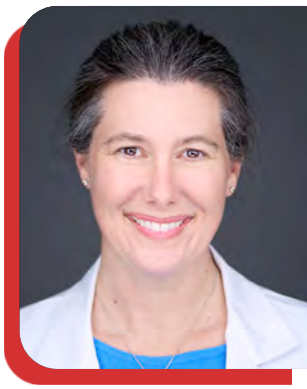
PERSPECTIVES IN HYPERTENSION



Are hypertensive disorders of pregnancy an overlooked predictor in cardiovascular risk assessment in women?

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Hypertensive disorders of pregnancy (HDP) – including gestational hypertension, preeclampsia and eclampsia – are associated with an average two-fold increased risk of long-term cardiovascular disease in women. The endothelial dysfunction and vascular injury related to these disorders has been linked to subclinical cardiac and vascular changes, which become clinically apparent in the first year postpartum and persist throughout a woman's life.[1-3] Numerous recent studies have shown that women with HDP have an increased risk of developing cardiovascular risk factors (e.g. chronic hypertension, hyperlipidemia, diabetes, renal dysfunction) as well as cardiovascular disease (e.g. coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease).[3-6] This association appears to correlate with the severity of HDP, earlier age of onset, earlier gestation of onset, and recurrence in subsequent pregnancies.[1, 3-4]

Although patients with HDP are sometimes regarded as high risk and monitored closely by our obstetrical colleagues during pregnancy, longitudinal care after the postpartum period is not standardized.[8] Internists and other subspecialists who care for these patients throughout their lifetime need to have a heightened awareness of a history of HDP. In response, international societies including the American Heart Association (AHA), American College of Cardiology (ACC), European Society of Cardiology (ESC), and International Society of Hypertension (ISH), have recommended incorporating a history of HDP into the risk assessment for primary prevention of cardiovascular disease.[1,8-10] However, there is no consensus in the recommended monitoring metrics and intervals across guidelines.

As practicing clinicians, we routinely assess individual cardiovascular risk for our patients in the context of office visits. Commonly used methods to estimate cardiovascular risk, including the Pooled Cohort Equation (PCE),[11] the Systematic Coronary Risk Equation 2 (SCORE2)[12] and the more contemporary Predicting Risk of cardiovascular disease EVENTs (PREVENT™) calculator,[13] account for a range of known risk factors such as age, sex, tobacco use as well as the presence of underlying hypertension, diabetes, hyperlipidemia, renal disease, and obesity. However, a history of HDP or other adverse pregnancy outcomes, a well-established marker of future cardiovascular risk, remains conspicuously absent (**Figure 1**).

Researchers have attempted to fill this gap by modeling how the inclusion of HDP may improve cardiovascular risk prediction with mixed findings. Stuart et al. found that the inclusion of HDP to the PCE did not improve 10-year risk prediction, which is likely due to the collinearity with existing risk factors in the PCE model.[14] A subsequent

study by Stuart et al. found that existing risk factors accounted for 84% of the risk conferred by gestational hypertension but only 57% of the risk conferred by preeclampsia.[15] This is consistent with findings that a history of preeclampsia is associated with a higher risk for cardiovascular disease than a history of gestational hypertension, highlighting the phenotypic heterogeneity within the umbrella of HDP.[3-4] In a Norwegian study, Markovitz et al. found that inclusion of HDP made only small improvements to cardiovascular disease risk prediction.[16] In a Canadian study, Gladstone et al found that inclusion of HDP reclassified many women into the high-risk category who otherwise would've been considered low risk.[17]

A major reason for why the addition of HDP into risk calculators has not shifted test characteristics significantly could be due to the lack of robust pregnancy data in the cohorts from which these equations are derived. As clinician-researchers, we should be asking about pregnancy history and adverse pregnancy outcomes when designing cohorts and clinical trials. Future studies should seek to find ways to capture that unaccounted risk, especially with the use of models that are built from updated and more diverse population data.

As nature's stress test, pregnancy provides clinicians a window into the subclinical cardiovascular dysfunction that may already be present in a woman's early to mid-life. Like

Figure 1. Comparison of cardiovascular risk factors included in PCE, SCORE2, and PREVENT calculators

Risk Factor	PCE (2013)[11]	SCORE2 (2021)[12]	PREVENT™ (2023)[13]
Age	x (40-75)	x (40-69)	x (30-79)
Sex	x	x	x
Race	x (optional)	-	-
Current Smoking	x	x	x
Total Cholesterol	x	x	x
HDL-C	x	x	x
Statin Use	-	-	x
Systolic BP	x	x	x
Antihypertensive Use	x	-	x
Diabetes	x	- (excluded)	x
HbA1c	-	-	x
BMI	-	-	x
eGFR	-	-	x
UACR	-	-	x
Geography	-	x (risk region)	x (zip code)

angina, HDP should be treated as a harbinger for elevated risk for subsequent cardiovascular disease. A step in the right direction, the AHA/ACC 2019 guidelines on the primary prevention of cardiovascular disease and 2025 guidelines on hypertension management included considering HDP as a sex-specific risk enhancer.[8, 18] The 2025 ESC guidelines also highlight the importance of primary care follow up after delivery for patients with adverse pregnancy outcomes to continue blood pressure monitoring at regular intervals.[19] However, in practice, the lack of its inclusion in standardized calculators make the adoption of this risk stratification difficult. We hope that future international society guidelines will evaluate emerging findings about the sequela of HDP to make stronger recommendations on long-term risk stratification and management, including the potential benefit of pharmacotherapy for primary prevention in this high-risk population.

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