

Title: Preeclampsia: Advances in Prediction, Prevention, and Management of a Critical Maternal–Fetal Disorder

Running title Precision Approaches in Preeclampsia

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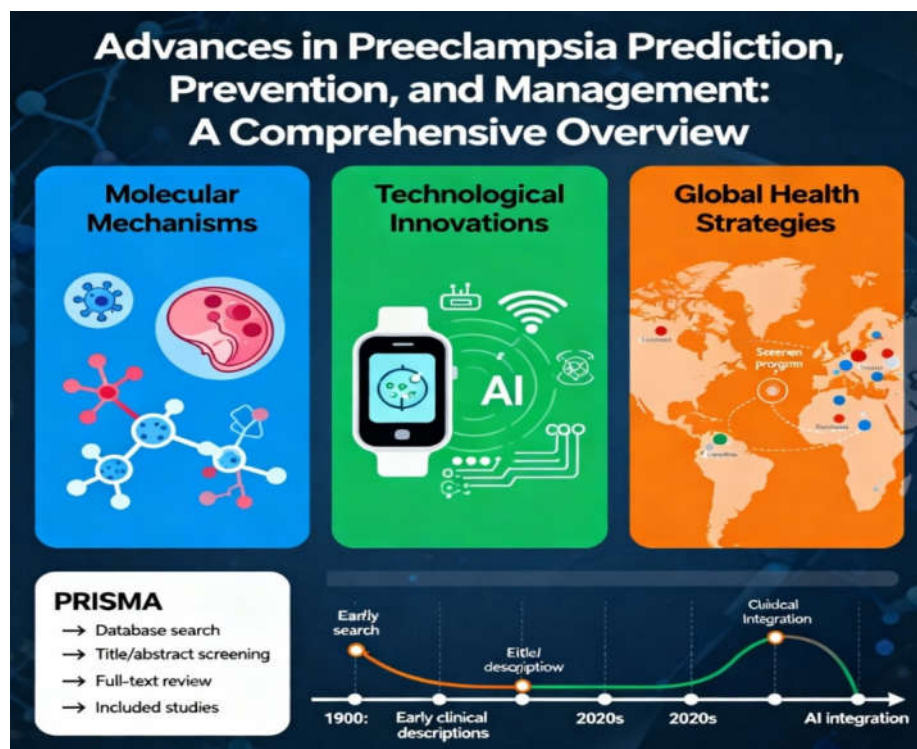
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Abstract

Preeclampsia remains one of the most formidable challenges in global maternal–fetal health, contributing substantially to preventable maternal and neonatal morbidity and mortality. Affecting an estimated 2–15% of pregnancies worldwide, this multisystem disorder arises from placental dysfunction that initiates widespread endothelial injury, systemic inflammation, and oxidative stress. Recent research has elucidated the pivotal role of angiogenic imbalance—particularly the elevation of soluble fms-like tyrosine kinase-1 (sFlt-1) and the concomitant reduction in placental growth factor (PlGF)—in its pathogenesis. Beyond conventional diagnostic parameters, the integration of genomic, transcriptomic, and epigenetic biomarkers has enhanced early risk prediction and laid the foundation for precision obstetrics. Artificial intelligence (AI) and multi-omics analytics now facilitate risk stratification by identifying molecular subtypes of preeclampsia and supporting individualized therapeutic algorithms. Preventive strategies have evolved beyond low-dose aspirin and calcium supplementation to include agents such as pravastatin, low-molecular-weight heparin, metformin, and nitric oxide donors, each targeting distinct molecular pathways of placental dysfunction. Precision management models integrating telemonitoring, wearable sensors, and digital decision-support systems are transforming care in high-risk pregnancies, enabling early detection and continuous maternal–fetal surveillance. Importantly, the sequelae of preeclampsia extend well beyond gestation, predisposing affected women to long-term cardiovascular and renal disease and their offspring to metabolic and developmental complications. Emerging interventions, including angiogenic modulators, CRISPR-based gene editing, and endothelial-targeted therapeutics, represent the next frontier in treatment. However, disparities in healthcare access, economic limitations, and ethical considerations surrounding AI-driven prediction continue to hinder equitable implementation. The convergence of molecular medicine, digital health, and global health policy offers the most promising pathway toward achieving truly personalized prediction, prevention, and management of this critical maternal–fetal disorder.

Keywords: Preeclampsia; Angiogenic imbalance; Placental dysfunction; Endothelial injury; Soluble fms-like tyrosine kinase-1 (sFlt-1); Placental growth factor (PlGF)

Graphical abstract



Introduction: The Evolving Challenge of Preeclampsia

Preeclampsia remains a significant and evolving challenge in maternal–fetal health, characterized by new-onset hypertension and often proteinuria after the 20th week of gestation, affecting 2–15% of pregnancies globally (1). It continues to be a leading cause of maternal and neonatal morbidity and mortality, accounting for approximately 76,000 maternal and 500,000 neonatal deaths annually (2). The disorder’s pathophysiology involves complex interactions among genetic, immunologic, and environmental factors, culminating in placental dysfunction, systemic inflammation, and endothelial injury (3,4). Recent advances have identified key angiogenic biomarkers, particularly soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF), which have enhanced early diagnosis and disease monitoring (5).

Despite these developments, preeclampsia remains a multifactorial condition with distinct subtypes—early-onset, late-onset, and superimposed forms—each associated with unique molecular and clinical characteristics that complicate prediction and prevention. Current management strategies primarily rely on antihypertensive therapy, magnesium sulfate for seizure prophylaxis, and expedited delivery as the definitive intervention (6). Among preventive measures, low-dose aspirin has shown efficacy in reducing the incidence of early-onset disease when initiated in high-risk women before 16 weeks of gestation (7).

However, the financial and healthcare burden associated with preeclampsia remains considerable, necessitating stronger public health policies and resource allocation to improve access to antenatal care (8). The condition’s impact extends well beyond pregnancy, with affected women facing heightened lifetime risks of cardiovascular and renal disorders, and offspring demonstrating increased susceptibility to metabolic and developmental complications (6). Comprehensive management—anchored in early screening, biomarker-based prediction, and multidisciplinary coordination—remains pivotal for improving outcomes (9). Continued innovation in diagnostic, predictive, and therapeutic strategies is essential to address this persistent global health challenge (10).

Molecular Pathophysiology: Placental and Endothelial Crosstalk

The molecular pathophysiology of preeclampsia (PE) involves intricate interactions between the placenta and maternal endothelium, characterized by a disruption in angiogenic balance and progressive endothelial dysfunction. The condition is marked by dysregulation of angiogenic and vasoactive mediators—most notably elevated soluble Fms-like tyrosine kinase-1 (sFlt-1) and endothelin-1—which are particularly pronounced in early-onset PE compared with normotensive pregnancies (11). The placenta serves as the primary source of these circulating factors that impair maternal endothelial function, culminating in systemic inflammation and vascular injury (12).

Endothelial dysfunction is further intensified by overactivation of the NLRP3 inflammasome, which enhances interleukin-1 β (IL-1 β) release and disrupts endothelial barrier integrity by downregulating VE-cadherin expression (13). This pro-inflammatory environment contributes to widespread endothelial activation and vasoconstriction, driven by anti-angiogenic and pro-inflammatory mediators released from the ischemic placenta (14). Moreover, degradation of the endothelial glycocalyx facilitates the liberation of inositol phosphoglycans and other angiogenic modulators, further compromising vascular integrity (12).

The crosstalk between endothelial cells and other tissue types—such as cardiomyocytes and podocytes—underscores the systemic nature of PE, reflecting shared mechanisms with chronic disorders like atherosclerosis and diabetic kidney disease, where endothelial-to-mesenchymal transition and impaired autophagy similarly play pathogenic roles (15). A comprehensive understanding of these molecular interactions at the maternal–fetal interface is therefore critical for identifying therapeutic targets and developing precision interventions aimed at mitigating adverse outcomes and improving long-term maternal and fetal health (16).

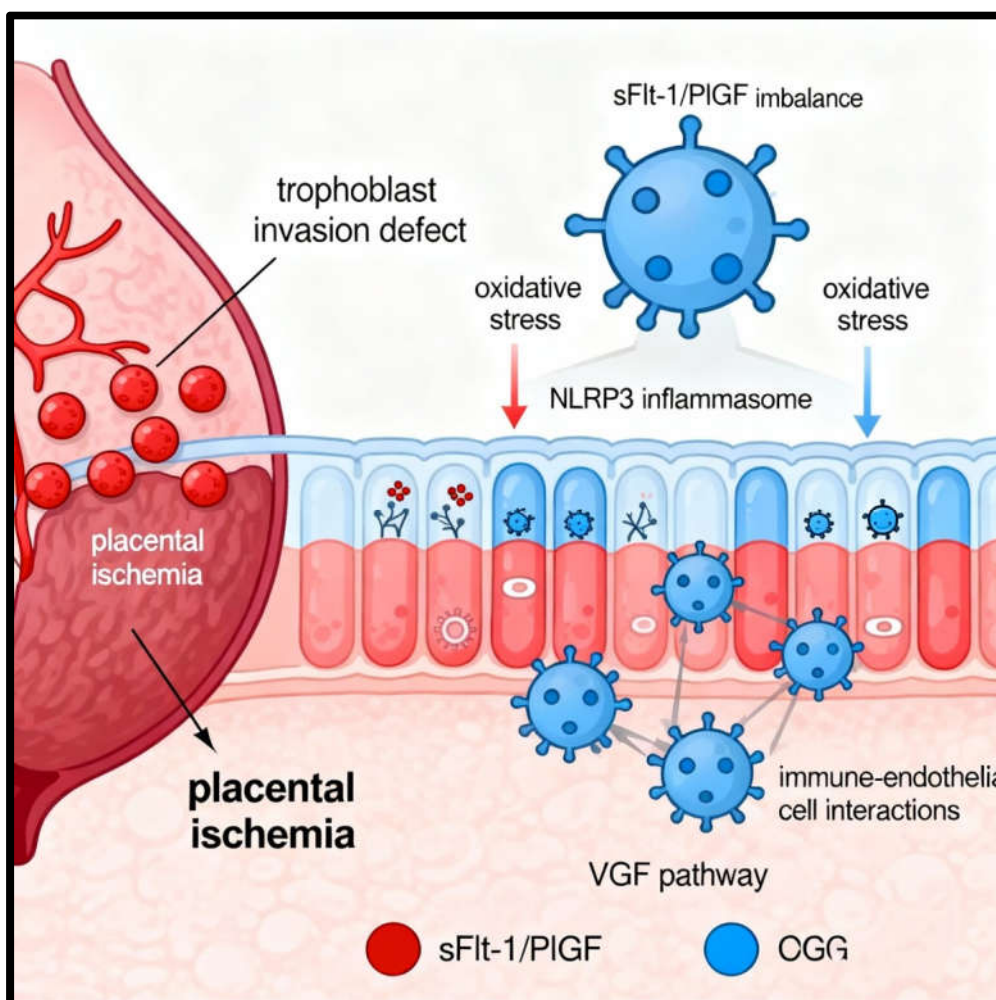


Figure 1: Placental ischemia from defective trophoblast invasion triggers oxidative stress and NLRP3 inflammasome activation, disrupting angiogenic balance (sFlt-1/PlGF) and endothelial function. This cascade leads to vascular dysfunction and systemic inflammation characteristic of preeclampsia.

Genomic and Epigenetic Biomarkers in Early Prediction

Genomic and epigenetic biomarkers have emerged as pivotal tools for the early prediction of complex diseases, including malignancies and neurodegenerative disorders. In breast cancer, recent advances have identified novel epigenetic biomarkers capable of predicting early disease onset, treatment response, and recurrence through the detection of aberrant DNA methylation patterns in tumor tissues and circulating plasma—signatures absent in healthy individuals (17). Similarly, in colorectal cancer (CRC), the methylation of specific genes such as *vimentin* (VIM),

syndecan-2 (SDC2), and *septin 9* (SEPT9) has been proposed as a potential diagnostic panel, although further validation is required before clinical translation (18).

In neurodegenerative conditions like Alzheimer's disease (AD), DNA methylation (DNAm) markers have been evaluated for their predictive potential. Longitudinal analyses reveal that while epigenetic age acceleration shows limited prognostic value, certain DNAm profiles can anticipate AD onset up to eight years in advance—though their predictive strength remains inferior to established genetic determinants such as *APOE ε4* (19,20). Reproducibility, however, remains a major challenge, as variability in CpG site associations across cohorts limits cross-study consistency (21).

Beyond oncology and neurodegeneration, epigenomic signatures are increasingly being explored in obstetric and perinatal contexts. In particular, studies on preterm birth and placental dysfunction have underscored the potential of stable methylation markers to reflect both genetic predisposition and environmental exposure, offering a window into early disease prediction (22). Collectively, while genomic and epigenetic biomarkers represent a transformative frontier for predictive medicine, their widespread clinical application will depend on rigorous validation across diverse populations and disease states (Table 1).

Table 1: Key Biomarkers Implicated in the Pathogenesis and Prediction of Preeclampsia

Category	Biomarker	Mechanism / Function	Clinical Utility
Angiogenic	sFlt-1, PlGF, sEng	Imbalance leads to endothelial dysfunction and vasoconstriction	Early diagnosis, disease severity assessment
Inflammatory	IL-6, TNF- α , CRP	Promote systemic inflammation and oxidative stress	Risk stratification and prognosis
Oxidative Stress	8-isoprostane, MDA, SOD	Reflect oxidative injury to endothelium	Marker of disease progression
Genetic / Epigenetic	miR-210, miR-155, DNA methylation of STOX1	Regulate trophoblast invasion and placental gene expression	Early prediction, personalized therapy
Metabolic	Uric acid, homocysteine, adiponectin	Endothelial dysfunction and vascular damage	Supportive diagnostic marker

Artificial Intelligence and Multi-Omics Approaches for Risk Stratification

Artificial intelligence (AI) and multi-omics technologies are increasingly shaping the landscape of precision medicine by enhancing disease classification, risk stratification, and personalized therapeutic design across a wide range of disorders. In hepatocellular carcinoma (HCC), the integration of multi-omics datasets—encompassing clinical, transcriptomic, genomic, and epigenomic profiles—has enabled the identification of distinct molecular subtypes, thereby improving prognostic accuracy and informing individualized treatment strategies. The development of an AI-derived risk score (AIDRS) further assists in predicting patient outcomes and optimizing therapeutic decisions (23).

Similarly, in psychiatric research, multi-omics frameworks have proven valuable. For instance, in schizophrenia, the combination of plasma proteomics, post-translational modification profiling, and metabolomics has facilitated the discovery of peripheral immune-coagulation biomarkers, substantially improving classification performance and providing deeper insights into disease pathophysiology (24). Comparable advances have been reported in glioblastoma, where machine-learning models integrating radiomic, pathomic, genomic, transcriptomic, and proteomic layers have successfully delineated clinically relevant subgroups, thereby refining prognostic models and unveiling new therapeutic targets (25)

In hematologic malignancies such as diffuse large B-cell lymphoma (DLBCL), AI-driven multi-omics and spatial multi-omics analyses have been instrumental in dissecting molecular heterogeneity and advancing the paradigm of precision oncology (26). The broader application of AI in cancer medicine further underscores its capacity to integrate diverse biological and clinical data to enhance subtyping, risk assessment, and clinical decision-making. Likewise, in acute myeloid leukemia (AML), longitudinal AI models leveraging electronic health record (EHR) data have demonstrated predictive performances comparable to traditional clinical criteria, offering dynamic, data-driven approaches to patient management (27) (table 2).

Table 2: Multi-Omics Approaches for Risk Stratification in Preeclampsia

Omics Layer	Key Insights	Applications in Preeclampsia	Analytical Tools
Genomics	Variants in FLT1, VEGF, STOX1, and HLA-G genes	Genetic predisposition and susceptibility profiling	GWAS, SNP microarrays
Transcriptomics	Dysregulated placental RNA and microRNA expression	Early detection, molecular subtyping	RNA-seq, qPCR
Proteomics	Altered plasma and placental protein signatures	Biomarker discovery and therapeutic targets	LC-MS/MS, ELISA
Metabolomics	Disturbed lipid and amino acid metabolism	Identification of metabolic pathways linked to PE	NMR, GC-MS
Epigenomics	DNA methylation and histone modifications	Fetal programming, long-term disease risk	B

Collectively, these advancements exemplify the transformative potential of AI-enabled multi-omics integration in advancing disease prediction and therapeutic precision. Although most evidence to date stems from oncology and neuroscience, the same analytical frameworks are now being adapted to obstetric medicine—particularly for disorders like preeclampsia—where integrating clinical, biochemical, and placental omics data may enable earlier prediction, refined risk categorization, and truly individualized management strategies.

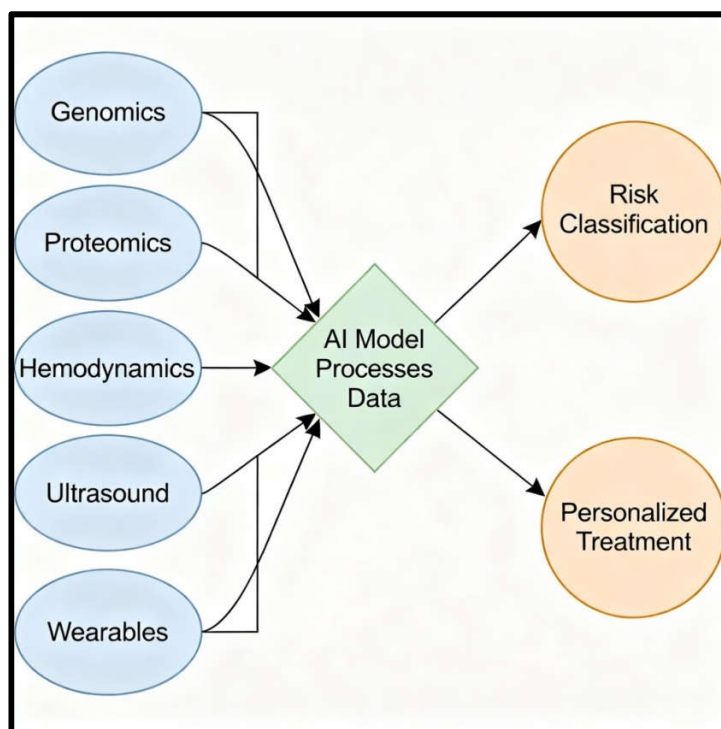


Figure 2. Artificial intelligence integrates genomic, proteomic, hemodynamic, ultrasound, and wearable data to process complex patterns, enabling early risk classification and personalized treatment strategies in preeclampsia.

Novel Preventive Strategies: Beyond Aspirin and Calcium

Recent advances in preventive medicine have expanded far beyond traditional interventions such as low-dose aspirin and calcium supplementation, reflecting a paradigm shift toward targeted and mechanism-based approaches. In the context of preeclampsia, several pharmacological strategies are being investigated for their ability to interrupt disease progression by modulating specific molecular pathways. These include low-molecular-weight heparins, pravastatin, proton pump inhibitors, metformin, nitric oxide donors, and L-arginine, each demonstrating potential in improving placental perfusion, endothelial function, and maternal–fetal outcomes (28).

Parallel innovations in other medical fields underscore this broader transition toward personalized prevention. In recurrent urolithiasis, emerging strategies such as probiotic supplementation to reduce oxalate absorption, genomic profiling for individualized intervention, and machine learning models for high-risk prediction exemplify this shift toward precision

prevention (28). Likewise, cardiovascular medicine is undergoing a comparable transformation, with the development of over a dozen novel plaque-stabilizing therapies designed to minimize lifelong pharmacologic exposure through shorter, more effective treatment regimens (30).

These advancements are complemented by progress in genetic and multi-omics risk stratification, which enables individualized assessment of predisposition and facilitates early, patient-specific preventive measures. Moreover, the incorporation of telemedicine, artificial intelligence, and community-based digital health interventions is revolutionizing early detection and risk monitoring, particularly in pregnancy-related disorders such as preeclampsia (31). Collectively, these innovations reflect a decisive shift toward a personalized, technology-driven, and multidisciplinary model of preventive medicine that aims to optimize outcomes and reduce the global healthcare burden (32).

-Novel Preeclampsia Preventive Strategies Comparative Table			
Medication	Mechanism	Pregnancy Stage	Evidence
Low-dose aspirin	Anti-platelet	First trimester	Level 1 evidence
Pravastatin	Angiogenic balance	Second trimester	Level 2 evidence
LMWH	Anti-inflammatory		Level 1 evidence
Metformin	AMPK activation	First trimester	Level 2 evidence
L-arginine	NO donor		Level 3 evidence

Figure 3. Comparative summary of emerging pharmacologic strategies for preeclampsia prevention. Each intervention targets distinct molecular mechanisms across pregnancy stages, supported by varying levels of clinical evidence.

Precision Management and Remote Monitoring in High-Risk Pregnancies

Precision management and remote monitoring technologies are redefining the care of high-risk pregnancies by enabling continuous surveillance, timely intervention, and data-driven decision-making. Telemonitoring systems, such as the model developed by Nazari et al., (33) exemplify this approach by automatically alerting healthcare centers upon discharge of high-risk pregnancies, ensuring ongoing support through digital platforms that capture medical data and clinical recommendations (33).

For disorders such as preeclampsia, integrating machine learning algorithms with biomarker-based monitoring has markedly improved prediction accuracy and diagnostic precision, paving the way for individualized management strategies (34). Evidence from studies such as that by Zizzo et al. demonstrates that remote self-monitoring of maternal and fetal health is a safe and effective alternative to conventional care, yielding excellent maternal outcomes and neonatal survival rates even in complex pregnancies. Furthermore, systematic reviews and meta-analyses indicate that remote fetal monitoring can reduce rates of neonatal asphyxia and lower healthcare costs, though further large-scale validation is needed across diverse high-risk populations (35).

Remote blood pressure surveillance, as evaluated in the REMOTE CONTROL trial, offers a cost-effective solution that minimizes the need for frequent clinical visits—an especially valuable innovation for rural or resource-limited settings (36). Similarly, the PREMOM II study emphasizes the integration of telehealth frameworks into prenatal care for gestational hypertensive disorders, promoting continuity of care and early detection (37). The INVU platform, which supports remote non-stress testing, further illustrates the potential of wearable and digital technologies to expand access to maternal-fetal monitoring, particularly among underserved populations (38).

Collectively, these innovations underscore the transformative role of precision digital health in obstetric care. By enhancing accessibility, reducing healthcare costs, and enabling personalized risk assessment, remote monitoring technologies have the potential to improve maternal and neonatal outcomes worldwide. However, sustained research, infrastructural investment, and

clinical validation remain essential to ensure safe, equitable, and scalable integration into high-risk pregnancy management (39).

Cardiovascular and Metabolic Sequelae in Mothers and Offspring

Cardiovascular and metabolic sequelae in both mothers and their offspring are profoundly influenced by maternal conditions such as gestational diabetes mellitus (GDM), metabolic syndrome (MetS), preeclampsia (PE), and obesity. Women with GDM exhibit a substantially elevated risk of developing type 2 diabetes mellitus, hypertension, and metabolic syndrome later in life, while their offspring are predisposed to obesity, insulin resistance, and early-onset cardiovascular diseases (CVD) extending from childhood into adolescence (40). Similarly, the presence of MetS during pregnancy is associated with adverse obstetric outcomes and long-term cardiovascular and metabolic dysfunction in both mother and child, compounded by ongoing challenges in identifying reliable early biomarkers for prevention (41).

Preeclampsia, which complicates approximately 2–8% of pregnancies, has been recognized as an independent risk factor for future cardiovascular morbidity. Affected women face a twofold increase in CVD risk, while their offspring demonstrate a higher incidence of cardiovascular disease and congenital heart defects—an association mediated by intertwined genetic, epigenetic, and environmental mechanisms (42). Maternal obesity further exacerbates these risks, being consistently linked to congenital heart malformations and a lifelong predisposition to cardiovascular disease in the progeny, driven by a complex interplay of metabolic programming, inflammation, and shared genetic susceptibility (43).

In addition, maternal metabolic disorders during gestation can disrupt fetal cardiac morphogenesis, leading to structural and functional abnormalities through epigenetic modifications in cardiac gene expression. Emerging evidence also suggests that the influence of parental MetS on offspring cardiometabolic risk varies according to sex, underscoring the necessity of incorporating sex-specific strategies into preventive and postnatal management frameworks (44). Furthermore, low first-trimester concentrations of pregnancy-associated plasma protein A (PAPP-A) have been correlated with heightened risks of metabolic and cardiovascular complications in both mothers and their offspring (45).

Collectively, these findings highlight the lasting intergenerational impact of maternal metabolic and hypertensive disorders. Early identification of high-risk pregnancies, coupled with long-term cardiovascular surveillance and tailored lifestyle interventions, is essential to mitigate these enduring health risks for both mother and child.

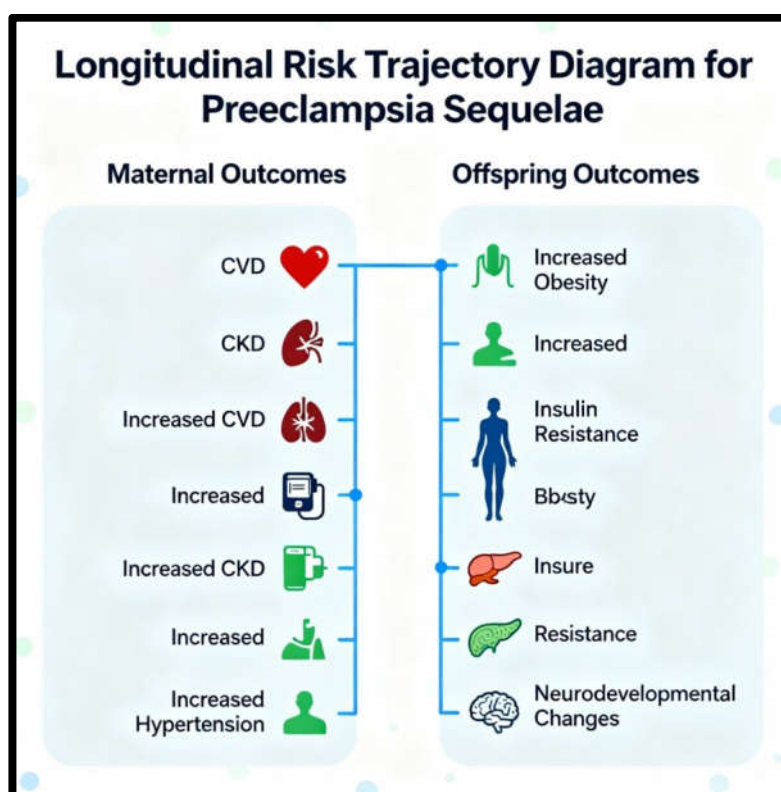


Figure 4. Long-term sequelae of preeclampsia in mothers and offspring. Maternal complications include increased risk of cardiovascular disease, chronic kidney disease, and hypertension, while offspring face heightened susceptibility to obesity, insulin resistance, and neurodevelopmental alterations.

Emerging Therapeutics: Angiogenic Modulators and Gene-Targeted Interventions

Emerging therapeutic approaches for angiogenic modulation and gene-targeted interventions have advanced rapidly in recent years, particularly in the field of neovascular age-related macular degeneration (nAMD). Although current anti-vascular endothelial growth factor (anti-VEGF) therapies have revolutionized disease management, their limitations—including frequent

intravitreal injections, waning long-term efficacy, and suboptimal real-world outcomes—highlight the need for more durable and precise therapeutic solutions (46).

Gene therapy has emerged as a particularly promising modality, with CRISPR–Cas9-based systems being investigated for their ability to permanently suppress pro-angiogenic mediators such as *VEGFA*. Experimental studies using paired guide RNAs have demonstrated enhanced gene ablation efficiency; however, these findings have not yet consistently translated into greater VEGF suppression in vivo, reflecting the complexity of bridging preclinical results to clinical efficacy (47). Parallel research into lentiviral vectors (LVs) for the delivery of anti-angiogenic agents, including aflibercept, has shown notable potential. Compared to adeno-associated viruses (AAVs), LVs offer stable transgene expression and larger cargo capacity, achieving sustained therapeutic levels of anti-VEGF proteins in preclinical ocular models (48).

Beyond VEGF inhibition, novel pharmacologic agents targeting complementary angiogenic pathways—such as VEGF-C and VEGF-D inhibitors—are under active development to overcome the resistance and partial responses observed with existing anti-VEGF regimens (49). The strategic integration of these gene-directed interventions with established pharmacotherapies may ultimately enhance treatment durability, efficacy, and patient compliance (50).

Despite these advances, several challenges remain. Off-target effects associated with CRISPR-based editing, immunogenicity of viral delivery systems, and the need for optimized dosing and vector safety continue to impede clinical translation (51). Nonetheless, as gene therapy platforms mature, the convergence of angiogenic modulation and genomic precision technologies holds immense potential not only for ocular neovascular disorders but also for systemic angiogenesis-related conditions such as preeclampsia, offering the prospect of more effective and less invasive therapeutic paradigms (51,52).

Global Health Perspectives and Implementation Challenges

Global health perspectives and their associated implementation challenges are inherently multifaceted, spanning domains from policy frameworks and governance structures to technological and infrastructural capacities. The International Health Regulations (IHR) underscore the necessity of robust global health governance; however, persistent obstacles—

including inadequate resource allocation, limited enforcement mechanisms, and weak international coordination—have been evident, particularly during the COVID-19 pandemic (53). Similarly, the European Union’s Global Health Strategy articulates strong commitments to health equity and system resilience but remains hindered by the absence of a dedicated funding framework and the fragmented integration of health priorities across policy sectors (54).

The growing burden of both emerging infectious diseases and chronic noncommunicable conditions demands coordinated global action and sustained public health investment to strengthen preparedness and enhance health security. Yet, the persistent inequities in access to precision medicine illustrate the broader challenges of global implementation. For instance, while precision oncology has made significant advances, high costs, technical complexity, and infrastructural gaps continue to limit its applicability in low- and middle-income countries (55). These disparities parallel similar challenges in maternal–fetal medicine, where innovations in biomarker testing, AI-based screening, and digital prenatal monitoring remain concentrated in high-resource settings (table 3).

Table 3: Global and Implementation Challenges in Precision Preeclampsia Care

Challenge	Description	Potential Solution
Resource limitations	Limited access to diagnostic assays (PlGF/sFlt-1) in LMICs	Subsidized kits, decentralized point-of-care platforms
Data inequity	AI algorithms trained predominantly on Western datasets	Inclusion of ethnically diverse populations
Technological integration	Lack of interoperability between hospital and telehealth systems	Unified electronic health infrastructure
Ethical and privacy concerns	Data protection, informed consent, AI transparency	Stronger regulatory and ethical frameworks
Implementation gap	Translation of research findings into practice is slow	Adoption of implementation-science models

Implementation science offers a promising framework to bridge the research-to-practice divide by emphasizing locally adapted, context-specific interventions and fostering community participation to advance equitable health outcomes (56). Complementary technological innovations such as digital health and telemedicine have demonstrated potential to improve healthcare delivery, but their long-term sustainability and scalability require rigorous evaluation

and policy integration (57). Moreover, the current distribution of artificial intelligence applications in healthcare remains disproportionately skewed toward developed nations, highlighting the need for global strategies to democratize AI adoption and ensure its responsible use across diverse populations (57).

The COVID-19 pandemic further exposed and amplified systemic weaknesses—ranging from disrupted medical supply chains to widening socioeconomic disparities—underscoring the urgent need for coordinated international action and behavioral health research to build more resilient systems. Ultimately, addressing these global health challenges necessitates a concerted and multidisciplinary approach: strengthening governance, fostering equitable access to emerging technologies, and promoting intergovernmental collaboration to achieve sustainable, inclusive, and equitable health outcomes worldwide (58).

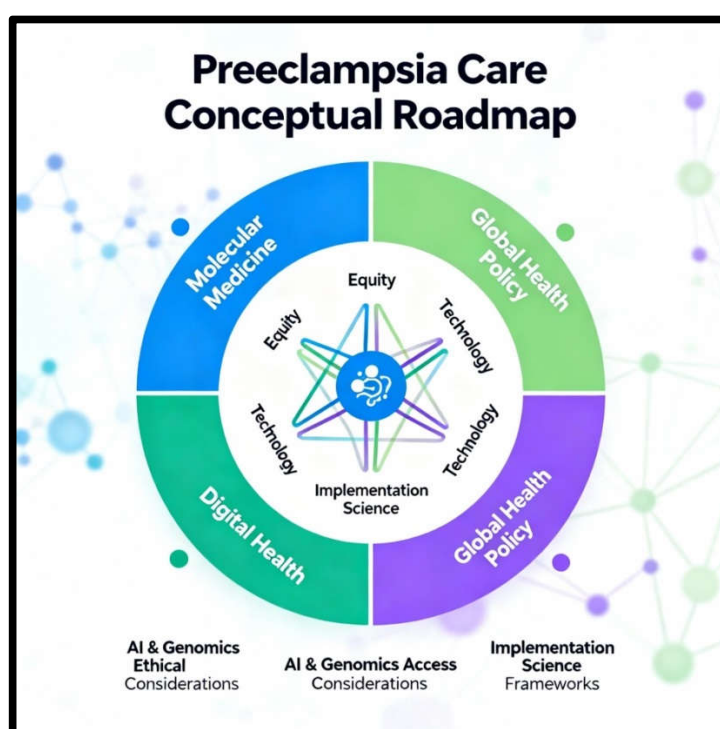


Figure 4. Long-term sequelae of preeclampsia in mothers and offspring. Maternal complications include increased risk of cardiovascular disease, chronic kidney disease, and hypertension, while offspring face heightened susceptibility to obesity, insulin resistance, and neurodevelopmental alterations.

Future Directions: Toward Personalized Prediction and Prevention

The future of personalized prediction and prevention in healthcare is being rapidly reshaped by the convergence of artificial intelligence (AI), genomics, and multi-omics technologies. Personalized medicine seeks to tailor preventive and therapeutic strategies to individual biological, genetic, and environmental characteristics—fundamentally moving beyond the conventional “one size fits all” paradigm. In Alzheimer’s disease (AD), for instance, personalized prevention frameworks integrating lifestyle modifications with disease-modifying interventions have shown potential to delay or even prevent cognitive decline, empowering patients to take an active role in managing their health (59). Similarly, in hypertrophic cardiomyopathy (HCM), AI-driven models have enhanced risk stratification and treatment individualization, although challenges such as data bias, validation standards, and regulatory oversight remain significant barriers to clinical translation (60).

In oncology, molecular profiling combined with AI-based analytics has transformed therapeutic precision, allowing clinicians to predict individual treatment responses and optimize care pathways (61). The integration of genomics, transcriptomics, and proteomics—supported by digital twin and systems biology modeling—has enabled real-time simulation of disease trajectories and personalized risk forecasting. Meanwhile, precision nutrition is emerging as a novel preventive discipline, utilizing genomic, epigenetic, and microbiome data to individualize dietary interventions aimed at improving metabolic health and preventing chronic disease (62). Comparable progress is evident in sleep medicine, where predictive, preventive, and personalized medicine (PPPM) frameworks employ AI and machine learning to analyze large-scale digital datasets, identifying sleep-related risk factors and guiding targeted behavioral interventions (63).

Across these disciplines, the integration of advanced analytics, real-time physiological data, and cross-sectoral collaboration is proving central to improving prediction accuracy and preventive effectiveness (64). However, the success of these technologies hinges on addressing persistent ethical, regulatory, and equity concerns—particularly those related to algorithmic bias, data privacy, and access disparities (65). In the context of maternal–fetal medicine, such precision approaches hold immense promise: AI-driven multi-omics models, digital twins of pregnancy,

and population-specific genomic profiling may soon allow for individualized risk prediction and proactive prevention of complex disorders such as preeclampsia.

Overall, the trajectory of personalized prediction and prevention is profoundly optimistic. As the integration of AI and multi-omics deepens, and ethical governance frameworks mature, healthcare systems are poised to transition toward a truly predictive, preventive, and personalized paradigm—transforming individual health outcomes and reshaping the future of global medicine.

Conclusion

Preeclampsia continues to represent one of the most complex and consequential challenges in maternal–fetal medicine, with profound implications for both short- and long-term health. Despite major advances in our understanding of its molecular, genetic, and immunologic underpinnings, preeclampsia remains a multifactorial disorder that demands an integrated, precision-based approach to prediction, prevention, and management. Disruption of placental angiogenic balance, endothelial dysfunction, and systemic inflammation form the core of its pathophysiology, yet ongoing discoveries in genomic, epigenetic, and proteomic biomarkers are gradually redefining its diagnostic landscape.

Emerging technologies—including artificial intelligence, multi-omics integration, and remote digital monitoring—offer unprecedented opportunities for early detection and risk stratification. At the same time, novel pharmacological and gene-targeted interventions, such as angiogenic modulators, statins, metformin, and CRISPR-based therapeutics, are expanding the therapeutic frontier. However, translating these innovations into real-world clinical benefit will require rigorous validation, equitable access, and strong implementation frameworks, particularly in low- and middle-income settings.

A future vision for preeclampsia management lies in the convergence of molecular medicine, digital health, and global health policy. Precision obstetrics—grounded in predictive biomarkers, AI-assisted decision tools, and personalized preventive care—has the potential to not only reduce maternal and neonatal morbidity but also mitigate the intergenerational burden of cardiovascular and metabolic disease. To achieve this, multidisciplinary collaboration among clinicians, researchers, data scientists, and policymakers is essential. Continued investment in research,

technology, and health equity will ultimately transform preeclampsia from a life-threatening complication into a model for personalized maternal care worldwide.

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