Preconception and Multigenerational Health:

Links Between Cardiovascular and Reproductive Health

Thursday May 2nd, 11.30-1pm CT

A webinar with Dr. Emily Harville, PhD

Emily W. Harville, associate professor
Department of Epidemiology
Tulane School of Public Health and Tropical Medicine
harville@tulane.edu

Webinar objectives

List	Ways in which cardiovascular health affects pregnancy outcomes and vice versa
Assess	Evidence for multigenerational influences on birth outcomes
Discuss	How life course and multigenerational health may contribute to disparities in perinatal outcomes

Reproductive and cardiovascular health are linked

Poorer health at birth

Low birthweight

Reduced fetal growth

Poorer cardiovascular health

Preconception hypertension

Preconception diabetes

Poorer health during pregnancy

Gestational hypertension

Gestational diabetes

Pre eclampsia

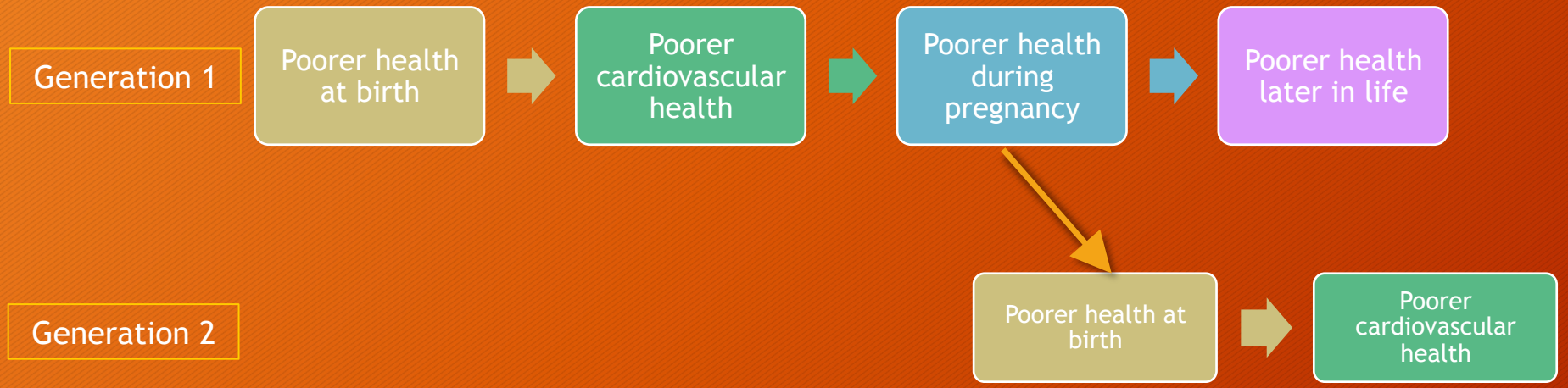
Poorer health later in life

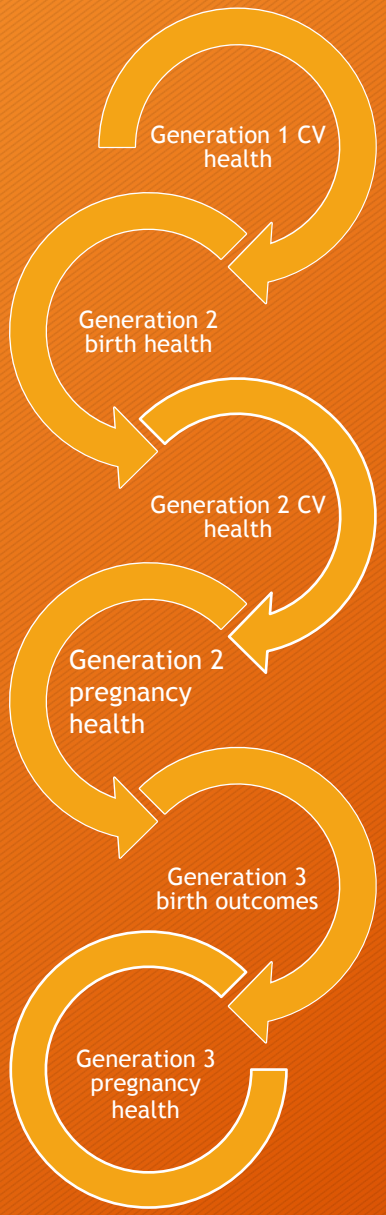
Diabetes

Hypertension

Cardiovascular disease

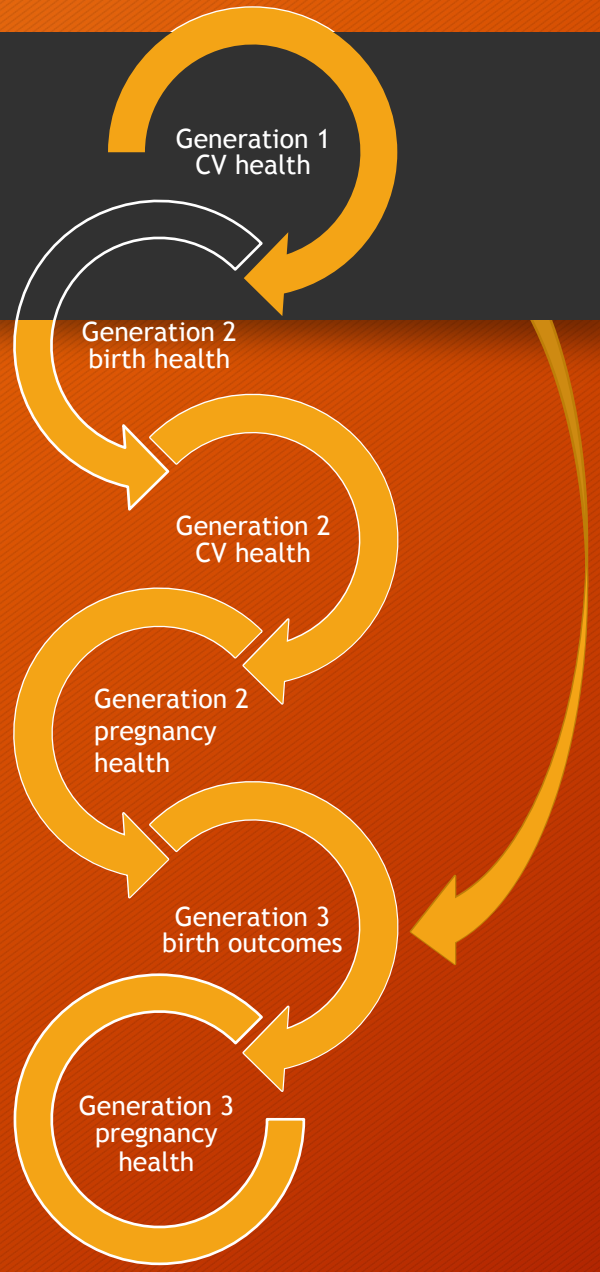
Cardiovascular and reproductive health are linked





Cardiovascular health and reproductive health across generations

Transgenerational effects?



Poor health at birth → cardiovascular health prior to pregnancy

Poorer health at birth

Low birthweight

Reduced fetal growth

Poorer cardiovascular health

Preconception hypertension

Preconception diabetes

Poorer health during pregnancy

Gestational hypertension

Gestational diabetes

Pre eclampsia

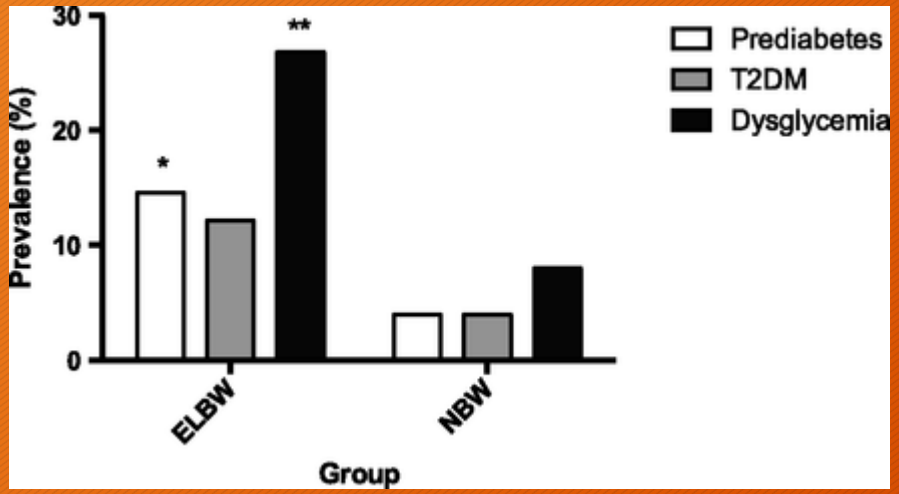
Poorer health later in life

Diabetes

Hypertension

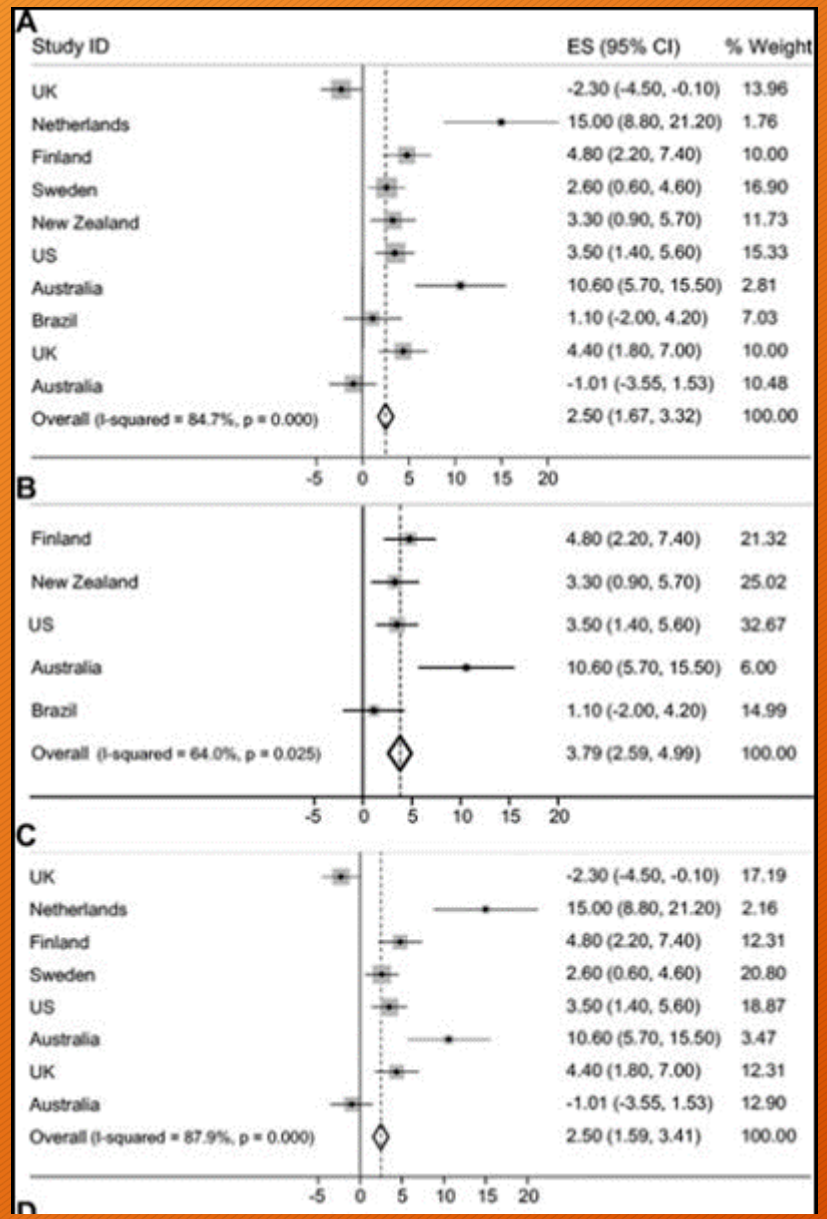
Cardiovascular disease

Low birthweight and cardiovascular health in adolescence and adulthood



Birthweight <1 kg
Mean GA 27.1 weeks
Mean age 31.8

Morrison KM, Ramsingh L, Gunn E, Streiner D, Van Lieshout R, Boyle M, Gerstein H, Schmidt L, Saigal S. Cardiometabolic Health in Adults Born Premature With Extremely Low Birth Weight. Pediatrics. 2016 Oct;138(4).



Meta-analysis of the difference in systolic blood pressure (SBP) between participants born preterm or very low birth weight (VLBW) vs term. B, adjusted for SES, C, adjusted for height/ weight/BMI

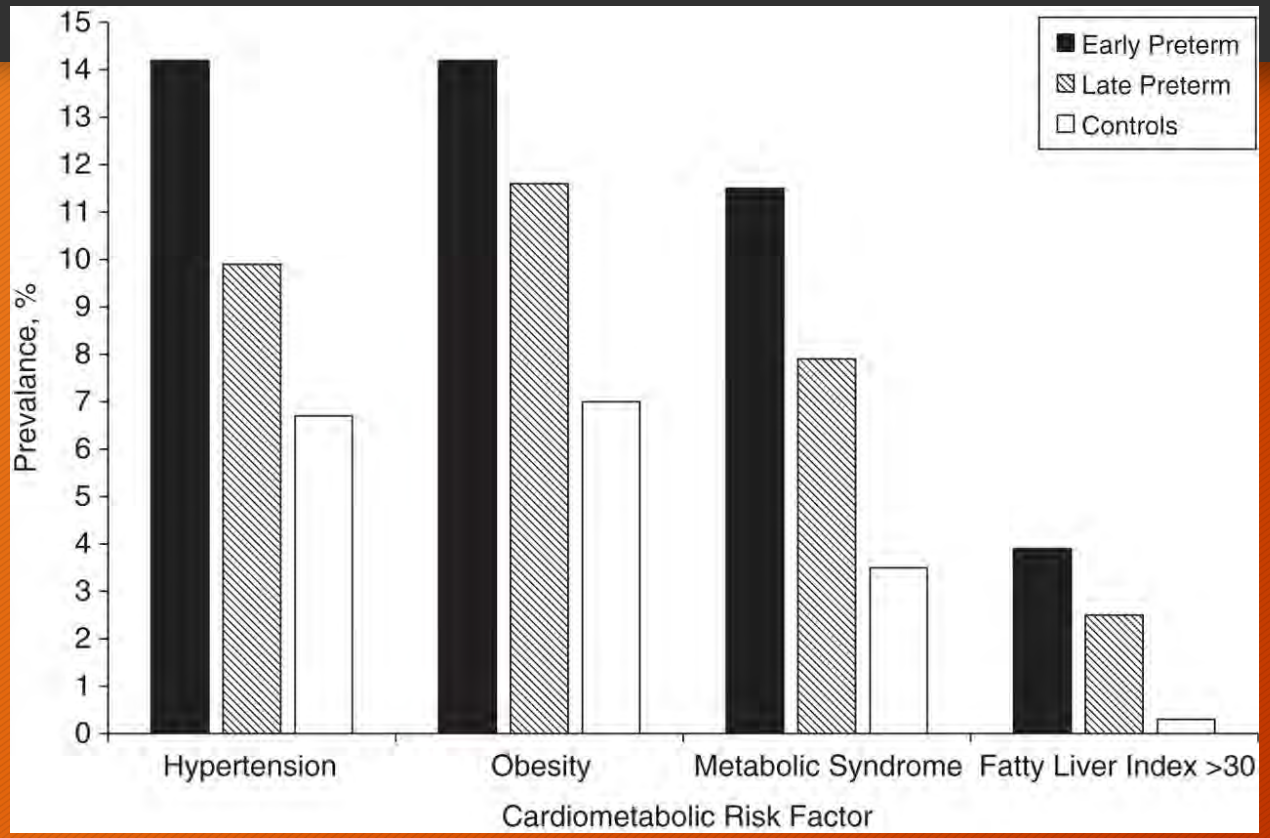
Mean age at BP measurement: 17.8

2.2 mm Hg (95% CI: 1.1-3.3 mm Hg) higher for preterm or VLBW versus term participants.
Most-adjusted: 2.5 mm Hg (95% CI: 1.7-3.3 mm Hg).
Higher-quality 3.8 mm Hg (95% CI: 2.6-5.0 mm Hg)

Systematic Review and Meta Analysis of Preterm Birth and Later Systolic Blood Pressure.
de Jong, Femke; Monuteaux, Michael; van Elburg, Ruurd; Gillman, Matthew; Belfort, Mandy

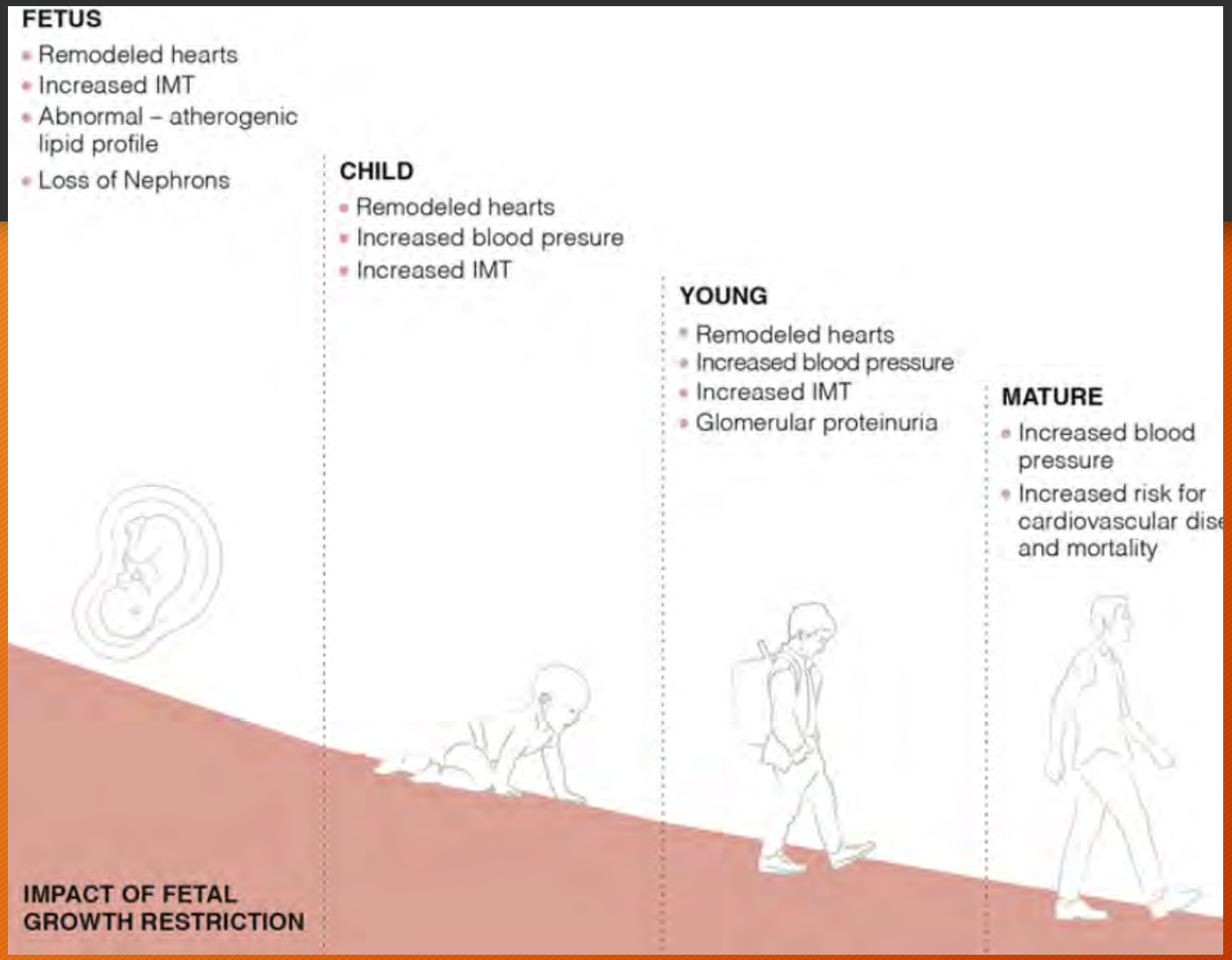
Hypertension. 59(2):226 234, February 2012.
DOI: 10.1161/HYPERTENSIONAHA.111.181784

Prevalence of hypertension, obesity, metabolic syndrome, and fatty liver index greater than 30 in adults who were born early preterm or late preterm compared with adults born at term (controls), Northern Finland, 2009–2011.



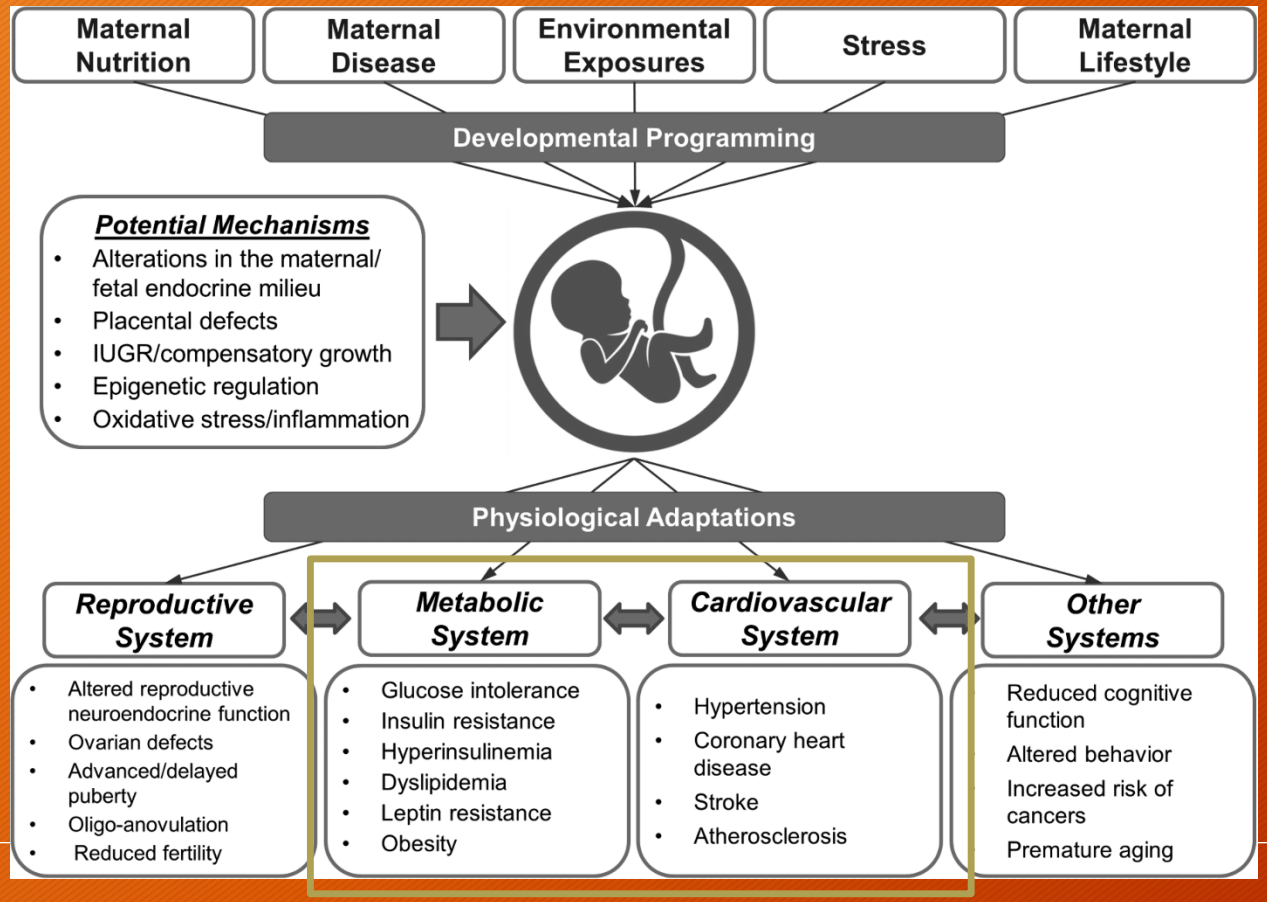
Ages 20-46

American Journal of Epidemiology, Volume 181, Issue 11, 1 June 2015, Pages 861–873, https://doi.org/10.1093/aje/kwu443



Crispi F, Miranda J, Gratacós E. Long-term cardiovascular consequences of fetal growth restriction: biology, clinical implications, and opportunities for prevention of adult disease. Am J Obstet Gynecol. 2018 Feb;218(2S):S869-S879. doi: 10.1016/j.ajog.2017.12.012.

Developmental Origins of Health and Disease



From: Developmental Programming, a Pathway to Disease
Endocrinology. 2016;157(4):1328-1340. doi:10.1210/en.2016-1003

Cardiovascular health prior to pregnancy → poorer health during pregnancy

Poorer health at birth

Low birthweight

Reduced fetal growth

Poorer cardiovascular health

Preconception hypertension

Preconception diabetes

Poorer health during pregnancy

Gestational hypertension

Gestational diabetes

Pre eclampsia

Poorer health later in life

Diabetes

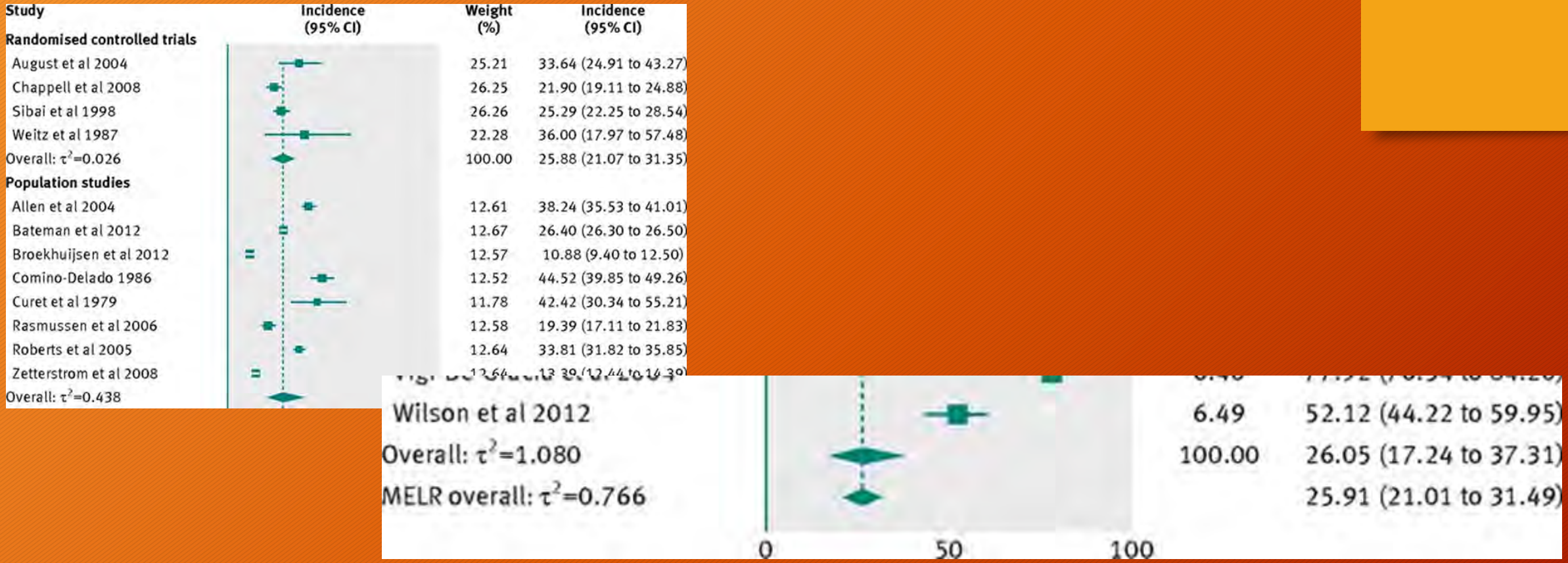
Hypertension

Cardiovascular disease

Preconception health

Typical levels of preconception exposures for young women in high-income countries (solid lines) and hypothesized optimal exposures before conception (dashed lines), with lack of evidence on exposure trajectories (grey area); adapted from Lancet 2018 Preconception health.[1]

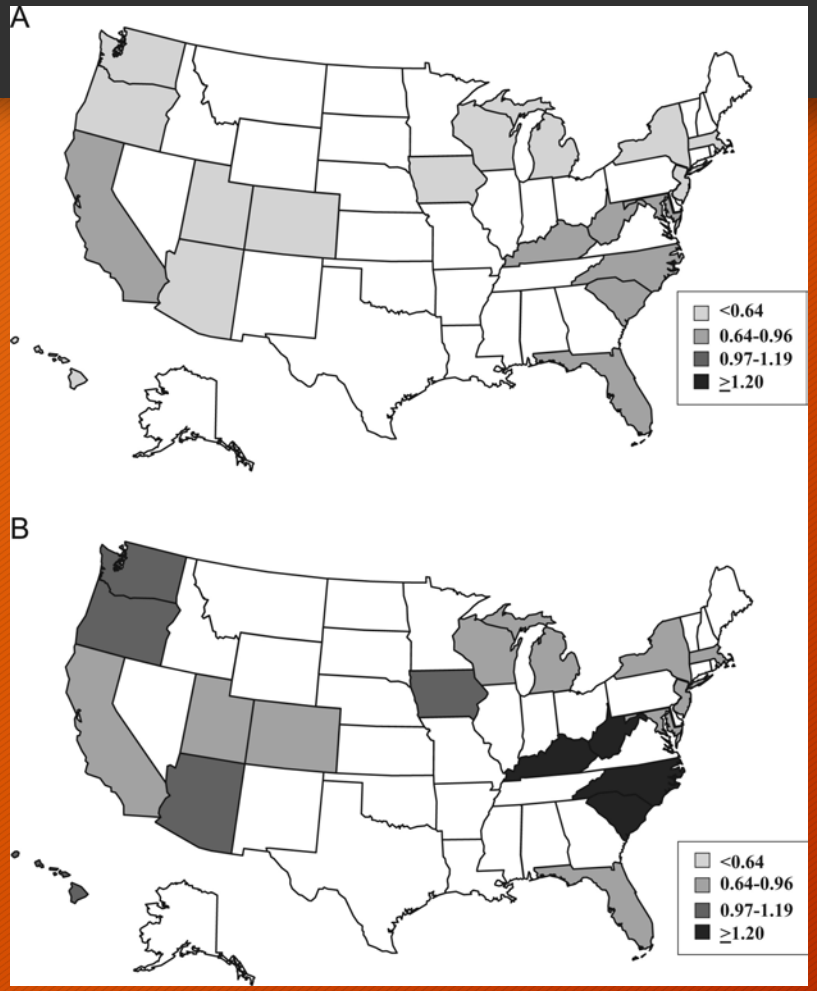
Forest plot of studies of superimposed pre-eclampsia in women with chronic hypertension stratified according to study design.



Kate Bramham et al. BMJ 2014;348:bmj.g2301

Preconception type 2 diabetes

(A) Prevalence of pre-pregnancy diabetes per 100 deliveries …2000. (B) Prevalence of pre-pregnancy diabetes per 100 deliveries … 2010.



Bardenheier BH, Imperatore G, Devlin HM, Kim SY, Cho P, Geiss LS. Trends in pre-pregnancy diabetes among deliveries in 19 U.S. states, 2000-2010. Am J Prev Med. 2015 Feb;48(2):154-161.

TABLE 2 Risk of maternal and neonatal adverse outcomes in women with type 2 diabetes compared to women without diabetes

Outcome	Type 2 diabetes (n = 138)	No diabetes (n = 27 075)	Crude OR (95% CI)	Adjusted OR (95% CI)
LGA†	28 (20.3)	2087 (7.7)	3.05 (1.99–4.67)	2.13 (1.37–3.32)
SGA†	22 (15.9)	3964 (14.7)	1.10 (0.70–1.74)	1.38 (0.87–2.20)
IOL‡	74 (53.6)	5738 (21.2)	4.30 (3.04–6.08)	4.03 (2.71–5.99)
Caesarean section‡	74 (53.6)	7116 (26.3)	3.24 (2.28–4.62)	2.10 (1.44–3.06)
Preterm birth§	31 (22.5)	2186 (8.1)	3.30 (2.16–5.04)	2.74 (1.78–4.24)
Gestational hypertension¶,‡‡	7 (5.1)	527 (2.0)	2.69 (1.26–5.77)	1.58 (0.73–3.43)
Pre-eclampsia	12 (8.7)	645 (2.4)	3.90 (2.15–7.08)	2.75 (1.49–5.10)
SCN**	98 (78.4)	4142 (15.9)	19.21 (12.50–29.52)	19.34 (12.37–30.25)
NICU‡‡	10 (7.4)	727 (2.7)	2.87 (1.50–5.47)	1.94 (0.94–4.01)
Hypoglycaemia¶,‡‡	31 (22.5)	1074 (4.0)	7.01 (4.66–10.56)	4.90 (2.79–8.61)
Jaundice‡‡	28 (20.3)	1737 (6.4)	3.71 (2.45–5.64)	2.58 (1.61–4.13)
Respiratory distress††,‡‡	10 (7.3)	1039 (3.8)	1.96 (1.03–3.71)	0.78 (0.38–1.60)
Shoulder dystocia§§	5/64 (7.8)	498/19 958 (2.5)	3.31 (1.34–8.19)	2.72 (1.09–6.78)
Apgar < 7 at five minutes‡‡,§§	5/64 (7.8)	577/19 887 (2.9)	2.83 (1.13–7.12)	0.91 (0.30–2.80)
Congenital malformation	6 (4.4)	996 (3.7)	1.19 (0.52–2.71)	1.00 (0.99–1.01)
Perinatal death	3 (2.2)	394 (1.5)	1.50 (0.48–4.75)	1.40 (0.44–4.46)

Data are presented as count (proportion), crude and adjusted odds ratios (OR) and 95% confidence interval (CI).
All outcomes are adjusted for age and BMI category (normal < 25 kg/m^2, overweight 25–29.9 kg/m^2, obese ≥ 30 kg/m^2). Additional adjustments:
†Parity, smoking, country of birth.
‡Parity, smoking, pre-eclampsia.
§Smoking, country of birth, pre-eclampsia.
¶Parity.
**Parity, smoking.
††Parity, country of birth.
‡‡Gestation at birth.
§§Apgar score < 7 at five minutes and shoulder dystocia are reported for vaginal delivery only. There was an interaction between the presence of T2D and gestational age on risk of hypoglycaemia: if born at term (8.61 (5.23–14.18)); if born preterm (1.56 (0.68–3.64)).
IOL, induction of labour; LGA, large for gestational age; NICU, neonatal intensive care unit; SCN, special care nursery; SGA, small for gestational age.

Abell SK, Boyle JA, de Courten B, Soldatos G, Wallace EM, Zoungas S, Teede HJ. Impact of type 2 diabetes, obesity and glycaemic control on pregnancy outcomes. Aust N Z J Obstet Gynaecol. 2017 Jun;57(3):308-314.

Treatment effects

Blood pressure control in hypertension

- Preconception care offers the option of lifestyle counseling and comorbidity and end-organ assessment
- Ideally hypertension should be controlled before conception to avoid severe hypertension
  - May be concerns about medication side effects
  - Severe hypertension should be avoided but tight control does not necessarily improve outcomes

Glycemic control in diabetes

- Preconception care reduces the risk of
  - Congenital anomalies
  - Perinatal mortality
  - Preterm delivery

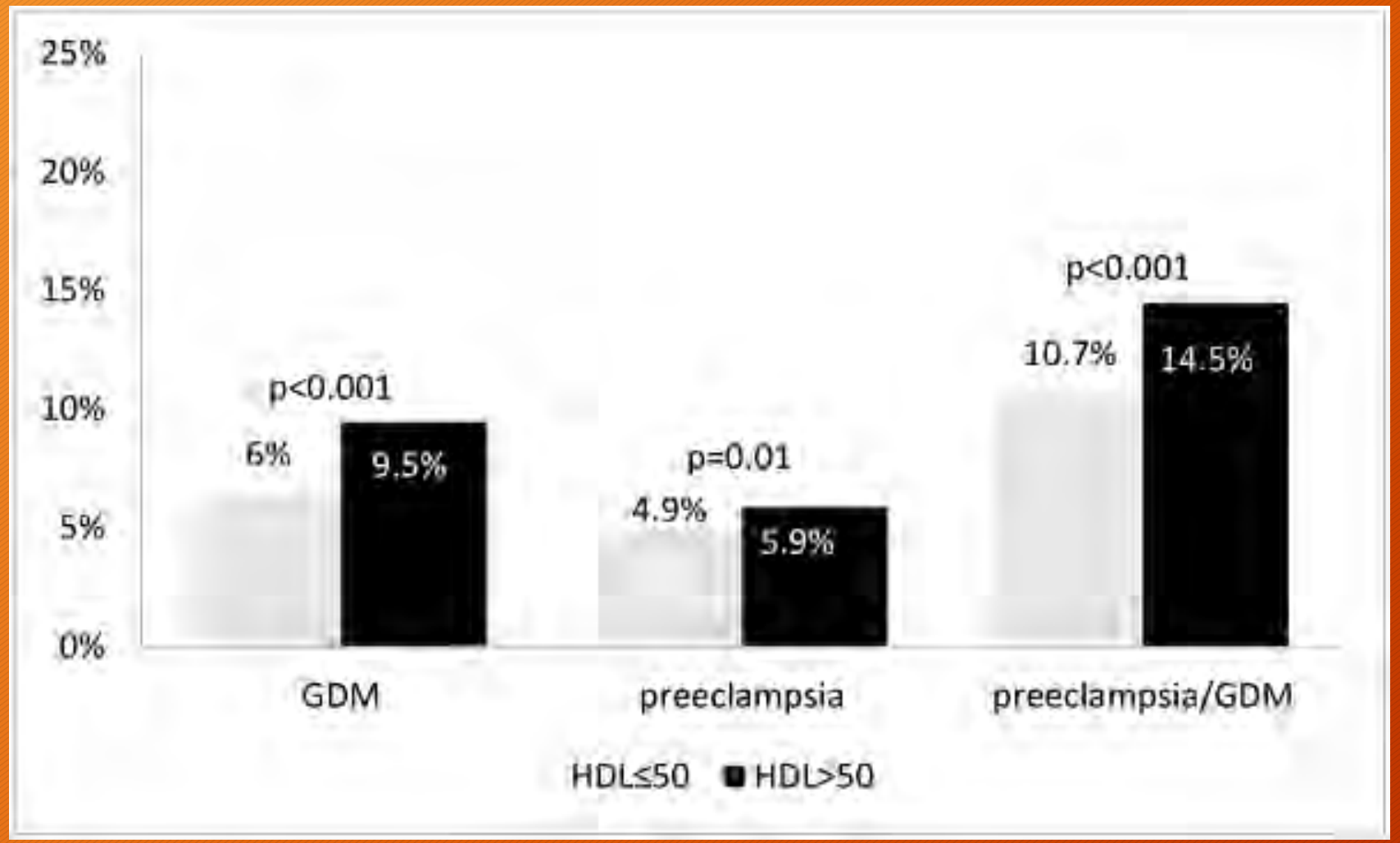
Non-clinical preconception cardiovascular health

	Gestational Diabetes		Pre-eclampsia	
	RR	95% CI	RR	(95% CI)
Cholesterol	1.51	(1.01, 2.25)	1.52	(0.87-2.66)
LDL-c	1.44	(1.00, 2.07)	1.22	(0.65-2.30)
Triglycerides	1.68	(1.25, 2.25)	1.70	(1.08-2.65)
Systolic blood pressure	1.06	(0.75, 1.50)	1.28	(0.71-2.29)
Diastolic blood pressure	1.12	(0.81, 1.55)	0.64	(0.22-1.87)

Harville et al. 2011

Cardiovascular Risk in Young Finns

Outcome rates in patients with triglyceride level above and below 150 mg/dL.



All deliveries in a medical center in Southern Israel

Baumfeld Y, Novack L, Wiznitzer A, Sheiner E, Henkin Y, et al. (2015) Pre Conception Dyslipidemia Is Associated with Development of Preeclampsia and Gestational Diabetes Mellitus. PLOS ONE 10(10): e0139164. https://doi.org/10.1371/journal.pone.0139164
https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0139164

PLOS ONE

Physical fitness and GDM

TABLE 2. Associations of baseline fitness with risk of gestational diabetes, the CARDIA study (1985–2011).

	Cardiorespiratory Fitness (METs)									
	Continuous[a]			Low ≤ 8.3		Intermediate 8.4–10.6		High ≥10.7		
Fitness Models	*n*	OR (95% CI)	*P*	*n*	OR (95% CI)	*n*	OR (95% CI)	*n*	OR (95% CI)	P_{trend}
Model 1	1333	0.78 (0.66–0.91)	**0.001**	204	1.00 (Ref)	523	0.63 (0.40–0.98)	606	0.52 (0.34–0.81)	**0.007**
Model 2	1274	0.72 (0.61–0.86)	**<0.001**	188	1.00 (Ref)	500	0.65 (0.41–1.05)	586	0.48 (0.29–0.80)	**0.005**
Model 3	1269	0.79 (0.65–0.95)	**0.013**	188	1.00 (Ref)	499	0.85 (0.51–1.42)	582	0.70 (0.39–1.25)	0.210
Model 4	1248	0.79 (0.65–0.96)	**0.017**	184	1.00 (Ref)	485	0.93 (0.54–1.57)	579	0.74 (0.41–1.35)	0.263

Model 1 is the unadjusted association. Model 2 is adjusted for center, time from baseline to delivery, race, age, parity, education, family history of diabetes, smoking, alcohol, and dietary fat. Model 3 is additionally adjusted for waist circumference. Model 4 is additionally adjusted for HOMA-IR and HDL-C. Bolded values are statistically significant ($P < 0.05$).
[a]Continuous models expressed per 1 SD of fitness (2.3 METs).

Whitaker et al., 2018

Subclinical risk factors and birth outcomes

Associations of Prepregnancy Cardiovascular Risk Factors with the Offspring's Birth Weight

Pål R. Romundstad[1], George Davey Smith[2], Tom I. L. Nilsen[1], and Lars J. Vatten[1]

[1] Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway.
[2] Department of Social Medicine, University of Bristol, Bristol, United Kingdom.

Received for publication May 22, 2007; accepted for publication August 22, 2007.

Low birth weight of offspring has been associated with increased risk of maternal cardiovascular mortality, and cardiovascular risk factors measured within pregnancy have been related to offspring birth weight. It is not clear whether cardiovascular risk factors assessed prior to pregnancy are associated with the offspring's birth weight. The authors combined baseline data from 3,461 women in the HUNT Study (1995–1997) and data on deliveries from the Medical Birth Registry of Norway up to 2005. They used linear regression to prospectively study associations between diastolic and systolic blood pressures, concentrations of triglycerides, serum total cholesterol, and high density lipoprotein cholesterol measured before conception and birth weight for gestational age of the offspring. Blood pressure measured before pregnancy was inversely associated with birth weight for gestational age, whereas unfavorable levels of serum total cholesterol, high density lipoprotein cholesterol, triglycerides, and glucose were positively associated with birth weight for gestational age. Thus, women with relatively high blood pressure tend to deliver small babies, whereas women with unfavorable lipid levels tend to give birth to large babies, suggesting reduced glucose tolerance. These findings suggest that low as well as high birth weight of the offspring may indicate increased cardiovascular risk for the mother.

Preconception cardiovascular health

TABLE 2. ORs for quartiles of plasma lipids according to PTB status; referent are women with term births (n = 792)

Prepregnancy lipid concentration	Crude analysis		Adjusted analysis[a]		Excluding women with hypertension in pregnancy[a]	
	34 to <37 wk (n = 146)	<34 wk (n = 72)	34 to <37 wk (n = 146)	<34 wk (n = 72)	34 to <37 wk (n = 103)	<34 wk (n = 51)
Total cholesterol (mg/dl)						
Quartile 4 (196–318)	1.48 (0.88, 2.51)	2.43 (1.08, 5.46)	1.38 (0.80, 2.36)	2.21 (0.97, 5.05)	1.55 (0.82, 2.93)	3.80 (1.21, 11.96)
Quartile 3 (173–195)	1.36 (0.80, 2.32)	2.24 (0.99, 5.06)	1.30 (0.75, 2.23)	2.11 (0.92, 4.85)	1.57 (0.84, 2.94)	3.53 (1.12, 11.18)
Quartile 2 (156–172)	Referent	Referent	Referent	Referent	Referent	Referent
Quartile 1 (94–155)	1.83 (1.09, 3.06)	3.10 (1.41, 6.85)	1.86 (1.10, 3.15)	3.04 (1.35, 6.81)	1.66 (0.89, 3.09)	5.02 (1.66, 15.16)
LDL cholesterol (mg/dl)						
Quartile 4 (124–233)	1.21 (0.72, 2.02)	0.95 (0.47, 1.94)	1.07 (0.63, 1.83)	0.86 (0.41, 1.78)	1.30 (0.70, 2.41)	0.96 (0.39, 2.36)
Quartile 3 (105–123)	1.02 (0.60, 1.73)	1.13 (0.57, 2.21)	0.96 (0.56, 1.66)	1.03 (0.52, 2.07)	1.05 (0.56, 1.98)	1.34 (0.59, 3.02)
Quartile 2 (89–104)	Referent	Referent	Referent	Referent	Referent	Referent
Quartile 1 (26–88)	1.50 (0.91, 2.48)	1.16 (0.58, 2.30)	1.60 (0.96, 2.68)	1.17 (0.58, 2.37)	1.40 (0.77, 2.54)	1.16 (0.50, 2.67)
Triglycerides (mg/dl)						
Quartile 4 (78–318)	0.88 (0.53, 1.46)	0.81 (0.39, 1.69)	0.99 (0.58, 1.67)	1.03 (0.48, 2.20)	1.02 (0.53, 1.94)	0.68 (0.27, 1.71)
Quartile 3 (58–77)	0.99 (0.60, 1.62)	1.10 (0.56, 2.18)	1.05 (0.63, 1.75)	1.22 (0.61, 2.47)	1.41 (0.77, 2.58)	1.09 (0.49, 2.42)
Quartile 2 (44–57)	Referent	Referent	Referent	Referent	Referent	Referent
Quartile 1 (16–43)	1.16 (0.71, 1.89)	1.42 (0.73, 2.76)	1.13 (0.68, 1.88)	1.30 (0.66, 2.58)	1.44 (0.78, 2.67)	1.19 (0.54, 2.60)
HDL cholesterol (mg/dl)						
Quartile 4 (64–118)	1.39 (0.86, 2.24)	1.27 (0.66, 2.45)	1.52 (0.92, 2.49)	1.36 (0.69, 2.70)	1.32 (0.76, 2.30)	1.29 (0.58, 2.89)
Quartile 3 (55–63)	0.90 (0.54, 1.52)	0.93 (0.46, 1.88)	0.95 (0.56, 1.62)	0.99 (0.48, 2.04)	0.72 (0.39, 1.36)	1.00 (0.42, 2.36)
Quartile 2 (47–54)	Referent	Referent	Referent	Referent	Referent	Referent
Quartile 1 (25–46)	1.06 (0.64, 1.77)	1.09 (0.55, 2.19)	1.05 (0.62, 1.79)	1.31 (0.64, 2.69)	0.98 (0.53, 1.82)	1.62 (0.70, 3.75)

[a] Adjusted for race, parity, BMI, physical activity at baseline, age at selected birth, ever gestational hypertension or preeclampsia during follow-up, time interval from baseline measurement to selected birth.

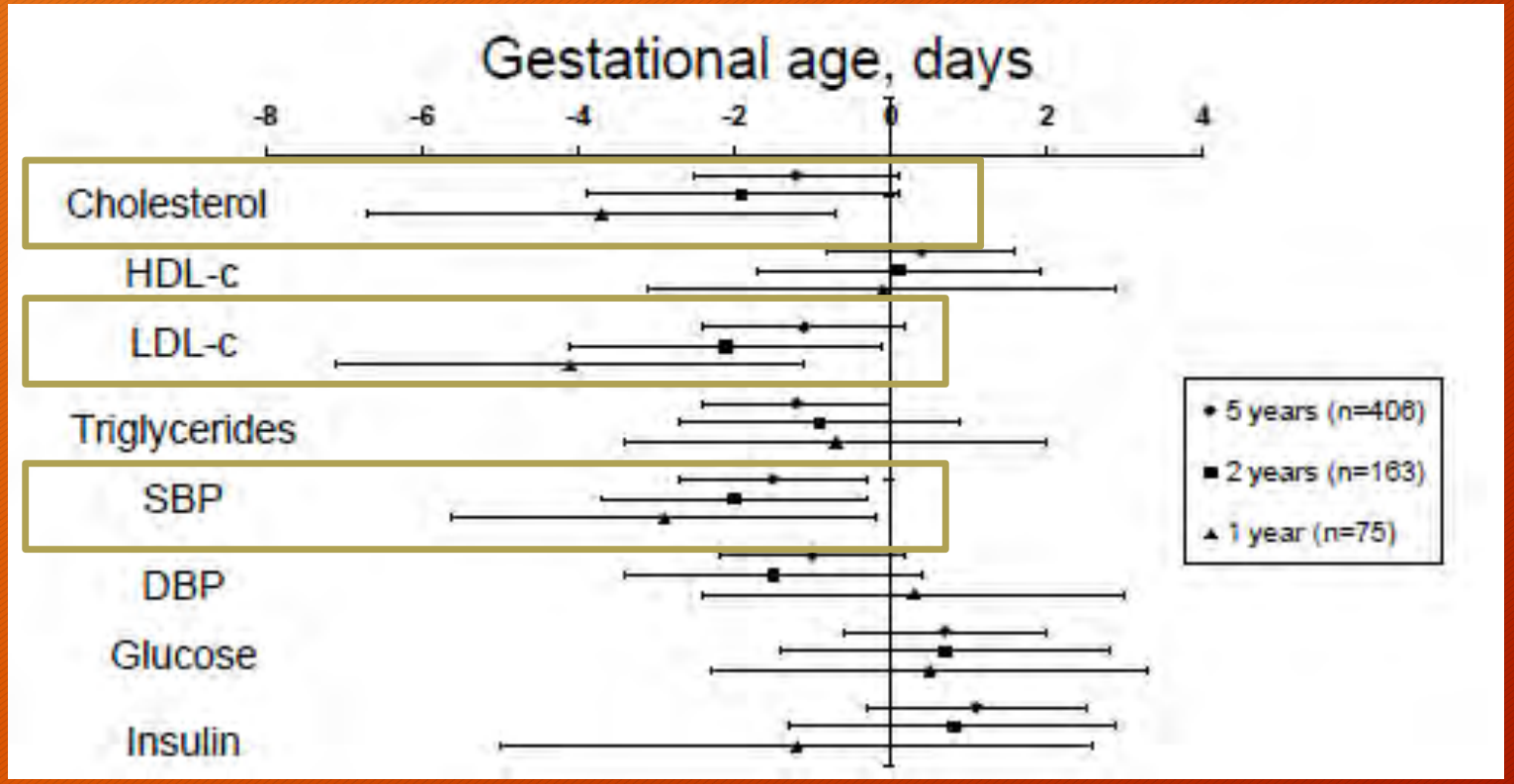
CARDIA study, US

Catov et al., 2010

Time relative to pregnancy

	PTB	LBW
	RR (95% CI)	RR (95% CI)
Systolic blood pressure	1.28 (1.05-1.57)	1.31 (0.97-1.76)
Diastolic blood pressure	1.19 (0.94-1.53)	1.14 (0.80-1.63)

Per 1 SD unit



Cardiovascular Risk in Young Finns Study

Harville et al, 2011

Pregnancy is also a window to later-life health

Poorer health at birth

Low birthweight

Reduced fetal growth

Poorer cardiovascular health

Preconception hypertension

Preconception diabetes

Poorer health during pregnancy

Gestational hypertension

Gestational diabetes

Pre eclampsia

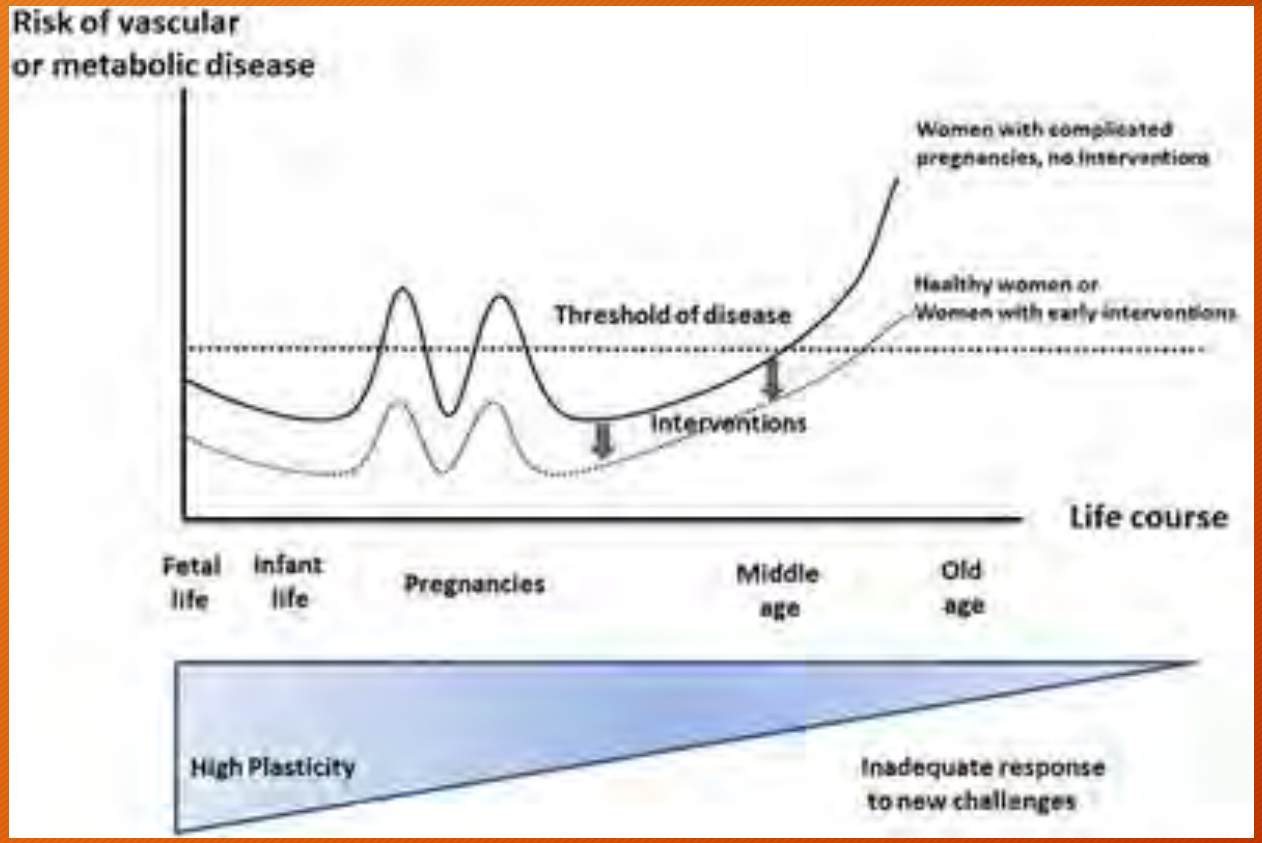
Poorer health later in life

Diabetes

Hypertension

Cardiovascular disease

Pregnancy as a window to future health



https://www.frontiersin.org/articles/10.3389/fped.2017.00069/full

Association Between a History of Hypertensive Disorder of Pregnancy or Gestational Diabetes Mellitus and Diagnosis of Hypertension and Hypercholesterolemia

Outcome	Model I	Model II	Model III
Hypertensive disorder of pregnancy			
Hypertension (n=2935)	2.04 (1.91–2.18)	2.12 (1.97–2.27)	2.12 (1.98–2.28)
Hypercholesterolemia (n=2070)	1.01 (0.94–1.08)	1.05 (0.97–1.12)	1.00 (0.93–1.08)
Gestational diabetes mellitus			
Hypertension (n=367)	0.87 (0.69–1.09)	0.91 (0.73–1.14)	0.83 (0.66–1.05)
Hypercholesterolemia (n=308)	0.92 (0.75–1.15)	1.04 (0.83–1.31)	1.05 (0.84–1.32)

Results obtained with multivariable logistic regression models and expressed as odds ratios with corresponding 95% confidence intervals. Model I: adjustment for cohort and gestational diabetes mellitus (only for hypertensive disorder of pregnancy outcomes) or hypertensive disorder of pregnancy (only for gestational diabetes mellitus outcomes). Model II: additional adjustment for age, BMI, current smoking, and current alcohol consumption at study enrollment. Model III: additional adjustment for history of myocardial infarction and stroke, prevalent diabetes mellitus, total cholesterol/HDL ratio (only for hypertension outcome), and hypertension (only for hypercholesterolemia outcome) at study enrollment. BMI indicates body mass index; and HDL, high-density-lipoprotein.

22 265 ever-pregnant women from the European Prospective Investigation into Cancer and Nutrition-NL study, aged 20 to 70 years at baseline (mean age 51-55)

Earlier Age of Onset of Chronic Hypertension and Type 2 Diabetes Mellitus After a Hypertensive Disorder of Pregnancy or Gestational Diabetes Mellitus.
Heida, Karst; Franx, Arie; van Rijn, Bas; Eijkemans, Marinus; Boer, Jolanda; Verschuren, Monique; Oudijk, Martijn; Bots, Michiel; van der Schouw, Yvonne

Hypertension. 66(6):1116-1122, December 2015.
DOI: 10.1161/HYPERTENSIONAHA.115.06005

Association Between History of Hypertensive Disorder of Pregnancy or Gestational Diabetes Mellitus and Cardiovascular Events and T2D After Follow-Up

Outcome	Events n/N	Model I	Model II	Model III
Hypertensive disorder of pregnancy				
CVD	810/2557	1.22 (1.11–1.33)	1.21 (1.10–1.32)	1.09 (1.00–1.20)
IHD	496/1478	1.29 (1.15–1.45)	1.28 (1.14–1.44)	1.16 (1.03–1.30)
Stroke	231/720	1.26 (1.07–1.49)	1.26 (1.06–1.48)	1.11 (0.94–1.32)
T2D	396/1089	1.44 (1.26–1.65)	1.27 (1.11–1.46)	1.11 (0.97–1.28)
Gestational diabetes mellitus				
CVD	104/2557	1.12 (0.85–1.49)	1.07 (0.81–1.42)	1.04 (0.78–1.38)
IHD	70/1478	1.25 (0.87–1.79)	1.21 (0.84–1.73)	1.14 (0.79–1.65)
Stroke	24/720	1.08 (0.62–1.88)	1.04 (0.60–1.82)	1.04 (0.59–1.82)
T2D	121/1089	3.82 (2.92–5.00)	3.58 (2.72–4.73)	3.68 (2.77–4.90)

Results obtained with Cox proportional hazard models and expressed as hazards ratios with corresponding 95% confidence intervals. The not exposed group was used as reference. Model I: adjustment for cohort and gestational diabetes mellitus (only for hypertensive disorder of pregnancy outcomes) or hypertensive disorder of pregnancy (only for gestational diabetes mellitus outcomes). Model II: additional adjustment for age, BMI, current smoking, and current alcohol consumption at study enrollment. Model III: additional adjustment for total cholesterol/HDL ratio, prevalent hypertension at study enrollment, and T2D (only for CVD, IHD, and stroke outcome). BMI indicates body mass index; CVD, cardiovascular disease; HDL, high-density lipoprotein; IHD, ischemic heart disease; n, number of events in the exposed group; N, total number of events in this cohort; and T2D, type 2 diabetes mellitus.

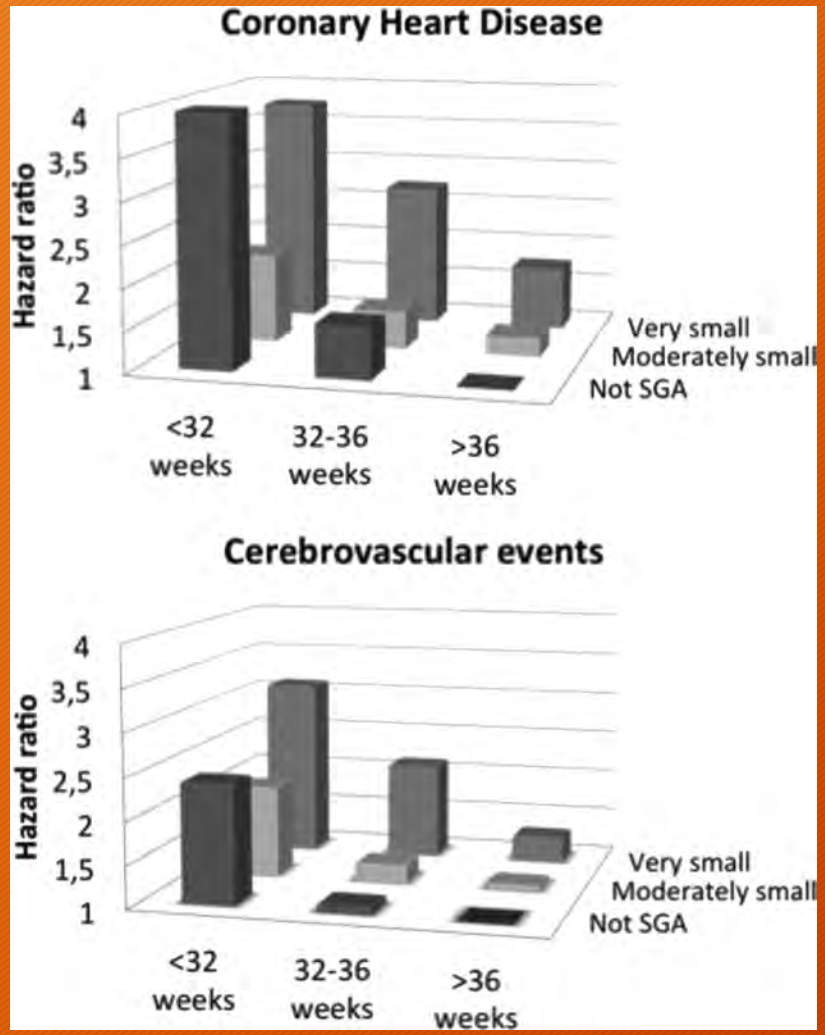
Follow-up until event or 9-15 years

Women with a history of HDP were diagnosed with hypertension 7.7 years earlier since first pregnancy (95% CI 6.9-8.5) without such history

Women with GDM were diagnosed with T2D 7.7 years earlier (95% CI 5.8-9.6) than women without such history

Earlier Age of Onset of Chronic Hypertension and Type 2 Diabetes Mellitus After a Hypertensive Disorder of Pregnancy or Gestational Diabetes Mellitus.
Heida, Karst; Franx, Arie; van Rijn, Bas; Eijkemans, Marinus; Boer, Jolanda; Verschuren, Monique; Oudijk, Martijn; Bots, Michiel; van der Schouw, Yvonne

Hypertension. 66(6):1116-1122, December 2015.
DOI: 10.1161/HYPERTENSIONAHA.115.06005



923686 Swedish women, 1983-2005

Birth Characteristics and Subsequent Risks of Maternal Cardiovascular Disease, Volume: 124, Issue: 25, Pages: 2839-2846, DOI: (10.1161/CIRCULATIONAHA.111.034884)

Experiencing multiple pregnancy complications is associated with a greater risk of cardiovascular disease, beyond single complications

Cirillo PM, Cohn BA. Pregnancy complications and cardiovascular disease death: 50-year follow-up of the Child Health and Development Studies pregnancy cohort. Circulation. 2015 Sep 29;132(13): 1234-42.

Table 2. Associations of Paired Pregnancy Complications With CVD Risk

Combinations of pregnancy complications*	HR	95% CI	
		Lower	Upper
SGA + preterm delivery	2.6	1.06	6.20
Gestational hypertension + hemoglobin decline	2.8	1.15	6.92
Preeclampsia† + SGA‡	3.7	1.12	12.10
Preterm delivery (weeks 35–36) + hemorrhage	3.9	1.63	9.56
SGA + preexisting hypertension	4.8	1.78	12.91
Gestational hypertension + preterm delivery‡	5.0	2.64	9.60
Preeclampsia† + preexisting hypertension	5.6	2.09	15.18
Preterm delivery + preexisting hypertension	7.1	3.49	14.55

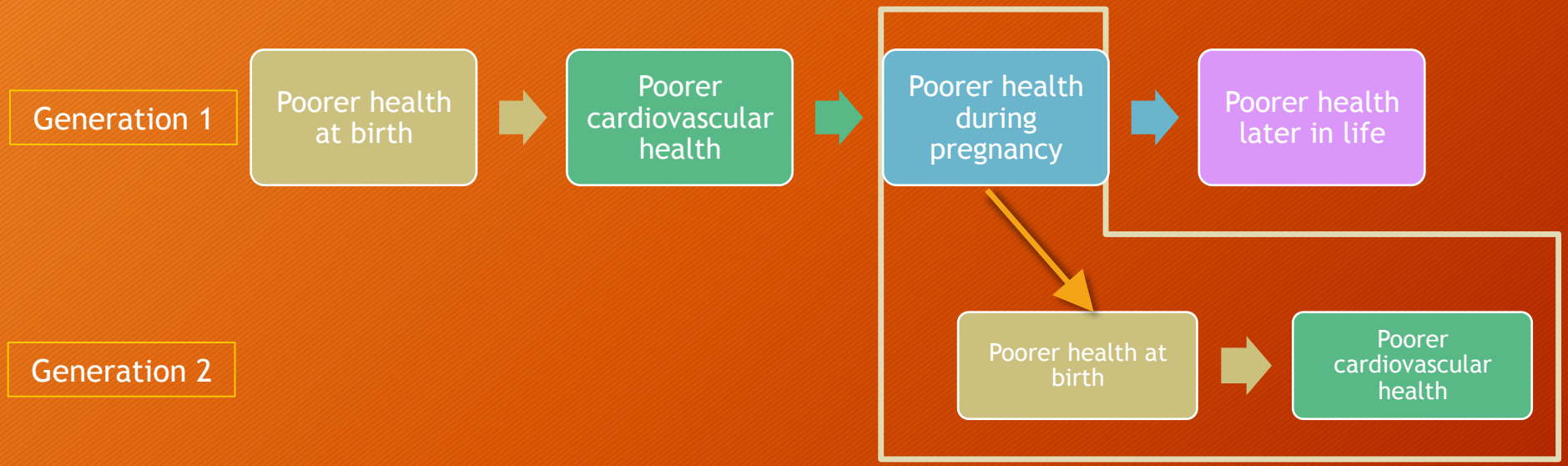
95% CI indicates 95% confidence interval (lower limit, upper limit); HR, hazard ratio; and SGA, small for gestational age.

*Risk was estimated for each combination of pregnancy complications separately by using a competing risks proportional hazards model. To avoid collinearity between paired pregnancy events, mutually exclusive dummy variables were included in each model. With the use of the first combination, SGA + preterm delivery as an example, 3 dummy variables were created to represent the following nonoverlapping scenarios: (1) SGA only and not preterm delivery, (2) preterm delivery only and not SGA, and (3) SGA plus preterm delivery combined. The association for the co-occurrence of both events is tabled here. Models were adjusted for age, race, and parity at the study pregnancy. Age is represented continuously. Parity is represented by using 2 dummy variables for primiparas and multiparas with ≥3 previous live births vs else.

†Early- and late-onset preeclampsia were combined to maximize power for investigating the risk of preeclampsia co-occurring with other pregnancy events.

‡Co-occurring events involving preeclampsia, and preterm and SGA delivery were tested for age dependence. Only the co-occurrence of gestational hypertension with preterm delivery and of preeclampsia with SGA were significantly age-dependent (P=0.0119 and P=0.0018, respectively). The hazard ratios for these paired events are estimated at 60 years of age for co-occurring gestational hypertension with preterm delivery, and at 55 years of age for co-occurring preeclampsia with SGA delivery.

Cardiovascular and reproductive health are linked



Offspring of hypertensive pregnancies

Table 5. Associations of Hypertensive Disorders of Pregnancy With Offspring BP (n=3876 With Complete Data on any Variable Included in Any Model)

	No Hypertensive Disorder of Pregnancy (n=5082)	Gestational Hypertension (n=1065)			Preeclampsia (n=196)		
		Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
SBP, mm Hg	Reference	3.17 (2.50–3.85)	2.04 (1.42–2.67)	2.50 (1.80–3.20)	2.23 (0.78–3.67)	2.05 (0.72–3.38)	1.13 (−0.35–2.60)
DBP, mm Hg	Reference	1.47 (1.00–1.94)	1.07 (0.60–1.54)	1.25 (0.76–1.73)	0.96 (−0.06–1.97)	1.00 (−0.01–2.01)	0.65 (−0.38–1.69)

Values are regression coefficients (95% CIs) and reflect the difference in offspring characteristic for maternal hypertensive disorder of pregnancy (ie, in this table, hypertensive disorder of pregnancy is the exposure, and offspring blood pressure (BP) the outcomes). Model 1, adjusted for offspring sex and age at the 9-year visit. Model 2, additionally adjusted for maternal age at delivery, parental prepregnancy BMI, parity, social class, and maternal smoking during pregnancy, plus offspring weight, height, and height squared at the 9-year visit (the confounder-adjusted model). Model 3, additionally adjusted for mode of delivery, gestational age at birth, and birth weight (to examine mediation by these determinants).

Geelhoed JJ, Fraser A, Tilling K, Benfield L, Davey Smith G, Sattar N, Nelson SM, Lawlor DA. Preeclampsia and gestational hypertension are associated with childhood blood pressure independently of family adiposity measures: the Avon Longitudinal Study of Parents and Children. Circulation. 2010 Sep 21;122(12):1192-9.

Offspring of hypertensive pregnancies

Table 2. Hospital Admissions or Deaths From Coronary Heart Disease and Stroke and the Occurrence of Hypertension Among Offspring Born at ≥37 Weeks of Gestation From Pregnancies Complicated by Gestational Hypertension or Pre-Eclampsia

		Gestational Hypertension (n=1592)				Pre-Eclampsia, Nonsevere (n=120)				Severe Pre-Eclampsia (n=164)			
Cardiovascular Outcome	All (n=6410) N of Cases	N of Cases	Relative Risk*	95% CI	*P*	N of Cases	Relative Risk*	95% CI	*P*	N of Cases	Relative Risk*	95% CI	*P*
Coronary heart disease	464	117	1.0	0.8–1.3	0.8	12	1.3	0.7–2.3	0.4	15	1.5	0.9–2.6	0.1
Stroke	272	81	1.4	1.0–1.8	0.03	8	1.8	0.9–3.7	0.1	11	2.2	1.2–4.1	0.01
Hemorrhagic	84	25	1.3	0.8–2.2	0.3	4	3.2	1.1–9.1	0.03	2	1.4	0.3–5.7	0.7
Thrombotic	173	55	1.5	1.1–2.2	0.02	4	1.4	0.5–3.8	0.5	8	2.5	1.2–5.2	0.01
Hypertension	1275	356	1.3	1.1–1.5	0.002	24	0.9	0.6–1.5	0.7	44	1.5	1.1–2.3	0.03

*Hazard ratios (adjusted for sex) for coronary heart disease and stroke; ORs (adjusted for sex and age) for hypertension using normotensive pregnancies as the comparison group.

Followed to age ~65-75

Kajantie E, Eriksson JG, Osmond C, Thornburg K, Barker DJ. Pre-eclampsia is associated with increased risk of stroke in the adult offspring: the Helsinki birth cohort study. Stroke. 2009 Apr;40(4):1176-80.

Offspring of gestational diabetes pregnancies

Clausen et al. [31]	GDM and type 1 diabetes	168 offspring of women with diet-treated GDM; 160 offspring of women with type 1 diabetes; 128 offspring from background population	~22 years	Two-fold risk of overweight in offspring of women with diet-treated GDM or type 1 diabetes compared with a background population, and the risk of metabolic syndrome was 4 and 2.5 times higher, respectively
Clausen et al. [33]	GDM and type 1 diabetes	168 offspring of women with diet-treated GDM; 160 offspring of women with type 1 diabetes; 128 offspring from a background population	~27 years	Adjusted ORs for type 2 diabetes or prediabetes (impaired glucose tolerance or impaired fasting glucose) of 7.76 (95% CI 2.58–23.39) in offspring of diet-treated GDM women, and 4.02 (95% CI 1.31–12.33) in offspring of type 1 diabetic women, by comparison with offspring from a background population

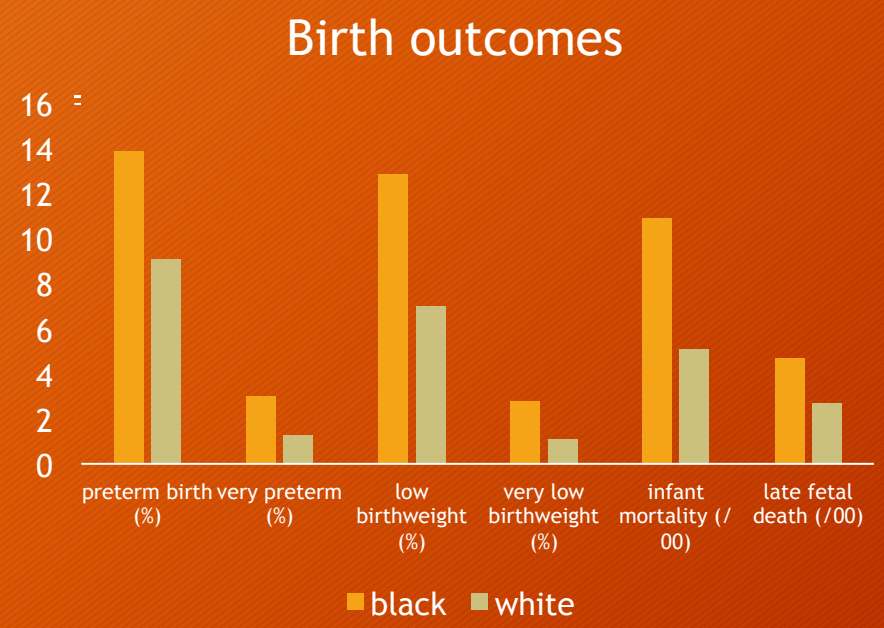
Burlina S, Dalfrà MG, Lapolla A. Short- and long-term consequences for offspring exposed to maternal diabetes: a review. J Matern Fetal Neonatal Med. 2019 Feb;32(4):687-694.

Adverse perinatal and cardiovascular outcomes take a particularly hard toll on vulnerable communities

Racial disparities

Generation 1

Poorer health at birth → Poorer cardiovascular health → Poorer health during pregnancy → Poorer health later in life

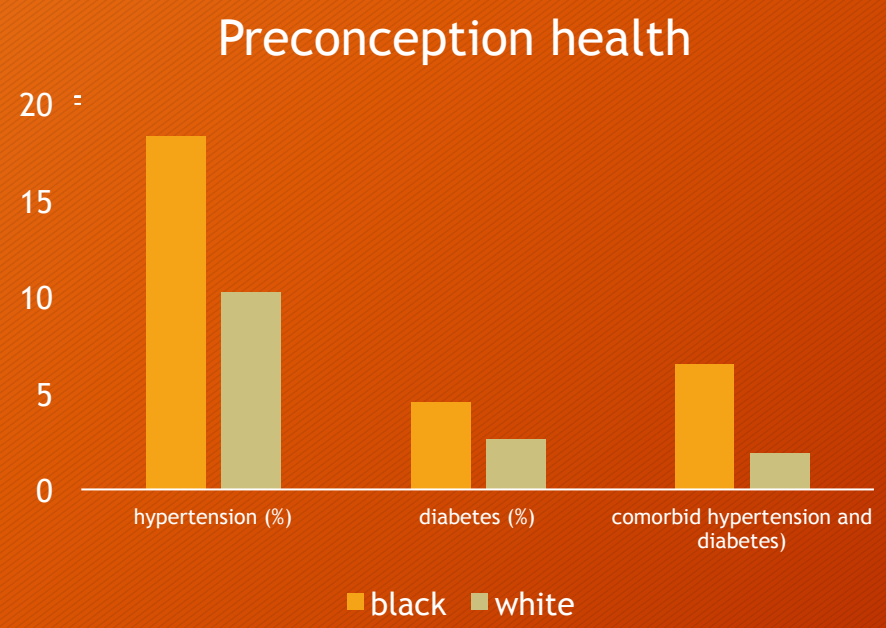


March of Dimes

Racial disparities

Generation 1

Poorer health at birth → Poorer cardiovascular health → Poorer health during pregnancy → Poorer health later in life

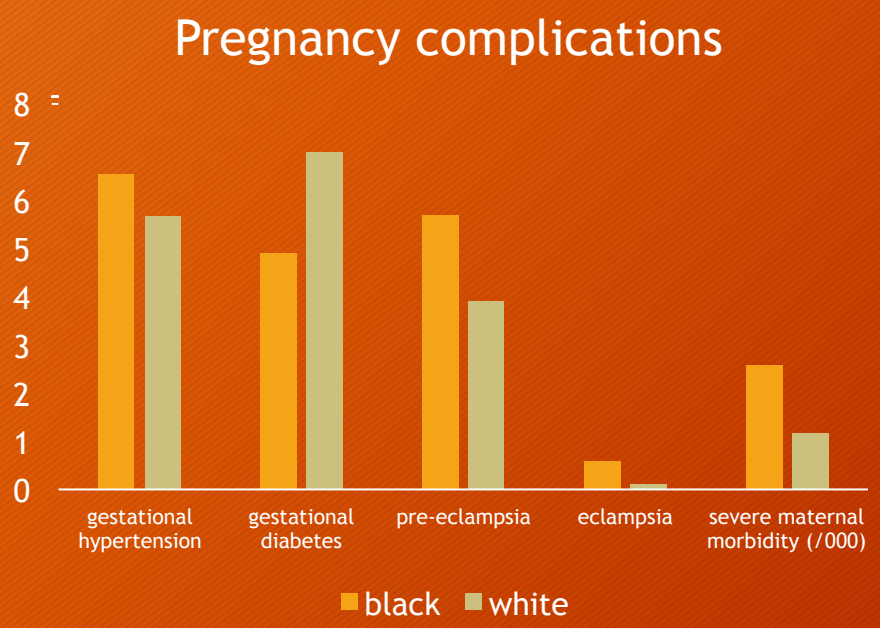


MMWR

Racial disparities

Generation 1

Poorer health at birth → Poorer cardiovascular health → Poorer health during pregnancy → Poorer health later in life

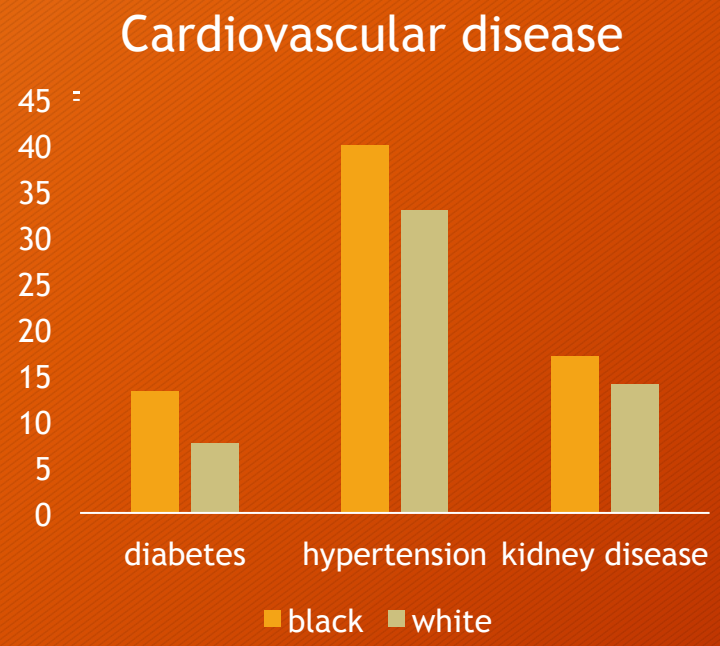


National Inpatient Sample, AHRQ, CA birth certificates, national birth cohort data

Racial disparities

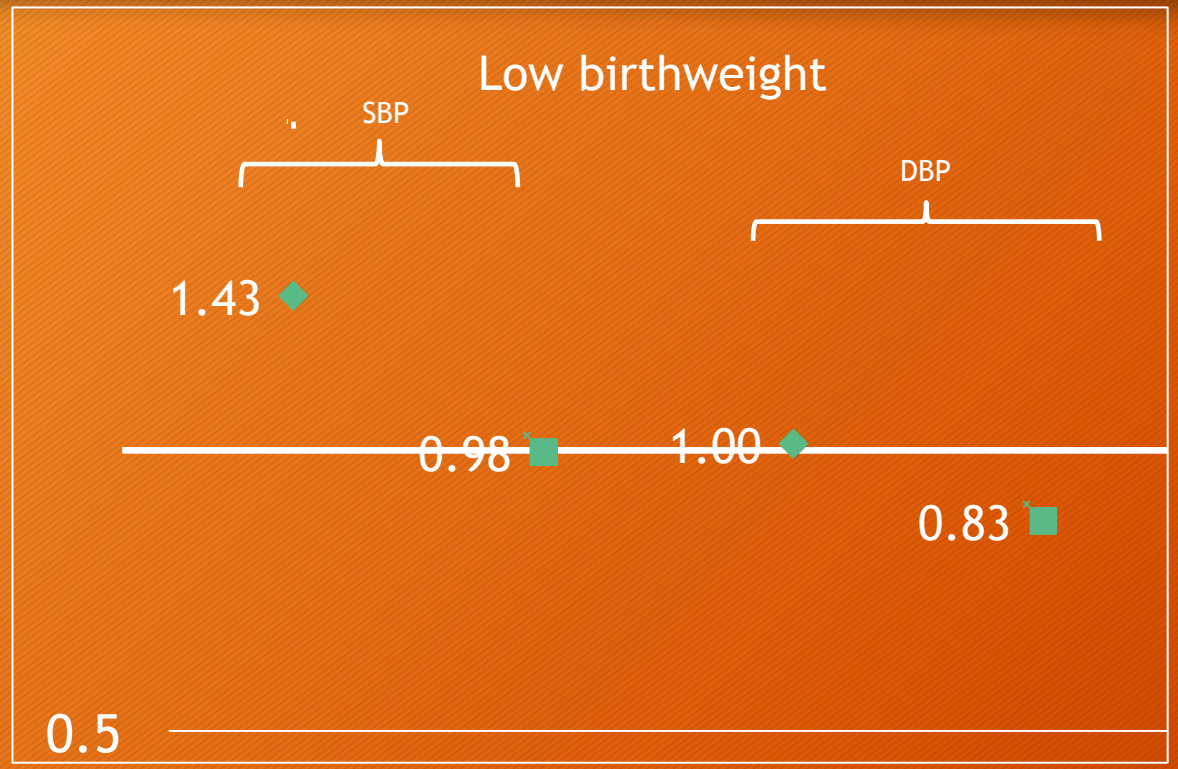
Generation 1

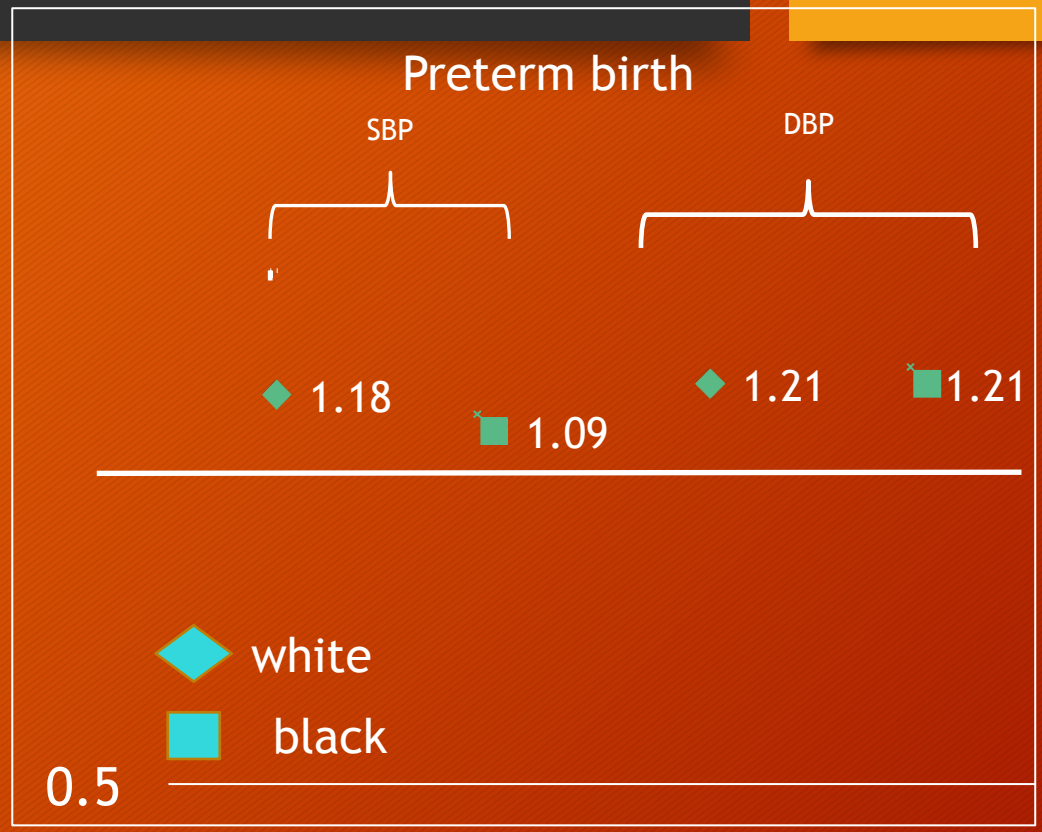
Poorer health at birth → Poorer cardiovascular health → Poorer health during pregnancy → Poorer health later in life



CDC, NIDDK

Racial differences – The Bogalusa Heart Study

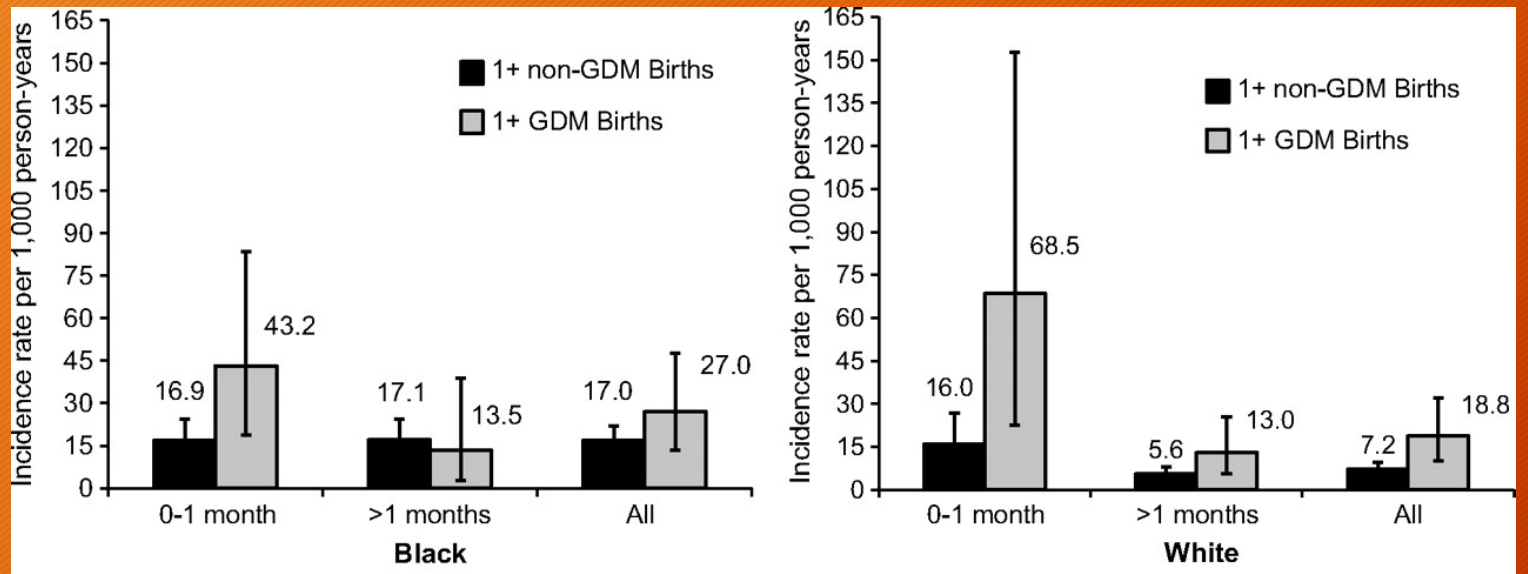




adjusted for cigarettes, Kotelchuck index, maternal education, parity, mother's age at child's birth, year of birth, BMI at last screening, and time (in years) between screening and birth

Harville et al., 2018

Crude incidence rates (95% CIs) of the metabolic syndrome during 20 years of follow-up for lactation categories by GDM status (1986–2006) and race (black and white).



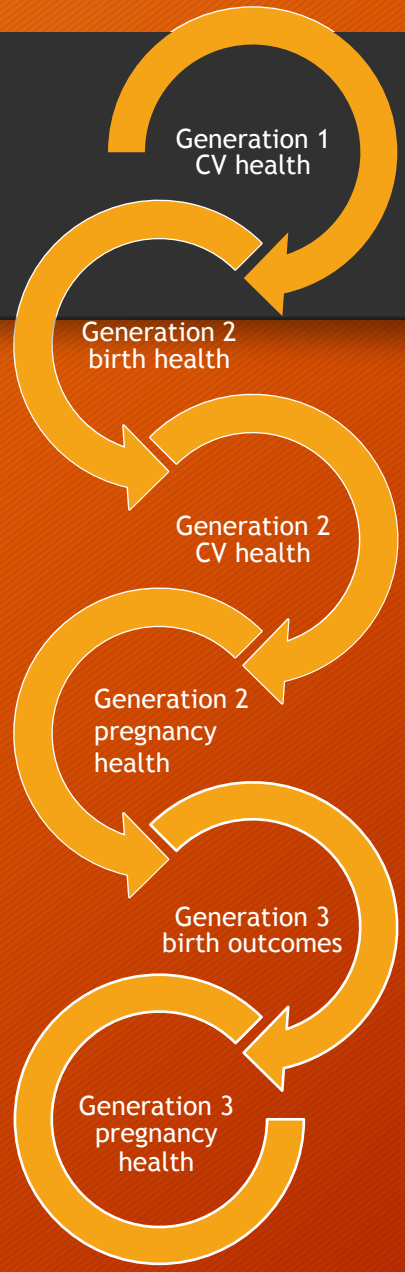
Race	Non-GDM		GDM	
	Duration of Lactation		Duration of Lactation	
	0-1 month	>1 months	0-1 month	>1 months
Black				
Cases, n	26	30	8	3
Person-yrs	1667	1,699	185	223
White				
Cases, n	14	27	4	8
Person-yrs	860	4,727	58	574
All				
Cases, n	40	57	12	11
Person-yrs	2,527	6.426	243	797

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

American Diabetes Association

Transgenerational effects

Why transgenerational effects?



Traditional genetic mechanisms explain only a small proportion of the familial clustering of obesity and cardiovascular disease

"The CAD loci with the strongest genetic effects, such as *SLC22A3-LPAL2-LPA* and chromosome 9p21, still only confer a 20–37% increased risk and the vast majority of the loci modulate risk by 10% or less. Furthermore, the ~60 loci for CAD collectively explain <20% of the heritability, raising the question of where to search for the remaining genetic risk."

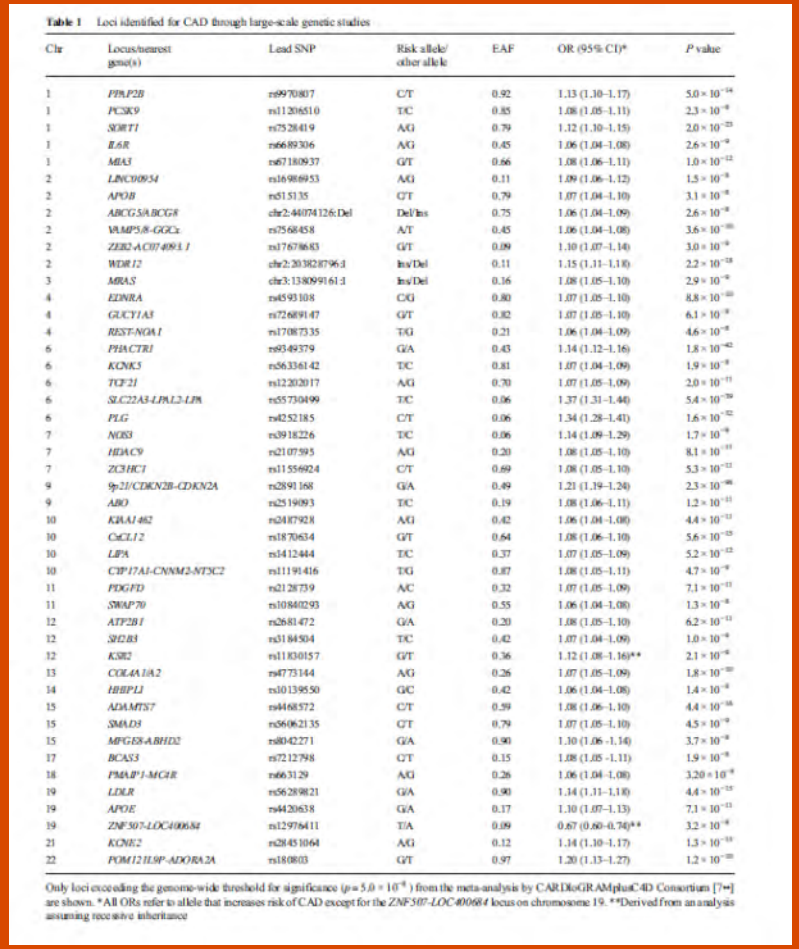


Table 1 Loci identified for CAD through large-scale genetic studies

Chr	Locus/nearest gene(s)	Lead SNP	Risk allele/ other allele	EAF	OR (95% CI)*	*P* value
1	*PBLP2B*	rs9970807	C/T	0.92	1.13 (1.10–1.17)	5.0×10^{-14}
1	*PCSK9*	rs11206510	T/C	0.85	1.08 (1.05–1.11)	2.3×10^{-8}
1	*SORT1*	rs7528419	A/G	0.79	1.12 (1.10–1.15)	2.0×10^{-23}
1	*IL6R*	rs6689306	A/G	0.45	1.06 (1.04–1.08)	2.6×10^{-9}
1	*MIA3*	rs67180937	G/T	0.66	1.08 (1.06–1.11)	1.0×10^{-12}
2	*LINC00954*	rs16986953	A/G	0.11	1.09 (1.06–1.12)	1.5×10^{-8}
2	*APOB*	rs515135	C/T	0.79	1.07 (1.04–1.10)	3.1×10^{-8}
2	*ABCG5/ABCG8*	chr2:44074126:Del	Del/Ins	0.75	1.06 (1.04–1.09)	2.6×10^{-8}
2	*VAMP5/8–GGCx*	rs7568458	A/T	0.45	1.06 (1.04–1.08)	3.6×10^{-10}
2	*ZEB2-AC074093.1*	rs17678683	G/T	0.09	1.10 (1.07–1.14)	3.0×10^{-9}
2	*WDR12*	chr2:203828796:I	Ins/Del	0.11	1.15 (1.11–1.18)	2.2×10^{-18}
3	*MRAS*	chr3:138099161:I	Ins/Del	0.16	1.08 (1.05–1.10)	2.9×10^{-9}
4	*EDNRA*	rs4593108	C/G	0.80	1.07 (1.05–1.10)	8.8×10^{-10}
4	*GUCY1A3*	rs7268947	G/T	0.82	1.07 (1.05–1.10)	6.1×10^{-9}
4	*REST-NOA1*	rs17087535	T/G	0.21	1.06 (1.04–1.09)	4.6×10^{-8}
6	*PHACTR1*	rs9349379	G/A	0.43	1.14 (1.12–1.16)	1.8×10^{-42}
6	*KCNK5*	rs6363142	T/C	0.81	1.07 (1.04–1.09)	1.9×10^{-8}
6	*TCF21*	rs12202017	A/G	0.70	1.07 (1.05–1.09)	2.0×10^{-11}
6	*SLC22A3-LPAL2-LPA*	rs55730499	T/C	0.06	1.37 (1.31–1.44)	5.4×10^{-29}
6	*PLG*	rs4252185	C/T	0.06	1.34 (1.28–1.41)	1.6×10^{-22}
7	*NOS3*	rs3918226	T/C	0.06	1.14 (1.09–1.29)	1.7×10^{-8}
7	*HDAC9*	rs2107595	A/G	0.20	1.08 (1.05–1.10)	8.1×10^{-11}
7	*ZC3HC1*	rs11556924	C/T	0.69	1.08 (1.05–1.10)	5.3×10^{-12}
9	*9p21/CDKN2B-CDKN2A*	rs2891168	G/A	0.49	1.21 (1.19–1.24)	2.3×10^{-96}
9	*ABO*	rs2519093	T/C	0.19	1.08 (1.06–1.11)	1.2×10^{-11}
10	*KIAA1462*	rs2487928	A/G	0.42	1.06 (1.04–1.08)	4.4×10^{-12}
10	*CxCL12*	rs1870634	G/T	0.64	1.08 (1.06–1.10)	5.6×10^{-15}
10	*LIPA*	rs1412444	T/C	0.37	1.07 (1.05–1.09)	5.2×10^{-12}
10	*C3P17A1-CNNM2-NT5C2*	rs11191416	T/G	0.87	1.08 (1.05–1.11)	4.7×10^{-9}
11	*PDGFD*	rs2128739	A/C	0.32	1.07 (1.05–1.09)	7.1×10^{-11}
11	*SWAP70*	rs10840293	A/G	0.55	1.06 (1.04–1.08)	1.3×10^{-8}
12	*ATP2B1*	rs2681472	G/A	0.20	1.08 (1.05–1.10)	6.2×10^{-12}
12	*SH2B3*	rs3184504	T/C	0.42	1.07 (1.04–1.09)	1.0×10^{-8}
12	*KSR2*	rs11830157	G/T	0.36	1.12 (1.08–1.16)**	2.1×10^{-8}
13	*COL4A1/A2*	rs4773144	A/G	0.26	1.07 (1.05–1.09)	1.8×10^{-10}
14	*HHIPL1*	rs10139550	G/C	0.42	1.06 (1.04–1.08)	1.4×10^{-8}
15	*ADAMTS7*	rs4468572	C/T	0.59	1.08 (1.06–1.10)	4.4×10^{-16}
15	*SMAD3*	rs56062135	G/T	0.79	1.07 (1.05–1.10)	4.5×10^{-9}
15	*MFGE8-ABHD2*	rs8042271	G/A	0.90	1.10 (1.06 -1.14)	3.7×10^{-8}
17	*BCAS3*	rs7212798	G/T	0.15	1.08 (1.05 -1.11)	1.9×10^{-8}
18	*PMAIP1-MC4R*	rs663129	A/G	0.26	1.06 (1.04–1.08)	3.20×10^{-8}
19	*LDLR*	rs56289821	G/A	0.90	1.14 (1.11–1.18)	4.4×10^{-15}
19	*APOE*	rs4420638	G/A	0.17	1.10 (1.07–1.13)	7.1×10^{-11}
19	*ZNF507-LOC400684*	rs12976411	T/A	0.09	0.67 (0.60–0.74)**	3.2×10^{-8}
21	*KCNE2*	rs28451064	A/G	0.12	1.14 (1.10–1.17)	1.3×10^{-13}
22	*POM121L9P-ADORA2A*	rs180803	G/T	0.97	1.20 (1.13–1.27)	1.2×10^{-10}

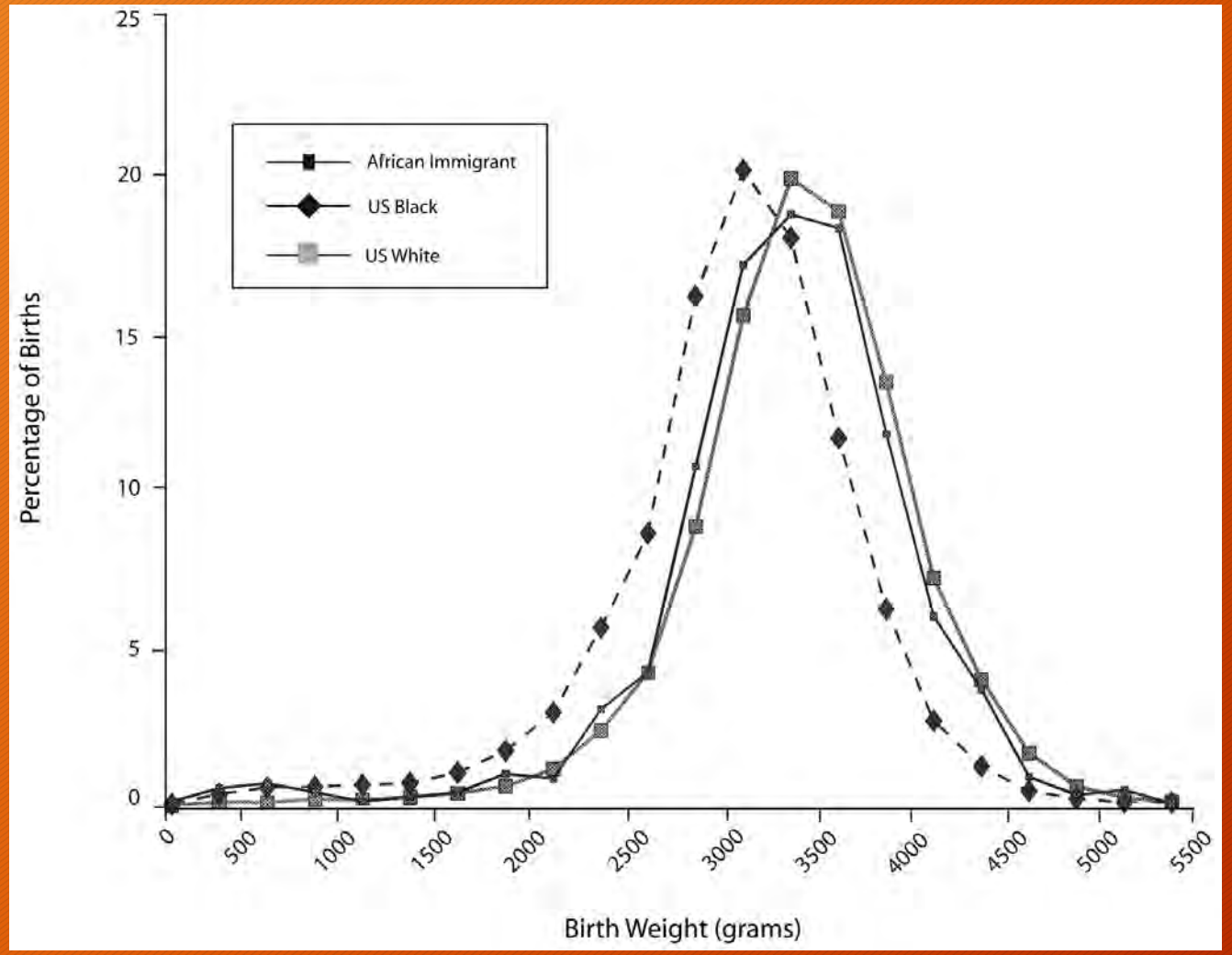
Only loci exceeding the genome-wide threshold for significance ($p = 5.0 \times 10^{-8}$) from the meta-analysis by CARDIoGRAMplusC4D Consortium [7••] are shown. *All ORs refer to allele that increases risk of CAD except for the *ZNF507-LOC400684* locus on chromosome 19. **Derived from an analysis assuming recessive inheritance

Hartiala J, Schwartzman WS, Gabbay J, Ghazalpour A, Bennett BJ, Allayee H. The Genetic Architecture of Coronary Artery Disease: Current Knowledge and Future Opportunities. Curr Atheroscler Rep. 2017 Feb; 19(2):6.

Genetics of cardiovascular disease

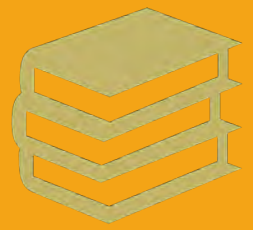
- Non-diabetic kidney disease - explained by genetic variants in apolipoprotein 1 (APOL1) gene
  - More common in SSAA; confers immunity against trypanosomiasis
- No convincing genetic variant linked with hypertension excess

Birthweight distributions of 3 Illinois subpopulations



David, R. et al. Am J Public Health 2007;97:1191-1197

Things that are not the cause of disparities



Poverty, education

Smoking

Reproductive outcomes

Percentage small-for-gestational-age[a] by maternal risk status and race; 1990–91 single live births, 34–42 weeks' gestation, to US-resident mothers

	ELR	Total
African-American: % SGA[a] [95% CI]	8.24 [7.89, 8.61]	15.85 [15.76, 15.94]
White: % SGA[a] [95% CI]	3.29 [3.23, 3.35]	8.03 [8.00, 8.06]
African-American/White SGA[a] risk ratio [95% CI]	2.64 [2.51, 2.78]	2.16 [2.14, 2.17]

[a]Small for gestational age (SGA) defined as less than the 10th percentile of birthweight for gestational age from the 1991 US Reference Curve. ELR, extremely low risk group; CI, confidence interval.

Alexander et al., Racial differences in birthweight for gestational age and infant mortality in extremely-low-risk US populations. *Paediatric & Perinatal Epidemiology* **13** (2), 205-217.

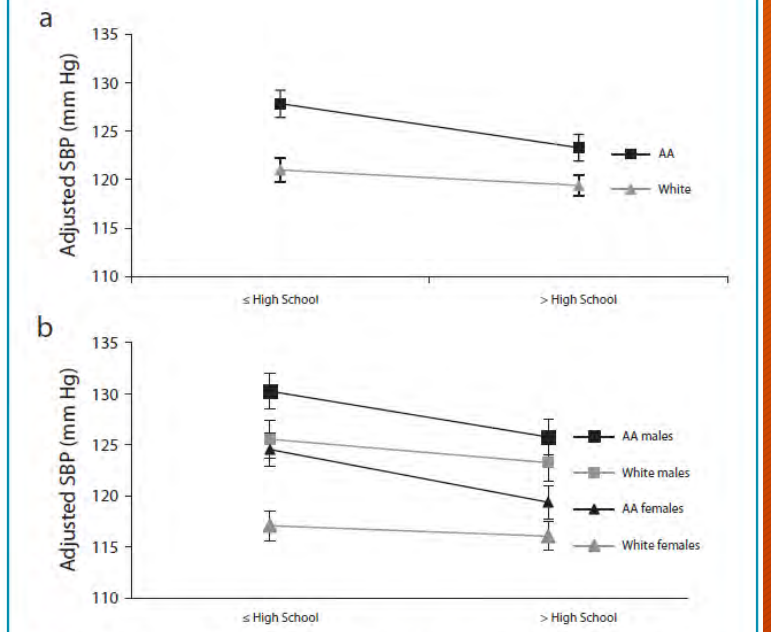
TABLE 3—Odds Ratios for Preterm Birth for US-Born Black Relative to White Women Delivering in California, Stratified by Socioeconomic Characteristics: Maternal and Infant Health Assessment, 2003–2010

Variables Included in the Model Predicting Preterm Birth	Model 1,[a] OR (95% CI)	Model 2,[b] OR (95% CI)	Model 3,[c] OR (95% CI)
Family income			
≤ 100% poverty	1.23 (0.91, 1.65)	1.19 (0.86, 1.63)	1.14 (0.78, 1.65)
> 100% poverty	2.03 (1.64, 2.50)	1.85 (1.48, 2.32)	1.82 (1.42, 2.34)
Maternal education			
< high-school graduate	0.93 (0.61, 1.42)	0.94 (0.58, 1.52)	0.91 (0.51, 1.61)
≥ high-school graduate	1.95 (1.64, 2.31)	1.69 (1.38, 2.08)	1.63 (1.29, 2.05)
Paternal occupation, excluding students			
Not working	0.82 (0.29, 2.31)	0.84 (0.22, 3.18)	0.97 (0.15, 6.09)
Lower status	1.52 (1.22, 1.89)	1.37 (1.07, 1.76)	1.25 (0.93, 1.69)
Higher status	2.12 (1.58, 2.85)	1.85 (1.30, 2.62)	1.90 (1.25, 2.88)
Census tract–level poverty			
≥ 25%	1.19 (0.75, 1.89)	1.16 (0.70, 1. 93)	0.99 (0.55, 1.76)
< 25%	1.91 (1.62, 2.26)	1.68 (1.39, 2.04)	1.61 (1.30, 1.99)

Note. CI = confidence interval; OR = odds ratio.
[a]Race only (unadjusted), comparing Blacks to Whites.
[b]Race + socioeconomic variables (family income [only for the > 100% poverty group], maternal education, paternal education, mother's parents' education, maternal occupation, paternal occupation, private insurance before and during pregnancy, census tract poverty [< 25% or ≥ 25%]), comparing Blacks to Whites.
[c]Race + socioeconomic variables + all other variables (maternal age, paternal age, parity, trimester of prenatal care initiation, adequacy of prenatal care visits, smoking during pregnancy, alcohol consumption during pregnancy, pregnancy intendedness, intimate partner violence, homelessness, job loss of respondent, job loss of partner, separation or divorce, moving, trouble paying bills, incarceration of respondent or partner, drug or alcohol problem in someone close, food insecurity, marital status, emotional support, practical support, prepregnancy health status, body mass index, adequacy of weight gain during pregnancy, gestational diabetes, gestational hypertension), comparing Blacks to Whites.

Braveman PA, Heck K, Egerter S, Marchi KS, Dominguez TP, Cubbin C, Fingar K, Pearson JA, Curtis M. The Role of Socioeconomic Factors in Black-White Disparities in Preterm Birth. Am J Public Health. 2014 Sep 11:e1-e9.

Hypertension



Note. AA = African American; SBP = systolic blood pressure. Interaction plots of education × self-identified race, with education divided into less than or equal to a high-school degree, or greater than a high-school degree (a), and separated by gender (b). SBP measures are adjusted for covariates of age, gender, age × gender, and body mass index (defined as weight in kilograms divided by the square of height in meters).

FIGURE 1—Interaction plots of self-identified race and education: US Family Blood Pressure Program, 1996–2000.

Smoking

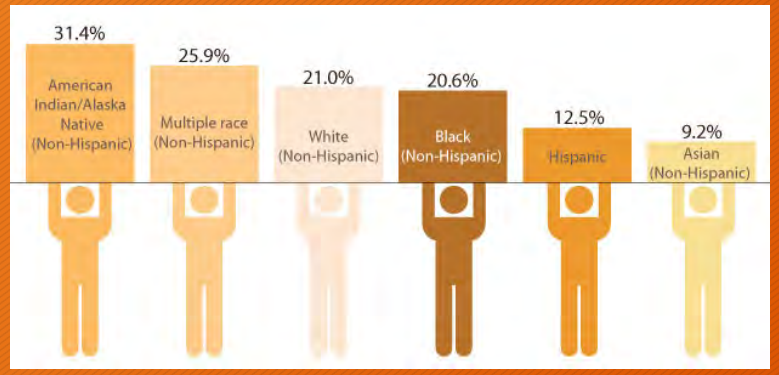
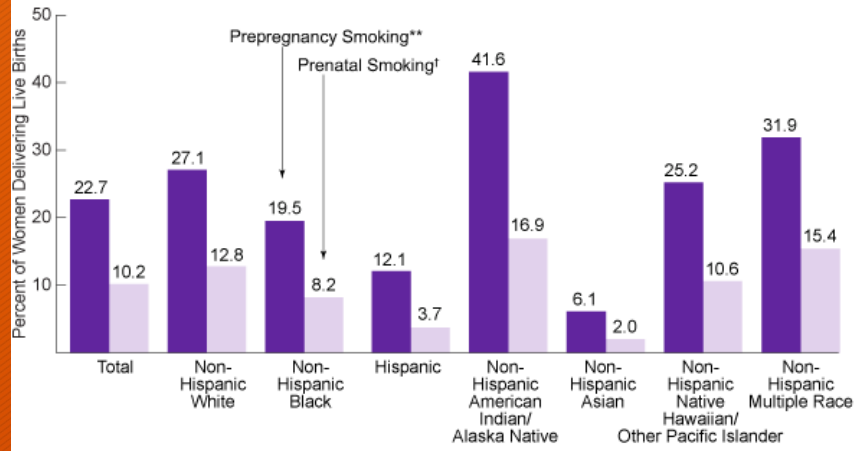


Figure 1. Cigarette Smoking Before and During Pregnancy, by Maternal Race/Ethnicity, 2011*

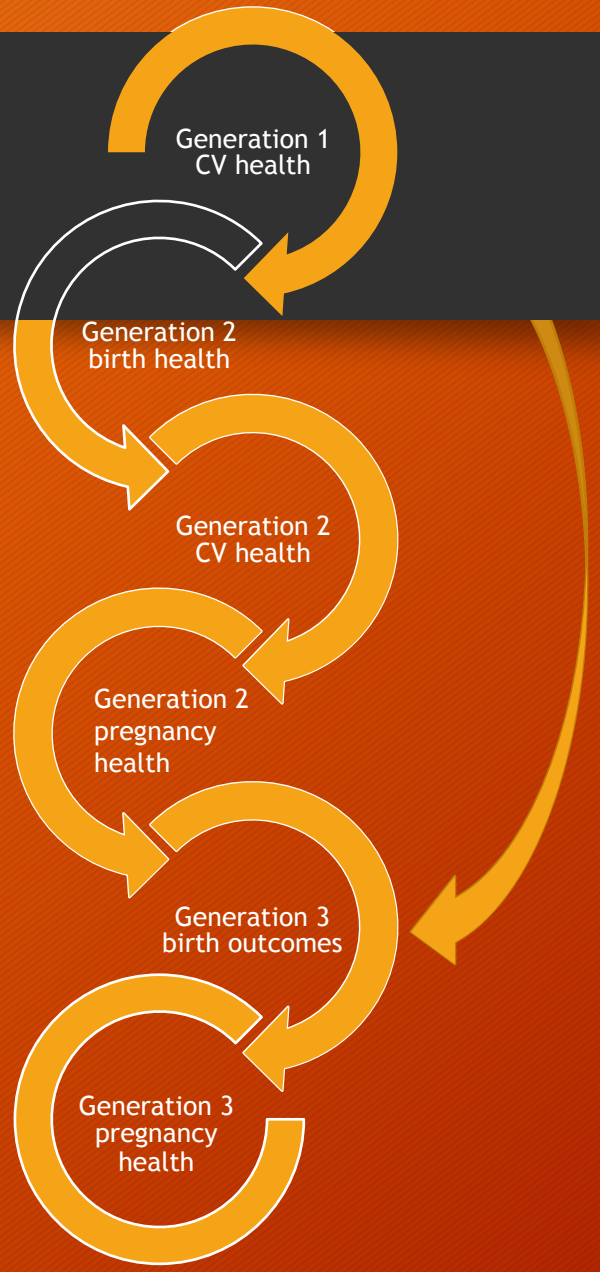


Includes data from 23 states (AR, CO, GA, HI, ME, MD, MI, MN, MO, NE, NJ, NM, NY, OK, OR, PA, RI, UT, VT, WA, WV, WI, WY) and New York City. Mothers completed surveys between 2 and 9 months postpartum. Multiple race data were not reported by 5 of 23 states (AR, HI, ME, NJ, WV); therefore, specific race categories may include multiple race mothers. Defined as the proportion of mothers who reported smoking in the 3 months before pregnancy. †Defined as the proportion of mothers who reported smoking in the last 3 months of pregnancy.*

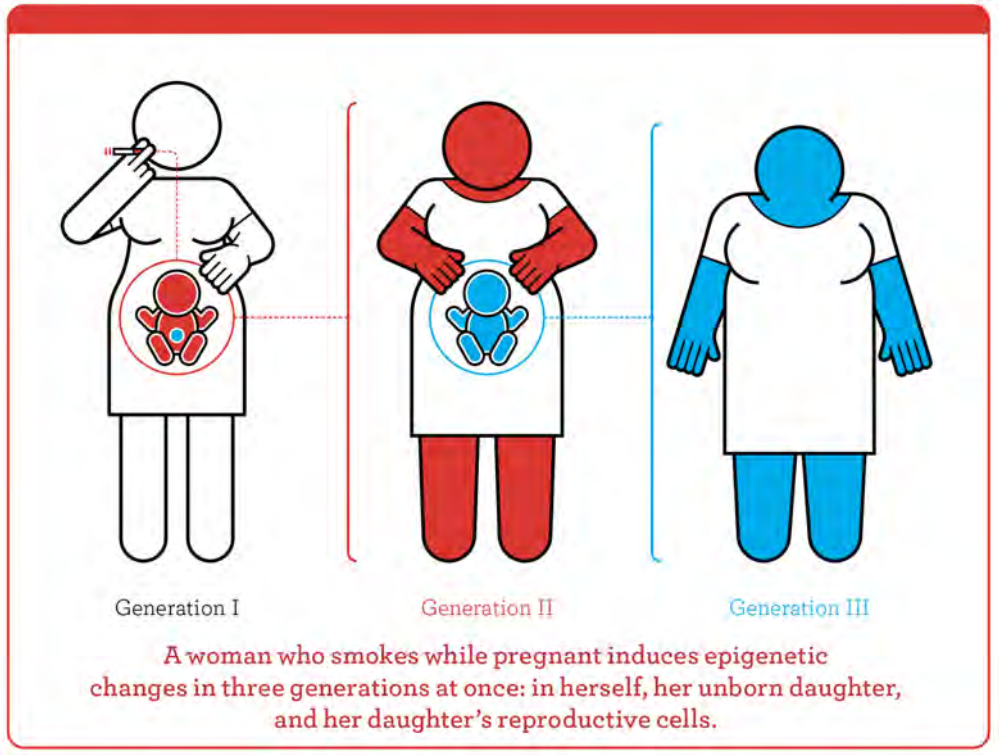
Source: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), Pregnancy Risk Assessment Monitoring System, 2011–2012. Analysis conducted by the CDC Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion.

CDC

Transgenerational effects?

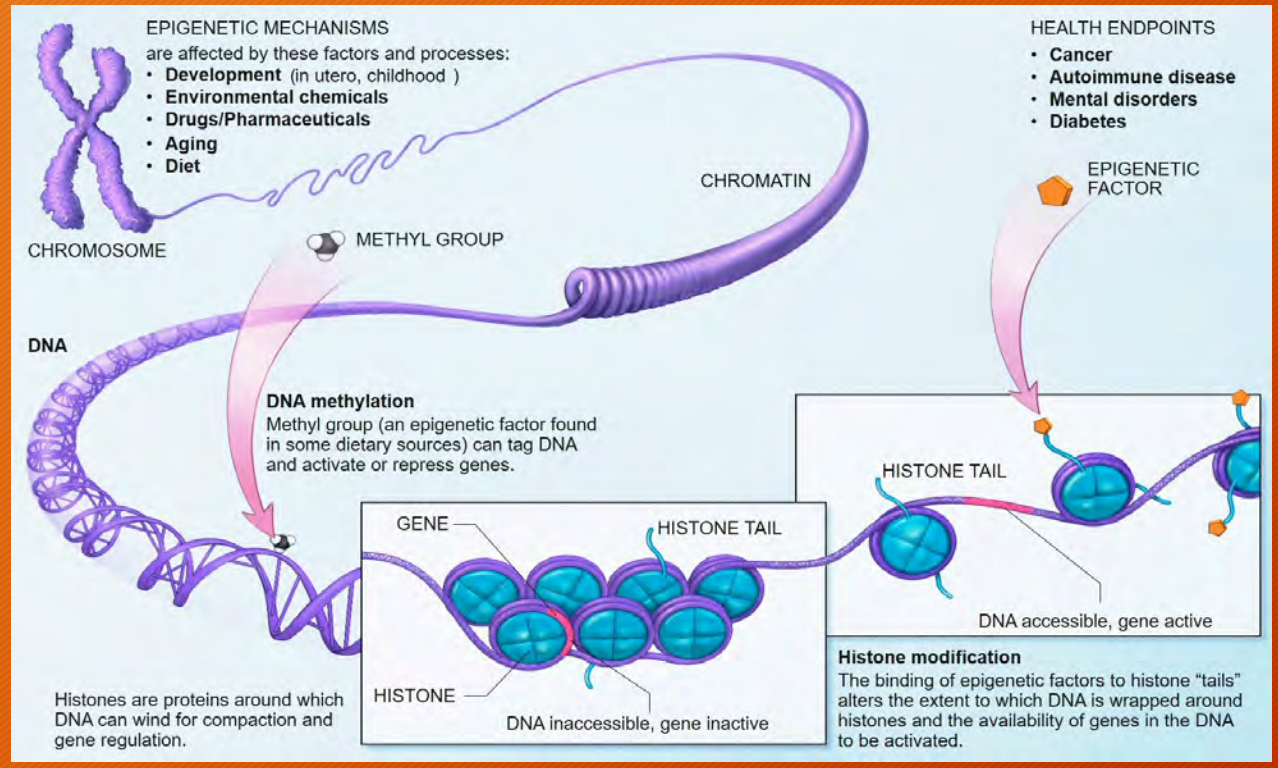


Transgenerational effects



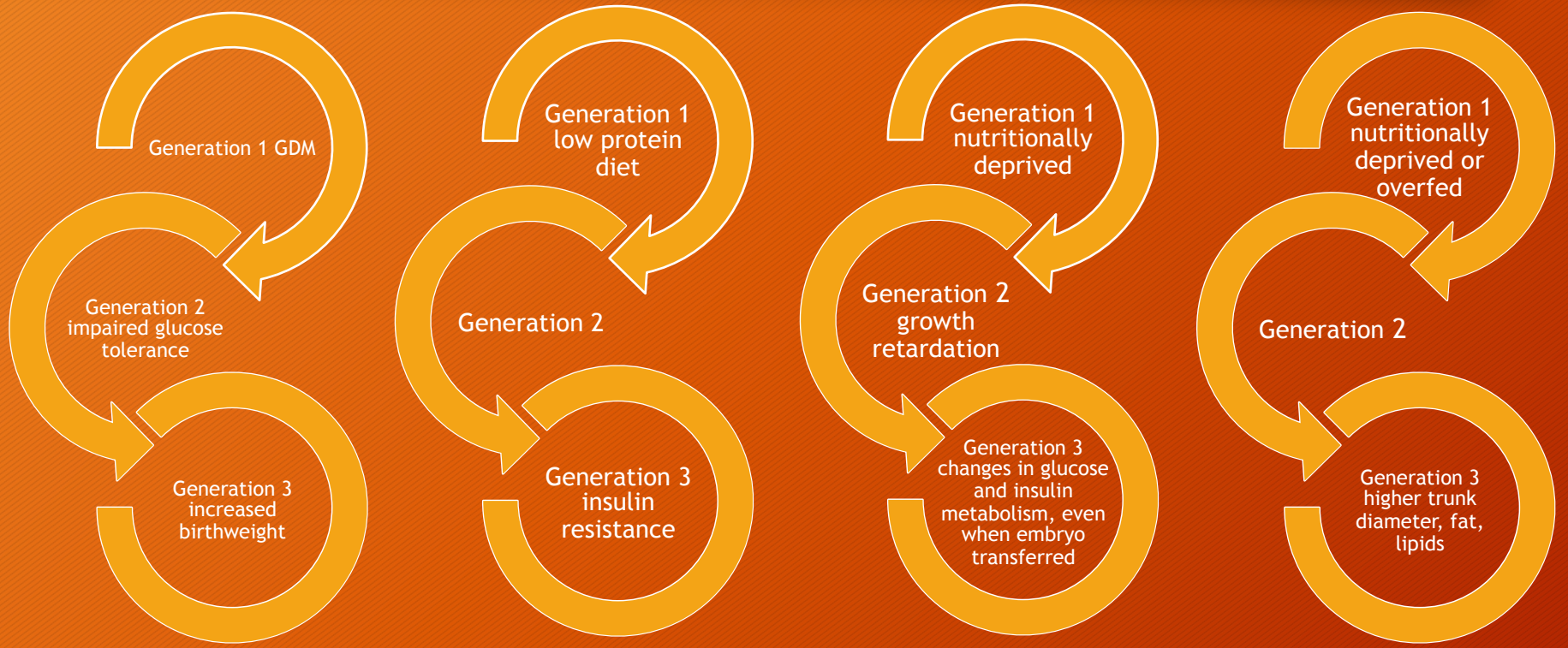
https://www.harvardmagazine.com/2017/05/is epigenetics inherited

Epigenetics



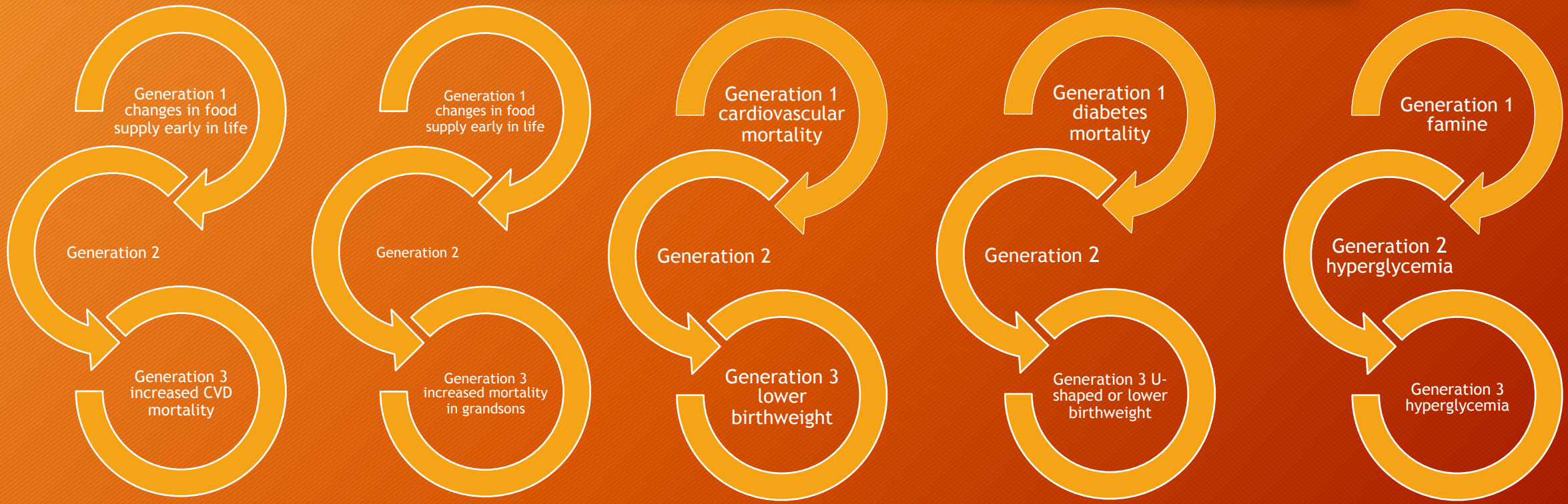
By National Institutes of Health http://commonfund.nih.gov/epigenomics/figure.aspx, Public Domain

Animal studies

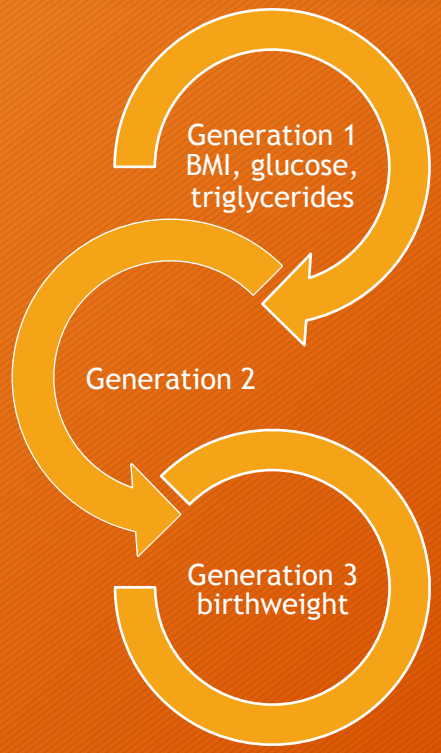


mice rats rats swine

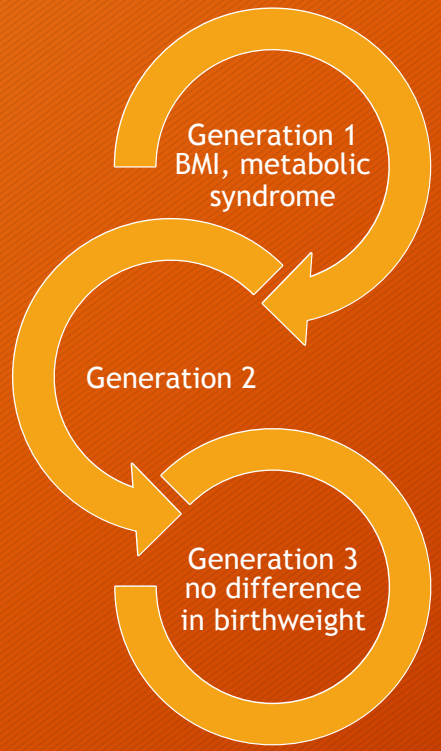
Human studies



Human studies

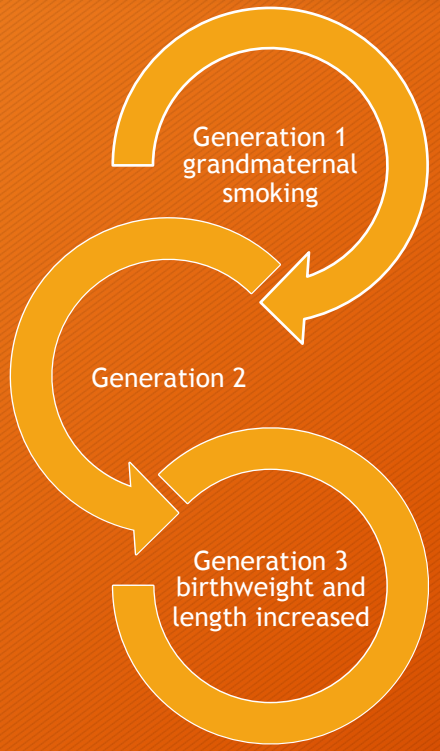


Bogalusa Heart Study

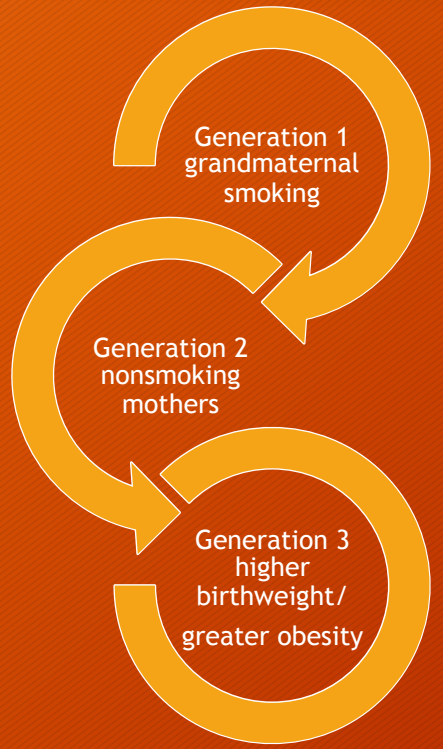


Malta, clinical records

Human studies

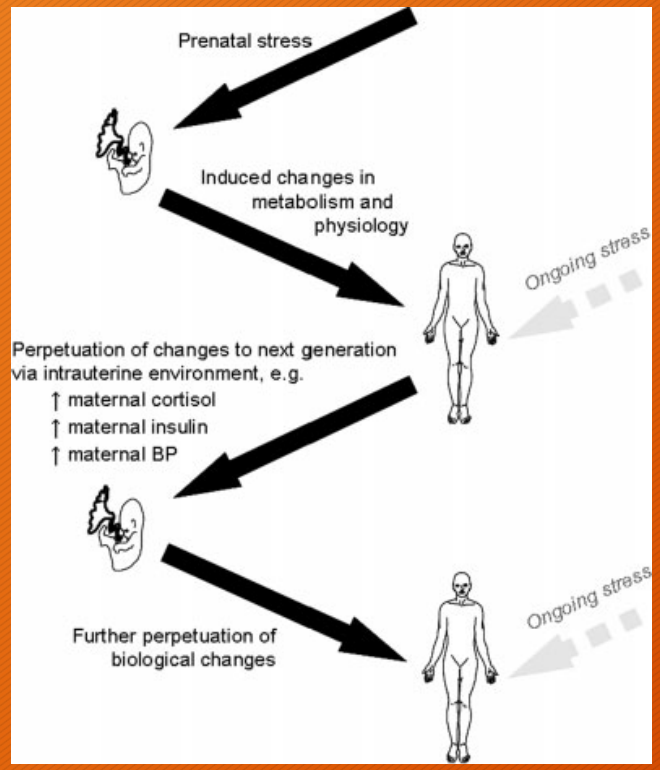


ALSPAC



Nurses' Health

Epigenetics may contribute to the embodiment of racial disparities



- Epigenetic differences are associated with CVD
- Stress during pregnancy has been associated with changes in methylation in the next generation

Kuzawa, 2009

Problems with studying transgenerational health

- Difficult to set up – long time frame or reliance on existing records, which may not have the necessary information
- Privacy/confidentiality for accessing data
- Quality of linkage across generations
- Difficulty of complete follow-up, especially through the male line
- Observed patterns may be consistent with many hypotheses
- Difficulty of testing hypotheses and confounder control, particularly for second-generation
- Missing data
- Fertility/socially patterned reproduction

Future directions – Transgenerational health

Expand	Include	Examine	Take advantage
Expand existing prospective cohorts, pregnancy, and child health studies	Include biological markers and test mechanisms	Examine mediation and pathway analyses	Take advantage of natural experiments and discrepant generations

How can we use these to improve women's health?

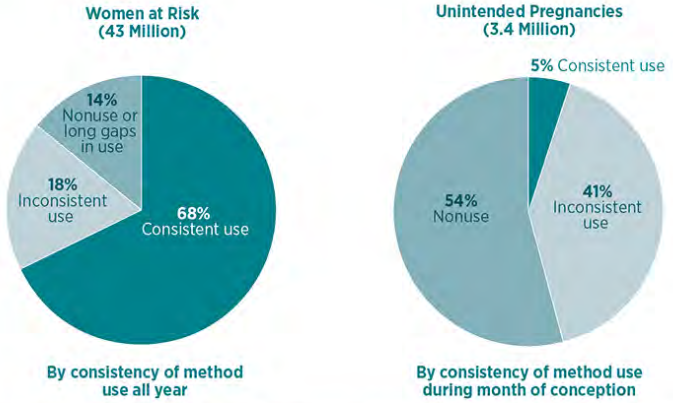
- Recognize that health is linked across the life course and across generations

How can we use these to improve women's health?

- Good health during pregnancy starts with good family planning

MODERN CONTRACEPTION WORKS

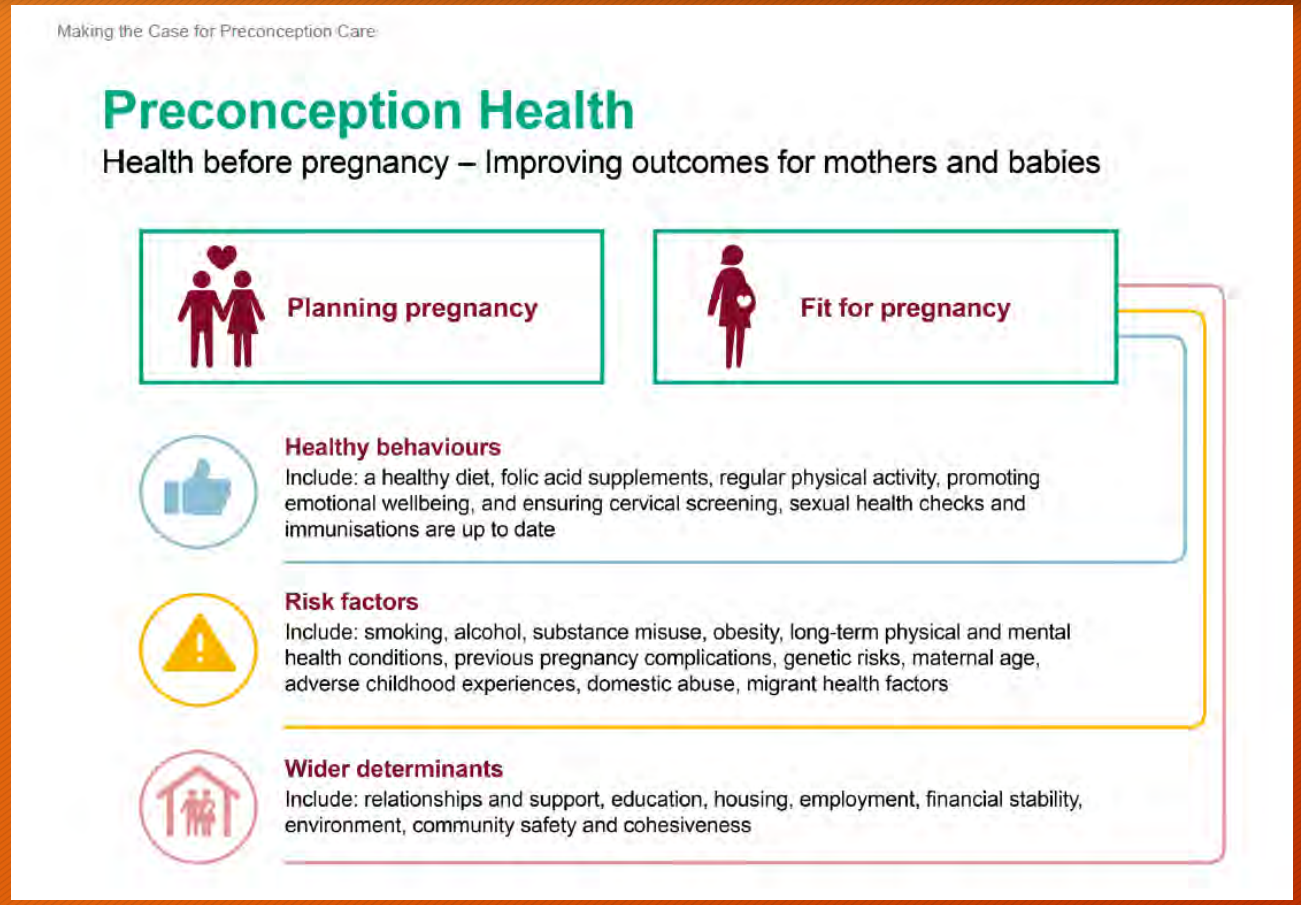
In 2008, the two-thirds of U.S. women at risk of pregnancy who used contraceptives consistently accounted for only 5% of unintended pregnancies.



NOTES: "Nonuse" includes women who were sexually active, but did not use any method of contraception. "Long gaps in use" includes women who did use a contraceptive during the year, but had gaps in use of a month or longer when they were sexually active. "Inconsistent use" includes women who used a method in all months that they were sexually active, but missed taking some pills, or skipped use or incorrectly used their barrier method or condom during some acts of intercourse. "Consistent use" includes women without any gaps in use who used their method consistently and correctly during all months when they were sexually active, including those who used a long-acting or permanent method.

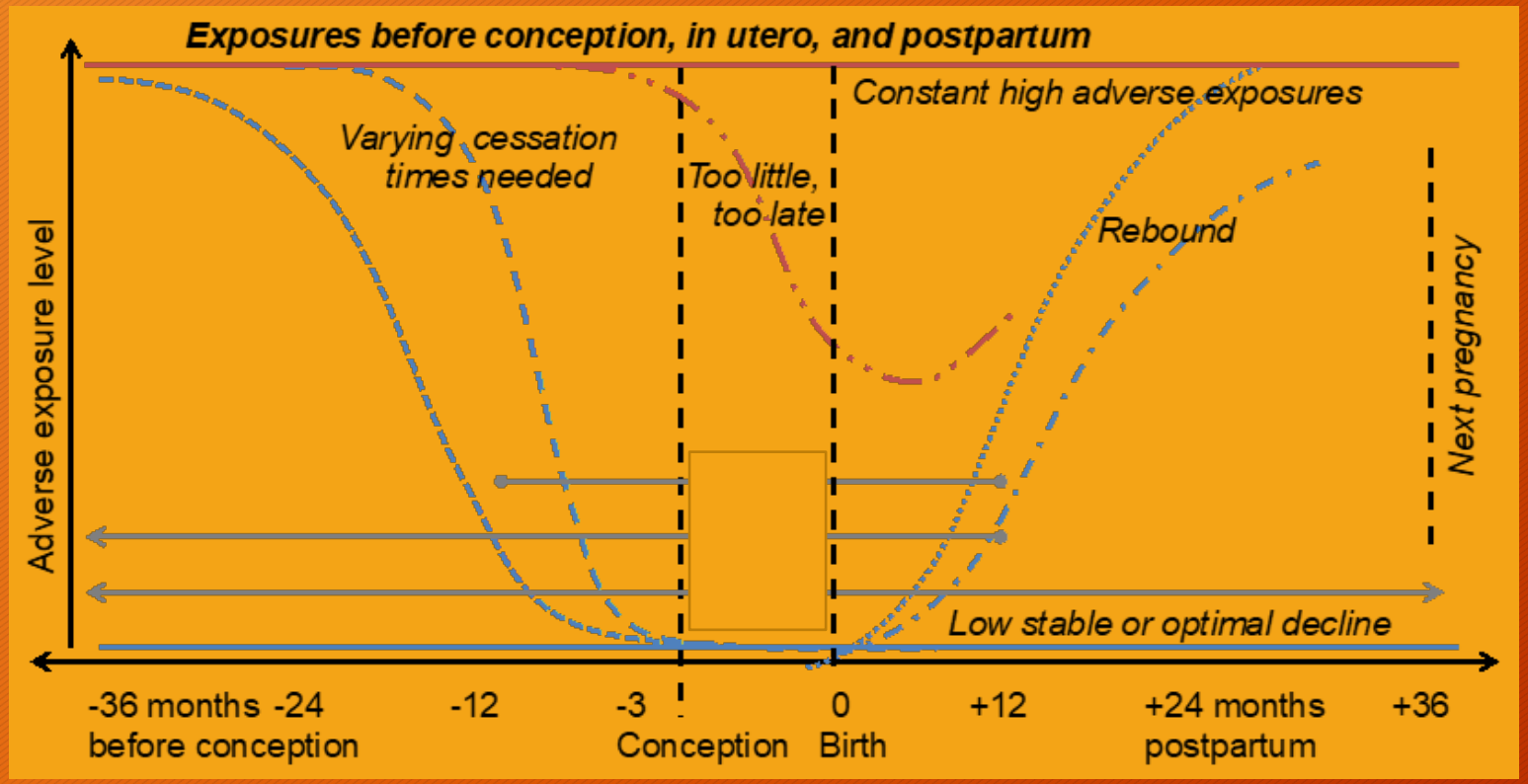
www.guttmacher.org

How can we use these to improve women's health?



Making the case for preconception care, Public Health England

Preconception health



How can we use these to improve women's health?

Follow-up for women who experience pregnancy complications

- Postpartum is a time when care continuum can fail
- Pediatricians treat children
- Obstetricians treat pregnant women
- PCPs may not ask about pregnancy history

Clinical care solutions

- Integrated and functioning EMR systems to establish flagging tools for certain conditions (e.g., GDM)
- Empower women to share their birth narratives
- Training on hand-off of care in medical/midwife/RN/PA students to know the right questions to ask or to identify when information is missing, especially for women of reproductive age
- Improve predictive analytics to identify women who are likely to progress to cardiovascular disease
- Expand payment models to bundle postpartum services with delivery and have a “well-mom” schedule parallel with well-baby

How could a life course/DOHaD perspective inform policy?

Goodman et al., Analyzing policy through a DOHaD Lens

- Paid family leave
  - May decrease stress among pregnant women either through offering an opportunity to stop working during pregnancy (antenatal leave) or through the anticipation of paid postpartum leave and this may result in more appropriate birthweight and decreased PTB
  - Appropriate birthweight is an indicator of fetal developmental processes that contribute to the long-term development of coronary heart disease, diabetes mellitus, and other conditions, thus amplifying the potential impact of PFL.
  - The influence of PFL may be further amplified through its well established connection to breastfeeding, providing a link to later life obesity and cardiometabolic disease through healthier infant weight gain
- Sugar sweetened beverage taxes
  - SSBs were the largest single dietary sources of energy consumed in pregnancy.
  - Observational evidence suggests that greater maternal SSB consumption in pregnancy is associated with adverse birth outcomes associated with life course disease risk in the offspring, including higher risk of PTB
  - Prenatal SSB consumption is also associated with greater adiposity in children
  - Applying a DOHaD lens to evaluate SSB tax policies requires integration of pregnant women as a subgroup of interest, and extending policy simulations to consider intergenerational effects. It also requires more empirical research on the intergenerational effects of consuming SSBs and their alternatives prior to, during, and after pregnancy, as well as consumption by fathers.
- Housing policy
  - Housing transitions and housing instability have been associated with increased risk of LBW among young, urban pregnant women
  - Effects of renewal policies that result in housing transitions are differential by race/ethnicity
    - Very high levels of gentrification were associated with increased PTB compared to non Hispanic blacks, but protective among non Hispanic whites
  - While the housing-related literature is beginning to concern itself with effects on pregnant women, the consideration of potential health effects stops at birth and fails to take into account the long-term health trajectory that birth outcomes set in.
  - A DOHaD lens considers the positive and negative consequences of what might seemingly be economic development policies, but also the potential effects of these policies on the second generation.

Int. J. Environ. Res. Public Health **2018**, *15*(12), 2906

COMMENT

HISTORY How James Watt moved from steam engines to sculpture p.134

RESILIENCE A treatise on the social roots of disasters p.135

CLIMATE CHANGE Threatened white possum is Australia's harbinger p.136

LAB LIFE Ethics codes could protect field workers from harassment p.138

MEGAMEVIZ TTY

Don't blame the mothers

Careless discussion of epigenetic research on how early life affects health across generations could harm women, warn **Sarah S. Richardson** and colleagues.

From folk medicine to popular culture, there is an abiding fascination with how the experiences of pregnant women imprint on their descendants. The latest wave in this discussion flows from studies of epigenetics — analyses of heritable changes to DNA that affect gene activity but not nucleotide sequence. Such DNA modification has been implicated in a child's future risk of obesity, diseases such as diabetes, and poor response to stress.

Headlines in the press reveal how these findings are often simplified to focus on the maternal impact: 'Mother's diet during pregnancy alters baby's DNA' (BBC), 'Grandma's Experiences Leave a Mark on Your Genes' (*Discover*), and 'Pregnant 9/11 survivors transmitted trauma to their children' (*The Guardian*). Factors such as the paternal contribution, family life and social environment receive less attention.

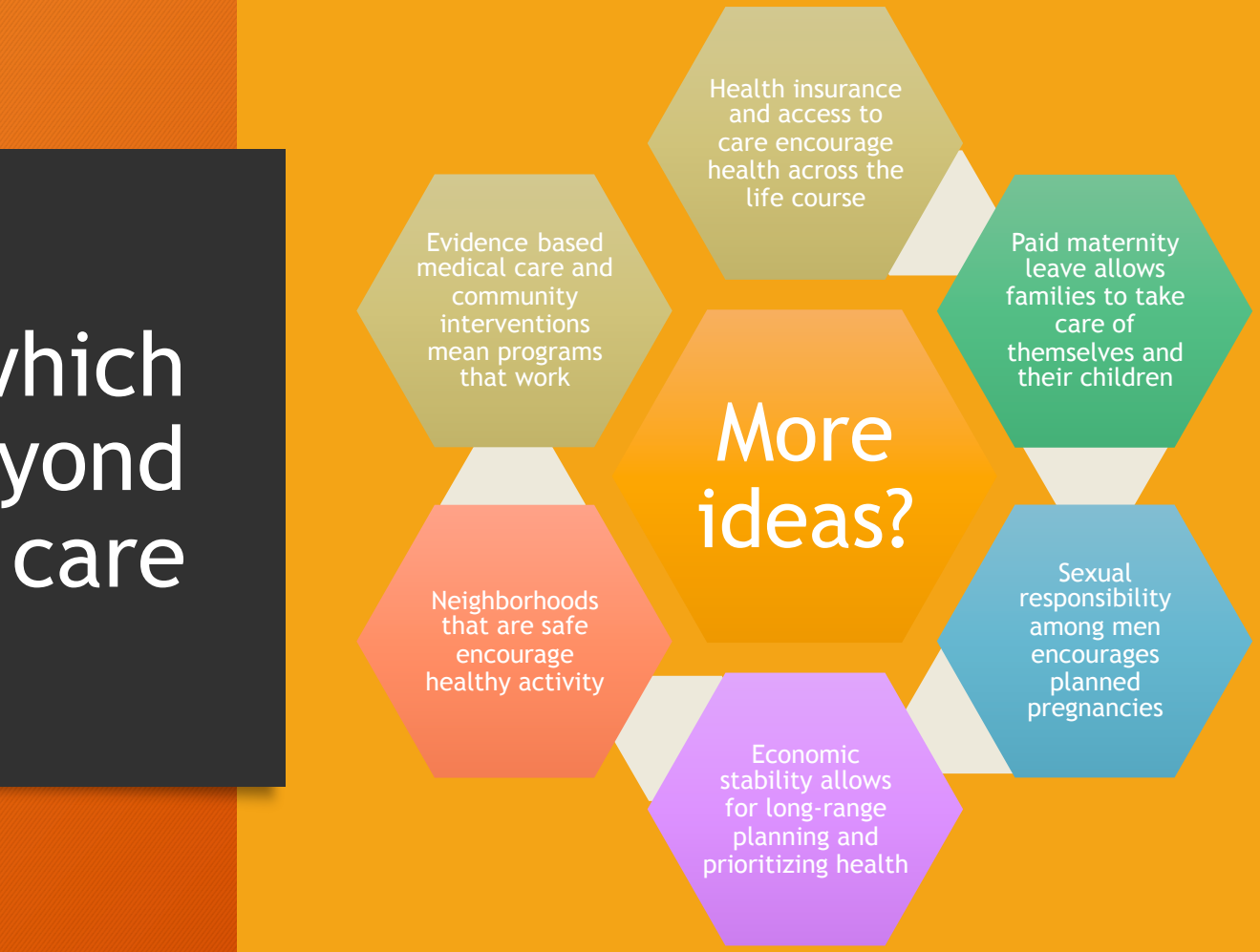
Questions about the long shadow of the uterine environment are part of a burgeoning field known as developmental origins of health and disease (DOHaD)[1]. For example, one study revealed[2] that 45% of children born to women with type 2 diabetes develop diabetes by their mid-twenties, compared with 9% of children whose mothers developed diabetes after pregnancy.

DOHaD would ideally guide policies that support parents and children, but exaggerations and over-simplifications are making scapegoats of mothers, and could even increase surveillance and regulation of pregnant women. As academics working in DOHaD and cultural studies of science, we are concerned. We urge researchers, press officers and journalists to consider the ramifications of irresponsible discussion.

ALARMING PRECEDENTS

There is a long history of society blaming mothers for the ill health of their children. Preliminary evidence of fetal harm has led to regulatory over-reach. First recognized in the 1970s, fetal alcohol syndrome (FAS) is a collection of physical and mental problems in children of women who drink heavily during pregnancy. In 1981, the US Surgeon General advised that no level of alcohol consumption was safe for pregnant women. Drinking during pregnancy was stigmatized and even criminalized. Bars and restaurants were required to display warnings that drinking ▸

All of which goes beyond clinical care



Goal: All babies born healthy!
All women healthy throughout life!

Questions?

Send me your baby and 4+ generation pictures!

harville@tulane.edu

504-988-7327

Department of Epidemiology, Tulane School of Public Health and Tropical Medicine