Treatment postpartum – immediate and long term

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SYNOPSIS
Hypertension may worsen transiently postpartum, especially between days 3 and 6 when blood pressure peaks. Hypertension and pre-eclampsia may even develop for the first time postpartum. Hypertension, proteinuria and the biochemical changes of pre-eclampsia begin to resolve by 6 weeks postpartum but may persist for longer, especially when those changes have been extreme. Care in the 6 weeks postpartum includes management of hypertension, ensuring resolution of biochemical changes, and screening for secondary causes of hypertension in women with resistant hypertension, impaired renal function, or abnormal urinalysis. Care providers should be aware of the mental health implications of the hypertensive disorders of pregnancy, such as anxiety, depression and post-traumatic stress disorder. The hypertensive disorders of pregnancy are also associated with a number of long-term complications and the postpartum period provides an ideal window of opportunity to address these risks, such as premature cardiovascular disease and chronic kidney disease. Women with a history of a hypertensive disorders of pregnancy should adopt a heart-healthy lifestyle and should be screened and treated for traditional cardiovascular risk factors according to locally accepted guidelines.

CARE IN THE FIRST 6 WEEKS AFTER BIRTH
Women and their maternity care providers may assume that, because delivery is the cure for pre-eclampsia, all aspects of the disease will improve postpartum. As such, it is important to manage expectations and prepare women for an alternative outcome.

Hypertension may antedate delivery in up to 50% of women with postpartum hypertension. Women with pre-existing hypertension who did not require antihypertensive medication antenatally may require such therapy after delivery. Those at greatest risk of postpartum hypertension are those who delivered preterm and, for multiparous women, those with higher urate levels. Postpartum deterioration of maternal end-organ function occurs in up to 25% of women with a hypertensive disorder of pregnancy; this deterioration usually occurs early in the puerperium, especially when women have had severe disease.

Hypertension that appears for the first time postpartum does so most commonly on days 3–6, when there is mobilisation of extracellular fluid and expansion of intravascular volume. Postpartum hypertension may be isolated or associated with pre-eclampsia-related end-organ dysfunction. Two-thirds of women with postpartum pre-eclampsia have no antenatal hypertensive disorder of pregnancy and their postpartum
pre-eclampsia/eclampsia usually develops within days, but occasionally up to 3 weeks, after delivery. Pre-eclampsia mimickers should be considered in women in whom pre-eclampsia worsens postpartum or in women who develop severe hypertension and HELLP (haemolysis, elevated liver enzymes, low platelet) syndrome in the postpartum period (see Chapter 3, for further details). The differential diagnosis includes disorders such as thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome (TTP/HUS), systemic lupus erythematosus and exacerbation of pre-existing renal disease. They are important to recognise because they require individualised therapeutic interventions. Key issues to consider are the urinary sediment (which must be collected by urinary catheter because of lochia), the time course of the abnormalities relative to delivery, and manifestations that may point to disease processes other than pre-eclampsia, such as a skin rash of lupus.

**Management of hypertension**

At minimum, blood pressure should be measured during the time of peak postpartum blood pressure elevation (for all postnatal women), on days 3–6 after delivery so that the rise in blood pressure, which may be to severe levels, does not go undetected. All severe hypertension should be treated, be it antenatally or postpartum. There are no reliable data to guide whether antenatal antihypertensive therapy should be continued postpartum. The potential advantages of continuing antihypertensives postpartum would be to decrease the risk of non-severe or severe hypertension postpartum. However, postnatal antihypertensive therapy has not been shown to decrease the development of postnatal severe hypertension, shorten hospital stay, or result in any other beneficial or adverse effects in very small published, randomised controlled trials (3 trials, 313 women). Based on data outside pregnancy, blood pressure should be treated to <140/90 mmHg but possibly to <130/80 mmHg in women with pre-gestational diabetes mellitus. Generally, antihypertensives are needed longer in women with pre-eclampsia (approximately 2 weeks) versus gestational hypertension (about 1 week). There is no clear best choice of antihypertensive agent. Any antihypertensive agent used should be based on a clinician’s familiarity with the drug. Antihypertensives used most commonly in pregnancy, as well as captopril and enalapril are ‘usually acceptable’ for breastfeeding. The available studies have been small and evaluated maternal serum/plasma drug and/or active metabolite concentrations, the same levels in breast milk, and infant serum/plasma/urine levels; few case reports or series have described any clinical adverse effects in infants. However, any breastfed baby who is potentially exposed to drugs through breast milk should be observed for any behavioural (e.g., excessive crying) and/or physiological (e.g., diarrhoea) concerns. Caution may be exercised in preterm and low birth weight infants owing to immature drug clearance and/or increased susceptibility to drug effects. There is particular concern about the angiotensin converting enzyme (ACE) inhibitors, at least initially until the premature baby is stabilised, but the concerns expressed by neonatologists are largely theoretical.

**Analgesia**

Control of postpartum pain is discussed in Chapter 10.

**Thromboprophylaxis**

Guidelines vary in their recommendations about risk factors, the number of risk factors that should prompt thromboprophylaxis, and the duration of that thromboprophylaxis. Risk factors agreed upon by most guidelines include pre-eclampsia, advanced maternal age, obesity, prolonged antenatal bed rest, postpartum haemorrhage and emergency Caesarean delivery. Pre-eclampsia is associated with an increased risk of venous thromboembolism (VTE) (adjusted odds ratio 2.9–3.1). The risk is further increased in women with pre-eclampsia and fetal growth restriction (adjusted odds ratio 5.8). The duration of thromboprophylaxis from delivery may vary from treatment until full mobilisation, to 4–6 weeks postpartum.

**CARE BEYOND THE FIRST 6 WEEKS AFTER BIRTH**

**Work-up to rule out underlying disease**

**After gestational hypertension**

Gestational hypertension usually resolves by 6 weeks postpartum. If it persists, particularly beyond 6 months postpartum, the woman has ‘pre-existing’ or ‘chronic’ hypertension, either
essential or secondary to another aetiology. Further investigation is warranted at that time.

Hypertension that is difficult to control (such as with three agents) in particular should prompt evaluation for a secondary cause of hypertension.

**After pre-eclampsia**

The hypertension of severe pre-eclampsia may take up to 3–6 months to resolve\(^\text{18}\). As following gestational hypertension, hypertension that persists beyond 6 months after delivery indicates chronic hypertension and warrants consideration of secondary causes.

Screening for underlying causes of pre-eclampsia may better inform management of the woman’s health after the current pregnancy, between pregnancies, and/or in subsequent pregnancies. These efforts are best undertaken at 3–6 months postpartum when pregnancy-related physiology can be relied upon to have resolved.

Screening for pre-existing hypertension and underlying renal disease should be undertaken if pre-eclampsia was: (1) of onset before 34 weeks or ‘severe’, or (2) was followed at 3–6 months postpartum by ongoing proteinuria, estimated glomerular filtration rate (eGFR) <60 mL/min, or abnormal urinary sediment. While it is essential to ensure resolution of target organ damage (e.g., proteinuria), routine measurement of microalbuminuria after pre-eclampsia resolution is not recommended without a specific renal indication. Appropriate specialist referral (e.g., internal medicine or nephrology) should be considered for women in whom blood pressure is difficult to control or a secondary cause (including renal disease) is suspected.

Special mention of thrombophilia screening is warranted. Thrombophilia confers, at most, a weakly increased risk of pre-eclampsia (and other placentally mediated pregnancy complications). Routine thrombophilia screening following pre-eclampsia is not recommended\(^\text{20}\) because of this weak association and, also, because treatment with thromboprophylaxis has not been demonstrated to improve outcomes\(^\text{21}\); an individual patient data meta-analysis is being performed to examine whether there is a high-risk subgroup of women who may benefit from thromboprophylaxis and therefore, could be screened for thrombophilia\(^\text{22}\). Until such time, the one subgroup of women who may benefit from antiphospholipid antibody screening is pre-eclampsia with delivery at <34 weeks, as these women would meet criteria for the antiphospholipid antibody syndrome (APAS) and the diagnosis would influence future management outside pregnancy (e.g., choice of contraception) at minimum\(^\text{23}\).

**Future pregnancy planning**

The recurrence risk of a hypertensive disorder of pregnancy depends in part on the disorder and its characteristics in the previous pregnancy and characteristics of the woman, particularly obesity. Recurrence is discussed in detail in Chapter 5. In brief, gestational hypertension is followed by a hypertensive disorder of pregnancy risk of about 25% in the subsequent pregnancy, and almost all is gestational hypertension (21%) rather than pre-eclampsia (4%). In contrast, pre-eclampsia is followed by a higher hypertensive disorder of pregnancy risk of 40%, with just over half as pre-eclampsia (22%) and the rest as gestational hypertension (15%); recurrence rates are higher (exceeding 50% in some reports) when pre-eclampsia was ‘severe’ or associated with HELLP syndrome specifically.

**Implications for long-term paediatric health**

The short-term implications for the fetus and newborn are discussed in Chapter 3. Discussed here is the fact that the hypertensive disorders of pregnancy may have long-term implications for the child beyond the complications of preterm delivery and/or fetal growth restriction. Although any potential impact on neurodevelopment is of keen interest to practitioners, there are other chronic diseases associated with the hypertensive disorders of pregnancy and/or preterm delivery of which the clinician should be aware.

**Neurodevelopment**

Pre-eclampsia superimposed on pre-existing hypertension (versus pre-existing hypertension alone) has no adverse effect on (or slightly better) intellectual development\(^\text{24}\). There is no literature available on the independent impact of antihypertensive therapy.

Gestational hypertension and pre-eclampsia may predict generally modest long-term effects on child development. Children of women with pre-eclampsia had better outcomes (i.e., reduced...
internalising morbidity such as anxiety) at ages 5 and 8 years, but children of women with gestational hypertension were more likely to have poorer behaviour from 8 years onwards, with the largest difference seen at 14 years; no information was provided on the potential impact of antihypertensive therapy. Both types of hypertensive disorders of pregnancy were associated with a small reduction in verbal ability of uncertain clinical significance. The neurodevelopmental effects of pre-eclampsia persisted even when matched or adjusted for gestational age and growth restriction. Although placental abruption is an additional risk factor for adverse neurodevelopmental outcomes, it has not been studied in conjunction with pre-eclampsia.

It should be noted that not all studies provide a consistent picture of the association between the hypertensive disorders of pregnancy and paediatric cognitive function. The mixed pattern of results likely arises from methodological differences, particularly varying study populations and study designs. The lack of much information on antihypertensive therapy is a major drawback to this literature. There are a handful of small randomised controlled trials that have examined paediatric neurodevelopment. Babies of antihypertensive (mainly methyldopa)-treated mothers (versus normotensive controls) more often had delayed fine-motor function at 6 months of age, while those of placebo-treated hypertensive mothers more frequently had 'questionable' neurological assessment and delayed gross-motor function at 12 months. In other small randomised controlled trials, antihypertensive therapy was not associated with negative effects on child development when assessed at 1 year, 18 months, or 7.5 years (methyldopa, 242 children), 18 months (atenolol, 190 children), or 7.5 years (nifedipine, 110 children). In contrast, in an observational controlled study, methyldopa (25 exposed children) (but not labetalol, 32 exposed children) was associated with lower intelligence quotient (IQ) scores, but in multivariable regression, IQ was associated with maternal IQ and duration of antihypertensive treatment.

Other long-term outcomes

Higher blood pressure A systematic review and meta-analysis found that children exposed to pre-eclampsia had higher systolic and diastolic blood pressure values during childhood and young adulthood when compared with controls. The degree of elevated blood pressure is related to preterm birth and higher body mass index (BMI) of the children. The blood pressure effects were present at age 21 years.

Stroke In the Helsinki birth cohort (6410 pregnancies), pre-eclampsia was associated with an increased risk of stroke in the adult offspring.

Pregnancy complications of their own In a population-based cohort study (24,119 women), hypertensive disorders of pregnancy and gestational diabetes mellitus (GDM) were increased in women who were themselves born preterm, especially before 32 weeks. Although this was a study of preterm birth in general, the hypertensive disorders of pregnancy were found to be an important cause of iatrogenic preterm birth.

Implications for long-term maternal health

Pregnancy is considered a biological 'stress test' that can predict a woman's health in later life. The hypertensive disorders of pregnancy, particularly pre-eclampsia, are associated with a number of future health risks. Identifying women at risk by virtue of the physiologic stress test of a pregnancy complicated by pre-eclampsia is a unique opportunity to address and prevent chronic illnesses.

Cardiovascular risk factors and disease

The American Heart Association has recognised pre-eclampsia and gestational hypertension as 'major' cardiovascular risk factors for women. Pre-eclampsia has a pathophysiology remarkably similar to cardiovascular disease, in terms of metabolic abnormalities (such as hyperlipidaemia and insulin resistance), a heightened inflammatory response, a hypercoagulable state and endothelial dysfunction.

It is likely that some women are predisposed to pre-eclampsia because of an adverse pre-pregnancy cardiovascular risk profile, which lowers the threshold for a hypertensive response to placentally derived products. The alternative hypothesis is that pre-eclampsia itself damages a woman's endothelium and produces permanent metabolic sequelae, leading to increased long-term cardiovascular risk.
A large prospective study examined the cardiovascular risk profiles of women who developed a hypertensive disorder of pregnancy and found that women with gestational hypertension and pre-eclampsia, compared with women who had a normotensive pregnancy, had higher BMI, lower levels of high density lipoprotein (HDL), and higher levels of triglycerides, low density lipoprotein (LDL) and total cholesterol.

A small case–control study conducted at 1 year postpartum showed asymptomatic left ventricular moderate–severe dysfunction/hypertrophy was significantly higher in women who had suffered from preterm pre-eclampsia (56%) compared with term pre-eclampsia (14%) or matched controls (8%; \( p < 0.001 \))46. This suggests that pre-eclampsia is associated with persistent postpartum cardiovascular impairment.

Three large systematic reviews have consistently demonstrated that women with a history of pre-eclampsia have a higher risk of cardiovascular and cerebrovascular disease47–49 (Table 11.1). The 2007 systematic review by Bellamy et al. included 25 studies, and approximately 3 million women of whom 25,000 had pre-eclampsia47. McDonald et al. in their 2008 review included 15 studies and a total of 118,990 women with a history of pre-eclampsia/eclampsia and 2,259,576 women with unaffected pregnancies49. A recent review by Brown et al. in 2013 included 50 papers but did not state the number of women included48. While there are methodological differences, the results have been generally similar amongst the reviews.

**Hypertension**

Bellamy et al. found that pre-eclampsia was associated with development of hypertension later in life, after a mean follow-up of 14 years with a relative risk of 3.7 (95% CI 2.70–5.05)47. For women with gestational hypertension, the risk of developing subsequent hypertension was similar to women with a risk of hypertension (RR 3.39, 95% CI 0.82–13.92) at a mean of 11 years postpartum47. Brown et al. had similar results with a relative risk of 3.13 (95% CI 2.51–3.89) for women with a history of pre-eclampsia/eclampsia48.

**Ischaemic heart disease**

In the systematic review of Bellamy et al., the relative risk of fatal or non-fatal ischaemic heart disease in women with pre-eclampsia was over twice that of women without pre-eclampsia (RR 2.16, 95% CI 1.86–5.20)47. The risk of ischaemic heart disease also occurred earlier at a mean of 11.7 years after the index pregnancy. In McDonald et al.‘s review, women with a history of pre-eclampsia/eclampsia had an increased risk of subsequent cardiac disease, in both case–control studies (odds ratio 2.47, 95% CI 1.22–5.01) and cohort studies (RR 2.33, 95% CI 1.95–2.78)49. Brown et al. found that women who experienced pre-eclampsia were at more than two fold increased odds of cardiovascular disease (OR 2.28, 95% CI 1.87–2.77) with similar results between the cohort and control studies48.

Bellamy et al. found that women with severe pre-eclampsia had a greater risk of developing later ischaemic heart disease (RR 2.86, 95% CI

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**Table 11.1** Risk of cardiovascular disease after pre-eclampsia (95% CI presented in parentheses)

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<tbody>
<tr>
<td><strong>Hypertension</strong></td>
<td></td>
<td>Not analysed</td>
<td>RR 3.13 (2.51–3.89)</td>
</tr>
<tr>
<td>Pre-eclampsia:</td>
<td>RR 3.7 (2.70–5.05)</td>
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<tr>
<td>Gestational hypertension:</td>
<td>RR 3.39 (0.82–13.92)</td>
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<tr>
<td><strong>Ischaemic heart disease</strong></td>
<td>RR 2.16 (1.86–5.20)</td>
<td>OR 2.47 (1.22–5.01)*</td>
<td>OR 2.28 (1.87–2.77)</td>
</tr>
<tr>
<td><strong>Stroke</strong></td>
<td>RR 1.81 (1.45–2.27)</td>
<td>OR 2.6 (1.5–4.3)*</td>
<td>RR 2.03 (1.54–2.67)*</td>
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<td></td>
<td></td>
<td>OR 1.77 (1.43–2.21)</td>
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* Case–control studies; †cohort studies
1.65–2.24) compared to women who had mild pre-eclampsia (RR 1.92, 95% CI 1.65–2.24) particularly if pre-eclampsia occurred before 37 weeks (RR 7.71, 95% CI 4.40–13.52)\(^47\). This ‘dose response’ effect was not, however, demonstrated in the review by Brown. The review by Brown compared outcomes for pre-eclampsia both with and without preterm birth using three studies whilst the data from Bellamy came from only one study\(^48\).

The risk of cardiovascular disease may be further increased in the presence of poor fetal outcomes. In a population-based retrospective cohort study of women with maternal placental syndrome (defined as pre-eclampsia, gestational hypertension, placental abruption, and/or placental infarction), the risk of premature cardiovascular disease was higher in the presence of poor fetal growth (adjusted hazard ratio (aHR) 3.1, 95% CI 2.2–4.5) or intrauterine fetal death (aHR 4.4, 95% CI 2.4–7.9)\(^50\). A Canadian population-based retrospective cohort study of 1985 women found that in middle-aged women (mean age 45 years) who underwent coronary revascularisation, prior maternal placental syndrome (such as pre-eclampsia) doubled the risk of death (aHR 1.61, 95% CI 1.00–2.58)\(^51\).

**Stroke**

Bellamy’s review found that the overall risk of fatal and non-fatal cerebrovascular disease (stroke or non-fatal stroke) after pre-eclampsia was 1.81 (95% CI 1.45–2.27) compared with women who had not developed pre-eclampsia. Subgroup analysis showed that the risk of fatal stroke (RR 2.98, 95% CI 1.11–7.96) was greater than that of non-fatal stroke (RR 1.76, 95% CI 1.40–2.2) after pre-eclampsia\(^57\). A diagnosis of pre-eclampsia before 37 weeks was associated with a further elevation in risk (RR 5.08, 95% CI 2.09–12.35) compared with pre-eclampsia after 37 weeks (RR 0.98, 95% CI 0.50–1.92). McDonald included only one eligible case–control study which reported an increased risk of 2.6 (95% CI 1.5–4.3) consistent with the pooled estimate in the six cohort studies (RR 2.03, 95% CI 1.54–2.67)\(^59\).

**Renal disease**

Pre-eclampsia has been associated with an increased risk of end-stage kidney disease in large observational studies.

A large retrospective cohort study from Norway (20,918 women with pre-eclampsia) found that pre-eclampsia in the first pregnancy was associated with a relative risk of end-stage kidney disease of 4.7 (95% CI 3.6–6.1). This risk increased further to 6.7 (95% CI 4.3–10.6) among women who also had pre-eclampsia only in their second pregnancy, and increased again if women had pre-eclampsia in both their first and second pregnancies or in three pregnancies (RR 15.5, 95% CI 7.8–30.8)\(^52\).

In a population-based study from Taiwan (8653 women with gestational hypertension, 17,998 women with pre-eclampsia), having had either gestational hypertension or pre-eclampsia was associated with a greater risk of chronic kidney disease (aHR 9.4, 95% CI 7.1–12.4) and end-stage renal disease (aHR 12.4, 95% CI 8.5–18.0), even after controlling for several factors including coronary artery disease, congestive heart failure, hyperlipidaemia and abruption\(^53\). The greatest risk of end-stage renal disease was associated with having had pre-eclampsia or eclampsia (aHR 14.0, 95% CI 9.4–20.7) compared with gestational hypertension (aHR 9.0, 95% CI 5.2–15.7)\(^53\).

**Other chronic diseases**

**Diabetes**

In a population-based study (50,598 women with a hypertensive disorder of pregnancy), women with a prior hypertensive disorder of pregnancy had a two-fold increased risk of developing diabetes when followed up to 16.5 years after pregnancy, even in the absence of a prior history of gestational diabetes\(^54\). A history of a hypertensive disorder of pregnancy and gestational diabetes together increased the risk associated with GDM alone\(^54\).

**Elevated thyroid stimulating hormone (TSH)**

In a nested case–control study of women with pre-eclampsia from two large cohort studies (Calcium for Pre-eclampsia Prevention trial\(^55\) and the Nord-Trondelag Health Study\(^56\)), women with prior pre-eclampsia had higher thyroid stimulating hormone (TSH) levels compared with controls who had no history of a hypertensive disorder of pregnancy\(^57\). Of note, women with prior pre-eclampsia were less likely to have thyroid peroxidase antibodies, suggesting that their hypothyroidism was occurring in the absence of an autoimmune process. The association between
pre-eclampsia and elevated TSH was especially strong (adjusted OR 5.8, 95% CI 1.3–25.5) if pre-eclampsia had occurred in both the first and the second pregnancies.

Central nervous system white-matter lesions Several studies have shown that women whose pregnancies were complicated by pre-eclampsia or eclampsia are more likely than controls to have white matter lesions; although these may reflect a predisposition to vascular disease, the significance of these lesions is currently unknown.

Mental health Pre-eclampsia can be very stressful for women and their partners, especially relative to expectations of a routine, normal pregnancy and no prior significant illness. Women may have to deal with postpartum recovery from hypertension, end-organ complications, and frequently, Caesarean delivery. In addition, women may have to deal with perinatal loss or illness, such as care in the neonatal intensive care unit (NICU).

A systematic review showed that while the evidence is not entirely consistent, in general, there is an association with prior pre-eclampsia or HELLP syndrome and more anxiety, depression and post-traumatic stress disorder (6 studies, 5636 women). Women who experienced severe maternal morbidity were shown to be at particular risk of post-traumatic stress disorder (1824 women). Women with severe pre-eclampsia who must deal with a perinatal death or NICU admission are at particular risk of poor health-related (especially mental health-related) quality of life. These effects of pre-eclampsia on mental health may persist beyond the short term; women with preterm birth owing to severe, early-onset pre-eclampsia (compared with women with preterm birth for other reasons) more often experienced post-traumatic stress symptoms an average of 7 years postpartum.

Postpartum care of women with pre-eclampsia should include evaluation and referral for postpartum psychological care. It is important for women to receive relevant information about not only their medical condition, but their psychological condition as well. It is also necessary to examine coping strategies after pre-eclampsia and offer adequate supportive interventions when they are needed.

Investigations and interventions to improve long-term health

Pregnancy and the immediate postpartum period may be one of the few times in a woman’s life when she accesses the health care system regularly. Therefore, the postpartum period provides a unique window of opportunity for early identification and reduction of primary cardiovascular risk.

Education/awareness

Among women A small study using focus groups found that women with prior pre-eclampsia were unaware of the link between pre-eclampsia and future cardiovascular disease, but were eager to learn about the link and motivated to achieve a healthy lifestyle. Another study found that women generally had a low level of cardiovascular risk factor knowledge.

Although some guidelines, such as those from NICE (UK), recommend that future cardiovascular risk should be communicated to the woman before discharge from maternal services, some argue that it may be too early for most women. Women may be recovering from serious morbidity whilst balancing the demands of the neonate; this may limit the efficacy of the communication. Women’s reactions to learning about the link between pre-eclampsia and future cardiovascular disease included both positive feelings (i.e., motivation, empowerment) and negative ones (i.e., being scared, angry, guilty, or isolated). Therefore, it is important that women are followed on an ongoing basis and receive information about cardiovascular health over time.

Recently, an educational intervention to promote cardiovascular knowledge and awareness was tested amongst women with a history of pre-eclampsia. The intervention, delivered by telephone given that postpartum women have many demands on their time, had several components: diet, exercise, medication compliance, screening for risk factors and symptoms of myocardial infarction. It was found to be a practical and effective method of contacting postpartum women following pre-eclampsia and increasing perception of cardiovascular risk.

Among health care providers There is also a lack of awareness amongst health care providers and gaps in identification and routine follow-up.
Though the American Heart Association recommends that health professionals disclose the future risk of cardiovascular disease to women with a history of pre-eclampsia, a study revealed that only a third of health professionals provide that counselling\(^\text{69}\). A review of the existing literature on engaging obstetricians and gynaecologists in cardiovascular risk reduction found that while they agreed that their role extended beyond reproductive care, there was variation in practice and they were unlikely to manage hypertension or elevated cholesterol. Obstetricians and gynaecologists identified knowledge and skill deficits, concerns about liability, and barriers to prevention presented by their practice structure. Some providers also emphasised difficulties completing referrals to primary care providers\(^\text{70}\). A Canadian survey of maternity care providers found that only 54% of participants were familiar with the long-term cardiovascular risks of pre-eclampsia\(^\text{71}\). A small retrospective review from The Netherlands examined cardiovascular risk factor management and found that only 50% of women with pre-eclampsia had their blood pressure measured by 3 months postpartum. Blood glucose and lipids were infrequently checked even though some of the women had cardiovascular risk factors prior to the index pregnancy\(^\text{72}\). Appendix 11.1 contains training materials for health care providers including multiple choice questions and a case study. Knowledge translation tools for health care providers are included in Appendix 11.2.

**Cardiovascular risk factor screening**

At present, there are no guidelines advising when to screen women with a prior hypertensive disorder of pregnancy or pre-eclampsia for cardiovascular risk factors. (Cardiovascular risk factor screening in women with pre-existing or chronic hypertension has been published by all national societies.) The very earliest would be at 3–6 months postpartum when the metabolic changes of pregnancy (such as dyslipidaemia) have resolved.

Traditional cardiovascular markers appear to be more abnormal in women who have suffered from pre-eclampsia, as early as 1 year postpartum\(^\text{73}\). A small study from the Maternal Health Clinic, a postpartum cardiovascular risk reduction clinic in Kingston, Canada, sought to determine whether women with a history of pre-eclampsia (N=99) compared with those without pre-eclampsia (N=118) had 10-year, 30-year and lifetime cardiovascular risk estimates that were high enough at 1 year postpartum to identify them as warranting further counselling and follow-up regarding lifestyle modification and/or pharmacotherapy\(^\text{74}\). Using traditional cardiovascular risk markers (i.e., sex, age, smoking, serum total cholesterol, serum LDL cholesterol, serum HDL cholesterol, fasting plasma glucose, systolic blood pressure, diastolic blood pressure and antihypertensive use), the study found that women who had suffered from pre-eclampsia (versus those who had not) more often had elevated 10-year cardiovascular risk (i.e., 18.2% vs. 1.7%, respectively; OR 13.1, 95% CI 3.4–85.5), 30-year cardiovascular risk (i.e., 31.3% vs. 5.1%, respectively, OR 8.4, 95% CI 3.5–23.2), and lifetime cardiovascular risk (i.e., 41.4% vs. 17.8%, respectively; OR 3.3, 95% CI 1.8–6.1)\(^\text{74}\). A follow-up study showed that the Maternal Health Clinic could identify a population of postpartum patients with increased 10- and 30-year cardiovascular risk\(^\text{75}\).

It remains unclear whether traditional risk factors, such as those used in the Maternal Health Clinic, are sufficient for cardiovascular risk screening. First, global risk assessment tools like the Framingham Risk Score may not accurately estimate cardiovascular risk in young women, especially in the short term; a study of 2333 women using the Framingham Offspring cohort showed that the 10-year model estimates negligible risks for young women, whereas the 30-year model suggests a risk that is 10 times higher\(^\text{76}\). Second, cardiovascular risk factors used in prediction models like the Framingham or Reynolds Risk Score may not fully explain the risk of cardiovascular disease after pre-eclampsia; in a literature based study that included 16 studies, a major part of the observed OR of cardiovascular disease after pre-eclampsia remained after adjustment for these traditional cardiovascular risk factors\(^\text{77}\).

**In summary**, it remains unclear both when cardiovascular risk screening should take place...
following pre-eclampsia, and at what threshold treatment should begin. There are public health implications and costs to consider. Although it may be appropriate to intervene at earlier stages in this population, we should await supportive research findings. In the meantime, it would seem prudent to screen women who have had pre-eclampsia for traditional cardiovascular risk markers according to national guidelines which should also dictate intervention for abnormal results.

A simple approach that has been proposed in this population of women is the identification of any of the components of metabolic syndrome as the syndrome does not predict clinical outcomes better than its individual components78. These components include:

- Blood pressure
- Weight and height are measured to calculate the BMI
- Lipid panel
- Glucose intolerance screening.

All women with gestational diabetes should undergo postpartum glucose tolerance testing. In addition, some recommend that postpartum testing for glucose intolerance should be ordered for all women with one of the other components of metabolic syndrome, such as obesity78. Abnormalities in any of the above components should be treated as per current national guidelines or prompt referral to an internal medicine specialist.

## Lifestyle change

What is appropriate and evidence-based for all is adoption of a heart-healthy diet and lifestyle to decrease cardiovascular risk (Table 11.2)40. Of course, neither is an easy intervention and there are barriers to change that are specific to postpartum women.

Women may be motivated by the knowledge that weight gain between pregnancies predicts pre-eclampsia and other pregnancy complications (e.g., gestational diabetes and Caesarean delivery)80,81, and weight loss between pregnancies may improve future pregnancy outcome in addition to long-term cardiovascular risk. However, there are many competing demands on a new mother’s time.

Major perceived barriers to lifestyle change identified in a qualitative (American) study of 20 postpartum women were lack of time, cost of healthy foods and family responsibilities65. Another (Dutch) study of 36 women identified additional barriers of poor postpartum physical and psychological recovery, and lack of postpartum medical and psychological support from health care providers82. Perceived facilitators have included knowledge of the link between pre-eclampsia and cardiovascular disease, a desire to stay healthy, and creating a healthy home for their children65. This link to child health may be a key motivator of change.

Currently, postpartum lifestyle interventions tailored specifically for women following a hypertensive disorder of pregnancy are lacking, although those demonstrated to be effective outside

### Table 11.2 Dietary and lifestyle modifications recommended for all women40 (with permission from Society of Obstetricians and Gynaecologists of Canada)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Details</th>
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<tbody>
<tr>
<td>Heart-healthy diet</td>
<td>Maintain a healthy balanced diet (high in fruits, vegetables, low-fat dairy products, reduced in saturated fat and cholesterol) in addition to dietary and soluble fibre, whole grains and protein from plant sources79</td>
</tr>
<tr>
<td>Regular physical activity</td>
<td>Undertake 150 minutes/week of moderate to vigorous-intensity aerobic physical activity (such as walking, jogging, cycling or swimming)</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Reduce alcohol consumption to &lt;2 drinks/day and &lt;9/week</td>
</tr>
<tr>
<td>Weight reduction</td>
<td>Attain and maintain ideal body weight (i.e., BMI 18.5–24.9 kg/m²)</td>
</tr>
<tr>
<td>Reduce waist circumference</td>
<td>Attain and maintain a waist circumference of &lt;88 cm</td>
</tr>
<tr>
<td>Salt intake</td>
<td>Reduce intake to &lt;1500 mg/d</td>
</tr>
<tr>
<td>Smoking cessation</td>
<td>Quit smoking in addition to ensuring a smoke-free environment</td>
</tr>
</tbody>
</table>

BMI, body mass index
pregnancy have been tested in unselected postpartum populations\(^8\). Among postpartum women in general (21 studies, 6288 women), most weight loss interventions (6 of 8) were effective, as were most smoking cessation interventions (4 of 5). Also effective were individualised tailoring of counselling, group counselling sessions, and use of diaries or other correspondence material. Of note, the Maternal Health Clinic (Kingston, ON) has designed ‘The Postpartum Mother’s Health Record’, a card that allows women to set goals and track weight loss\(^8\). The timing of data collection coincides with the infant’s scheduled visits and immunisations, linking maternal and child health going forward – a practical and potentially more feasible approach for the new mother. Appendix 11.2 highlights knowledge translation tools for women including mobile apps, programmes and research studies.

Focus groups with women with prior pre-eclampsia indicated potential interest in a web-based programme focused on lifestyle strategies to decrease cardiovascular risk\(^6\). This approach was tested in a small feasibility study (20 women) of a web-based, tailored health education intervention related to diet and exercise, in conjunction with counselling by a psychologist (Dutch ProActive study, Postpartum Rotterdam Appraisal of Cardiovascular Health and Tailored Intervention)\(^8\). The intervention was initiated at 6 months postpartum and continued for 3 months. In all 60\% of women participated and anthropometric measurements at 13 months postpartum improved significantly, although metabolic parameters did not\(^8\).

**Bariatric surgery for women with morbid obesity**

Women who are morbidly obese and have failed lifestyle interventions to achieve weight loss are candidates for bariatric surgery without considering potential effects on future pregnancy, which are mixed. There are no randomised controlled trials for women planning pregnancy, but in a retrospective cohort study of insurance claims data (585 women)\(^8\) and two controlled registry studies (identifying 1085 women with prior bariatric surgery)\(^8\), women who had undergone bariatric surgery (vs. those who had not) experienced lower rates of all hypertensive disorders of pregnancy (including pre-eclampsia)\(^8\), gestational diabetes and large-for-gestational infants\(^8\), as well as fewer emergency Caesarean deliveries\(^8\) following adjustment for confounders. However, these benefits have not been consistently demonstrated, with one registry study demonstrating higher rates of hypertension and gestational diabetes following bariatric surgery\(^8\). In addition, potential benefits appear to come at the price of more gastrointestinal problems\(^8\), lower birth weight\(^8\), more small-for-gestational age (SGA) infants\(^8\), earlier delivery\(^8\) and, possibly, higher perinatal mortality\(^8,8\) and admission to NICU\(^8\). Therefore, at present, there are insufficient data to support recommendations to undergo bariatric surgery to favourably affect future pregnancy outcomes.

### BEST PRACTICE POINTS

(Please see Appendix 11.3 for the evaluation of the strength of the recommendations and the quality of the evidence on which they are based.)

**Care in the 6 weeks after birth**

1. Blood pressure should be measured during the time of peak postpartum blood pressure, at days 3–6 after delivery.
2. Women with postpartum hypertension should be evaluated for pre-eclampsia (either arising de novo or worsening from the antenatal period).
3. Antihypertensive therapy may be continued postpartum, particularly in women with antenatal pre-eclampsia and those who delivered preterm.
4. Severe postpartum hypertension must be treated with antihypertensive therapy, to keep systolic blood pressure <160 mmHg and diastolic blood pressure <110 mmHg.
5. Antihypertensive therapy may be used to treat non-severe postpartum hypertension, to keep blood pressure at <140/90 mmHg for all but women with pre-gestational diabetes mellitus among whom the target should be <130/80 mmHg.
The priorities for postpartum care of women with hypertensive disorders of pregnancy in under-resourced settings are outlined in Table 11.3. A sample policy brief that focuses on postnatal care is contained in Appendix 11.4.

In LMICs, routine postnatal care has the potential to improve both maternal and neonatal outcomes. In LMICs, almost 40% of women experience complications after delivery and an estimated 15% develop potentially life-threatening problems. More than half of maternal deaths occur postpartum and the vast majority (i.e., 80%) of those occur in the first week postpartum. Such visits are most likely to detect early complications that may be addressed by referral for specialist care.

Also, postnatal care has the potential to identify neonatal sepsis and asphyxia/hypothermia, the leading causes of neonatal death in LMICs. Finally, postnatal care helps to promote healthy maternal behaviours, such as exclusive breastfeeding and proper care of babies with low birth weight.

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**Care beyond the first 6 weeks after birth**

1. Women with a history of severe pre-eclampsia (particularly those who presented or delivered at <34 weeks) should be screened for pre-existing hypertension and underlying renal disease.
2. Referral for internal medicine or nephrology consultation should be considered for women with postpartum hypertension that is difficult to control, or women who had pre-eclampsia and have at 3–6 months postpartum ongoing proteinuria, decreased eGFR (<60 mL/min), or another indication of renal disease (such as abnormal urinary sediment).
3. Women who are overweight should be encouraged to attain a healthy body mass index to decrease risk in future and for long-term health.
4. Women with pre-existing hypertension or persistent postpartum hypertension should undergo the following investigations (if not done previously): urinalysis; serum sodium, potassium and creatinine; fasting glucose; fasting lipid profile; and standard 12-lead electrocardiography.
5. Women who are normotensive but who have had a hypertensive disorder of pregnancy, may benefit from assessment of traditional cardiovascular risk markers.
6. All women who have had a hypertensive disorder of pregnancy should pursue a healthy diet and lifestyle.

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**Priorities for Under-Resourced Settings**

The priorities for postpartum care of women with hypertensive disorders of pregnancy in under-resourced settings are outlined in Table 11.3. A sample policy brief that focuses on postnatal care is contained in Appendix 11.4.

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Antihypertensive agents acceptable for use in breastfeeding include nifedipine XL, labetalol, methyldopa, captopril and enalapril.

- There should be confirmation that end-organ dysfunction of pre-eclampsia has resolved.
- Non-steroidal anti-inflammatory drugs (NSAIDs) should not be given postpartum if hypertension is difficult to control, there is evidence of kidney injury (oliguria and/or an elevated creatinine) (≥90 μmol/L) or platelets are <50 × 10⁹/L.
- Postpartum thromboprophylaxis should be considered in women with pre-eclampsia who have other risk factors for thromboembolism.

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"By the 6th week the child is due for pentavalent. That is... the diphtheria, tetanus and all... at that 6 week [mark]. That is the time (when) the lady is also due for the 6 week postnatal review. But many a time the postnatal review is not done... because of lack of manpower at the PHC. You have a lot of children and... so sometimes to attend to mother, and educate and counsel takes time."

Stakeholder, Local Government in Ogun, Nigeria

Postnatal care is reported at much lower rates than for other maternal and infant health services. In a review of Demographic and Health Survey (DHS) data from 1990 to 2009 in 38 countries in four regions (i.e., sub-Saharan Africa; North Africa/West Asia/Europe; South/Southeast Asia; and Latin America and the Caribbean), approximately half of the countries with data (i.e., 8 of 18) provided at least one demonstrated postnatal visit to more than half (64–92%) of postpartum women within 41 days after giving birth. Even within those countries, postnatal visits varied from 64% to...
92% of relevant women. Although there was a strong relationship between receiving postnatal care and both more antenatal visits and having skilled birth attendance, the major determinant of postnatal care was delivery in facility. (A recent systematic review found that inequities in the use of postnatal services is also based on socioeconomic status, education, ethnicity and geographical location94.) Following delivery in facility, at least two-thirds of women reported postnatal care in all countries except Uganda and Zimbabwe where less than half of the women reported postnatal checkups. Women who delivered in a health facility (compared with those who did not) were more likely to report postnatal visits, to have the first visit within 2 days after birth, and to receive postnatal care from a doctor, nurse, or midwife. Among women who did not deliver at a health facility, postnatal care was reported for less than 50% with the exception of a few countries in South/Southeast Asia (i.e., Cambodia and the Philippines), sub-Saharan Africa (i.e., Ghana and Madagascar), and Latin America and the Caribbean (i.e., Bolivia, the Dominican Republic and Peru).

In recognition of the postnatal period as “. . . a critical phase in the lives of mothers and newborn babies”, the 2013 WHO guidelines on postnatal care95 recommend the following:

- A health care visit within 24 hours after the birth and then again at least three more times – on day 3, in the second week, and again at 6 weeks;
- Blood pressure measurement shortly after birth and at 6 hours, although there is no guidance around blood pressure measurement during the rest of the postpartum period;
- Counselling about the signs and symptoms of pre-eclampsia at each postpartum visit.

Global initiatives that address the link between a woman’s reproductive health and long-term health are lacking. To prevent non-communicable diseases in the offspring, the International Federation of Gynaecology and Obstetrics (FIGO) recently announced that it is partnering with other agencies and organisations that focus on enforcing interventions, such as good nutrition and minimisation of harmful environmental exposures during pregnancy97. While this initiative

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**Table 11.3** Priorities for postpartum care in under-resourced settings

<table>
<thead>
<tr>
<th></th>
<th>Initial priority</th>
<th>Ultimate goal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Community</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary health care centre (detect, stabilise and refer)</td>
<td>A health care visit within 24 hours after the birth and then again at least three more times – on day 3, in the second week, and again at 6 weeks</td>
<td>A health care visit within 24 hours after the birth and then again at least three more times – on day 3, in the second week, and again at 6 weeks</td>
</tr>
<tr>
<td></td>
<td>BP measurement shortly after birth and at 6 hours</td>
<td>BP measurement shortly after birth and at 6 hours</td>
</tr>
<tr>
<td></td>
<td>Counselling about the signs and symptoms of pre-eclampsia at each postpartum visit</td>
<td>Counselling about the signs and symptoms of pre-eclampsia at each postpartum visit</td>
</tr>
<tr>
<td><strong>Facility</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary-level facility (detect, manage and refer if necessary)</td>
<td>Delivery in facility of all women with a HDP Management of women with HDPs, including postpartum pre-eclampsia (see Table 4.4, Chapter 4)</td>
<td>Delivery in facility of all women with a HDP Management of women with HDPs, including postpartum pre-eclampsia (see Table 4.4, Chapter 4)</td>
</tr>
<tr>
<td>Tertiary-level (referral) facility (detect and manage definitively)</td>
<td>Counselling about BP monitoring as well as heart-healthy diet and lifestyle following a HDP</td>
<td>Counselling about BP monitoring as well as heart-healthy diet and lifestyle following a HDP</td>
</tr>
</tbody>
</table>

BP, blood pressure; HDP, hypertensive disorder of pregnancy
acknowledges the role of non-communicable diseases within the reproductive, maternal, neonatal and child health continuum, it does not address the long-term chronic illnesses that may develop as a result of a complicated pregnancy.

WHAT INTERNATIONAL GUIDELINES SAY (APPENDIX 11.5)


Most international guidelines highlighted that pre-eclampsia may develop de novo or worsen in the postpartum period (AOM, ACOG, NICE, SOGC, QLD).

The majority of guidelines stated that blood pressure may increase postpartum and recommended continuing antihypertensive therapy that women had been taking antepartum (NICE, ACOG, SOGC). Importantly, no guideline recommended that antenatal antihypertensive therapy be stopped. Although the treatment of severe hypertension followed similar recommendations to those antenatally, treatment targets for non-severe hypertension were generally lower and varied amongst guidelines (NICE, SOGC, ACOG). Most commonly, clinicians are recommended to aim for a blood pressure <150/100 mmHg for women with gestational hypertension or pre-eclampsia (NICE, ACOG).

Most of the guidelines specifically mentioned the association between the hypertensive disorders of pregnancy (particularly pre-eclampsia) and future cardiovascular health, and suggested lifestyle counselling as the logical response (AOM, ACOG, NICE, SOGC, QLD, SOMANZ).

SUMMARY

Care in the immediate postpartum period should focus on the management of hypertension using treatment options that are acceptable during breastfeeding. Consideration should be given to postpartum thromboprophylaxis in women with a hypertensive disorder of pregnancy if other risk factors are present. NSAIDs should be avoided if hypertension is difficult to control or there is either a coagulopathy or renal dysfunction. All women with pre-eclampsia should be followed closely after delivery to ensure resolution of end-organ damage. Women should be screened for underlying disease that may have predisposed to pre-eclampsia and pre-eclampsia mimickers should also be ruled out. Finally, the postpartum period offers a unique window of opportunity to address short- and long-term risks of hypertensive disorders of pregnancy. Women should be counselled about the ideal inter-pregnancy interval as well as risks in future pregnancies. Women should be evaluated for risk factors for premature cardiovascular disease as well as other complications such as chronic kidney disease. Currently, the focus should be on the adoption of a heart-healthy lifestyle and screening for traditional cardiovascular risk factors.

PRIORITIES FOR FUTURE RESEARCH

Given the global rise in non-communicable diseases and the risk stratification that pregnancy appears to provide, there is an urgent need to identify how a woman’s pregnancy history can be added to currently available cardiovascular disease risk scoring systems to identify and manage women at increased risk for cardiovascular disease.

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