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PERIPARTUM AND LONG-TERM MATERNAL CARDIOVASCULAR HEALTH AFTER PRE-ECLAMPSIA

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ABSTRACT

There is widespread acceptance of the increased prevalence of cardiovascular disease occurring within one to two decades in women following a pre-eclamptic pregnancy. More recent evidence suggests that the deranged biochemical and echocardiographic findings in women do not resolve in the majority of pre-eclamptic women following giving birth. Many women continue to be hypertensive in the immediate postnatal period with some exhibiting occult signs of cardiac dysfunction. There is now promising evidence that with close monitoring and effective control of blood pressure control in the immediate postnatal period, women may have persistently lower blood pressures many years after stopping their medication. This review highlights this evidence that delivering effective medical care in the 'fourth trimester' of pregnancy as a means of improving the long-term cardiovascular health of women after a pre-eclamptic birth.

Key words: Pre-eclampsia, Pregnancy, Postpartum, Hypertension, Cardiovascular risk, Cardiac remodeling, Cardiovascular prevention

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What we know	What this review adds
<ul style="list-style-type: none"> HDP results in increased long-term risk of cardiovascular disease, chronic kidney disease and metabolic syndrome 	<ul style="list-style-type: none"> The risk of persistent hypertension is exceptionally high in the puerperium There is a high rate of progression to persistent hypertension in the first year after a HDP pregnancy
<ul style="list-style-type: none"> Altered cardiac geometry persists after birth and is associated with the increased risk of hypertension years later. Enalapril can help improve altered cardiac geometry 	<ul style="list-style-type: none"> Peripartum cardiac imaging in women with HDP could help identify those who require closer follow-up to prevent cardiovascular morbidity, and to target enalapril use to those who will benefit the most
<ul style="list-style-type: none"> Postpartum PE is underdiagnosed as postnatal BP monitoring in the “fourth” trimester is infrequently undertaken after HDP 	<ul style="list-style-type: none"> Postpartum BP self-management offers an acceptable, safe and well-tolerated means of improving postpartum BP control and identifying postpartum PE.

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PERIPARTUM CARDIOVASCULAR HEALTH

Magnitude and time course of postnatal hypertension

The development of chronic hypertension after pregnancies complicated by hypertensive disorders of pregnancies (HDP) explains most of the increased risk of developing cardiovascular diseases (CVD), especially coronary artery disease and heart failure in this cohort of women.¹ This makes the prompt diagnosis and treatment of hypertension in women with a history of HDP a clinical priority. The increased risk of developing chronic hypertension is substantial and occurs much earlier after pregnancies complicated by HDP.^{2,3} In a Danish registry-based cohort study that included 1.5 million primiparous women, the adjusted risk of hypertension was 4-10 times in women with HDP compared with women with a normotensive pregnancy in the first five years after pregnancy. Notably, the cumulative incidence of hypertension at ten years postpartum was 10% in women aged 20-29 years with a previous HDP, which is higher than in women aged 40-49 years with previous normotensive pregnancies.³ Furthermore, the earlier the onset and more severe the HDP, the higher the risk of developing postpartum hypertension.^{3,4}

Recent evidence has shown that the risk of having persistent hypertension is exceptionally high shortly after giving birth with HDP, with about two-thirds of women with a pregnancy complicated by HDP remained hypertensive at six months postpartum.^{5,6} A meta-analysis of postnatal hypertension, showed that the OR (95% CI) of postpartum hypertension was 5.42 (95% CI 3.12-9.41) in the period up to one year and 7.24 (95% CI 4.44-11.80) between one to two years after HDP (Figure 1).⁶ Similarly, a recent French National Health Data study demonstrated that the risk for hypertension 3 years following birth was higher after any HDP, even after adjusting for certain pre-existing cardiovascular risk factors such as age, social deprivation, smoking etc.^{4,7} The mechanisms underlying the association between HDP and subsequent development of CVD, are highly debated. Pre-eclampsia (PE) and other HDP might contribute independently to the development of postpartum CVD by causing persistent endothelial damage, dysregulation of the renin-angiotensin-aldosterone system and/or an enduring high inflammatory state.⁸ On the other hand, an impaired

cardiovascular system might be unmasked by the increased cardiovascular demands required during pregnancy, which functions as a cardiovascular stress test.⁹

Peripartum and postpartum echocardiographic assessment

Profound echocardiographic changes are evident in the majority of pregnant women affected by HDP and these persist in the postpartum period in a significant proportion of these women (Figure 2). Maternal echocardiography can detect HDP-associated increased left ventricle mass, cardiac remodeling and diastolic dysfunction.¹⁰⁻¹² Patients with severe and/or preterm PE, particularly if they present with dyspnea or signs of volume overload, would probably benefit from an echocardiographic evaluation in the peripartum period to evaluate systo-diastolic function. HDP is also the major risk factor for peripartum cardiomyopathy (PPCM), where women with PPCM and PE exhibit more severe symptoms and signs of heart failure compared to PPCM without hypertension.¹³ Also, Vaught *et al.* reported that all women with severe PE who developed pulmonary edema (10%) had high left ventricular filling pressures assessed by an elevated E/E' ratio.¹²

Although removal of the placenta at birth is said to 'cure' HDP, the impact of HDP extends well beyond birth, with persistent cardiac remodeling and dysfunction detectable by postpartum trans-thoracic echocardiography.¹⁴ In a multicenter observational study of 321 women with preterm PE, 10% of women had a left ventricle ejection fraction <55% and/or diastolic dysfunction at six months postpartum.¹¹ Melchiorre *et al.* demonstrated in PE patients with normal BP at 1 year after delivery that those with moderate-severe echocardiographic left ventricle anomalies were more likely to develop hypertension at two years postpartum (50% risk) in comparison to those with normal or mild left ventricle alterations (3.5% risk).¹⁵ Women with a history of PE have altered cardiac structure and evidence of diastolic and myocardial dysfunction in the first years after delivery, which may then translate to a trend toward long-term CVD.^{14,16} In PE, subclinical signs of myocardial dysfunction, such as abnormal GLS, might be present long before the onset of the overt cardiac condition after HDP.¹⁷⁻²⁰ Women with HDP who develop chronic hypertension within a decade, have shown the most pronounced echocardiographic differences in left

ventricular remodeling and diastolic function indices compared to women with only hypertension without previous HDP.²¹ Despite this evidence, there are no recommendations on whether, when or how often a cardiac evaluation should be carried out after HDP.

New-onset postpartum pre-eclampsia

A poorly studied complication is new-onset postpartum PE, defined as new-onset hypertension (SBP \geq 140 mmHg or DBP \geq 90 mmHg) and end-organ involvement or severe new-onset hypertension (SBP \geq 160 mmHg or DBP \geq 110 mmHg) 48 hours to six weeks after delivery in the absence of other identifiable causes.²² Its incidence varies considerably among studies (0.3–27.5%) and only in 40% of cases is there a diagnosis of HDP.^{23,24} Pre-existing maternal cardiovascular risk factors for postpartum PE are similar to those for antepartum PE and both conditions share the finding of an anti-angiogenic imbalance in the maternal circulation.^{25,26} Postpartum PE challenges the paradigm that removing the placenta at birth cures HDP and brings into question the role of the placenta as the undisputed trigger for HDP.²⁷ Postpartum PE is often underdiagnosed, as BP monitoring in the “fourth” trimester is not universally recommended for women without HDP and only infrequently undertaken after HDP.²⁸ The most common presenting symptoms of postpartum PE are neurological (e.g., headache) or signs of volume overload.^{22,28} Due to under-diagnosis, women who develop postpartum PE are at increased risk of severe maternal morbidity, particularly eclampsia and stroke.²⁹ Current studies on long-term cardiovascular risk after HDP have not reported the onset of postpartum PE, and as a result, there is a paucity of epidemiological data on new-onset postpartum PE and future risk of CVD.²² After delivery, women should be informed how to recognize symptoms of postpartum PE. Although risk factors for postpartum cardiovascular morbidity could be identified at the time of discharge, their effectiveness in identifying subsequent disease is unknown.³⁰ A predictive model based on these risk factors would be invaluable in tailoring postpartum follow-up for women at risk of severe maternal morbidities.

Factors that influence persistent postpartum CVS dysfunction

HDP and CVD share common pathophysiological pathways and processes which may explain their close and dose-dependent association.³¹ These findings have led to the acknowledgement of HDP as a crucial female-specific risk factor for CVD later in life.³²⁻³⁴ However, there is no consensus regarding optimal screening, prevention and managing CVD risk after HDP.³⁵ In addition, not all women who experience HDP develop CVD in later life, indicating different levels of future risk.^{36,37} Epidemiological studies have shown that the severity of HDP, the need for preterm birth for HDP and other obstetric complications might help identify women at increased risk of CVD.^{38,39} In addition, early-life factors of women with HDP, such as being born preterm or small-for-gestational age themselves, are associated with increased cardiovascular risk, early-onset high BP and cardiovascular dysfunction.⁴⁰

Better cardiovascular health in early pregnancy, defined by markers such as BP, lipid profile and glucose, has been associated with better pregnancy and postpartum cardiovascular outcomes in women with HDP.^{41,42} Imbalances in circulating angiogenic factors, such as sFlt-1 and its ligand PlGF, are considered responsible for maternal signs and symptoms of PE as it induces microangiopathy in target organs and also vascular remodeling in coronary artery disease or heart failure.^{43,44} Higher sFlt1 levels are associated with cardiovascular dysfunction during pregnancy and increased sFlt1/PlGF ratio in HDP was associated with postpartum hypertension.^{25,45} Moreover, lower PlGF concentrations in HDP have been associated with worse cardiac structure, increased BP levels and higher lipid levels in the postpartum follow-up.^{46,47} In one small study of echocardiographic variables at the time of PE diagnosis, women who were hypertensive four years postpartum had significantly thicker left ventricle posterior walls on their initial antenatal echocardiogram.⁴⁸

Prediction models for postpartum CVS dysfunction

Women with a history of PE, have an elevated Framingham risk score compared to those who experienced uncomplicated pregnancies.^{37,49,50} However, adding pregnancy complication history, particularly HDP, in an established cardiovascular risk score did not substantially improve discrimination or reclassification.^{51,52} The incremental information

provided by adverse pregnancy outcomes may have been partly captured by any subsequent increases in hypertension, diabetes, and dyslipidemia. Current CVD risk calculators have not been designed to be used in women of reproductive age with a low overall CVD risk, highlighting the urgent need to develop models to assess long-term CVD risk which include sex-specific risk factors such as HDP. To achieve this, it might be helpful to target prediction of cardiovascular risk factors such as hypertension, diabetes and dyslipidemia instead of CVD that occurs several decades after HDP. Indeed, hypertension and obesity are essential targets for cardiovascular prevention in women after HDP because they explain most of the excess risk of CVD in women with a history of HDP.

LONG-TERM MATERNAL HEALTH AFTER PRE-ECLAMPSIA

Cardiovascular disease mortality and hospitalization

There is an abundance of evidence demonstrating the development of cardiovascular disease and its risk factors after PE pregnancy (Table 1 and supplementary Table) and recent meta-analyses that suggest CVD morbidity and mortality increase throughout the lifetime.^{53,54} The most recent meta-analysis of over 10 million women showed that the overall risk of composite adverse CVD outcomes in the decade after birth is 2-times higher for women who had experienced a PE pregnancy compared to those who had uncomplicated pregnancies.⁵³ Consistent with this association, Langlois *et al.* showed a 17% increased risk of hospitalization for CVD after PE compared to uncomplicated pregnancies and this finding seems to extend throughout lifetime and include an increased risk of all-cause mortality.⁵⁵ However, specific CVD mortality studies show that a history of PE increases risk of dying 2 to 5-fold from CVD regardless of follow-up time.⁵⁶⁻⁵⁹ PE appears to increase the long-term risk of cardiovascular morbidity and mortality throughout the lifetime.

Influence of PE on the future development of conventional CVD risk factors

PE is associated with increased long-term development of conventional CVD risk factors with hypertension appearing to be most prominent.⁶⁰ At more than 10 years after a PE pregnancy, hypertension occurs roughly 2 to 4-times more frequently than after uncomplicated pregnancies.^{58,61} Ghossein *et al.* show that 8% of women who were normotensive at 6 weeks following a PE birth, were hypertensive at 6 years and that most women who were hypertensive postpartum, remained hypertensive at 6 years.⁶² The average mean difference for total cholesterol is higher after PE, but does not necessarily lead to dyslipidaemia.^{54,60} Dyslipidemia may occur 2-times more frequently, but there is no apparent correlation with cholesterol level.^{47,61,63} Even though one study demonstrated a 15.6% prevalence of metabolic syndrome within one year following PE, this finding is not supported by subsequent smaller studies.^{47,64,65} There is a mixed picture as to whether PE increases the risk of developing type 2 diabetes mellitus (T2DM) with increased risk being evident with longer-term follow-up up to 35 years.⁵³

Atherosclerotic disease

Placental decidual vasculopathy in PE has a similar pathophysiological process to atherosclerosis – leading to the hypothesis that PE could induce development of systematic atherosclerosis at an accelerated rate leading to an increased incidence of CVD.⁶⁶ This is supported in a national registry study with 50-year follow-up showing a 50% increase in risk of atherosclerotic events after PE.⁶⁷ CT angiography has also demonstrated subclinical coronary atherosclerosis in 30% of 45-55 year-old women consistent with a systematic review of seven studies showing a 50% increase in coronary artery disease (CAD).^{38,68} In addition to coronary events, a meta-analysis including nine studies demonstrated a 40% increased risk of developing a stroke after PE. PE may also affect cerebral microvasculature with evidence at 5 to 10 years, that cerebral white matter lesions related to microvascular disease occur more frequently.^{69,70} Although most long-term studies did not demonstrate an increased risk of developing dementia, the largest study with 283,902 participants showed a significant six-fold increased risk for vascular dementia specifically.⁷¹

Heart failure and arrhythmia

Heart failure and related hospital admissions are increased 2-fold after PE pregnancy, with hypertension being the key determinant driving cardiac dysfunction.^{17,64} This finding is echoed in a study of 1,303,365 women followed up for an average of 10 years with a 2-fold hazard ratio.⁵⁸ There is also an increased risk of dysrhythmias after PE, but this relationship is no longer evident when adjusted for confounding factors such as diabetes, hypertension and renal disease.⁵⁵

Renal dysfunction

There is robust evidence of a five-fold increase in the risk of developing end stage renal disease after PE.⁷² In contrast, there is a less data on the development of CKD with one study showing a four-fold increase in risk for hypertensive and diabetic CKD a two-fold increase for glomerular/proteinuric CKD at 20 years following a PE pregnancy.⁷³

POSTPARTUM MONITORING AND MANAGEMENT

Blood pressure pattern during pregnancy and the puerperium

Identifying these longitudinal BP patterns is vital to our understanding of maternal cardiovascular adaptation in HDP and to shape postpartum treatments to reduce cardiovascular morbidity. A recent retrospective cohort study of almost 1000 women with HDP⁷⁴ showed a decrease of 3.5 mmHg in SBP and 4.4 mmHg in DBP during the first trimester so that BP was below preconception levels, with a very small drop from 1st to 2nd trimester similar to a normal pregnancy.⁷⁵ SBP subsequently peaks on the day of the delivery and then reached similar highs up to day 5, whereas DBP peak later at 5-7 days postpartum. SBP gradually decreased and fell below the preconception level by day 15 postpartum, but DBP falls more gradually not reaching preconception level until 6 weeks postpartum. Therefore, prior to the typical 7–10 day routine postpartum medical check, BP varies significantly, and this is when cardiovascular morbidities typically occur.

What is the long-term BP course following hypertensive pregnancy?

Many argue that HDP is not causal in accelerating cardiovascular risks but, rather is a marker of a pre-existing sub-clinical disease. These conclusions are supported by the longitudinal follow up of the Norwegian Nord-Trondelag HUNT 1, 2 and 3, population-based, open cohort studies from 21 years prior to pregnancy up to 41 years after a women's first delivery. This cohort contains 22,308 normotensive women, 1092 of whom developed PE and 478 of whom developed gestational hypertension.⁷⁶ The HUNT studies demonstrate that BP trajectories remain higher in the HDP cohort compared to normotensive women, and that progression of cardiovascular risk factors to 60 years of age occurs in parallel for women with and without a history of HDP, with greater increases in systolic BP and adiposity in HDP women. However, the data does highlight that the diastolic BP does not return to 'normal' postpartum in the HDP cohort – a finding not explained by differences prior to pregnancy. Without intervention, BP can remain unstable for up to 50% of women for several months after HDP, and it may well be that uncontrolled BP in the puerperium directly affects cardiac and vascular remodeling, known to occur in the weeks after a hypertensive pregnancy in both mother and child.⁷⁷

Optimal measurement of blood pressure

Hypertension is largely identified during routine annual checks or opportunistically assessing BP in a primary care setting. However, between 1/3 to 1/2 of hypertensive patients remain undiagnosed, indicating the need for better screening.⁷⁸ UK guidance for hypertension in pregnancy makes no specific recommendation, but the general adult guidance⁷⁹ recognizes the value of Home BP monitoring (HBPM) and 24hr ambulatory blood pressure monitoring (ABPM)⁸⁰. Trials of self-monitoring outside of pregnancy, repeatedly show it can improve BP control, and it is an increasingly common part of hypertension management. It is well tolerated by patients and is a better predictor of end organ damage than clinic measurement.⁸¹ In 2018, the TASMINE-H4 randomized trial⁸² showed that using self-monitored BP to titrate anti-hypertensives, achieved better BP control when using telemonitoring. Trials have now shown that telemonitoring postpartum is also safe and effective when compared to standard care, with 8-fold fewer hypertension-related readmissions.⁸³ The role for HBPM, which is both liked by patients, widely available, practical and cost-

effective makes this an attractive option for facilitating postpartum BP care.⁸⁴ Two recent large trials in the UK (BUMP1 and 2) assessed whether self-monitoring improves the detection and/or control of hypertension during pregnancy itself^{85,86}. Once a person has been found to have high BP, 24-hour ambulatory blood pressure monitoring (ABPM) is still the most accurate way to diagnose hypertension.^{87,88} The BUMP trials demonstrated that remote self-monitoring resulted in equivalent pregnancy outcomes compared to clinic-based BP monitoring in the antenatal and postpartum period. Home telemonitoring following HDPs may also reduce ethnic health disparities in postpartum care. When engaged in a virtual BP monitoring program in one trial, both black and non-black women demonstrated compliance rates of more than 90%.⁸⁹

Frequency of BP measurement

In a trial by Hoppe *et al.*, severe hypertension (>160/110mmHg) occurred in approximately one in four women following discharge, and over half had increased BPs that required treatment after discharge⁸³. Systematic reviews show the latency to the first severe hypertension reading, and to the first BP level that necessitated treatment being ~6 days.⁹⁰ These findings suggest that it is sensible to measure BP for at least the first ten days postpartum. Given the significant diurnal variation in BP in HDP, with the BP climbing in the afternoon and evening in approximately 50% of women, twice daily readings would seem appropriate⁹¹. If the HBPM was timed in the morning and afternoon it would allow early recognition and adjustment 'in office hours' of medication. Frequency could be increased but at the risk of reducing compliance and thus a balanced approach is needed based on the clinical scenario.

Clinical benefits of improved-BP control during the puerperium

Tele-monitoring can be combined with self-titration or self-management, which can take the form of in person, or remote doctor support by telephone, text messages or an app. The SNAP-HT RCT compared self-management to usual GP and mid-wife led care following HDP⁹². It allowed women to self-monitor their BP and provided self-management via remotely medication advice feedback (Table 2). The results demonstrated the technique was

acceptable; women self-monitored daily with 85% adherence, a median accuracy of 94%, and there was a significant improvement in BP control. Not surprisingly, BP control was better whilst on treatment with the difference most marked at 6 weeks, but another striking finding was the diastolic BP being a mean 4.5 mmHg lower six months postpartum, long after stopping medication. The SNAP-HT Extension at four years postpartum went on to demonstrate that DBP was more than 7 mmHg lower in those originally randomized to postpartum BP self-management versus those treated with standard care (Figure 3)⁹³. This work suggests there is a window to optimize long-term cardiovascular risk in the puerperium and if the DBP difference were to be maintained long-term, it correlates to an approximate 40% life-time reduction in stroke and 20% life-time reduction in coronary heart disease risk.⁹⁴

The role for specific drug interventions in the postpartum period

Beyond the AHA recommendation of incorporating HDPs as a risk-enhancing factor to guide statin prescribing, no other specific guidelines exist to direct screening strategies or therapies for long-term cardiovascular risk reduction in these women. The PICK-UP trial, was a randomized double-blind placebo-controlled feasibility trial of enalapril in the highest risk early-onset PE group⁹⁵. At randomization, 88% of women had diastolic dysfunction and 68% had concentric remodeling/hypertrophy. There was no difference in the primary outcome (total vascular resistance) at 6 months postpartum but, women treated with enalapril had significantly better diastolic function at 6 months than those treated with placebo, as measured by E/E'. Enalapril use was also associated with improved LV remodeling at 6 months as well as a significant improvement in DBP in the intervention arm. A 2nd RCT specifically assessed the role of targeted calcium therapy in the puerperium, as part of a sub-group analysis of the WHO Calcium and preeclampsia study. Recruitment fell short of the sample size needed in the power calculation, but there was a statistically significant reduction in DBP in the sub-group of women who had a pregnancy previously affected by severe PE.⁹⁶ Another RCT in just under 400 women of a 5-day course of 20 mg oral furosemide vs. placebo in women with HDP demonstrated a 60% reduction in the prevalence of persistently elevated BP at 7 days in the furosemide group⁹⁷. AHA/ACC guidelines encourage statin use in women with prior HDP⁹⁸ and intermediate

calculated 10-year ASCVD risk, although no trials to date have specifically evaluated the role of statins in cardiovascular and cerebrovascular risk reduction after HDP.

Optimal postpartum treatment regimen

Larger validation studies of BP self-management are ongoing at present with mechanistic evaluation of peripheral resistance, cardiac output and function at rest, and on exercise.⁹⁹ This will hopefully help us answer the question of 'what is the optimal treatment regime' but there is no doubt there is a role for self-monitoring, self-management and ACEi in the future of postpartum BP treatment.^{83,95,100}

CONCLUSION AND FUTURE DIRECTIVES

HDP have a more immediate and detrimental impact on maternal cardiovascular health than previously known. These observations hold irrespective of whether these findings preceded the pregnancy and/or were caused by HDP. It is evident that maternal HBPM self-monitoring combined with effective BP control in the immediate postpartum period is associated with long-term benefits to the mother including an increased likelihood of normotension off medication. The evidence that effective care may increase the likelihood that women may be more likely to be normotensive off BP medication long-term deserves closer attention. Heightened awareness of these findings should drive increased research into clarifying the optimal BP measurement method and frequency as well as the appropriate treatment regimen with allied self-titration protocols. Improved healthcare delivery in the 'fourth trimester' of pregnancy has important implications for women, clinicians and public health policy.

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AUTHORS' CONFLICT OF INTEREST

None

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FIGURE LEGENDS

Figure 1. Risk of postnatal hypertension within 2 years of delivery after hypertensive disorders of pregnancy including (◆) or excluding (●) women with pre-existing chronic hypertension. Modified by Giorgione et al.⁶

Figure 2. Cardiac changes in pregnancies complicated by hypertensive disorders of pregnancy during pregnancy and throughout the postpartum. HDP Hypertensive disorders of pregnancy, GLS global longitudinal strain, LV left ventricle, LVMI left ventricular mass index, CHT chronic hypertension, DM diabetes mellitus.

Figure 3. Longitudinal diastolic blood pressure trajectories from SNAP-HT into SNAP-HT EXTENSION from antenatal booking blood pressure to 3.6 ± 0.4 years postpartum.

Table 1. Table summarizing the most recent key literature indicating the risk (based on hazard ratios) of developing various types of CVD split by number of years after PE. PE Pre-eclampsia, CVD Cardiovascular disease, CKD Chronic Kidney Disease, ESRD End Stage Renal Disease. Citations to support level of risk are shown in the Supplementary Table

Years after PE	CVD hospitalization	CVD mortality	All-cause mortality	Hypertension	Dyslipidemia	Metabolic syndrome	Type 2 diabetes mellitus	Ischemic heart disease	Stroke	Heart failure	Dysrhythmia	CKD	ESRD	Peripheral artery disease	Dementia
5-10		++	++	+++		+++		++	+	++	+	+		+	
10-20	+			+++		++		+	+	+/-	+/-	+	+++	+	
>20	++	++	+/-	+	+		+	+	+/-	+	+	+			++

+/- risk may not be raised

+ mildly increased risk (HR <2 in most studies)

++ moderately increased risk (HR >2 in most studies)

+++ markedly increased risk (HR >3 in most studies).

Table 2. Traffic-light system to guide frequency of blood pressure readings post-partum or women with HDP whilst on anti-hypertensive treatment. 'No action' prompts an app notification to continue daily readings.⁹⁹

Colour	Level	BP	Action
Red	Very high	Sys 160 or more OR Dia 110 or more OR Symptoms	Repeat BP in 5 minutes. If this is a repeat reading: contact local maternity unit immediately for urgent assessment today.
Orange	High	Sys 150-159 OR Dia 100-109	Repeat BP in 5 minutes. If this is a repeat reading: Call from study physician 9-5pm AND to see own GP/midwife for an URGENT (same-day) appointment.* Switch to twice daily readings until back in yellow/green
Yellow	Raised	Sys 140-149 OR Dia 90-99	No action.
Green	High normal	Sys 130-139 OR Dia 80-89	No action
Blue	Low normal	Sys 100-129 AND Dia < 80	Switch to twice daily readings and if in this zone for 2 consecutive days, medication titration will be signed off by study doctor and instructions sent via app to participant
Purple	Low	Sys < 100 AND Dia < 80	Repeat BP in 5 minutes. If this is a repeat reading: option of opting for a call from study physician 9-5pm vs. opting to see own GP/midwife for an URGENT appointment*. Switch to twice daily readings until back in yellow/green