

## Associations of maternal hypertensive disorders during pregnancy with offspring risks of ischemic heart disease and stroke: a Nordic cohort study

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**Background:** A substantial body of evidence suggests that children exposed to maternal hypertensive disorders during pregnancy (HDP) have increased risks of preterm birth, fetal growth restriction and several cardiovascular risk factors (e.g., hypertension, obesity, diabetes) later in life. However, the direct evidence on the link between maternal HDP and the risk of severe cardiovascular diseases such as ischemic heart disease (IHD) and stroke in the offspring is very limited.

**Objective:** To investigate the associations between maternal HDP and the risk of IHD and stroke in the offspring.

**Methods:** We conducted a population-based cohort study by linking several national registers in Sweden and Finland. Live singleton births from the Swedish Medical Birth Register (1973–2014) and the Finnish Medical Birth Register (1987–2014) were followed for IHD and stroke until 2014 by the national patient and cause of death registers. We performed Cox regression models to examine the association between maternal HDP and its subtypes, i.e., pre-existing chronic hypertension, gestational hypertension, and preeclampsia, and the risk of IHD, and stroke in the offspring while adjusting for relevant maternal and pregnancy-related confounders. We conducted sibling analyses to control for unmeasured shared familial (genetic and/or environmental) risk factors.

**Results:** Among the 5,807,122 singletons included in the study, 218,322

(3.76%) children were born to mothers with HDP. During the up to 41 years of follow-up, 2,340 (0.04%) offspring were diagnosed with IHD and 5,360 (0.09%) were diagnosed with stroke. Offspring exposed to maternal HDP had an increased risk of IHD (adjusted hazard ratio (aHR), 1.29; 95% confidence interval (CI), 1.01–1.63), and stroke (aHR, 1.33; 95% CI, 1.14–1.56). Significantly increased rates of stroke were also observed in children exposed to the subtypes of maternal HDP: pre-existing chronic hypertension (aHR, 1.64; 95% CI, 1.03–2.60), gestational hypertension (HR, 1.38; 95% CI, 1.08–1.77), and preeclampsia (HR, 1.26; 95% CI, 1.02–1.55). The associations between maternal HDP and offspring's IHD and stroke were independent of preterm birth and small for gestational age at birth. Maternal HDP remained associated with stroke in the offspring (aHR, 1.94; 95% CI, 1.16–3.22), but not with IHD (aHR, 0.89; 95% CI, 0.47–1.67) in the sibling analyses.

**Conclusion:** Children to mothers with HDP have increased rates of IHD and stroke from childhood to young adulthood. While the link between maternal HDP and IHD in the offspring seemed to be attributed to confounding by familial factors, the relation between maternal HDP and stroke persisted even when considering such confounding. Persons born to mothers with HDP may benefit from early screening and prevention efforts to reduce the risk of IHD and stroke later in life.