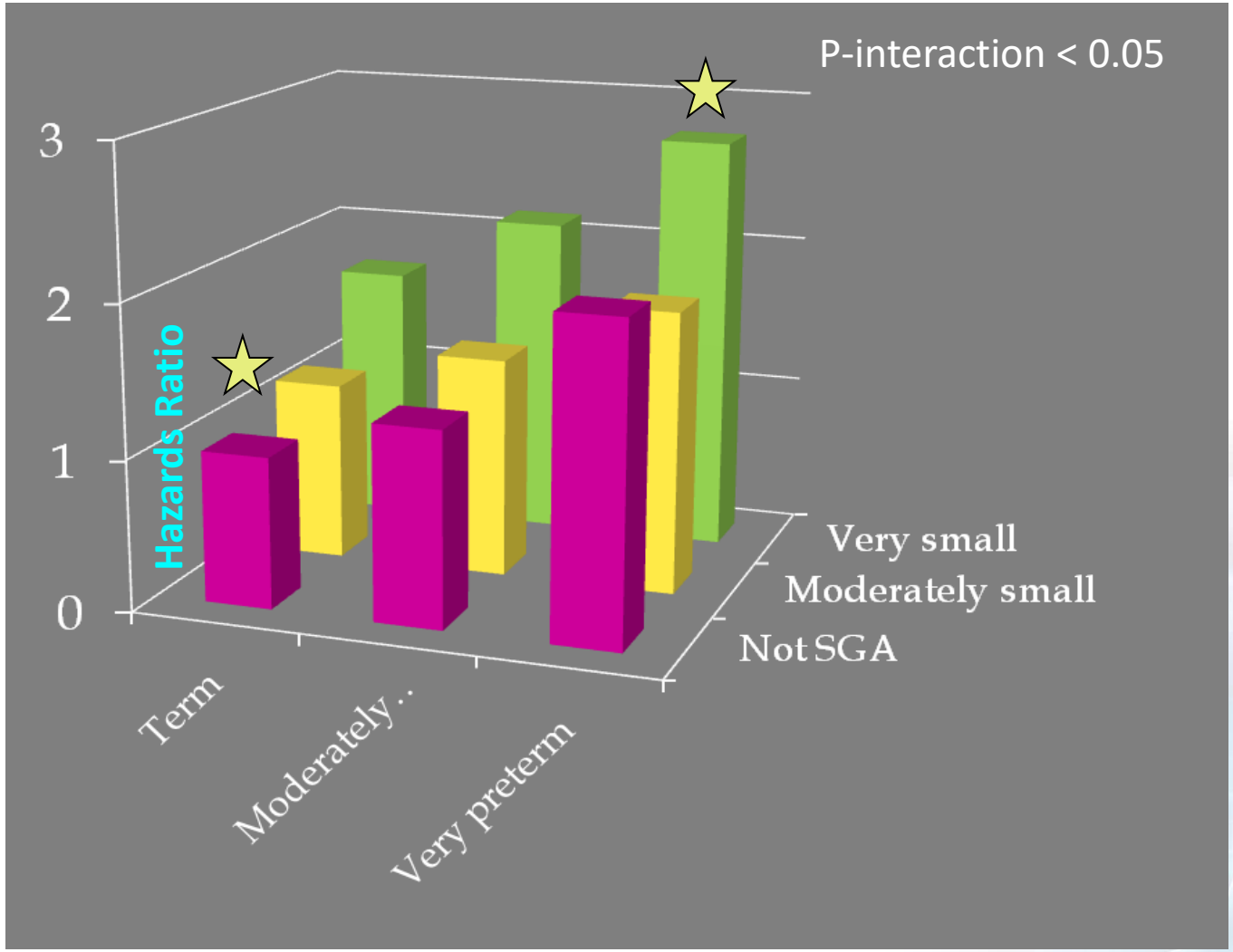
Severe Preeclampsia

OR, 2.74 [95% CI, 2.48–3.04]).



Grandi SM et al Circulation. 2019

Delivery of Preterm and Small-for-Gestational Age Baby and Maternal CVD in 1.3 million Swedish Women, (mean age at CVD diagnosis = 40.5 yrs)

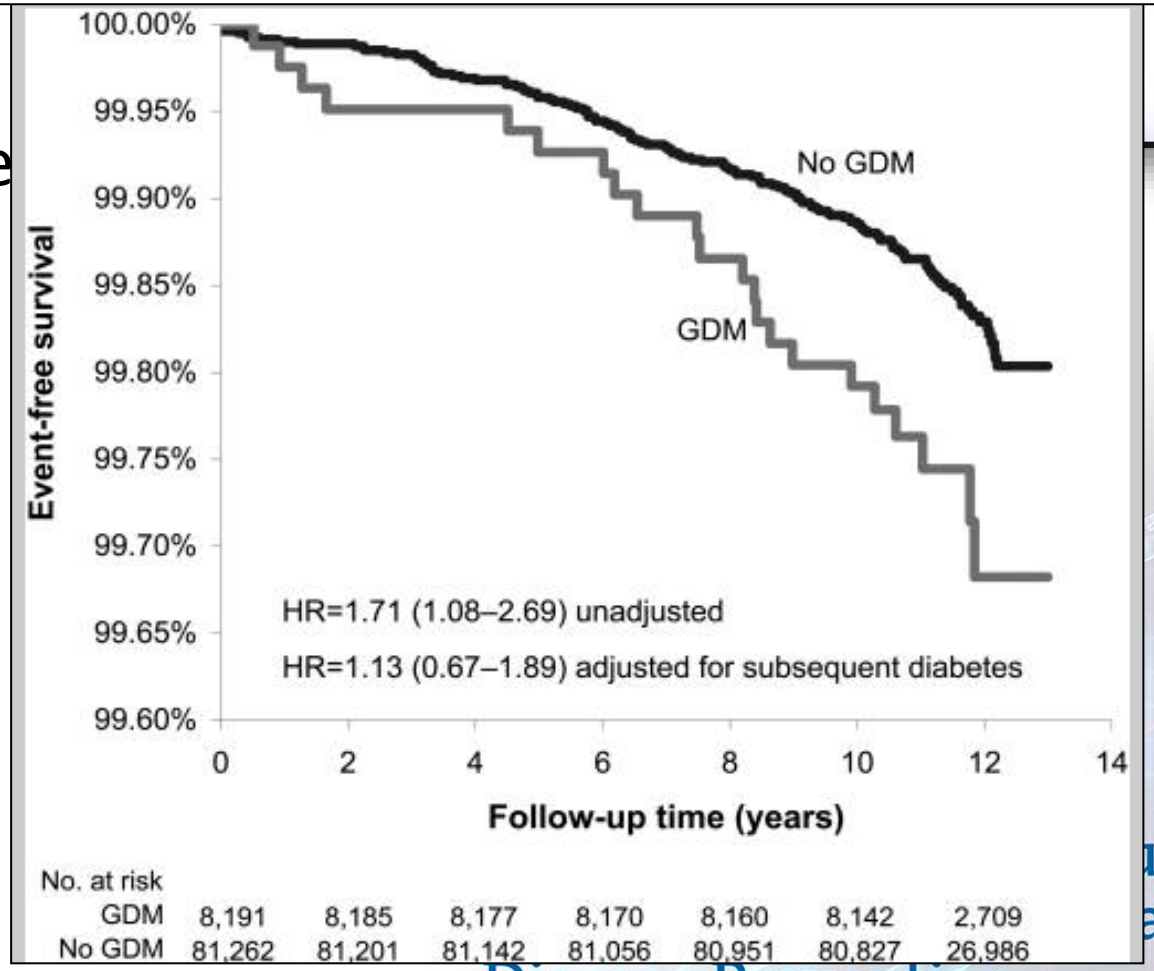


Edstedt- Bonamy et al, Circulation 2011

Gestational diabetes (G

- Occurs in 2-8% of pregnancies in
- > 220,000 cases annually
- $ 1.3 billion dollars in yearly US he

Gestational Diabetes Mellitus and CVD: Ontario Diabetes Database 351,685 Women



Shah, Diabetes Care 2008

Li, Diabetes Res Clin Pract 2018

Dall, Diabetes Care 2014

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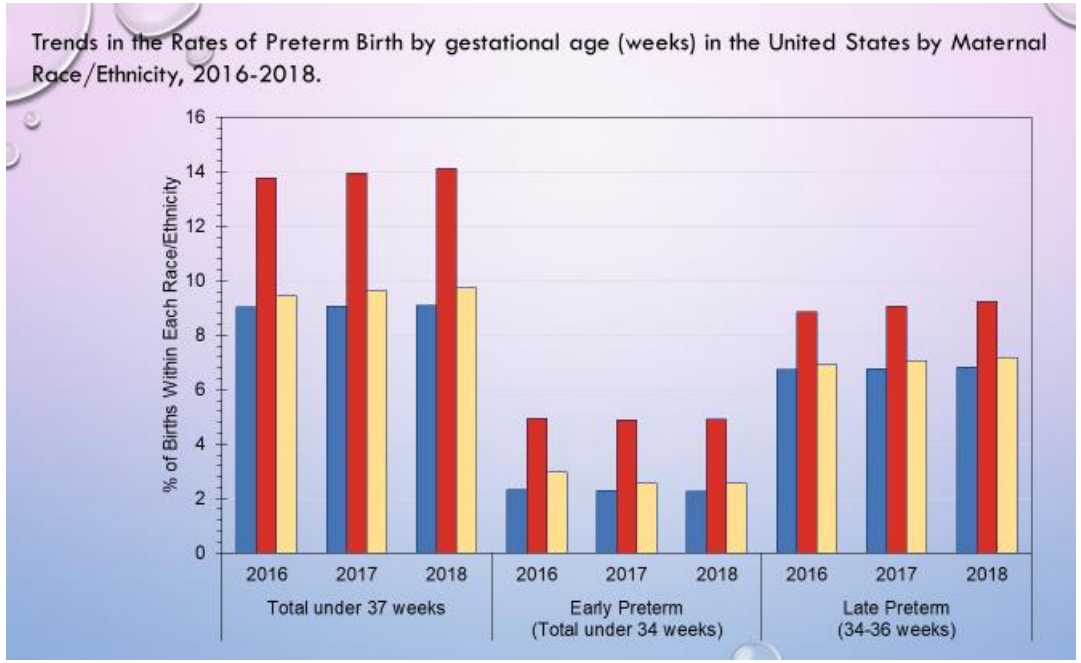
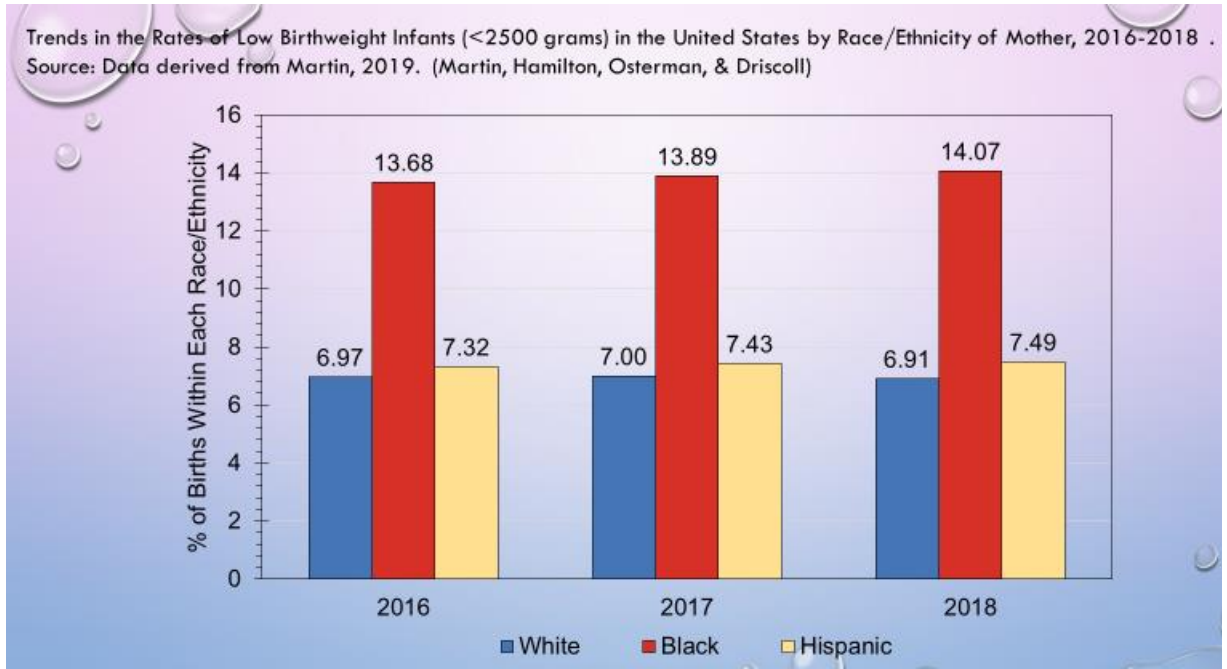
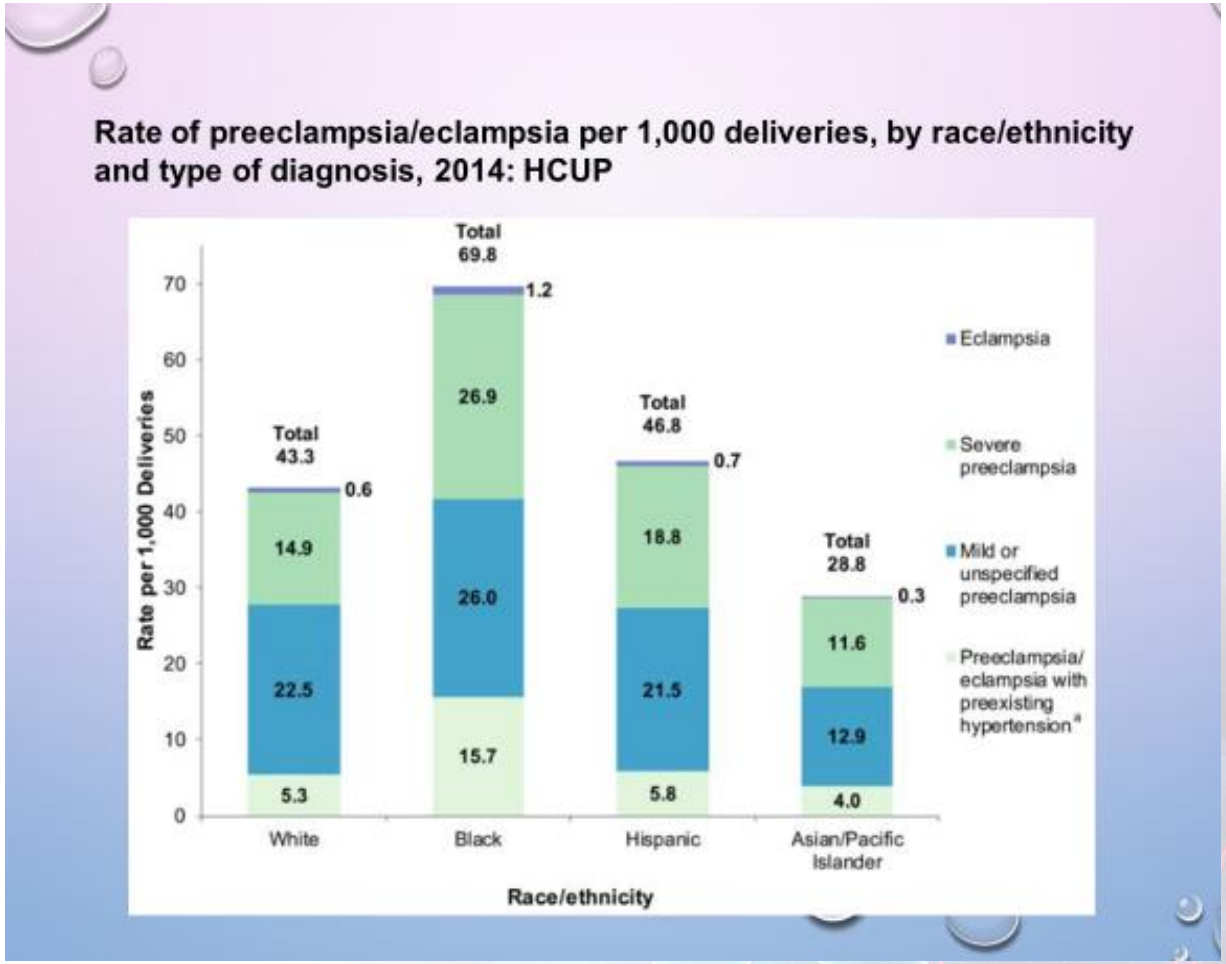
Disease Prevention

Higher burden of birthweight, preterm birth, preeclampsia in Black women







Health Disparities in Cardiovascular Diseases in Pregnancy Among Black Women: Prevalence, Preventive Care, and Peripartum Support Networks

1. Being Black during pregnancy is a risk factor for CVD related-morbidity and mortality.
    * Factors driving this risk are still unclear.

2. Concerted efforts needed to improve maternal CVD outcomes among black women in pregnancy.

3. Larger cohort studies and registry data are needed to fill in gaps in knowledge regarding:
    * genetic predisposition, institutional and demographic influences, other factors

4. Comprehensive, community-based approach for high-risk pregnant women can help lessen:
    * Contributions from lack of health insurance, low income, distrust in the medical system, and low health literacy

5. We need to continue an open dialog:
    * Among healthcare professionals, patients, and their allies
    * To increase awareness and provide a safe space and support for these women.

Njorge J and Parikh NI, Current CV Risk Reports 2020

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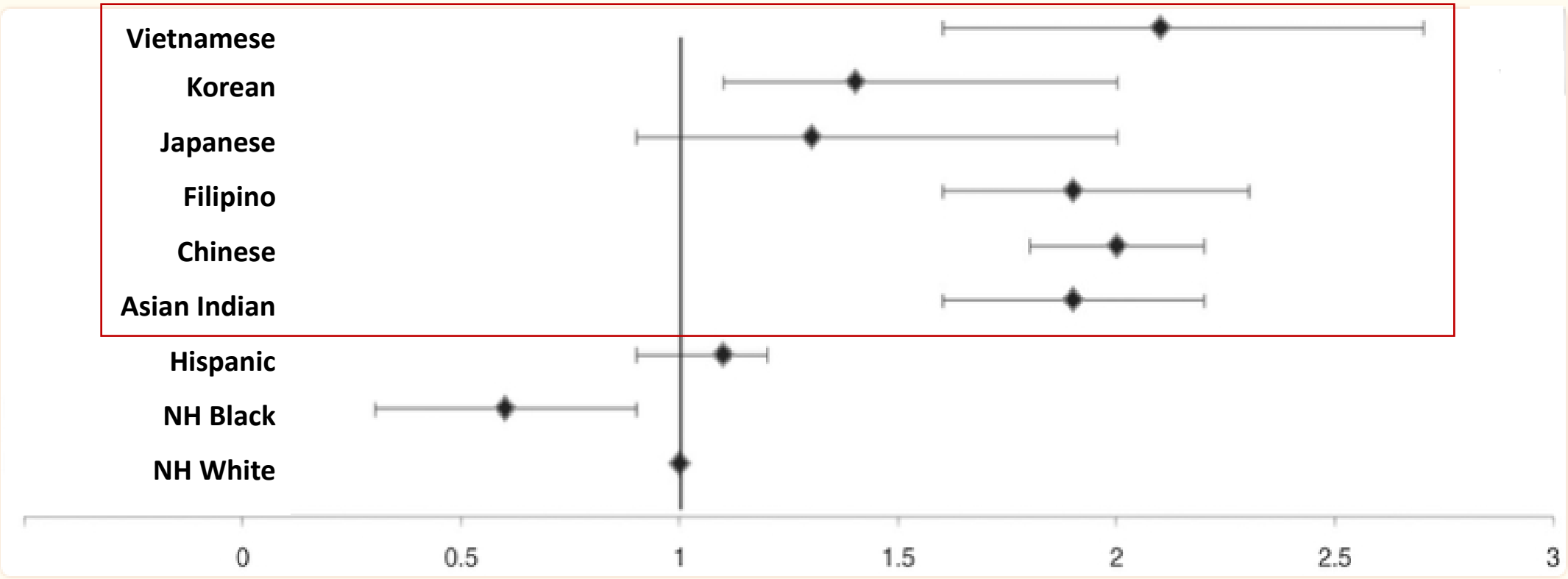
Adjusted relative risks* (95% CI) of GDM by race/ethnicity, higher risks In Asian women in California



*adjusted for maternal education, parity, smoking, insurance type

Pu et al Paediatr Perinat Epidemiol 2019

Risk factors for GDM in Asian women in CA

- Overweight/obesity
- Advanced maternal age
- Family history of type 2 diabetes
- Foreign-borne status

Pu et al Paediatr Perinat Epidemiol 2019

Social determinants of health, beyond SES

- **Unstable housing, eviction** (PTB) (Pantell et al, *am J OG MFM*; Himmelstein G et al. *JAMA Pediatr*. 2021)
- **Intimate partner violence** (SGA, PTB) (Alhusen et al, J Wom H 2015)
- **Perceived racism and discrimination** (GDM, SGA, PTB) (Macgregor et al, *AJOG MFM*. 2020; Van Daalen et al, *BMJ Glob Health*. 2022)
- **Lower social support** (PTB, SGA) (Grobman et al Obstet Gynecol. 2018)
- **Acculturation in United States** (HDP) (Zahid et al JACC: Advances. 2022)
- **Immigrant status** (GDM) (Mogos et al, J Immigr Minor Health. 2017)
- **Patient and provider trust, implicit bias, structural racism**

PTB=preterm birth, SGA=small for gestational age, GDM= gestational diabetes, HDP= hypertensive disorders of pregnancy

Pregnancy loss and CVD

Risk of Cardiovascular Disease Among Postmenopausal Women with Prior Pregnancy Loss: The Women's Health Initiative

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Mary O'Sullivan, MD
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Charles B. Eaton, MD, MS

ABSTRACT

PURPOSE Metabolic, hormonal, and hemostatic changes associated with pregnancy loss (stillbirth and miscarriage) may contribute to the development of cardiovascular disease (CVD) in adulthood. This study evaluated prospectively the association between a history of pregnancy loss and CVD in a cohort of postmenopausal women.

METHODS Postmenopausal women (77,701) were evaluated from 1993-1998. Information on baseline reproductive history, sociodemographic, and CVD risk factors were collected. The associations between 1 or 2 or more miscarriages and 1 or more stillbirths with occurrence of CVD were evaluated using multiple logistic regression.

RESULTS Among 77,701 women in the study sample, 23,538 (30.3%) reported a history of miscarriage; 1,670 (2.2%) reported a history of stillbirth; and 1,673 (2.2%) reported a history of both miscarriage and stillbirth. Multivariable-adjusted odds ratio (OR) for coronary heart disease (CHD) for 1 or more stillbirths was 1.27 (95% CI, 1.07-1.51) compared with no stillbirth; for women with a history of 1 miscarriage, the OR = 1.19 (95% CI, 1.08-1.32); and for 2 or more miscarriages the OR = 1.18 (95% CI, 1.04-1.34) compared with no miscarriage. For ischemic stroke, the multivariable odds ratio for stillbirths and miscarriages was not significant.

CONCLUSIONS Pregnancy loss was associated with CHD but not ischemic stroke. Women with a history of 1 or more stillbirths or 1 or more miscarriages appear to be at increased risk of future CVD and should be considered candidates for closer surveillance and/or early intervention; research is needed into better

Parker et al Ann Fam Med 2014

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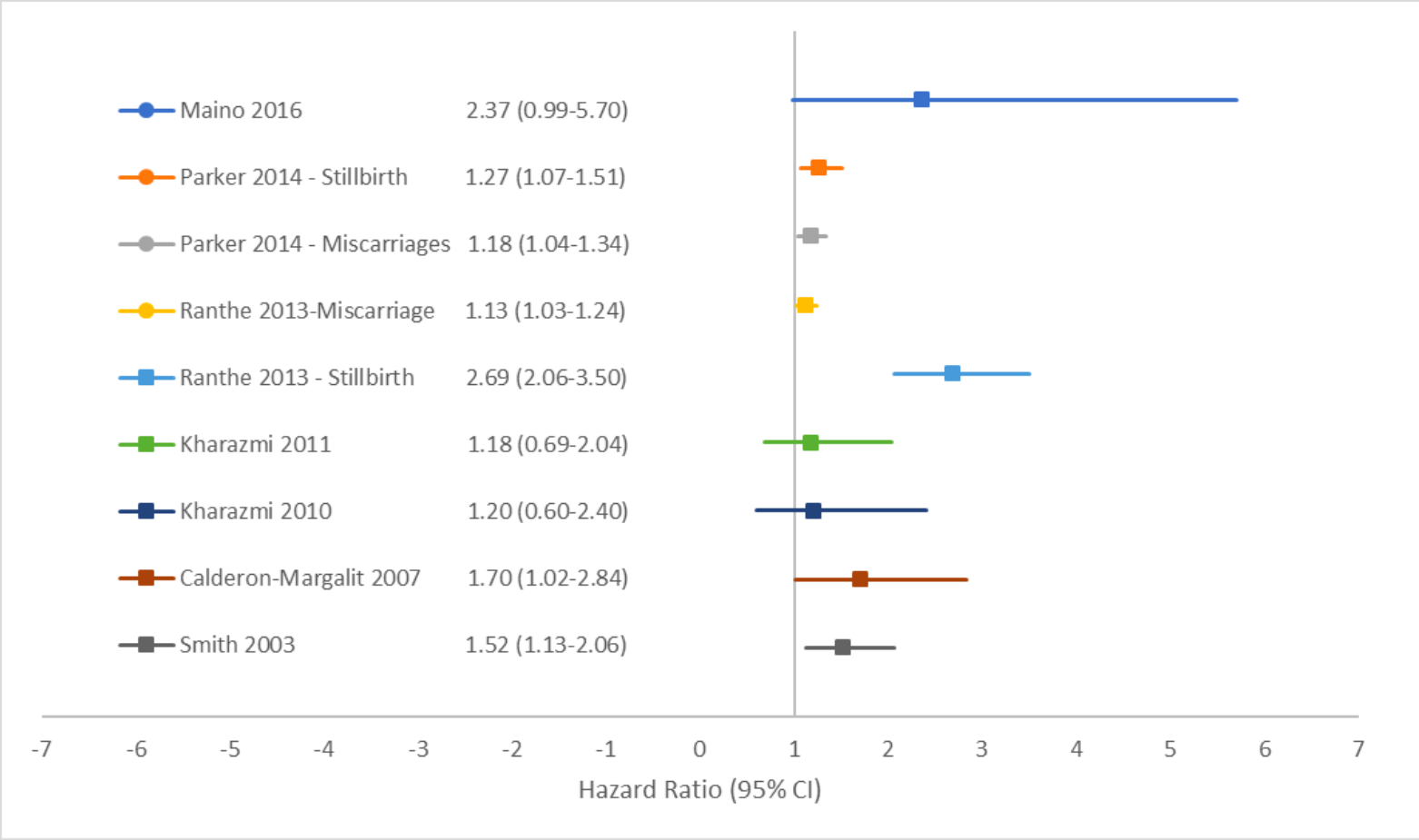
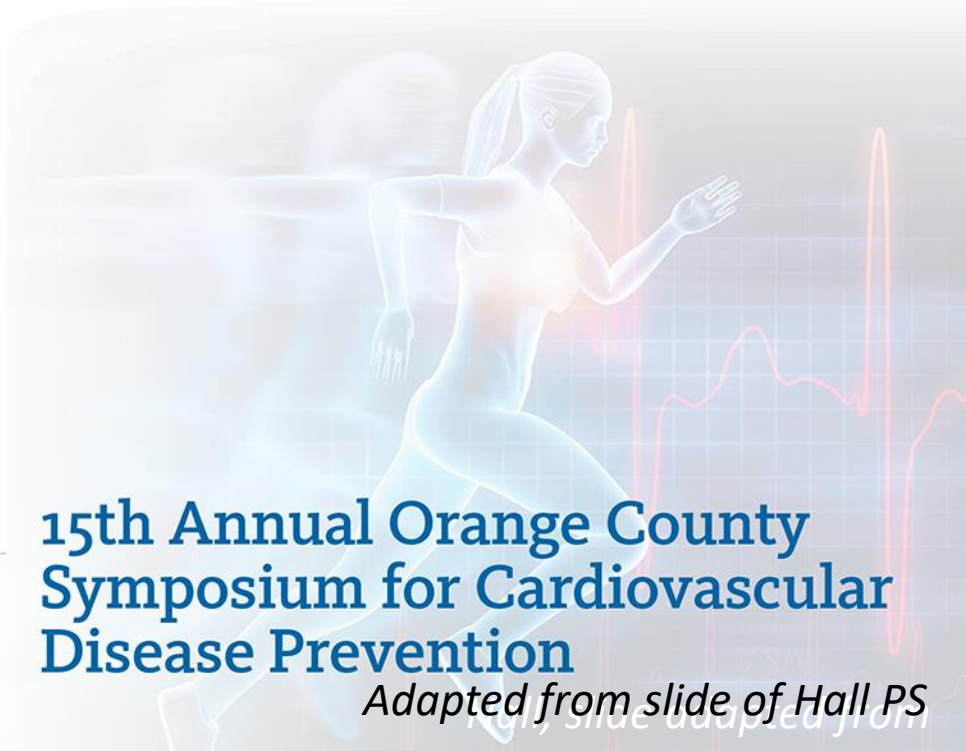
Pregnancy loss and maternal CVD- prior studies

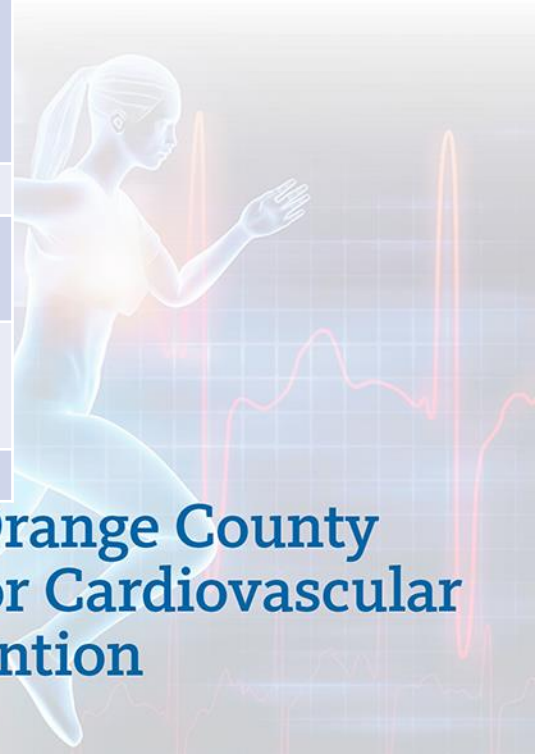




Adapted from slide of Hall PS

Pregnancy Loss and Established CVD RFs in WHI: Results

Patient Characteristics	With Pregnancy Loss 27,272 (34.5%)	Without Pregnancy Loss 51,849 (65.5%)	p
Number of Pregnancies	4.8 (±1.7)	3.0 (±1.4)	
BMI	28.2 (±5.9)	27.7 (±5.7)	<0.0001
HTN	8,926 (32.7%)	15,741 (30.4%)	<0.0001
SBP	127.7 (±17.6)	126.9 (±17.4)	0.008
Diabetes	1,246 (4.6%)	2,020 (3.9%)	0.003
Hyperlipidemia	3,376 (12.4%)	6,231 (12.0%)	0.47
Smoking status			<0.0001
Current smoker	13,775 (50.5%)	27,799 (53.6%)	
Former smoker	2,014 (7.4%)	3,159 (6.1%)	
Never smoker	11,483 (42.1%)	20,891 (40.3%)	
Socioeconomic Status Index	75.7 (±8.7)	76.2 (±8.1)	0.01
Psychosocial history of Depression	6,461 (23.7%)	11,478 (22.1%)	<0.0001
Physical Activity, MET-hours/week	12.3 (±13.5)	12.7 (±13.7)	0.01
Healthy Eating Index	64.2 (±10.8)	64.7 (±10.7)	<0.0001



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Hall PS et al Am J Cardiology 2019

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Circulation. 2016 May 31; 133(22): 2149–2158. doi:10.1161/CIRCULATIONAHA.115.017854.

Reproductive Risk Factors and Coronary Heart Disease in the Women's Health Initiative Observational Study

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Table 3

CHD discrimination among WHI women who have ever been pregnant for established CHD risk factors, reproductive factors and combined models.

Model	C-statistic (n=72,982)	C Difference from Established Risk Factor Model	Bootstrap 95% CI for difference from Established Risk Factor Model (n=72,982)
Age + reproductive risk factors *	0.675		
Established risk factors †	0.726		
Established risk factors + age at first birth	0.728	0.0019	(0.0010, 0.0032)
Established risk factors + number of stillbirths	0.727	0.0005	(0.0001, 0.0013)
Established risk factors + number of miscarriages	0.727	0.0010	(0.0004, 0.0020)
Established risk factors + breast feeding	0.726	0.0001	(−0.00002, 0.0005)
Established risk factors + significant reproductive factors ‡	0.730	0.0033	(0.0022, 0.0051)

* Reproductive risk factors include menstrual irregularity, age at first birth, still births, miscarriages, and breastfeeding ≥ 1 month.

† Established risk factors modeled include age, high cholesterol requiring pills, currently taking pills for hypertension, log of systolic blood pressure, current smoker, diabetes.

‡ Significant reproductive risk factors include age at first birth, still births, miscarriages, and breastfeeding ≥ 1 month.

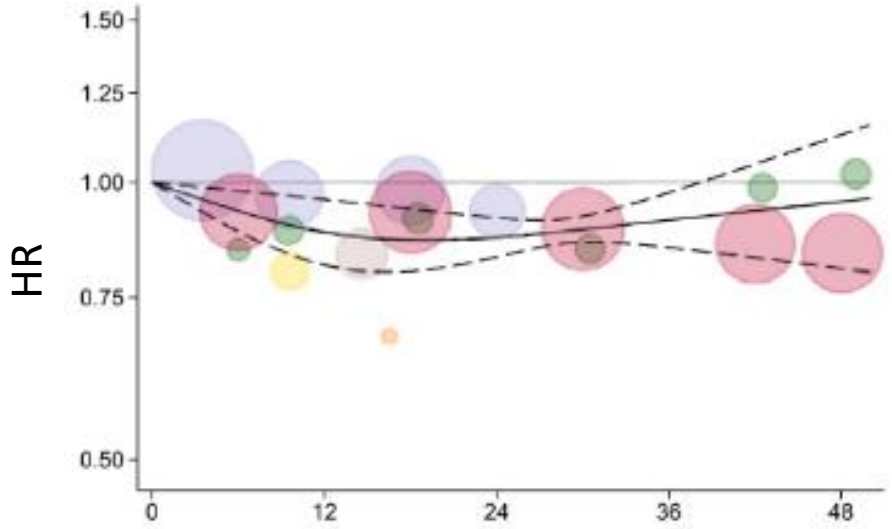
Clinical Perspectives

When considered together, the following reproductive factors are independently associated with post-menopausal coronary heart disease in women: early age at first birth, number of stillbirths and miscarriages, irregular menses and lack of breastfeeding for ≥ 1 month. When considered along with established risk factors these reproductive factors do not improve our ability to risk stratify coronary heart disease in post-menopausal women. However, our study suggests that a reproductive history may be useful as an "early window", before the onset of established CHD risk factors, to predict which women are most likely to experience a future coronary heart disease event.

Parikh et al Circulation 2016

Breastfeeding reduces CVD risk in women: meta-analysis

Study	No. of parous women	No. of outcomes	Level of adjustment	Hazard ratio (95% CI)	Weight (%)
CVD					
HUNT2[12]	20,007	1,049*	++	0.68 (0.49, 0.95)	3.66
JPHC[13]	37,496	996*	++	0.84 (0.71, 0.98)	10.43
EPIC[9]	266,607	1,970*	++	0.80 (0.70, 0.91)	12.41
45&Up[7]	100,864	3,846	++	0.84 (0.76, 0.92)	15.37
Gallagher[11]	254,116	2,578*	○	0.92 (0.86, 0.99)	17.90
CKB[8]	285,603	43,787	+	0.91 (0.86, 0.97)	19.26
WHI[15]	138,681	NR	++	0.99 (0.96, 1.03)	20.98
Overall random-effects, I^2 (95% CI): 79.4% (57.8%, 89.9%)				**0.89 (0.83, 0.95)**	**100.00**
Overall fixed-effects				**0.95 (0.92, 0.97)**	



* for each additional month of breastfeeding HR is 0.91 (95% CI, 0.84–0.99; *P*=0.031) for CVD

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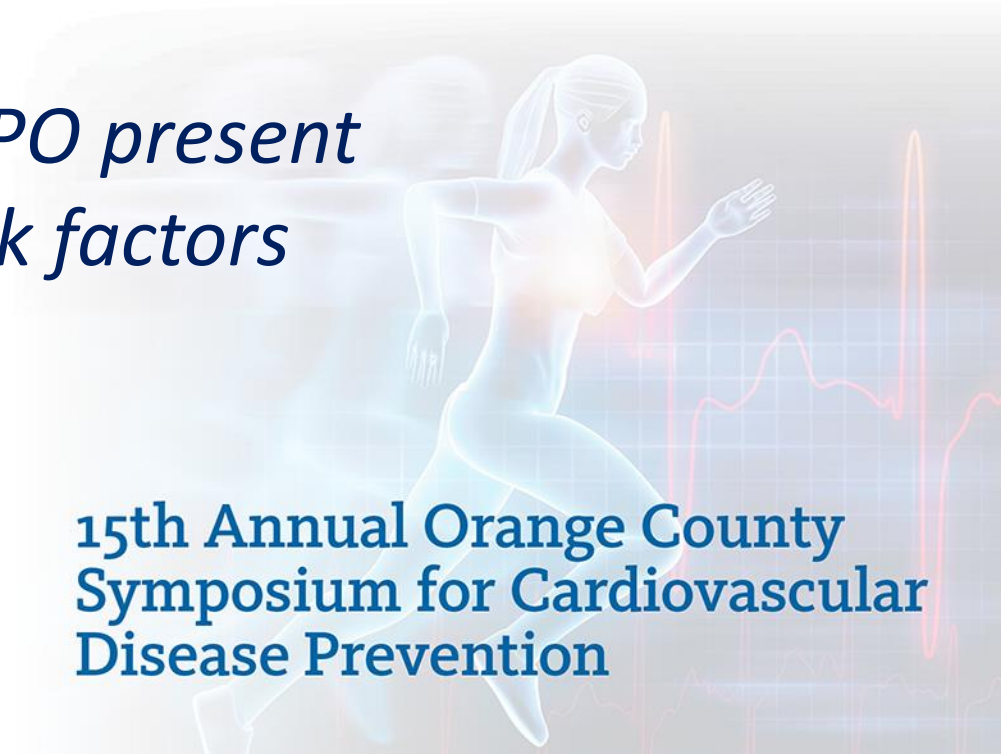
Tschiderer L et al, JAHA 2022

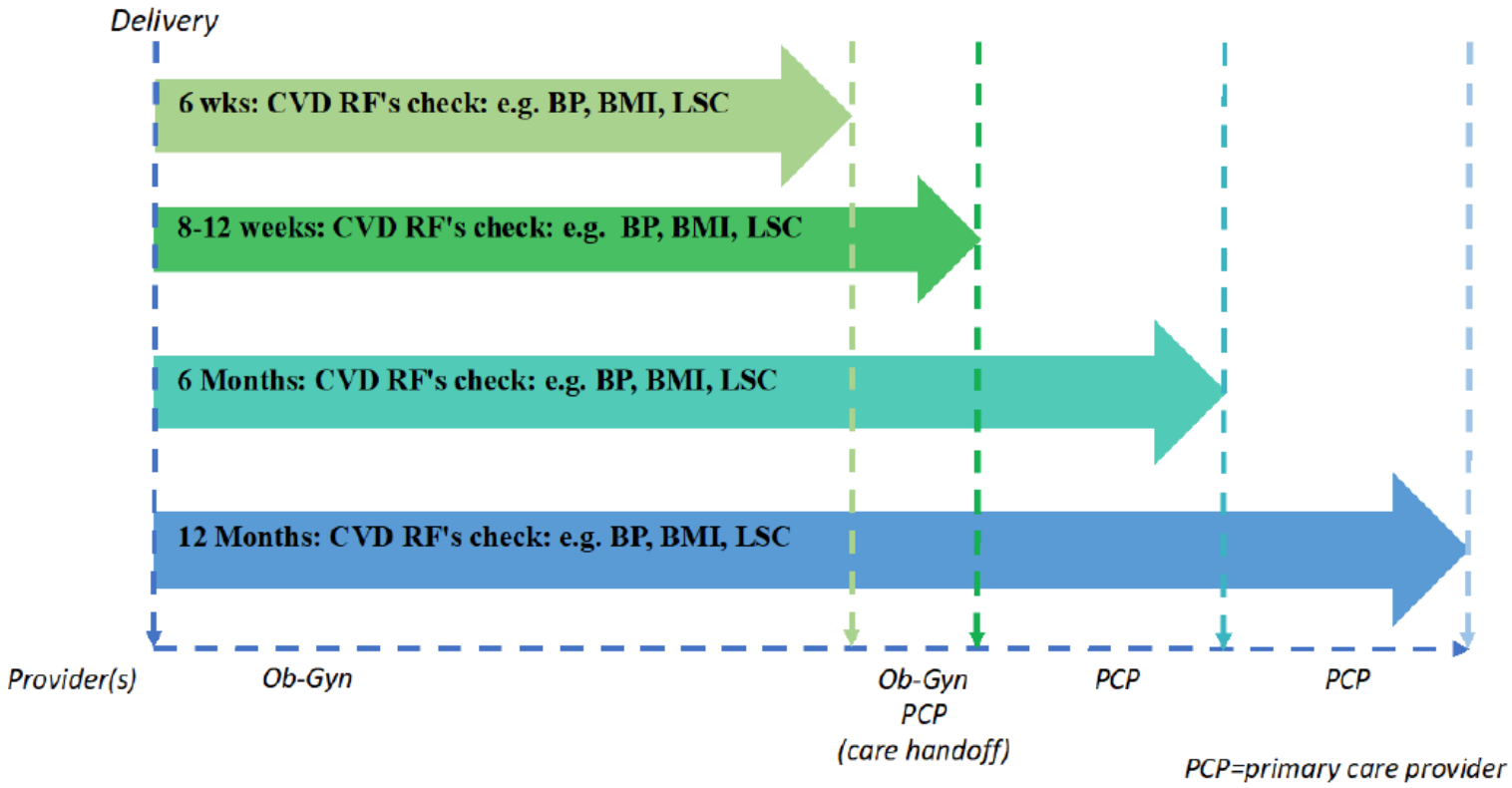
When does CVD risk originate?

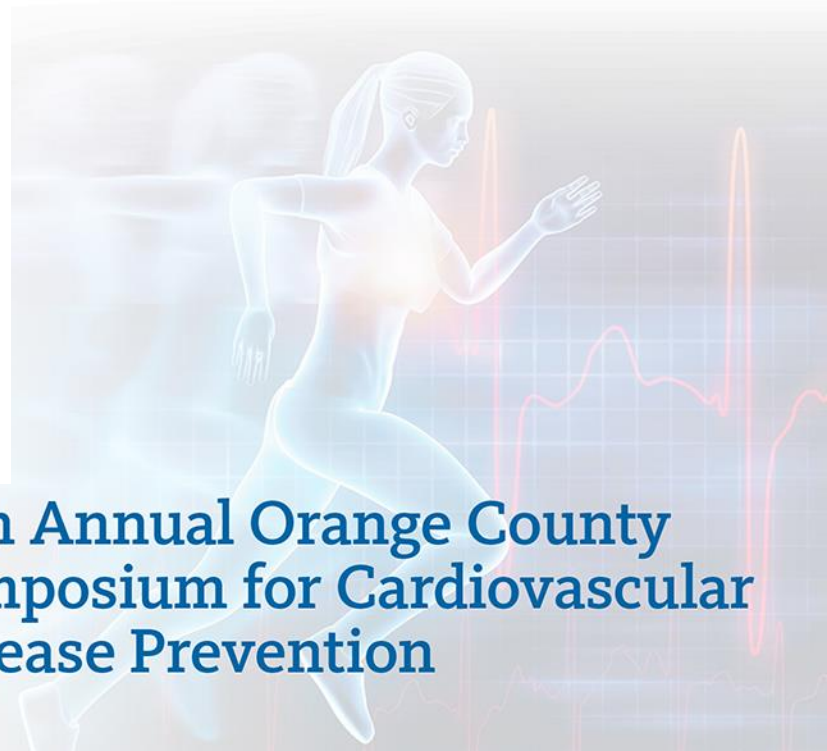
Evidence suggests:

- ✓ *pre-pregnancy*
- ✓ *during pregnancy, especially with APO present*
- ✓ *post pregnancy via elevated CVD risk factors*



Timing of CVD RF Assessment and RF modification, Lifestyle Counseling in Woman with an APO





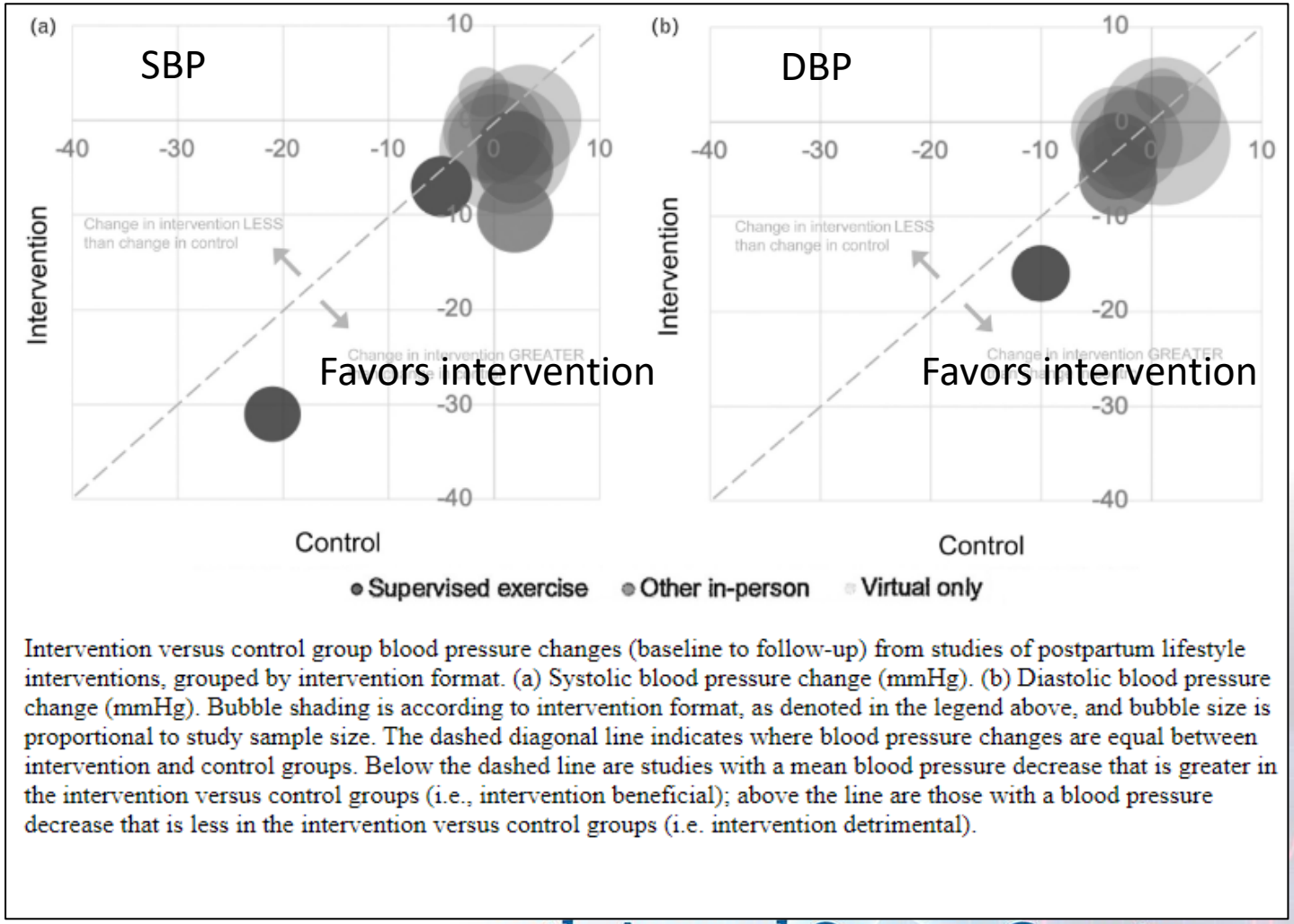
AHA Pregnancy and CVD Statement 2021

Handoff of a patient's care from Ob-Gyn to PCP and/or cardiologist: patient with adverse pregnancy outcome (APO)

Timing	Provider(s)	Evaluation and management
1. Diagnosis of APO 2. During and/or at discharge from L&D	Ob-Gyn and multidisciplinary care team (MD,RN,NP, midwife)	Introduce concept of pregnancy as a cardiometabolic stress test - Need to monitor BP - Lifestyle modification (diet, activity, stress/mood, sleep) - Importance of lactation
6 weeks PP	Ob-Gyn	Reinforce the concept of APO's as a cardiometabolic stress test, importance of lifestyle modification OGTT (6-12 weeks PP), BP check Refer to PCP
8-12 weeks PP	PCP and/or cardiologist	BP, diet, activity, stress/mood, sleep, breastfeeding
6 months PP	PCP and/or cardiologist	BP, diet, activity, stress/mood, sleep, breastfeeding
12 months PP	PCP and/ or cardiologist	BP, diet, activity, stress/mood, sleep, breastfeeding If lactation has ceased, consider checking lipids

Research gap: The effect of postpartum lifestyle interventions on blood pressure: a systematic literature review

- 9 studies met inclusion criteria.
- RCTs with sample sizes <100.
- Nearly all participants identified as White
- No statistical effect on BP
- Most interventions were associated with improvements in physical activity
- Possible signal of



Intervention versus control group blood pressure changes (baseline to follow-up) from studies of postpartum lifestyle interventions, grouped by intervention format. (a) Systolic blood pressure change (mmHg). (b) Diastolic blood pressure change (mmHg). Bubble shading is according to intervention format, as denoted in the legend above, and bubble size is proportional to study sample size. The dashed diagonal line indicates where blood pressure changes are equal between intervention and control groups. Below the dashed line are studies with a mean blood pressure decrease that is greater in the intervention versus control groups (i.e., intervention beneficial); above the line are those with a blood pressure decrease that is less in the intervention versus control groups (i.e. intervention detrimental).

Murray Horwitz et al, *Journal of Hypertension 2023*

Menopause

DECREASED ESTROGEN with several other pathophysiologic changes:

- DYSLIPIDEMIA: Increase in Total, LDL-C, Triglycerides, Decrease in HDL-C
- BLOOD PRESSURE: increase in BP, salt sensitivity
- ADIPOSITY and VISCERAL FAT

ACCELERATION OF CVD RISK in SUSCEPTIBLE WOMEN

STILL PAY ATTENTION TO HISTORY OF APO's!!! → Collect your patient's history of APO's

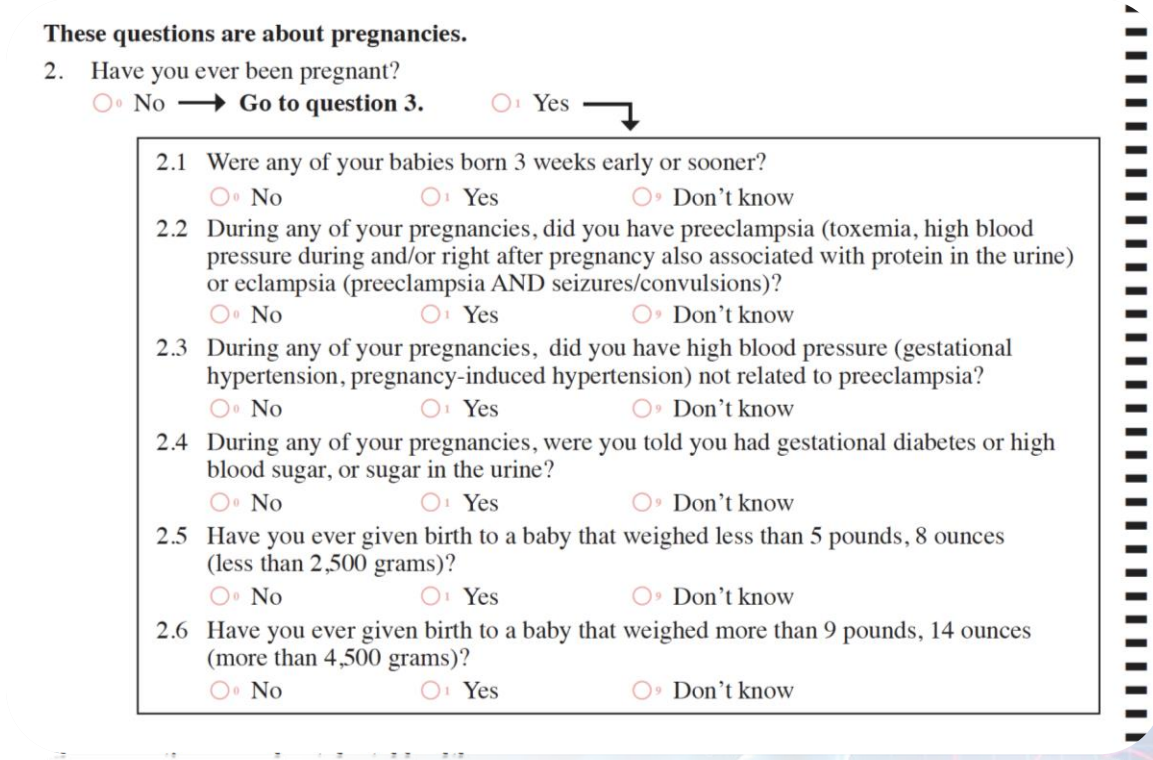
Post menopause

CVD is the major cause of death in women 65+

Do APO’s matter at this age?

Adverse Pregnancy Outcomes and CVD in WHI

- Form 158
- Allows for study of:
  - A large # of women
  - Diverse race-ethnicities
  - Adjudicated CVD
  - Study of post-menopausal women
  - Novel biologic pathways linking APO's and CVD (study of omics panels)



These questions are about pregnancies.

2. Have you ever been pregnant?
   ○0 No → **Go to question 3.** ○1 Yes →

2.1 Were any of your babies born 3 weeks early or sooner?
○0 No ○1 Yes ○9 Don't know

2.2 During any of your pregnancies, did you have preeclampsia (toxemia, high blood pressure during and/or right after pregnancy also associated with protein in the urine) or eclampsia (preeclampsia AND seizures/convulsions)?
○0 No ○1 Yes ○9 Don't know

2.3 During any of your pregnancies, did you have high blood pressure (gestational hypertension, pregnancy-induced hypertension) not related to preeclampsia?
○0 No ○1 Yes ○9 Don't know

2.4 During any of your pregnancies, were you told you had gestational diabetes or high blood sugar, or sugar in the urine?
○0 No ○1 Yes ○9 Don't know

2.5 Have you ever given birth to a baby that weighed less than 5 pounds, 8 ounces (less than 2,500 grams)?
○0 No ○1 Yes ○9 Don't know

2.6 Have you ever given birth to a baby that weighed more than 9 pounds, 14 ounces (more than 4,500 grams)?
○0 No ○1 Yes ○9 Don't know

JAMA Network™

From: **Association of Adverse Pregnancy Outcomes With Risk of Atherosclerotic Cardiovascular Disease in Postmenopausal Women**

JAMA Cardiol. 2020;5(12):1390-1398. doi:10.1001/jamacardio.2020.4097

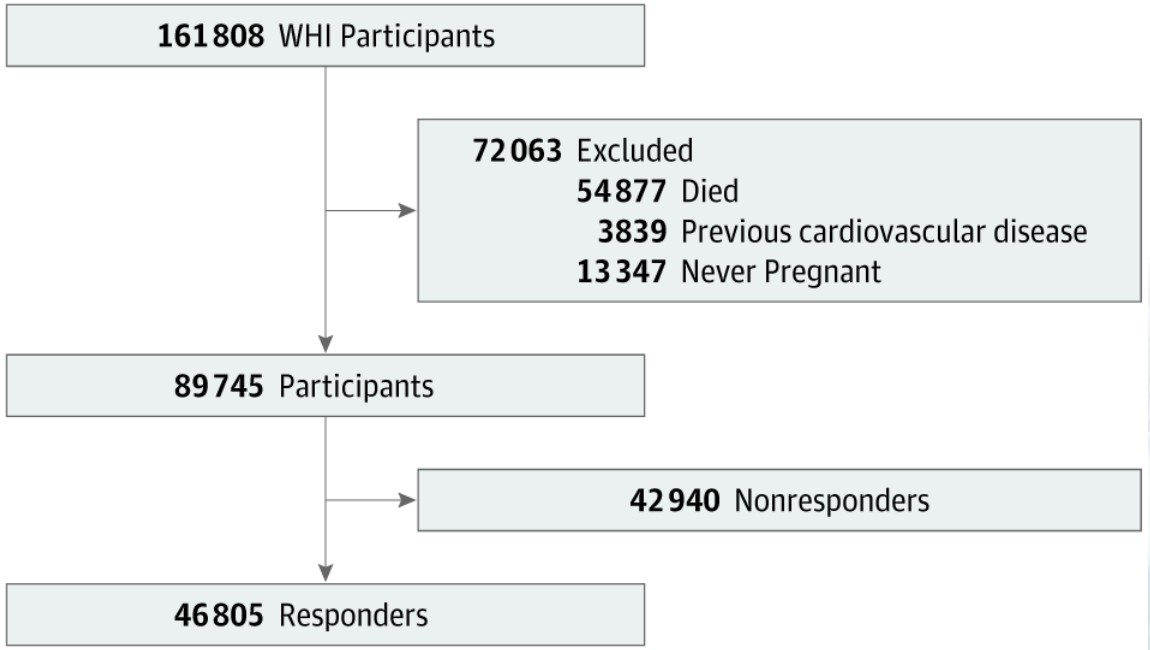


Figure Legend:

Flow Diagram for the Selection of the Study Participants From the Women's Health Initiative (WHI)

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Sondergaard et al, Jama Card 2020

JAMA Network™

From: **Association of Adverse Pregnancy Outcomes With Risk of Atherosclerotic Cardiovascular Disease in Postmenopausal Women**

JAMA Cardiol. 2020;5(12):1390-1398. doi:10.1001/jamacardio.2020.4097

APO	Odds ratio (95% CI)
Gestational diabetes	
Unadjusted	1.45 (1.15-1.81)
Adjusted	1.32 (1.02-1.67)
Low birth weight	
Unadjusted	1.29 (1.16-1.43)
Adjusted	1.25 (1.12-1.39)
High birth weight	
Unadjusted	1.18 (1.02-1.37)
Adjusted	1.07 (0.91-1.25)
Preterm delivery	
Unadjusted	1.23 (1.12-1.36)
Adjusted	1.23 (1.10-1.36)
Hypertensive disorders of pregnancy	
Unadjusted	1.61 (1.41-1.83)
Adjusted	1.38 (1.19-1.58)

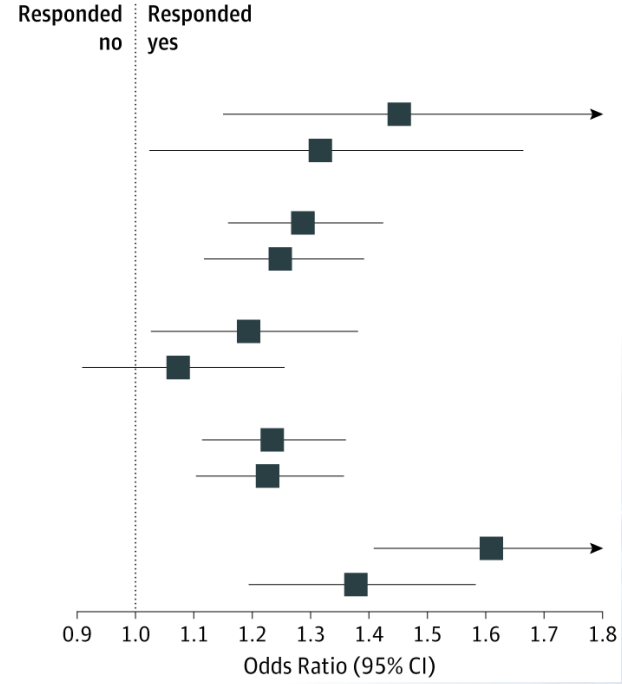

Figure Legend:

Association of Individual Adverse Pregnancy Outcomes (APOs) With Atherosclerotic Cardiovascular Disease (ASCVD)Each line displays the odds ratio and its 95% CI from the comparison of yes and no responses based on a multinomial logistic model. For each APO, the top line shows the odds ratio for the APO from an unadjusted model and the bottom line shows the odds ratio for the APO from a model that adjusted for all traditional ASCVD risk factors, including age, hyperlipidemia, hypertension, diabetes, and smoking.

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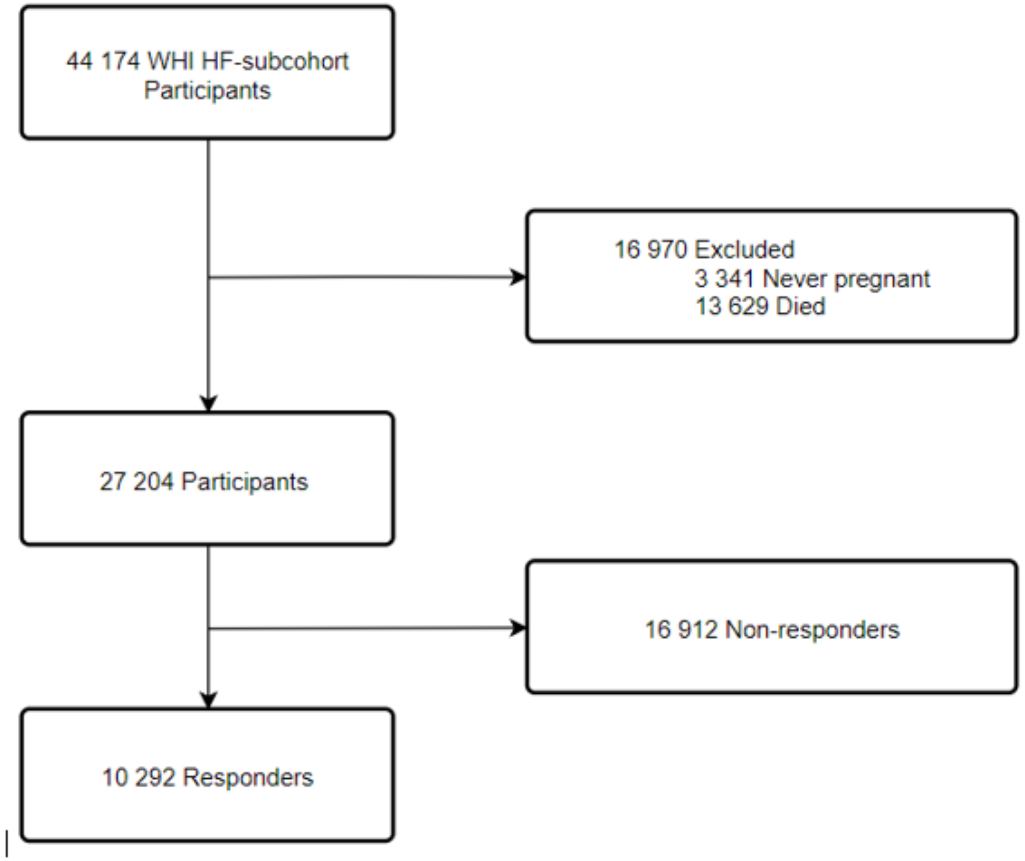
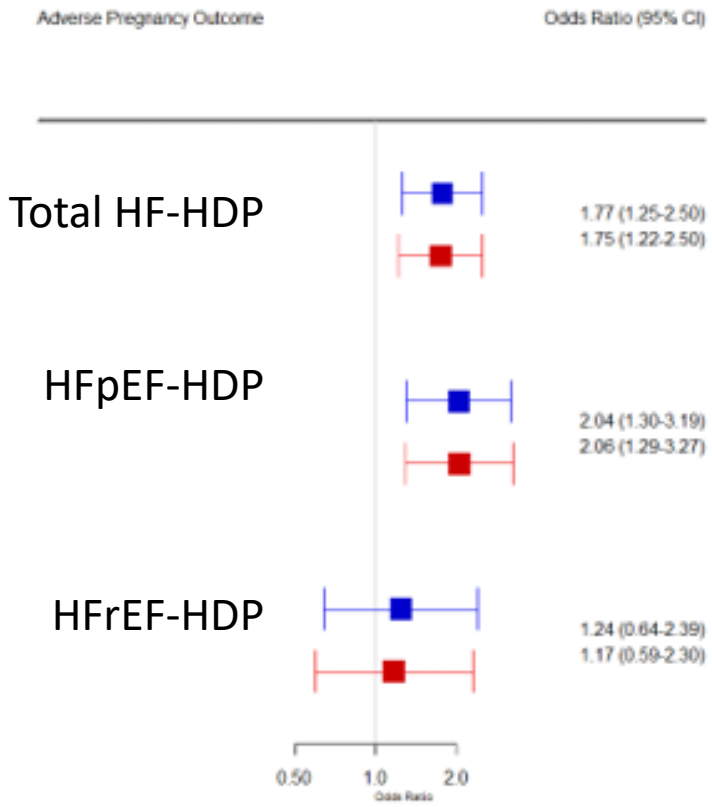
APOs and HF in WHI

Figure 1 – Flow diagram for the selection of study participants





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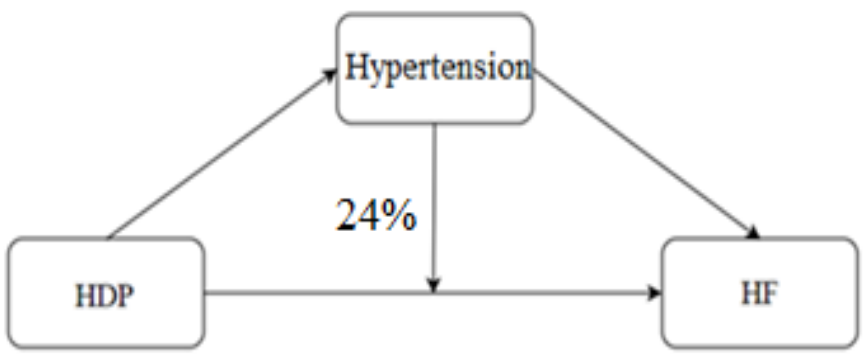
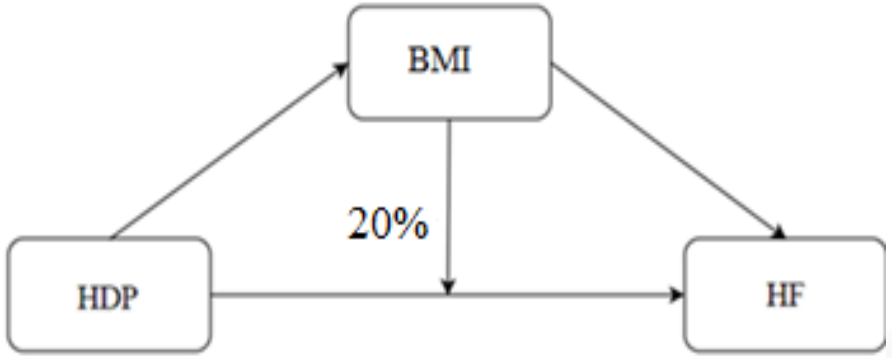
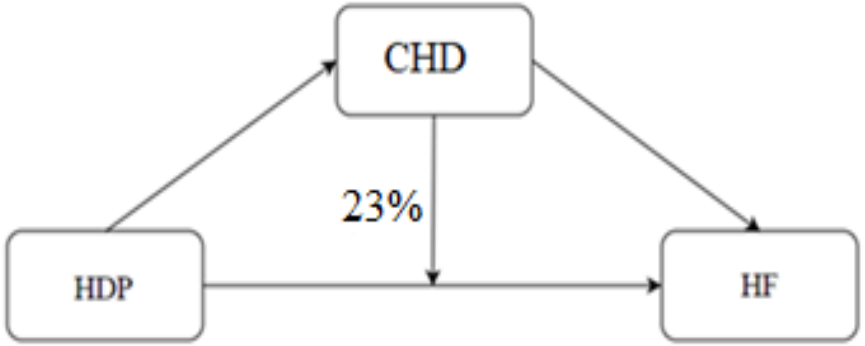
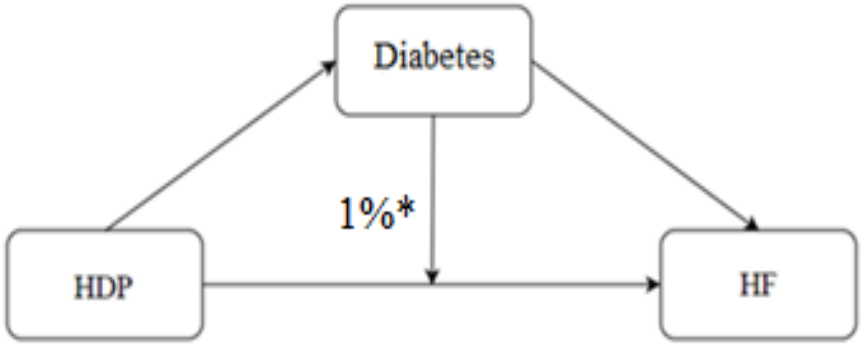
APOs and HF in WHI: mediation









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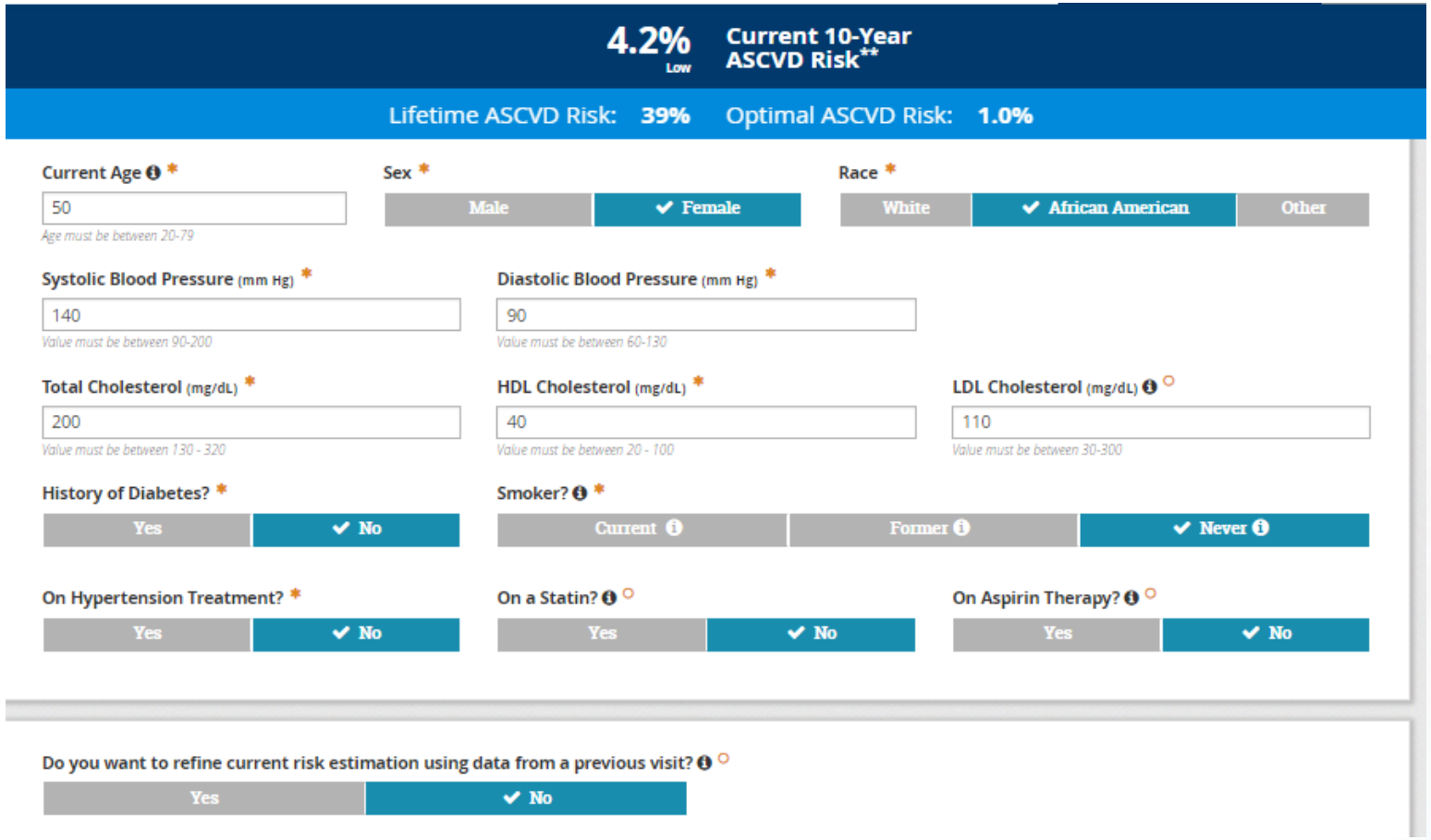
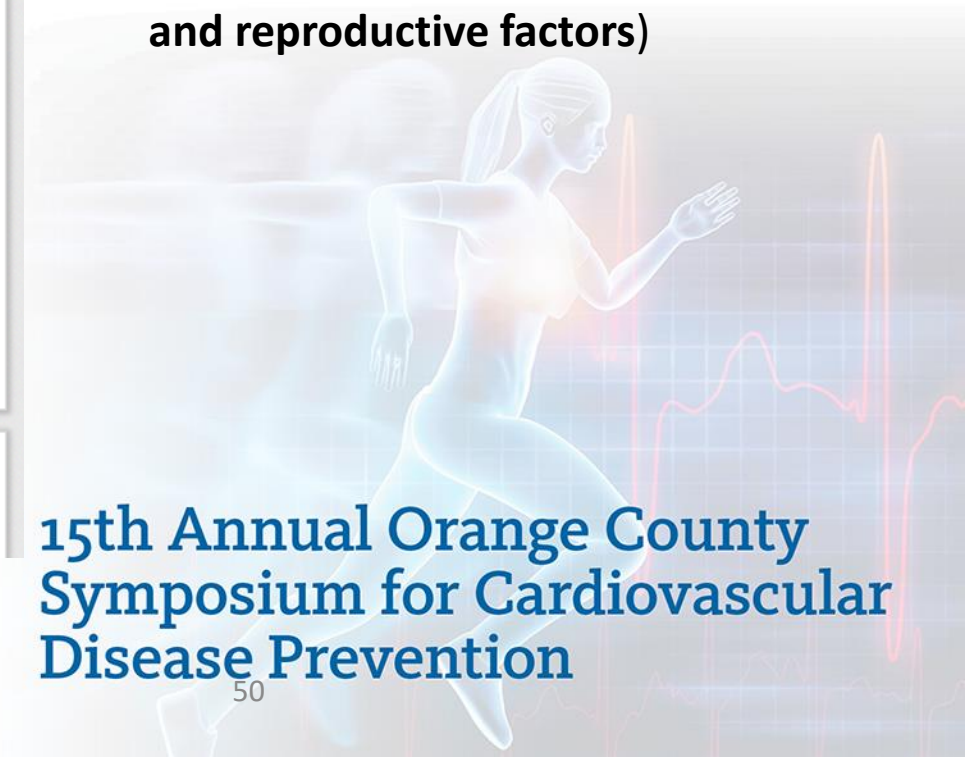
Atherosclerotic cardiovascular disease risk calculator (ASCVD) and risk enhancers



Risk enhancers: Factors not in The ASCVD risk calculator that can enhance a person's risk of ASCVD (e.g., chronic kidney disease, autoimmune diseases, **pregnancy and reproductive factors**)



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My Cardiovascular-focused reproductive and pregnancy history*

- Gravida, Para
- Number Miscarriages
- Number of Stillbirths

- Preeclampsia
- Preterm delivery
- Gestational Diabetes
- Low birth weight or small baby
- Placental abruption

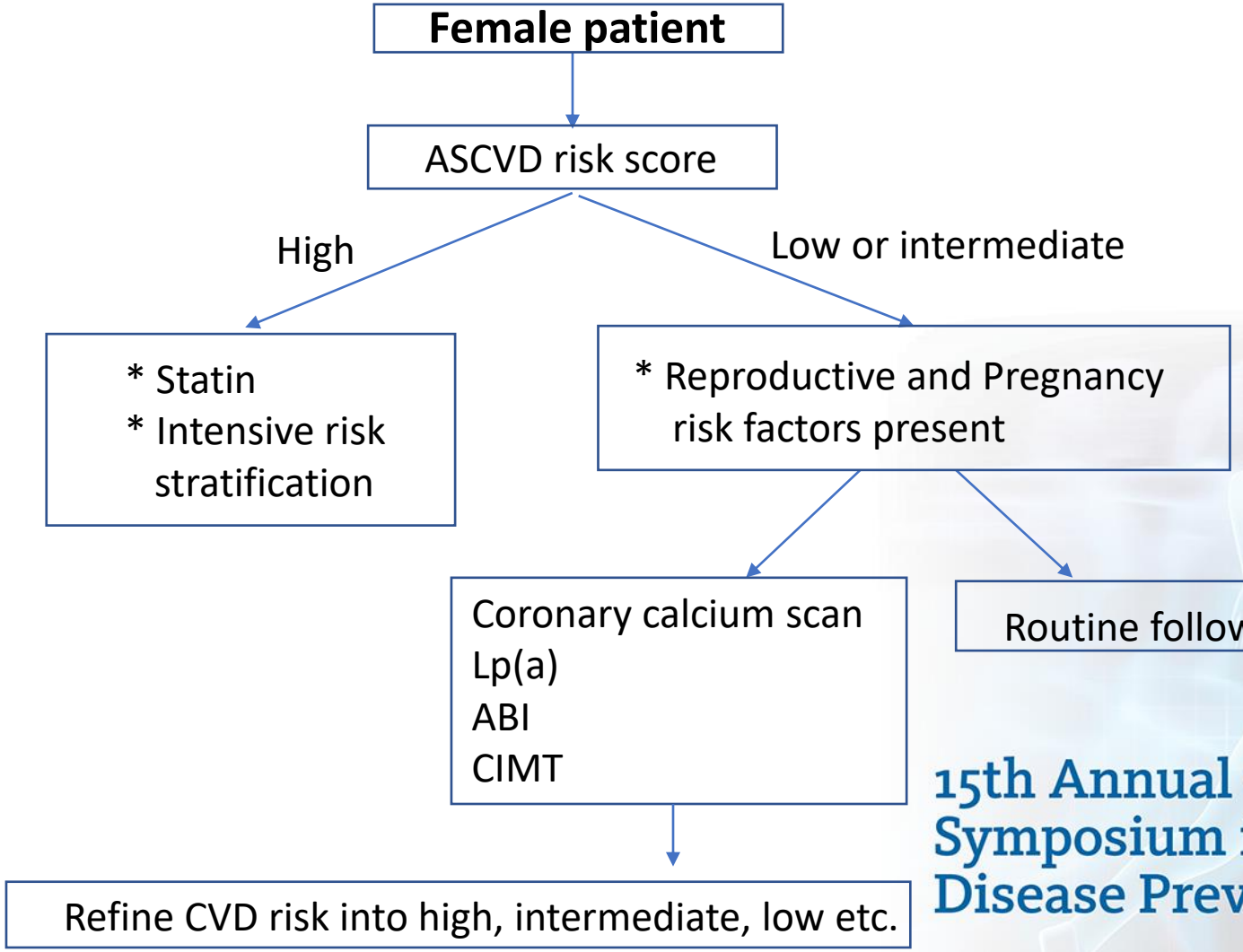
- Breastfeeding duration total

- Menopause
- What age?
- Surgical?

- History of Polycystic Ovarian Syndrome
- Any menstrual irregularity? {MILD/MOD/SEVERE}
- Difficulty conceiving for >=1 year when trying?
- For how many years have you had difficulty conceiving?

** To identify risk enhancers*

Algorithm for APOs in CVD risk stratification

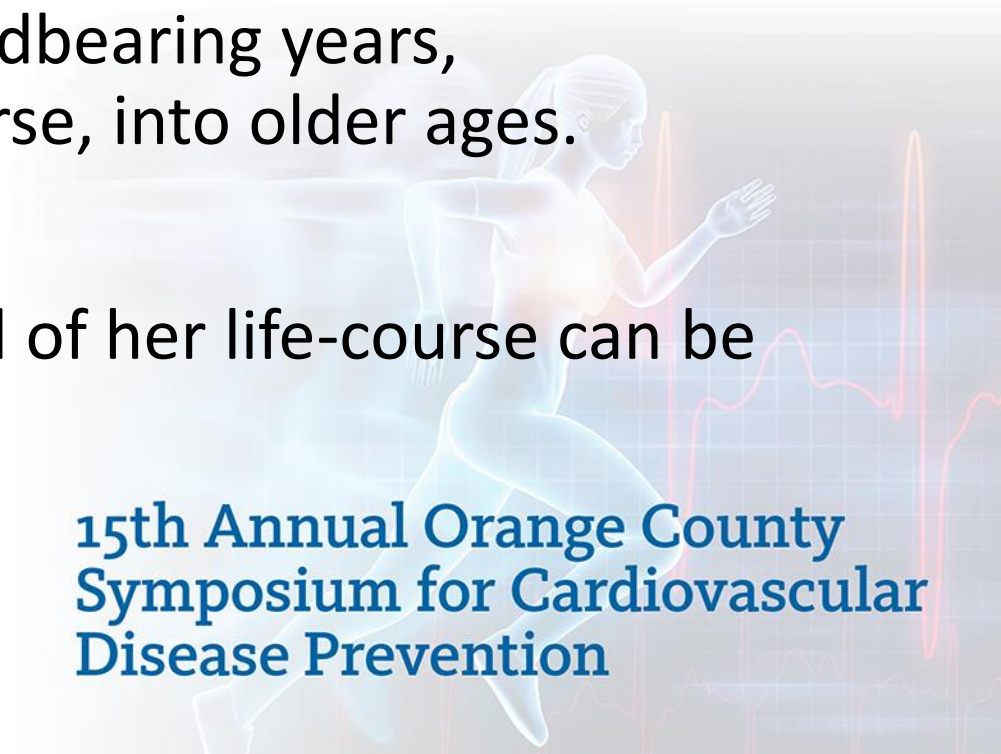


Conclusions

- In adolescence and teenage years early age at first birth at < 20 years may be associated with CVD in women.

- APO's are important to recognize in the childbearing years, postpartum throughout a woman's life-course, into older ages.

- For women, APO history during each period of her life-course can be leveraged to prevent CVD.



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