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Review

The programming of women's health: A narrative review detailing insights into regenerative medicine-based approaches for cardiovascular disease intervention

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From the Contents

Abstract

Fetal programming (Barker's hypothesis) is a key concept in the current vision of health and disease. The fetal programming hypothesis of adult diseases suggests that the fetus adapts to environmental influences, and those changes in its regulatory systems could have long-term effects on child and adult health. The theory stems from the widely held finding that infants who are lower in weight at birth are more likely to die from cardiovascular disease later in life. There is certainly sex-specific cardiovascular disease. There is evidence that women who have given birth to low-birth-weight babies have an increased level of arterial hypertension. Pre-eclampsia is a well-known risk factor for cardiovascular disease and its complications. A review of the literature focused on analyzing the factors affecting women's health programming from the antenatal stage to elderly age. Fetal programming arose from food blockade in the Netherlands during World War II. The weak point in Barker's hypothesis is the absence of different situations associated with low birth weight. This could be due to premature birth or fetal growth restriction. Fetal growth restriction is a satellite of pre-eclampsia. An analysis of the literature data revealed that mothers of children who are small for gestational age have an increased risk of cardiovascular disease of up to 3 times, whereas mothers with pre-eclampsia and preterm birth have an increased risk of cardiovascular disease of up to 9 times. Therefore, pregnancy complications are an early marker of a woman's predisposition to develop cardiovascular disease and require preventive measures. Menopause typically begins as aging starts, often resulting in various diseases. There are no evident markers of fetal programming atherogenicity during the reproductive period in women without severe comorbidities. Hypoestrogenism is a trigger for a considerable number of comorbid menopausal disorders. Close monitoring of menopausal patients permits the determination of priorities in the implementation of the following therapeutic strategies, reducing the risk of cardiovascular disease. Dietary nutrition and physical activity are important components of preventive medicine for reducing insulin resistance, dyslipidemia, and chronic inflammation. In conclusion, the analysis of the risk factors for cardiovascular disease and other pathologies in women revealed the significant role of placenta-related disorders. Great obstetric syndromes can affect both fetal and maternal health programming, with long- and short-term consequences. Maternal polycystic ovary syndrome is a cause of metabolic syndrome, type 2 diabetes mellitus, and disturbed development of the fetal reproductive system. Menopause is a time for initiative-taking health measures that support longevity. Creating gender-focused cardiovascular disease prevention programs in regenerative medicine could further advance human health.

Key Words: aging; anti-aging; cardiovascular disease; fetal growth restriction; fetal programming; menopause; placental-related disorders; polycystic ovarian syndrome; pre-eclampsia; regenerative medicine

Introduction

Fetal programming (Barker's hypothesis) is a key concept in the current vision of health and disease, recognizing the influence of the prenatal and early postnatal environment on health status throughout life.[1] The fetal programming hypothesis of adult diseases suggests that the fetus adapts to environmental influences, and those changes in its regulatory systems could have long-term effects on child and adult health. The theory stems from the widely held finding that infants who are lower in weight at birth are more likely to die from cardiovascular disease (CVD) later in life.[2,3] The model, first used for cardiometabolic phenotypes, now also covers the nervous system and mental health disorders. The range of laboratory markers for diseases that begin before birth is still not fully understood. The development of a personalized patient-centered screening program assessing perinatal pathology is one of the current challenges.[4]

There is certainly sex-specific CVD. The highest level of CVD manifestation occurs during early aging in the process of the transition to menopause. This life interval requires the greatest attention to lipid profiles, carbohydrate metabolism, body mass index (BMI), and blood pressure (BP). Gestational disorders and low birth weight are linked to menopause.[5] It is also known that women who have given birth to low-birth-weight babies have an increased level of arterial hypertension.[6]

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A review of the literature focused on analyzing the factors affecting women's health programming from the antenatal stage to elderly age.

Literature Search

For this review, literature searches were performed using PubMed, Scopus, or Web of Science from 2010 to 2025. The following keywords were used: "fetal programming," "women's health programming" OR "cardiovascular disease programming." The articles included in this review were selected based on their relevance to the topic. The results were further screened according to the title and abstract and whether they included animal experiments, in vitro studies, clinical trials, and database or software applications. **Figure 1** shows the literature screening process.

Developmental Origins

Role of gestational pathologies

Pre-eclampsia (PE) is a well-known factor for CVD and its complications.[7] PE is a severe complication of pregnancy that affects 5%–8% of pregnancies worldwide. PE is a great obstetric syndrome. These pathologies are characterized by disturbed placentation. These diseases also include fetal growth restriction, preterm birth, and gestational diabetes mellitus. PE is characterized by high blood pressure and multiple organ failure, typically occurring after 20 weeks of pregnancy. PE is the main cause of maternal and perinatal morbidity and mortality. Although its exact cause is unknown, PE is associated with placental ischemia resulting from inadequate invasion of trophoblastic cells into the spiral arterioles or impaired adaptation of the maternal cardiovascular system to pregnancy (**Figure 2**). Risk factors include a history of PE, chronic hypertension, diabetes mellitus, obesity, and autoimmune diseases. Symptoms include arterial hypertension, proteinuria, headache, visual disturbances, and abdominal pain. Without treatment, PE can lead to seizures, stroke, preterm labor, or even death. The termination of pregnancy (induction of labor) is the most effective treatment. PE significantly increases the long-term risk of CVD, including hypertension, coronary heart disease, and stroke.[8] This is due to shared mechanisms such as endothelial malfunction and chronic inflammation. Women with severe PE are at increased risk of CVD, often developing chronic hypertension within a decade of delivery. It also affects offspring, with daughters at increased risk of PE and CVD. PE causes hemodynamic changes such as left ventricular hypertrophy and diastolic malfunction, which increase the risk of heart failure with a preserved ejection fraction and coronary atherosclerosis. The use of antihypertensives in PE is not only associated with BP control but also with preventing cardiac remodeling.[9,10] Long-term monitoring and lifestyle interventions are crucial for risk management, and research on genetic and biological mechanisms offers the potential for targeted prevention.

Several approaches exist for managing pregnant women at risk of, or showing signs of, PE.[11] The use of low doses of acetylsalicylic acid to prevent PE in the population at risk is known. An elevated pulsatile index and a dicrotic notch in early diastoles during uterine artery Doppler flow can indicate PE risk as early as the end of the first trimester. Automated PE risk analysis programs have incorporated these biophysical markers. Among the biochemical markers, screening studies include measurements of pregnancy-associated protein P (a protease of the insulin-like growth factor transport protein), human chorionic gonadotropin, placental growth factor (PlGF, an angiogenic substance) and tyrosine-like receptors (sFlt-1, an antiangiogenic substance). The last two substances maximally characterize the process of uteroplacental vascular gestational transformation.

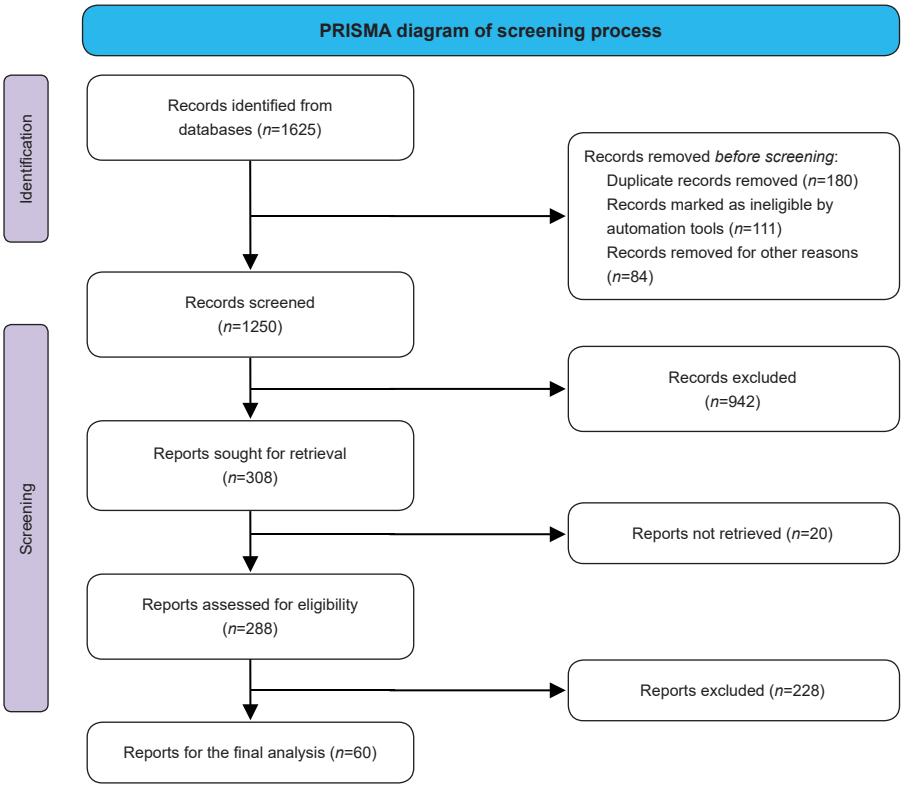

Figure 1 | **The stages of paper selection included in the study.**
PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Combined biophysical and biochemical screening models are designed to be performed at the end of the first trimester of pregnancy. They are more specific for early-onset PE (occurring before 34 weeks of pregnancy and are, in most cases, severe). Physicians are more interested in the prediction or early detection of PE at any stage of pregnancy. Since disturbed placentation is the key event in the pathogenesis of PE, markers of placental angiogenesis are the most evident and promising indicators for continual laboratory monitoring. sFlt-1 is an antiangiogenic factor important for the regulation of angiogenic homeostasis during pregnancy. During normal pregnancy, the concentration of sFlt-1 increases steadily during the third trimester. However, it increases prematurely in women who develop PE, as well as in cases of fetal growth restriction. The level of sFlt-1 in maternal blood increases approximately 5 weeks before the onset of symptoms of PE. sFlt-1 binds to PlGF, blocking its activity. The decrease in PlGF concentration is largely mediated by an excess of circulating sFlt-1. PlGF is an angiogenic substance that is expressed in the placenta and enhances the action of vascular endothelial growth factor A (VEGF-A), which is also involved in uterine spiral vessel transformation. The concentration of PlGF in the mother initially increases in the first and second trimesters, reaches a peak in mid-pregnancy, and then gradually decreases until the term of delivery. A decrease in the PlGF concentration occurs prematurely in women with PE and is detected even before the onset of symptoms. An increase in sFlt-1 levels and a decrease in PlGF levels lead to an increase in the sFlt-1/PlGF ratio. Therefore, this ratio may be a useful tool for predicting and/or diagnosing great obstetric syndromes, including PE, SBP, stillbirth, and preterm labor.[12]

Data from the multicenter PETRA (Pre-eclampsia Triage by Rapid Assay Trial) trial revealed that low PlGF levels (≤ 100 pg/mL) in women with suspected PE before 35 weeks of gestation had a sensitivity of 76% and a specificity of 69%.[13] This study revealed an increased rate of maternal complications in a cohort of women with low PlGF (≤ 100 pg/mL). Low maternal PlGF levels also help predict PE requiring delivery within the next 14 days. The prospective multicenter PELICAN (Plasma Placental Growth Factor in the Diagnosis of Women with Pre-Eclampsia Requiring Roding Within 14 Days) trial revealed that in women with suspected PE before 35 weeks of gestation, PlGF levels < 100 pg/mL were associated with a greater risk of PE.[14] The 5th percentile had a sensitivity of 96%, specificity of 55%, and negative predictive value (NPV) of 98% for predicting the development of PE. It also requires preterm delivery within the next 14 days, with a sensitivity of 96%, specificity of 56%, and negative predictive value of 98%. The PARROT (Placental Growth Factor Repeat Sampling for Reduction of Adverse Perinatal Outcomes in Women with Suspected Pre-eclampsia) trial revealed that testing PlGF significantly reduced the median time to clinical confirmation of PE from 4.1

to 1.9 days ($P = 0.027$).[15] The PlGF trial significantly reduced the incidence of severe adverse maternal outcomes but had no effect on perinatal morbidity. In addition, the trial revealed no differences between groups in terms of delivery time.

The sFlt-1/PlGF ratio predicts PE and adverse perinatal outcomes. The PROGNOSIS (Prediction of Short-term Outcomes in Pregnant Women with Suspected Preeclampsia Study) is a prospective, multicenter study that enrolled women with suspected PE from 24 to 36^{+6} weeks of gestation. The study confirmed a cutoff of sFlt-1/PlGF ≤ 38 to exclude the development of PE within 1 week of testing, with a sensitivity of 80.0%, specificity of 78.3%, and negative predictive value of 99.3%. The study also demonstrated improved prediction of PE with an sFlt-1/PlGF ratio of > 38 to detect the development of PE within 4 weeks of testing, with a sensitivity of 66.2%, specificity of 83.1% and positive predictive value of 36.7%. These cutoff values of the sFlt-1/PlGF ratio were then evaluated in Asian women in the PROGNOSIS Asia study.[16] Furthermore, the results of the INSPIRE (Interventional Study Evaluating the Short-Term Prediction of Preeclampsia/Eclampsia In Pregnant Women with Suspected Preeclampsia) study demonstrated that clinical examination combined with an sFlt-1/PlGF ratio > 38 identified 100% of women with PE that would develop within the following week.[17]

In one prospective pilot study, women with a sFlt-1/PlGF ratio > 85 were found to be more likely to have severe PE (90.9% *versus* 8.0%, $P < 0.001$), a higher combined rate of adverse maternal outcomes (18.2% *versus* 0, $P = 0.04$), and preterm delivery (32.6 *versus* 37.4 weeks, $P = 0.001$) than women with a sFlt-1/PlGF ratio < 85.[18] Pregnant women with PE who had severe angiogenic factor imbalance (sFlt-1/PlGF ratio ≥ 85) had a significantly higher rate of preterm birth within 14 days of examination and small-for-gestational-age fetuses than women with PE who had no imbalance (sFlt-1/PlGF ratio ≤ 38) or moderate imbalance (sFlt-1/PlGF ratio between 38 and 85) in terms of angiogenic factors ($P < 0.001$). Currently, screening for preterm birth due to severe PE within the next 4 weeks is performed at 31–34 weeks of gestation by combining maternal risk factors with sFlt-1 and PlGF values or by using the sFlt-1/PlGF ratio alone. Therefore, compared with PlGF, the sFlt-1/PlGF ratio has similar sensitivity for predicting and diagnosing PE but higher specificity.[19] This is why many current guidelines recommend the use of the sFlt-1/PlGF ratio for diagnosing PE.

Research on the sFlt-1/PlGF ratio is currently an effective approach for the prediction, diagnosis, and selection of interventions for managing women with PE. In pregnant women with already confirmed PE (high blood pressure and proteinuria), the sFlt-1/PlGF ratio can be useful for determining the severity of the disease. Therefore, the assistance of a specialist in laboratory diagnosis to an obstetrician-gynecologist is the main factor in the success of timely detection of PE and prevention of complications of this disease.

According to the described cut-off values of the sFlt-1/PlGF ratio, three "subgroups" of women should be considered: a sFlt-1/PlGF ratio < 38. These women are unlikely to develop PE for at least 1 week; with a -sFlt-1/PlGF ratio > 85 (early-onset PE) or > 110 (late-onset PE), these women are very likely to have PE; with a -sFlt-1/PlGF ratio of 38–85 (early-onset PE) or 38–110 (late-onset PE), these women do not have a definite diagnosis of PE but are highly likely to develop PE within 4 weeks. Therefore, this screening program could be beneficial during any day of the second or third trimester of pregnancy. The national health service systems in low-income countries should stimulate the introduction of this program by monitoring high-risk groups for PE at the regional level.

In recent years, folic acid deficiency has been of foremost importance in the pathogenesis of pregnancy pathology and CVD. Folic acid supplementation is useful for the health of both the mother and the newborn. One study examined awareness, attitudes, and adherence to folic acid supplementation among Saudi women.[20] Comprehensive national surveys were carried out across Saudi Arabia between January 1 and February 28, 2025.[20] Sixty percent of the participants recognized the importance of folic acid during pregnancy. A considerable proportion recognized dietary sources of folic acid, although they misinterpreted the timing of supplementation. A significant majority (83.5%) preferred supplements and natural food sources, while 10.7% relied only on prescribed supplements. Just under half (45%) reported having health care personnel who facilitated adherence to the regimen, while 39.1% cited a lack of knowledge as a barrier to adherence. Although folic acid awareness is increasing, Saudi women continue to face knowledge gaps and adherence challenges. Improving educational programs and integrating folic acid counseling into routine medical practice are essential to ensure consistent supplementation and improve maternal and fetal health.

Currently, the risk of mortality in women over 55 years of age from CVD in developed countries worldwide is increasing. In the USA, black women have the highest rates of cardiovascular morbidity and mortality.[21] There is no doubt that women with a history of PE should control their BP and receive antihypertensive drugs if necessary. Postpartum management for women in this category involves coordinated consultations with specialists in cardiology, neurology, and nephrology. Chronic non-infectious inflammation, dyslipidemia, and obesity are known pathogenetic events of these diseases. All these factors may be associated with pathological pregnancy. Is it necessary to conduct rehabilitation measures for women with other types of great obstetric syndromes? Is there a certain risk of arterial hypertension after premature birth or antenatal fetal death? There are opinions that systemic vasculopathy requires further correction.[22]

The results of a recent study of the first pregnancy consequences and monitoring of CVD in the future provide answers to these issues.[23] More than one-fifth of the women who participated in this study had adverse pregnancy outcomes. Among them, the most common were hypertensive disorders during pregnancy (13.6%), which were associated with PE in 6.6% of the patients and with chronic arterial hypertension in 7.0% of the patients. Preterm births occurred in 8.6% of the study participants. Labor began spontaneously in 4.9% of the cases, while it was induced in 3.7% of the cases. Fetal growth restriction occurred in 4.2% of the patients; antenatal fetal death occurred in 0.4%. A total of 59.9% of women who had induced preterm labor experienced hypertensive disorders during pregnancy. Among women who had adverse pregnancy outcomes, the following characteristics were more common: age under 21 years or over 35 years, body mass index greater than 25 kg/m^2, African race, low education level, public or military health insurance, and smoking within 3 months prior to pregnancy. Gestational diabetes mellitus is also significantly more common in this category of women.[24]

Elevated BP and abnormal triglyceride (TG) levels are known to be associated with adverse pregnancy outcomes.[25] Stage 2 hypertension is widely regarded as a predictor of PE, but the relevance of other categories of blood pressure elevation for prognosis is still under discussion. This study evaluated how early pregnancy blood pressure and TG levels influence PE risk and helped identify high-risk groups needing clinical attention. Among the 78,016 patients, 2204 (2.83%) developed PE. Multivariate logistic regression revealed that both stage 1 and stage 2 hypertension in early pregnancy significantly increased the risk of PE (adjusted odds ratio (OR) 3.40 [95% confidence interval (CI), 3.05–3.80]; OR 6.96 [95% CI, 6.15–7.88]). The generalized models revealed that high TGs significantly increased the likelihood of PE with increasing BP. Stratification by BP and TG levels revealed that patients with high TG levels and stage 1 or 2 arterial hypertension had a significantly higher risk of PE than patients with normotensive and reference TG levels did, with RRs of 5.52 (95% CI, 4.61–6.62) and 10.13 (95% CI, 8.23–12.46), respectively. Interaction analysis revealed that stage 1 hypertension and high TG levels were associated with a 1.5-fold synergistic risk of PE (OR = 1.50, $P = 0.021$). The combination of elevated BP and high TG levels significantly increased the risk of PE. These results suggest that the co-occurrence of stage 1 hypertension with high TG levels should be considered a significant risk factor for PE, capturing the level of risk associated with stage 2 hypertension alone.[25]

Several studies have examined disrupted fetal autonomic development in PE and fetal growth restriction. Delayed fetal autonomic development has been observed in fetuses with growth restriction.[26,27] A lack of maternal and fetal autonomic coupling was found in fetal growth restriction and sympathetic overactivity in mothers and fetuses with PE.[28,29] However, these findings are not evident markers for the fetal programming of adult-life diseases.

The weak point in Barker's hypothesis is the absence of different situations associated with low birth weight. This could be due to premature birth or fetal growth restriction. Fetal growth restriction is a type of PE. This is a placenta-related pathology and one of the great obstetric syndromes.[30] An analysis of the literature data revealed that mothers of children who are small for gestational age have an increased risk of CVD of up to 3 times, whereas mothers with PE and preterm birth have

an increased risk of CVD of up to 9 times. The smallest 3% had a CVD hazard ratio of 1.44 (95% confidence interval: 1.38, 1.51).[3] Among women with only one lifetime pregnancy, the increase in the risk of cardiovascular death was greater than that for those with two or more children (3.4 (2.6–4.6) after term PE; 9.4 (6.5–13.7) after preterm PE).[31] Therefore, pregnancy complications are an early marker of a woman's predisposition to develop CVD and require preventive measures. From a public health perspective, Barker's hypothesis regarding the risk of CVD in low-birth-weight children is less convincing than the issue of CVD risk among mothers with pregnancy complications.

Internal diseases are maternal comorbidities that complicate gestational and perinatal outcomes

Medical complications of pregnancy have a multifactorial influence, depending on the following: the impact of pregnancy on the current main disease; difficulty in verifying the diagnosis during pregnancy; limited treatment and diagnostic options; the impact of the main disease on the current pregnancy, labor and delivery, and the postpartum period; specific obstetric risks and great obstetric syndromes; preterm birth and prematurity; and the effect of drugs on the fetus.[32] Preconception preparation should take a holistic approach. Conventional questions for the clinician include the degree of risk of future pregnancy for the health and life of the woman, the need to continue drug treatment during pregnancy and its possible negative impact on the fetus, the child's risk of congenital (hereditary) disease in the future, the woman's expected life duration and her ability to care for the child. The international experience of interdisciplinary cooperation in the management of pregnant women with comorbidities highlights the need to expand the network of specialized clinics that assist such women. Conducting training for obstetricians-gynecologists or family doctors on maternal medicine is a current issue. Providing systematic training in obstetrics for internists addresses the fact that some consultants may not have prior experience with pregnant patients. Priority should be given to obstetricians in choosing the route of delivery (Cesarean section). The goal is to form a separate community of obstetricians and gynecologists involved in maternal medicine. Pregnancy in women with severe comorbidities shortens their lives and contributes to the progression of the disease.[33]

Impact of war

Fetal programming arose from food blockade in the Netherlands during World War II.[34] Now, we have a war in Ukraine. Changes in the health status of pregnant women in the frontline city of Kharkiv were identified in a recent study.[35] During hostility, pregnant women in Kharkiv experienced more internal diseases, notably increased endocrine disorders such as diabetes and urinary tract infections. The increase in the prevalence of vaginal infections led to an increase in the incidence of vaginal and perineal tears during labor and delivery. These peculiarities require attention to monitoring the infection and timely sanitation of the birth canal. The use of preventive measures allows the level of great obstetric syndromes in the form of premature birth, PE, and the level of complications of the birth act to remain quite stable.

Role of artificial fertilization

Assisted reproductive technologies (ART), such as intrauterine insemination, in vitro fertilization, and intracytoplasmic sperm injections, have become much more common, as global infertility rates, now at 17.5%,[36] continue to rise. The levels of fetal growth restriction and preterm birth are increased in ART.[37] Placental perfusion was found to be better in frozen embryo transfer.[38] The epigenetic mechanisms of cardiac remodeling after ART are not clear. However, subfertility may not be a reason for maldevelopment of the cardiovascular system.[39] More than nine million children have been born through ART, which is widely regarded as safe and effective. Concerns about their association with prenatal and long-term health risks, particularly CVD, warrant careful investigation. Recent evidence regarding cardiac remodeling in fetuses conceived via ART is reviewed, emphasizing the potential for subclinical dysfunction and ongoing cardiovascular abnormalities that may extend into adolescence. The perinatal complications associated with ART and the effects of the renin–angiotensin system, epigenetic modifications, and altered microRNA expression on fetal cardiovascular development were also examined. The analysis further differentiates the cardiac effects of fresh and frozen ART cycles and investigates the persistence of these changes after birth. Given the increased risk of CVD among individuals conceived with ART, proactive interventions, including lifestyle modifications, have been proposed to mitigate potential adverse outcomes. There is a critical need for ongoing research and intervention strategies to protect the cardiovascular health of the growing number of individuals conceived with ART.

Repercussions of fetal programming on the kidneys

Prenatal programming has recently been applied to chronic kidney disease (CKD).[40] Early detection of CKD can prevent disease progression and associated complications, reduce the risk of CVD, and reduce mortality. The urinary system screening test uses serum creatinine to assess kidney function and urine albumin to assess kidney and endothelial damage. Assessment of causes and risk factors for CKD includes testing for diabetes mellitus, BP, and BMI. Widespread screening for CKD and active case detection in high-risk populations could reduce the burden of kidney disease worldwide. Early CKD is asymptomatic. It can be diagnosed, and newer treatments for CKD, including sodium–glucose cotransporter-2 inhibitors, have led to improved outcomes. This supports a cost–benefit analysis for screening or case–finding programs. There are several obstacles, such as inefficient resource allocation, limited health financing, and low levels of awareness of kidney disease among both health professionals and the public. Key kidney non-governmental organizations can work together to place kidney health on the agendas of governments in developed countries and coordinate early detection interventions with existing programs to achieve effective outcomes.

Programming of reproductive health in women

Polycystic ovary syndrome

Pathological pregnancy affects the development of the reproductive system of the fetus. Adverse intrauterine conditions can permanently alter fetal physiology, increasing the risk of disease and accelerating aging later in life. Pathological pregnancy may negatively affect reproductive potential in the first generation and compromise offspring health in the second generation due to alterations in oocytes. It is necessary to research the impact of various adverse factors of the intrauterine period of life on the reproductive system of female offspring. Maternal malnutrition, overeating/obesity, hypoxia, smoking, hyperandrogenism, endocrine-disrupting chemicals, and pollutants during pregnancy have important consequences. The available data indeed indicate that an unfavorable antenatal environment alters the reproductive physiology of female offspring, with consequences for future reproductive capacity. These changes are mediated by programmed changes in the hypothalamic–pituitary–gonadal axis and the structure and function of reproductive tissues, particularly the ovaries. Reproductive programming may result in a shifted timing of puberty or menopause, reduced reproductive function, changes in the menstrual cycle, polycystic ovary syndrome (PCOS), and a greater risk of reproductive cancers.[41] These findings may impact the fertility of female offspring. However, further research is needed to better define the possible impact of these programmed changes on subsequent generations.

Recently, "female-centered" or "female-only" cardiac rehabilitation has been developed to improve women's participation and adherence in standard programs.[42] Recent research has investigated the effects of cardiac rehabilitation programs designed for women on psychological and physical outcomes, along with patient adherence.[43] Female-centered cardiac rehabilitation significantly improved depressive symptoms (standardized mean difference = –0.40, 95% CI [–0.61, 0.19]) but had no significant effect on anxiety (standardized mean difference = –0.15, 95% CI [–0.55, 0.25]). Currently, individualized or supervised cardiac rehabilitation requires adherence to both regular exercise and educational programs. Cardiac rehabilitation targeted at women may provide psychological benefits, particularly in reducing depressive symptoms, but further high-quality research is necessary for a better understanding of its effects on physical outcomes and adherence. Healthier lifestyles lead to lasting epigenetic changes that can be inherited, helping combat arterial hypertension across generations.

Women with PCOS have persistently elevated circulating androgen levels during pregnancy, which is an independent risk factor for pregnancy complications and adverse outcomes for offspring.[44] Additional research is needed to determine how increased androgen levels affect placental function in specific cell types and fetal

development. A study was conducted in mice with PCOS-like pathology caused by chronic androgen exposure. PCOS mice exhibited impaired placental and embryonic development, leading to mid-gestational pregnancy loss. Concomitant treatment with the androgen receptor blocker flutamide prevented these complications, including germ cell differentiation. Comprehensive placental profiling using genome and RNA sequencing revealed reduced Cdx2 expression. Reduced expression of Gcm1, Synb, and Prl3b1 is associated with decreased numbers of syncytiotrophoblast and sinusoidal giant trophoblast cells, which disrupts the formation of placental circulation. Importantly, human trophoblast organoids exposed to androgens exhibit similar changes, indicating that impaired trophoblast cell differentiation is a key feature of pregnancy complications associated with PCOS. These results provide new insights into potential cellular targets for future therapies. Thus, hyperandrogenemia is a reason for lifelong monitoring and therapeutic intervention.

Women with PCOS constitute a risk group for metabolic disorders.[45,46] According to Aziz et al.,[47] the history of PCOS dates back approximately 40 thousand years. In the Paleolithic era, the harsh living conditions prompted the suppression of fertility and the accumulation of fat reserves.[47] The wave of migration of primitive people from Africa to Europe led to the need to survive harsh winters and food shortages. Higher insulin levels and the growth of adipose tissue contribute to the build-up of extra energy reserves. Reduced fertility also increased the chances of survival of women at that time. PCOS helps preserve humanity and may be viewed as an endocrine disorder inherited from ancestors with insulin resistance.

A recent study revealed that the RR of arterial hypertension and dyslipidemia in women with PCOS was 1.7. The CVD RR in obese women in this study was 2.4. Additionally, over 30% of patients with PCOS presented blood pressure levels equal to or greater than 130/85 mmHg.[48] In a Chinese study, women with PCOS also had hypertension, dyslipidemia, hyperglycemia, and hyperinsulinemia. Overall, 18% of women with PCOS had elevated TG (> 1.7 mM). Insulin resistance has been shown to contribute to CVD. As BP increases, lipid profiles and pancreatic β-cell function deteriorate in women with PCOS as they age. Importantly, BMI varies greatly between patients with different phenotypes.[49]

Aging is a significant risk factor for type 2 diabetes mellitus. Obesity, a sedentary lifestyle, an unbalanced diet, smoking, excessive alcohol consumption, and the use of certain medications contribute to the development of this disease. Both vitamin D3 and calcium deficiency increase the risk of both types of diabetes. Central obesity is the main factor in the progression of carbohydrate metabolism disorders. Osteopenia syndrome and osteoporosis are separate problems. It has recently been reported that women with osteopenia have impaired intestinal microflora. The treatment of intestinal dysbiosis could neglect the pro-inflammatory changes in patients with PCOS and diabetic women.[50]

Since lipid metabolism disorders are known events in the development of endothelial malfunction, the pathogenesis of cardiovascular pathology in perimenopausal women is becoming fully understood. Hypertrophied adipocytes have a significant number of genes involved in inflammation and produce cytokines. The presence of tissue hypoxia may lead to the accumulation of macrophages and other immune cells in adipose tissue. Inflammation is the "fate" of every person and can lead to atherosclerosis. Inflammatory events in adipose tissue cause impaired carbohydrate metabolism in the liver and reduce the sensitivity of skeletal muscles to insulin.[45] Therefore, insulin resistance and dyslipidemia are central parts of the pathogenesis of metabolic disorders in perimenopausal women. Therefore, determining the HOMA index and studying the blood lipid spectrum by calculating the atherogenic index is an especially important aspect of the examination that determines therapeutic interventions. It is also advisable to determine the levels of the universal inflammation markers C-reactive protein and several pro-inflammatory cytokines, such as interleukin (IL)-1 and IL-6.[51]

In postmenopausal women with PCOS, hyperandrogenism remains, and the levels of C-reactive protein and inflammatory markers (IL-18, TNF-α, and IL-6) are elevated. An increased level of pro-inflammatory cytokines in the blood is involved in the development of atherosclerosis and chronic inflammation. IL-6 is recognized as a biomarker associated with the risk of developing atherosclerosis, coronary heart disease, and arterial hypertension. IL-6 is a potential inducer of the synthesis of C-reactive protein by hepatocytes. An increase in the concentration of C-RP suggests the presence of a severe atherosclerotic process, the risk of myocardial infarction and stroke.[52] PCOS is a well-known risk factor for CVD. This approach provides promising preventive measures for the target population.

Impact of premenstrual syndrome

In the Nurses' Health Study II, 1257 women with premenstrual syndrome (PMS) (1991–2005) and 2463 women of the same age with isolated premenstrual symptoms were identified. Participants were monitored for arterial hypertension from 6 to 20 years until 2011. In women with PMS, the OR for arterial hypertension was 1.4 (95% CI: 1.2–1.6) compared with women without PMS. In women with PMS under the age of 40, the risk of developing arterial hypertension was 3-fold increased (RR=3.3; 95% CI: 1.7, 6.5; $P = 0.0002$). The risk of hypertension associated with PMS was not altered by oral contraceptive or antidepressant use but was reduced in women with high thiamine and riboflavin intakes ($P < 0.05$). These results suggest that PMS may be associated with the development of arterial hypertension in the future and that this risk is modifiable. The mechanism providing the link between PMS and elevated BP may be a malfunction of the renin-angiotensin-aldosterone system.[53]

Menopausal Transition and Cardiovascular Disease

Menopause is an important stage in a woman's life. Menopause marks the beginning of aging and often leads to various diseases. There are no evident markers of fetal programming atherogenicity during the reproductive period in women without severe comorbidities. Hypoestrogenism contributes to many menopausal comorbidities.[54] Aging is the sum of conditions preceding the disease and certain diseases. Sometimes, the development of complications precedes the clinical manifestation of the main disease. An example is nephropathy or retinopathy before the diagnosis of type 2 diabetes mellitus. Preventive treatment helps prevent disease. Progression from preliminary stages to disease occurs during early or late aging. Aging without diseases or healthy aging should be the norm. It slows aging, prevents the development of degenerative processes and prolongs longevity. However, which diseases should be prioritized for prevention, and what is the volume of laboratory tests for menopausal women?

Atherosclerosis and arterial hypertension harm the nervous system. Elderly people constitute the fastest-growing segment of the population in Europe and the USA. CVDs are significantly more common among elderly patients, leading to excess morbidity, mortality, and health care utilization. Cognitive impairment is also found in elderly people with CVD.[42] These conditions progress in parallel with comorbid CVDs, as both conditions share the same risk factors and common pathogenesis. CVDs also exacerbate cognitive impairment through arterial hypertension, cerebral hypoperfusion, inflammation, arrhythmia, embolism, and drug side effects. In addition, cognitive impairment could complicate the treatment of patients with CVD owing to insufficient medical literacy, non-adherence to recommendations, and even the likelihood that drug and/or interventional treatments will be prescribed in insufficient quantities. Patients with cognitive impairment are also more likely to experience delays in seeking medical care and a lack of CVD diagnosis. The development of a modern, effective management strategy for older patients should be based on understanding the different types of cognitive impairment common among patients with CVD; capturing the pathophysiology and mechanisms of cognitive impairment in adults with CVD; translating the bidirectional impact of cognitive impairment and CVD; and using evidence-based treatments to mitigate cognitive impairment in patients with CVD. Hormonal replacement therapy started before 60 years of age could improve cardiovascular health in elderly women.[54,55]

Development of a Novel Strategy: the Way to Go

Close monitoring of menopausal patients permits the determination of priorities in the implementation of the following therapeutic strategies: reducing the risk of CVD; preventing coagulation system disorders; preventing osteopenia syndrome and screening for osteoporosis; combating disorders of nervous regulation (early vasomotor disorders); screening for mood disorders and cognitive disorders, senile dementia and Alzheimer's disease; breast cancer screening; screening for hypothyroidism; and

preventing urinary disorders.[56] Laboratory tests support the diagnosis and monitoring of these disorders. **Table 1** presents possible diagnostic and preventive interventions.

Dietary nutrition and physical activity are important components of preventive medicine. Reducing BMI in perimenopausal women is a guarantee for improving autonomic nervous system regulation and metabolic processes. It involves the use of preventive strategies based on a reduced diet and physical activity that allows overcoming insulin resistance, dyslipidemia, and chronic inflammation. Since adipose tissue is involved in inflammatory conditions and promotes oxidative stress and endothelial malfunction, its ability to reduce fat and carbohydrate metabolism contributes to improving the condition of the cardiovascular system. Supporting the health of the heart and blood vessels is an especially principal issue in modern health care and a real challenge of today.[57,58] Extending the creative longevity of women of older age groups is possible following high-quality diagnostics and anti-aging preventive measures.[59,60]

The main issue of life extension strategies is the different levels of health care in low- and high-income countries. The prospect is to ameliorate current approaches to healthy aging worldwide.

Table 1 | **Possible diagnostic measures and preventive interventions during the lifespan**

Period of life	Diagnostic marker	Preventive intervention
Antenatal stage	Ultrasonic biometry, Doppler ultrasound velocimetry, cardiotocography	Not known
Childhood and adolescence	HOMA index, blood serum lipids, free androgen index	Diet, antiandrogens
Reproductive period	HOMA index, blood serum lipids, free androgen index, transvaginal ultrasound	Folic acid, diet, combined oral pills, antiandrogens
Pregnancy	Soluble Fms-like tyrosine kinase-1/placental growth factor, blood serum lipids	Low dose acetylsalicylic acid, calcium, statins, l-arginine, antihypertensives.
Menopause	HOMA index, blood serum lipids, free androgen index	Hormonal replacement therapy, diet, l-arginine, physical activity.

HOMA: Homeostasis Model Assessment Index.

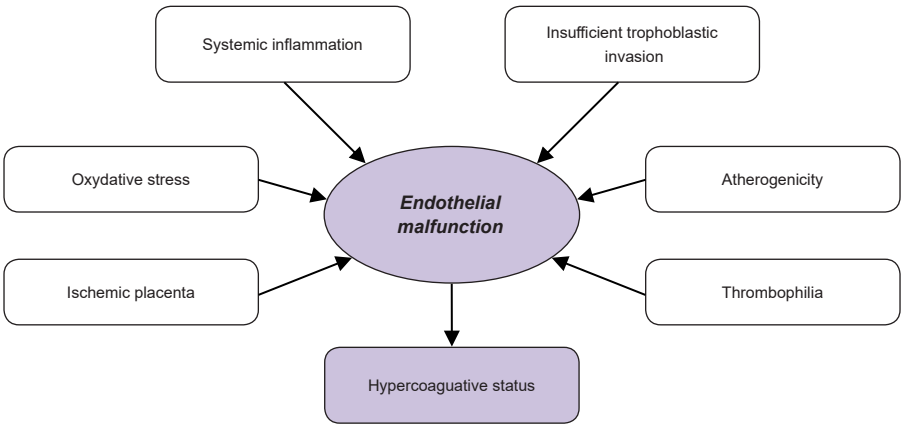

Figure 2 | **Maternal factors of programming in pre-eclampsia.**

Limitations

The main limitation of the review is the limited scope of pathologies affecting cardiovascular health included in the study.

Conclusion

The analysis of the risk factors for CVD and other pathologies in women revealed the significant role of placenta-related disorders. Great obstetric syndromes can affect both fetal and maternal health programming, with long- and short-term consequences. Maternal PCOS is a cause of metabolic syndrome, type 2 diabetes mellitus, and disturbed development of the fetal reproductive system. Menopause is a time for initiative-taking health measures that support longevity. Creating gender-focused CVD prevention programs in regenerative medicine could further advance human health.

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References

1. Jebasingh F, Thomas N. Barker hypothesis and hypertension. *Front Public Health.* 2022;21(9):767545. doi: 10.3389/fpubh.2021.767545.
2. Alnefaie K, Dungan JR. Reproductive-associated risk factors and incident coronary heart disease in women: an umbrella review. *Am Heart J Plus.* 2025;55:100558. doi: 10.1016/j.ahjo.2025.100558.
3. Wyatt S, Skjærven R, Vatten L, et al. Hypertensive disorders of pregnancy, preterm delivery, and infant size: which mothers have highest cardiovascular disease mortality? *Paediatr Perinat Epidemiol.* 2025;39(6):515-523. doi: 10.1111/ppe.70033
4. Glover V, O'Connor TG, O'Donnell KJ. Fetal programming and public policy. *J Am Acad Child Adolesc Psychiatry.* 2023;62(6):618-620. doi: 10.1016/j.jaac.2022.11.010
5. Cohen NJ, Rifas-Shiman SL, Soria-Contreras DC, et al. Associations of gestation length and offspring birthweight for gestational age with menopausal symptoms and age of natural menopause at midlife among women enrolled in a prebirth longitudinal cohort. *Menopause.* 2025;32(4):323-330. doi: 10.1097/GME.0000000000002495
6. Cortés YI, Brooks M, Barinas-Mitchell E, Matthews KA, Thurston RC, Catov JM. Impact of prior preterm or term small for gestational age birth on maternal blood pressure during the menopause transition in the Study of Women's Health Across the Nation. *Menopause.* 2021;28(3):255-262. doi: 10.1097/GME.0000000000001739
7. Palmiero P, Caretto P, Ciccone MM, et al. Long-term cardiovascular risk and maternal history of pre-eclampsia. *J Clin Med.* 2025;14(9):3121. doi: 10.3390/jcm14093121
8. Jenkinson B, Charlton V, Hardiman L, et al. Women's health and healthcare experiences in the years after gestational diabetes or hypertensive disorders of pregnancy. *BMC Pregnancy Childbirth.* 2025;25(1):158. doi: 10.1186/s12884-025-07296-7
9. Moustakli E, Potiris A, Zikopoulos A, et al. Sex differences in hypertension risk: insights from placental genomics and pregnancy-driven vascular programming. *Int J Mol Sci.* 2025;26(13):6034. doi: 10.3390/ijms26136034
10. Lan L, Zhang C, Geng J, Li Q. Echocardiographic assessment of the maternal heart: a review of the structural and functional changes during pregnancy. *Echocardiography.* 2025;42(6):e70220. doi: 10.1111/echo.70220
11. Capdeville G, Godinez-Medina A, Copado-Mendoza DY, et al. Prediction of preeclampsia before 11th week of gestation: a secondary analysis of the ASPIRIN trial. *AJOG Glob Rep.* 2025;5(3):100521. doi: 10.1016/j.xagr.2025.100521.
12. Kamphof HD, Marijnen MC, Damhuis SE, et al. Predictive value of fetal Doppler velocimetry, fetal growth trajectory and maternal serum biomarkers for short-term adverse perinatal outcome: secondary analysis of DRIGITAT study. *Ultrasound Obstet Gynecol.* 2025;66(4):470-479. doi: 10.1002/uog.29266
13. Parchem JG, Brock CO, Chen HY, et al. Placental growth factor and the risk of adverse neonatal and maternal outcomes. *Obstet Gynecol.* 2020;135(3):665-673. doi: 10.1097/AOG.0000000000003694
14. Sharp A, Chappell LC, Dekker G, et al. Placental Growth Factor informed management of suspected pre-eclampsia or fetal growth restriction: The MAPPLE cohort study. *Pregnancy Hypertens.* 2018;14:228-233. doi: 10.1016/j.preghy.2018.03.013

15. Hurrell A, Sparkes J, Duhig K, et al. Placental growth factor repeat sampling for reduction of adverse perinatal Outcomes in women with suspecTed pre-eclampsia: study protocol for a randomised controlled trial (PARROT-2). *Trials.* 2022;23(1):722. doi: 10.1186/s13063-022-06652-8
16. Gao J, Huang X, Di W, et al. Short-term prediction of preeclampsia in chinese women using the soluble fms-like tyrosine kinase 1/placental growth factor ratio: a sub-analysis of the PROGNOSIS Asia Study. *Front Cardiovasc Med.* 2021;8:602560. doi: 10.3389/fcvm.2021.602560
17. Yuan D, Huang Y, Liu H, Tang H, Liu J. Worldwide research trends of pregnancy hypertension in epigenetics field. *Front Public Health*. 2025;13:1506992. doi: 10.3389/fpubh.2025.1506992
18. Giardini V, Santagati AA, Marelli E, et al. Decoding placental dysfunction with a new angiogenic classification of PlGF and sFlt-1. *Eur J Obstet Gynecol Reprod Biol*. 2025;312:114539. doi: 10.1016/j.ejogrb.2025.114539.
19. Bremner L, Gill C, Seed PT, et al. Rule-in and rule-out of pre-eclampsia using DELFIA Xpress PlGF 1-2-3 and sFlt-1: PlGF ratio. *Pregnancy Hypertens*. 2022;27:96-102. doi: 10.1016/j.preghy.2021.12.008
20. Zayd AA, Shaikh A, Makkawi M, Alasmari S. Health implications of folic acid deficiency during pregnancy: women's awareness and attitudes. *Afr J Reprod Health.* 2025;29(6):72-81. doi: 10.29063/ajrh2025/v29i6.7
21. Haas DM, Parker CB, Marsh DJ, et al. Association of adverse pregnancy outcomes with hypertension 2 to 7 years postpartum. *J Am Heart Assoc.* 2019;8(19):e013092. doi: 10.1161/JAHA.119.013092
22. Lakhno IV, Reyes-Lagos JJ, Adam I, Brownfoot FC. Editorial: The repercussions of maternal inflammation in pre-eclampsia on fetal health and neurodevelopment. *Front Immunol*. 2024;15:1434260. doi: 10.3389/fimmu.2024.1434260
23. Saarela T, Peltomäki L, Kivioja A, Jääskeläinen T, Haukka J, Laivuori H. External causes are leading causes of death in women of reproductive age: a registry study on maternal perinatal health, hypertensive pregnancy disorders and mortality in Finland. *J Epidemiol Community Health*. 2025;79(9):691-697. doi: 10.1136/jech-2024-223438
24. Sharma R, Singh U, Kamal R, Kumar R. From pregnancy to postpartum: the cardiovascular risks associated with gestational diabetes. *Curr Cardiol Rev.* 2025. doi: 10.2174/011573403X354645250329171327
25. Zhu Y, Wang H, Wei SY, et al. Early pregnancy triglycerides and blood pressure: a combined predictor for preeclampsia. *BMC Pregnancy Childbirth*. 2025;25(1):704. doi: 10.1186/s12884-025-07761-3
26. Hoyer D, Żebrowski J, Cysarz D, et al. Monitoring fetal maturation-objectives, techniques and indices of autonomic function. *Physiol Meas*. 2017;38(5):R61-R88. doi: 10.1088/1361-6579/aa5fca.
27. Hoyer D, Schmidt A, Gustafson KM, et al. Heart rate variability categories of fluctuation amplitude and complexity: diagnostic markers of fetal development and its disturbances. *Physiol Meas.* 2019;40(6):064002. doi: 10.1088/1361-6579/ab205f
28. Lakhno IV. The hemodynamic repercussions of the autonomic modulations in growth-restricted fetuses. *Alex J Med*. 2017;53(4):333-336. doi: 10.1016/j.ajme.2016.12.007
29. Lakhno I. The impact of preeclampsia on fetal ECG morphology and heart rate variability. *Arch Perinat Med.* 2014;20 (1):7-10.
30. Wilcox AJ. Invited Commentary: Beyond barker-Mothers are the ones at risk. *Am J Epidemiol*. 2023;192(6):878-881. doi: 10.1093/aje/kwad056
31. Skjaerven R, Wilcox AJ, Klungsøyr K, et al. Cardiovascular mortality after pre-eclampsia in one child mothers: prospective, population based cohort study. *BMJ.* 2012;345:e7677. doi: 10.1136/bmj.e7677
32. Toledo I, Czarny H, DeFranco E, Warshak C, Rossi R. Delivery-related maternal morbidity and mortality among patients with cardiac disease. *Obstet Gynecol.* 2025;145(1):e1-e10. doi: 10.1097/AOG.0000000000005780
33. Chen C, Zheng X, Liao S, et al. The diabetes mellitus multimorbidity network in hospitalized patients over 50 years of age in China: data mining of medical records. *BMC Public Health.* 2024;24(1):1433. doi: 10.1186/s12889-024-18887-y
34. Obladen M. Historical notes on immaturity. Part 2: surviving against the odds. *J Perinat Med*. 2011;39(5):571-577. doi: 10.1515/jpm.2011.057
35. Lakhno I. The insight into obstetric care near the front line in Kharkiv. *Acta Med Litu.* 2022;29(2):236-244. doi: 10.15388/Amed.2022.29.2.10
36. Tasias K, Papamichail M, Fasoulakis Z, Theodora M, Daskalakis G, Antsaklis P. Investigation of cardiac remodeling and cardiac function on fetuses conceived via artificial reproductive technologies: a review. *J Perinat Med.* 2025;53(3):286-296. doi: 10.1515/jpm-2024-0346
37. Bi WJ, Cui L, Xiao YJ, et al. Assessing cardiovascular remodelling in fetuses and infants conceived by assisted reproductive technologies: a prospective observational cohort study protocol. *BMJ Open.* 2019;9(10):e031452. doi: 10.1136/bmjopen-2019-031452
38. Huluta I, Wright A, Cosma LM, Dimopoulou S, Nicolaides KH, Charakida M. Fetal cardiac function at midgestation and conception by in-vitro fertilization. *Ultrasound Obstet Gynecol*. 2023;61(5):587-592. doi: 10.1002/uog.26207
39. Boutet ML, Casals G, Valenzuela-Alcaraz B, et al. Subfertility versus ART: unraveling the origins of fetal cardiac programming. *Hum Reprod*. 2023;38(10):1961-1969. doi: 10.1093/humrep/dead160
40. Vassalotti JA, Francis A, Santos ACSD Jr, et al. Are your kidneys ok? Detect early to protect kidney health. *J Bras Nefrol.* 2025;47(4):e20250106. doi: 10.1590/2175-8239-JBN-2025-0106en
41. Bernstein SR, Kelleher C, Khalil RA. Gender-based research underscores sex differences in biological processes, clinical disorders and pharmacological interventions. *Biochem Pharmacol*. 2023;215:115737. doi: 10.1016/j.bcp.2023.115737
42. Jamil Y, Krishnaswami A, Orkaby AR, et al. The impact of cognitive impairment on cardiovascular disease. *J Am Coll Cardiol.* 2025;85(25):2472-2491. doi: 10.1016/j.jacc.2025.04.057
43. Yao S, Lopez-Tello J, Sferruzzi-Perri AN. Developmental programming of the female reproductive system-a review. *Biol Reprod*. 2021;104(4):745-770. doi: 10.1093/biolre/ioaa232
44. Franks MM, Mason MB, August KJ, et al. Women managing heart disease: involvement of spouse and non-spouse care partners. *Am J Lifestyle Med.* 2025:15598276251358184. doi: 10.1177/15598276251358184
45. Osumi A, Kanejima Y, Kitamura M, Ishihara K, Izawa KP. Effects of cardiac rehabilitation on female patients with heart disease: A systematic review and meta-analysis. *Maturitas.* 2025;199:108653. doi: 10.1016/j.maturitas.2025.108653
46. Lu H, Jiang H, Li C, et al. Dissecting the impact of maternal androgen exposure on developmental programming through targeting the androgen receptor. *Adv Sci (Weinh).* 2024;11(36):e2309429. doi: 10.1002/advs.202309429
47. Aziz M, Sidelmann JJ, Faber J, et al. Polycystic ovary syndrome: cardiovascular risk factors according to specific phenotypes. *Acta Obstet Gynecol Scand.* 2015;94(10):1082-1089. doi: 10.1111/aogs.12706
48. Ntikoudi A, Spyrou A, Evangelou E, Dokoutsidou E, Mastorakos G. The effect of menopausal status, insulin resistance and body mass index on the prevalence of non-alcoholic fatty liver disease. *Healthcare (Basel).* 2024;12(11):1081. doi: 10.3390/healthcare12111081
49. Geng L, Yang X, Sun J, et al. Gut microbiota modulation by inulin improves metabolism and ovarian function in polycystic ovary syndrome. *Adv Sci (Weinh).* 2025;12(20):e2412558. doi: 10.1002/advs.202412558
50. Dilliyappan S, Kumar AS, Venkatesalu S, et al. Polycystic ovary syndrome: Recent research and therapeutic advancements. *Life Sci*. 2024;359:123221. doi: 10.1016/j.lfs.2024.123221
51. Dokras A. Polycystic ovary syndrome in 2025-insights and innovations. *Fertil Steril.* 2025;124(5 Pt 2):907-909. doi: 10.1016/j.fertnstert.2025.09.025
52. Glenn AJ, Lo K, Jenkins DJA, Boucher BA, et al. Relationship between a plant-based dietary portfolio and risk of cardiovascular disease: findings from the women's health initiative prospective cohort study. *J Am Heart Assoc.* 2021;10(16):e021515. doi: 10.1161/JAHA.121.021515
53. Bertone-Johnson ER, Whitcomb BW, Rich-Edwards JW, Hankinson SE, Manson JE. Premenstrual syndrome and subsequent risk of hypertension in a prospective study. *Am J Epidemiol*. 2015;182(12):1000-1009. doi: 10.1093/aje/kwv159
54. Machuca JN, Rosales-Alvarez CP. Cardiovascular disease in women and the role of hormone replacement therapy. *Cureus.* 2024;16(9):e69752. doi: 10.7759/cureus.69752
55. Prentice RL, Aragaki AK, Van Horn L, et al. Low-fat dietary pattern and cardiovascular disease: results from the Women's Health Initiative randomized controlled trial. *Am J Clin Nutr.* 2017;106(1):35-43. doi: 10.3945/ajcn.117.153270
56. Ko SH, Kim HS. Menopause-associated lipid metabolic disorders and foods beneficial for postmenopausal women. *Nutrients*. 2020;12(1):202. doi: 10.3390/nu12010202
57. Purohit A, Kim YJ, Michos ED. Cardiovascular disease prevention in women - the current state in 2023. *Curr Opin Cardiol.* 2024;39(1):54-60. doi: 10.1097/HCO.0000000000001099
58. Lakhno I. Dyslipidemia in internally displaced middle aged women in Kharkiv during the war. *Med Mod.* 2024;31(4):331-336. doi: 10.31689/rmm.2024.31.4.331
59. Lakhno I, Korovai S, Struk T, Pak S. The pathogenic pathways of cardiovascular disease in perimenopausal women. *Prz Menopauzalny.* 2023;22(2):59-63. doi: 10.5114/pm.2023.127902
60. Guo H, Liu Y, Yang R, et al. Relationship between biological ageing, premature mortality, life expectancy, and number of live births: a prospective cohort study of the UK women. *BMC Public Health.* 2025;25(1):3239. doi: 10.1186/s12889-025-24534-x