

## Long-Term Cardiovascular Risk in Women with Hypertensive Pregnancy: Insights from Polygenic Risk Scores

### Authors:

*Anna Kivioja, Jaakko Tyrmi, Elli Toivonen, Heini Huhtala, FinnGen, Tiina Jääskeläinen, Johannes Kettunen, Tanja Saarela, Hannele Laivuori*

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### Abstract

The well-documented association between pre-eclampsia (PE) and cardiovascular disease (CVD) remains incompletely understood. We aimed to investigate, how polygenic risk scores (PRSs) for PE, high systolic blood pressure (SBP), coronary artery disease (CAD) and stroke modify the risk of CVD in addition to history of PE or other hypertensive disorder of pregnancy (HDP) compared to women with normotensive pregnancies.

The study was conducted in the FinnGen cohort of 242,852 Finnish women. A total of 8818 PE and 18345 HDP women were included with 234,034 parous controls. All participants were classified based on their PRSs in three groups: low (<20%), moderate (20-80%) and high (>80%) genetic risk.

Women with a high PE-PRS had in the three groups elevated risk for CVD: a history of PE HR 1.87 (p-value  $2 \times 10^{-16}$ ), a history of HDP HR 2.06 (p-value  $2 \times 10^{-16}$ ), a history of normotensive pregnancies, HR 1.07 (p-value < 0.001). The risk for CVD was further elevated in women with a high SBP-PRS: 2.31 (p-value  $2 \times 10^{-16}$ ), 2.39 (p-value  $2 \times 10^{-16}$ ), 1.32 (p-value  $2 \times 10^{-16}$ ), respectively. The trend was similar when combining the pregnancy history and high CAD- or stroke-PRS.

In women with a high genetic risk for CVD, a history of PE or other HDP further increases the risk compared to women with a history of normotensive pregnancies. With all tested PRSs, the role of PE and HDP was more significant compared to the genetic risk and the risk remained elevated until 80 years of age.