



Hypertensive Disorders of Pregnancy and Future Maternal Health: How Can the Evidence Guide Postpartum Management?

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Abstract

Purpose of Review To review the postpartum management of hypertensive disorders of pregnancy.

Recent Findings Hypertensive disorders are associated with an increased risk of future cardiovascular disease; however, there is a poor understanding of the underlying mechanisms and few recommendations to guide care in the postpartum period. Recent studies have shown high rates of masked hypertension and home blood pressure monitoring in the first year postpartum may be a promising opportunity to monitor health given evidence of high maternal adherence to this approach. In longer term, women with a history of a hypertensive disorder of pregnancy have higher blood pressures, increased risk of metabolic syndrome, and perhaps excess diastolic dysfunction. Triaging risk and improving handoff from the obstetrician to the primary care provider or subspecialist should be a priority in this population.

Summary Hypertensive disorders of pregnancy remain an untapped opportunity to identify excess cardiovascular risk in affected women at a time when mitigating that risk during the reproductive years has the potential to improve future pregnancy health as well as improve women's long-term cardiometabolic health.

Keywords Preeclampsia · Hypertensive disorders of pregnancy · Postpartum management · Hypertension · Cardiovascular imaging · Prevention

Introduction

Hypertensive disorders of pregnancy, including gestational hypertension and preeclampsia, complicate 8–10% of pregnancies in the USA [1]. Gestational hypertension is the presence of new-onset hypertension (≥ 140 mmHg/90 mmHg) detected during pregnancy in a previously normotensive

woman [1]. Preeclampsia is a heterogeneous syndrome characterized by new-onset hypertension and proteinuria and/or end-organ dysfunction. It is thought to result from uteroplacental insufficiency and leads to systemic endothelial dysfunction. In the severe form, in addition to higher blood pressures (≥ 160 mmHg/110 mmHg), end-organ dysfunction (such as eclampsia or acute renal or hepatic failure) develops, which often necessitates immediate delivery, and can lead to significant maternal and neonatal morbidity. Outside of delivery, care is otherwise supportive, with no effective treatments to prolong pregnancy or reverse the disease process. After delivery, women are often initiated on anti-hypertensive medication if blood pressures exceed 150 mmHg/100 mmHg and medication is down titrated as blood pressure normalizes in the first few weeks postpartum [1, 2]. Prevention of hypertensive disorders in future pregnancies is an active area of investigation. Currently, the only effective preventive strategy is low-dose aspirin starting in the late first trimester, which is recommended for women at high risk of preeclampsia, including women with pre-gestational diabetes, chronic hypertension, renal disease, a history of preeclampsia, or other well-established risk factors [1]. Several newer modalities for

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prevention are under investigation, including statins and metformin [3, 4].

The association of preeclampsia with later-life cardiovascular disease (CVD) is well established and has been replicated in diverse populations across multiple studies [2, 5–7]. The biologic plausibility of this relationship is reinforced by the observation that the risk is amplified in women with recurrent preeclampsia, early-onset disease, or more severe forms [7, 8]. While many hypotheses have been proposed to explain this association, the underlying mechanisms are poorly understood. Proposed mechanisms for this increased risk include the presence of shared risk factors in preeclampsia and CVD, the possibility of common physiologic processes, or the distinct possibility that preeclampsia generates lasting endothelial dysfunction and causes the increased risk of CVD [9–11]. These mechanistic pathways are not mutually exclusive. *In this article, we review the postpartum management of hypertensive disorders of pregnancy with a focus on identifying clinical opportunities and gaps in the evidence with the goal of improving subsequent pregnancy outcomes and long-term women's cardiometabolic health.*

Immediate Postpartum Management

After delivery, the primary management of hypertensive disorders of pregnancy is continued by the obstetrician in most cases. Immediately postpartum, the focus is on maternal stabilization and normalization of blood pressures with medication if indicated. The American College of Obstetricians and Gynecologists (ACOG) suggest maintaining blood pressures < 150/100 in the postpartum period, although initiation, titration of medication, and selection of the anti-hypertensive agent is based on clinical judgment, as there are no standardized management guidelines for specific anti-hypertensive agents or parameters for postpartum medication titration [12]. At present, in the USA, women are typically discharged from the hospital on postpartum day 2–4 and ACOG recommends a single blood pressure check between 3–10 days postpartum for women with a hypertensive disorder of pregnancy. Women with persistent hypertension or the need for titration of anti-hypertensive medications are typically seen more frequently in the postpartum period for medication management; however, this varies by institution [12]. Subsequently, women are typically seen at 4–6 weeks postpartum for a comprehensive postpartum visit and referred to their primary care physician (PCP) if there are additional needs for anti-hypertensive medication management [1].

One barrier to management in this period is the underutilization of postpartum care. There are limited data on the adherence to the 3–10 days postpartum blood pressure check, with one study showing that only 44% of eligible women were seen for this visit [13•]. Similarly, up to 40% of women are not

seen for a traditional 4–6 weeks postpartum visit [14]. Attendance rates are even lower among populations with limited resources, which likely contribute to health disparities in these groups [14, 15]. ACOG and others have recommended implementation of innovative interventions to improve adherence to care in the immediate postpartum period, such as remote monitoring. Within the context of small randomized trials or research studies, text message-based home postpartum hypertension monitoring programs have been shown to increase patient engagement and improve compliance with blood pressure management follow-up [13•, 16, 17]. One such randomized trial compared a text-based remote monitoring protocol using home blood pressure monitoring for postpartum hypertension compared with usual care in a small cohort of women. They demonstrated increased compliance with having a single blood pressure value recorded in the first 10 days postpartum in the text messaging group compared with the standard care group [13•]. Remote hypertension monitoring may improve compliance with ACOG recommendations surrounding blood pressure assessment within the first 3–10 days postpartum and may identify women with otherwise unrecognized blood pressure elevations requiring medication in this period [1, 14]. However, whether broad implementation of remote monitoring programs improve maternal morbidity and mortality in this period or improve long-term outcomes has not been studied.

Management in the First Year Postpartum

Increasing evidence suggests high rates of progression to chronic hypertension or persistent hypertension in the first year following a hypertensive disorder of pregnancy [18, 19•, 20]. A recent study utilizing ambulatory and in-office BP monitoring found that 42% of women with preeclampsia with severe features had persistent hypertension at 1 year postpartum, with 17.5% of these cases only detected by APBM, suggesting that masked hypertension may contribute significantly to increased CVD risk in this population [19•]. Similarly, Smith et al. demonstrated that 56% of women with preeclampsia were hypertensive by 1-year postpartum [18]. Certain factors appear to amplify this risk, including overweight and obesity, Black race, and the severity of hypertensive disorder of pregnancy [15, 20].

Few interventions have been studied to improve blood pressure or prevent chronic hypertension in the first year postpartum following a hypertensive disorder of pregnancy. Small trials have examined the impact of various anti-hypertensive agents on acute control of hypertension either at the time of delivery or in the first few days postpartum [21, 22]. Similarly, ACOG guidelines address treatment of acute, severe hypertension immediately after delivery, but do not provide guidance on management in the weeks and months following

delivery [23]. One small study showed that a lifestyle intervention designed to improve cardiometabolic risk factors following a complicated pregnancy in the first year postpartum was feasible and effective [24]. The recently published SNAP-HT trial demonstrated that systematic titration of anti-hypertensive medications in the postpartum period not only shortens the duration of anti-hypertensive therapy, but also may have a longer term benefit on blood pressure that persisted up to 6 months postpartum [25]. The authors hypothesized that this beneficial impact is secondary to more favorable cardiovascular remodeling. These findings indicate that the first year postpartum may be critical to triage of risk and to facilitating identification of women with persistent or unresolved hypertension following a hypertensive disorder of pregnancy.

Barriers to Care in the Postpartum Period

Few healthcare providers carry out postpartum CVD risk counseling or screening, despite the fact that the postpartum period may be a time when women are motivated to modify their lifestyle [26]. While some providers are acutely aware of the risk of future CVD and attempt to educate patients in a timely manner, they encounter a variety of barriers to risk reduction. Identifying the appropriate timing and venue for this counseling as well as implementing recommended interventions for risk reduction is challenging. Much of this counseling occurs immediately after delivery, which is often a busy and emotional period for women. Amidst the birth of a newborn, many physical changes, pain, and sleep deprivation, it is not surprising that women do not retain all of the information that providers relay to them at the time of delivery [27]. While remote monitoring of blood pressure may be a promising method of improving adherence with care in the postpartum period, blood pressure monitoring is often not reimbursed by insurance, thus potentially disadvantaging women of lower socioeconomic status. Postpartum care after a hypertensive disorder of pregnancy is often fragmented, with no cohesive transition from the obstetrician to internist or cardiologist [26]. Further compounding this poor follow-up are the underlying socioeconomic issues that impact care in this period. The USA is one of the few developed countries without paid parental leave, which disparately impacts the most disadvantaged women. Similarly, access to care is a consideration, as many women with public insurance who were insured only during pregnancy lose insurance coverage within 60 days postpartum, significantly limiting their follow-up after a pregnancy complication, with specifics varying from state to state [14, 28]. Finally, emerging data suggest a significantly higher rate of posttraumatic stress disorder among women with a hypertensive disorder of pregnancy [29, 30]. These women may be less likely to return to the healthcare system

for follow-up care after a prior traumatic delivery experience. Attending to the postpartum period within a trauma-informed care model may be beneficial but is to date untested [31].

Future Reproductive Health: Pre-Conception Care

Inter-pregnancy care focuses on care of women between pregnancies with the overall goal of improving outcomes for women and future infants. The Society for Maternal Fetal Medicine (SMFM) and ACOG recommend inter-pregnancy care for women with a history of hypertensive disorders of pregnancy [32]. In particular, they emphasize the importance of inter-pregnancy care to maximize women's wellness not just between pregnancies and during subsequent pregnancies but along her entire life course. This inter-pregnancy care should actually start during the prenatal care period of the initial pregnancy, with SMFM recommending that during prenatal care, providers should discuss who will provide primary care after the immediate postpartum period, discuss contraception options, provide anticipatory guidance regarding breastfeeding and maternal health, and discuss the associations between pregnancy complications and long-term maternal health. At the 4–6 weeks comprehensive postpartum visit, providers should review complications of pregnancy and their implications for future maternal health and ensure that the patient has a primary medical home for ongoing care. Specifically, for women with a pregnancy complicated by preeclampsia or gestational hypertension, SMFM recommends that BP should be evaluated for resolution of hypertension and recommends that BP be maintained < 120/80 mmHg, with consideration for medication initiation or referral to a primary care physician if BP goals are not met. In addition, they recommend that women should achieve a normal BMI and that aspirin should be discussed for future pregnancies. In women with underlying chronic hypertension, in addition to the abovementioned recommendations, testing should be considered for ventricular hypertrophy, retinopathy, and renal disease in women with longstanding or uncontrolled hypertension [32].

Multidisciplinary Care and Transition of Care

Several centers throughout the USA and Canada have reported on multidisciplinary maternal health clinics for women with a hypertensive disorder of pregnancy [33, 34]. These clinics typically involve combinations of obstetricians, cardiologists, and primary care physicians with a goal of addressing care inequities for young women. A structured cardiovascular screening program ensures adequate follow-up after a hypertensive disorder of pregnancy and provides an opportunity for lifestyle counseling and interventions [26]. One such

clinic, The Maternal Health Clinic in Ontario, Canada, identifies women with a pregnancy complication at the time of delivery and systematically refers them to the follow-up clinic [18]. Women undergo a complete assessment including screening history, physical examination, fasting bloodwork, and urinalysis at 6 months postpartum [35]. Similarly, Celi et al. report on successful implementation of a postpartum transition clinic after a hypertensive pregnancy in Boston. In their model, women are seen for multiple visits beginning in the immediate postpartum period. They demonstrate successful incorporation of home blood pressure monitoring, adjustment of anti-hypertensive medications, and implementation of preventative measures such as a nutritionist referral and follow-up with primary care physicians in a racially and socioeconomically diverse population. Follow-up in a dedicated postpartum preeclampsia clinic may help facilitate transition of care and provide a unique window for providers to focus on improving cardiometabolic health prior to a subsequent pregnancy, primary prevention of CVD, and counseling on risk factor modification.

Unfortunately, most women in the USA are not seen in such novel multidisciplinary clinics, and communication about future risk relies on relaying information from the obstetrician to both the patient and her primary care provider. In addition to improving this communication and counseling in the immediate postpartum period, consideration should be made for implementation of innovative interventions to improve this handoff. Examples include the utilization of standardized best practice alerts in the electronic medical record, which could more reliably incorporate pregnancy history into a patient's history and facilitate risk identification. One recent study described a rule-based computerized algorithm to characterize preeclampsia by mining prenatal clinical notes within a large healthcare organization, which had a sensitivity of 88% and a specificity of 99% [36]. Until such innovative interventions can be implemented on a larger scale, focus should be on improving patient-provider education and communication surrounding the long-term implications of hypertensive disorders of pregnancy for women's future CV health.

Management of Women with a History of Hypertensive Disorders of Pregnancy: Beyond the Postpartum Period

In the years after delivery, management of women with a history of hypertensive disorders of pregnancy becomes the responsibility of primary care physicians, family practitioners, and subspecialists such as cardiologists and nephrologists. It is often easy for these women to get lost to follow-up, as they are generally young and otherwise healthy. As part of the 2011 Guideline Update for the Prevention of CVD in Women, the American Heart Association (AHA) recommended that

providers meeting female patients for the first time should take a detailed pregnancy history and ask specifically about pregnancy complications such as preeclampsia, gestational hypertension, preterm birth, and gestational diabetes [37]. These guidelines consider a history of preeclampsia or gestational hypertension to be a major risk factor for CVD. Thus, they recommend that women with a history of hypertensive disorders of pregnancy should have careful screening, monitoring, and control of other CVD risk factors such as hypertension, dyslipidemia, and diabetes. In the general population, it is recommended that CV risk factor screening be obtained every 4 to 6 years. In a higher risk population such as those with a history of hypertensive disorders of pregnancy, there are no specific data to guide our management, but we suggest that regular BP and cholesterol screening should be more frequent and should start as soon as 1 year postpartum.

Women with a history of preeclampsia and gestational hypertension are at increased risk of hypertension in later life. In the 14 years after preeclampsia, women are 3.7 times more likely to develop hypertension than those with normotensive pregnancies [6]. Thirty-eight percent of women with a history of early-onset preeclampsia had developed hypertension by the 5th decade of life [38]. Starting at age 30, women with a history of hypertensive disorders of pregnancy are more likely to be treated for hypertension and on average, systolic blood pressure was ~10 mmHg higher in these women until age 55 [39]. There are no clear guidelines on frequency of blood pressure monitoring in this population. However, in patients with elevated risk for hypertension, the United States Preventive Services Task Force (USPSTF) task force recommends at least yearly in-office measurements [40]. Extrapolating from these recommendations, we also suggest yearly blood pressure measurements for the high-risk population of women with a history of hypertensive disorders of pregnancy. There is a growing body of evidence that suggests that we may be missing those with masked hypertension and that providers should consider obtaining home blood pressure measurements or ambulatory blood pressure measurements, especially in high-risk populations [41, 42]. Elevated home blood pressures and ambulatory blood pressures are associated with higher CVD risk and warrant treatment [43, 44]. According to the 2017 American College of Cardiology (ACC) and AHA Guidelines on Management of High Blood Pressure in Adults, stage 1 hypertension was redefined as systolic BP 130–139 mmHg or diastolic BP 80–89 mmHg [41]. Low-risk adults with stage 1 hypertension can be treated with nonpharmacologic therapy and repeat measurement in 3–6 months. However, those with stage 1 hypertension and high-ASCVD risk (>10% 10-year ASCVD risk) should be treated with both nonpharmacologic therapy and anti-hypertensive medications. Without specific mention from the ACC/AHA on treatment of women with a history of hypertensive disorders of pregnancy, we recommend following guidelines for the general population.

The ACC and the AHA incorporate preeclampsia into the newest Cholesterol Management Guidelines published in 2018 [45]. On first contact with a healthcare provider, young adults should have one screening cholesterol measurement and measured every 4 to 6 years thereafter. In their primary prevention section, preeclampsia is listed as a CVD “risk enhancer.” For women in the age range of 40 to 75 years old with an LDL between 70 and 190 mg/dL who do not have diabetes mellitus and who are at “borderline” (5 to < 7.5%) or “intermediate” (≥ 7.5 to 20%) 10-year ASCVD risk, the presence of a risk enhancer such as preeclampsia merits initiation of at least a moderate intensity statin. If decision on statin initiation is still uncertain, obtaining a coronary artery calcium (CAC) measurement can help risk stratify patients. The use of statins for primary prevention specifically among women with a history of hypertensive disorders of pregnancy has not been studied. Aspirin use may be beneficial for stroke prevention in this population, but evidence supported by randomized control trials is needed [46].

As for all women, those with a history of hypertensive disorders of pregnancy should be counseled on healthy lifestyle practices. This should include recommendation to follow diets such as the “DASH” diet, which are diets low in salt and animal fat and include a majority of fruits and vegetables and more plant-based protein. In addition, women should be advised to do moderate exercise for at least 30 min a day, 5 times per week [47]. Providers should discuss weight loss strategies with women who are overweight or obese. Women who smoke cigarettes should be counseled on smoking cessation. Online education modules and meeting with a lifestyle coach may be helpful motivators for women with a history of hypertensive disorders of pregnancy [48].

Although it is well known that preeclampsia is an independent risk factor for CVD including ischemic heart disease as well as heart failure [5, 6], hypertensive disorders of pregnancy have not yet been successfully incorporated into CVD risk prediction models. Traditional risk models, such as the Framingham or Modified Framingham Risk Score, tend to underestimate CV risk among younger women. Multiple studies have attempted to include a history of hypertensive disorders of pregnancy into 10-year CVD risk prediction models, but did not find an improvement in discrimination or reclassification [49, 50]. Women who are within 10 years postpartum are generally less than age 40 and thus, their overall CVD risk is still very low. In addition, women with hypertensive disorders of pregnancy also are more likely to have other traditional CVD risk factors and comorbidities that may mask contributions of hypertensive disorders of pregnancy to CVD risk estimation. In fact, those with a history of hypertensive disorders of pregnancy are more likely to have ASCVD risk scores greater than 7.5% [39]. Using longer term models that evaluate 30 year or lifetime risk may be better at identifying a higher risk group [51]. Overall, development of risk models

targeted at assessing longer term CV risk for younger women that include sex-specific risk factors such as hypertensive disorders of pregnancy is desperately needed.

Noninvasive Cardiovascular Imaging Tools

Beyond risk factor screening, the use of noninvasive cardiovascular imaging techniques may help identify women who may be at higher risk to develop clinical CVD. Around the time of delivery, women with preeclampsia are more likely to have structural cardiac changes assessed by transthoracic echocardiogram compared with women who are normotensive during pregnancy. These structural changes include more abnormal diastolic parameters such as an exaggerated reduction in E/A mitral inflow ratio and increased E/e' ratio corresponding to increased left atrial and left ventricular pressures [52–54]. Additionally, women with gestational hypertension and women with preeclampsia are more likely to have an increase in the left ventricular (LV) mass, a finding associated with worse CV outcomes in the general adult population [52, 53, 55, 56]. Severe and preterm preeclampsia carries a poorer clinical prognosis and are associated with more pronounced peripartum structural changes on echocardiogram including increased right ventricular (RV) systolic pressure and abnormal right ventricular strain [57, 58].

A limited number of studies have evaluated echocardiographic changes in later life for women with a history of hypertensive disorders of pregnancy. For women 9 to 16 years after index pregnancy, preeclampsia history was associated with thicker LV walls and more abnormal diastolic function parameters such as an increased E/e' ratio suggestive of increased left ventricular pressure [59]. Other studies have shown an association of preeclampsia history with concentric LV remodeling and preclinical heart failure 4 to 10 years after delivery; however, these associations were attenuated after accounting for metabolic syndrome and hypertension [60, 61]. There are additional studies that did not find a significant difference in echocardiogram parameters in the 10-year follow-up time period for women with preeclampsia compared with normotensive controls [62]. This area warrants further study to identify characteristics associated with an increased risk for early structural cardiac changes and to evaluate the association with higher risk outcomes in this population. Intervention studies to determine if these structural changes and increased risk are reversible are also warranted.

Cardiac MRI is an alternative noninvasive imaging technique that can provide more accurate and reproducible measures of cardiac chamber sizes as well as ventricular and atrial function. Gadolinium contrast during cardiac MRI also allows the assessment of myocardial infiltrative processes and late gadolinium enhancement (LGE) has been shown to be associated with adverse outcomes and arrhythmias. In patients

with hypertension, cardiac MRI is a useful tool to differentiate etiology of left ventricular hypertrophy and provides a more accurate assessment of myocardial ischemia, especially small vessel disease [63]. Cardiac MRI has also helped evaluate medication treatment benefits on reversal of left ventricular remodeling with use of medications such as angiotensin receptor blockers among patients with hypertension or metformin among patients with diabetes [64, 65]. Given the association of left ventricular remodeling with worse CV outcomes, reversal of remodeling has potential implications for CVD risk modification [66]. For women with a history of preeclampsia, cardiac MRI may be a way to evaluate those who have evidence of structural cardiac changes following a preeclamptic pregnancy. However, there are very limited published data on cardiac MRI among patients with a history of pregnancy complications to guide our practice patterns [67].

At delivery and at 1 year postpartum, women with a history of preeclampsia have evidence of subclinical vascular changes that include abnormalities in their carotid intima media thickness with a thicker intima/media ratio [68]. Differences in CIMT among women with a history of preeclampsia tend to persist in the 10 years after delivery [69–71]. Considering coronary artery calcium, in one study with women ~3 decades after pregnancy, women with preeclampsia were found to be more likely to have a higher CAC score compared with those who were normotensive during pregnancy, a finding that persisted even after adjustment for traditional risk factors [72]. A history of pregnancy complications including preeclampsia has been shown to be associated with non-

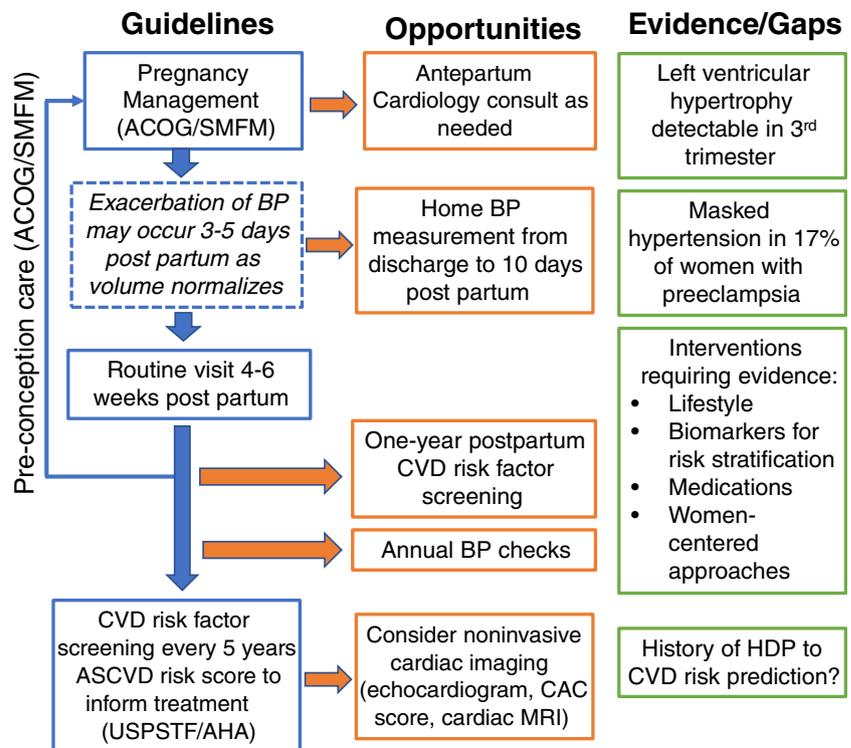
obstructive and obstructive coronary artery disease on coronary CT angiogram in asymptomatic women [73, 74]. It is possible that optimizing CV health during and shortly after pregnancy may improve subclinical measures such as CIMT or coronary artery calcification, but randomized control trials are needed to confirm these potential benefits [75].

Leveraging noninvasive CV imaging tools may help providers identify subclinical vascular and structural cardiac changes which could guide targeted therapies for those who may be at higher risk to develop clinical CVD. Differentiating women at lower risk from those at moderate to high risk via imaging modalities will allow providers to triage patients for more aggressive treatment in the higher risk group. To date, however, there are large gaps in the data regarding use of CV imaging among women with hypertensive disorders of pregnancy and provide an opportunity for further study.

Conclusions

While the evidence linking hypertensive disorders of pregnancy with future CVD is robust and compelling, there remain many unanswered questions on management both in the immediate postpartum period as well as longer term. First, in the USA, care in the postpartum period is fragmented and poorly attended by patients. This results in an inconsistent transition of care from the obstetrician to the primary care physician and communication about future risk. One limitation to research on effective interventions and assistance in guideline

Fig. 1 Guidelines, opportunities, evidence, and gaps regarding the improvement of postpartum health among women with hypertensive disorders of pregnancy



development is the time interval between a pregnancy complication and a cardiovascular event. The authors propose consideration of two-tiered endpoints when evaluating screening, interventions or risk score calculators. As hypertension contributes to more cardiovascular events in women compared with men, its clinical importance as a primary endpoint should not be overlooked [76]. Finally, we propose modeling clinical care following a hypertensive disorder of pregnancy after the guidelines for management after a pregnancy complicated by gestational diabetes (GDM). Following GDM, the American Diabetes Association recommends screening for type 2 diabetes with an oral glucose tolerance test at 4–8 weeks postpartum and again every 1 to 3 years thereafter [77]. While this approach is untested following hypertensive disorders of pregnancy, future studies could provide evidence about its feasibility, efficacy, and cost-effectiveness.

Hypertensive disorders of pregnancy are still an untapped opportunity to identify excess CVD risk in affected women at a time when mitigating that risk during the reproductive years has the potential to improve future pregnancy health as well as improve women's long-term cardiometabolic health. We have summarized the evidence and gaps in the postpartum care of women with hypertensive disorders of pregnancy (Fig. 1). We also propose opportunities that can be tested to leverage the postpartum years as a unique sex-specific time to improve women's health.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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