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Review

Cardiovascular Risk Assessment Across the Female Life Course: Key Time Windows for Earlier Identification and Prevention

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Abstract

Cardiovascular disease remains the leading cause of death in women, yet risk is frequently underestimated, particularly during early and middle adulthood. A life-course perspective may identify periods in which female-specific factors reveal or accelerate cardiovascular vulnerability. This narrative review examines cardiovascular risk across adolescence, reproductive life, pregnancy, the postpartum period, menopause, and older age. Relevant literature was identified through a targeted PubMed search, supplemented by major international guidelines and reference screening. The review addresses reproductive and pregnancy-related risk factors, female-predominant conditions, limitations of

current prediction models, and the potential contribution of biomarkers and imaging, including coronary artery calcium and breast arterial calcification. Cardiovascular prevention in women should move beyond isolated 10-year risk estimates towards longitudinal assessment that incorporates reproductive history and female-specific risk modifiers. Pregnancy and the postpartum period are underused opportunities for early prevention, whereas selected imaging tools may improve risk classification when conventional scores are uncertain. Future progress will require structured follow-up pathways, multidisciplinary care, systematic capture of female-specific risk factors, and prediction models validated in diverse female populations. We distinguish epidemiological associations from independently validated risk prediction and from interventions with demonstrated clinical benefit, and propose a staged, guideline-anchored pathway for reassessment at key life transitions.

Keywords: cardiovascular prevention; cardiovascular risk assessment; female-specific risk factors; life-course approach; women's cardiovascular health

1. Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide [1,2]. In Europe and the United States, CVD accounts for more deaths in women than breast cancer, lung cancer, and chronic lung disease combined [3]. Although major advances in prevention and treatment have improved cardiovascular outcomes, recent data suggest that the burden of cardiovascular disease among younger women remains substantial. Mortality from ischemic heart disease among women aged 35–54 years appears to be increasing compared with men [4], while the incidence of ST-segment elevation myocardial infarction has risen among women younger than 45 years [5]. Despite these observations, cardiovascular risk in women remains insufficiently recognized. Traditional risk factors play a central role in the development of cardiovascular disease, but their impact is often influenced by biological and reproductive factors that are unique to women and may emerge at different stages of life. A woman's cardiovascular risk profile evolves across the lifespan. Adolescence, reproductive age, pregnancy, the postpartum period, menopause, and ageing represent key phases during which cardiovascular risk may become apparent or accelerate. Considering these stages as part of a continuous trajectory may help identify women at increased risk earlier than conventional approaches based exclusively on short-term risk estimation. This review summarizes the main stages of the female life course that may influence cardiovascular risk assessment and discusses how a life-course approach could contribute to earlier recognition and more effective prevention of cardiovascular disease in women.

Scope, Literature Identification and Interpretation

This is a narrative, clinically oriented review rather than a systematic review or meta-analysis. The original targeted PubMed search was supplemented by a focused literature update through 5 November 2026. Search concepts were combined in English using terms for women or female sex, cardiovascular prevention or risk prediction, and life-course exposures (menarche, polycystic ovary syndrome, pregnancy complications, gestational diabetes, postpartum health, menopause, frailty), together with coronary phenotypes, race and ethnicity, social determinants, metabolomics, coronary calcium and breast arterial calcification. Reference lists of relevant articles and contemporary ESC, AHA/ACC, ADA and menopause guidance documents were also reviewed. Priority was given to clinical guidelines, scientific statements, randomized trials, large prospective cohorts and

meta-analyses; smaller mechanistic studies were considered where clinical data were limited. Selection was based on relevance to risk assessment and actionable prevention, without formal protocol registration, duplicate screening or quantitative quality scoring. Accordingly, the review does not claim exhaustive capture of the literature or formal certainty grading.

Throughout the manuscript, we use three distinct levels of inference: (i) epidemiological association, which can identify a potential risk marker; (ii) independent prognostic information or improved model performance, which requires appropriate adjustment and external validation; and (iii) clinical utility, which requires evidence that using the marker changes decisions or improves outcomes. An association alone is not treated as justification for a test, treatment threshold or scheduled specialist referral.

2. Conceptual Life Course Framework

A life-course approach provides a useful framework for cardiovascular prevention in women, as it captures the interaction between traditional risk factors and female-specific exposures emerging at different stages of life. This framework emphasizes cumulative exposure to traditional cardiovascular risk factors together with female-specific exposures occurring during biologically vulnerable periods, including puberty, reproductive age, pregnancy, the menopausal transition, and ageing. Traditional risk factors remain major determinants of cardiovascular events but may interact differently with sex-specific exposures across a woman's life course. Current calculators (PCE, SCORE2, QRISK and others) are calibrated to short-term cardiovascular outcomes and may fail to adequately capture long-term risk in young and middle-aged women, particularly in the presence of female-specific conditions [6]. In 2020, the American College of Cardiology highlighted the importance of incorporating female-specific factors into cardiovascular risk assessment and prevention strategies [7]. The impact of these non-traditional factors is particularly evident in young and middle-aged women, who may not show signs of high CVD risk until later in life. Since most current calculators do not incorporate these female-specific factors, cardiovascular risk may be underestimated in some women [8,9]. The main stages of the female life course and the corresponding sex-specific factors influencing cardiovascular risk assessment are summarized in Table 1 and illustrated in Figure 1.

The added value of the life-course framework is not a new numerical score. Rather, it is a clinical sequence for asking the right questions when reproductive information becomes available, reassessing conventional risk when circumstances change, and escalating investigations only when the result is likely to alter management. These distinctions are especially important because reproductive exposures may be markers of shared antecedent risk rather than independent causes of later disease.

Mechanistic interpretation of Table 1 requires attention to timing and confounding. Early menarche may reflect childhood adiposity, insulin resistance, altered leptin signalling and earlier exposure to ovarian hormones, whereas late menarche may arise from low energy availability, endocrine disorders or other chronic conditions. Both ends of the menarche-age distribution have shown associations with later vascular events, but these pathways cannot be assumed to be causal in every woman [10–12]. In PCOS, androgen excess, impaired insulin sensitivity, visceral adiposity and endothelial dysfunction may act together; in pregnancy, abnormal placentation and angiogenic imbalance can expose pre-existing vascular susceptibility; and during menopause, redistribution of adiposity, changes in lipoprotein metabolism and endothelial responses modify the cardiometabolic milieu [13–20]. These mechanisms support targeted assessment of modifiable risk factors, not automatic pharmacological treatment solely because of the reproductive event.

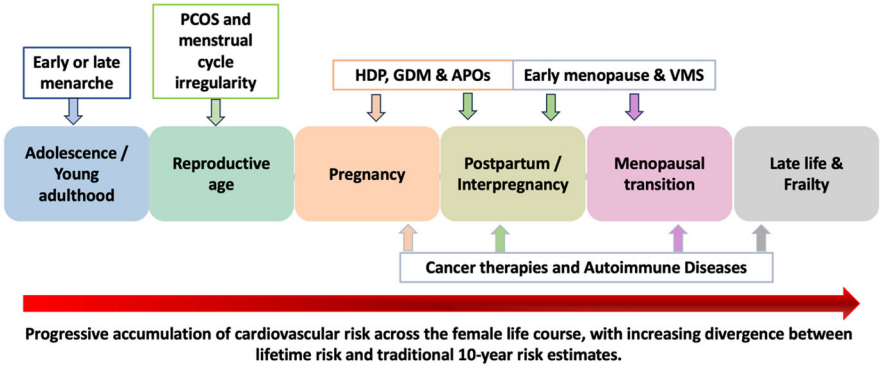


Figure 1. Key moments across the female life course influencing cardiovascular risk assessment. Female-specific conditions emerging across the life course may modify cardiovascular risk beyond traditional risk factors. Pregnancy complications, reproductive disorders, menopause, and ageing represent important opportunities for cardiovascular risk reassessment and preventive intervention. Abbreviations: PCOS, polycystic ovary syndrome; HDP, hypertensive disorders of pregnancy; GDM, gestational diabetes mellitus; APOs, adverse pregnancy outcomes; VMS, vasomotor symptoms.

Table 1. Key moments across a woman's life for cardiovascular risk assessment.

Life-Course Stage	Main Female-Specific or Female-Predominant Risk Factors	Suggested Clinical Evaluation/Implications
Adolescence and pre-pregnancy years	Early or late menarche, polycystic ovary syndrome (PCOS), menstrual cycle irregularity, adolescent obesity, systemic inflammatory/autoimmune disorders	Assess blood pressure, body mass index/waist circumference, fasting glucose and lipid profile; identify family history of premature CVD and early cardiometabolic risk markers
Pregnancy	Hypertensive disorders of pregnancy, pre-eclampsia, gestational diabetes mellitus, preterm delivery, adverse pregnancy outcomes, peripartum cardiomyopathy	Consider pregnancy as a cardiovascular stress test; document obstetric history carefully and identify women who may require structured postpartum cardiovascular follow-up
Postpartum and interpregnancy period	Persistent hypertension, dysglycaemia, metabolic syndrome, subclinical cardiac dysfunction after complicated pregnancy	Reassess blood pressure, glucose/HbA1c, lipid profile and weight; promote lifestyle intervention and periodic cardiovascular follow-up, especially after hypertensive disorders of pregnancy or gestational diabetes
Midlife transition and menopause	Early menopause, premature ovarian insufficiency, vasomotor symptoms, sleep disturbance, depression, adverse changes in lipids and adiposity	Reassess global cardiovascular risk; optimise control of blood pressure, lipids and glycaemia; consider coronary artery calcium scoring in selected women at borderline/intermediate risk
Later life and frailty	Frailty, multimorbidity, polypharmacy, heart failure with preserved ejection fraction, atrial fibrillation, microvascular disease	Tailor preventive strategies according to biological age, functional status, competing risks and treatment burden; integrate cardiovascular assessment with geriatric evaluation
Across the life course	Autoimmune diseases, breast cancer therapies, infertility, endometriosis, social determinants of health, chronic stress and caregiving burden	Record these conditions systematically as risk modifiers; consider intensifying prevention and improving multidisciplinary follow-up when conventional risk scores appear to underestimate risk

3. Adolescence and Pre-Pregnancy Years

During adolescence and young adulthood, several factors may promote early endothelial dysfunction and systemic inflammation, potentially contributing to premature cardiovascular disease. Both early (≤10 years) and late (≥17 years) menarche have been associated with an increased risk of future cardiovascular events [10–12]. Adolescent obesity contributes to the development of metabolic syndrome and pro-thrombotic pathways. Data from the Framingham study showed that women with obesity had a 64% higher risk of CHD compared to 46% of men with obesity [21]. Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age, affecting approximately 6–20% of this population. It is characterized by a cluster of metabolic abnormalities, including insulin resistance, dyslipidaemia, and hyperandrogenism, which are associated with an increased risk of type 2 diabetes (T2D), hypertension, and premature subclinical atherosclerosis [13–15]. Beyond these metabolic alterations, growing evidence suggests that women with PCOS may develop early endothelial dysfunction and subclinical vascular changes, potentially contributing to an adverse long-term cardiovascular risk profile. Moreover, PCOS has increasingly been recognized as a potential early marker of cardiometabolic vulnerability within the female life course, highlighting the importance of early screening and preventive strategies in young women [13–15].

Nevertheless, the relationship between PCOS and clinical cardiovascular events has become clearer over recent years. Earlier evidence suggested that, despite a higher prevalence of cardiometabolic risk factors, women with PCOS did not have a significantly increased risk of non-fatal coronary artery disease, although an increased risk of non-fatal cerebrovascular events was observed [13]. However, accumulating evidence from larger contemporary meta-analyses and nationwide cohort studies has substantially strengthened the association between PCOS and adverse cardiovascular outcomes. A recent meta-analysis including more than one million women demonstrated that PCOS is associated with a significantly higher risk of composite cardiovascular disease, ischemic heart disease, myocardial infarction, and stroke [16]. These findings are consistent with the 2023 International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome, which recognizes the increased cardiovascular risk associated with PCOS and recommends comprehensive cardiovascular risk assessment throughout adult life [17]. Furthermore, a large Nordic nationwide cohort study showed that the increased cardiovascular risk persisted even among women with normal body mass index and without type 2 diabetes, supporting the concept that PCOS should be considered not only a reproductive and metabolic disorder but also an early marker of long-term cardiovascular vulnerability [22].

Menstrual cycle characteristics may also provide useful information on future cardiovascular risk. Increasing evidence supports an association between menstrual cycle abnormalities, cardiometabolic risk factors, and cardiovascular disease [23]. Notably, only a small proportion of the association between menstrual cycle regularity and duration and cardiovascular risk appears to be explained by chronic hypertension, type 2 diabetes, and hypercholesterolaemia, suggesting that menstrual cycle dysfunction may represent an early marker of future cardiovascular risk [24]. Premenstrual syndrome has also been associated with fluctuations in arterial stiffness and blood pressure [25], while more severe premenstrual symptoms may be associated with an increased risk of developing hypertension before the age of 40 years [26]. Among overweight or obese women with PCOS, lifestyle interventions may improve several cardiometabolic risk factors [27]. More broadly, the cumulative duration of exposure to cardiovascular risk factors is important, as lifetime risk is strongly influenced by early and persistent cardiometabolic abnormalities. Cardiovascular assessment during early adulthood should include family history of premature CVD, early-onset hypertension, diabetes, dyslipidaemia, PCOS, systemic

inflammatory diseases, and exposure to tobacco, vaping, or recreational drugs. Blood pressure, lipid profile, BMI or waist circumference, and glucose levels should ideally be evaluated before a first pregnancy.

Menarche timing and menstrual irregularity should therefore be interpreted as contextual information. They may prompt screening for obesity, hypertension, glucose intolerance or an underlying endocrine disorder, but their incremental predictive value over routinely measured risk factors, and the benefit of any menarche-based surveillance schedule, have not been established. A patient with a normal menstrual history can still have substantial vascular risk, and conversely an early or late menarche does not itself establish high absolute cardiovascular risk [10–12,23,24].

4. Pregnancy as a Cardiovascular Stress Test

Pregnancy may unmask susceptibility to endothelial dysfunction, abnormal vascular remodelling, and metabolic disturbances [28]. Hypertensive disorders of pregnancy (HDP), including gestational hypertension, pre-eclampsia, eclampsia, and chronic hypertension with superimposed pre-eclampsia, are associated with a twofold or greater long-term risk of CVD, including CAD, stroke, heart failure (HF), heart valve disease, atrial fibrillation, and permanent arterial hypertension [29]. Women show a more rapid increase in blood pressure (BP) than men, starting as early as age 30 [30], and those who have had HDP have a 2 to 7.7 times greater risk of developing CAD [31]. Women who have had early pre-eclampsia (<34 weeks of gestation) have the highest risk of developing future cardiovascular events [31]. These observations support the concept that pregnancy complications should be regarded as important markers of future cardiovascular risk rather than isolated obstetric events. These observations are further supported by the 2025 AHA/ACC hypertension guideline, which emphasizes early identification and appropriate management of hypertension during pregnancy. These recommendations further support the concept that pregnancy should be considered a critical opportunity for cardiovascular risk assessment and timely implementation of preventive strategies [32].

In the short term, women who have had HDP have a higher risk of developing hypertension, dyslipidemia and diabetes. Long-term follow-up studies have shown that approximately one-third of women develop hypertension before the age of 40 after a pregnancy complicated by HDP [33]. The severity of pre-eclampsia also appears to influence long-term cardiovascular risk. In fact, a recent study observed that 41.5% of women with severe pre-eclampsia experienced an increase in BP one year after giving birth [34]. Most HDPs are explained by the formation of pro-inflammatory products from a dysfunctional placenta during pregnancy. Together with hypertension, dyslipidaemia, insulin resistance, circulating angiogenic proteins, and dysregulation of the renin–angiotensin–aldosterone system, these mechanisms may accelerate vascular dysfunction and contribute to earlier development of atherosclerosis, microvascular disease, and heart failure [18,35–37]. In addition, women with HDP have an increased burden of subclinical atherosclerosis, confirmed by increased carotid intima-media thickness and higher coronary artery calcium (CAC) score compared to age-matched controls [38,39]. Recent large-scale analyses based on Mendelian randomization and population data support a causal contribution of genetic predisposition to HDP to subsequent CVD, reinforcing the concept that pregnancy complications are not only indicators but actual risk factors [40,41]. Gestational diabetes mellitus (GDM) and preterm delivery confer additional cardiovascular risk, accelerating diabetes and subsequent atherosclerotic events, and should be documented and treated as significant risk factors [42].

The biological link between pre-eclampsia and later CVD extends beyond a nonspecific statement of chronic inflammation. Defective placental vascular remodelling, antiangiogenic signalling (including excess soluble fms-like tyrosine kinase-1 relative to

placental growth factor), oxidative stress, endothelial nitric-oxide dysfunction and microvascular injury are implicated in the acute syndrome. Subsequent hypertension, endothelial activation, persistent metabolic abnormalities and subclinical cardiac remodelling may contribute to longer-term risk [18,20,35–37]. Nevertheless, overlap between pre-pregnancy susceptibility and effects of the pregnancy itself complicates causal attribution; even genetic evidence does not establish that all observed excess risk is mediated by the obstetric episode.

In particular, approximately 10% of pregnant women develop GDM [43] and after delivery are exposed to a higher cardiometabolic risk, including T2D, hypertension and hypercholesterolemia [44,45]. Women with previous GDM have approximately double the risk of future cardiovascular events, and even in the absence of postpartum T2D, cardiovascular risk remains significantly increased [46].

In the Coronary Artery Risk Development in Young Adults (CARDIA) study, women with previous gestational diabetes showed a higher prevalence of subclinical atherosclerosis approximately 15 years after pregnancy [47]. In addition, both mothers with GDM and their offspring appear to have an increased long-term cardiovascular risk [48]. Other adverse pregnancy outcomes (APOs), including spontaneous abortions, small or large for gestational age babies, and preterm delivery, are also associated with an increased risk of developing future cardiovascular disease [49]. A J-shaped relationship between parity (number of pregnancies) and future CVD risk has been described [49,50]; in fact, multiparity has been associated with an even greater risk of CVD, with the risk of CAD within 10 years of delivery being 2.26 times higher [51]. Conversely, breastfeeding is considered a protective factor associated with reduced risk of CVD and T2D [52,53], as confirmed by Magnus et al., who observed a lower risk of CVD among women with HDP who breastfed compared to those who did not [54].

5. Postpartum and Interpregnancy Window

The first decade after HDP or gestational diabetes is characterized by a substantial increase in chronic hypertension, metabolic syndrome, and subclinical cardiac dysfunction, including phenotypes resembling HFpEF. Women with a history of pre-eclampsia or gestational hypertension often develop chronic hypertension within a decade and show increased left ventricular hypertrophy and diastolic dysfunction that predispose them to heart failure and coronary artery disease [6]. Despite this, systematic cardiovascular follow-up after complicated pregnancies is rare, and few guidelines specify structured postpartum pathways. Risk assessment at 6–12 weeks postpartum, followed by periodic reassessment, should include blood pressure, BMI or waist circumference, fasting lipids, glucose or HbA1c, and lifestyle counselling. However, evidence regarding the optimal frequency of follow-up and treatment thresholds remains limited. In fact, no randomized clinical trial has evaluated the effects of postpartum interventions on long-term maternal CVD outcomes. Pregnancy and the postpartum period may represent unique opportunities to promote cardiovascular prevention, particularly among women planning future pregnancies.

Current cardiovascular risk calculators may underestimate long-term cardiovascular risk in young women after pregnancies complicated by HDP in stratifying risk for primary cardiovascular follow-up and prevention, as these calculators neglect the impact of pregnancy complications and are often not applicable below the age of 40 [55]. In clinical practice, these women may benefit from closer cardiovascular follow-up and earlier management of modifiable risk factors. In contrast, conventional risk scores may provide more appropriate estimates in older women; however, the potential benefit of preventive interventions may be attenuated when risk factors are addressed late in life [56]. The FIGO (International Federation of Gynecology and Obstetrics) has recommended follow-up at

6–12 weeks after a pregnancy complicated by HDP or any other complication associated with placental dysfunction, including BP measurements and the possibility of considering screening for other risk factors [57]. Recent hypertension guidelines have further emphasized the importance of long-term cardiovascular surveillance in women with previous hypertensive disorders of pregnancy [58]. If postpartum or interpregnancy assessment identifies a woman at high risk of recurrent pre-eclampsia, low-dose aspirin should be considered during a subsequent pregnancy, according to current obstetric and cardiovascular guidelines, rather than as a treatment during the postpartum period itself.

However, access to good-quality healthcare remains a problem not only in low-income countries, but also in high-income countries that do not have a healthcare system that guarantees equity and universal access to healthcare services. In the postpartum period, women who developed hypertension during pregnancy are advised to continue antihypertensive therapy and to discontinue it gradually depending on whether or not the target blood pressure has been achieved [59].

As many women are discharged three to seven days after delivery, postpartum pre-eclampsia may often go undiagnosed in some previously normotensive women. Therefore, it is important to plan for follow-up after discharge in a woman with HDP, which may include specialist hospital/outpatient follow-up and/or community healthcare system follow-up, depending on available resources [18]. In addition, home BP monitoring (HBPM) may also be an adequate solution for some populations, helping them to achieve normotension after delivery. A recent randomized clinical trial reported improved blood pressure control at 9 months postpartum among women using self-monitoring strategies [60].

Importantly, subsequent imaging substudies of the POP-HT trial suggested that the benefits of optimized postpartum blood pressure management extended beyond blood pressure control. At 9 months, women assigned to blood pressure self-monitoring with physician-guided antihypertensive titration showed more favorable cardiac remodelling, including lower left ventricular mass, higher biventricular ejection fractions, and lower left atrial volumes [61]. More recent vascular data also showed lower pulse wave velocity and greater aortic distensibility, further supporting the postpartum period as a potential window for early cardiovascular intervention after hypertensive pregnancy [62].

As recently emphasized by the American Heart Association, women of childbearing age should ideally optimize their cardiovascular health before subsequent pregnancies by avoiding tobacco, alcohol, and recreational drugs, maintaining a healthy weight and balanced diet, and engaging in regular physical activity. These measures may reduce the risk of hypertensive disorders of pregnancy and placental dysfunction while also contributing to improved long-term cardiovascular health [63].

The Diabetes Prevention Programme (DPP) has shown that intensive lifestyle intervention aimed at weight loss and physical activity successfully reduced the incidence of diabetes by 50% compared to placebo among patients with a history of gestational diabetes [64]. Subsequently, other randomised clinical trials were conducted using the lifestyle intervention proposed by the DDP in the postpartum period, with significant effects on body weight outcomes. Specifically, the components of the intervention included lifestyle coaching, goal-setting for calorie intake and physical activity, self-monitoring and feedback on weight, diet and healthy behaviours related to physical activity, and multimedia educational materials [65–68].

Women with gestational diabetes should be screened for blood glucose 4 to 12 weeks after delivery with a 2-h 75 g oral glucose tolerance test [69]. For women who do not complete this test, glucose screening with hemoglobin A1c or fasting blood glucose should be considered within the first year after delivery. In addition, ongoing screening for diabetes or prediabetes is recommended every 1–3 years for patients with a history of GDM and

may be considered in those with a history of any APO. Within the first year after delivery, it is reasonable to perform a lipid profile to establish a baseline value in order to detect familial hypercholesterolemia and assess CVD risk [70]. In addition, in patients with suspected familial hypercholesterolemia or those who have difficulty accessing primary care, a lipid profile may be indicated at the 6-week postpartum visit. The peripartum period is a vulnerable time for maternal sleep disorders, and women generally experience increased night-time awakenings, more fragmented sleep and reduced sleep efficiency. Maternal sleep disorders associated with obstructive sleep apnea may increase the risk of CVD, so it is necessary to improve subjective sleep quality through non-pharmacological interventions such as massage and exercise and to treat apnea with a sleep medicine specialist after delivery [71,72]. Finally, postpartum depression affects up to 10% of women during the first year after delivery and should be actively screened for during routine follow-up visits [73–75].

The immediate postpartum pathway differs by complication. After HDP, blood pressure should be reviewed early, generally within 3–10 days after discharge, with earlier assessment in severe or uncontrolled cases; home measurement and medication adjustment may help bridge gaps in care [32]. Assessment of persistent hypertension and cardiometabolic risk can be revisited around 6–12 weeks and subsequently in primary care. After GDM, the priority is a 75-g oral glucose tolerance test at 4–12 weeks postpartum, because early postpartum HbA1c alone may miss dysglycaemia; lifelong diabetes screening every 1–3 years is recommended even when the initial test is normal [76]. Lipids, weight, smoking and family history can be evaluated after pregnancy-related physiological changes have settled, with treatment or specialist referral driven by actual abnormalities and standard indications. Programmes of home BP monitoring have improved intermediate outcomes, but convincing evidence of fewer long-term myocardial infarctions or strokes is not yet available [32,60–62].

6. Midlife Transition and Menopause

Natural menopause typically occurs at around age 50 [77]. During the menopausal transition, declining estrogen levels are associated with adverse changes in body fat distribution, lipid metabolism, vascular stiffness, and autonomic regulation, contributing to accelerated atherosclerosis beyond normal ageing. In particular, there is an increase in total cholesterol, LDL (low-density lipoprotein) cholesterol, triglycerides, and apolipoprotein B levels, with a decrease in HDL (high-density lipoprotein) cholesterol [19,78]. During this period, the incidence of ischaemic heart disease and stroke begins to increase significantly, and traditional risk factors (particularly high blood pressure, dyslipidemia and T2D) become highly prognostic in women [79]. In fact, the risk of CVD is higher in postmenopausal women than in premenopausal women of the same age [80]. The Framingham study suggested that higher levels of BP, total cholesterol and other CVD risk factors before menopause are associated with early menopause, regardless of smoking [81]. A similar result emerged in another study, in which the occurrence of a first CVD episode at a young age (before 35 years) was associated with a doubling of the risk of early menopause, confirming that poorer premenopausal cardiovascular health can influence the onset of menopause [82]. In addition, several meta-analyses have found that women with early menopause are at significantly higher risk of CAD, as well as an increased risk of heart failure, compared to those who enter menopause from the age of 45 onwards [83,84]. A longer duration of menopause may prolong exposure to adverse cardiometabolic changes, including higher levels of LDL cholesterol, triglycerides, total cholesterol, and lipoprotein(a), thereby promoting cardiovascular disease [85,86]. In contrast, the SWAN study reported that blood lipid levels peaked during late perimenopause and early postmenopause compared to the premenopausal phase [87]. Vasomotor symptoms (VMS),

commonly referred to as hot flushes, are frequent during menopause and have been associated with an unfavorable cardiometabolic profile and increased cardiovascular risk [88,89]. In particular, very severe, frequent or persistent vasomotor symptoms are associated with an increased risk of future CVD, even after taking into account traditional risk factors for CVD [90,91]. This was observed in the SWAN study, in which women who experienced hot flushes had reduced flow-mediated dilation and increased aortic calcification compared to those who did not, regardless of traditional risk factors and estradiol levels [92]. Several studies have reported associations between poor sleep quality, metabolic syndrome, and carotid atherosclerosis, which remained significant even after accounting for estradiol levels, cardiovascular risk factors, and hot flushes [93,94]. Furthermore, according to data from the SWAN study, women aged 46 to 59 with ≥3 episodes of depression had greater coronary artery calcification [95]. Lifestyle interventions may also play an important role during the menopausal transition. Several randomized trials and meta-analyses have evaluated the effects of dietary modification and physical activity in this setting. In the Women's Healthy Lifestyle Project (WHLP), a combined diet and exercise program attenuated the increase in LDL cholesterol, prevented weight gain during the transition from premenopause to peri- and postmenopause, and improved several cardiometabolic parameters, including blood pressure, glucose, insulin, and triglyceride levels [96]. Menopausal hormone therapy (MHT) has complex cardiovascular effects. Large randomized trials and meta-analyses have reported a low absolute cardiovascular risk among healthy women younger than 60 years or within 10 years of menopause. However, an increased risk of venous thromboembolism and, in selected settings, ischemic events has also been reported [8]. Menopausal hormone therapy (MHT) should be considered for an established menopausal indication, chiefly troublesome vasomotor symptoms, not for primary cardiovascular prevention. Lipid-lowering treatment addresses dyslipidaemia and atherosclerotic risk but is not a therapy for hot flushes. Choice of MHT requires assessment of age, time since menopause, uterine status, personal history of breast or endometrial cancer, previous venous thromboembolism or stroke, known coronary disease, severe hypertriglyceridaemia and other relevant contraindications. Systemic therapy may have a more favourable benefit–risk profile when started before age 60 or within 10 years of menopause in appropriately selected women; route, dose and the need for progestogen matter. Transdermal oestrogen may be preferable to oral treatment in women with selected thrombotic or metabolic risk factors, but individualized specialist discussion is essential when cardiovascular disease is established [97–99]. For selected women whose primary-prevention treatment decision remains uncertain after conventional risk estimation and consideration of risk enhancers, CAC scoring can provide further information on atherosclerotic burden; it is not a prerequisite for MHT nor a general screening test for menopausal symptoms [100]. When atherosclerotic burden is significant, lipid-lowering therapy may be warranted. Recent US recommendations [100] have further strengthened the role of coronary artery calcium (CAC) scoring in this context. In individuals with borderline or intermediate estimated risk, CAC can help refine risk stratification and support shared decision-making regarding lipid-lowering therapy. In particular, the absence of coronary calcification may justify a more conservative approach focused on lifestyle measures, whereas the presence of CAC, especially at higher levels, identifies individuals who are more likely to benefit from earlier and more intensive preventive strategies. This approach is particularly relevant in women during the menopausal transition, when traditional risk estimation may not fully capture the underlying burden of atherosclerosis. Although women remain underrepresented in many lipid-lowering trials, available evidence supports the benefit of statins in appropriately selected women undergoing primary prevention. In the JUPITER trial, rosuvastatin significantly reduced cardiovascular events in women without established CVD, with a relative risk

reduction comparable to that observed in men; this finding was further supported by a meta-analysis of primary prevention statin trials [101]. The main limitation of lipid-lowering therapy is that current cardiovascular prevention guidelines do not offer personalized recommendations for women, but classify them into broader special population groups [8]. Beyond the menopausal transition, cardiovascular risk continues to increase with ageing. Older women frequently present with multimorbidity, atrial fibrillation, HFpEF, and polypharmacy, factors that should be considered when individualizing preventive strategies.

The menopause transition should be distinguished from chronological ageing and from premature ovarian insufficiency. Oestrogen withdrawal affects hepatic lipoprotein handling, visceral adiposity, endothelial nitric-oxide signalling and arterial stiffness, while sleep disturbance and vasomotor symptoms may indicate an unfavourable vascular phenotype without proving a causal pathway. Earlier menopause has been linked to higher subsequent cardiovascular risk in observational cohorts, but shared vascular risk preceding menopause and possible reverse causation remain important considerations [19,77–84]. MHT prescribing should therefore follow symptom-oriented menopause guidance and individualized safety assessment, while statins, antihypertensive drugs and other preventive treatments should follow established cardiovascular indications [99,100].

7. Late Life and Frailty

In older women, the absolute risk of CVD is high and often coexists with multimorbidity, frailty, and polypharmacy. HFpEF, atrial fibrillation (AF), microvascular angina, and myocardial infarction with non-obstructive coronary arteries (MINOCA) are particularly prevalent in older women and may present with greater dyspnea, atypical fatigue, and other non-classical symptoms compared with men [6]. Although hypertension is less prevalent in younger women, its prevalence increases markedly with age and eventually exceeds that observed in men [102]. Ageing is associated with rising blood pressure in both sexes, although sex-specific trajectories have been described. In particular, although systolic blood pressure is lower in young women, BP increases more rapidly with age, as demonstrated by four large US cohorts involving over 32,000 adults [30]. Traditional risk scores become less discriminative in advanced age, when multimorbidity and competing non-cardiovascular causes of death increasingly influence prognosis. Clinical judgement is therefore essential, particularly when considering the potential benefits and risks of menopausal hormone therapy [98].

When lifestyle interventions alone are insufficient, the intensity of preventive strategies should be individualized by considering the competing risk of non-cardiovascular death, together with relevant findings from geriatric assessment, including cognitive status, risk of falls, and functional capacity.

Evidence remains limited regarding optimal blood pressure targets and LDL-C goals in frail older women, largely because this population remains underrepresented in clinical trials [79].

8. Female-Specific and Female-Predominant Risk Factors

Several female-specific and female-predominant conditions should be systematically considered during cardiovascular risk assessment in women [103]. In particular, as suggested by the Lancet Commission, risk factors for female CVD can be divided into three general categories: (1) well-known (modifiable) risk factors that affect both sexes; (2) female-specific risk factors (PCOS, premature ovarian failure, early and/or surgical menopause) or risk factors that affect women more than men (systemic autoimmune diseases, migraine with aura, radiotherapy and systemic therapies for breast cancer, depression,

psychiatric disorders); (3) risk factors related to gender and the environment in which a woman lives (partner violence, chronic stress and caregiving burden) [104]. Autoimmune diseases are more prevalent in women and may accelerate both atherosclerosis and coronary artery disease. In a large British study of over 22 million people, women with autoimmune diseases were shown to have a higher risk of incident CVD than age-matched controls, and this risk increased progressively with the number of autoimmune diseases present. In particular, systemic sclerosis, Addison's disease, systemic lupus erythematosus (SLE) and type 1 diabetes mellitus had the highest risk of CVD [105]. Infertility has also emerged as a potential marker of increased cardiovascular risk in women. In the Nurses' Health Study, women with a history of infertility had a 13% higher risk of CAD. The association appeared stronger among women reporting infertility at a younger age (≤25 years) and in women whose infertility was secondary to ovulatory disorders such as PCOS or endometriosis [106]. Endometriosis is associated with an increased risk of hypercholesterolemia and hypertension, and in fact, women with endometriosis have a 23% higher risk of developing CVD than healthy women [107]. Chronic inflammation is thought to represent one of the main mechanisms linking endometriosis to accelerated atherosclerosis and cardiovascular disease [108]. Social and environmental determinants of health are frequently overlooked despite their potential impact on cardiovascular risk. In particular, socioeconomic disparities at every stage of life disproportionately affect women's future cardiovascular health; these include family income, education, literacy, language barriers, healthcare systems, marital status, social support, physical environment, economic stability, racism, culture, sexual orientation, and gender identity [109–112]. Particular attention should be paid to women with systemic immune-mediated diseases, given their increased risk of cardiovascular mortality [113]. Many of these factors are not incorporated into current risk prediction models and may contribute to underestimation of cardiovascular risk in women. Their recognition should support more individualized preventive strategies [103].

Race, ethnicity and social position also shape when risk is recognized and which preventive options are accessible. In the United States, Black women experience a disproportionate burden of hypertension and hypertensive pregnancy disorders, whereas risk patterns within Hispanic/Latina, Asian and other communities vary substantially by national origin, migration history, cardiometabolic profile and access to care [114,115]. These broad labels are social and epidemiological descriptors, not interchangeable biological categories; rates should not be compared without accounting for age, geography and how outcomes were ascertained. South Asian ancestry, for example, may coexist with elevated cardiometabolic risk at a lower body mass index, while other Asian subgroups have different patterns. Where data are available, reporting disaggregated categories is preferable to a single aggregate estimate.

Socioeconomic gradients operate through differential exposure and differential opportunity for prevention. Material deprivation, precarious employment, food insecurity, housing instability, neighbourhood conditions, racism, caregiving responsibilities, low health literacy and insurance or transport barriers can influence blood pressure control, obesity, diabetes detection and postpartum attendance [109–112,115]. These factors should be recorded where clinically relevant and linked to practical responses—accessible appointments, culturally appropriate counselling, medication affordability, home BP monitoring and continuity between obstetric and primary care—rather than used as a surrogate for an individual patient's physiology. Evidence that a risk association differs across populations should not automatically be interpreted as proof of intrinsic ethnic susceptibility.

8.1. Coronary Phenotypes: Obstructive and Non-Obstructive Disease

A life-course discussion of coronary risk is incomplete if all ischaemic presentations are treated as conventional plaque-driven stenosis. Women experience obstructive atherosclerotic CAD, but are relatively more likely than men to present with ischaemia with non-obstructive coronary arteries (INOCA), coronary microvascular dysfunction, vasomotor disorders, myocardial infarction with non-obstructive coronary arteries (MINOCA) or spontaneous coronary artery dissection (SCAD). These are not mutually exclusive labels: MINOCA is a working diagnosis after an infarction presentation, SCAD is a non-atherosclerotic coronary lesion, and INOCA describes an ischaemic syndrome requiring mechanism-oriented investigation [116,117].

In a large infarction cohort summarized by the 2026 ESC scientific statement, MINOCA occurred in approximately 10.5% of women versus 3.4% of men presenting with myocardial infarction; around 90% of patients with SCAD were women [116]. These proportions are context-dependent and should not be interpreted as screening prevalence in the general population. Women with symptoms or objective ischaemia despite no obstructive lesions should not be reassured solely on the basis of angiography; assessment may include coronary functional testing, stress perfusion imaging or cardiac magnetic resonance according to the clinical setting. Treatment depends on the mechanism and does not follow a single pathway applicable to all non-obstructive phenotypes [116,117].

The sex differences in Table 2 concern diagnosis and secondary prevention once symptoms or an acute event have occurred. They do not justify population imaging or angiography in asymptomatic young women solely because of sex or reproductive history.

Table 2. Coronary disease phenotypes relevant to sex-sensitive risk assessment. Clinical proportions refer to selected symptomatic cohorts and are not population screening rates [116,117].

Phenotype	Sex-Related Pattern	Typical Mechanism/Presentation	Implication for Assessment
Obstructive atherosclerotic CAD	Common in both sexes; men generally have a greater epicardial plaque burden at younger ages	Epicardial plaque and stenosis; ACS or chronic coronary syndrome	Treat conventional risk factors; use established diagnostic and secondary-prevention pathways.
INOCA/coronary microvascular dysfunction	Relatively frequent among symptomatic women without obstructive CAD	Impaired microvascular vasodilator reserve and/or microvascular spasm; exertional or rest angina	Avoid ruling out ischaemic disease from a non-obstructive angiogram alone; consider mechanism-specific evaluation.
Vasospastic angina	Occurs in both sexes; sex differences vary by referral population	Transient epicardial or microvascular spasm with angina and ischaemic ECG changes	Assess vasomotor mechanisms when clinically indicated; treatment differs from fixed obstructive CAD.
MINOCA	Approximately 10.5% in women versus 3.4% in men among MI presentations in one large cohort	Working diagnosis; causes include plaque disruption, SCAD, spasm, embolism and microvascular dysfunction	Use additional investigation (including CMR when indicated) to identify cause; avoid a one-size-fits-all regimen.
SCAD	Approximately 90% of affected patients are women in contemporary series	Non-atherosclerotic dissection/intramural haematoma; ACS often in early or middle adulthood	Recognize pregnancy-associated and other triggers; individualize acute care and longer-term counselling.

8.2. Weight of Evidence for Female-Specific Risk Modifiers

Reported associations differ markedly in precision, independence from traditional risk factors and clinical usefulness. Relative risk estimates describe associations in the

populations studied; they are not transferable treatment thresholds. Table 3 therefore separates the type of evidence from the action that can reasonably follow. Estimates are intentionally illustrative rather than pooled de novo across heterogeneous studies.

Table 3. Representative associations, evidence type and clinical implications of risk factors across the female life course. Values are illustrative, not new meta-analytic estimates; they should be interpreted alongside absolute baseline risk [10–12,16,17,22,31,46,49,83,84,105,113,118].

Exposure	Illustrative Evidence/Estimate	Interpretive Caveat	Proportionate Clinical Action
Hypertensive pregnancy disorders	Meta-analytic cohorts: approximately twofold or greater long-term CVD association [31,49]	Shared antecedent risk and severity affect estimates; prevention trials with CVD endpoints lacking	Early BP review; later BP, lipid and glycaemic assessment; treat established abnormalities.
Gestational diabetes	Observational meta-analysis: approximately twofold future CVD risk [46]	Partly mediated by later type 2 diabetes; no direct proof that a novel CVD score improves care	75-g OGTT 4–12 weeks postpartum, then diabetes screening every 1–3 years [76].
Polycystic ovary syndrome	Cohorts/meta-analyses associate PCOS with incident cardiometabolic disease and selected CVD outcomes [16,17,22]	CVD endpoint estimates vary by age, adjustment, BMI and outcome	Screen BP, glycaemia and lipids; manage metabolic risk using existing guidance [17].
Early/late menarche	U-shaped associations with later vascular disease in large observational cohorts [10–12]	Potential residual confounding by adiposity, deprivation, nutrition and illness	Investigate accompanying clinical abnormalities; no menarche-only intervention threshold.
Early menopause/ovarian insufficiency	Prospective and pooled cohort associations with CHD and HF [83,84]	Chronological ageing, prior vascular health and potential reverse causality complicate interpretation	Reassess BP, lipids, glucose and smoking; distinguish MHT symptom treatment from CVD prevention.
Systemic autoimmune diseases	Large observational cohorts and meta-analysis show elevated incident CVD and cardiovascular death [105,113]	Disease activity, inflammation and drugs may modify risk	Control conventional risk factors and coordinate care with disease specialists.
Menopause-associated metabolomic signatures	UK Biobank prospective cohort: HR 1.18 per SD of signature for composite CVD [118]	Association after adjustment; insufficient external validation and clinical utility data	Research use; no routine omics-based treatment escalation.

Evidence of independent association does not establish improved discrimination, calibrated reclassification or net benefit. For example, a statistically significant hazard ratio for a reproductive exposure may add little to a model that already includes blood pressure, diabetes and lipids. Only prospective evaluations of clinical decisions and outcomes can establish whether explicitly incorporating the exposure improves preventive care.

9. Performance and Limitations of Current Risk Scores

Established cardiovascular risk scores differ in their derivation cohorts, eligible ages, geographical calibration, outcomes and prediction horizons; several have sex-specific equations and include large numbers of women, but most do not directly incorporate reproductive history. Their performance in women may be limited because they do not fully account for female-specific conditions, cumulative lifetime exposure to risk factors, ethnic diversity, or social determinants of health. In addition, several derivation cohorts included

relatively older populations. Further data are needed to improve risk prediction in younger women. These risk calculators work best at the population level (i.e., reflecting an average risk in a group) but less well at the individual level. It is not appropriate to rank these models solely on whether they were introduced recently: discrimination and calibration depend on the population and endpoint in which they are tested. PREVENT was developed in a contemporary cohort that included a substantial proportion of women and younger individuals, potentially improving its applicability across different populations [119]. PREVENT offers both 10-year and 30-year estimates in eligible adults and incorporates cardiovascular–kidney–metabolic information, but it does not directly encode obstetric history; despite extensive development and validation datasets, calibration and net benefit must still be assessed in the population and clinical setting where it is applied [100,119].

Distinct Prediction Horizons and Target Populations

PCE, SCORE2, QRISK3 and PREVENT should not be pooled as interchangeable 10-year calculators. SCORE2 is calibrated by European risk region and targets fatal and non-fatal atherosclerotic events; QRISK3 includes ethnicity and deprivation but was developed in English primary care; the US PCE and PREVENT equations use different generations of data, outcomes and eligible ages [8,9,100,119,120]. PREVENT can report risk at 10 and 30 years; its 30-year estimate is especially relevant to discussions with younger adults, but is not itself evidence that long-term treatment triggered by that number improves outcomes. Choice of model should therefore follow the locally endorsed guideline and the patient's eligibility, and estimates should not be directly compared as if they measured the same endpoint. The main characteristics, prediction horizons, target populations, and limitations of these cardiovascular risk assessment models are summarized in Table 4.

Table 4. Comparison of commonly used primary-prevention prediction systems. Age ranges describe general intended applications, not all local treatment indications [8,9,100,119,120].

Model	Typical Age and Setting	Horizon and Principal Outcome	Caution for Female Life-Course Care
PCE (US)	40–79 years; historical US cohorts	10-year first hard ASCVD events (non-fatal MI, CHD death, stroke)	No pregnancy history; race-based coefficients and historic calibration limit transferability.
SCORE2 (Europe)	40–69 years, apparently healthy; regional calibration	10-year fatal/non-fatal MI and stroke	Not designed for very young adults; reproductive exposures not direct inputs.
SCORE2-OP (Europe)	≥70 years; country risk calibration, older population	10-year fatal/non-fatal CVD with competing-risk adjustment	Frailty and competing morbidity still require bedside judgement.
QRISK3 (UK)	25–84 years; English general practice	10-year composite CVD including CHD, stroke/TIA	Includes ethnicity, deprivation and several comorbidities; not specifically validated for every non-UK population.
PREVENT (US)	30–79 years for 10- and 30-year risk; contemporary US cohorts	10- and 30-year ASCVD; related equations also estimate broader CVD including HF	Accounts for kidney/metabolic information but not obstetric factors; external calibration and local guidance matter.

For example, a 35-year-old woman with severe prior pre-eclampsia may have low short-term estimated risk because of her age. Her obstetric history should prompt an assessment of blood pressure, glycaemia, lipids and family history, not unvalidated numerical inflation of the calculated risk or automatic CAC imaging. In contrast, a 52-year-old

with uncertain primary-prevention lipid treatment eligibility may be a candidate for shared decision-making about CAC after conventional risk factors and risk-enhancing conditions have been reviewed [49,100].

Emerging approaches, including polygenic risk scores, cardiovascular imaging, and circulating biomarkers, may further refine risk assessment in women but are not yet routinely incorporated into guideline-endorsed prediction models [103].

Multi-omics approaches may eventually clarify the mechanisms and heterogeneity of female cardiovascular risk. Metabolomics and proteomics can describe signatures of insulin resistance, inflammation, lipoprotein remodeling and vascular injury that shift during pregnancy and menopause; integrated longitudinal profiles may be informative even when a traditional risk score is low. In a UK Biobank analysis of 67,582 postmenopausal women, a menopause-duration-associated plasma metabolomic signature was associated with incident CVD after adjustment (HR 1.18, 95% CI 1.15–1.21 per standard deviation), providing a promising research signal [118]. Yet a prognostic association is not the same as improved clinical decisions: assay standardization, replication across ancestries, calibration, decision-curve performance, cost-effectiveness and intervention trials are required before omics are incorporated into routine screening. Polygenic risk scores have analogous limitations, including ancestry-dependent transportability.

The main limitations of currently used cardiovascular risk prediction models in women are summarized in Figure 2. The recent US guidelines promote a broader and more longitudinal approach to cardiovascular risk assessment, integrating traditional risk estimation with additional modifiers and, when appropriate, imaging tools such as CAC. This combined strategy allows a more individualized evaluation of risk, particularly in subjects whose estimated risk falls into borderline or intermediate categories [100].

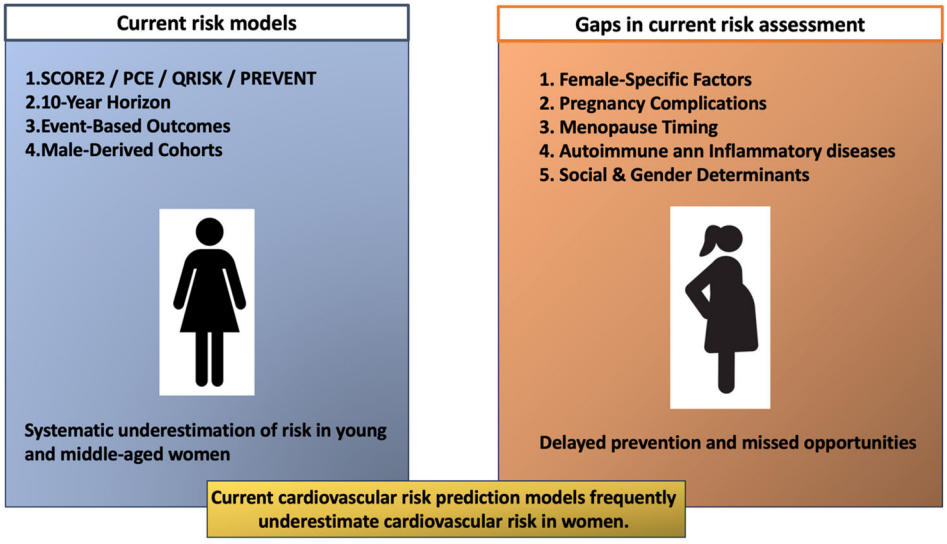


Figure 2. Limitations of current cardiovascular risk assessment tools in women. Risk models differ by age eligibility, endpoint, prediction horizon and geographical derivation. Although several use sex-specific equations and include women in development cohorts, reproductive and obstetric histories are generally absent from predictor sets. Some younger women may therefore have deceptively low short-term absolute risk despite risk-enhancing exposures; calibration should be tested rather than assuming uniform underestimation across all female populations. Abbreviations: SCORE2, Systematic COronary Risk Evaluation 2; PCE, Pooled Cohort Equations; QRISK, QResearch Cardiovascular Risk Algorithm; PREVENT, Predicting the Risk of Cardiovascular Events.

10. Imaging and Biomarkers Across the Life Course

Coronary artery calcium (CAC) scoring is a non-invasive imaging tool that may improve risk stratification in women with borderline or intermediate estimated risk, helping to guide preventive strategies and statin allocation [121]. CAC burden is a strong predictor of future cardiovascular events. The 2026 US ACC/AHA dyslipidaemia guideline considers CAC in selected primary-prevention adults whose treatment decision is uncertain, generally men aged ≥40 or women aged ≥45 years with borderline or intermediate estimated 10-year risk. In the guideline population, CAC 1–99 (below the 75th percentile) supports moderate-intensity statin treatment with an LDL-C goal <100 mg/dL (Class IIa); CAC 100–299 or at least the 75th standardized percentile supports an LDL-C goal <70 mg/dL with ≥50% reduction (Class I); CAC 300–999 supports the same <70 mg/dL goal (Class I), with intensification toward <55 mg/dL reasonable in selected patients (Class IIa); and CAC ≥1000 supports an LDL-C goal <55 mg/dL (Class I). These are US guideline recommendations for a defined population, not sex-specific trial-proven LDL-C targets or universal European rules. CAC = 0 can reduce the apparent need for immediate pharmacotherapy in selected settings but should not overrule major risk-enhancing conditions or clinical judgement. Figure 3 explicitly separates the conceptual accumulation of risk from actual CAC-guided management [100,122,123]. At the same CAC score, women have a higher risk of future CVD than men, and women with more extensive CAC in multiple vessels have higher cardiovascular mortality than men [123]. However, the absence of CAC in middle age does not imply the absence of risk when female-specific factors are present (e.g., severe preeclampsia, early menopause, breast cancer therapy). Although uncertainty remains regarding the optimal timing and frequency of CAC assessment in these subgroups, CAC may provide useful additional risk stratification, even in relatively young women [124,125]. Current risk assessment algorithms only partially incorporate female-specific factors, despite evidence suggesting important sex-related differences in the prognostic significance of CAC. Measurement of lipoprotein(a) at least once is supported in contemporary lipid guidance, whereas the additional value of routinely measuring high-sensitivity C-reactive protein, natriuretic peptides, troponin, adiponectin or novel biomarkers depends on the clinical question and has not been established for universal female-specific screening [100,126]. However, prospective female-specific data and cost-effectiveness analyses remain limited. In this framework, CAC is increasingly used not only as a prognostic marker but also as a practical tool to guide preventive strategies, helping clinicians tailor both the initiation and intensity of lipid-lowering therapy according to the underlying atherosclerotic burden.

Breast arterial calcifications (BAC), incidentally detected on routine mammography, have emerged as a potential opportunistic marker of cardiovascular risk in women. Recent meta-analyses have shown that the presence of BAC is associated with a higher risk of cardiovascular events and underlying coronary disease, as well as with stroke, heart failure, cardiovascular mortality, and all-cause mortality [127,128].

More recently, automated quantification of BAC using artificial intelligence was evaluated in a large, multi-institutional cohort of more than 120,000 women and showed a graded association with major adverse cardiovascular events, providing additional prognostic information beyond the PREVENT risk score [129]. BAC can be observed on mammograms obtained for breast cancer screening without a new examination. This makes it an appealing opportunistic signal for cardiovascular risk assessment, not an established independent screening indication. Although some studies show incremental prognostic associations beyond conventional scores, improvements in discrimination, calibration and clinically meaningful reclassification have not been consistently established, and no randomized evidence demonstrates that routine BAC notification improves cardiovascular outcomes. Reporting practices and quantification are heterogeneous; the downstream

costs, patient anxiety and testing consequences also require evaluation. A prudent response to an incidental BAC finding is to review conventional risk factors and prevention eligibility rather than automatically order CAC or initiate treatment solely on the basis of BAC [127–130].

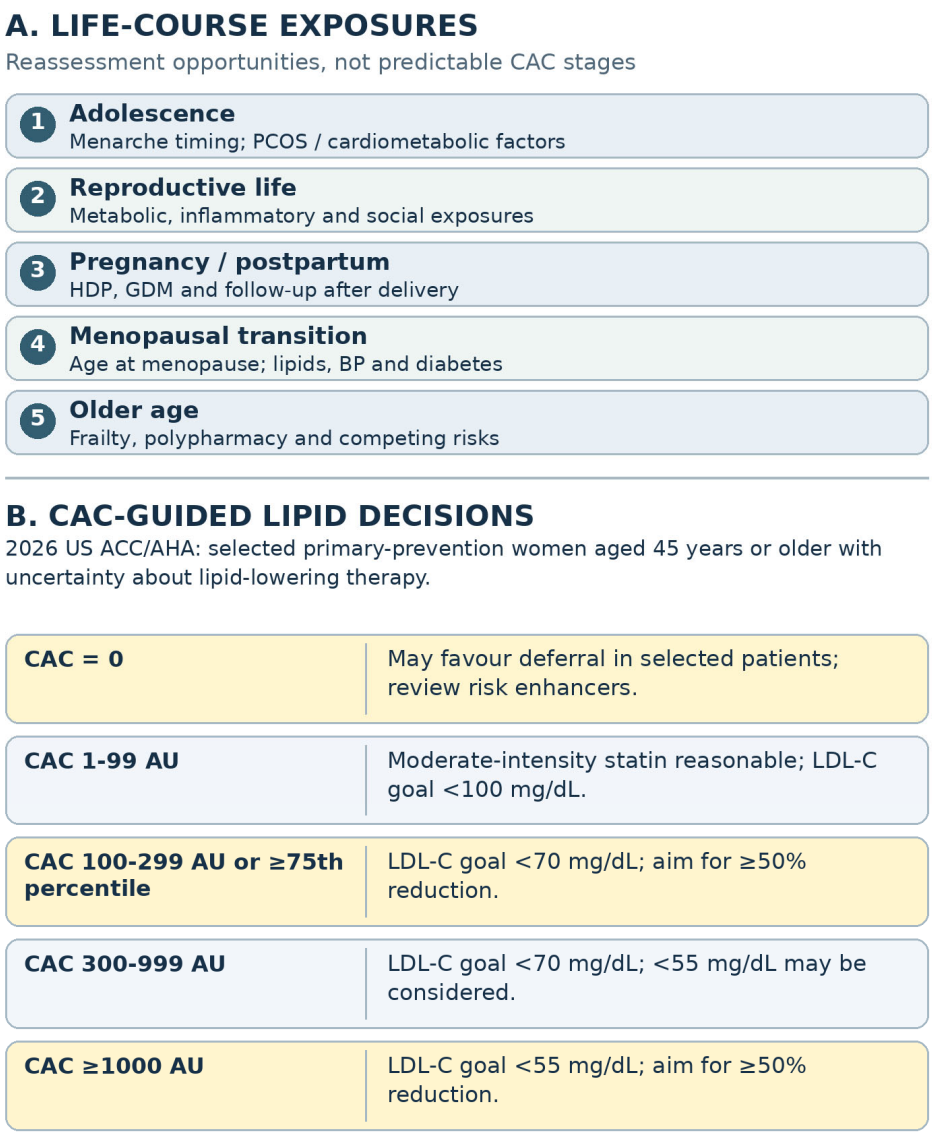


Figure 3. Life-course exposures (**A**) and separate CAC-guided lipid decisions (**B**). CAC thresholds are based on the 2026 US ACC/AHA guideline [100]; they do not define chronological stages. CAC, coronary artery calcium; AU, Agatston units.

A Pragmatic Clinical Pathway Across Life Transitions

We propose a two-stage approach: universal opportunities to document female-specific exposures and measure modifiable cardiovascular risk factors, followed by selective escalation only when a measurable abnormality, multiple modifiers, symptoms or uncertainty over a preventive decision warrants it. Table 5 identifies the relevant clinical encounters and separates established recommendations from reasonable but not formally validated follow-up suggestions. Figure 4 depicts the sequence of decisions and explicitly

excludes indiscriminate imaging in asymptomatic younger women. Neither should be interpreted as a validated female-only risk score.

Table 5. Proposed, guideline-anchored risk assessment and follow-up pathway by life-course window. The timing of general reassessment is individualized unless explicitly supported by a stated guideline [17,32,49,57,76,99,100].

Window/Trigger	Timing and Core Clinical Measures	Escalation or Referral	Evidence Boundary
Adolescence/PCOS	At recognition, check BP, adiposity, smoking, family history; assess lipids and glycaemia according to PCOS/metabolic guidance	Refer for hypertension, dysglycaemia, severe dyslipidaemia or suspected endocrine disorder	PCOS metabolic assessment is guideline-supported; no PCOS-only CVD drug threshold [17].
During pregnancy/HDP	Document HDP phenotype, severity and gestational timing; manage obstetric BP and complications	Obstetric/cardiology input for severe, persistent or complicated disease	Obstetric BP management follows pregnancy guidelines, not a generic CVD score [32].
Postpartum after HDP	BP review ~3–10 days after discharge; reassess persistent BP and cardiometabolic status around 6–12 weeks; follow up longitudinally	Persistent hypertension, symptoms or cardiac dysfunction warrant targeted care	Early BP review supported by guidance; optimal lifelong CVD visit interval not established [32,57].
Postpartum after GDM	75-g OGTT at 4–12 weeks; lifelong glycaemic screening every 1–3 years; assess weight and lipids	Diabetes, prediabetes or other metabolic abnormalities trigger standard treatment/referral	Specific glycaemic intervals are recommended by ADA; CV outcome benefit of intensified visits unknown [76].
Menopause/premature ovarian insufficiency	Reassess BP, lipid profile, glycaemia, smoking, family history and menopausal history at transition	Manage risk factors; decide MHT for symptoms with risk and contraindication review; selective CAC if lipid treatment uncertain	MHT is not CVD prevention; CAC subject to age, risk and guideline eligibility [99,100].
Later life/frailty	Periodically reassess competing risks, function, BP, medication burden and preventive priorities	Use shared decisions; refer for symptomatic CVD or complex multimorbidity	Avoid imposing unvalidated risk targets or routine imaging in frail older women [8,100].

For adult women without known CVD, symptom assessment and standard risk-factor measurement remain the first decision point. Persistently elevated BP, abnormal glycaemia, major dyslipidaemia or strong family history prompt guideline-based management irrespective of a low 10-year score. If eligibility for lipid-lowering treatment remains uncertain, a validated tool appropriate to age and geography should be used; sex-specific modifiers may inform shared decision-making, while CAC is selective and age-appropriate [8,9,100]. There is no evidence-based recommendation to obtain serial CAC scans, routine omics panels or universal cardiovascular specialist visits after every adverse reproductive event. The proposed pathway needs prospective evaluation for clinical impact and equity.

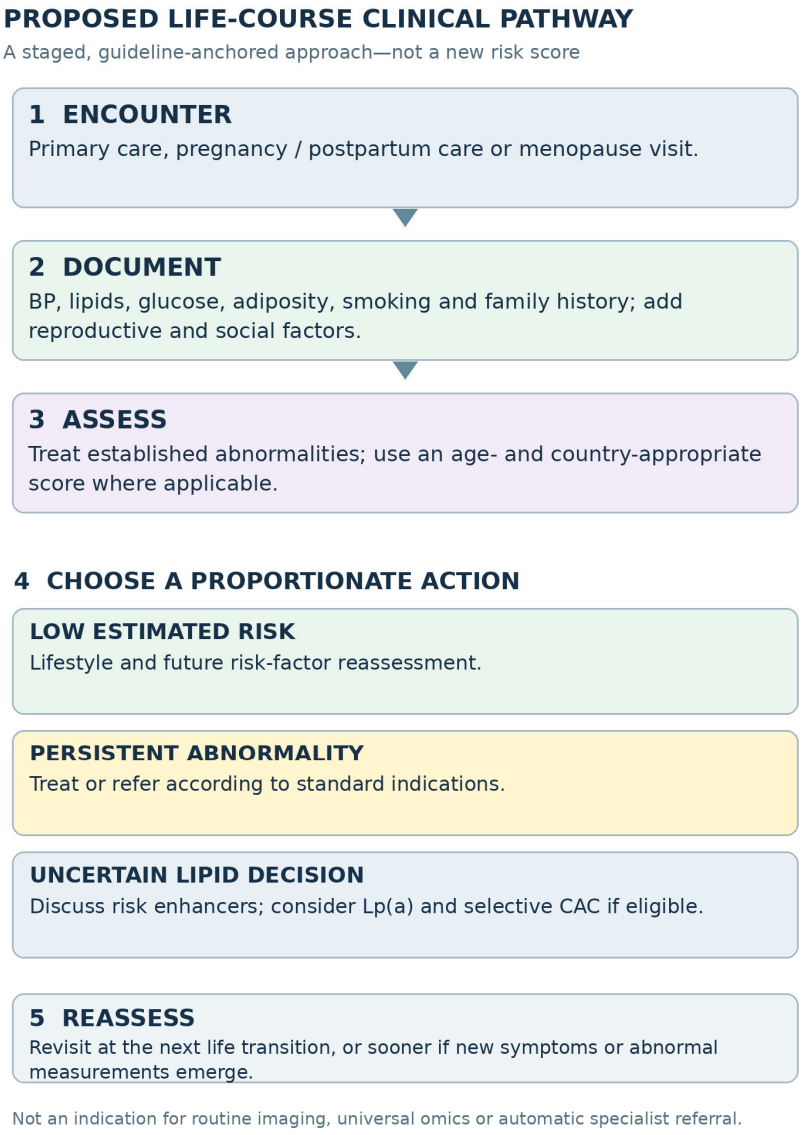


Figure 4. Proposed clinical pathway combining life-course risk history, conventional assessment, selective tests and follow-up; the algorithm is not yet prospectively validated.

11. Key Evidence Gaps

Several important evidence gaps persist across the female life course, including the underrepresentation of women in clinical trials, limited sex-specific analyses, scarce data on non-obstructive CAD, microvascular dysfunction, and HFpEF, and uncertainty regarding optimal treatment targets in women with female-specific risk conditions. Although recent postpartum interventions have improved blood pressure control and cardiovascular remodelling, it remains unknown whether these strategies reduce long-term maternal cardiovascular events [60–62].

In a study of 132 women with a mean age of 38 years, having a history of HDP approximately 10 years earlier than women with pregnancies uncomplicated by HDP was associated with a higher prevalence of left ventricular remodelling. Although physiological left ventricular remodelling occurs during pregnancy, it remains unclear whether pathological remodelling after delivery reflects persistent cardiovascular alterations related to APOs. Alternatively, these abnormalities may predate pregnancy and identify women who are already at increased cardiovascular risk [131]. A recent review of international guidelines showed that pregnancy complications and menopause are

increasingly recognized as important cardiovascular risk modifiers. However, clear management strategies remain limited because of the lack of adequately powered randomized trials. Data are particularly limited in low- and middle-income countries, among women from ethnic minorities, those with intersecting vulnerabilities (poverty, violence, migration), and women with disabilities.

Priority questions include whether adding standardized reproductive histories improves prediction beyond current equations, whether explicit changes in care pathways reduce events rather than merely increase testing, and whether approaches perform similarly across underrepresented ancestry and socioeconomic groups. New molecular markers must show transportability, calibration, feasible thresholds and incremental decision value. Prospective trials should measure absolute benefit, harms, healthcare utilization and patient-reported outcomes before a life-course algorithm can be adopted as an independent recommendation [100,115,118,130].

12. Conclusions

Cardiovascular risk in women develops across a continuum shaped by traditional risk factors, reproductive history, pregnancy-related complications, menopause, ageing, and female-predominant conditions. A life-course approach may identify cardiovascular vulnerability earlier than strategies based solely on short-term risk estimates. Polycystic ovary syndrome, hypertensive disorders of pregnancy, gestational diabetes, early menopause, autoimmune disease, and exposure to cardiotoxic cancer therapies should therefore be considered during routine cardiovascular assessment. Pregnancy and the postpartum period are particularly important opportunities for early recognition and prevention, although structured long-term follow-up remains inconsistent. In women whose estimated risk is uncertain, selected biomarkers and imaging tools, including coronary artery calcium scoring, may provide additional risk information. Breast arterial calcification detected on routine mammography may also serve as an opportunistic marker, although standardised reporting and management pathways are still needed. Integrating female-specific risk factors into longitudinal, multidisciplinary care may support more timely and individualised cardiovascular prevention. The practical contribution of this review is a staged assessment pathway that links documented exposures to measurable risk factors, correctly selected prediction tools and proportionate follow-up. This should be viewed as a clinical proposal for evaluation, not as a validated risk score or evidence that every female-specific association warrants additional testing or treatment.

13. Expert Opinion

The main challenge in cardiovascular prevention in women is no longer demonstrating that female-specific factors are relevant, but deciding how this information should change clinical practice. Conventional risk scores remain useful, yet their focus on short-term events may be reassuring in younger women even when lifetime exposure to risk is substantial. In our view, reproductive history should be considered part of the cardiovascular history rather than background obstetric information. Age at menopause, polycystic ovary syndrome, infertility, hypertensive disorders of pregnancy, gestational diabetes, preterm delivery, and exposure to cardiotoxic cancer therapies should be recorded systematically and interpreted together with traditional risk factors. Implementation should make use of healthcare encounters that already take place across the female life course. Preconception visits, antenatal care, postpartum assessment, consultations for menopausal symptoms, mammography, and routine primary care all provide opportunities to identify women who may benefit from earlier evaluation. This does not imply referral of every woman with a reproductive risk factor to a cardiologist. A practical first step would

be a standardised assessment of blood pressure, lipid and glucose profile, smoking, adiposity, and family history, followed by targeted referral when abnormalities persist, several risk enhancers coexist, or the estimated risk is inconsistent with the clinical history. Selected biomarkers, including lipoprotein(a), may provide additional information in specific settings [126]. Electronic health records could facilitate this process by making obstetric and reproductive information visible across specialties, but automated prompts should be linked to clear actions to avoid adding to alert fatigue. The postpartum period may offer the greatest immediate opportunity for improvement. Women with hypertensive disorders of pregnancy or gestational diabetes are identified at a stage when vascular and metabolic abnormalities may still be modifiable, but long-term follow-up is often lost when obstetric care ends. The vascular and myocardial consequences associated with preeclampsia support the need to view these complications as part of long-term cardiovascular care [20]. Shared pathways involving obstetricians, primary care physicians, cardiologists, endocrinologists, and maternal–foetal medicine specialists could improve continuity. Home blood pressure monitoring and digital follow-up may increase access, although their value should ultimately be assessed through sustained risk-factor control and cardiovascular outcomes rather than short-term engagement alone. Imaging should remain selective. Coronary artery calcium scoring may be particularly useful when conventional estimates are borderline, intermediate, or discordant with a woman's clinical profile. It should not become routine screening for all young women with reproductive risk factors, because the optimal age for testing, the meaning of a zero score at younger ages, and the cost-effectiveness of repeat assessment remain uncertain. Breast arterial calcification is promising because it can be detected during an examination already performed for another purpose. However, routine reporting should be accompanied by standardised quantification and a defined pathway for cardiovascular reassessment; otherwise, incidental findings may lead to anxiety and additional testing without proven clinical benefit. Important barriers remain. Care is still divided between specialties, pregnancy complications are not consistently transferred into cardiovascular records, and responsibility for long-term follow-up is often unclear. Most available evidence is observational, while women with frailty, ethnic and socioeconomic diversity, or intersecting vulnerabilities remain underrepresented. There is also a risk of overmedicalising common reproductive events if epidemiological associations are translated directly into treatment without considering absolute risk and patient preferences. The goal should be more accurate and timely prevention, not simply the expansion of the population labelled as high risk. This is increasingly relevant given projections of a rising burden of hypertension, diabetes, obesity, and cardiovascular disease among women [114]. Future research should prioritise prospective cohorts with standardised reproductive phenotyping, external validation of prediction models in diverse female populations, and randomised trials testing whether postpartum interventions reduce cardiovascular events. Studies should also establish when imaging provides clinically meaningful information beyond traditional risk factors and whether opportunistic markers such as breast arterial calcification improve treatment uptake and cost-effectiveness. Over the next five years, we expect cardiovascular risk assessment in women to become more longitudinal and more closely integrated into electronic health records. Reproductive and obstetric history will probably be captured more consistently, with targeted prompts for metabolic assessment and follow-up after adverse pregnancy outcomes. Conventional scores are unlikely to disappear, but will increasingly be complemented by female-specific modifiers and, in selected women, measures of subclinical atherosclerosis. Progress will depend less on the development of another score than on practical care pathways that convert information already available across a woman's life into timely and proportionate preventive action. The proposed framework differs from a list of female risk enhancers by specifying where information is obtained, when it should be

revisited, what is measured at that visit, and which findings change management. A prospective implementation study should test whether such a pathway improves sustained blood pressure and lipid control, postpartum glucose testing completion and appropriate referral without increasing unnecessary imaging. Future studies should report these outcomes across disaggregated racial, ethnic and socioeconomic groups and assess potential harms from overdiagnosis.

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