A review of maternal overweight and obesity and its impact on cardiometabolic outcomes during pregnancy and postpartum

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Abstract: The rates of maternal overweight and obesity, but also excess gestational weight gain, are increasing. Pregnancy complications, including gestational diabetes mellitus, gestational hypertension, pre-eclampsia and delivery of a preterm or growth restricted baby, are higher for both women with overweight and obesity and women who gain excess weight during their pregnancy. Other conditions such as polycystic ovary syndrome are also strongly linked to overweight and obesity and worsened pregnancy complications. All of these conditions place women at increased risk for future cardiometabolic diseases. If overweight and obesity, but also excess gestational weight gain, can be reduced in women of reproductive age, then multiple comorbidities associated with pregnancy complications may also be reduced in the years after childbirth. This narrative review highlights the association between maternal overweight and obesity and gestational weight gain, with gestational diabetes, pre-eclampsia, polycystic ovary syndrome and delivery of a preterm or growth restricted baby. This review also addresses how these adverse conditions are linked to cardiometabolic diseases after birth. We report that while the independent associations between obesity and gestational weight gain are evident across many of the adverse conditions assessed, whether body mass index or gestational weight gain is a stronger driving factor for many of these is currently unclear. Mechanisms linking gestational diabetes mellitus, gestational hypertension, pre-eclampsia, preterm delivery and polycystic ovary syndrome to heightened risk for cardiometabolic diseases are multifactorial but relate to cardiovascular and inflammatory pathways that are also found in overweight and obesity. The need for post-partum cardiovascular risk assessment and follow-up care remains overlooked. Such early detection and intervention for women with pregnancy-related complications will significantly attenuate risk for cardiovascular disease.

Keywords: cardiometabolic, cardiovascular disease, gestational weight gain, obesity, polycystic ovary syndrome, pregnancy, risk factors

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Introduction

Obesity is a significant public health concern. Globally, there is a trend of increasing body mass index (BMI) in both adults and children, with obesity rates tripling since 1975.[1] Obesity is one of the leading risk factors for premature death related to cardiovascular disease (CVD), type 2 diabetes, cancer and poor mental health, and accounted for 4.7 million deaths globally in 2017.[2] The World Health Organization reported that 39% of adults aged 18 years and above had overweight in 2016, and 13% had obesity.[3] The rise in obesity prevalence has been most prominent in women of reproductive age (post-adolescent and pre-menopausal),[4] with women tending to gain 0.5–1 kg each year from early adulthood until

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middle age.[5] Critically, it appears that even young women are at risk of unhealthy weight gain as they approach child-bearing years.[6] This has significant impacts on reproductive health in women as they enter pregnancy at a higher BMI.

Women with obesity take a longer time to conceive,[7] and women with a BMI ⩾40 kg/m^2 have a near 7-fold higher risk for taking more than 12 months to conceive than those with a normal BMI.[8] Pregnancy complications, including gestational diabetes mellitus (GDM), gestational hypertension and pre-eclampsia, are also higher for women with overweight or obesity.[9,10] In addition, meta-analyses report that having overweight or obesity during pregnancy is associated with preterm birth, with different effects depending on BMI category and preterm birth subtype.[11] Polycystic ovary syndrome (PCOS)[12] is closely linked with obesity and cardiometabolic risk factors, and also amplifies the risk of GDM and gestational hypertension.[13] All of these outcomes place women at heightened risk for developing type 2 diabetes and related cardiometabolic conditions.[14–16] The long-term consequences of obesity have been reported in studies relating to the developmental origins of health and disease[17,18] with both Caucasian and minority ethnic groups having risk factors early tracking into adulthood which predict adult disease risks.[19] Reducing overweight and obesity in reproductive-aged women could improve a broad spectrum of complications in pregnancy and also in the years after childbirth.

In addition to overweight and obesity prior to and during pregnancy, the amount of weight that women gain during pregnancy [gestational weight gain (GWG)] is important for optimal maternal and child outcomes. Women with obesity prior to pregnancy are more likely to have excessive GWG compared with normal weight women.[20] However, excess GWG is an independent risk factor for a number of pregnancy complications,[21] thereby also placing women at increased risk for future cardiometabolic conditions.

To our knowledge, there has been no review examining how cardiometabolic diseases are related to pregnancy complications as a consequence of maternal overweight and obesity and GWG. This narrative review highlights the association between maternal overweight and obesity and GWG, with GDM, pre-eclampsia, PCOS and delivery of a preterm or growth restricted baby. This review also addresses how these adverse conditions are linked to cardiometabolic diseases after birth.

Table 1. Recommendations for gestational weight gain in singleton pregnancies.[a]

Preconception body mass index categories		Total gestational weight gain
Underweight	<18.5 kg/m^2	12.5–18 kg
Normal	18.5–24.9 kg/m^2	11.5–16 kg
Overweight	25–29.9 kg/m^2	7–11.5 kg
Obese	⩾30 kg/m^2	5–9 kg

[a]Adapted from the Institute of Medicine Guidelines (2009).[20]

Obesity and GWG in pregnancy

Globally, the estimated number of pregnant women with overweight or obesity in 2014 was 8.9 and 14.6 million, respectively.[22] Country-specific data indicate that 25.6% of women giving birth in Australia in 2017 had overweight and 20% had obesity,[23] 32% of Swedish pregnant women had overweight or obesity in 2008–2010,[24] 25% and 10% had overweight or obesity in Scotland,[25] and in Africa, maternal obesity has ranged from as low as 6.5% up to as high as 50.7%.[26]

The Institute of Medicine (IOM) has developed universally endorsed recommendations in the general population for GWG based on women's preconception BMI (Table 1).[20] Despite Asian women having different risk profiles in pregnancy,[27] there are no specific GWG guidelines for women from Asia. The weight gained during pregnancy is primarily due to the weight of the developing foetus and to increases in maternal body water and fat. GWG has also increased in addition to an increase in obesity,[28] and women with obesity prior to pregnancy are more likely to have excessive GWG compared with women in the normal weight range.[20] Using 2010–2011 data from Pregnancy Risk Assessment Monitoring System, 47.2% of women had excessive GWG, with around two-thirds of women with overweight or obesity class I (BMI = 30–34.9 kg/m^2) having the highest prevalence of excessive GWG.[29]

However, between 20% and 40% of women with a normal or underweight BMI also had excessive GWG.[29] Furthermore, in a population cohort study among women from Sweden, those gaining the most weight in pregnancy (⩾1.50 SD, i.e. ⩾15.9 kg in underweight women) were more likely to have a BMI in the underweight category.[30] Concerningly, excessive GWG is related to post-partum weight retention and has implications for future pregnancies which are influenced by BMI in the index pregnancy. In a meta-analysis of observational studies, a BMI gain ⩾3 kg/m^2 between pregnancies was associated with a 2-fold higher risk for GDM, pre-eclampsia and gestational hypertension.[31] This highlights that weight management is important for women of all BMI categories planning a pregnancy as they all may be susceptible to excess GWG.

Risks associated with obesity and GWG in pregnancy

The impact of obesity in pregnancy has been studied for decades, demonstrating both immediate and long-term adverse consequences for the mother and child.[32] A meta-analysis demonstrated women with overweight or obesity had an approximate 2-fold increased risk of spontaneous miscarriage [odds ratio (OR) = 1.67, 95% confidence interval (CI) = 1.25, 2.25],[33] and in a systematic review of reviews, there was a 2-fold increased risk of stillbirth among women in the highest BMI category [relative risk (RR) = 2.19; 95% CI = 2.03, 2.36] compared with women with a normal BMI.[34] There is consistent evidence that overweight or obesity in pregnancy increases the risk for pre-eclampsia,[35] GDM[34,36] and preterm birth.[37] Recent reviews have also demonstrated the impact of maternal pre-pregnancy overweight or obesity on offspring outcomes, contributing to increased infant birthweight (macrosomia and large for gestational age) and higher BMI in adolescent offspring.[38,39]

Similar adverse outcomes to obesity also occur with excess, and even inadequate, GWG. In a meta-analysis of more than 1 million women, GWG below guidelines was associated with a higher risk of small for gestational age (SGA) [USA/Europe (OR = 1.51; 95% CI = 1.39, 1.63), Asia (OR = 1.63; 95% CI = 1.45, 1.82)] and preterm birth [USA/Europe (OR = 1.35; 95% CI = 1.17, 1.56), Asia (OR = 1.06; 95% CI = 0.78, 1.44)], and GWG above guidelines was associated with a higher risk of large for gestational age (LGA) [USA/Europe (OR = 1.93; 1.81–2.06), Asia (OR = 1.68; 95% CI = 1.51, 1.87)] and macrosomia [USA/Europe (OR = 1.87; 95% CI = 1.70, 2.06), Asia (OR = 2.18; 95% CI = 1.91, 2.49)].[40] Key to this review is the comparison of Asian studies applying regional BMI categories compared with the World *Health Organization (WHO)* BMI categories. The analysis showed that across all pre-pregnancy BMI categories and in different ethnicities, insufficient GWG was associated with increased risk of SGA and preterm birth, whereas excess GWG was associated with increased risk of LGA, macrosomia and caesarean section. In a meta-analysis of 13 studies, women who had GWG above the IOM were more likely to have hypertensive disorders of pregnancy (HDP; OR = 1.82; 95% CI = 1.53, 2.17), pre-eclampsia (OR = 1.92; 95% CI = 1.36, 2.72) or gestational hypertension (OR = 1.67; 95% CI = 1.43, 1.95).[41]

The independent or combined effect of BMI and GWG on pregnancy outcome

The impact of overweight and obesity and excess GWG on maternal and neonatal outcomes can be difficult to disentangle when risks for various outcomes are comparable. Using data from 196,670 participants within 25 cohort studies, the absolute risk for any adverse outcome, that is, the presence of 1 or more of pre-eclampsia, gestational hypertension, GDM, caesarean delivery, preterm birth, SGA or LGA increased across pre-pregnancy BMI, which was largely independent of GWG.[42] That is, the lowest absolute risks were found for women who had a low to normal BMI ⩽25 kg/m^2, with a moderate to high GWG, whereas higher absolute risks were found for women with a BMI ⩾30 kg/m^2 and high GWG.[42] This meta-analysis, however, did not assess pregnancy outcomes separately, and all outcomes were treated equally; thus, the independent or combined effect of BMI and GWG cannot be established for individual outcomes.

In a meta-analysis of 8 studies (n = 13,748 participants) which authors generally reported as medium quality, the effect of GWG on GDM did not differ depending on maternal pre-pregnancy BMI category.[43] In a meta-analysis of individual participant data, diet and lifestyle interventions to reduce GWG demonstrated a reduction in GDM

of 24% (OR = 0.76; 95% CI = 0.65, 0.89) and caesarean section by 9%.[44] Moreover, the effect was observed irrespective of maternal BMI.[44] Consistent evidence for an independent effect of GWG is apparent for HDP. In a meta-analysis of 21 studies, the increased odds of HDP were greatest among women with overweight and obesity pre-pregnancy, and gained weight in excess of the IOM guidelines (OR = 2.17; 95% CI = 1.56, 3.02).[41] The effect of pre-pregnancy BMI and GWG on preterm birth is unclear, and risk may be different depending on the population studied and type of preterm birth. In a multicentre study in Brazil (n = 3273 preterm birth, n = 920 term births), insufficient GWG, regardless of the initial BMI, increased risk for spontaneous preterm birth by 76% (OR = 1.76; 95% CI = 1.34, 2.31) and also excess GWG increased risk for preterm birth in women with overweight (OR = 1.43; 95% CI = 1.16, 1.77) and obesity (OR = 1.76; 95% CI = 1.37, 2.26).[45] In a retrospective cohort study in Peru (n = 8964), there was an independent association between GWG and preterm birth, with a protective effect seen for underweight women (OR = 0.91; 95% CI = 0.82, 1.00).[46]

Despite both BMI and GWG being independent risk factors for a range of pregnancy outcomes, further high-quality research is needed on their independent and additive effects.

Management of overweight and obesity in pregnancy

Standard guidelines for lifestyle management as a component of antenatal care involve advice relating to eating the recommended number of daily serves of the five food groups,[47] drinking plenty of water, and advice that low- to moderate-intensity physical activity during pregnancy is associated with a range of health benefits and is not associated with adverse outcomes.[48] In addition to this, health professionals should also offer appropriate advice relating to folic acid supplementation, food hygiene, including how to reduce the risk of a food-acquired infection and advice relating to smoking cessation, and the implications of recreational drug use and alcohol consumption in pregnancy.[49] Guidelines also highlight offering women the opportunity to be weighed and to give women advice about appropriate weight gain during pregnancy in relation to either their pre-pregnancy BMI if recorded or their BMI at the first antenatal visit. At every antenatal visit, health professionals should encourage self-monitoring of weight gain and discuss weight gain, diet and level of physical activity with all women.[48]

During pregnancy, women with overweight or obesity may require additional monitoring of foetal growth, GDM, HDP, neural tube defects and potential complications during birth, including anaesthetic risk. They may also need a referral to an accredited dietitian.[48] Women are recommended to gain less weight over the course of their pregnancy, specifically 7–11.5 kg for women with overweight and 5–9 kg for women with obesity (Table 1).[20] Antenatal lifestyle (diet and physical activity) interventions are recommended to achieve this and resulted in significantly less GWG compared with control (−0.70 kg; 95% CI = −0.92, −0.48) and reduced the odds of caesarean section (0.91 kg; 95% CI = 0.83, 0.99).[44] To achieve this in clinical practice, interventions also need to move beyond monitoring and provision of advice. These should practically support women in achieving lifestyle changes and include health professional training and embedding in the workforce with further implementation research warranted in this field. With regard to specific physical activity advice, women should be informed that moderate physical activity during pregnancy has a range of health benefits, particularly for women with overweight or obesity. With regard to specific dietary recommendations, women should be advised limiting additional serves and avoiding energy-dense foods to limit excessive weight gain.[48,50] Folic acid supplementation is also recommended to be increased from 500 µg/day to 5 mg/day for women with a BMI $>30\ kg/m^2$.[51] The International Federation of Gynecology and Obstetrics' (FIGO) Pregnancy and Non-Communicable Diseases (PNCD) Committee has also recently emphasised that management of obesity in pregnancy should be considered in the context of a life course approach, linking with preconception and post-partum and interconception services to prevent excess weight gain before and during pregnancy.[52] Advice on GWG, particularly for women with an obese BMI is also highlighted in the FIGO guideline for the management of pre-pregnancy, pregnancy and post-partum obesity.[53]

It must also be acknowledged that there are a wide variety of individual and environmental factors affecting food and physical activity choices. Current guidelines[54] for optimising lifestyle

recognise this complex relationship which can be understood through models such as the Social-Ecological Model encompassing social and cultural norms and values, sectors (systems, organisation, and business and industries), settings and individual factors.[55] They highlight that support and active engagement from a range of sectors of society are required to both optimise individual diet and physical activity and achieve improvements in population health.

Adverse conditions during pregnancy and their relationship to cardiometabolic diseases

Polycystic ovary syndrome

PCOS is a common endocrinopathy, affecting 13% of reproductive-aged women.[56] It is characterised by irregular menstrual cycles, clinical/biochemical hyperandrogenism and polycystic ovaries on ultrasound.[57] PCOS is associated with increased risk of metabolic (including type 2 diabetes, hypertension, dyslipidaemia and thrombosis), reproductive (including anovulatory infertility and pregnancy complications) and psychological (including anxiety, depression and poor quality of life) disorders.[58,59] Overweight or obesity is present in up to 88% of women with PCOS, with insulin resistance as a key pathophysiological factor influencing clinical outcomes in PCOS.[60] Women with PCOS and overweight and obesity usually present with a more severe phenotype of the condition.[61]

The higher BMI commonly observed in women with PCOS extends into their pregnancies with women with PCOS having a higher BMI around conception [standard mean difference (SMD) = 0.63 kg/m^2; 95% CI = 0.42, 0.84] and a higher GWG (SMD = 0.26 kg/m^2; 95% CI = 0.03, 0.50), compared with women without PCOS.[13] It is not clear if this higher GWG in PCOS is clinically significant.[62] Furthermore, ongoing pregnancies in PCOS are more likely to be complicated with GDM, gestational hypertension and pre-eclampsia.[13,63–66] The adverse maternal outcomes are worsened by, but occur independent of, obesity in PCOS, evidenced by the risks in women with and without PCOS when comparing the outcomes in women with a BMI >30 kg/m^2 around conception.[13] With regard to infant complications, infants born to women with PCOS are up to 2 times more likely to be born premature, LGA, and require intensive neonatal care at birth.[64,66] The main risk factors for adverse infant outcomes in PCOS are not known. However, these could be secondary to the higher rate of maternal pregnancy complications, particularly as the higher preterm and LGA births in PCOS are probably explained by maternal BMI at conception[67] with similar risk for infant outcomes observed in women with and without PCOS with obesity.[13] The driving factor could potentially be insulin resistance, which fades away in those with obesity.[68] There is relatively limited research assessing GWG in PCOS and the impact of GWG on adverse pregnancy outcomes in PCOS is still unclear.[62] However, it may contribute to higher BMI and longitudinal weight gain, higher type 2 diabetes and cardiovascular risk factors, post-pregnancy, in women with PCOS.[69–71]

Lifestyle and management. The first-line treatment in women with PCOS is lifestyle management.[72,73] A 5–10% weight loss in PCOS can improve presentations, including infertility. Given that infertility is an independent risk factor for pregnancy complications, where women with PCOS lose weight preconception they may have a higher likelihood of spontaneous conception and a lower BMI at conception which would offer further benefits for reducing the risk of pregnancy complications.[74] Lifestyle and weight management in PCOS should be as per the recommendations for the general population for a healthy balanced diet and optimal levels of physical activity and sedentary time.[72] This should involve a multidisciplinary support with inclusion of allied health professionals such as dietitians, exercise physiologists and psychologists where required.[72] Given the higher risk profile for pregnancy complications in PCOS, additional risk factors for pregnancy complications including smoking, alcohol consumption and high caffeine intake should be particularly focused on preconception and during pregnancy.[61] After conception, women with PCOS should be advised to monitor their GWG and aim for a healthy GWG.[62] Given that there is no GWG guidelines specific to PCOS, women with PCOS should follow the IOM guidelines[20] and follow the recommendations for the general population with a healthy balanced diet,[75] and exercise and physical activity.[75,76]

PCOS and future cardiometabolic diseases. Women with PCOS have a 2- to 3-fold elevated prevalence of *type 2 diabetes* and

risk factors for CVD including hypertension, thromboembolism and dyslipidaemia compared with women without PCOS.[58,59] Despite this, there is inconclusive evidence as to whether PCOS independently increases the risk of clinical CVD events.[77] Insulin resistance is a characteristic feature of PCOS presenting in 75% of lean and 95% of women with overweight or obesity,[59] which worsens the reproductive, metabolic and psychological presentations. Excess weight further exacerbates insulin resistance and the features of PCOS, including cardiometabolic risk.[78] Women with PCOS also have higher longitudinal weight gain[71] and prevalence of overweight/obesity.[60] Given the consistent associations with cardiovascular risk factors in women with PCOS, and potential links to future cardiometabolic diseases, it highlights the need for interventions for improving risk factors in PCOS.

Gestational diabetes mellitus

GDM is defined as 'any degree of glucose intolerance with onset or first recognition during pregnancy'.[79] It is one of the most common metabolic complications in pregnancy, affecting 5–25% of all pregnant women worldwide, depending on screening approaches (universal or targeted) and diagnostic criteria.[80] The intergenerational cycle of diabetes and obesity, that is, the association between maternal diabetes, GDM and maternal obesity with increased risk of diabetes and obesity in the offspring, has been neatly articulated in a review by Ma and Popkin.[81]

Both obesity and GWG have also demonstrated independent effects on babies born large for gestational age. In a retrospective analyses of 9,835 women, in those without GDM, 21.6% of infants born LGA were attributable to maternal overweight and obesity; with the combination of having overweight or obesity *and* having GDM, accounting for a similar 23.3%, of infants born LGA.[82] Similarly, in a cohort of 9,270 Spanish women with or without obesity and in women with and without GDM, had significantly higher odds of having an infant born LGA than those of normal weight.[83] In a recent Australian study, almost one-quarter of all macrosomia was attributable to overweight and obesity.[84] Encouragingly, it was estimated that 15.9% of macrosomia could be prevented if women with overweight or obesity were to move down one BMI category over a 4-year period.[84] While diet and physical activity interventions aimed at reducing GWG can reduce the incidence of GDM compared with standard care, the effects vary by BMI.[85] This highlights the importance of future studies addressing BMI and GWG to reduce GDM and potential offspring outcomes.

The relationship between obesity, GDM and related adverse pregnancy outcomes is complex and is modified by ethnicity. In a population-based, cross-sectional study among 5,562 women, compared with non-Hispanic white women, Asian women had a 2-fold higher likelihood for GDM (OR = 2.44; 95% CI = 1.81, 3.29).[86] Ethnic minority origin was also an independent predictor for GDM in South Asians [OR = 2.24 (95% CI = 1.26, 3.97)] and Middle Eastern women [OR = 2.13 (95% CI = 1.12, 4.08)], after adjusting for age, pre-pregnancy BMI and parity.[87] Ethnicity may be a blunt but implementable surrogate marker for specific physiologic glucometabolic profiles accounting for different clinical phenotypes. Although important, ethnicity cannot be considered in isolation because translation into a system-based approach should recognise the important independent effects of cultural and linguistic identity especially where lifestyle-based interventions are predominant.

Lifestyle and management. Treatment of GDM is directed at reducing blood glucose levels to near normal levels. Target blood glucose levels vary based on how institutional and/or national clinical practice guidelines have operationalised evidence from two interventional trials, where a combination of lifestyle measures and insulin treatment reduced adverse pregnancy outcomes in women with mild hyperglycaemia consistent with contemporary diagnostic criteria.[88,89] Lifestyle-based interventions are the foundation of treatment[90,91] and are effective at adequately controlling blood glucose levels during pregnancy for the majority of women.[88,89] Where blood glucose levels are inadequately controlled with lifestyle measures alone, pharmacologic therapy is instituted. Pharmacologic therapy most commonly consists of metformin and/or insulin, with preference varying internationally.[90,91] It is evident that lifestyle management for GDM rarely focuses on healthy GWG which may prove a useful strategy in future intervention studies.

Gestational diabetes and future cardiometabolic diseases. GDM is associated with a number of longer term health complications to mother and offspring beyond the immediate risks to pregnancy. In women with a history of GDM, the risk of recurrent GDM is about 30–84%.[92] This is not surprising as GDM and type 2 diabetes both sit on the same continuous spectrum of glucose abnormality, albeit the former a milder state of impairment which is unmasked by a surge in placental hormones required to support glucose transfer to the foetus and promote insulin resistance. Therefore, at completion of pregnancy with the rapid dissipation of placental hormones, GDM rapidly resolves. In a prospective cohort study with up to 18 years of follow-up, baseline BMI (i.e. within 2 years of GDM diagnosis), most recent BMI and weight gain after GDM were significantly and positively associated with risk of progression from GDM to type 2 diabetes, suggesting the need for managing weight at onset of GDM and post-partum, to reduce risk for type 2 diabetes.

In the longer term, GDM is a well-established risk factor for future cardiovascular events mediated by an increased risk of type 2 diabetes, metabolic syndrome, hyperlipidaemia, atherosclerosis and obesity.[93–95] Impaired glucose tolerance or upper normal glycaemic level in the normoglycaemic obstetric population, termed 'maternal dysglycaemia', is an increasingly recognised risk factor for future cardiovascular risk, with an estimated 13% increase in risk for every 1 mmol/L increment in blood glucose.[96] This highlights the importance of antenatal glucose screening and interval monitoring with early identification of future cardiovascular risk.

Hypertensive disorders of pregnancy

HDP are classified into two main groups: first, hypertension known prior to pregnancy or presenting during the first 20 weeks, which includes chronic hypertension, white coat hypertension and masked hypertension; and second, hypertension arising at or after 20 weeks, which includes transient gestational hypertension, gestational hypertension and pre-eclampsia.[97] Chronic hypertension is the most prevalent HDP, with 14% of women experiencing during pregnancy; a further 2–5% of pregnancies are affected by gestational hypertension or pre-eclampsia.[97] The prevalence of HDP has increased rapidly over the past 10 years, potentially due to corresponding increases in overweight, obesity, diabetes and advanced maternal age.[97]

Overweight and obesity are identified as strong clinical risk factors for pre-eclampsia. A pre-pregnancy BMI of >25 and >30 kg/m^2 has been demonstrated in meta-analysis to be associated with an increased risk of pre-eclampsia (overweight RR = 2.1, 95% CI = 2.0, 2.2; obesity RR = 2.8, 95% CI = 2.6, 3.1).[98] Guidelines from the International Society for the Study of Hypertension in Pregnancy (ISSHP) indicate that while there is no test available during the first or second trimester of pregnancy to accurately predict pre-eclampsia, all women should be screened during the first trimester for risk factors known to be strongly associated with pre-eclampsia.[97] Risk factors include maternal BMI >30 kg/m^2, history of pre-eclampsia, chronic hypertension, pre-gestational diabetes, antiphospholipid syndrome and assisted reproduction pregnancies.[97] Women identified as having clinical risk factors for pre-eclampsia, including obesity, are recommended to be treated with aspirin (75–165 mg/day) before 16 weeks' gestation as an intervention to prevent pre-eclampsia.[97]

Lifestyle and management. A 2019 systematic review of 23 randomised controlled trials explored the efficacy of diet and/or exercise interventions among pregnant women with overweight or obesity, as a strategy to prevent pre-eclampsia.[99] The review identified that despite achieving significantly lower weight gain in the intervention groups, there was no significant difference in the risk of pre-eclampsia between groups (diet and/or exercise *versus* usual/expectant care). These results are consistent with other systematic reviews of antenatal weight management interventions, which also found no impact on pre-eclampsia incidence.[100] Therefore, further research is required to explore the role of weight management pre-pregnancy, inter-pregnancy and during pregnancy on the occurrence of HDP, particularly among women with a previous hypertensive pregnancy.

HDP and future cardiometabolic diseases. A diagnosis of HDP has a significant impact on maternal CVD risk, with an 8-fold risk of developing cardiovascular risk factors and up to 5-fold risk of

premature CVD.[101–103] Although the exact mechanisms remain unclear, an interplay between pre-pregnancy predisposition and the cardiometabolic effects of HDP has been proposed.[102,104] The occurrence of endothelial dysfunction leading to accelerated atherogenesis is a common theory.[105] The prevalence and onset of cardiovascular risk factors among women appear to correlate with both the severity of HDP and the presence of other pregnancy-related complications such as SGA births and preterm delivery.[102] Following recurrent pre-eclampsia (i.e. women with a history of pre-eclampsia in a previous pregnancy), risk for ischaemic heart disease (RR = 2.40; 95% CI = 2.15, 2.68) and cerebrovascular disease (RR = 1.69; 95% CI = 1.21, 2.35) is higher compared with women with an uncomplicated pregnancy.[106]

There is emerging evidence of the contribution of overweight and obesity post-pregnancy to the higher risk of cardiovascular risk factors among women following HDP. Analysis of the Nurses' Health Study II cohort study (n = 54,588),[107] and the 45 and Up cohort study (n = 71,819)[108] both found that a history of HDP and a higher BMI following pregnancy were associated with the greatest risk of chronic hypertension. However, research in this area is in its infancy, and further research is needed to examine the contribution of overweight and obesity, and associated risk factors (e.g. poor diet, physical inactivity) on the cardiovascular health of women following HDP.

Preterm birth

Preterm birth is a heterogeneous condition with multiple attributable factors such as systemic inflammation, infection or vascular diseases.[109,110] While maternal BMI and increased GWG has been associated with delivery of a preterm baby,[11,21,40] other studies have also reported a protective effect of obesity.[111]

Women with previous preterm deliveries have a higher burden of atherogenesis, atherogenic lipid accumulation and carotid intima-media thickness detected in later life.[112] Thus, dysregulation in cardiometabolic factors may be a common pathway partly explaining the potential relationship between preterm birth and future CVD. This may be driven, in part, by a higher incidence of postpartum hypertension, hypercholesterolaemia, type 2 diabetes mellitus and elevated BMI in women with preterm delivery.[113]

Over the last 20 years, increasing evidence highlights that preterm delivery poses an increased risk of future maternal cardiovascular health. Most notably, a recent meta-analysis included 21 studies with over 5.8 million women, with more than 338,000 women with previous preterm deliveries.[114] Preterm birth was associated with an increased risk of a range of CVD outcomes by up to 2-fold, including maternal future CVD (RR = 1.43; 95% CI = 1.18, 1.72), death from CVD (RR = 1.78; 95% CI = 1.42, 2.21), coronary heart disease (RR = 1.49, 95% CI = 1.38, 1.60), death from coronary heart disease (RR = 2.10; 95% CI = 1.87, 2.36) and stroke (RR = 1.65; 95% CI = 1.51, 1.79).[114] This highlights clear and consistent associations between preterm delivery and increased risk for future maternal adverse cardiovascular outcomes. Although the authors discussed that follow-up guidelines recommend the consideration of preterm delivery in CVD prevention, it was also recommended that a detailed evaluation of a screening programme for CVD in women with a history of preterm birth should be conducted.[114]

Lifestyle and management. Lifestyle factors have important implications for both women's reproductive health and cardiovascular outcomes. The adverse cardiovascular effects of smoking, alcohol, recreational substance use, sedentary lifestyle and obesity also increase the risk of low birthweight and preterm birth.[115] Conversely, moderate exercise has been associated with reduced preterm birth and more favourable pregnancy and cardiovascular outcomes, particularly in women with raised BMI.[116–118]

Foetal growth restriction

Foetal growth restriction occurs when a foetus does not grow according to its genetic growth potential. Most commonly, SGA is defined as a birthweight below the 10th percentile for gestational age on the normative population growth curve and intrauterine growth restriction with birthweight less than 5th percentile. Maternal obesity is associated with SGA and intrauterine growth restriction (IUGR),[119] and both maternal obesity[120] and growth restriction are associated with placental insufficiency. This occurs when the placenta cannot deliver an adequate

supply of nutrients and oxygen to the foetus which can lead to foetuses with structural and functional cardiovascular changes which can persist through infancy, childhood and adolescence.[121] An infant born growth restricted has increased blood pressure, arterial stiffness and aortic intima-media thickness, a marker of preclinical atherosclerosis.[122]

Women who delivered an SGA infant are at an approximately 2-fold greater risk for developing future CVD,[123,124] with risk increasing with severity of growth restriction.[123] Women who gave birth to a moderate or very SGA infant (i.e. less than 1–2 standard deviations below the mean based on Swedish reference curves) and who was also born at less than 31 weeks' gestation had up to 4-fold increased risk for CVD.[123] One major causal factor behind preterm birth and growth restriction is maternal pre-eclampsia.[125] As highlighted earlier, women who had pre-eclampsia are at higher risk for future CVD. Pre-eclampsia and related HDP may be a driving factor in the relationship between foetal growth restriction and CVD. Further studies assessing these relationships are warranted, along with mechanisms linking maternal risk for future CVD following delivery of a growth restricted baby.

Lifestyle and management. Maternal energy and protein deficiency are associated with foetal growth restriction; however, dietary intervention studies have been inconsistent in terms of increasing birthweight.[119,126] While other lifestyle factors such as smoking[127,128] and maternal BMI also increase the risk for growth restriction, there are currently no specific diet and lifestyle guidelines aimed at preventing foetal growth restriction. Given the links between maternal obesity, pre-eclampsia and growth restriction, similar management strategies may also support appropriate foetal growth.

Post-partum follow-up care

Clinically, post-partum follow-up care for GDM is based around managing the risks of recurrent GDM and progression to cardiometabolic disease, that is, type 2 diabetes and CVD, predominantly through lifestyle measures. These include dietary interventions focused around caloric restriction, physical activity, sleep optimisation, stress management and the tackling contributory factors such as low mood and identification and treatment of a range of medical causes of obesity. Numerous recommendations suggest a follow-up of glycaemic status after pregnancy, using WHO criteria for the diagnosis of diabetes 6 weeks to 3 months post-partum,[129,130] with additional follow-up every 1–3 years.[91] Adherence to a follow-up programme after GDM is typically low.[131–133]

For HDP, many clinical guidelines recognise HDP as a primary risk factor specifically for CVD, to be considered as part of follow-up care.[134] A recent review of clinical guidelines, however, acknowledged there is currently no international consensus for post-partum follow-up care after its diagnosis. This includes consensus for the role of different health professionals, along with the timing, duration or focus of care. One of the more detailed guidelines is that of the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ).[135] The SOMANZ guidelines recommend counselling women with a history of HDP regarding lifestyle risk factors (i.e. excess body weight, physical inactivity, poor diet and smoking), along with monitoring blood pressure annually, and serum lipids and blood glucose at least every 5 years as a CVD preventive strategy. The SOMANZ guidelines also acknowledge the need to provide advice to women following HDP (>6 weeks post-partum) about optimising risk factors, such as obesity, prior to subsequent pregnancies.

There is evidence to suggest, however, that follow-up care consistent with clinical guidelines is not routinely being provided. For example, a survey of 127 Australian women, aged ⩾18 years with recent (⩽2 years) pre-eclampsia, found 34% were unaware of their increased risk of CVD, and while 95% reported monitoring of their blood pressure, less than half (41%) reported monitoring of their cholesterol and/or glucose, and <25% had received advice/counselling on lifestyle risk factors.[136] Notably, a 2019 systematic review of post-partum interventions to reduce long-term CVD risk in women after HDP located only two published randomized controlled trials evaluating such interventions.[137] They acknowledged the paucity of intervention trials and concluded research is urgently required to determine the best method of CVD risk reduction following HDP. Additional trials are currently underway that may provide further guidance on the efficacy and implementation of post-partum follow-up care for CVD prevention.[138]

There is no literature assessing lifestyle or post-partum follow-up care for women with preterm birth or growth restriction. Further work in this area is needed to identify and initiate risk-reduction strategies for future cardiovascular risk.

Conclusion

Obesity is a clear contributor to a range of pregnancy complications, including GDM, HDP and delivery of a preterm or growth restricted baby, but also to PCOS as an adverse condition, which is itself associated with worsened pregnancy outcomes. GWG also contributes to a range of pregnancy complications; however, further studies investigating which is a stronger driving factor will help tailor lifestyle interventions. Nevertheless, all of these conditions discussed pose significant increased risk for future cardiometabolic-related diseases. If overweight and obesity, but also excess GWG and post-partum weight retention, can be reduced through lifestyle interventions, then multiple comorbidities associated with pregnancy complications may also be reduced in the years after childbirth. The need for post-partum cardiovascular risk assessment and follow-up remains under-recognised, and further research in this area is warranted.

Author contributions

L.J.M. designed the review and J.A.G. contributed to the concept of this work. All authors contributed to interpretation of data, drafted the article and revised it critically for important intellectual content, approved the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest statement

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