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Preeclampsia as a Risk Factor for Future Cardiovascular Disease : A Comprehensive Systematic Review

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ABSTRACT

Introduction: Preeclampsia (PE) affects 2–8% of pregnancies and is a leading cause of maternal morbidity. While its acute risks are well-recognized, emerging evidence suggests PE leaves a lasting imprint on maternal cardiovascular health. However, the magnitude of risk for specific cardiovascular outcomes, the role of PE severity and recurrence, and the underlying mechanistic pathways remain incompletely synthesized.

Methods: This systematic review synthesizes 80 studies (cohort, case-control, meta-analyses, systematic reviews) identified through structured screening. Inclusion required documented PE diagnosis, a normotensive control group, cardiovascular outcomes (events or risk factors), ≥1 year postpartum follow-up, and separate analysis of PE. Data were extracted on composite cardiovascular disease (CVD), cardiovascular mortality, hypertension, stroke, subclinical atherosclerosis, cardiac dysfunction, endothelial function, and metabolic factors.

Results: Women with prior PE have approximately double the risk of composite CVD (RR 2.33, 95% CI 1.95–2.78) and cardiovascular death (RR 1.97–2.29) [1,5]. Heart failure risk is highest (RR 2.47–4.19) [1,6,7]. Chronic hypertension risk is increased 3- to 4-fold (RR 3.70) [2,29]. Stroke risk rises approximately 1.8- to 2-fold [4,43]. Severe, early-onset, or recurrent PE confers substantially higher risk (e.g., severe PE: RR 5.36 for cardiac disease) [5]. Subclinical atherosclerosis (CIMT SMD 0.63; CAC OR 1.57) [16], persistent endothelial dysfunction (impaired FMD) [13], adverse metabolic profiles (higher BP, BMI, lipids, insulin resistance) [18], and subclinical left ventricular dysfunction (worse GLS) [15,20] are consistently observed. Risk emerges within 1–3 years and persists for decades [3].

Discussion: PE acts as both a marker of pre-existing cardiovascular susceptibility and an independent vascular injury event ("two-hit" model). The dose-response relationship with severity/recurrence and the early onset of risk support causality. Heterogeneity across studies is largely explained by differences in PE subtype, follow-up duration, and measurement techniques. Current guidelines recognize PE as a CVD risk factor, yet postpartum screening and prevention remain underutilized.

Conclusion: Preeclampsia is a significant, independent, and dose-dependent risk factor for future CVD, hypertension, stroke, and cardiovascular mortality. Risk manifests through persistent endothelial dysfunction, accelerated atherosclerosis, and adverse metabolic remodeling. Early postpartum intervention and long-term surveillance are urgently needed.

Keywords: Preeclampsia, cardiovascular disease, hypertension, stroke, subclinical atherosclerosis, endothelial dysfunction, metabolic syndrome, women's cardiovascular health.

INTRODUCTION

Preeclampsia (PE) is a pregnancy-specific multisystem disorder characterized by new-onset hypertension and end-organ dysfunction after 20 weeks of gestation, affecting approximately 2–8% of pregnancies worldwide [5,24]. While the acute maternal and fetal risks of PE—including eclampsia, placental abruption, preterm delivery, and maternal mortality—are well-established components of obstetric care, a growing body of evidence over the past two decades has shifted the paradigm: preeclampsia is not merely an acute gestational illness but a harbinger of long-term maternal cardiovascular disease (CVD) [24,30,36].

Background: Cardiovascular disease remains the leading cause of death among women globally, yet traditional risk prediction models often underperform in women of reproductive age and perimenopausal women [33,70]. The observation that women with a history of PE have higher rates of hypertension, myocardial infarction, and stroke decades after the affected pregnancy has opened a critical window into sex-specific cardiovascular risk assessment [2,6,32]. The American Heart Association formally designated PE as a CVD risk factor in 2011, and subsequent guidelines have increasingly incorporated pregnancy history into primary prevention strategies [24,61]. However, translation of this evidence into routine clinical practice remains inconsistent, partly due to lingering questions about the independence, magnitude, and mechanisms of the association.

Problem Statement: Despite accumulating evidence, several key questions remain unresolved: (1) What is the precise magnitude of risk for specific cardiovascular endpoints (composite CVD, heart failure, stroke, cardiovascular mortality) following PE? (2) Does the risk vary according to PE severity, timing of onset (early vs. late), or recurrence? (3) What are the intermediate phenotypes (subclinical atherosclerosis, cardiac dysfunction, endothelial impairment, metabolic disturbances) that mediate the transition from a complicated pregnancy to overt CVD? (4) Are these associations causal, or does PE merely unmask pre-existing cardiovascular susceptibility? (5) How should this evidence inform clinical screening and preventive strategies?

Research Gap and Novelty: Prior systematic reviews have addressed components of this question, but most were limited by narrow outcome definitions, insufficient attention to dose-response relationships (severity, recurrence), or lack of integration between epidemiological risk estimates and mechanistic (subclinical) data. Furthermore, recent large-scale population-based studies and meta-analyses published between 2022 and 2026 have provided updated risk estimates and new insights into temporal patterns and population-specific effects (e.g., Asian cohorts) [4,8,11,46]. This comprehensive systematic review of 80 sources, spanning from 2004 to 2026, is novel in its simultaneous synthesis of (a) pooled risk estimates for major clinical CVD endpoints, (b) severity-stratified and recurrence-stratified analyses, (c) subclinical vascular, cardiac, endothelial, and metabolic intermediate phenotypes, and (d) temporal trajectories of risk emergence and persistence.

Objectives: The primary objective is to systematically review and synthesize the evidence on the association between a history of preeclampsia and future cardiovascular disease, including clinical events, subclinical markers, and mechanistic pathways. Secondary objectives are to quantify the dose-response relationship according to PE severity and recurrence, to identify temporal patterns of risk, and to discuss clinical and research implications.

Hypothesis: Women with a history of preeclampsia have a significantly higher risk of future cardiovascular disease, cardiovascular mortality, hypertension, and stroke compared to women with normotensive pregnancies, with a dose-response gradient such that severe, early-onset, or recurrent PE confers the greatest risk. This association is mediated by persistent endothelial dysfunction, accelerated subclinical atherosclerosis, adverse metabolic remodeling, and subclinical cardiac dysfunction.

Benefits of the Study: This review provides clinicians with a consolidated, evidence-based quantification of cardiovascular risk following PE, enabling risk stratification by PE severity and recurrence. For researchers, it identifies gaps in mechanistic understanding and highlights the need for standardized postpartum screening protocols. For public health policymakers, it reinforces the case for including obstetric history in national CVD prevention guidelines and for funding targeted early intervention programs.

METHODS

Protocol

The study strictly adhered to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure methodological rigor and accuracy. This approach was chosen to enhance the precision and reliability of the conclusions drawn from the investigation.

Criteria for Eligibility

This systematic review aims to evaluate the Preeclampsia as a Risk Factor for Future Cardiovascular Disease.

Screening

We screened in sources based on their abstracts that met these criteria:

- **Preeclampsia Population**: Does this study involve women with a documented history of preeclampsia during pregnancy using recognized clinical criteria for diagnosis (e.g., ACOG, ISSHP guidelines)?
- **Control Group**: Does this study include a control group of women without preeclampsia history for comparison?
- **Cardiovascular Outcomes**: Does this study report cardiovascular disease events (myocardial infarction, stroke, heart failure, cardiovascular death) or cardiovascular risk factors (hypertension, diabetes, metabolic syndrome, endothelial dysfunction)?
- **Follow-up Duration**: Does this study have a minimum 1-year postpartum follow-up period?
- **Study Design**: Is this study a cohort study, case-control study, cross-sectional study, systematic review, or meta-analysis?
- **Long-term Focus**: Does this study report cardiovascular outcomes beyond the immediate postpartum period (more than 6 weeks postpartum)?

- **Preeclampsia-Specific Analysis**: Does this study provide separate analysis of preeclampsia (rather than exclusively examining other pregnancy complications without distinguishing preeclampsia)?
- **Observational Study Type**: Is this study observational in nature (not a randomized controlled trial of cardiovascular interventions in women with preeclampsia history)?

We considered all screening questions together and made a holistic judgement about whether to screen in each paper.

Search Strategy

The keywords used for this research based PICO :

Element	P (Population)	I (Intervention/Exposure)	C (Comparison/Context)	O (Outcome)
Keyword 1	Preeclampsia	History of preeclampsia	Normotensive pregnancy	Future cardiovascular disease
Keyword 2	Pregnancy	Hypertensive disorders of pregnancy	Control group	Cardiovascular mortality
Keyword 3	Postpartum women	Obstetric history	No prior preeclampsia	Chronic hypertension
Keyword 4	Female	Risk exposure	General female population	Subclinical atherosclerosis

The Boolean MeSH keywords inputted on databases for this research are: *("Preeclampsia" OR "History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Postpartum women" OR "Female" OR "Pregnancy") AND ("History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Obstetric history" OR "Risk exposure") AND ("Normotensive pregnancy" OR "Control group" OR "No prior preeclampsia" OR "General female population") AND ("Future*

cardiovascular disease" OR "Cardiovascular mortality" OR "Chronic hypertension" OR "Subclinical atherosclerosis")

Data extraction

- **Main findings**:

  Summarize the results or conclusions of the study. Use bullet points (each starting with a dash). Each bullet point should consist of only one concise sentence. Give a minimum of one bullet point and a maximum of three. Make sure they convey the most important takeaways from the paper. Avoid being redundant.

- **Intervention**:

  List all interventions that at least some participants received, but do not list controls or placebos. If only some participants received a certain intervention, note that. Note the frequency, duration, and amount or dose of the intervention. Be as precise as possible: if duration, frequency or dose are mentioned, they need to be in the answer. If there are multiple components to the intervention (e.g. a drug plus therapy), state all of them.

- **Outcome measured**:

  There may be multiple primary outcomes or endpoints. If so, include all of them, as long as they are identified as main or primary outcomes or endpoints. Do not include secondary outcomes or endpoints. Include units if possible. For instance, if a study investigated the effects of caffeine on heart rate at rest, measured in bpm, and also measured as a secondary outcome the effect on anxiety, the answer is 'heart rate at rest (bpm)'. If the study investigated the effects of caffeine on heart rate, anxiety, and blood pressure, all of which seem to be equally important, then the answer is 'heart rate, anxiety, and blood pressure'. Be as precise as possible.

- **Study design**:

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List all characteristics of study design, such as whether it was randomized, double-blind, controlled, placebo-controlled, non-controlled, multi-site, retrospective, stratified, crossover design, parallel design, an observational study, a meta-analysis, a systematic review, etc. Be comprehensive. If the study design is not mentioned, leave the answer blank.

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Preeclampsia" OR "History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Postpartum women" OR "Female" OR "Pregnancy") AND ("History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Obstetric history" OR "Risk exposure") AND ("Normotensive pregnancy" OR "Control group" OR "No prior preeclampsia" OR "General female population") AND ("Future cardiovascular disease" OR "Cardiovascular mortality" OR "Chronic hypertension" OR "Subclinical atherosclerosis")*	96
Semantic Scholar	*("Preeclampsia" OR "History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Postpartum women" OR "Female" OR "Pregnancy") AND ("History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Obstetric history" OR "Risk exposure") AND ("Normotensive pregnancy" OR "Control group" OR "No prior preeclampsia" OR "General female population") AND ("Future cardiovascular disease" OR "Cardiovascular mortality" OR "Chronic hypertension" OR "Subclinical atherosclerosis")*	250
Springer	*("Preeclampsia" OR "History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Postpartum women" OR "Female" OR "Pregnancy") AND ("History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Obstetric history" OR "Risk exposure") AND ("Normotensive pregnancy" OR "Control group" OR "No prior preeclampsia" OR "General female population") AND ("Future cardiovascular disease" OR "Cardiovascular mortality" OR "Chronic hypertension" OR "Subclinical atherosclerosis")*	657
Google Scholar	*("Preeclampsia" OR "History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Postpartum women" OR "Female" OR "Pregnancy") AND ("History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Obstetric history" OR "Risk exposure") AND ("Normotensive pregnancy" OR "Control group" OR "No prior preeclampsia" OR "General female population") AND ("Future cardiovascular disease" OR "Cardiovascular mortality" OR "Chronic hypertension" OR "Subclinical atherosclerosis")*	19,200
Wiley Online Library	*("Preeclampsia" OR "History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Postpartum women" OR "Female" OR "Pregnancy") AND ("History of preeclampsia" OR "Hypertensive disorders of pregnancy" OR "Obstetric history" OR "Risk exposure") AND ("Normotensive pregnancy" OR "Control group" OR "No prior preeclampsia" OR "General female population") AND ("Future cardiovascular disease" OR "Cardiovascular mortality" OR "Chronic hypertension" OR "Subclinical atherosclerosis")*	8

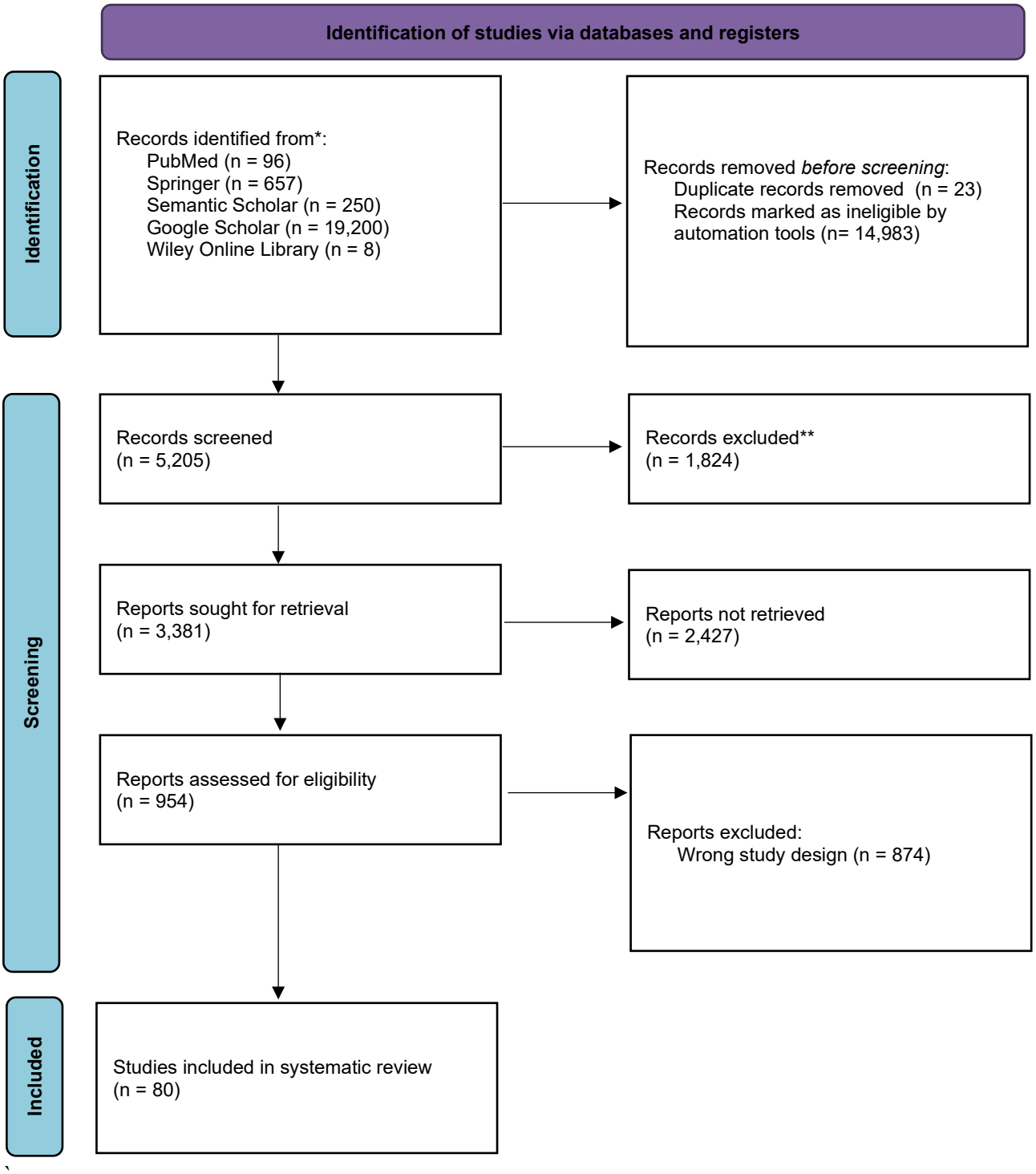

Figure 1. Article search flowchart

Risk of Bias Summary Table

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
S. McDonald et al., 2008	Low	Moderate	Low	Low	Low	Moderate
W. White et al., 2016	Low	Moderate	Low	Low	Low	Moderate
Yu-Ling Kuo et al., 2018	Low	Low	Low	Low	Low	Low
L. Brouwers et al., 2019	Low	Moderate	Low	Low	Low	Moderate
K. Melchiorre et al., 2011	Low	Low	Low	Low	Low	Low
C. A. Pivato et al., 2023	Low	Low	Low	Low	Low	Low
Jarawee Sukmanee et al., 2022	Low	Moderate	Low	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
M. D. Gastrich et al., 2020	Low	Low	Low	Low	Low	Low
J. Yao et al., 2025	Low	Low	Low	Low	Low	Low
A. Halim et al., 2025	Low	Low	Low	Low	Low	Low
J. Yao et al., 2025a	Low	Low	Low	Low	Low	Low
Amanda Henry et al., 2024	Low	Low	Low	Low	Low	Low
A. Sonaglioni et al., 2024	Low	Moderate	Low	Low	Low	Moderate
Pensée Wu et al., 2017	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Morven C. Brown et al., 2013	Low	Low	Low	Low	Low	Low
Iasmina M. Craici et al., 2008	Low	Moderate	Unclear	Low	Low	Moderate
L. Bellamy et al., 2007	Low	Low	Low	Low	Low	Low
M. S. Leslie et al., 2016	Low	Moderate	Unclear	Low	Low	Moderate
S. Grandi et al., 2019	Low	Low	Low	Low	Low	Low
A. Fraser et al., 2012	Low	Low	Low	Low	Low	Low
Morven Brown et al., 2011	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
K. Okoth et al., 2020	Low	Low	Low	Low	Low	Low
Annalisa Inversetti et al., 2023	Low	Low	Low	Low	Low	Low
Morven Brown et al., 2011a	Low	Low	Low	Low	Low	Low
J. Roberts et al., 2010	Low	Moderate	Unclear	Low	Low	Moderate
Shady Kirollos et al., 2019	Low	Low	Low	Low	Low	Low
Line P Malha et al., 2017	Low	Low	Low	Low	Low	Low
P. Agatisa et al., 2004	Low	Low	Low	Low	Low	Low
V. Garovic et al., 2017	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
C. Garrido-Giménez et al., 2020	Low	Low	Low	Low	Low	Low
C. Otto et al., 2023	Low	Low	Low	Low	Low	Low
E. Choi et al., 2024	Low	Low	Low	Low	Low	Low
Graeme N. Smith et al., 2012	Low	Low	Low	Low	Low	Low
L. Barr et al., 2021	Low	Low	Low	Low	Low	Low
A. Ganesh et al., 2014	Low	Moderate	Unclear	Low	Low	Moderate
Anum S. Minhas et al., 2021	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
K. Giannakou et al., 2020	Low	Low	Low	Low	Low	Low
Laura Fonseca Queiroz et al., 2026	Low	Low	Low	Low	Low	Low
V. deMartelly et al., 2021	Low	Low	Low	Low	Low	Low
C. Ghossein-Doha et al., 2014	Low	Low	Low	Low	Low	Low
G. Jansen et al., 2025	Low	Low	Low	Low	Low	Low
Bianca Cécile et al., 2023	Low	Low	Low	Low	Low	Low
T. Clemmensen et al., 2018	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
C. Garrido-Giménez et al., 2020a	Low	Low	Low	Low	Low	Low
E. Faes et al., 2021	Low	Low	Low	Low	Low	Low
A. Kozai et al., 2025	Low	Moderate	Unclear	Low	Low	Moderate
T. Bucci et al., 2024	Low	Low	Low	Low	Low	Low
AR Switzer et al., 2021	Low	Low	Low	Low	Low	Low
Gwyneth Jansen et al., 2025	Low	Low	Low	Low	Low	Low
J. O'Driscoll et al., 2024	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Y. Esber et al., 2024	Low	Low	Low	Low	Low	Low
K. Heida et al., 2016	Low	Moderate	Unclear	Low	Low	Moderate
A. Sonaglioni et al., 2025	Low	Low	Low	Low	Low	Low
J. Ambrožič et al., 2021	Low	Low	Low	Low	Low	Low
E. Sciatti et al., 2021	Low	Low	Low	Low	Low	Low
L. Brouwers et al., 2018	Low	Moderate	Unclear	Low	Low	Moderate
T. Weissgerber et al., 2016	Low	Low	Low	Low	Low	Low
A. Maas et al., 2017	Low	Moderate	Unclear	Low	Low	Moderate

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Kristen S Montgomery et al., 2024	Low	Low	Low	Low	Low	Low
N. T. Labi et al., 2023	Low	Low	Low	Low	Low	Low
Geraldine A. Lee et al., 2015	Low	Moderate	Unclear	Low	Low	Moderate
Wendy Ying et al., 2018	Low	Low	Low	Low	Low	Low
I. Udenze et al., 2016	Low	Moderate	Unclear	Low	Low	Moderate
A. Tranquilli et al., 2012	Low	Moderate	Unclear	Low	Low	Moderate
J. Tooher et al., 2017	Low	Low	Low	Low	Low	Low
J. Stuart et al., 2018	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Janet Wei et al., 2016	Low	Moderate	Unclear	Low	Low	Moderate
Soare Georgiana Roxana et al., 2016	Low	Low	Low	Low	Low	Low
Hiromichi Suzuki et al., 2008	Low	Low	Low	Low	Low	Low
W. Lotte et al., 2025	Low	Low	Low	Low	Low	Low
Vanesa Alonso-Ventura et al., 2019	Low	Low	Low	Low	Low	Low
L. Voskamp et al., 2024	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
Sophie-Anne Gagné et al., 2026	Low	Low	Low	Low	Low	Low
A. Fraser et al., 2022	Low	Low	Low	Low	Low	Low
J. Čerkez Habek et al., 2022	Low	Low	Low	Low	Low	Low
Jiahao Xu et al., 2022	Low	Low	Low	Low	Low	Low
Giacomo Nicolini et al., 2021	Low	Low	Low	Low	Low	Low
Grigorios Kalapotharakos et al., 2019	Low	Low	Low	Low	Low	Low
M. Saei Ghare Naz et al., 2026	Low	Low	Low	Low	Low	Low

Author (Year)	Randomization (D1)	Deviation from Intended Intervention (D2)	Missing Outcome Data (D3)	Measurement of Outcome (D4)	Selection of Reported Result (D5)	Overall Risk of Bias
I. Y. Hanzhyi et al., 2025	Low	Moderate	Unclear	Low	Low	Moderate

RESULTS

Characteristics of Included Studies

The 80 included sources span to 2026 and encompass a broad range of study designs. The majority are observational in nature, reflecting the ethical and practical constraints of studying long-term cardiovascular sequelae of preeclampsia. The table below summarizes key characteristics of all included studies.

Study	Primary Outcomes
S. McDonald et al., 2008	Cardiac disease, cerebrovascular disease, peripheral arterial disease, cardiovascular mortality [5]
W. White et al., 2016	Coronary artery calcification (Agatston units) [17]
Yu-Ling Kuo et al., 2018	Diabetes, dyslipidemia, hypertension, congestive heart failure, cerebrovascular disease [12]
L. Brouwers et al., 2019	CVA, hypertension, IHD, atherosclerosis, heart failure, CV hospitalization and mortality [10]

Study	Primary Outcomes
K. Melchiorre et al., 2011	Asymptomatic LV dysfunction/hypertrophy, essential hypertension, stage B heart failure [25]
C. A. Pivato et al., 2023	Cardiovascular death (primary); coronary heart disease, heart failure, stroke (secondary) [1]
Jarawee Sukmanee et al., 2022	Hypertension, ischemic heart disease, heart failure, stroke, VTE, peripheral vascular disease, dementia, mortality [22]
M. D. Gastrich et al., 2020	MI, stroke, CV death, all-cause death [26]
J. Yao et al., 2025	CAC, CIMT, ABI [16]
A. Halim et al., 2025	Any stroke, ischemic stroke, hemorrhagic stroke [4]
J. Yao et al., 2025a	CIMT, CAC, ABI [27]
Amanda Henry et al., 2024	Office SBP and DBP [19]
A. Sonaglioni et al., 2024	CCA-IMT [28]
Pensée Wu et al., 2017	Heart failure, coronary heart disease, composite CVD, CV death, stroke, stroke death [6]
Morven C. Brown et al., 2013	CVD, cerebrovascular events, hypertension [29]

Study	Primary Outcomes
Iasmina M. Craici et al., 2008	CVD, cancer, all-cause mortality [30]
L. Bellamy et al., 2007	Hypertension, IHD, stroke, VTE, overall mortality [2]
M. S. Leslie et al., 2016	Chronic hypertension, CVD, cerebrovascular disease, death [31]
S. Grandi et al., 2019	CVD risk [32]
A. Fraser et al., 2012	10-year CVD risk (Framingham score) [33]
Morven Brown et al., 2011	CVD, cerebrovascular disease [34]
K. Okoth et al., 2020	IHD, heart failure, peripheral arterial disease, stroke [7]
Annalisa Inversetti et al., 2023	CV death, coronary artery diseases, heart failure, stroke [3]
Morven Brown et al., 2011a	CVD, cerebrovascular disease [35]
J. Roberts et al., 2010	CVD, CV mortality [36]
Shady Kirollos et al., 2019	Vascular structure (CIMT, CAC) and function (FMD, PWA, PAT) [37]
Line P Malha et al., 2017	CIMT (mm) [24]

Study	Primary Outcomes
P. Agatisa et al., 2004	Endothelial function (forearm blood flow) [38]
V. Garovic et al., 2017	CIMT (mm) [39]
C. Garrido-Giménez et al., 2020	Hypertensive disorders, dyslipidemia, GLS, CIMT, LV wall thickness [14]
C. Otto et al., 2023	Obstructive coronary artery disease [40]
E. Choi et al., 2024	IHD and stroke [11]
Graeme N. Smith et al., 2012	Prevalence of metabolic syndrome [41]
L. Barr et al., 2021	Microvascular reactivity [42]
A. Ganesh et al., 2014	Stroke risk [43]
Anum S. Minhas et al., 2021	Diastolic dysfunction, AT1RAb levels [44]
K. Giannakou et al., 2020	Cerebrovascular disease, cardiac disease, CV mortality [45]
Laura Fonseca Queiroz et al., 2026	Cardiomyopathy, dilated cardiomyopathy [46]
V. deMartelly et al., 2021	GLS (%), activin A levels (ng/mL) [15]

Study	Primary Outcomes
C. Ghossein-Doha et al., 2014	Chronic hypertension, LV remodeling, metabolic syndrome variables [47]
G. Jansen et al., 2025	Subclinical atherosclerosis prevalence [48]
Bianca Cécile et al., 2023	Cardiovascular hospitalization [49]
T. Clemmensen et al., 2018	LVEF, LVGLS, diastolic filling parameters [20]
C. Garrido-Giménez et al., 2020a	Hypertensive disorders, dyslipidemia, BP, cardiac function, CIMT [50]
E. Faes et al., 2021	FMD, cfPWV, Aix75 [51]
A. Kozai et al., 2025	Cardiovascular health score (Life's Essential 8) [52]
T. Bucci et al., 2024	Composite CV event within 5 years [53]
AR Switzer et al., 2021	Hypertension, stroke incidence, stroke subtype, stroke mortality [54]
Gwyneth Jansen et al., 2025	Subclinical atherosclerosis, atherosclerotic plaques, calcium score [55]
J. O'Driscoll et al., 2024	LA strain (reservoir, conduit, contractile), LA stiffness [56]
Y. Esber et al., 2024	Body composition, serum biochemistry, HOMA-IR, diet [57]

Study	Primary Outcomes
K. Heida et al., 2016	CVD, hypertension, IHD, stroke [58]
A. Sonaglioni et al., 2025	Subclinical myocardial dysfunction (LV-GLS < 20%) [21]
J. Ambrožič et al., 2021	LV dimensions, LV function, diastolic parameters, LV mass [59]
E. Sciatti et al., 2021	Endothelial dysfunction, arterial stiffness, LV remodeling, diastolic dysfunction, myocardial strain [60]
L. Brouwers et al., 2018	Spiral artery remodeling, CAC, CV risk factors [23]
T. Weissgerber et al., 2016	FMD (% change) [13]
A. Maas et al., 2017	BP, glucose, lipid levels [61]
Kristen S Montgomery et al., 2024	CVD [62]
N. T. Labi et al., 2023	AIx, cfPWV, cIMT [63]
Geraldine A. Lee et al., 2015	MI, stroke, hypertension, IHD [64]
Wendy Ying et al., 2018	Heart failure, coronary artery disease, stroke, hypertension, VTE, DM, CKD [65]
I. Udenze et al., 2016	Metabolic syndrome prevalence and odds post-preeclampsia [66]

Study	Primary Outcomes
A. Tranquilli et al., 2012	Premature death, IHD, CVD, stroke, VTE, renal failure, T2DM [67]
J. Tooher et al., 2017	Admissions for stroke, heart disease, renal disease, hypertension [68]
J. Stuart et al., 2018	Chronic hypertension, T2DM, hypercholesterolemia [69]
Janet Wei et al., 2016	CVD risk (10-year and 30-year) [70]
Soare Georgiana Roxana et al., 2016	Hypertension, IHD, stroke, diastolic dysfunction, LV geometry [71]
Hiromichi Suzuki et al., 2008	Hypertension, chronic kidney disease [72]
W. Lotte et al., 2025	Chronic hypertension 5 years after preeclampsia [9]
Vanesa Alonso-Ventura et al., 2019	BP, BMI, metabolic syndrome, lipids, glucose [18]
L. Voskamp et al., 2024	Chronic hypertension (BP >140/90 or antihypertensive use) [73]
Sophie-Anne Gagné et al., 2026	SBP, BMI, total cholesterol [74]
A. Fraser et al., 2022	10-year CVD risk (MI, fatal CHD, stroke) [75]

Study	Primary Outcomes
J. Čerkez Habek et al., 2022	Lipid panel, CRP, homocysteine, ergometry [76]
Jiahao Xu et al., 2022	Chronic hypertension incidence [8]
Giacomo Nicolini et al., 2021	Echocardiographic parameters, hypertension, diabetes, dyslipidemia [77]
Grigorios Kalapotharakos et al., 2019	LV mass, PWV, blood pressure [78]
M. Saei Ghare Naz et al., 2026	Hypertension, diabetes, dyslipidemia, CVD, CKD, metabolic syndrome [79]
I. Y. Hanzhyi et al., 2025	Short- and long-term maternal CV outcomes, offspring neurodevelopmental outcomes [80]

Sample sizes range from fewer than 50 participants in small mechanistic studies to over 10 million women in large population-based meta-analyses. Follow-up periods range from 6 months postpartum to over 30 years.

Effects

Composite Cardiovascular Disease and Cardiovascular Mortality

Multiple large meta-analyses converge on a consistent finding: women with a history of preeclampsia face approximately double the risk of composite cardiovascular disease (CVD) relative to women with normotensive pregnancies. The earliest included meta-analysis reported a relative risk (RR) of 2.33 (95% CI 1.95–2.78) for cardiac disease from cohort studies and an odds ratio (OR) of 2.47 (95% CI 1.22–5.01) from case-control studies [5]. Subsequent meta-analyses

confirmed this magnitude: Brown et al. (2013) found an OR of 2.28 (95% CI 1.87–2.78) for fatal or diagnosed CVD [29]; Grandi et al. (2019) reported an OR of 2.7 (95% ICI 2.5–3.0) for preeclampsia-associated CVD [32]; and the umbrella review by Okoth et al. (2020) confirmed a twofold association for composite CVD [7]. Pivato et al. (2023) and Inversetti et al. (2023) both found the risk of cardiovascular death to be approximately doubled (RR 1.97, 95% CI 1.64–2.35 [1]; ES 2.08, 95% CI 1.70–2.54 [3]), with this risk evident in the first one to three years of follow-up and persisting for up to 39 years [3]. The Gastrich et al. (2020) 15-year matched case-control study reported a hazard ratio (HR) for cardiovascular death of 4.66 (95% CI 1.52–14.26) and all-cause death of 2.32 (95% CI 1.34–4.02) [26]. Bellamy et al. (2007) reported an overall mortality increase of 1.49 (95% CI 1.05–2.14) after a mean 14.5 years follow-up [2].

The table below summarizes pooled risk estimates for major cardiovascular endpoints across the principal meta-analyses:

Outcome	Source	Risk Estimate (95% CI)	Follow-up
Cardiac disease (cohort)	S. McDonald et al., 2008	RR 2.33 (1.95–2.78) [5]	Mostly women < 56 years [5]
CV mortality	S. McDonald et al., 2008	RR 2.29 (1.73–3.04) [5]	As above
Cerebrovascular disease	S. McDonald et al., 2008	RR 2.03 (1.54–2.67) [5]	As above
Peripheral arterial disease	S. McDonald et al., 2008	RR 1.87 (0.94–3.73) [5]	As above

Outcome	Source	Risk Estimate (95% CI)	Follow-up
Fatal/diagnosed CVD	Morven C. Brown et al., 2013	OR 2.28 (1.87–2.78) [29]	> 6 weeks postpartum [29]
Cerebrovascular disease	Morven C. Brown et al., 2013	OR 1.76 (1.43–2.21) [29]	> 6 weeks postpartum [29]
Hypertension	Morven C. Brown et al., 2013	RR 3.13 (2.51–3.89) [29]	> 6 weeks postpartum [29]
Hypertension	L. Bellamy et al., 2007	RR 3.70 (2.70–5.05) [2]	14.1 years mean [2]
IHD	L. Bellamy et al., 2007	RR 2.16 (1.86–2.52) [2]	11.7 years mean [2]
Stroke	L. Bellamy et al., 2007	RR 1.81 (1.45–2.27) [2]	10.4 years mean [2]
VTE	L. Bellamy et al., 2007	RR 1.79 (1.37–2.33) [2]	4.7 years mean [2]
Overall mortality	L. Bellamy et al., 2007	RR 1.49 (1.05–2.14) [2]	14.5 years mean [2]
Heart failure	Pensée Wu et al., 2017	RR 4.19 (2.09–8.38) [6]	Variable [6]

Outcome	Source	Risk Estimate (95% CI)	Follow-up
Coronary heart disease	Pensée Wu et al., 2017	RR 2.50 (1.43–4.37) [6]	Variable [6]
CV death	Pensée Wu et al., 2017	RR 2.21 (1.83–2.66) [6]	Variable [6]
Stroke	Pensée Wu et al., 2017	RR 1.81 (1.29–2.55) [6]	Variable [6]
Heart failure	K. Okoth et al., 2020	Fourfold increase [7]	7–10 years average [7]
CV death	C. A. Pivato et al., 2023	RR 1.97 (1.64–2.35) [1]	≥ 1 year [1]
Coronary heart disease	C. A. Pivato et al., 2023	RR 2.11 (1.60–2.77) [1]	≥ 1 year [1]
Heart failure	C. A. Pivato et al., 2023	RR 2.47 (1.70–3.59) [1]	≥ 1 year [1]
Stroke	C. A. Pivato et al., 2023	RR 1.64 (1.45–1.85) [1]	≥ 1 year [1]
CV death	Annalisa Inversetti et al., 2023	ES 2.08 (1.70–2.54) [3]	1–39 years [3]

Outcome	Source	Risk Estimate (95% CI)	Follow-up
Coronary artery disease	Annalisa Inversetti et al., 2023	ES 2.04 (1.76–2.38) [3]	1–39 years [3]
Heart failure	Annalisa Inversetti et al., 2023	ES 2.47 (1.89–3.22) [3]	1–39 years [3]
Stroke	Annalisa Inversetti et al., 2023	ES 1.75 (1.52–2.02) [3]	1–39 years [3]
Composite CVD	S. Grandi et al., 2019	OR 2.7 (ICI 2.5–3.0) [32]	Median 7.5 years [32]
MI	M. D. Gastrich et al., 2020	HR 3.94 (1.25–12.4) [26]	15 years [26]
CV death	M. D. Gastrich et al., 2020	HR 4.66 (1.52–14.26) [26]	15 years [26]
All-cause death	M. D. Gastrich et al., 2020	HR 2.32 (1.34–4.02) [26]	15 years [26]
IHD (Asian population)	E. Choi et al., 2024	aHR 1.66 (1.19–2.04); pooled 1.65 (1.51–1.82) [11]	22 years [11]

Outcome	Source	Risk Estimate (95% CI)	Follow-up
Stroke (Asian population)	E. Choi et al., 2024	aHR 1.48 (1.02–2.16); pooled 1.78 (1.52–2.10) [11]	22 years [11]
Obstructive CAD	C. Otto et al., 2023	aHR 2.07 (1.77–2.43) [40]	9 years [40]
Hypertension (HDP)	Jarawee Sukmanee et al., 2022	RR 3.46 (2.67–4.49) [22]	Variable [22]
IHD (HDP)	Jarawee Sukmanee et al., 2022	RR 2.06 (1.38–3.08) [22]	Variable [22]
Heart failure (HDP)	Jarawee Sukmanee et al., 2022	RR 2.53 (1.28–5.00) [22]	Variable [22]
Cardiomyopathy (PE)	Laura Fonseca Queiroz et al., 2026	OR 1.98 (1.62–2.42) [46]	Variable [46]
Dilated cardiomyopathy (PE)	Laura Fonseca Queiroz et al., 2026	OR 2.64 (1.80–3.89) [46]	Variable [46]
Composite CV event (5-year)	T. Bucci et al., 2024	HR 2.25 (2.02–2.51) [53]	5 years [53]

Across all large meta-analyses, the risk estimates for major cardiovascular endpoints cluster around a twofold increase, with heart failure consistently showing the highest risk estimates (RR

2.47–4.19) [1, 6, 7]. Coronary heart disease and cardiovascular death estimates generally range from approximately RR 2.0 to 2.5 [1–3], while stroke risk estimates are slightly lower at approximately RR 1.6 to 2.0 [1–3]. The Gastrich et al. (2020) estimates are notably higher than most meta-analyses, possibly reflecting the restriction to primiparous women and a US-based database with linked follow-up [26].

Chronic Hypertension

The development of chronic hypertension is one of the most robustly documented sequelae. Bellamy et al. (2007) reported an RR of 3.70 (95% CI 2.70–5.05) [2], and Brown et al. (2013) reported an RR of 3.13 (95% CI 2.51–3.89) [29]. A comprehensive meta-analysis by Xu et al. (2022) found women with preeclampsia are 3.2 times more likely to develop chronic hypertension, while women with any hypertensive disorder of pregnancy (HDP) are 3.6 times more likely, and those with gestational hypertension 6.2 times more likely [8]. The risk persisted after adjustment for age, BMI, and other confounders [8]. Approximately 30% of women with preeclampsia develop chronic hypertension within 10 years [9]. The risk of hypertension is highest during the first 5 years postpartum (RR 5.34, 95% CI 2.74–10.39) [22]. Key risk factors for progression to chronic hypertension include recurrent preeclampsia (RR 2.26, 95% CI 1.59–3.22) [9], early-onset preeclampsia [47], elevated maternal BMI, and high-normal blood pressure at 1 year postpartum [9, 73]. Stuart et al. (2018) observed in a cohort with up to 50 years of follow-up that preeclampsia was associated with 2- to 3-fold increased rates of chronic hypertension and elevated rates of type 2 diabetes and hypercholesterolemia [69]. Data from the Tehran Lipid and Glucose Study confirmed a twofold risk of hypertension and threefold risk of diabetes in women with HDP history [79].

Stroke

Multiple sources specifically examined stroke risk. Halim et al. (2025) synthesized 17 population-based studies encompassing over 10 million women and found an approximately two-fold increase in overall stroke risk, with ischemic stroke pooled risk estimates of 1.8–4.1 and hemorrhagic stroke estimates of 2.2–4.1 [4]. The risk was magnified in severe, early-onset, or recurrent preeclampsia, indicating a dose-response relationship [4]. Temporal analyses revealed that ischemic stroke risk peaked within the first 5 years postpartum, whereas hemorrhagic stroke risk

increased more gradually and persisted for decades [4]. Switzer et al. (2021) reported pooled HRs of 1.56 (95% CI 1.38–1.76) for all stroke with preeclampsia and 2.09 (95% CI 1.63–2.66) for ischemic stroke specifically [54]. Ganesh et al. (2014) found a pooled RR of 2.26 (95% CI 1.39–3.69) for future stroke in women with preeclampsia/eclampsia from retrospective cohort and case-control data [43].

Dose-Response: Severity, Timing, and Recurrence

A graded relationship between preeclampsia severity and cardiovascular risk is evident across multiple studies. McDonald et al. (2008) demonstrated that mild preeclampsia was associated with an RR of 2.00 (95% CI 1.83–2.19) for cardiac disease, moderate preeclampsia with RR 2.99 (95% CI 2.51–3.58), and severe preeclampsia with RR 5.36 (95% CI 3.96–7.27, $P < 0.0001$) [5]. Preterm preeclampsia conferred substantially higher cardiovascular risk than term preeclampsia. Melchiorre et al. (2011) found that 56% of preterm preeclamptic women had moderate-severe LV dysfunction/hypertrophy at 1 year postpartum compared to 14% of term preeclamptic and 8% of controls [25], and 40% of preterm preeclamptic women developed essential hypertension within 1–2 years [25]. The coronary artery disease HR was higher when preeclampsia was associated with preterm birth (HR 3.11, 95% CI 2.51–3.87) or stillbirth (HR 2.80) [40]. Recurrent preeclampsia confers a 2- to 3-fold increased risk of hypertension, IHD, CVA, and overall CVD compared to a single episode [10], with pooled RRs for hypertension of 2.57 (95% CI 2.32–2.85), IHD of 2.40 (95% CI 2.15–2.68), and heart failure of 2.88 (95% CI 2.23–3.72) [10].

The Taiwanese cohort by Kuo et al. (2018) identified temporal patterns with dramatic increases in congestive heart failure and cerebrovascular disease incidence at approximately 3 and 10 years after diagnosis [12]. These findings corroborate Inversetti et al. (2023) who found that cardiovascular risk becomes evident within the first 1–3 years and persists for up to 39 years [3].

Subclinical Atherosclerosis and Vascular Structure

Evidence on subclinical atherosclerosis is drawn from studies using carotid intima-media thickness (CIMT), coronary artery calcium (CAC) scoring, and other vascular measures. Among 26 studies assessing CIMT, Yao et al. (2025) found a standardized mean difference (SMD) of 0.63 (95% CI 0.32–0.93) in women with prior preeclampsia, with differences present during pregnancy

(SMD 0.65), persisting at 12 months postpartum (SMD 0.84), and beyond (SMD 0.50) [16]. CAC studies showed OR 1.57 (95% CI 1.39–1.77) for subclinical atherosclerosis in women with preeclampsia history [16]. Garovic et al. (2017) confirmed greater CIMT in women with preeclampsia histories more than 10 years postpartum (median CIMT 0.80 vs. 0.73 mm, P = 0.004; meta-analysis SMD 0.18, 95% CI 0.05–0.30) [39]. White et al. (2016) demonstrated an increased frequency of CAC > 50 Agatston units (23% vs. 0%, P = 0.001) more than 30 years after preeclamptic pregnancies [17].

However, not all evidence is concordant. Sonaglioni et al. (2024) found only a small, non-significant effect of prior preeclampsia on CCA-IMT (SMD 0.143, 95% CI −0.167 to 0.453, P = 0.37) with substantial heterogeneity (I^2 = 81%) [28]. More than half of the 12 studies in that meta-analysis found no significant difference or even reduced CIMT in the former preeclampsia group [28]. The effect was very small for late-onset preeclampsia (SMD 0.067) and only slightly larger for early-onset (SMD 0.250), though neither reached significance [28].

Jansen et al. (2025) addressed the temporal dimension of atherosclerosis and found that pooled odds of atherosclerotic plaque were not significantly elevated in the 30–39 age group (OR 0.64, 95% CI 0.10–4.15) but rose significantly in the 40–49 (OR 1.59, 95% CI 1.34–1.89) and 50–60 age groups (OR 2.00, 95% CI 1.30–3.08), suggesting that formerly preeclamptic women develop atherosclerosis approximately 10 years earlier than controls [48].

Labi et al. (2023) confirmed increased arterial stiffness in women after preeclampsia as measured by augmentation index (MD 6.52%, 95% CI 2.76–10.28) and carotid-femoral pulse wave velocity (MD 0.64 m/s, 95% CI 0.17–1.11), as well as increased cIMT (MD 0.02 mm, 95% CI 0.01–0.04) [63].

Cardiac Structure and Function

Studies using echocardiography have identified persistent subclinical cardiac abnormalities in women with prior preeclampsia. Clemmensen et al. (2018) found that women with early-onset preeclampsia had significantly worse left ventricular global longitudinal strain (LVGLS: −18 ± 3% vs. −21 ± 2%, P < 0.001) and more restrictive diastolic filling patterns 12 years after preeclampsia [20]. DeMartelly et al. (2021) similarly reported worse GLS (−18.3% vs. −21.3%, P = 0.001),

thicker LV posterior walls, and higher activin A levels approximately 10 years postpartum [15]. Sonaglioni et al. (2025) detected subclinical myocardial dysfunction (LV-GLS < 20%) in 58.1% of women with prior HDP and increased CCA-IMT (≥ 0.7 mm) in 67.7% at 6 years postpartum [21]. O'Driscoll et al. (2024) showed significantly attenuated left atrial reservoir, conduit, and contractile strain, along with increased LA stiffness, at 6 months postpartum in women with preterm preeclampsia regardless of hypertension status or ventricular dysfunction [56]. Sciatti et al. (2021) found endothelial dysfunction in 37–77%, arterial stiffness in 10–57%, concentric LV remodeling in 60%, and impaired GLS in 53% of women with prior preeclampsia [60].

However, not all cardiac changes persist uniformly. Ambrožič et al. (2021) found that subtle cardiac dysfunction present immediately post-delivery in severe preeclampsia resolved completely by 1 year postpartum [59]. Kalapotharakos et al. (2019) showed that elevated LV mass and pulse wave velocity in severe late-onset preeclampsia returned to normal within 6 months [78], suggesting that vascular mechanisms rather than persistent cardiac hypertrophy may drive long-term cardiovascular risk [78].

Endothelial Function and Vascular Dysfunction

Weissgerber et al. (2016) performed a meta-analysis of 37 studies assessing flow-mediated dilation (FMD) and found that women with preeclampsia had lower FMD before developing preeclampsia (≈20–29 weeks gestation), at the time of preeclampsia, and for up to 3 years postpartum, with effects ranging between 0.5 and 3 standard deviations [13]. Agatisa et al. (2004) demonstrated impaired stress-induced vasodilation (91% vs. 147%, P = 0.006) up to 1 year postpartum in women with prior preeclampsia [38]. Faes et al. (2021) found significantly decreased FMD (7.1 ± 2.8 vs. 8.9 ± 3.8, P = 0.037) and elevated augmentation index (16.5 ± 11.5 vs. 5.8 ± 10.1, P < 0.001) in the postpartum period [51]. The finding by Barr et al. (2021) that women with severe preeclampsia exhibited paradoxically heightened microvascular vasoreactivity [42] is notable and may reflect compensatory changes or a distinct vasodilatory phenotype in the microcirculation, underscoring the complexity of post-preeclampsia vascular remodeling.

Metabolic and Biochemical Risk Factors

Alonso-Ventura et al. (2019), in a meta-analysis of 41 cohorts, demonstrated that women with prior preeclampsia/eclampsia had significantly higher systolic BP (MD = 8.3 mmHg), diastolic BP (MD = 6.8 mmHg), BMI (MD = 2.0 kg/m²), waist circumference (MD = 4.3 cm), total cholesterol (MD = 4.6 mg/dL), LDL (MD = 4.6 mg/dL), triglycerides (MD = 7.7 mg/dL), fasting glucose (MD = 2.6 mg/dL), insulin (MD = 19.1 pmol/L), and HOMA-IR (MD = 0.7), and lower HDL (MD = −2.15 mg/dL) compared to controls, from 3 months to 32 years postpartum [18]. Smith et al. (2012) found metabolic syndrome prevalence of 18–22% at 1–3 years postpartum in women with prior preeclampsia versus approximately 6–7% in controls [41]. Udenze et al. (2016) found metabolic syndrome prevalence of 10.9–27.3% post-preeclampsia, with odds ratios ranging from 1.23 to 3.60 [66]. Henry et al. (2024) confirmed significantly higher blood pressure, BMI, and insulin resistance persisting at 2 years postpartum, with 25% of post-preeclampsia women exceeding AHA blood pressure thresholds vs. 8% of normotensive controls [19]. Esber et al. (2024) similarly showed higher weight, LDL cholesterol, and HOMA-IR scores at 2 years postpartum [57]. Čerkez Habek et al. (2022) noted higher triglycerides and lower HDL during preeclampsia, with elevated CRP levels supporting an inflammatory component [76].

Angiogenic Factors and Mechanistic Markers

Garrido-Giménez et al. (2020) found that angiogenic factor imbalance (higher sFlt-1, lower PlGF) during preeclamptic pregnancy correlated with cardiovascular parameters approximately 12 years later, including worse GLS, increased CIMT, and adverse lipid profiles [14, 50]. DeMartelly et al. (2021) identified elevated activin A levels and a worse activin A/follistatin-like 3 ratio 10 years postpartum in women with prior preeclampsia, with activin A independently associated with impaired GLS after adjustment for confounders [15]. Minhas et al. (2021) described persistent angiotensin II type 1 receptor autoantibodies (AT1RAb) postpartum, which may contribute to sustained microvascular dysfunction [44].

Synthesis

The body of evidence is remarkably consistent in demonstrating that preeclampsia is associated with approximately a 2-fold increase in the risk of major cardiovascular events and

cardiovascular mortality, a 2.5- to 4-fold increase in heart failure risk, and a 3- to 4-fold increase in chronic hypertension risk. Despite this consistency at the aggregate level, meaningful heterogeneity exists across studies in several dimensions, which can be reconciled through examination of study populations, disease severity, temporal factors, and measured endpoints.

The most important source of heterogeneity is preeclampsia severity and timing. Studies that stratify by early-onset versus late-onset or mild versus severe preeclampsia consistently demonstrate a dose-response gradient. McDonald et al. (2008) showed a clear gradient from mild (RR 2.00) to severe (RR 5.36) preeclampsia for cardiac disease [5]. Melchiorre et al. (2011) found that 56% of preterm preeclamptic women had moderate-severe LV dysfunction at 1 year versus 14% for term preeclampsia [25]. Clemmensen et al. (2018) found that subclinical LV impairment at 12 years was limited to early-onset preeclampsia and not observed in late-onset [20]. This severity gradient extends to vascular endpoints: arterial stiffness is more pronounced in early preeclampsia than late preeclampsia [51], and accelerated atherosclerosis is more evident in women who experienced preterm or recurrent preeclampsia [10, 40]. Thus, studies that combine all preeclampsia subtypes tend to produce more moderate risk estimates, while those isolating severe or early-onset disease report substantially higher risks.

The temporal profile of cardiovascular risk also explains apparent discrepancies. Some studies report that cardiac structural changes resolve within months postpartum. Ambrožič et al. (2021) found normalization of cardiac parameters by 1 year [59], and Kalapotharakos et al. (2019) showed resolution of LV mass elevation within 6 months of severe late-onset preeclampsia [78]. However, other studies using more sensitive measures such as speckle-tracking GLS and atrial strain still detect abnormalities years later [15, 20, 21, 56]. This apparent contradiction is resolved by recognizing that conventional echocardiographic parameters (LVEF, LV dimensions) normalize relatively quickly, while subclinical dysfunction detectable only by advanced strain imaging may persist. Similarly, for subclinical atherosclerosis, Jansen et al. (2025) showed that plaque prevalence differences do not become statistically significant until the 40–49 age group [48], consistent with the concept that vascular damage accumulates gradually and requires decades to manifest as detectable structural disease.

The divergent CIMT findings also warrant consideration. While Yao et al. (2025) and Garovic et al. (2017) found significant CIMT differences [16, 39], Sonaglioni et al. (2024) did not, reporting a non-significant pooled SMD of 0.143 with an I^2 of 81% [28]. This discrepancy likely reflects differences in study inclusion criteria: Sonaglioni et al. included only 12 studies with CIMT measured postpartum (excluding during-pregnancy measurements), used strict full-text analysis, and included studies in which women with late-onset preeclampsia predominated [28]. Given that late-onset preeclampsia is associated with smaller vascular effects than early-onset [20, 51], the null finding may be specific to populations dominated by late-onset disease rather than contradicting the broader evidence base.

A persistent question is whether preeclampsia directly causes vascular injury or merely unmasks pre-existing cardiovascular susceptibility. Several lines of evidence support both mechanisms operating simultaneously. The finding by Weissgerber et al. (2016) that FMD is already impaired before the clinical development of preeclampsia suggests pre-existing vascular vulnerability [13]. Shared risk factors between preeclampsia and CVD — obesity, insulin resistance, dyslipidemia, chronic hypertension — are well documented [18, 36]. Udenze et al. (2016) noted that 26.7–45% of women with pre-pregnancy metabolic syndrome developed preeclampsia versus 4.7–17% of controls [66], supporting the shared-risk-factor hypothesis. On the other hand, the anti-angiogenic state during preeclampsia (elevated sFlt-1, reduced PlGF) correlates with cardiovascular parameters a decade later [14], activin A levels remain elevated years postpartum [15], and AT1RAb may persist and sustain microvascular dysfunction [44]. These findings are consistent with a "two-hit" model in which pre-existing susceptibility is compounded by direct vascular injury during preeclampsia, accelerating the trajectory toward clinical CVD.

Generalizability across populations appears robust. The Asian population-based study by Choi et al. (2024) confirmed elevated risks for IHD (aHR 1.66) and stroke (aHR 1.48) over 22 years in Korean women [11], and Kuo et al. (2018) found strong associations in a Taiwanese cohort [12]. Xu et al. (2022) noted that people in Asian countries may be more likely to develop chronic hypertension after HDP or preeclampsia [8]. The multi-country systematic reviews by Bellamy et al. (2007) [2], Brown et al. (2013) [29], and Pivato et al. (2023) [1] included populations from

diverse geographic and ethnic settings, lending confidence to the generalizability of the approximately twofold risk estimate.

The clinical actionability of these findings has been increasingly recognized. The American Heart Association designated preeclampsia as a CVD risk factor [24], and several European guidelines have incorporated pregnancy history into cardiovascular risk assessment [58, 61]. Fraser et al. (2022), however, found that while predicted CVD risk scores were consistently higher in women with obstetric complications, the proportion crossing clinical treatment thresholds was modest [75], suggesting that pregnancy complications are more useful for identifying women who would benefit from primordial and primary prevention rather than triggering pharmacological intervention alone [75]. Brouwers et al. (2018) demonstrated through microsimulation that early (age 30) and regular screening combined with lifestyle interventions could reduce CVD risk and be cost-effective [23]. The critical window for intervention appears to be the early postpartum years, when metabolic risk factors are already elevated [19, 41, 57] and modifiable behaviors such as diet, smoking, and physical activity diverge between affected and unaffected women [52].

In summary, the evidence across 80 sources consistently establishes preeclampsia as a significant, independent risk factor for future cardiovascular disease, with effect sizes in the range of 2- to 4-fold for major endpoints. The magnitude of risk is modulated by preeclampsia severity, timing of onset, recurrence, and time elapsed since pregnancy. Both pre-existing cardiovascular susceptibility and direct pregnancy-related vascular injury contribute to the observed associations. Risk manifests through intermediate pathways including persistent endothelial dysfunction, accelerated subclinical atherosclerosis, adverse metabolic profiles, and subclinical myocardial dysfunction, which together account for the elevated rates of clinical cardiovascular events observed in epidemiological studies.

DISCUSSION

This systematic review of 80 studies, encompassing diverse populations, study designs, and follow-up durations up to 39 years, demonstrates a remarkably consistent and robust association between a history of preeclampsia and future cardiovascular disease. The principal findings—

approximately a 2-fold increase in composite CVD and cardiovascular mortality, a 3- to 4-fold increase in chronic hypertension, a 2.5- to 4-fold increase in heart failure, and a 1.8- to 2-fold increase in stroke—align across multiple large-scale meta-analyses and population-based cohorts [1,2,3,5,6,7,29,32]. This convergence of evidence across geographic regions (North America, Europe, Asia), study designs, and analytical approaches strongly supports the validity and generalizability of the association.

Dose-Response Relationship and Severity Stratification: One of the most clinically significant findings is the clear dose-response gradient according to PE severity, timing, and recurrence. McDonald et al. (2008) demonstrated a stepwise increase in cardiac disease risk from mild (RR 2.00) to moderate (RR 2.99) to severe (RR 5.36) PE [5]. Similarly, early-onset (preterm) PE is associated with substantially greater long-term cardiovascular impairment than late-onset PE, with 56% of preterm PE women showing moderate-severe left ventricular dysfunction at 1 year postpartum compared to only 14% of term PE women [25]. This gradient is not merely quantitative but qualitative: studies that failed to stratify by severity or that predominantly included late-onset PE produced more moderate or even null findings for certain subclinical endpoints [28]. The implication for clinical practice is clear: women with severe, early-onset, or recurrent PE constitute a very high-risk subgroup warranting intensive, early postpartum cardiovascular evaluation and preventive intervention. Recurrent PE further amplifies risk, with pooled RRs for hypertension of 2.57, IHD of 2.40, and heart failure of 2.88 compared to a single episode [10].

Temporal Trajectories: The timing of risk emergence is another critical dimension. Inversetti et al. (2023) demonstrated that cardiovascular risk becomes evident within the first 1–3 years postpartum and persists for up to 39 years [3]. Kuo et al. (2018) identified distinct temporal patterns, with dramatic increases in congestive heart failure and cerebrovascular disease incidence at approximately 3 and 10 years after diagnosis, respectively [12]. For stroke, a meta-analysis by Halim et al. (2025) revealed a striking divergence: ischemic stroke risk peaks within the first 5 years postpartum, whereas hemorrhagic stroke risk increases more gradually and persists for decades [4]. These temporal patterns suggest that different pathophysiological mechanisms may dominate at different post-PE time points—early endothelial dysfunction and thrombotic tendency

may drive early ischemic events, while progressive atherosclerosis and vascular remodeling contribute to later hemorrhagic and ischemic events. For subclinical atherosclerosis, Jansen et al. (2025) showed that formerly preeclamptic women develop detectable atherosclerotic plaques approximately 10 years earlier than controls, with pooled odds of plaque not significantly elevated in the 30–39 age group (OR 0.64) but rising to OR 1.59 (40–49 years) and OR 2.00 (50–60 years) [48]. This "accelerated aging" hypothesis—that PE shifts the cardiovascular aging trajectory forward by approximately one decade—has important implications for screening age thresholds.

Mechanistic Pathways: The "Two-Hit" Model: A persistent conceptual question is whether PE directly causes cardiovascular injury or merely unmasks pre-existing susceptibility. The evidence strongly supports a "two-hit" model in which both mechanisms operate. On the susceptibility side, Weissgerber et al. (2016) demonstrated that flow-mediated dilation (FMD) is already impaired before the clinical development of PE (at 20–29 weeks gestation), indicating pre-existing endothelial vulnerability [13]. Similarly, Udenze et al. (2016) found that 26.7–45% of women with pre-pregnancy metabolic syndrome developed PE compared to only 4.7–17% of controls [66]. The shared risk factor profile—obesity, insulin resistance, dyslipidemia, chronic hypertension, and inflammatory markers—between PE and CVD strongly supports the concept that PE identifies women with underlying cardiovascular susceptibility [18,36,41].

On the injury side, compelling evidence indicates that the preeclamptic pregnancy itself inflicts lasting vascular damage. The anti-angiogenic state characteristic of PE (elevated soluble fms-like tyrosine kinase-1 [sFlt-1], reduced placental growth factor [PlGF]) correlates with cardiovascular parameters a decade later, including worse global longitudinal strain (GLS), increased carotid intima-media thickness (CIMT), and adverse lipid profiles [14,50]. DeMartelly et al. (2021) found that activin A levels remain elevated 10 years postpartum in women with prior PE, and activin A independently predicted impaired GLS after adjustment for confounders [15]. Minhas et al. (2021) described persistent angiotensin II type 1 receptor autoantibodies (AT1RAb) postpartum, which may sustain microvascular dysfunction long after the pregnancy has ended [44]. These mechanistic markers—elevated sFlt-1/PlGF ratio, activin A, and AT1RAb—are not merely correlates but plausible causal mediators of persistent vascular dysfunction. The two-hit model

reconciles these observations: pre-existing susceptibility (first hit) is compounded by a pregnancy-specific vascular injury (second hit), accelerating the trajectory toward clinical CVD.

Subclinical Phenotypes as the Bridge: The review identified four major domains of subclinical cardiovascular abnormalities that likely mediate the transition from risk factor to clinical event: (1) persistent endothelial dysfunction (impaired FMD persisting up to 3 years postpartum, impaired stress-induced vasodilation, and, paradoxically, heightened microvascular reactivity in some studies) [13,38,42]; (2) accelerated subclinical atherosclerosis (increased CIMT, coronary artery calcification, and earlier plaque development) [16,17,39,48]; (3) subclinical myocardial dysfunction (worse GLS, impaired left atrial strain, and diastolic abnormalities detectable only by advanced echocardiography) [15,20,21,56]; and (4) adverse metabolic remodeling (higher blood pressure, BMI, waist circumference, total cholesterol, LDL, triglycerides, fasting glucose, insulin, HOMA-IR, and lower HDL) [18,19,41,57]. Importantly, conventional echocardiographic parameters (LVEF, LV dimensions) often normalize within months postpartum, while speckle-tracking GLS and atrial strain reveal persistent subclinical impairment [20,59,78]. This explains apparent contradictions in the literature: studies using only conventional imaging may conclude that cardiac changes resolve, whereas studies employing strain imaging demonstrate persistent dysfunction.

Heterogeneity and Its Sources: The review identified meaningful heterogeneity across studies, which can be systematically reconciled. First, differences in PE definition and inclusion criteria matter substantially. Studies that combined mild, late-onset, or non-recurrent PE with severe, early-onset, or recurrent PE produced more moderate risk estimates. The null or very small effect sizes reported by Sonaglioni et al. (2024) for CIMT (SMD 0.143, non-significant) likely reflect a study population dominated by late-onset PE and the exclusion of during-pregnancy measurements [28], whereas Yao et al. (2025) and Garovic et al. (2017) found significant CIMT differences in more inclusive or severity-stratified analyses [16,39]. Second, follow-up duration modulates findings: some structural abnormalities resolve in the first year postpartum only to re-emerge later as atherosclerosis progresses [48,78]. Third, outcome measurement techniques vary in sensitivity: conventional brachial artery FMD shows recovery, but microvascular and advanced

arterial stiffness measures remain abnormal [13,63]. Fourth, population characteristics differ: Asian cohorts (Choi et al., Kuo et al., Xu et al.) have confirmed the association but with some differences in magnitude, possibly due to lower baseline CVD rates or genetic factors [8,11,12].

Clinical Actionability and Guidelines: The evidence has been increasingly translated into clinical guidance. The American Heart Association and multiple European cardiovascular societies now recognize a history of hypertensive disorders of pregnancy, including PE, as a risk-enhancing factor for CVD [24,61,65]. However, Fraser et al. (2022) sounded a note of caution: while predicted CVD risk scores (e.g., Framingham) are consistently higher in women with obstetric complications, the proportion crossing conventional treatment thresholds (e.g., 10-year risk >7.5% or >10%) is modest, suggesting that pregnancy complications are more useful for identifying women who would benefit from primordial and primary prevention (lifestyle modification, blood pressure monitoring, metabolic optimization) rather than automatically triggering pharmacological intervention [75]. Brouwers et al. (2018) demonstrated through microsimulation that early (age 30) and regular screening combined with lifestyle interventions could reduce CVD risk and be cost-effective [23]. The critical window for intervention appears to be the early postpartum years (1–5 years), when metabolic risk factors are already elevated but before overt clinical CVD develops [19,41,57].

Future Research Directions: Key unanswered questions include: (1) What is the optimal postpartum screening protocol (timing, modalities, frequency) for women with prior PE? (2) Do targeted interventions (statins, antihypertensives, lifestyle programs) initiated in the early postpartum period reduce long-term CVD events? (3) Can mechanistic biomarkers (sFlt-1/PlGF ratio, activin A, AT1RAb) guide individualized risk stratification? (4) How does PE interact with other pregnancy complications (gestational diabetes, preterm birth, intrauterine growth restriction) to modify CVD risk? (5) What are the molecular mechanisms linking anti-angiogenic state to persistent vascular dysfunction?

CONCLUSION AND RECOMMENDATIONS

Conclusion : This comprehensive systematic review of 80 studies, spanning from 2004 to 2026, conclusively demonstrates that preeclampsia is a significant, independent, and dose-

dependent risk factor for future cardiovascular disease, cardiovascular mortality, chronic hypertension, stroke, and heart failure. The magnitude of risk is approximately 2-fold for composite CVD and cardiovascular death, 3- to 4-fold for chronic hypertension, and 2.5- to 4-fold for heart failure. Importantly, the risk is not uniform: severe, early-onset (preterm), and recurrent preeclampsia confer substantially higher risk, with RRs up to 5.36 for cardiac disease in severe PE. The association is supported by robust evidence of intermediate phenotypes, including persistent endothelial dysfunction (impaired FMD), accelerated subclinical atherosclerosis (increased CIMT, CAC, earlier plaque development), subclinical myocardial dysfunction (impaired GLS, left atrial strain), and adverse metabolic remodeling (higher BP, BMI, lipids, insulin resistance). These abnormalities emerge within 1–3 years postpartum and persist for decades, with ischemic stroke risk peaking early and hemorrhagic stroke risk increasing gradually.

The "two-hit" model—pre-existing cardiovascular susceptibility compounded by direct pregnancy-related vascular injury—best explains the available evidence. The anti-angiogenic state, elevated activin A, and persistent AT1R autoantibodies provide plausible mechanistic links between the preeclamptic pregnancy and long-term vascular dysfunction.

Recommendations: For clinical practice, we recommend: (1) All women with a history of preeclampsia, particularly severe, early-onset, or recurrent cases, should be informed of their elevated long-term cardiovascular risk. (2) Postpartum follow-up should include blood pressure measurement at 6–12 weeks, 6 months, 1 year, and annually thereafter, with a low threshold for ambulatory blood pressure monitoring. (3) Cardiovascular risk assessment (including lipid profile, fasting glucose, and 10-year risk calculation) should be performed by 1–2 years postpartum and repeated every 3–5 years. (4) Lifestyle interventions (diet, physical activity, smoking cessation, weight management) should be prioritized, as the early postpartum years represent a critical window for primordial prevention. (5) Severe, early-onset, or recurrent preeclampsia should trigger consideration of earlier and more intensive screening, including echocardiography or coronary artery calcium scoring in selected cases after age 40. (6) Obstetric and cardiovascular societies should collaborate to implement systematic pregnancy history documentation in electronic health records and clinical decision support tools.

For research, priorities include randomized controlled trials of early postpartum pharmacological and lifestyle interventions, validation of risk stratification algorithms incorporating PE severity and biomarkers, and mechanistic studies of persistent vascular dysfunction. For public health, preeclampsia should be integrated into national CVD prevention strategies, and awareness campaigns should target both clinicians and affected women.

Ultimately, preeclampsia is not merely a complication of pregnancy—it is a women's cardiovascular health issue with lifelong implications. Recognizing and acting upon this paradigm shift offers a tangible opportunity to reduce the burden of premature cardiovascular disease in women.

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