



Preeclampsia and Future
Cardiovascular Disease in Women
What Do We Know and What Can We Do?

Preeclampsia Foundation Position Paper

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This position paper summarizes current research findings and provides best practice recommendations related to preeclampsia and future cardiovascular disease endorsed by the Preeclampsia Foundation.

Introduction

Trying to provide accurate estimates of the incidence of preeclampsia, and more broadly hypertensive disorders of pregnancy (HDP), presents multiple challenges. This can involve variations in definitions, underrepresented populations, and the quality of data collection and reporting. Overall, HDP is estimated to occur in 5-10% of pregnancies worldwide.¹ Data from U.S. Birth Certificates in 2016 showed a rate of 6.25% (246,010 women).²

Globally, hypertension in pregnancy accounts for as much as 14% of maternal mortality and results in 10-25% of perinatal (infant) deaths.³⁻⁵ A review of preeclampsia rates in the U.S. from 1980 to 2010 found 3.4% of pregnancies in 2010 were affected specifically by preeclampsia, which represents 136,000 women per year. Preeclampsia is also responsible for 9% of maternal deaths.³ African-American women in the U.S. are nearly three times more likely to die from preeclampsia than white women.⁶ For the U.S., between 1980 and 2003, the number of women with severe preeclampsia increased 322%.³

Heart disease is the leading cause of death for women ages 65 and older in the U.S. One in every 3.2 women dies of cardiovascular causes as compared to one in 4.7 dying from breast cancer. Heart disease kills more women than cancer, lung disease, and diabetes combined. Despite advances in diagnosis and treatment, cardiovascular disease (CVD) still kills almost 400,000 women each year in the U.S.⁷ Globally, in 2013 the age-standardized death rate for all CVD was 293.2 per 100,000 for men and women combined. For ischemic heart disease, the rate was 137.8 per 100,000.⁸ Early identification of women at high risk for CVD may lead to more aggressive primary prevention, earlier diagnosis, more effective treatment, and improved survival.

In 2011, the American Heart Association (AHA) issued guidelines for the prevention of CVD in women. Chief among the recommendations for determining a woman's cardiovascular risk was the assessment of pregnancy history and complications. Within the guidelines, preeclampsia, eclampsia, pregnancy-induced hypertension, and gestational diabetes are identified as *major risk factors* for CVD.⁹ In addition, the American College of Obstetricians and Gynecologists (ACOG) acknowledges the association between HDP and future development of CVD.¹⁰ Thus, the presence of preeclampsia provides an important opportunity for early detection of women at risk for CVD to guide appropriate follow-up care and enable women to adopt lifestyle changes that may help to reduce such consequences.

Qualitative research found that women with a history of preeclampsia were relatively unaware of their added risks for morbidity and mortality – but also that they were interested in knowing about the link and in modifying behaviors to lessen risk.¹¹ Those who have experienced preeclampsia or other HDPs deserve education on what they can do to improve their health as well as clinical follow up with a focus on preventive measures. This paper discusses the specific HDP, their shared physiology with CVD, evidence concerning the significant association between HDP and future CVD morbidity and mortality, as well as preventive measures and appropriate follow-up care.

Hypertensive Disorders of Pregnancy

Screening for Hypertension in Pregnancy

When considering the benefits of screening in health care, it is critical to evaluate feasibility as well as what can be accomplished with the information provided. In this case, both the potential

severity of preeclampsia as well as the possibility of a sudden onset requires timely diagnosis. In addition, once diagnosed, effective treatments can be utilized to reduce risk to mother and infant. Routine blood pressure screening, at each prenatal visit, is now recommended for all women in pregnancy by the U.S. Preventive Services Task Force (USPSTF).¹²

The efficacy of other methods of screening such as urine tests for protein and risk-prediction models was limited because resources required to use them are not routinely found in primary care settings.¹² In addition, per the guidelines on diagnosis of preeclampsia from ACOG, the presence of proteinuria is no longer required for diagnosis.¹⁰

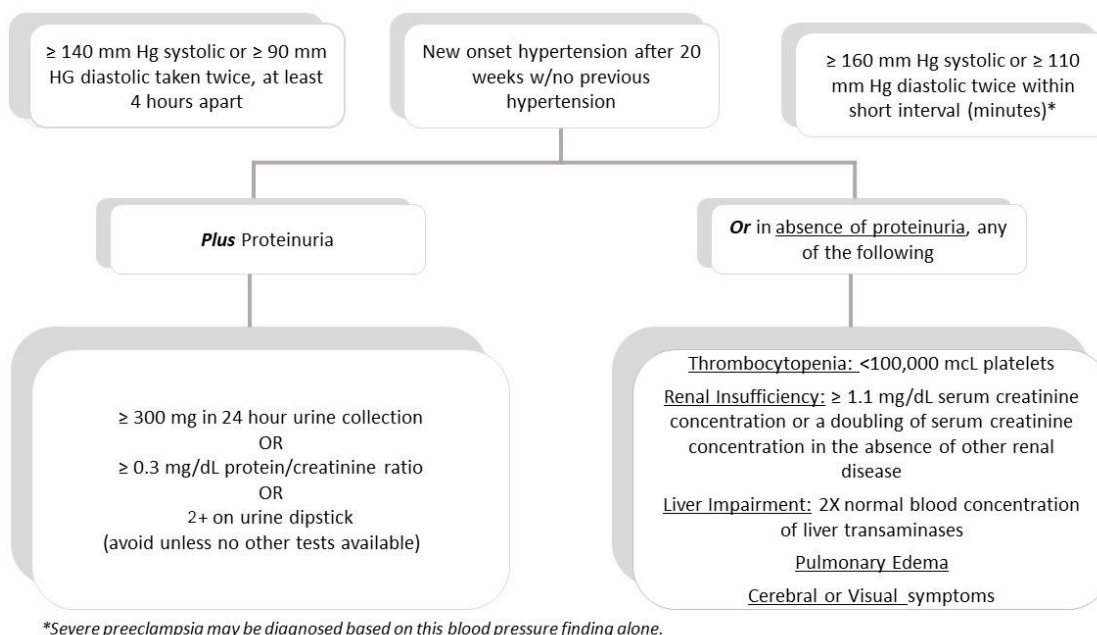
Classification and Diagnosis

The classification of hypertensive disorders during pregnancy includes preeclampsia-eclampsia (described below), chronic hypertension (pre-existing high blood pressure that continues during pregnancy), preeclampsia superimposed on chronic hypertension, and gestational hypertension (blood pressure that is elevated after 20 weeks in pregnancy without meeting the diagnostic criteria for preeclampsia) (Figure 1).¹⁰

Many terms have been used to describe these disorders including pregnancy-induced hypertension (PIH) and HDP. In addition, past classification systems have included categorization of symptoms, such as mild and severe. However, the nature of preeclampsia is that it is a progressive disease. Eclampsia occurs when a woman with preeclampsia has seizures. While most women who have preeclampsia do not develop eclampsia, it is important to remember that a diagnosis based on a single moment in time does not provide reliable assurance as to how far the disease will or will not progress, or how rapidly. For this reason, current diagnostic criteria use the term *preeclampsia-eclampsia*. Similarly, former categorizations of preeclampsia into levels of severity have been removed and symptoms indicative of increasing severity are noted. The ACOG Task Force on Hypertension in Pregnancy recommends avoiding the use of the term “mild preeclampsia” and suggests instead “preeclampsia without severe features”.¹⁰ Also of note, the diagnosis of gestational hypertension can only be confirmed *after* the pregnancy has ended, because further symptom development indicative of preeclampsia/eclampsia is always a possibility.

Figure 1 shows the current criteria for diagnosing preeclampsia recommended by ACOG and the International Society for the Study of Hypertension in Pregnancy.^{10,13} Important changes over previous guidelines include the removal of edema as a criterion and the fact that proteinuria is no longer a *required* component. In the absence of proteinuria, other factors are used to confirm diagnosis. Because of this, the term ‘atypical preeclampsia’ (once used to describe preeclampsia without proteinuria) is no longer used.

Figure 1. Diagnostic Criteria for Preeclampsia



Adapted from *Hypertension in Pregnancy: Report of the American College of Obstetricians and Gynecologists Task Force on Hypertension in Pregnancy (2013)*.¹⁰

Research shows that the severity of preeclampsia is associated with increased morbidity and mortality around the time of pregnancy. In addition, it is also linked to increased risks in the woman's future cardiovascular health. Once a woman has met the criteria for preeclampsia as described above, the additional diagnosis of *increased severity* is associated with *new or additional* onset of *any* of these signs and symptoms:

- Thrombocytopenia
- Impaired renal function
- Impaired liver function
- Pulmonary edema
- Neurological symptoms⁷

Note that other than blood pressure, the criteria for the diagnosis of increased severity are the same as those used to diagnose preeclampsia when proteinuria is absent – but it is the *new* onset of these signs and symptoms after initial diagnosis that warrants an assessment of severe preeclampsia. Eclampsia is diagnosed when a woman with preeclampsia develops new onset grand mal seizures. This can occur before, during, or after labor and birth.¹⁰

The etiology of preeclampsia has been the subject of rigorous study. One theory suggests that the disease consists of two stages.¹⁴ The first stage involves incomplete trophoblastic remodeling of the uterine spiral arteries at the time of implantation. In the second stage, the incompletely restructured arteries result in intermittent placental ischemia due to decreased perfusion. This causes the release of cytokines and other substances that lead to maternal systemic inflammation, endothelial dysfunction, and a pro-thrombotic condition. This stage is characterized

by hypertension and, in more severe cases, signs of target organ damage, such as proteinuria or elevated creatinine levels (kidney), elevated liver enzymes (liver), or neurological symptoms (brain). Another hypothesis builds on the fact that many of the precursors to preeclampsia are also precursors to CVD pointing to a genetic etiology that leads to metabolic syndrome, inflammation, and endothelial dysfunction.¹⁵

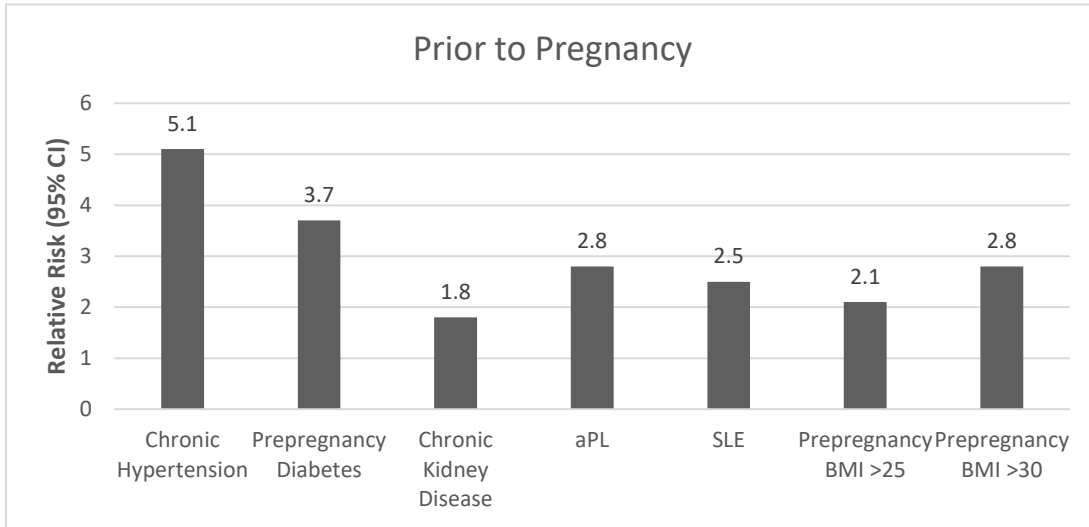
Community Summary: Hypertensive Disorders of Pregnancy

- There are four main disorders related to high blood pressure during pregnancy:
 - 1a. **Preeclampsia:**
 - You start pregnancy with normal blood pressure and
 - Your blood pressure increases up to or above 140/90mmHg during your pregnancy and
 - You have high levels of protein in your urine or your doctor finds you have high platelets or new liver, kidney, lung, or brain illness
 - 1b. **Eclampsia:**
 - You are diagnosed with preeclampsia (see #1) during your pregnancy and
 - You have seizures
 - 2. **Chronic hypertension:**
 - You start pregnancy with high blood pressure and
 - Your high blood pressure stays high during your pregnancy
 - 3. **Preeclampsia superimposed on chronic hypertension:**
 - You start pregnancy with high blood pressure and
 - You also get diagnosed with preeclampsia (see #1) during your pregnancy
 - 4. **Gestational hypertension:**
 - You start pregnancy with normal blood pressure and
 - Your blood pressure increases during your pregnancy but not high enough to be diagnosed with preeclampsia
- Together these disorders are called hypertensive disorders of pregnancy, or HDP.
- Why and how preeclampsia happens is not fully understood yet. But doctors and scientists have a good guess (or “theory”) from the research that has been done so far:
 - Stage 1: At the very beginning of pregnancy, the cells of the placenta are supposed to travel a short distance into the wall of your uterus and help make some of the blood vessels of the uterus bigger. This helps your uterus send extra blood to the placenta as your baby grows. It is thought that in women who get preeclampsia, these cells do not do this well enough and your uterus’ blood vessels stay small.
 - Stage 2: Because the cells of the placenta did not remodel the uterus’ blood vessels to be big enough, this means not enough blood gets to your placenta and your placenta can get sick. This sick placenta makes the rest of your body sick too.

Risk Factors for Preeclampsia in Pregnancy

A systematic review of large sample cohort studies in 2016 reported on risk factors for preeclampsia based on over 25 million pregnancies.¹⁶ Risks for preeclampsia can be considered in three categories: those that occurred in a previous pregnancy, those present in the current pregnancy, and conditions that existed before pregnancy. Based on this study, Figure 2 provides the relative risk (95% CI) of developing preeclampsia associated with common pre-existing conditions. (Relative risk is a measure of an event happening in one group compared to the risk of it occurring in another group. So, for instance, in this chart, someone with chronic hypertension is five times more likely to develop preeclampsia than someone who does not have it before pregnancy.)

Figure 2: Risk Factors for Developing Preeclampsia: Conditions Prior to Pregnancy

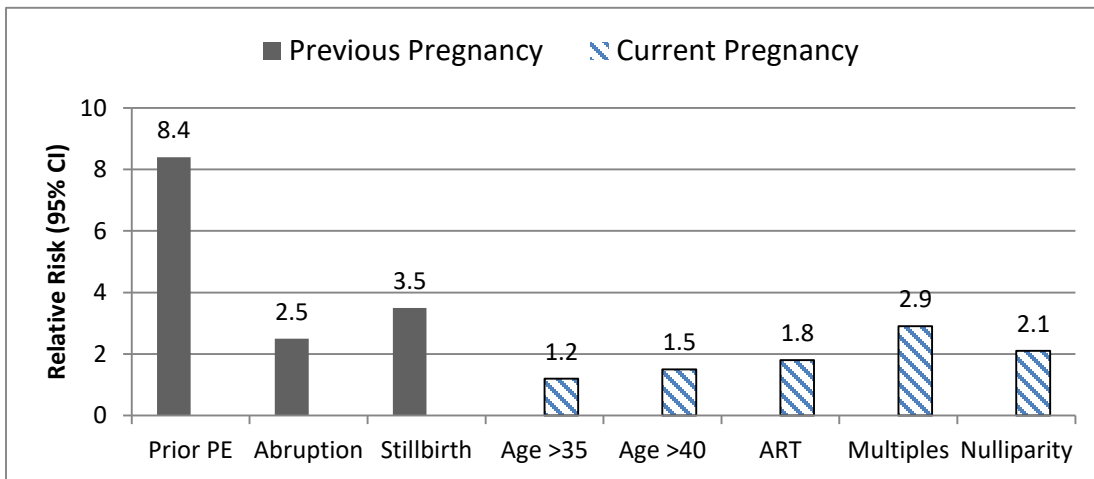


Note: aPL = anti-phospholipid syndrome; SLE = systemic lupus erythematosus

Adapted from: Bartsch, E., Medcalf, K.E., Park, A.L., Ray, J.G., High Risk of Pre-eclampsia Identification Group. *Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies.* (2016).¹⁶

For risk factors that may develop during a current or previous pregnancy, Figure 3 shows the relative risk of developing preeclampsia. Of note, the greatest risk factor for having preeclampsia in any pregnancy is a previous pregnancy with preeclampsia. Without any other risks being present, this one attribute can make a woman as much as eight times more likely to develop preeclampsia than another woman with no history of preeclampsia.

Figure 3: Risk Factors for Developing Preeclampsia: Previous and Current Pregnancy



Note: PE = preeclampsia; ART = assisted reproductive technology

Adapted from: Bartsch, E., Medcalf, K.E., Park, A.L., Ray, J.G., High Risk of Pre-eclampsia Identification Group. *Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies.* (2016).¹⁶

A 2005 review of preeclampsia risk factor cohort studies reported similar findings. In addition to the factors described above, the authors found a 1.3 times increased risk for preeclampsia each year when a woman is over 40. If she has a first-degree relative with preeclampsia, her risk is increased threefold. For women with five or more years between births, the risk for preeclampsia increased 1.8 times.¹⁷

Community Summary: Risk Factors for Preeclampsia in Pregnancy

- Doctors and researchers have identified conditions and habits that can increase your chance for preeclampsia. These are called “risk factors.”
- Conditions that can increase your chance of getting preeclampsia (meaning risk factors for preeclampsia) include:
 - 1. *Factors that you already had before you got pregnant:*
 - Having high blood pressure before you got pregnant
 - Having diabetes before you got pregnant
 - Having chronic kidney disease before you got pregnant
 - Being overweight or obese before you got pregnant
 - 2. *Factors that happened during your last pregnancies:*
 - Having had preeclampsia before
 - Having had a placenta abruption
 - Having delivered a stillborn baby
 - 3. *Factors that are happening during your pregnancy now*
 - Being pregnant for the first time
 - Being 35 years old or older
 - Having used assisted reproductive technology, like IVF, to get pregnant
 - Being pregnant with multiples (twins, triplets, etc.)
 - Waiting five or more years between your last pregnancy and current pregnancy
- Having had preeclampsia before is the *greatest risk factor* for having preeclampsia in a future pregnancy.

Survivor’s Action Steps

- *Know your risk:* Review the risk factors for preeclampsia above and talk to your OB/GYN doctor about how your last pregnancy (or pregnancies) turned out, your health before you became pregnant, your health when you got pregnant, and how you feel during this pregnancy.

Cardiovascular Disease in Women

While atherosclerosis of the coronary arteries occurs in both women and men, CVD in women involves some mechanisms not as commonly seen in their male counterparts. Men predominantly develop obstructive coronary artery disease in the larger vessels of the heart. In addition, atherosclerotic lesions or plaques in men are more prone to rupture, causing myocardial infarction. By contrast, the most common cause of myocardial infarction among women is plaque erosion (the cap of the plaque wears thin to expose vessel components that activate the formation of clots). Further, women often have microvascular (small vessel) disease not visualized by standard coronary angiography.¹⁸ This microvascular disease is reactive dysfunction that has both an endothelial and non-endothelial component.¹⁹ Also, women may more frequently experience coronary artery spasm or dissection.^{20,21}

Microvascular disease is difficult to detect or diagnose. It is not detected with standard coronary angiography and therefore diagnosis of microvascular disease and coronary spasm often involves testing that delivers medications that evoke vessel spasms, making them higher risk procedures. Women who present with chest discomfort and normal-appearing major coronary

arteries may be misdiagnosed as not having CVD when, in fact, they do experience a lack of adequate blood flow to the heart muscle. This diagnostic challenge can lead to delayed treatment or complete omission of therapies directed at the management of CVD and prevention of complications.

Mortality rates following acute myocardial infarction, angioplasty, and coronary artery bypass are higher in women compared to men. Women appear to be under-screened and under-treated, sometimes despite falling into a high-risk category by traditional scoring methods.²² In order to change this pattern, the National Heart, Lung, and Blood Institute, in conjunction with national and community organizations, has developed “The Heart Truth,” a campaign to direct attention to heart disease among women, including those with non-traditional risk factors such as preeclampsia, who may need a more aggressive approach than previously taken.²³

Community Summary: Cardiovascular Disease in Women

- Cardiovascular disease is a disease of the heart and blood vessels.
- Cardiovascular disease can *look* differently in women because the *causes* of cardiovascular disease can be different for women. This makes it harder to spot cardiovascular disease in a woman compared to a man.
- There is a higher chance a woman who *does* have cardiovascular disease will be have a missed or delayed diagnosis.
- Missed and delayed diagnoses of cardiovascular disease in women have caused the number of deaths from cardiovascular disease to be *higher in women* compared to men.
- “The Heart Truth” campaign was started to teach people about cardiovascular disease in women. The goal is to improve diagnosis and treatment of cardiovascular disease in women.

Survivor’s Action Steps

- Learn the signs and symptoms of heart events in women: <https://www.heart.org/en/health-topics/heart-attack/warning-signs-of-a-heart-attack/heart-attack-symptoms-in-women>
- Visit The Heart Truth and make a commitment to your heart: <https://www.nhlbi.nih.gov/health/educational/hearttruth/index.htm>

Risk Factors for Cardiovascular Disease

Risk factors for CVD in women are similar to those in men, and include age, smoking, hypertension, diabetes, and dyslipidemia. Some risk factors are unique to women, such as estrogen exposure and postmenopausal state. Among these factors, age is the most influential. In general, CVD predominantly affects women ages 65 or older; however, there are certain subgroups who are at increased risk at earlier ages. Among these groups are women who have a history of HDP. In fact, women with preeclampsia have been noted to have CVD and thromboembolic events as early as five to 10 years following the index pregnancy.²⁴

Identifying and determining the influence of CVD risk factors helps to establish the threat of CVD for specific individuals. Traditional Framingham risk scoring relies on risk factors common to both men and women, and may underestimate the risk for cardiovascular events in some women. In 2013, new pooled cohort CVD risk equations based on several longitudinal studies that included more women and non-Hispanic African-Americans were adopted and published by the AHA and the American College of Cardiology (ACC). These new risk calculators provide gender- and race-specific risk assessments for white and non-Hispanic African-American men and women.²⁵ Of note, within these tools, the risk contribution of HDP was not directly addressed.

In a guideline specifically addressing CVD prevention in women, the AHA recommends categorizing women as high risk, at risk, or optimal risk, or unclassified based on the number and types of risk factors identified. Women at high risk have one or more of the following: a) known coronary heart disease, b) cerebrovascular disease, c) peripheral arterial disease, d) abdominal aortic aneurysm, e) chronic kidney disease, f) diabetes, or g) a 10-year predicted CVD risk of 10% or more (using a risk calculation tool). Women considered to be in the at-risk category include those who have one or more major risk factors. Importantly, HDP were identified as major risk factors along with smoking, hypertension, dyslipidemia, obesity, poor diet, physical inactivity, metabolic syndrome, systemic autoimmune collagen-vascular disease, family history of premature CVD, evidence of subclinical atherosclerosis, and poor exercise capacity.⁹

Community Summary: Risk Factors for Cardiovascular Disease

- Doctors and researchers have identified habits and conditions that can increase your chance for cardiovascular disease. These are called “risk factors.”
- Examples of risk factors for cardiovascular disease are: your age, your blood pressure, if you smoke, if you have diabetes, and if you have gone through menopause. The strongest risk factor for cardiovascular disease is your *age*: the older you are, the higher your risk for cardiovascular disease. Some factors are unique to women, like menopause or pregnancy history.
- Preeclampsia (and other conditions of high blood pressure in pregnancy) is a risk factor for future cardiovascular disease. This means **if you have had preeclampsia, you have a higher chance of having cardiovascular disease.**
- *Risk factors for heart disease for women include:* coronary heart disease, cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm, chronic kidney disease, diabetes, calculated risk score more than 10%, history of preeclampsia, history of high blood pressure that only occurred during pregnancy, history of gestational diabetes, smoking, high blood pressure, high cholesterol, obesity, poor diet, physical inactivity, family history of early heart disease, metabolic syndrome, early atherosclerosis, poor exercise test results, or lupus.
- You can figure out your chance of having cardiovascular disease by counting how many risk factors you have.
- Doctors classify women into three “risk categories” for cardiovascular disease: *high risk, at risk, or optimal risk.* Ask your doctor or see *Survivor’s Action Steps* below to figure out your risk.

Survivor’s Action Steps

- *Tell your doctor!* Let your doctor know if you have had preeclampsia or any other risk factors. Tell her or him you want to keep your heart healthy and ask about your cardiovascular disease risk.
- See “Questions to Ask Your Doctor” to help guide your conversation at <https://www.nhlbi.nih.gov/health/educational/hearttruth/lower-risk/ask-doctor.htm>.
- You can also estimate your chance of cardiovascular disease by yourself (below).
- Calculate your chance of getting cardiovascular disease within the next 10 years with this tool: <http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/>
- Know which risk group you fall into:
 - You are at “*high risk*” for cardiovascular disease if you have *one or more* of these risk factors: coronary heart disease, cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm, chronic kidney disease, diabetes, or calculated risk score more than 10%.
 - You are “*at risk*” for cardiovascular disease if you have *one or more* of these risk factors: history of preeclampsia, history of high blood pressure that only occurred during pregnancy, history of gestational diabetes, smoking, high blood pressure, high cholesterol, obesity, poor diet, physical inactivity, family history of early heart disease, metabolic syndrome, early atherosclerosis, poor exercise test results, or lupus.
 - You have “*ideal cardiovascular health*” if you have *all* of these factors: total cholesterol less than 200mg/dL, blood pressure less than 120/80mmHg, fasting blood sugar less than 100mg/dL, are not overweight or obese, do not smoke, physically active at least 150 minutes a week at moderate intensity or at least 75 minutes a week at vigorous intensity, and eat a healthy diet.

Cardiovascular Disease after Hypertensive Disorders in Pregnancy

Cardiovascular sequelae of preeclampsia have prompted a search for a common mechanism or predisposing factors. It is unclear whether the physiological demands of pregnancy unmask underlying metabolic and vascular disease, or whether HDP cause damage to the vasculature or trigger inflammatory, autoimmune, or other responses.²⁶ Some authors propose that both mechanisms play a role.²⁷ Research related to each of these hypotheses continues.

Pathophysiology and Shared Risk Factors

One theory suggests that preeclampsia does not cause future health issues, but rather that it shares many of the same physiological features associated with CVD, for example endothelial dysfunction. At the tissue level, what is known is that both women with preeclampsia and those with CVD demonstrate inflammation and endothelial dysfunction.^{28,29} In fact, Noori et al. postulated that endothelial dysfunction may be a pre-existing condition in women who go on to develop preeclampsia.³⁰ This group also found that brachial artery flow-mediated dilation, a test of endothelial function, was abnormal throughout the pregnancies of women with preeclampsia. Further, Chambers et al. found that preeclamptic women continued to have lower brachial artery flow-mediated dilation up to three years after the reference pregnancy.³¹ Endothelial dysfunction conveys significant risk for CVD. Bairey, Merz et al. synthesized the results of 15 studies and found that women with endothelial dysfunction had nearly a tenfold increased risk for experiencing adverse CVD events compared to individuals without this problem.³² From this perspective, having preeclampsia in pregnancy may serve as an early and important marker for increased risk of heart disease and vascular disorders.

While they may share mechanisms or risk factors at the cellular level, preeclampsia and CVD have more easily observable shared risk factors. These include family history of CVD, chronic hypertension, pre-existing diabetes mellitus, dyslipidemia, and obesity. Family history of premature CVD (before the age of 65 for women and 55 for men) is a risk factor for the development of CVD. Additionally, for women having a first-degree female relative with CVD is a greater risk factor than having a male family member with the disease.³³ Despite this relationship, family history is not included in frequently used risk prediction tools, as this factor has not been demonstrated to improve initial risk prediction.³⁴ Patient history of a first-degree relative with premature CVD can be used by providers to revise the risk assessment upward when the recommendation for pharmacological therapy is uncertain.²⁵

Family History

Following a pattern similar to CVD, family history of preeclampsia increases a woman's risk of developing preeclampsia herself. Interestingly, a family history of CVD is also associated with an increased risk of preeclampsia. Ness et al. found an increased prevalence of coronary artery disease and stroke among relatives of women who developed preeclampsia.³⁵ Having two or more relatives with CVD almost doubled the risk of preeclampsia (1.9, CI 95% 1.1 – 3.2), and having two or more relatives with coronary artery disease or cerebrovascular accident more than tripled the risk (3.2, CI 95% 1.4 – 7.7). Specific mechanisms of disease were not studied in this epidemiologic investigation.

Thrombophilia

Small cases control studies initially suggested an association between preeclampsia and common inherited thrombophilic conditions, such as Factor V Leiden and prothrombin gene

mutation.^{24,36} However, more recent, large retrospective, prospective cohort studies and meta-analyses have supported either a weak association⁸⁵ or no relationship at all⁸⁶. Based on these conflicting results, the ACOG practice bulletin on hypertension in pregnancy states that there is insufficient evidence to conclude that inherited thrombophilia disorders are associated with an increased occurrence of preeclampsia. Routine screening for these disorders in pregnancy is not recommended.¹⁰

Obesity

In recent years increasing attention has been focused on weight as a risk factor for CVD. Obesity increases the risk of CVD by threefold.²⁶ High maternal body mass index (BMI) is a strong predictor of several adverse pregnancy outcomes, including gestational hypertension and preeclampsia.^{37,38} Low BMI is associated with protection against preeclampsia, whereas women with high BMI have a greater risk for severe preeclampsia and early onset preeclampsia.^{39,40}

In a study of 1,179 primiparous women (women pregnant for the first time), Bodnar, et al. found that a woman with a BMI of 26 kg/m² has double the risk of preeclampsia compared to a woman with a BMI of 21. Further, a BMI of 30 represents triple the risk and when severe obesity is present (≥ 35), there is 3.5 times the risk for developing preeclampsia.⁴¹ In women with normal weight in pregnancy, gaining weight between pregnancies also increases the risk of preeclampsia. An increase of just 1–2 BMI units between pregnancies increases the risk for preeclampsia by 23% – and the risk almost doubles with a gain of 3 BMI units.⁴²

While some studies have shown that obesity is a risk factor for preeclampsia, a small retrospective case-controlled study of women with preeclampsia matched to normal pregnancy controls by BMI, age, and parity found no relationship between BMI and preeclampsia. Instead, this study found that preeclampsia was associated with an increase in prevalence of the components of the metabolic syndrome. Importantly, evidence of metabolic syndrome was 10 times more common in preeclamptic women than BMI matched controls.⁴³

Metabolic Syndrome

Criteria for metabolic syndrome in women include abdominal adiposity (abdominal circumference >35 inches), elevated blood pressure (above 130/85 mm Hg), elevated fasting glucose (above 110 mg/dL), and dyslipidemia (high-density lipoprotein or HDL below 50 mg/dL and triglycerides above 150 mg/dL).⁴⁴ High BMI is not specifically listed as a criterion for metabolic syndrome; however, obesity is more common in metabolic syndrome patients and abdominal adiposity is a criterion.

Metabolic syndrome has been implicated in pathogenesis of CVD, diabetes, non-alcoholic fatty liver disease, kidney disease, and sleep-disordered breathing.⁴¹ There is no current consensus on whether or not metabolic syndrome is a stronger predictor of CVD than the sum of each of its components. Women with a history of preeclampsia in pregnancy frequently exhibit features of metabolic syndrome.^{28,43,45} Risk factors for CVD such as hypertension, obesity, and dyslipidemia are shared between metabolic syndrome and atherosclerosis.⁴⁶ Other commonalities include endothelial dysfunction and inflammation. Recognition of metabolic syndrome may facilitate implementation of lifestyle interventions that may prevent progression of the syndrome and potentially prevent diseases associated with it.⁴⁷

Another feature of metabolic syndrome is elevated blood glucose and insulin resistance.⁴⁸ Women with preeclampsia frequently demonstrate insulin resistance.⁴³ Normal pregnancy is associated with increased insulin levels; however, fasting insulin is higher in preeclamptic pregnancy, even prior to the onset of clinical disease.⁴⁹ Insulin resistance and increased sympathetic tone in pregnancy are thought to potentially contribute to the development of vasoconstriction associated with preeclampsia.⁵⁰ More importantly, insulin resistance does not reverse in the postpartum period. Women with a history of preeclampsia have insulin resistance up to 20 years after the index pregnancy.^{51,52} Insulin resistance is an important risk factor for CVD in women.⁵³

Diabetes

More severe forms of insulin-related abnormalities are found in diabetes mellitus, which is also a risk factor shared by preeclampsia and CVD. The most common form of diabetes, Type 2 diabetes, is caused by insulin resistance. Diabetes increases the risk of developing preeclampsia by two- to four-fold.⁵⁴ CVD risk is doubled by type 2 diabetes and the risk is higher in women than in men, especially among women between the ages of 40 and 59 years.⁵⁵ Recent research has also demonstrated that pregnant women with type 1 diabetes who have an elevated level of Serum Fatty Acid Binding Protein 4 (FABP4) are at increased risk for preeclampsia. A second trimester elevation was independently associated with preeclampsia (OR 2.87). This suggests that FABP4 could be used as a biomarker for preeclampsia risk in women with type 1 diabetes.⁵⁶

Dyslipidemia

Dyslipidemia is yet another risk factor shared by preeclampsia and CVD. It is also a component of the metabolic syndrome. Elevated levels of cholesterol and low-density lipoprotein (LDL) pre-pregnancy are associated with increased risk of preeclampsia.⁴⁶ Lower levels of HDL and elevated levels of total cholesterol, LDL, and triglycerides have long been known to be associated with an increased risk of CVD disease. Hyperlipidemia causes endothelial dysfunction, another common thread between HDP and CVD.⁵⁷

Community Summary: Cardiovascular Disease after Hypertensive Disorders in Pregnancy

- **Women who have had preeclampsia have a higher chance of having cardiovascular disease.** Doctors and researchers have two theories for this:
 - 1. Perhaps preeclampsia causes long-term damage to the body, especially the heart and blood vessels, and this damage could put women at high risk for cardiovascular disease later in life.
 - 2. Perhaps a woman who gets preeclampsia already had a less healthy heart and blood vessels. Then, when she gets pregnant, her pregnancy stresses her blood vessels and heart even more and results in preeclampsia.
- To help understand the link between preeclampsia and cardiovascular disease, doctors and researchers have looked at similarities between the risk factors of both preeclampsia and cardiovascular disease and found that:
 - A family history of preeclampsia increases a woman's risk for both preeclampsia and cardiovascular disease.
 - Obesity (body mass index [BMI] greater than 30 kg/m²) increases a woman's risk for both preeclampsia and cardiovascular disease.; also having a low BMI has been shown to protect women against preeclampsia.
 - Metabolic syndrome (diagnosed by the presence of at least three of these factors: large waist circumference, elevated blood pressure, elevated fasting blood sugar, low HDL [the "good" cholesterol], and/or elevated triglycerides) increases a woman's risk for both preeclampsia and cardiovascular disease.
 - Diabetes increases a woman's risk for both preeclampsia and cardiovascular disease.
 - Elevated levels of cholesterol and low-density lipoprotein (dyslipidemia) increase a woman's risk for both preeclampsia and cardiovascular disease.

Evidence for the Link between HDP and Future CVD

Evidence on the association of HDP and future CVD and death has been increasing steadily. As mentioned previously, debate continues as to whether preeclampsia itself causes the increased risk for subsequent CVD or whether preeclampsia and CVD share physiologic features and risk factors, such that preeclampsia serves as a marker for women who are already at increased risk. One large prospective study in Finland of more than 10,000 women followed for an average of 39.4 years showed that HDP was associated with an increased incidence of CVD, renal disease, and diabetes even in those women without traditional cardiac risk factors.⁵⁸ In another study of 302,686 women in Florida who experienced placental syndromes (preeclampsia, placental infarction, or placental abruption) there was a 39% increase in their risk of a CVD event within five years of the index pregnancy.⁵⁹

The vast majority of the evidence of a link between HDP and CVD comes from cohort studies. A systematic review with meta-analysis is the highest quality method of synthesizing results of multiple studies with similar characteristics. Three systematic reviews with meta-analysis have been published on the association of preeclampsia and later CVD.^{24,36,60} These reviews provide important information from a combination of 48 unique studies representing over 3.5 million pregnancies (after eliminating duplicates between reviews).⁶¹

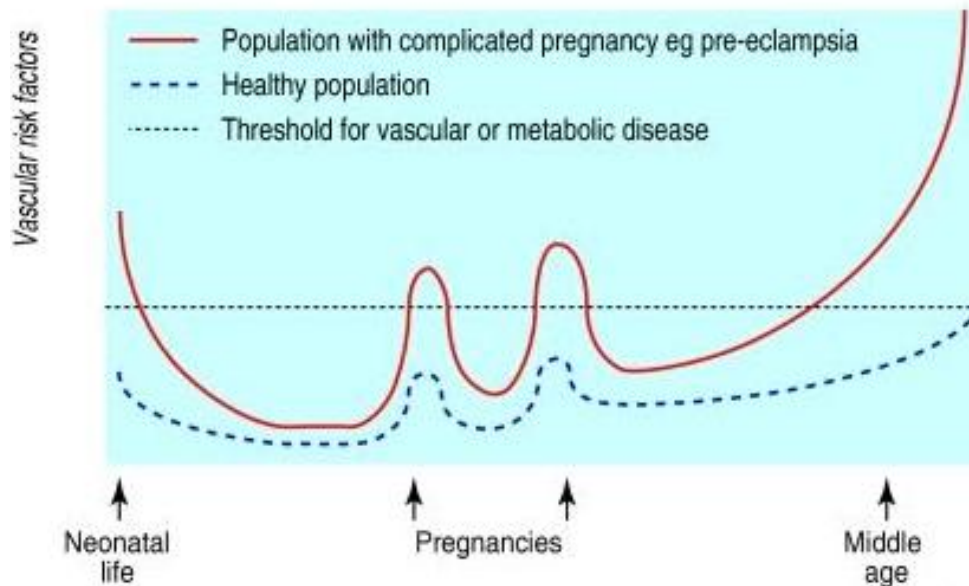
When reviewing evidence, it is important to note that individual studies vary in what parameters were measured and how terms such as preeclampsia were defined. The studies represented in these reviews took place over long periods of time during which the diagnostic criteria for preeclampsia evolved. Most significantly, the requirement for proteinuria as a criterion for preeclampsia predominated the period when these studies were conducted. Due to this more stringent definition, it is likely that preeclampsia and other HDPs were under-diagnosed. Appendix 1 provides a detailed table of the findings of the three reviews. A summary of those results is presented here.

As summarized in the review by Leslie and Briggs, women have a greater than twofold increase for developing CVD after having preeclampsia in pregnancy. The likelihood of dying from ischemic heart disease, heart failure, or stroke is also more than doubled. Women with a history of preeclampsia also have a 1.8 times greater risk for venous thromboembolism and peripheral arterial disease.⁶¹

Certain factors within the pregnancy can increase these risks. These include premature birth, the severity of the disease, and the gestational age at which problems began. Premature birth is an independent risk factor for CVD. Compared to a woman having a term birth (≥ 37 weeks), a preterm birth increases the chances of subsequent CVD nearly 1.5 times (HR, 1.42). In very preterm births (< 32 weeks), there is double the incidence of CVD later in life.⁶² When preterm delivery occurs in a pregnancy affected by preeclampsia, the risk for subsequent CVD is nearly eight times higher than it is for a mother without preeclampsia and a term birth.⁶¹

For survivors of preeclampsia, the likelihood of developing CVD increases exponentially depending on the woman's age at the time of the evaluation. This is because the risk for CVD itself increases over time for all women. The incidence of CVD in young women is low (0.6% for women ages 20-39 years) and in middle age is intermediate (5.6% for women ages 40-50 years). Women older than 50 years have a lifetime risk of 32.9% for CVD. In addition to the age-related increases, having preeclampsia in pregnancy can multiply the risk. For example, both a 20-year-old and a 40-year-old woman after preeclampsia have approximately double their baseline risk for CVD.

However, their baseline risks are age dependent. So, the 20-year-old woman with a baseline risk of 0.6% now has a CVD risk of 1.2%, whereas the 40-year-old woman with a history of preeclampsia sees a jump from 5.6% to 11.2% in the likelihood of having CVD. In this case, it is not the age at the time of pregnancy, but a woman's current age that is significant. This exponential increase in risk provides strong rationale for the importance of early intervention starting as soon after preeclampsia occurs as possible.²⁴



Sattar N, Greer LA. Pregnancy complications and maternal cardiovascular risk: opportunities for intervention and screening? BMJ. 2002 Jul 20;325(7356):157-60.

In addition to impacting the future health of the preeclampsia survivor, HDP may affect their children. They may be at increased risk for childhood and adult hypertension, stroke, diabetes, cardiovascular disorders, mood and anxiety disorders, and reduced cognitive function.⁶³ Research in this area is expanding and high-quality studies with large numbers of subjects are needed to provide a clearer picture.

Community Summary: Evidence for the Link Between HDP and Future CVD

- *Reminder.* “HPD” or “hypertensive disorders of pregnancy” is a term for the group of disorders involving high blood pressure specifically in pregnancy, including preeclampsia, eclampsia, chronic hypertension, preeclampsia superimposed on chronic hypertension, and gestational hypertension.
- Research has shown over and over that having a “hypertensive disorder of pregnancy” is linked to future cardiovascular disease:
 - A large study of more than 10,000 women from Finland found women who had a “hypertensive disorder of pregnancy” were more likely to have cardiovascular disease, kidney disease, and diabetes by the age of 40 years old.
 - Another large study of more than 300,000 women in Florida, USA found that women who had preeclampsia or another placenta syndrome (infarction or abruption) had a 39% higher chance of having cardiovascular disease just five years after having their babies.
 - Combining data from multiple studies to make a giant study of more than 3.5 million women, investigators found **women have double the chance of getting cardiovascular disease if they had preeclampsia.** Also found in this study, women who had preeclampsia have over two times higher chance of dying from heart disease, heart failure, or a stroke.
 - Interestingly, other pregnancy complications are also linked to future cardiovascular disease. For example, women who deliver their baby preterm (meaning less than 37 weeks’ gestation) have a 40% higher chance for having cardiovascular disease.
- Just as a woman’s risk of cardiovascular disease increases with age, if she has had preeclampsia, her cardiovascular disease risk increases even quicker. This means it is very important to start “interventions” to try to prevent cardiovascular disease as soon as possible.
 - An “intervention” can mean seeing your doctor regularly, staying or becoming a healthy weight, taking medicine, etc.
 - See the next section about how to reduce your risk and how survivors should follow up with their doctors after having preeclampsia.
- Children of women with a “hypertensive disorder of pregnancy” also have an increased risk of disease. A child’s chance of having high blood pressure, stroke, diabetes, cardiovascular disorder, and mood and anxiety disorders as an adult is higher if s/he was born from a mother with a hypertensive disorder during pregnancy.

Survivor’s Action Steps

- *Keep reading!* These numbers can be scary, especially for survivors and their loved ones. The best action you can take is to learn about your health and take action to make your health better. Now that you know the numbers, the next section is all about how to reduce your risk for cardiovascular disease.

Risk Reduction and Follow-Up Care

Preeclampsia survivors frequently receive information about the risk for future recurrence of preeclampsia; however, they are rarely advised on their increased cardiovascular risk and available interventions for risk reduction. Evidence on effective interventions for these women is limited. Berks et al. used statistical modeling to estimate the effects of lifestyle modifications, such as regular exercise and a healthy diet, on the risk of CVD in women with a history of preeclampsia and found that such interventions could decrease the risk by between 4% and 13%.⁶⁴

Until additional information is available, recommendations provided by AHA’s *Effectiveness-based Guidelines for the Prevention of Cardiovascular Disease in Women: 2011 Update*⁹ along with the recommendations of ACOG regarding later-life CVD in women with prior preeclampsia provide the best available guidance.¹⁰ These recommendations are synthesized below:

Pregnancy History

When possible, actual prenatal and delivery records should be obtained and entered into a woman's medical record. If records are not available, a history may be sufficient for further risk stratification. Women with preeclampsia and preterm delivery (less than 37 weeks) or recurrent preeclampsia face significantly increased risk for cardiovascular events and thus constitute the highest risk group.^{10,24} These women should have an annual assessment of their blood pressure, lipids, fasting glucose, and BMI.¹⁰ Gestational diabetes and gestational hypertension are also associated with increased cardiovascular risk.⁹

Medical and Family History

The ACC and AHA guidelines for the assessment of CVD risk recommend that all men and women ages 20 to 79 be screened for traditional risk factors every four to six years.²⁵ Women with chronic hypertension, diabetes, and other comorbid conditions that may have contributed to the development of preeclampsia are at increased cardiovascular risk due to the nature of these comorbidities, which should be managed in accordance with national guidelines. A family history of premature CVD may identify women who need early aggressive risk-factor modifications. A population-based cardiovascular risk calculator should be used to determine a woman's 10-year risk of CVD. For women ages 20-59 years, who are not at high 10-year risk (> 7.5%), the 30-year risk calculation can be considered to guide management.²⁵ It should be noted though that none of the existing calculators incorporate pregnancy complications (such as preeclampsia) in estimating this risk. A history of HDP can significantly increase a woman's risk as previously described and until a risk calculator includes pregnancy history, the accuracy of the predicted risk cannot be assumed. Assessing for symptoms of CVD and depression is also advocated by AHA.⁹

Metabolic Syndrome Assessment

Women with a history of HDP need to be assessed for obesity (BMI and waist circumference), hypertension, and dyslipidemia (elevated total cholesterol, LDL, and triglycerides, or low HDL) as well as abnormal glucose metabolism (impaired fasting glucose, impaired glucose tolerance, or diabetes), as these disorders are risk factors for CVD and preeclampsia. Lipid testing can be performed within 12 weeks postpartum and post-lactation and then annually.⁶⁵ Glucose testing should be performed within six weeks if the woman experienced gestational diabetes. All women with a history of HDP should have glucose screening annually.¹⁰

Counseling and Goal Setting

Lifestyle Modifications:

All women should engage in lifestyle modifications as the first step in preventing CVD. The AHA defines "ideal health behaviors" as not smoking, having a BMI of less than 25 kg/m², engaging in moderate physical activity for at least 150 minutes per week, and consuming a healthy diet.⁶⁶ One of the cornerstones of promoting a healthy lifestyle is smoking cessation. Any patient who smokes tobacco should be routinely advised to quit given the significantly increased cardiovascular risk associated with tobacco use. In the Interheart Study, a large multinational study examining CVD risk factors, cigarette smoking almost tripled the risk of acute myocardial infarction, especially for younger individuals.⁶⁷

Current dietary recommendations call for consumption of more vegetables and fruits as well as foods that are low in saturated and trans-fat, and high in fiber. Sodium intake should also be

limited to between 1,500 and 2,400 mg per day. Diets that incorporate these recommendations include the Dietary Approaches to Stop Hypertension (DASH) diet, the USDA Food Pattern, and the AHA diet.⁶⁸ In addition, a recent study found that being overweight after HDP was associated with an increased risk for chronic hypertension.⁶⁹

The more components of a healthy lifestyle that are adopted, the greater the risk reduction is for women. A recent large study of women ages 27 to 44 years from the Nurses' Health Study II found that engaging in six healthy lifestyle activities decreased the risk of CVD by 92%. These activities were: a) not smoking, b) having a normal BMI, c) engaging in activity at least 2.5 hours per week, d) viewing less than seven hours of television per week, e) eating a healthy diet, and f) drinking no more than one alcoholic beverage per day.

Blood Pressure Control

Hypertensive disorders are common in the general population and may be more prevalent in preeclampsia survivors. ACOG recommends that women diagnosed with gestational hypertension, preeclampsia, or preeclampsia superimposed on chronic hypertension have their blood pressure monitored for at least 72 hours postpartum and again seven to 10 days following delivery.¹⁰ Hypertension that continues for more than three months postpartum is considered to be chronic hypertension.⁷⁰

Blood pressure should be monitored for those women with readings that are above the optimal range (<120 mm Hg systolic and < 80 mm Hg diastolic). At minimum, blood pressure screening should occur within six months to one year postpartum.⁷¹ Benchop et al (2018) suggest ambulatory monitoring may detect hypertension in 24% more individuals than using office blood pressures alone.⁷²

There is little research to guide decisions on what level of blood pressure to treat, what target blood pressure to use, or how long to continue any medication therapy for women who experienced HDP. Antihypertensive medicine is recommended by ACOG for persistent postpartum hypertension if systolic four to six hours apart. If the systolic blood pressure \geq 160 mm Hg or diastolic blood pressure \geq 110 mm Hg or higher, antihypertensive treatment should begin within one hour. For women who are still within childbearing years, especially if they are considering future pregnancy, avoidance of angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), and mineralocorticoid antagonists is recommended as these medications may have adverse effects on any fetus. Methyldopa is safe both in pregnancy and while breastfeeding.¹⁰ Given the possible increased risk of kidney disease in preeclampsia survivors, screening for proteinuria and microalbuminuria should be considered standard of care for these patients.²⁸

Management of Lipid Disorders

Disorders of lipid metabolism often occur in conjunction with hypertension as well as impaired insulin sensitivity. A fasting lipid panel should be checked periodically in preeclampsia survivors due to an increased incidence of abnormal cholesterol levels in this population.⁴³ The 2013 ACC/AHA guideline for the treatment of cholesterol removed absolute LDL goals for lipid lowering. In addition, it identified specific groups who should receive statin therapy and the intensity level of that treatment. Lifestyle changes were advocated as the first line of any intervention.⁷³ Omega-3 fatty acids in the form of fish or capsules can be added.⁹ The guideline task force identified four groups for whom HMG-CoA reductase inhibitors (statins) should be recommended. These are individuals with: a) clinical atherosclerotic cardiovascular disease (ASCVD) for secondary

prevention, b) an LDL level > 190 mg/dL for primary prevention, c) diabetes ages 40-75 who have an LDL of 70-189 mg/dL, and d) no diabetes and an estimated 10-year ASCVD risk $\geq 7.5\%$ who are between the ages of 40 and 75 years with a LDL of 70-189 mg/dL.⁷³

The benefits of statin use by women requires future research. In the Justification for the Use of Statins in Primary Prevention (JUPITER) trial, rosuvastatin did not prevent myocardial infarction, stroke, or death in women; however, women taking the drug had less chest pain and fewer hospitalizations.⁷⁴ Pravastatin has been found to be protective for the endothelium and there is a trial currently underway in the U.S. to evaluate the maternal and fetal safety in women at high risk for preeclampsia.⁷⁵

Statins should not be avoided altogether in women of reproductive age due to fear of potential exposure in pregnancy. Instead, benefits and risks of therapy as well as plans for future pregnancy should be discussed. Women of reproductive age requiring aggressive lipid-lowering therapy, including statins, should use effective contraception to avoid exposure to such agents during pregnancy.

Insulin Resistance and Diabetes

Women with a history of preeclampsia were identified in several studies as a population with a higher incidence of insulin resistance.^{26,43} Given that finding, it may be reasonable to screen patients with a history of preeclampsia for diabetes or impaired fasting glucose. Spaan, et al. recommend screening at three to six months postpartum and every other year thereafter.⁷⁶

For women with a history of gestational diabetes, the American Diabetes Association (ADA) and ACOG recommend follow-up screening for diabetes mellitus between six and 12 weeks postpartum and if normal, every three years after that.^{10,77} The preferred test is a 75 gm two-hour oral glucose tolerance test, but a fasting glucose is also acceptable. Intensive lifestyle modifications have been demonstrated to be an effective tool in preventing the progression from impaired glucose tolerance to diabetes, and should be routinely recommended to patients with insulin resistance.⁷⁷

The ADA does not recommend routine testing for type 2 diabetes for asymptomatic adults under 45 years old. Those with a BMI ≥ 25 kg/m² (or ≥ 23 kg/m² with Asian descent) plus one additional risk factor should be tested. A history of a previous delivery with an infant weighing > 9 lbs. is one of these risk factors. For complete information on diabetes diagnosis and care in pregnancy, see the *ADA 2016 Standards of Medical Care in Diabetes*.⁷⁸

Aspirin Therapy

Antiplatelet therapy is one of the cornerstones of secondary prevention of CVD. Low-dose aspirin (75-162 mg) is recommended for all patients with pre-existing coronary heart disease who do not have contraindications, such as allergy or gastrointestinal bleeding risk.⁷⁹ According to the most recent recommendations from the USPSTF, aspirin (81 mg daily) is recommended for primary prevention of CVD in adults ages 50-59 years and a 10% or greater risk of CVD in 10 years. The USPSTF found inadequate evidence to recommend aspirin to persons younger than 50 years or older than 69 years.⁷⁹ This recommendation made no distinction between benefits for women versus men. The prior USPSTF recommendations indicated that aspirin only be used for stroke prevention in women ages 55-79 years when the benefits of therapy outweigh the potential bleeding risks.⁷⁹

The USPSTF and ACOG both recommend low dose aspirin for the prevention of this disorder in pregnancy. Specifically, low dose aspirin is to be given to women at high-risk of preeclampsia including those with a history of preeclampsia with a preterm birth before 34 weeks, preeclampsia occurring in more than one pregnancy or when more than one risk factor for preeclampsia is present. The number of women likely to be helped by taking aspirin is small, but evidence supports its efficacy for these women and the safety of providing it for all women.^{10,80} This therapy should be initiated late in the first trimester or at the beginning of the second trimester. Neither USPSTF nor ACOG guidelines recommend aspirin use by young women for the prevention of CVD.

Community Summary: Risk Reduction

- Preeclampsia survivors rarely receive information about their increased risk of cardiovascular disease.
- The American Heart Association published a recommendation called “Effectiveness-based Guidelines for the Prevention of Cardiovascular Disease in Women” in 2011. Here is a short summary of the Counseling and Goal Setting information for **how preeclampsia survivors can reduce their risk for cardiovascular disease**:

Healthy Lifestyle

As a first step to prevent cardiovascular disease, all women should try to:

- Not smoke
- Not have overweight or obesity
- Exercise at least 150 minutes each week
- Eat a healthy diet (more vegetables and fruits; eat foods high in fiber and low in saturated and trans-fats; eat only 1500-2400mg of sodium each day). Helpful diets that match these eating recommendations are:
 - DASH diet: <https://www.nhlbi.nih.gov/health-topics/dash-eating-plan>
 - USDA Food Pattern: <https://www.cnpp.usda.gov/USDAFoodPatterns>
- *Note:* These are all called “ideal health behaviors.” The more ideal health behaviors you do, the more your chance for cardiovascular disease goes down.

Blood Pressure

- **Immediately after preeclampsia:** After a woman with preeclampsia delivers her baby, her blood pressure should be checked for at least three days and then again seven to 10 days after delivery.
- **One year after preeclampsia:** Blood pressure should be checked within six months to one year after delivery to see if levels are back to normal (<120/80mmHg). If blood pressure stays high longer than three months after having her baby, a woman will be diagnosed with high blood pressure.
- There is little research about exactly what level of blood pressure to treat (“treat” meaning prescribe medications to lower blood pressure), what are the best blood pressure numbers doctors should aim for, and how long women should be on medicine to lower their blood pressure after preeclampsia. Because of the little amount of research, different doctors will treat your blood pressure differently after preeclampsia.
- Methyldopa is a medicine that is safe in pregnancy and while breastfeeding that can help women lower their blood pressure should your doctor decide to treat your blood pressure.

Lipids

- Preeclampsia survivors have a higher chance of having high cholesterol. It is recommended survivors have their lipids (this is a measurement of the cholesterol and fats in your blood) checked every now and then.

Diabetes

- Preeclampsia survivors have a higher chance of having insulin resistance (meaning their bodies don’t listen to insulin as well as they are supposed to). Some doctors recommend checking for diabetes every year in preeclampsia survivors.

Aspirin Therapy

- Aspirin is a medicine that is recommended to lower your chance of cardiovascular disease in adults between 50 and 59 years old.
- If you have a high risk of getting preeclampsia during your pregnancy (things that make you “high risk”: you have had preeclampsia before and delivered your baby before 34 weeks, you have had preeclampsia more than once, you have more than one risk factor for preeclampsia), doctors are recommended to give you aspirin to lower your chance of preeclampsia *during pregnancy*, starting in the end of your first trimester or the beginning of your second trimester.

Follow Up

Due to the long-term consequences of HDP, multiple experts recommend follow up and referral from obstetrics to primary care or cardiology.^{9,10,45,76,81} Bokslag et al. suggest screening in the fifth decade of life.⁸² Recent evidence points to new options for measuring the degree of CVD risk after preeclampsia. Computed tomography calcium scores may help define and track an individual's level of risk for CVD.^{83,84} Until now, assessing the development of CVD after preeclampsia in pregnancy was based predominantly on symptom development. The ability to identify a specific level of risk at a given point in time can help to tailor treatment specific to the individual woman.

Knowledge of the connection between HDP and future CVD among obstetricians and other providers is not universal and globally there are low rates of referral.⁸¹ A multidisciplinary cardiovascular risk management program has been recommended.⁷⁶ One clinic in Canada has reported their experience with this model.⁴⁵

In addition, consideration should be given to follow up for the children of mothers with preeclampsia. Given findings showing increased risks for multiple conditions (previously discussed), both patients and providers should be educated about and alert to the potential impact on the future health of children born from pregnancies where preeclampsia is present.⁶³

Community Summary: Follow Up

- Doctors and researchers recommend preeclampsia survivors should be “followed up” (meaning you should see a doctor) after pregnancy by a primary care doctor or a cardiologist (a doctor that deals with hearts and blood vessels).
- Sadly, the link between preeclampsia and future cardiovascular disease is not always known by OB/GYNs and other doctors. This means that sometimes survivors may have to speak up and ask their doctor to refer them for this recommended “follow up”.

Conclusions

1. In several large studies, women with a history of preeclampsia have been found to develop CVD disorders and mortality at an increased rate compared to women with a history of normotensive pregnancies. Preeclampsia and heart disease share several risk factors, including family history, insulin resistance, microvascular dysfunction, and metabolic syndrome.
2. Women with a history of preeclampsia – particularly early morbid preeclampsia – may especially benefit from careful monitoring for conventional cardiovascular risk factors, aggressive lifestyle modifications aimed at prevention of cardiovascular disease, and counseling about implications for future pregnancies and future cardiovascular health.
3. Care provided by a multidisciplinary team that includes obstetricians, primary care physicians, and advance practice clinicians as well as cardiologists may be beneficial.
4. Future studies should be focused on further elucidation of the link between preeclampsia and heart disease, screening for early cardiovascular disease in preeclampsia survivors, and preventive strategies to improve maternal health following adverse pregnancy outcomes.

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Appendix A

Table 2. Outcomes of Included Studies on Relationship of Hypertensive Disorders in Pregnancy and Risk for Future Disease				
Systematic Reviews with Analysis	Risk of Future Hypertension	Risk of Future Cardiovascular Disease	Risk of Future Cerebrovascular Event	Risk of Future Mortality
Bellamy, Casas, Hingorani, & Williams (2008)	Future HTN after preeclampsia: RR, 3.7; 95% CI, 2.7-5.05 Gestational HTN: RR, 3.39; 95% CI, 0.82-13.92	Fatal and nonfatal ischemic heart disease after preeclampsia: RR, 2.16; 95% CI, 1.86-2.52 Gestational HTN: RR, 1.66; 95% CI, 0.62-4.41 Venous thromboembolism after preeclampsia: RR, 1.79; 95% CI, 1.37-2.23	Fatal and nonfatal stroke after preeclampsia: RR, 1.81; 95% CI, 1.45-2.27 Cerebrovascular event after preeclampsia: OR, 1.77; 95% CI, 1.43-2.21	Overall mortality after preeclampsia: RR, 1.49; 95% CI, 1.05 - 2.14 Fatal ischemic heart disease after preeclampsia: RR, 2.6; 95% CI, 1.94-3.49 Fatal stroke after preeclampsia: RR, 2.98; 95% CI, 1.11-7.96
Brown et al (2013)	HTN after preeclampsia: RR, 3.13; 95% CI, 2.51-3.89	CVD after preeclampsia: OR, 2.28; 95% CI, 1.87-2.78	Cerebrovascular event after preeclampsia: OR, 1.77; 95% CI, 1.43-2.21	
McDonald et al (2008)		CVD after preeclampsia: Case-control studies: OR, 2.47; 95% CI, 1.22-5.01 Cohort studies: RR, 2.33; 95% CI, 1.95-2.78 Peripheral arterial disease after preeclampsia (cohort studies): RR, 1.87; 95% CI, 0.94-3.73	Cerebrovascular disease after preeclampsia: RR, 2.03; 95% CI, 1.54-2.67	CVD mortality after preeclampsia: RR, 2.29; 95% CI, 1.73-3.04 Cerebrovascular mortality after preeclampsia: RR, 2.26; 95% CI, 1.11-4.57

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; GA, gestational age; HR, hazard ratio; HTN, hypertension; OR, odds ratio; RR, relative risk.

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Please note:

“Although there is clear evidence of an association between preeclampsia and later-life cardiovascular disease, the value and appropriate timing of assessment is not yet established. Healthcare providers and patients should make this decision based on their judgment of the relative value of extra information versus expense and inconvenience.” (ACOG, P 130)

For preeclampsia survivors with a preterm birth before 37 weeks, preeclampsia in more than one pregnancy, or severe preeclampsia, ACOG recommends annual blood pressure evaluation, lipid panel, fasting blood glucose, and BMI assessment.

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