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Risks of cardiometabolic diseases in women with history of adverse pregnancy outcomes

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Cardiometabolic diseases (CMDs) arise from shared pathophysiological pathways characterized by insulin resistance, dysglycemia, inflammation, adipokine dysregulation, and endothelial dysfunction. Pregnancy represents a natural cardiovascular stress test, involving hemodynamic adaptations such as increased blood volume, reduced vascular resistance, and elevated cardiac output. Adverse pregnancy outcomes (APOs) reflect maladaptive responses to this stress and are strongly associated with future CMDs. These outcomes are linked to an increased incidence of hypertension, ischemic heart disease, and stroke in later life. Proposed underlying mechanisms include impaired cardiac remodeling, chronic inflammation, and persistent dyslipidemia. Despite robust evidence linking APOs to future cardiometabolic risk, current cardiovascular disease (CVD) and diabetes prediction tools systematically overlook pregnancy history, leading to significant underestimation of risk in women. This problem is compounded by suboptimal postpartum screening. This review summarizes evidence supporting the role of APOs as early markers of CMDs. We propose a risk-stratification framework that incorporates APOs into CMDs risk assessment, supported by biomarker profiling, and promotes multidisciplinary postpartum care pathways along with individualized interventions such as dietary and physical activity programs. Future research should focus on developing risk prediction models that include APOs and on evaluating early preventive strategies to mitigate the long-term burden of CMDs in this high-risk population.

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INTRODUCTION

Cardiometabolic diseases (CMDs)—including type 2 diabetes mellitus(T2DM), hypertension, dyslipidemia, stroke and coronary heart disease—represent a major public health concern with profound implications for women's long-term health [1–4]. Strong evidence links adverse pregnancy outcomes(APOs) such as gestational hypertension(GH), preeclampsia(PE), gestational diabetes mellitus(GDM), preterm birth(PTB), recurrent pregnancy loss(RPL) and fetal growth restriction(FGR)/small for gestational age(SGA) to a substantially elevated risk of subsequent cardiovascular disease (CVD) and endocrinometabolic disorder, both shortly after delivery and later in life [2, 5].

Pregnancy serves as a physiological stress test, unmasking latent cardiometabolic vulnerability through its hemodynamic and metabolic adaptations [6]. These include increased blood volume, reduced vascular resistance, and altered insulin sensitivity—changes essential for fetal development. When compromised by impaired placentation or trophoblast dysfunction, APOs arise, offering a critical window for identifying women at elevated future CMDs risk.

Recent guidance from key academic associations including the American College of Obstetricians and Gynecologists (ACOG), the American Heart Association (AHA) and the European Society of Cardiology (ESC) advocates for the inclusion of APOs in cardiovascular risk evaluation. This consensus underscores the necessity for systematic documentation, lifestyle counselling, and coordinated long-term follow-up, to be implemented consistently across both obstetric and primary care settings. [7–9]. This represents a paradigm shift toward recognizing APOs as female-specific CVD risk factors.

This review synthesizes current evidence on APOs and subsequent CMDs risk, examines underlying mechanisms, and discusses strategies for improving lifelong cardiovascular and endocrinometabolic health in women through interdisciplinary approaches.

RESEARCH METHODOLOGY

Literature search strategy

A systematic search was conducted across PubMed, and Web of Science from inception to October 2025. Key search terms combined Medical Subject Headings (MeSH) and free-text keywords:

- Population: ("pregnancy" OR "postpartum") AND ("adverse pregnancy outcomes" OR "gestational hypertension" OR "preeclampsia" OR "gestational diabetes mellitus" OR "preterm birth" OR "recurrent miscarriage/pregnancy loss" OR "fetal growth restriction" OR "small for gestational").
- Outcome: ("cardiometabolic disease" OR "cardiovascular disease" OR "diabetes" OR "metabolic syndrome" OR "insulin resistance").
- Mechanism: ("pathophysiology" OR "inflammation" OR "insulin resistance" OR"oxidative stress" OR "placental dysfunction" OR "epigenetic").

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Data sources and study selection
Inclusion Criteria:

- Study designs: prospective/retrospective cohorts, case-control studies, randomized trials, and systematic reviews.
- Population: women with history of APOs.
- Outcomes: incident CMDs (T2DM, CVD, hypertension, dyslipidemia, stroke, obesity) or mechanistic biomarkers.
- Language: English-language publications.

Exclusion Criteria:

- Case reports, abstracts without full text.
- Studies lacking comparison groups (e.g., no non-APOs controls).

Screening Process: Two investigators independently screened titles/abstracts, followed by full-text review. Discrepancies were resolved by consensus or third-author arbitration.

Data synthesis and analysis
Given significant heterogeneity in APOs definitions and outcomes, a narrative synthesis was performed. Data were stratified by:

- APOs type (GH/PE, GDM, PTB, RPL, FGR/SGA).
- CMDs outcome (CVD, T2DM, metabolic syndrome, obesity).
- Pathophysiological theme (inflammation, placental pathology, metabolic/epigenetic mechanisms).

THE ASSOCIATION BETWEEN APOS AND RISK OF CMDS IN WOMEN

Gestational hypertension and preeclampsia

GH and PE are recognized as distinct pathophysiological entities originating from placental dysfunction. In the Cardiovascular Health After Maternal Placental Syndromes (CHAMPS) cohort, which included over 13,000 women, a composite cardiovascular endpoint occurred significantly more often in those with a history of hypertensive disorders of pregnancy (HDP)—with a hazard ratio (HR) of 2.6 (95% CI 2.3–2.9). This increased risk remained significant after multivariable adjustment for participant age at the time of discharge from hospital after the index delivery, length of stay in hospital, socioeconomic quintile and rural residence (HR 2.0; 95% CI 1.7–2.2). These findings underscore that GH and PE are not merely transient obstetric complications, but important clinical indicators of long-term vascular and metabolic vulnerability. Further analysis revealed elevated risks for specific cardiovascular outcomes: coronary artery disease (HR 2.0; 95% CI 1.7–2.3), cerebrovascular disease (HR 1.9; 95% CI 1.4–2.5), and peripheral arterial disease (HR 3.0; 95% CI 1.9–4.8) [10].

Preterm birth

PTB is a multifactorial syndrome associated not only with immediate neonatal risks but also with significant long-term cardiometabolic consequences for the mother. Robust meta-analyses have established spontaneous PTB as an independent predictor of future maternal CMDs [11]. Specifically, it is associated with a significantly elevated risk of overall CVD (HR 2.01, 95% CI 1.52–2.65), with further increases in the risks of ischemic heart disease (HR 1.38, 95% CI 1.22–1.57) and stroke (HR 1.71, 95% CI 1.53–1.91) [11]. The magnitude of this long-term risk is influenced by both gestational age and recurrence. Women delivering at late preterm gestation (32–36 weeks) exhibit a 1.89-fold increased risk of subsequent T2DM (95% CI 1.69–2.10) and a 1.42-fold increased risk of thromboembolism (95% CI 1.24–1.62). Notably, those with recurrent PTB (two preterm deliveries) face the highest compounded risk, with a 2.30-fold increase in T2DM (95% CI 1.71–3.10) and a 1.80-fold increase in thromboembolism (95% CI 1.29–2.50) [12]. Importantly, even when a subsequent pregnancy reaches term, a history of PTB remains a significant predictor of future metabolic dysfunction, associated with a 1.58-fold increased risk of T2DM (95% CI 1.34–1.86) and a 1.18-fold increased risk of thromboembolism (95% CI 0.96–1.44) [12]. These findings reinforce the concept of a shared pathophysiological continuum, in which APOs such as PTB unmask or amplify a woman's underlying predisposition to future CMDs.

Recurrent pregnancy loss

RPL is increasingly recognized as a clinical marker of underlying maternal cardiovascular dysfunction [8]. This condition is thought to reflect a subclinical state of vascular endotheliopathy and hypercoagulability, which may translate into persistent cardiovascular risk beyond the reproductive years. Evidence from large cohorts indicates that a history of three or more miscarriages is associated with a 1.56-fold increased risk of ischemic heart disease (HR 1.56, 95% CI 1.14–2.15) [13]. Epidemiological studies further suggest a dose-dependent relationship, whereby cardiovascular risk increases with the number of prior pregnancy losses [14]. Notably, in women with established atherosclerosis, a history of RPL is associated with a markedly elevated risk of recurrent cardiovascular events (HR 4.3, 95% CI 1.7–10.9) [13]. These findings position RPL as a critical but often underrecognized marker of underlying cardiovascular susceptibility, necessitating increased clinical vigilance and dedicated cardiovascular risk evaluation in this population to facilitate timely intervention and enhance long-term health prospects.

Fetal growth restriction/small for gestational age

A large-scale analysis of primiparous women demonstrated that delivering a SGA infant, as part of a spectrum of placental syndromes, was associated with a 19% increase in the mother's future CVD risk (adjusted HR 1.19, 95% CI 1.07–1.32). Importantly, this study revealed a synergistic effect: when SGA co-occurred with PTB, maternal CVD risk was substantially amplified, reaching a 45% increase (adjusted HR 1.45, 95% CI 1.24–1.71) [15]. While these epidemiological associations are well established, their interpretation requires consideration of shared underlying risk factors. A landmark Swedish twin study investigating the association between low birthweight (LBW) and adult CMDs provided critical insight. The study initially confirmed a strong overall association (OR 1.39, 95% CI 1.27–1.52) [16]. However, in a subsequent co-twin matched analysis that controlled for shared genetic and early-life environmental factors, this association was substantially attenuated and lost statistical significance (OR 1.21, 95% CI 0.94–1.56) [16]. These findings reveal a critical insight: the association between LBW and later CMDs is not merely causal but reflects a shared underlying biological or genetic predisposition. This perspective aligns with the Developmental Origins of Health and Disease (DOHaD) hypothesis and highlights the need for an integrated, mechanism-informed approach to risk stratification in women with a history of SGA.

Gestational diabetes mellitus

GDM represents one of the most significant APOs in predicting future metabolic morbidity, serving as an early clinical indicator of T2DM and conferring a substantially elevated long-term CVD risk. The risk of T2DM is both acute and pronounced: longitudinal studies indicate that women with a history of GDM face a 2.3-fold increased risk of progressing to prediabetes or T2DM within five years postpartum (adjusted HR 2.28, 95% CI 1.48–3.51). Underlying this progression is not only insulin resistance but, more critically, a primary impairment in pancreatic β-cell function (HR 3.1, 95% CI 2.0–4.8) [17], which emerges as the dominant determinant of dysglycemia—often outweighing the influence of obesity or

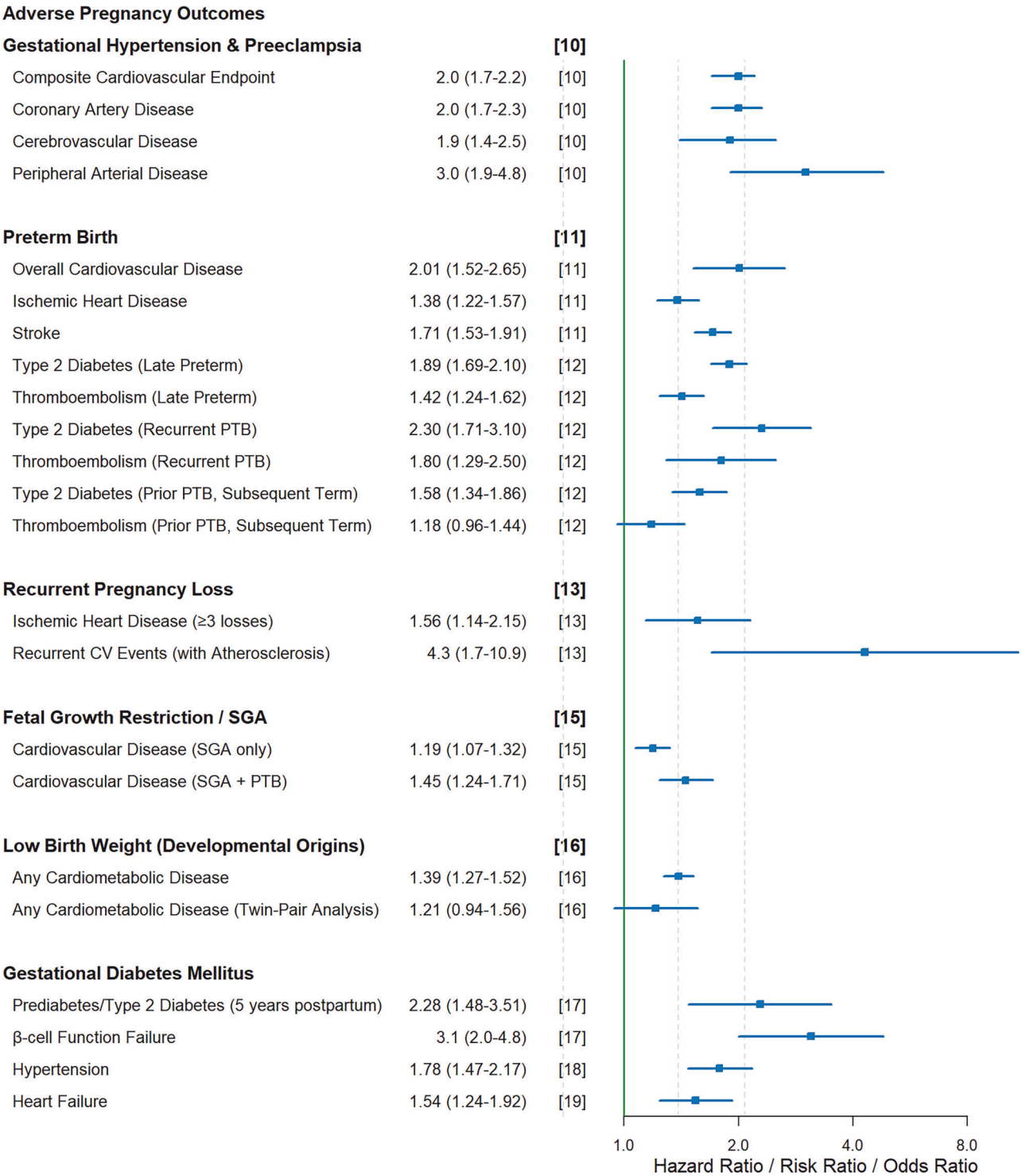

Fig. 1 Association Between Adverse Pregnancy Outcomes and Long-Term maternal Cardiometabolic Disease.

insulin resistance. This metabolic dysfunction directly translates into increased CVD risk, independent of subsequent T2DM development. A systematic review and meta-analysis focusing on hypertensive outcomes revealed that GDM is associated with a 78% higher risk of future hypertension (pooled RR 1.78, 95% CI 1.47–2.17) [18], a relationship that persists after adjustment for potential confounders such as antenatal psychological stress. Furthermore, women with a history of GDM face a 54% increased risk of heart failure (RR 1.54, 95% CI 1.24–1.92) [19], suggesting a potential role for GDM in promoting adverse myocardial remodeling. Figure 1 presents a forest plot summarizing the associations between APOs and subsequent CMDs.

PATHOPHYSIOLOGICAL MECHANISMS LINKING APOS TO CMDS

The association between APOs and subsequent CMDs is mediated by shared pathways of vascular, metabolic, and epigenetic

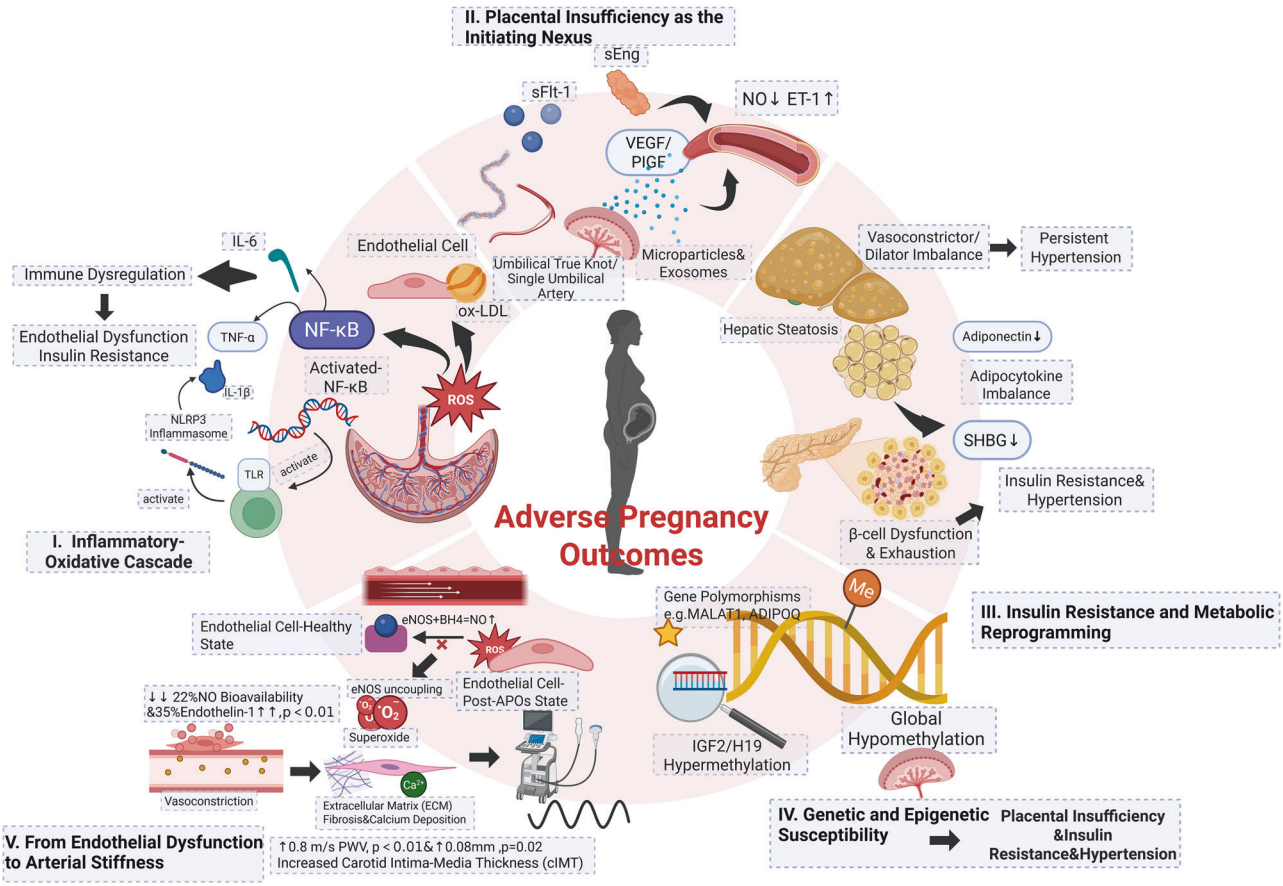

Fig. 2 Pathophysiological Mechanisms Linking Adverse Pregnancy Outcomes to Long-Term Cardiometabolic Diseases.

dysregulation that originate in placental dysfunction. This leaves a persistent pathophysiological imprint that drives accelerated vascular aging in the postpartum period, as summarized in Fig. 2.

Inflammation and oxidative stress cascade

Placental ischemia induces mitochondrial dysfunction, resulting in the overproduction of reactive oxygen species (ROS). This state of oxidative stress initiates a deleterious inflammatory cascade that perpetuates vascular injury. A key mechanism involves ROS-mediated activation of the nuclear factor kappa B (NF-κB) pathway, which stimulates the release of pro-inflammatory cytokines—including IL-1β and TNF-α—as well as damage-associated molecular patterns (DAMPs) [20]. Furthermore, placental ischemia specifically triggers activation of the Nucleotide-binding oligomerization domain, leucine-rich repeat and pyrin domain-containing protein 3(NLRP3) inflammasome, leading to caspase-1-dependent maturation and secretion of IL-1β [21]. The synergy between oxidative stress and inflammation sustains a state of subclinical inflammation postpartum, characterized by elevated C-reactive protein (CRP) and IL-6 levels [22]. This persistent inflammatory milieu contributes to the development of insulin resistance and metabolic syndrome, thereby extending cardiovascular and metabolic risk beyond the index pregnancy.

Placental insufficiency as the initiating nexus

Placental insufficiency, the failure to maintain adequate fetal nutrient and oxygen supply (underlying PE and FGR), serves as trigger for CMDs. Its mechanisms involve structural defects and remote systemic signaling via placental factors.

- **Umbilical Cord Abnormalities and Perfusion Defects:** Aberrant umbilical cord coiling (e.g., abnormal umbilical coiling index [UCI] <0.26 or >0.46 coils/cm) and structural lesions (e.g., single umbilical artery) restrict fetal blood flow, directly contributing to placental insufficiency, FGR, and increased stillbirth risk. These structural defects reflect early vascular developmental defects and indicate chronic placental hypoxia [23].
- **Placental Insufficiency and Metabolic Stress:** Impaired placental perfusion leads to ischemia-reperfusion injury, activating maternal systemic inflammation and oxidative stress, which induces core CMDs features like endothelial dysfunction and maternal insulin resistance. Histopathological features of fetal vascular malperfusion (FVM), such as avascular villi, further confirm chronic placental hypoxia and the release of inflammatory cytokines (e.g., TNF-α, IL − 6) that damage maternal endothelium [23].
- **Placental Deportation of Vesicles and Soluble Factors:** Crucially, the failure of physiological spiral artery remodeling—a hallmark of PE and FGR—results in the influx of high-pressure, turbulent maternal blood into the intervillous space. This aberrant flow generates significant shear stress, directly damaging the syncytiotrophoblast and promoting the release of syncytial knots and key soluble factors into the maternal circulation [24–26]. Subsequent placental ischemia drives the systemic release of extracellular vesicles (EVs) and anti-angiogenic factors. Among these, soluble fms-like tyrosine kinase-1 (sFlt-1) and soluble endoglin (sEng) are pivotal; they are often carried by syncytiotrophoblast-derived exosomes, which act as vectors for remote vascular injury [27]. sFlt-1 binds to and sequesters vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), thereby inhibiting their pro-angiogenic and endothelial repair functions. This disruption contributes directly to systemic endothelial dysfunction. Although the sFlt-1/PlGF ratio is a well-established biomarker

for the acute diagnosis and management of PE, its utility in predicting long-term risk of CMDs remains uncertain and requires further validation, as current evidence is conflicting [28].

Insulin resistance and metabolic reprogramming

Insulin resistance represents a central mechanism in the persistent susceptibility to CMDs following APOs, particularly GDM. This susceptibility is reflected in alterations in sex hormone-binding globulin (SHBG), adipocytokine profiles, lipid metabolism, and β-cell function—changes that are mediated by chronic insulin resistance, inflammation, and lipotoxicity.

- **β-Cell Dysfunction:** An insufficient compensatory expansion of β-cell mass during pregnancy is a key pathophysiological feature in GDM and underlies the rapid deterioration of glycemic control often observed postpartum. This persistent β-cell dysfunction strongly predicts subsequent progression to T2DM (HR 3.1; 95% CI 2.0–4.8) [17].
- **SHBG Dysregulation:** Reduced circulating SHBG levels are an independent predictor of GDM (OR 1.8; 95% CI 1.2–2.7) [29]. Mechanistically, this association is linked to insulin resistance —reflected by elevated Homeostatic Model Assessment for Insulin Resistance(HOMA-IR)—and is exacerbated by impaired hepatic insulin sensitivity, which further promotes hyperinsulinemia.
- **Lipotoxicity and Adipose Tissue Dysfunction:** Early pregnancy dyslipidemia, characterized by elevated first-trimester lysophosphatidylcholine (LPC 16:0) and ceramide (Cer 14:0), promotes lipotoxicity and hepatic steatosis, accounting for up to 27% of the attributable risk of GDM. Furthermore, low antenatal adiponectin levels are a significant predictor of postpartum β-cell dysfunction ($\beta = -0.32$; $P < 0.001$) [30].
- **Ethnic Disparities in Postpartum Glucose Metabolism:** Chinese women with GDM exhibit a 4.5-fold higher risk of postpartum dysglycemia compared to Malay women. This disparity is attributed to a lower β-cell functional reserve and differences in lipid metabolism profiles [31].

Genetic and epigenetic susceptibility

Epigenetic alterations at the maternal–fetal interface represent potential early biomarkers of future CMDs risk:

- **Genome-Wide Changes:** The placenta demonstrates a characteristic pattern of global hypomethylation relative to somatic tissues [32].
- **Imprinted Gene Dysregulation:** Aberrant methylation of imprinted genes is associated with APOs. For example, hypermethylation of the adiponectin, C1Q and collagen domain containing(ADIPOQ) promoter in placentas from GDM pregnancies is correlated with disturbances in fetal metabolic programming and may heighten maternal susceptibility to long-term obesity [33].

Endothelial dysfunction and vascular remodeling

Chronic inflammation and oxidative stress drive persistent impairments in vascular function and structure, which play a critical role in the pathogenesis of hypertension and maladaptive vascular remodeling in women with a history of APOs.

- **Imbalance in Vasoconstrictor and Vasodilator Systems:** APOs induce endothelial nitric oxide synthase (eNOS) uncoupling, thereby reducing the bioavailability of the vasodilator nitric oxide (NO) and increasing superoxide generation. This disturbance shifts the vascular balance towards constriction, as evidenced by elevated circulating endothelin-1 (ET-1) and reduced NO metabolites during the postpartum period. Concurrently, a state of chronic inflammation—characterized by elevated CRP—upregulates NADPH oxidase activity, which in turn increases ROS production. These ROS promote oxidation of tetrahydrobiopterin (BH4), an essential eNOS cofactor. The resulting BH4 deficiency perpetuates eNOS uncoupling, establishing a self-sustaining cycle of NO deficiency and enhanced vasoconstriction [20, 27].
- **Structural Vascular Remodeling and Stiffness:** Endothelial dysfunction progresses to measurable structural vascular injury that persists long-term following an affected pregnancy. Women with a history of PE demonstrate significantly impaired flow-mediated dilation (FMD), reflecting persistent endothelial dysfunction. This functional impairment typically precedes the development of structural alterations, such as increased carotid intima-media thickness (cIMT)—a well-established marker of subclinical atherosclerosis. Concomitant activation of vascular smooth muscle cells and enhanced collagen deposition promote arterial fibrosis and stiffening. These changes are quantifiably reflected by elevated pulse wave velocity (PWV), which serves as a key indicator of accelerated vascular aging [34].

THE IMPERATIVENESS OF EARLY POSTPARTUM RISK ASSESSMENT AND INTERVENTION

Postpartum window: a critical transition period within 5 years after pregnancy

Emerging evidence indicates that pregnancy and the postpartum period may unmask or amplify underlying vascular and metabolic dysfunction, offering a unique opportunity for early risk stratification and intervention. A meta-analysis involving over 3.48 million women confirmed that preeclampsia is associated with a 2.16-fold increased long-term risk of ischemic heart disease (95% CI: 1.86–2.52) and a 1.81-fold increased risk of stroke (95% CI: 1.45–2.27) [35].

The first five years postpartum represent a particularly vulnerable transitional phase for CMDs progression. In a prospective cohort of 4 484 women followed for a mean of 3.2 years after their first delivery, those with APOs had a 2.4-fold increased risk of hypertension (95% CI: 1.8–3.1) compared to those without. This risk was consistently elevated across individual APOs, including PE (RR 2.8, 95% CI: 2.0–4.0) and PTB (RR 2.7, 95% CI: 1.9–3.8), with the highest risk observed in women experiencing both hypertensive disorders and indicated PTB (RR 4.3, 95% CI: 2.7–6.7) [36].

Furthermore, a large population-based study ($n = 41{,}155$) demonstrated that women with prepregnancy hypertension and superimposed HDP faced markedly elevated risks of coronary heart disease (aHR 3.79, 95% CI: 3.09–4.65) and stroke (aHR 3.10, 95% CI: 2.09–4.60) within five years postpartum. Notably, HDP alone remained a significant predictor of early cardiovascular events even in the absence of prepregnancy hypertension [37]. Recent data further suggest that the postpartum trajectory of blood pressure and metabolic parameters may serve as a strong predictor of future cardiovascular health [38].

In response to these findings, major professional societies now recommend systematic postpartum cardiovascular risk assessment. The International Society for the Study of Hypertension in Pregnancy (ISSHP) advises annual evaluation for all women with a history of HDP, beginning within the first year after delivery [39]. Similarly, the 2025 ESC Guidelines recommend early screening for cardiovascular risk factors in women with any history of APOs [9].

Key implementation barriers in the management of women with APOs

A persistent challenge in the long-term management of women with prior APOs is the absence of standardized protocols for

Table 1. Clinical Practice Recommendations and Identified Gaps for Postpartum CMDs Screening in Women with a History of APOs.

Characteristics	Current Guideline Recommendations (Selected Key Examples)	Key Gaps and Unresolved Issues
Target Population	All women with a history of HDP (ISSHP 2021) [39], GDM (ADA 2023) [53], preterm birth, delivery of SGA infant, or placental abruption (AHA 2011, 2021) [54].	Lack of standardized risk stratification within the APOs population (e.g., early-onset vs. late-onset preeclampsia, severity of GDM,late/very/extremely preterm).
Timing for Screening	Initial screening: ACOG recommends a comprehensive visit within 3 months postpartum. Optimizing postpartum care. [7] Within 6 months to 1 year postpartum (ISSHP 2021 [39], ADA 2023) [53]. Long-term: Annual risk factor assessment and lifelong monitoring (AHA 2021) [54].	The ideal frequency of screening between the first postpartum visit and annual assessments is not defined. Lack of evidence for very early screening (e.g., <3 months postpartum).
Core Screening Metrics	Blood pressure: Ambulatory BP monitoring recommended if office BP elevated (ISSHP 2021) [39]. Metabolic panel: Fasting glucose or HbA1c, lipid profile (AHA 2021, ADA 2023) [53, 54]. Anthropometrics: BMI, waist circumference (AHA 2021) [54].	Limited guidance on screening for subclinical vascular dysfunction (e.g., pulse wave velocity, endothelial function) in clinical practice. Sleep apnea and renal function screening are often overlooked.
Intervention Threshold	Apply general population thresholds for hypertension, diabetes, and dyslipidemia (e.g., ACC/AHA2025, ESC guidelines 2025) [9, 54].	It is unclear if more aggressive treatment targets are warranted for this high-risk population. Lack of RCTs on optimal BP goals specifically for women with history of APOs.
Lifestyle Intervention	Universal recommendation for heart healthy diets (DASH, Mediterranean), physical activity, and weight management (ISSHP2021) [39].	Lack of standardized, evidence-based lifestyle programs tailored to postpartum women with APOs. Barriers to adherence (e.g., childcare, fatigue) are not adequately addressed.
Care Model & Follow-up	Recommend transition from obstetric care to primary care/ internal medicine for long-term monitoring (AHA 2021) [54].	Major gaps in care coordination. Lack of structured transition protocols, leading to high dropout rates from follow-up.
Special Considerations	Recognition has been added for the protective effects of breastfeeding, encouraging it to reduce the long-term CVD risk in mothers [9, 54].	The dose-response relationship between the duration and intensity of breastfeeding and its cardiovascular benefits remains unclear.

ACC American College of Cardiology, *ACOG* American College of Obstetricians and Gynecologists, *ADA* American Diabetes Association, *AHA* American Heart Association *APOs* adverse pregnancy outcomes, *BMI* body mass index, *BP* blood pressure, *CMDs* cardiometabolic diseases, *CVD* Cardiovascular Disease, *DASH* Dietary Approaches to Stop Hypertension, *ESC* European Society of Cardiology, *GDM* gestational diabetes mellitus, *HDP* hypertensive disorders of pregnancy, *ISSHP* International Society for the Study of Hypertension in Pregnancy, *RCT* randomized controlled trial, *SGA* small for gestational age.

transitioning from obstetric to primary or specialist care. This systemic gap contributes to substantial under-monitoring in the postpartum period. For example, global completion rates for postpartum oral glucose tolerance testing (OGTT) remain consistently low, ranging from 31–49% [40]. A systematic review of nine U.S. studies reported that postpartum diabetes screening rates following GDM did not exceed 58% within four months after delivery, indicating minimal improvement over the past decade [41]. Although blood pressure is more frequently measured in women with HDP, it is often unclear whether abnormal readings prompt appropriate follow-up or intervention.

These deficiencies are compounded by poorly defined responsibilities among obstetricians, general practitioners, midwives, endocrinologist, and cardiologists, leading to fragmented care and significant loss to follow-up [42]. In addition, many healthcare providers demonstrate limited familiarity with guideline recommendations and underestimate the long-term cardiometabolic implications of APOs. In up to 49% of cases, missed postpartum glucose screening has been attributed to providers not ordering the test [43].

Further barriers operate at the patient and community level, including low perceived severity of conditions such as GDM, cultural norms requiring spousal approval for healthcare access, and health illiteracy.

In summary, the implementation gap in postpartum cardiometabolic care arises from a combination of insufficient awareness among patients and providers, ambiguous clinical responsibility, and the absence of structured, feasible transition pathways—even where evidence-based guidelines exist.

Current guidelines recommendations

An emerging consensus within international societies endorses the incorporation of reproductive history into the assessment of cardiometabolic risk in women. However, as summarised in Table 1, the implementation of these recommendations in clinical practice remains limited. Several critical barriers hinder effective postpartum screening: a lack of standardised protocols for the early postpartum period, the systematic underestimation of risk by conventional calculators in young women [44], and, most notably, a 60–70% loss to follow-up rate attributable to fragmented care [45]. Addressing these challenges requires a paradigm shift towards integrated care models and more nuanced risk assessment.

Advanced Risk Tools

Risk stratification must move beyond conventional measures by adopting pregnancy-enhanced models (e.g., Predicting Risk of Cardiovascular Events Early(PREVENT) score, $\kappa = 0.55$) [46] and integrating the routine application of advanced vascular assessments, such as PWV, to detect sub-clinical arterial stiffening [47].

- **Digital Health and Fragmentation Solutions**: To address the continuity gap, telehealth and remote monitoring are significantly underutilized tools [48, 49]. Digital platforms, leveraging bluetooth-enabled BP cuffs and virtual consultations, enable timely detection of persistent hypertension in the critical early postpartum period (< 3 months) and facilitate a structured, multidisciplinary transition of care, thereby improving adherence to long-term screening protocols.

- **Targeted Intervention Gaps:** While intensive lifestyle interventions, such as adherence to a Mediterranean dietary pattern, have demonstrated significant long-term CVD event reduction (HR = 0.72) in secondary prevention trials [50], high-level RCT evidence is still lacking regarding the efficacy of novel pharmacotherapies (e.g., SGLT2 inhibitors and GLP − 1 receptor agonists) and optimal BP control targets in this specific high-risk population.

CONCLUSION AND FUTURE PERSPECTIVES

APOs are now unequivocally recognized as powerful, sex-specific indicators of a woman's long-term CMDs risk. They represent not merely transient obstetric events, but critical physiological stress tests that reveal underlying predispositions. The 3~5 years postpartum constitute a crucial window for preventive intervention.

This risk continuum is driven by synergistic pathways: placental ischemia-induced oxidative stress and inflammatory cascades (e.g., NLRP3/IL-1β) perpetuate endothelial dysfunction, while concurrent metabolic reprogramming establishes persistent diabetogenic phenotypes. Key biomarkers include suppressed SHBG and progressive β-cell exhaustion. Epigenetic dysregulation further entrenches this susceptibility.

Translating this knowledge into practice remains the paramount challenge. Conventional risk scores systematically underestimate risk in these women. Future efforts must prioritize enhanced stratification—integrating advanced vascular assessments and pregnancy-enhanced prediction models—alongside evidence-based interventions such as Mediterranean dietary patterns. The absence of structured postpartum transition pathways and a 60–70% loss to follow-up rate are critical barriers. This systemic fragmentation compromises lifelong maternal health and perpetuates an intergenerational cycle of risk. Future research must generate robust RCT evidence for targeted therapies and establish the cost-effectiveness of systematic screening programs.

The DOHaD hypothesis underscores the profound intergenerational implications of APOs [22]. Offspring exposed to suboptimal intrauterine environments undergo metabolic programming that predisposes them to cardiometabolic dysfunction later in life. Specifically, LBW is associated with a significantly increased risk of metabolic syndrome in adulthood (OR 1.37, 95% CI 1.17–1.61) and greater insulin resistance (WMD 0.28, 95% CI 0.19–0.36) [51]. Furthermore, young adults born preterm demonstrate early markers of cardiovascular impairment, including myocardial fibrosis and diastolic dysfunction, indicating heightened susceptibility to future heart failure and ischemic heart disease. These findings necessitate a fundamental shift toward family-centric health models that integrate obstetric, primary, and pediatric care. APOs should be recognized as sentinel events heralding cardiometabolic vulnerability across generations. Clinical practice must adopt a lifecourse perspective: pediatric and primary care providers should systematically document birth history as a key cardiovascular risk factor and initiate routine screening for blood pressure, dyslipidemia, and dysglycemia from childhood [52]. Nutritional and physical activity counseling should be provided family-wide, with careful management of rapid catch-up growth in infancy following fetal growth restriction, given its paradoxical amplification of long-term cardiometabolic risk [22]. Through such integrated strategies, the intergenerational cycle of CMDs can be effectively interrupted.

SUMMARY

What is known about the topic?

- APOs are established predictors of future maternal CMDs.
- Placental vascular dysfunction (e.g., impaired spiral artery remodeling) is a central mechanistic link between APOs and persistent endothelial/insulin resistance pathologies.

What this study adds

- **Novel risk stratification framework:** Proposes the systematic integration of APOs into cardiovascular risk assessment tools – currently excluded from major guidelines (e.g., ASCVD/Framingham) – to address the critical underestimation of women's long-term risks.
- **Actionable clinical pathway:** Introduces a step-by-step postpartum care model that combines:
  - Biomarker-enhanced screening (hs-CRP/homocysteine).
  - Multidisciplinary coordination (OB/GYN-cardiology collaboration).
  - Early lifestyle interventions (DASH diet/physical activity protocols).
- **Lifespan health perspective:** APOs are positioned as pivotal early warnings that necessitate lifelong cardiometabolic surveillance, filling the current care gaps where <fewer than 50% of high-risk women receive guideline-recommended follow-up.

DATA AVAILABILITY

Data sharing is not applicable to this article as no new datasets were generated or analysed during the current study.

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AUTHOR CONTRIBUTIONS

LQ contributed to the study's design, execution, and paper collection. WR took the lead in drafting the manuscript. WR and CYM performed formal analyses and interpretation. WL was responsible for project administration and resources. All authors drafted the manuscript and critical revision for important intellectual content. Each author has read and approved the final version of the manuscript and agrees to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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All the authors declare no conflict of interest.

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ADDITIONAL INFORMATION

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