Circulation

AHA SCIENTIFIC STATEMENT

# Adverse Pregnancy Outcomes and Cardiovascular Disease Risk: Unique Opportunities for Cardiovascular Disease Prevention in Women

## A Scientific Statement From the American Heart Association

**ABSTRACT:** This statement summarizes evidence that adverse pregnancy outcomes (APOs) such as hypertensive disorders of pregnancy, preterm delivery, gestational diabetes, small-for-gestational-age delivery, placental abruption, and pregnancy loss increase a woman's risk of developing cardiovascular disease (CVD) risk factors and of developing subsequent CVD (including fatal and nonfatal coronary heart disease, stroke, peripheral vascular disease, and heart failure). This statement highlights the importance of recognizing APOs when CVD risk is evaluated in women, although their value in reclassifying risk may not be established. A history of APOs is a prompt for more vigorous primordial prevention of CVD risk factors and primary prevention of CVD. Adopting a heart-healthy diet and increasing physical activity among women with APOs, starting in the postpartum setting and continuing across the life span, are important lifestyle interventions to decrease CVD risk. Lactation and breastfeeding may lower a woman's later cardiometabolic risk. Black and Asian women experience a higher proportion APOs, with more severe clinical presentation and worse outcomes, than White women. More studies on APOs and CVD in non-White women are needed to better understand and address these health disparities. Future studies of aspirin, statins, and metformin may better inform our recommendations for pharmacotherapy in primary CVD prevention among women who have had an APO. Several opportunities exist for health care systems to improve transitions of care for women with APOs and to implement strategies to reduce their long-term CVD risk. One proposed strategy includes incorporation of the concept of a fourth trimester into clinical recommendations and health care policy.

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Pregnancy leads to many vascular, metabolic, and physiological adaptations in the mother, including increased insulin resistance, adipose deposition, hypercoagulability, cardiac remodeling, and decreased vascular resistance. These changes support fetal growth and development and prepare the mother for the increased energy and nutritional demands of lactation to support the newborn's postnatal growth.[1] The physiological stress of pregnancy may unmask adverse maternal and fetal pregnancy outcomes (APOs) such as gestational diabetes (GD), hypertensive disorders of pregnancy, intrauterine growth restriction, small-for-gestational age (SGA) delivery, placental abruption, and preterm delivery in women with prepregnancy elevated cardiometabolic risk factors or genetic or environmental predisposition to these abnormalities[2–5] (Table 1).

For instance, women with prepregnancy insulin resistance, a family history of diabetes, or elevated blood pressure are more likely to develop GD during their pregnancy compared with women without these predisposing factors.[21] Similarly, women with obesity and elevated prepregnancy blood pressures are more susceptible to developing preeclampsia or gestational hypertension.[22] Fetal size is determined by several factors, including maternal and paternal age, genetics, nutrition, interpregnancy interval, and parity. A baby who is determined to be SGA (according to their birth weight for gestational age) may have been affected by placental insufficiency (resulting from insufficient implantation of the placenta into the uterus) or vascular insufficiency (caused by abnormal maternal uterine artery flow resulting in an inability to supply adequate oxygen and nutrients to the placental or fetal unit). Thus, having a small baby, that is, an SGA baby, a baby with low birth weight, or a baby with fetal (intrauterine) growth restriction, may uncover preexisting vascular dysfunction in the mother that later predisposes her to cardiovascular disease (CVD; including coronary heart disease, stroke, and heart failure). Experiencing an APO may also accentuate cardiovascular and metabolic risk factor trajectories for women, which also contributes to the higher risk of subsequent CVD.[23] Because response to the stress of pregnancy is a harbinger of women's later CVD risk, the 2011 update of the American Heart Association effectiveness-based guidelines for the prevention of CVD

**Table 1. Obstetric Definitions and Prevalence of APOs**

| Term/condition | Definition | Women with condition, % |
|---|---|---|
| APO | One of several maternal or fetal complications, including preeclampsia, gestational hypertension, GD, preterm delivery, fetal growth restriction, having a neonate with a low birth weight or a low birth weight indexed to a referent sample based on gestational age (SGA), and placental abruption. | 10–15[6,7]* |
| Preeclampsia | Pregnancy disorder associated with new-onset hypertension, which occurs most often after 20 wk of gestation and frequently near term. It is often but not always accompanied by new-onset proteinuria. | 2–8[8]† |
| Gestational hypertension | Defined as a systolic blood pressure of ≥140 mm Hg, a diastolic blood pressure of ≥90 mm Hg, or both on 2 occasions at least 4 h apart after 20 wk of gestation in a woman with a previously normal blood pressure. | 2–3[9]† |
| Hypertensive disorder of pregnancy[10] | Preeclampsia, chronic hypertension, chronic hypertension with superimposed preeclampsia, eclampsia, or gestational hypertension. | 6–8[11]† |
| GD | Any degree of glucose intolerance with onset or first recognition during pregnancy. | 2–10[12] |
| Gestational age | Time elapsed since the first day of the last menstrual period (also known as menstrual age). | … |
| Placental abruption | Premature separation of a normally implanted placenta from the uterus before delivery of the fetus. | 1[13]† |
| Preterm delivery | After 20 wk gestation and before the completion of 37 wk of gestation regardless of birthweight. | 10[14]† |
| Low birth weight | Neonate with birthweight <2500 g (or <5 lb 8 oz). | 8[14]† |
| SGA | Neonate whose weight is below the 10th percentile for the gestational age based on a reference standard (often national reference standards for weight for gestational age. Other defined cut points include weight below the third percentile). Some published cut points are sex and race specific. Reference standards generally have excluded nonsingleton deliveries and congenital malformations.[15] | 10[16] |
| Large for gestational age | Neonate whose weight is above the 90th percentile for the gestational age. | 8–13[17] |
| Fetal growth restriction (intrauterine growth restriction) | Condition in which a fetus is unable to achieve its genetically determined potential size.[18,19] Fetal growth restriction describes fetuses with an estimated fetal weight that is less than the 10th percentile for gestational age. To assess for fetal growth restriction, 4 biometric measures are commonly used: (1) biparietal diameter, (2) head circumference, (3) abdominal circumference, and (4) femur length. The biometric measurements can be combined to generate an estimated fetal weight.[20] | 5–15[8,19]† |

APO indicates adverse pregnancy outcome; GD, gestational diabetes; and SGA, small for gestational age.
*Across all of a woman's pregnancies.
†Per pregnancy or delivery.

**Table 2. APOs and Associations With Mortality and CVD Outcomes**

| 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.

in women recommends that a history of APOs (GD, preeclampsia, preterm birth, or birth of an SGA infant) should be considered part of CVD risk assessment in women.[24] Furthermore, the updated 2018 cholesterol treatment guidelines briefly list these APOs as CVD risk enhancers that would be critical to consider when deciding on use of a statin for CVD prevention.[25] This current American Heart Association statement reviews the epidemiological evidence relating individual APOs and CVD risk and discusses potential lifestyle modifications to ameliorate this risk among women with a history of APOs. We also consider health systems approaches that could dually enhance women's long-term cardiovascular health and improve the health of her future pregnancies after an APO.

## PREGNANCY COMPLICATIONS AND THE RISK OF CVD EVENTS

There is a substantial and consistent body of evidence showing that APOs, including hypertensive disorders of pregnancy, preterm delivery, GD, delivering an SGA baby, placental abruption, and pregnancy loss, are associated with clinical CVD events in later life (Table 2 and Supplemental Table 1). The body of evidence was considered strong (Strength of Evidence A) for meta-analyses that tested for (and excluded) publication bias and for primary studies based on objective contemporaneous record of pregnancy complications.

### Hypertensive Disorders of Pregnancy

A history of gestational hypertension has consistently been associated with an increased risk of CVD (odds ratio [OR], 1.67 [95% CI, 1.28–2.19]; meta-analysis of 9 studies)[26] and with increased odds of stroke (OR, 1.83 [95% CI, 1.79–4.22]; a meta-analysis of 4 studies).[26] The associations with CVD were progressively stronger for moderate preeclampsia (OR, 2.24 [95% CI, 1.74–1.93]) and severe preeclampsia (OR, 2.74 [95% CI, 2.48–3.04]).[26] Other meta-analyses and more recent primary studies show similar associations of these hypertensive disorders of pregnancy with CVD.[27–37]

### Gestational Diabetes

A history of GD was associated with CVD (OR, 1.68 [95% CI, 1.11–2.52]) in a meta-analysis of 8 studies,[26] which was confirmed by another systematic review with similar consolidated results.[38]

### Preterm Delivery

Preterm delivery was associated with CVD mortality (OR, 1.93 [95% CI, 1.83–2.03]) in a recent meta-analysis of 4 studies.[26] Although 1 recent study showed no association of preterm delivery with future CVD,[30] a large body of other studies and meta-analyses demonstrate strong associations of preterm delivery (alone and in conjunction with hypertensive disorders of pregnancy) with coronary heart disease, stroke, and CVD.[29,33,39,40]

### Birth Weight

Delivering an SGA baby was nonsignificantly associated with CVD (OR, 1.29 [95% CI, 0.91–1.83]) in a recent meta-analysis of 4 studies,[26] largely consistent with other individual studies and meta-analyses (some of which had statistically significant associations that were similar in magnitude).[29,30,33,36,41,42] One study suggested that a large-for-gestational-age delivery might also be associated with increased risk of CVD (hazard ratio [HR], 3.0 [95% CI, 2.0–4.6]).[43]

### Pregnancy Loss and Placental Abruption

A history of placental abruption was associated with increased risk of CVD (HR, 1.82 [95% CI, 1.42–2.33]) in a recent meta-analysis of 4 studies.[26] Stillbirth was also associated with increased risk of CVD (HR, 2.23 [95% CI, 1.92–2.62]).[26] Other individual studies have also shown an association between pregnancy loss (miscarriages or stillbirths or combined) and future cardiovascular events.[29,44–46]

## PREGNANCY COMPLICATIONS IN ASSOCIATION WITH LATER CVD RISK FACTORS

Most APOs are associated with future development of ≥1 CVD risk factors, including hypertension, diabetes, and dyslipidemia, which may, in part, mediate the

**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]; $P<0.001$]).

increased risk of late CVD that has consistently been documented in meta-analyses (Table 3). Placental abruption has not been well studied in terms of its association with later CVD risk factors.

## Hypertensive Disorders of Pregnancy and CVD Risk Factors

The evidence is strong that women who experienced preeclampsia have a much higher risk of subsequently developing chronic hypertension. A meta-analysis of 43 studies found a pooled risk ratio for hypertension of 3.13 (95% CI, 2.51–3.89) after preeclampsia.[59] Prior pooled data suggest that 20% of women with preeclampsia develop hypertension within 15 years.[63] Thus, screening programs for hypertension could begin in a woman's fourth decade.[63] Women with hypertensive disorders of pregnancy also have a greater risk of developing subsequent diabetes[60] and lipid abnormalities.[61]

## GD and CVD Risk Factors

GD is well established as a risk factor for the development of later type 2 diabetes, with a nearly 10-fold elevation in type 2 diabetes across 20 studies[62] (risk ratio, 9.51 [95% CI, 7.14–12.67]). The risk of developing type 2 diabetes after GD was higher in women with a higher body mass index, a family history of diabetes, multiparity, advanced maternal age, and more severe GD and in those with concomitant hypertensive disorders of pregnancy or preterm delivery.[64] The associations between GD and subsequent development of hypertension,[47,48] and dyslipidemia[49–51] have been inconsistent across studies.

## Preterm Delivery and CVD Risk Factors.

Evidence for an association between preterm delivery and CVD risk factors is less strong than for hypertensive disorders of pregnancy or GD (with CVD risk factors). Five prior studies demonstrated that preterm delivery is associated with elevated blood pressure and a greater risk of hypertension later in life.[39,48,52–54] The earlier in pregnancy that preterm delivery occurs, the more strongly it is associated with later development of high blood pressure.[48] The association between preterm delivery and later high blood pressure may be the result of its close association with hypertensive disorders of pregnancy.[51,55] Preterm delivery was a modest risk factor for later type 2 diabetes in some[39,55] but not all[51] prior studies. Evidence for the association of preterm birth with dyslipidemia is inconsistent, with 2 positive[39,55] and 3 negative studies.[51,53,56]

## SGA Delivery and CVD Risk Factors

Delivery of an SGA baby has been associated with later elevations in maternal systolic[48,51] and diastolic blood pressures[53] and with hypertension,[48,51] although a fourth smaller study found no such associations.[55] SGA birth is also associated with later development of diabetes[53] and elevated fasting glucose[55] but not with lipid abnormalities.[53]

## Pregnancy Loss and CVD Risk Factors

All forms of pregnancy loss are associated with risk of elevated blood pressure[44] or hypertension,[44,57,58] with a particularly higher risk for hypertension after either late-term or recurrent pregnancy loss.[26,43,44] Women with spontaneous pregnancy loss or stillbirth also have higher rates of type 2 diabetes in later life.[44,58] Evidence for an association between pregnancy loss and dyslipidemia has been mixed,[44] but the Nurses' Health Study has found that women with spontaneous abortion had modestly elevated risks of hypercholesterolemia.[58]

# STUDIES ASSESSING THE UTILITY OF APOS IN CVD RISK STRATIFICATION

Relatively few published studies have rigorously evaluated the utility of adding information about APOs to conventional CVD risk stratification.[30,34,36,45] These

studies suggest that although APOs may provide an early window to the development of CVD, they may not materially add to CVD prediction or to net reclassification of CVD after accounting for established risk factors. The incremental information provided by APOs may have been partly captured by any subsequent increases in hypertension, diabetes, and dyslipidemia. Prior studies have evaluated the additional information provided by the following APOs: pregnancy loss,[45] hypertensive disorders of pregnancy,[34] preterm delivery and preeclampsia,[36] and preeclampsia, gestational hypertension, preterm delivery, or SGA delivery.[30] The incremental predictive capacity of APOs may be limited by their lower prevalence compared with traditional CVD risk factors and the more contemporary data provided by current risk factor levels. Moreover, CVD risk stratification studies considering APOs have been conducted in middle-aged and older women, and by these ages, women are more likely to have developed conventional CVD risk factors, thereby limiting the potential contribution of APOs to identifying women at higher long-term risk for CVD.

## LIFESTYLE MODIFICATION FOR CVD RISK FACTOR REDUCTION AMONG WOMEN WITH APOS

### Dietary Patterns to Optimize Cardiovascular Health in Women of Reproductive Age and Pregnant Women

Healthy dietary patterns can optimize the cardiovascular health of all women, which may be especially important before pregnancy.[65,66] Epidemiological cohort studies suggest that healthy dietary patterns up to 3 years before pregnancy (ie, characterized by high intake of fruits, vegetables, legumes, nuts, and fish and low intake of red and processed meats) are associated with lower risks of hypertensive disorders of pregnancy, GD, and preterm delivery.[67] Maternal nutrition in the 12 months before conception may affect fetal growth, development, gestational age, and infant birth weight.[68] Among women with uncomplicated pregnancies, the DASH (Dietary Approaches to Stop Hypertension) diet was associated with lower blood pressure than other dietary patterns.[69] A diet high in protein and fruits was associated with a lower risk of preterm delivery, whereas a diet high in fat and sugar was associated with an increased risk for preterm delivery in 1 study.[68] Among women with GD, the DASH diet was associated with better pregnancy outcomes, including a lower use of insulin.[70] Following the DASH diet during pregnancy was associated with a decreased risk of preterm delivery in a separate study.[71] These associations could be confounded by other favorable lifestyle and medical factors, yet recommending consumption of a healthy dietary pattern is widely accepted. The American College of Obstetricians and Gynecologists has not specifically endorsed or counseled against a DASH diet during pregnancy and postpartum, and it is likely important for more scientific studies to be conducted to confirm efficacy.

### Special Considerations to Optimize Dietary Intake in Women of Reproductive Age and in Pregnant Women With GD or Preeclampsia

It is recommended that women of reproductive age consume supplemental folate and iron in addition to a healthy dietary pattern.[72,73] Adherence to dietary and physical activity recommendations may reduce the risk of developing GD.[74] The higher risk of developing type 2 diabetes among women who had GD suggests that adoption of a healthy diet may be particularly valuable in preventing late diabetes.[75,76] Although a strong body of evidence documents the effect of a healthy dietary pattern to lower blood pressure in the general population,[77–79] data are inconsistent about its value in preventing the development of chronic hypertension after preeclampsia.[80] Future clinical trials could investigate the efficacy of dietary changes to prevent the development of CVD risk factors in women who have experienced an APO, particularly GD and hypertensive disorders of pregnancy.

### Physical Activity to Optimize Cardiovascular Health in Women of Reproductive Age and Pregnant Women

Maternal obesity is related in the short term to maternal difficulties with lactation (which as reviewed in this document has protective effects on cardiometabolic health) and in the long term with postpartum weight retention, type 2 diabetes, and increased risks of subsequent hypertensive disorders of pregnancy.[81] Health professional–led interventions may have greater efficacy at weight reduction than delivery by nonhealth professionals, and combined diet and exercise showed greater average weight reduction in a recent meta-analysis.[82] The American College of Obstetricians and Gynecologists recommends that women experiencing uncomplicated pregnancies regularly engage in moderate-intensity physical activity for at least 20 to 30 min/d on most or all days of the week.[83] Similarly, the 2008 Physical Activity Guidelines for Americans recommended 150 min/wk of moderate-intensity aerobic activity during pregnancy and postpartum spread throughout the week and continuation of vigorous activity in women who engaged in vigorous activity before pregnancy.[84]

## Other Lifestyle Factors

Maternal cigarette smoking is strongly discouraged intrapartum and postpartum given its adverse effects on fetal short- and long-term health, including preterm birth, fetal growth restriction, low birth weight, sudden infant death syndrome, neurodevelopmental and behavioral problems, obesity, hypertension, type 2 diabetes, impaired lung function, and asthma.[85] These recommendations also have bearing on CVD reduction in women with smoking-related APOs because cigarette smoking is one of the most important modifiable risk factors in premenopausal women.[86] The topics of postpartum sleep and stress, including depression/anxiety, and later CVD in women have not been well studied but represent an important area for further research and a potential opportunity for future lifestyle recommendations unique to women in their childbearing years.

# RACIAL AND ETHNIC DISPARITIES IN PREGNANCY COMPLICATIONS AND CVD

Non-White women are at an increased risk for APOs that are associated with increased maternal CVD risk. In particular, non-Hispanic Black women are at an increased risk for hypertensive disorders of pregnancy, GD, and having a miscarriage, stillbirth, preterm delivery, or low-birth-weight infant compared with non-Hispanic White women.[21,63,87–91] Hispanic women are at an increased risk of preterm birth.[90] Asian women are at an increased risk of delivering a low-birth-weight or SGA infant and for developing GD.[92]

Black women have a higher incidence of preeclampsia than White women,[87,93] and preeclampsia is increasing more rapidly among Black women than among White women.[87] Clinical presentations[87] and outcomes are commonly more severe among women of color than among White women.[94,95] For instance, the case fatality rate for preeclampsia is 2.7 times higher among Black women than among White women (73.5 versus 27.4 deaths per 100 000 cases),[93] which may be attributable to inequalities in access to prenatal care and racial disparities in obesity and other prepregnancy risk factors.[87,93] However, the Bogalusa Heart Study suggested that only a small proportion of the racial disparities in pregnancy complications can be explained by differences in established risk factors between Black and White women.[96]

Pregnancy-related mortality rates between 2011 and 2013 were much higher in non-Hispanic Black women (43.5 deaths per 100 000 live births) than among non-Hispanic White women (12.7 deaths per 100 000 live births), Hispanic women (11.0 deaths per 100 000 live births), and women of other races (14.4 deaths per 100 000 live births).[97] This disparity may be related to structural, institutional, and systemic factors that disproportionally affect Black women in the United States, including lack of adequate health care insurance and access to care and other social determinants of health that have not been uniformly or fully accounted for in prior studies.[87,98]

Although it is known that non-Hispanic Black and Hispanic women are at increased risk for both pregnancy complications and CVD risk factors and events,[87,99] the relationships among these factors are poorly understood, largely because existing cohorts may have had limited follow-up and insufficiently diverse populations to fully study these associations. Indeed, most relevant study populations include 80% to 95% White women.[26] Only 18 of the 48 articles in a recent meta-analysis adjusted for race or ethnicity, and only 2 articles examined race as a potential effect modifier.[26] In 1 study of 77 701 women from the Women's Health Initiative, race was not shown to modify the relationship between pregnancy loss and CVD,[100] but Cirillo and Cohn[101] found a significant interaction by race ($P$=0.04) in the association between gestational hypertension and CVD (HR, 1.7 [95% CI, 1.1–2.7] among Black women; HR, 0.92 [95% CI, 0.6–1.4] among non-Black women).

Studies such as the Black Women's Health Study, the largest cohort study of Black women in the United States, have the potential to examine the strength of these relationships among Black women.[102] Future studies are also needed in more diverse populations that are adequately powered to test whether race and ethnicity modify the association between pregnancy complications and CVD.

# ROLE OF LACTATION/BREASTFEEDING IN POSTPARTUM CVD PREVENTION IN WOMEN

Lactation is the second segment of the reproductive continuum and fosters recovery of maternal physiological systems to their preconception state. From this perspective, breastfeeding not only benefits the infant but also counterbalances and promotes recovery from the increased cardiometabolic stresses of normal pregnancy for the mother.[103]

Lactating women have more favorable cardiometabolic profiles, with lower fasting blood glucose, triglycerides, insulin resistance,[104] and blood pressure[105] and higher high-density lipoprotein cholesterol levels.[106–108] These favorable effects on maternal metabolism result from conserving maternal energy stores for milk production with minimal maternal weight loss (1–2 kg over a year).[107,109–111] The physiological effects of breastfeeding may reduce long-term cardiovascular risk and protect against breast and ovarian cancers.[112,113]

The CARDIA study (Coronary Artery Risk Development in Young Adults) of women 18 to 30 years of age found that longer breastfeeding was associated with higher high-density lipoprotein cholesterol levels[109] and less nonalcoholic fatty liver disease[114] and type 2 diabetes.[115] Longer-term studies found that breastfeeding was associated with a lower risk of early atherosclerosis[111] that was independent of lifestyle behaviors.[115,116] Lactation may lower CVD risk by lowering blood pressure and preventing hypertension.[117,118] The Black Women's Health Study found that longer breastfeeding duration was associated with lower risk of incident hypertension during middle age (40–49 years) but not at older ages (50–65 years).[119,120]

Studies of middle-aged and older women of Northern European ancestry found that a history of breastfeeding was associated with a 23% lower risk of myocardial infarction, coronary heart disease, subclinical CVD, and CVD events later in life.[45,121–125] Among women of childbearing age, prospective studies show somewhat stronger associations of breastfeeding with subsequent CVD events.[126]

The associations between breastfeeding duration and CVD mortality do not show consistent strength of associations or clear threshold or dose-response associations. Both ever breastfeeding and average breastfeeding duration per child (from 6–12 months) have been associated with lower risk of incident CVD hospitalization and mortality and incident ischemic heart disease or stroke compared with never breastfeeding.[124,125,127] Associations for lifetime breastfeeding duration with CVD mortality have been inconsistent.[121,128]

Evidence that breastfeeding influences CVD risk factors and outcomes among women who experience APOs has been much less available, particularly because APOs may diminish breastfeeding success, especially among Black women.[120,129,130] A cross-sectional study of women with any APOs evaluated breastfeeding status at 6 months after delivery and found more favorable cardiometabolic risk factors associated with current breastfeeding status or duration.[131] Another study of women with hypertensive disorders of pregnancy found that longer breastfeeding duration was associated with lower mean blood pressure at 9 months after delivery among women with previous gestational hypertension but not among women who were normotensive or developed preeclampsia.[132] Breastfeeding among women with a history of GD was associated with a lower incidence of subsequent type 2 diabetes, even after adjustment for weight change across the childbearing years.[115,116,133]

Breastfeeding during the first year postpartum may play an important role in reducing future risk of CVD outcomes in women, particularly for racial/ethnic groups susceptible to increased risk of APOs and CVD and who have lower prevalence rates of breastfeeding. Well-designed longitudinal studies are needed to fill major research gaps related to lactation (breastfeeding history) and future CVD risk among women with APOs.

## PHARMACOTHERAPY

Whereas several studies have investigated use of pharmacotherapy to prevent the development of APOs, very few studies have focused on preventive CVD treatment specifically among women who have had an APO.

### Intrapartum APO Prevention

Low-dose aspirin is effective in reducing the development of preeclampsia and is recommended by the Society for Maternal-Fetal Medicine, the American College of Obstetricians and Gynecologists, and the US Preventive Task Force. Guidelines recommend low-dose aspirin for women at high risk of preeclampsia (those with a history of preeclampsia, advanced maternal age, chronic hypertension, etc), starting therapy between 12 and 28 weeks of gestation (optimally before 16 weeks) and continuing until delivery.[134] Data suggest a 30% reduction in preeclampsia onset after the institution of these recent guidelines.[135] A recent randomized study of low-dose aspirin initiated after 6 and up to 13 weeks of pregnancy in low- and middle-income countries demonstrated a modest reduction in preterm birth.[136] Whether these findings extend to high-income countries is not yet known but should be investigated comprehensively. Statin therapy may have a role in the prevention and treatment of preeclampsia during pregnancy. However, there are also concerns about the safety of statins during pregnancy, and no large clinical trials have proven efficacy.[137,138]

### Postpartum CVD Prevention

Metformin has been shown to reduce the incidence of type 2 diabetes in the general population and specifically in women with a history of GD. In the subgroup of woman with GD (n=350), the Diabetes Prevention Program found that metformin reduced diabetes incidence initially and by 35% in the subsequent 10 years after study randomization compared with placebo, which is similar to the effect of intensive lifestyle modification.[139,140] Whereas a UK trial found that metformin significantly reduced the frequency of preeclampsia and maternal weight gain,[141,142] the role of metformin for women with a history of preeclampsia remains unknown.

Whereas no clinical trials have specifically tested the use of statins for CVD prevention in women with a history of APOs, the 2018 American Heart Association cholesterol treatment guidelines classify GD, preeclampsia, preterm birth, or birth of an SGA infant as

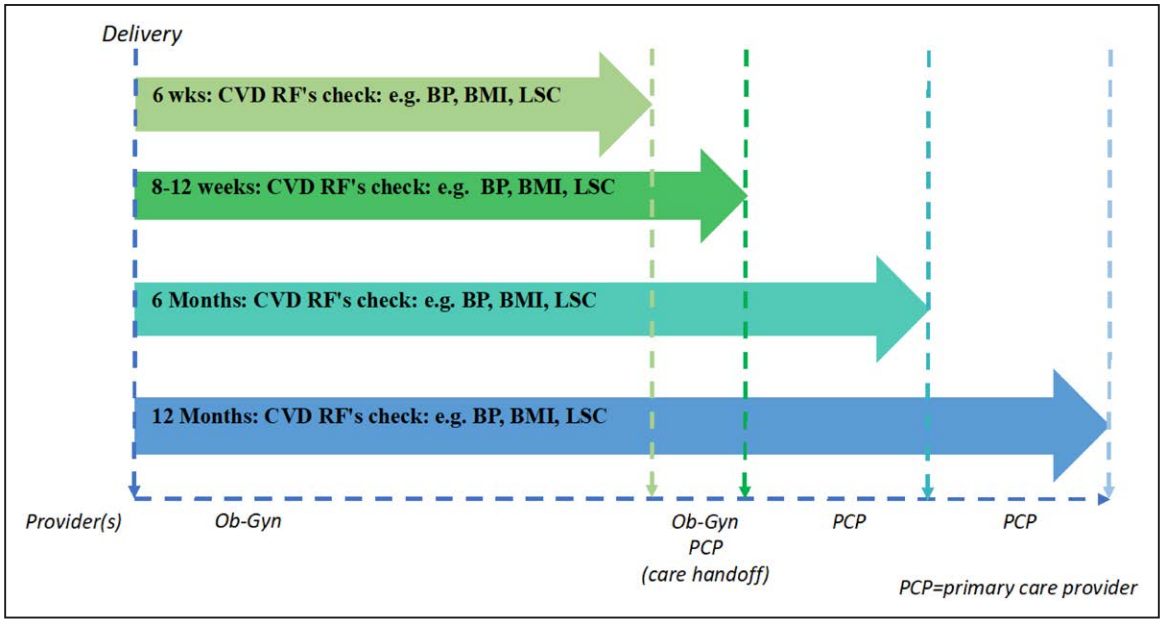


**Figure. Postpartum timing of cardiovascular disease risk factor (CVD RF) assessment and lifestyle counseling (LSC) in a woman with an adverse pregnancy outcome.**
BMI indicates body mass index; BP, blood pressure; Ob-Gyn, obstetrician-gynecologist, and PCP, primary care provider.

risk enhancers that could be discussed with the patient when deciding whether to initiate statins for primary prevention of CVD.[25] Further studies in this area are needed to clarify the role of statins in primary CVD prevention among women with APO histories.

Regrettably, most large primary prevention randomized clinical trials did not collect data on participants' history of APOs, and it is unknown whether aspirin, statins, and metformin have a special role in prevention of CVD after APOs. A recent analysis in the observational California Teachers Study showed a benefit of aspirin for primary prevention of stroke in middle age in women with a history of hypertensive disorders of pregnancy.[143] This approach has not been tested in any interventional trials.

## HEALTH CARE SYSTEMS CHANGES TO IMPROVE TRANSITIONS IN CARE FROM OBSTETRICIANS/ GYNECOLOGISTS TO PRIMARY CARE

Delivery of health care is often segmented, and information about APOs has been the concern primarily of obstetricians only. However, the period after birth is a critical period for women to set the stage for the long-term health of themselves and of their families. The American College of Obstetricians and Gynecologists has recently called this period the fourth trimester to expand the focus beyond the traditional single postpartum visit.[144] Longer coverage for postpartum care such that the obstetrician/gynecologist or other health care providers can screen for the development of CVD risk factors and provide adequate CVD risk prevention counseling, rather than simply offering a single postpartum visit, would improve long-term risk reduction for patients with APOs. Improved patient education is also necessary. Patients often do not know that having had a pregnancy complication might increase their future CVD risk.[144] Primary care physicians also may not appreciate the impact of APOs (including hypertensive disorders of pregnancy, preterm delivery, GD, SGA delivery, placental abruption, and pregnancy loss) on increased CVD risk, and these providers should be targeted for education[144] (Figure).

Another opportunity for improvement of postpartum care of women with APOs lies in more seamless communication between obstetrics providers and primary care physicians. Specifically, the separation of obstetric records from the general chart and inconsistencies in electronic record documentation may limit opportunities for CVD preventive care after an APO. This may occur even if the delivery occurred in the same institution where the woman receives primary care.[145] Improving transfer of information from obstetric providers to primary care clinicians within the permanent medical record and potentially harnessing electronic medical record information transfer and communication automation will ultimately improve the ability to deliver appropriate referrals and counseling.

Furthermore, current CVD risk assessment tools do not consider any female-specific risk factors, including APOs. The recent cholesterol treatment guidelines update did not address all APOs reviewed in this statement in terms of their recommended role as risk enhancers.[25] A recent international guideline statement from the United Kingdom

recommends, with a moderate quality of evidence, that women with hypertensive disorders of pregnancy be screened for thrombophilia subsequently and counseled to maintain a normal range of body mass index.[146] Aside from the American College of Cardiology/American Heart Association moderate-quality evidence–supported recommendations to evaluate and treat CVD risk factors among women with preeclampsia,[24] several other international societies have cited low- or very low-quality bodies of scientific evidence to make recommendations for women with hypertensive disorders of pregnancy to optimize their lifestyle for the aim of CVD prevention.[147]

Women with pregnancies complicated by hypertensive disorders of pregnancy, GD, placental abruption, and preterm delivery should be advised that these disorders are associated with a higher lifetime risk of CVD, and they should undergo CVD risk assessment.[7,24] Approaches could include a telephone education intervention[148] or use of other mobile coaching applications (apps) to enhance lifestyle change.[149] The postpartum period should be considered an opportunity to focus on lifestyle choices that optimize cardiovascular health, including weight management, smoking cessation, physical activity assessment, and nutritional counseling, particularly among those with pregnancy complications associated with increased CVD risk.[145] Currently, gaps in health insurance coverage may impede continuity of care among uninsured women. Indeed, insurance coverage by either Medicaid or the Children's Healthcare Insurance Program extends just 60 days postpartum (the latter having implications for offspring of a pregnancy and for pregnant adolescent girls, who themselves may be at a relatively higher CVD risk by way of early age at first pregnancy[150]). Legislation to continue coverage farther into the postpartum period, particularly for women with pregnancy complications, would provide better access to preventive care, as well as care of higher-risk individuals. Evaluation of CVD risk, with monitoring of blood pressure, lipids, fasting glucose, and body mass index, is recommended for women with a history of preeclampsia.[10,24] Evaluation for diabetes is recommended for women with a history of GD, including initial screening with an oral glucose tolerance test 4 to 12 weeks postpartum and further glycemic evaluation (glycohemoglobin, fasting glucose, or glucose tolerance test) every 1 to 3 years.[147]

Health care systems also need to improve follow-up for women with pregnancy complications. Consistent documentation of pregnancy complications in the medical record and coordination between obstetric and primary care providers are key. Postpartum transition clinics have proved to be an effective strategy.[151] Technology can also be used to improve cardiovascular health for women. Software algorithms can trigger patient education, referrals, and ambulatory blood pressure device monitoring. In a recent postpartum study of remote blood pressure monitoring in women who had gestational hypertension or preeclampsia, 42% of women had antihypertensive medications initiated or titrated through the program, and 88% returned for the 6-week postpartum visit.[152] Mobile phone-based apps allow consumers to monitor and enhance their health. Medical technology research in the arena of prevention and intervention strategies for behavioral change holds great promise to improve care and potentially reduce health disparities because these strategies can reach most populations.[76] Specifically, app-based coaching for increasing physical activity and making dietary behavioral changes in pregnancy and postpartum is promising but requires further study to prove efficacy.[153]

## KNOWLEDGE GAPS AND CONSIDERATIONS

APOs provide a window into women's long-term cardiovascular risk and thus can provide an opportunity to help patients engage in CVD prevention. A larger body of evidence-based studies on the timing and specific components of lifestyle modification programs that are tailored to women in the postpartum setting and during her childbearing years are needed. Better education of patients and providers, coordination of care, female-specific risk prediction models, and testing of effective interventions to reduce long-term risk are urgently needed. Given the advent of the concept of the fourth trimester of pregnancy, the obstetrician/gynecologist or other health care provider may want to use this critical period to screen for the development of CVD risk factors and to provide adequate risk prevention counseling, rather than offering simply a single 6-week postpartum visit (Figure). This concept of a fourth trimester might also be used as public policy to extend the pregnancy-related insurance coverage for several months rather than a few weeks.

## SUMMARY OF FINDINGS AND IMPLICATIONS

1. APOs (hypertensive disorders of pregnancy, preterm delivery, GD, SGA delivery, placental abruption, and pregnancy loss) increase a woman's risk of developing CVD risk factor development and later CVD.
2. Consideration of APOs is essential when evaluating CVD risk in women, although their value in reclassifying risk may not yet be established.
3. More vigorous primordial prevention of CVD risk factors and primary prevention of CVD for women with a history of APOs.
4. Adopting a heart-healthy diet and increasing physical activity among women with APOs, starting in the postpartum setting and continuing

across the life span, are important lifestyle interventions to decrease CVD risk.
5. Lactation and breastfeeding may lower a woman's later cardiometabolic risk.
6. Black, Asian, and Hispanic women experience a higher proportion of APOs, with more severe clinical presentation and worse outcomes than in White women.
7. More studies examining the association of APOs and CVD in non-White populations of women and health care implementation improvements can help to better address these health disparities.
8. Future studies of aspirin, statins, and metformin may better inform our recommendations for pharmacotherapy in primary CVD prevention among women who have had an APO.
9. Health care systems need to improve transitions of care for women with APOs and implement targeted strategies to reduce their long-term CVD risk.

## ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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*Modest.

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*Modest.

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