

Genome-wide polygenic risk scores for hypertensive disease during pregnancy identify women at risk for long-term cardiovascular disease

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Background & Aims

- Previous studies suggest that hypertensive disease during pregnancy (HDP) increase the risk of long-term cardiovascular disease later in life, and clinical guidelines recommend including HDP as important female specific factor in risk assessment.

- However, it has not been issued whether genetic trait for HDP determines the development of subsequent cardiovascular disease.

- In the current study, we developed polygenic risk scores for HDP (HDP-PRS) from genome-wide associated study (GWAS) data and evaluated its impact on long-term cardiovascular outcome.

Methods

- From the UK biobank, we included unrelated Caucasian women with at least one live birth and available genetic data.
- HDP-PRS was calculated by LDpred using the summary statistics from FinnGen, another large-scale biobank.
- Subjects were divided according to the genetic risk categorized by HDP-PRS and were evaluated for incident cardiovascular disease.

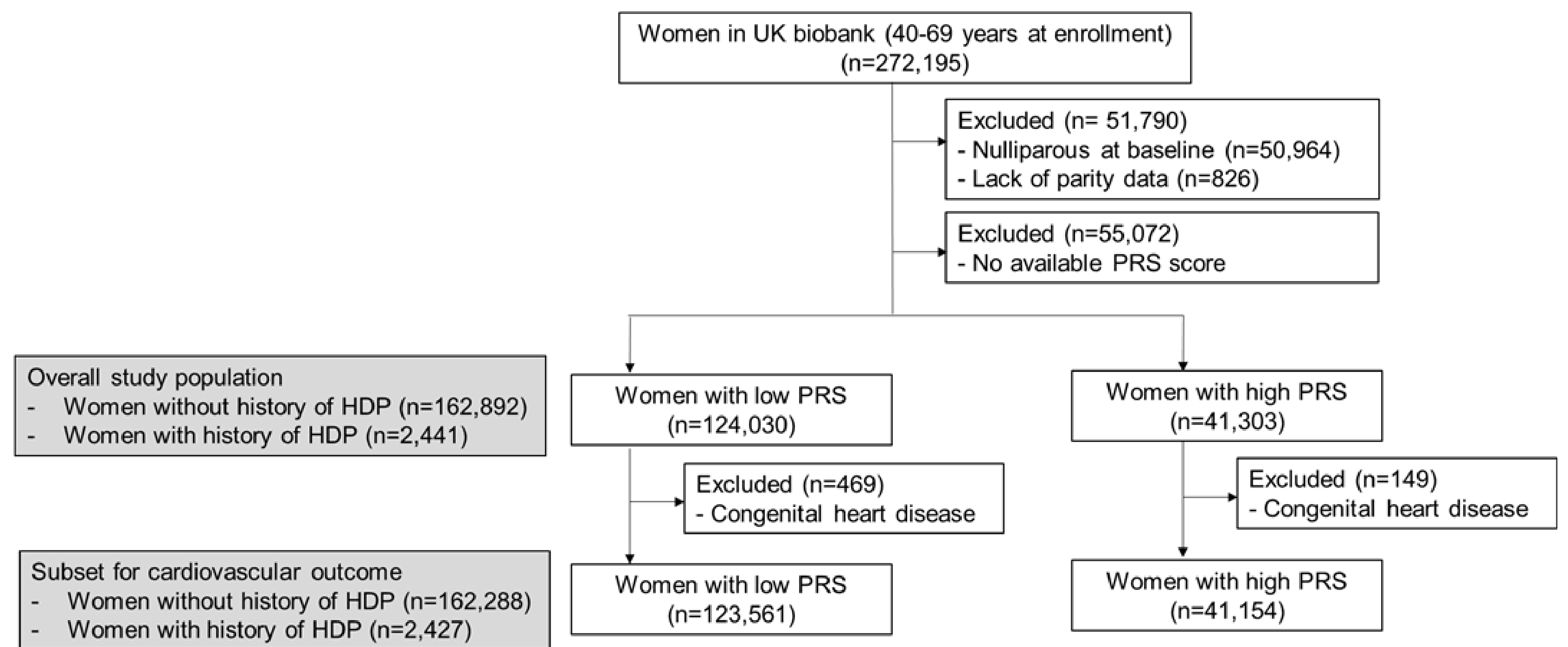


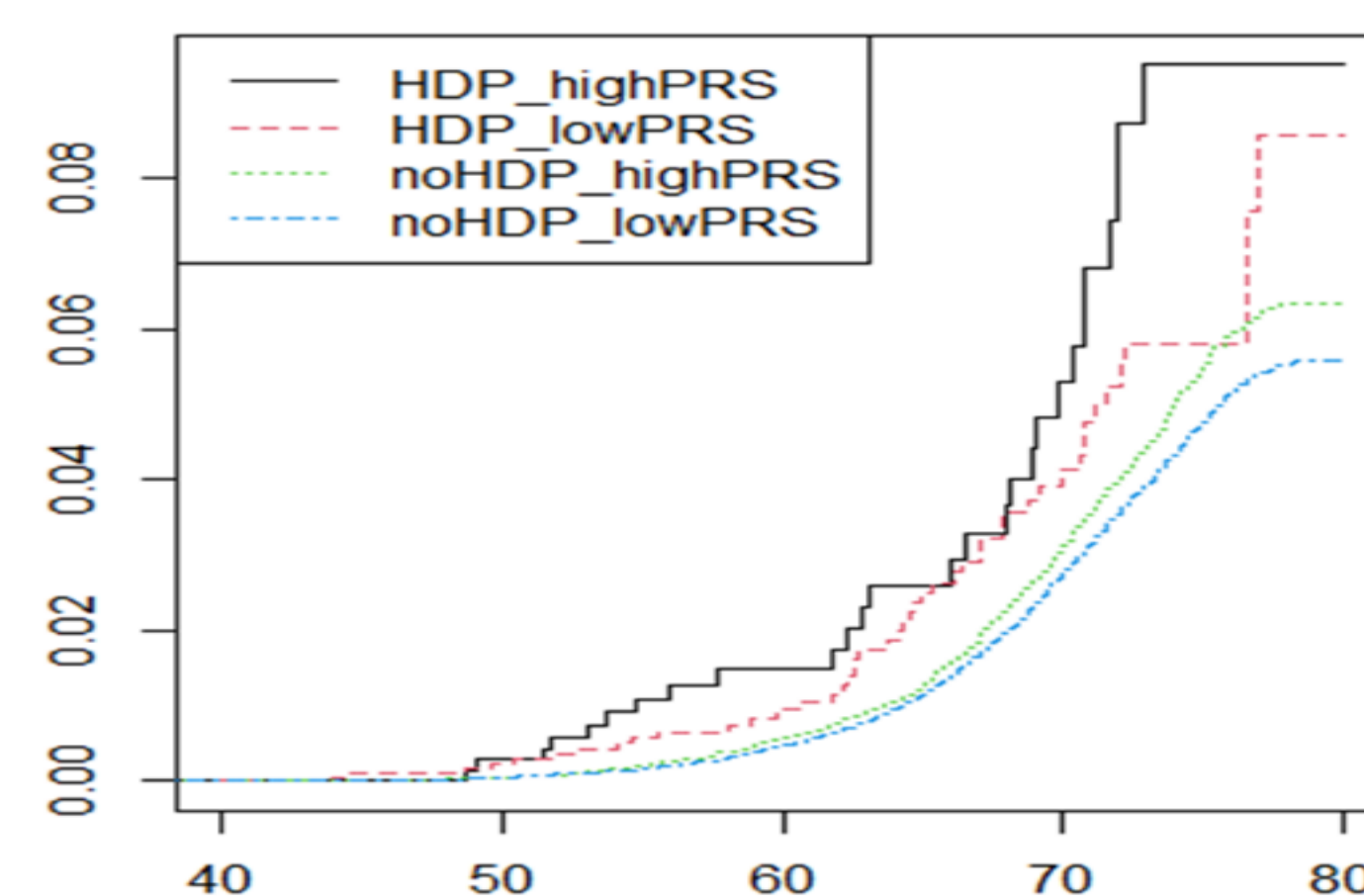
Table. Baseline clinical features

Characteristics	Low PE-PRS ($\leq 75p$) (n = 124,030)	High PE-PRS ($> 75p$) (n = 41,303)	P-value
Baseline characteristics at enrollment			
Age (years)	57.2 ± 7.7	57.2 ± 7.6	0.664
BMI	27.0 ± 5.0	27.3 ± 5.2	<0.001
Age at first live birth	25.4 ± 4.5	25.2 ± 4.5	<0.001
Number of live births	2.2 ± 0.9	2.2 ± 0.9	0.658
Mean duration between first birth and enrollment	32.2 ± 9.5	32.3 ± 9.5	0.024
Ever smoking	50583 (40.8%)	16932 (41.0%)	0.452
Use of medication			
- Aspirin	12439 (10.0%)	4486 (10.9%)	<0.001
- Anti-hypertensive	22507 (18.1%)	9111 (22.1%)	<0.001
- Cholesterol lowering agent	17213 (13.9%)	6327 (15.3%)	<0.001
Blood pressure at enrollment			
- Systolic blood pressure	135.8 ± 19.3	137.3 ± 19.3	<0.001
- Diastolic blood pressure	80.5 ± 9.9	81.4 ± 9.9	<0.001
Prevalent comorbidity at baseline			
Hypertension	30225 (24.4%)	12015 (29.1%)	<0.001
Diabetes	4086 (3.3%)	1618 (3.9%)	<0.001
Dyslipidemia	14509 (11.7%)	5296 (12.8%)	<0.001

Data are presented as proportion (%) or mean ± standard deviation. Abbreviations: BMI, body mass index; PE, preeclampsia

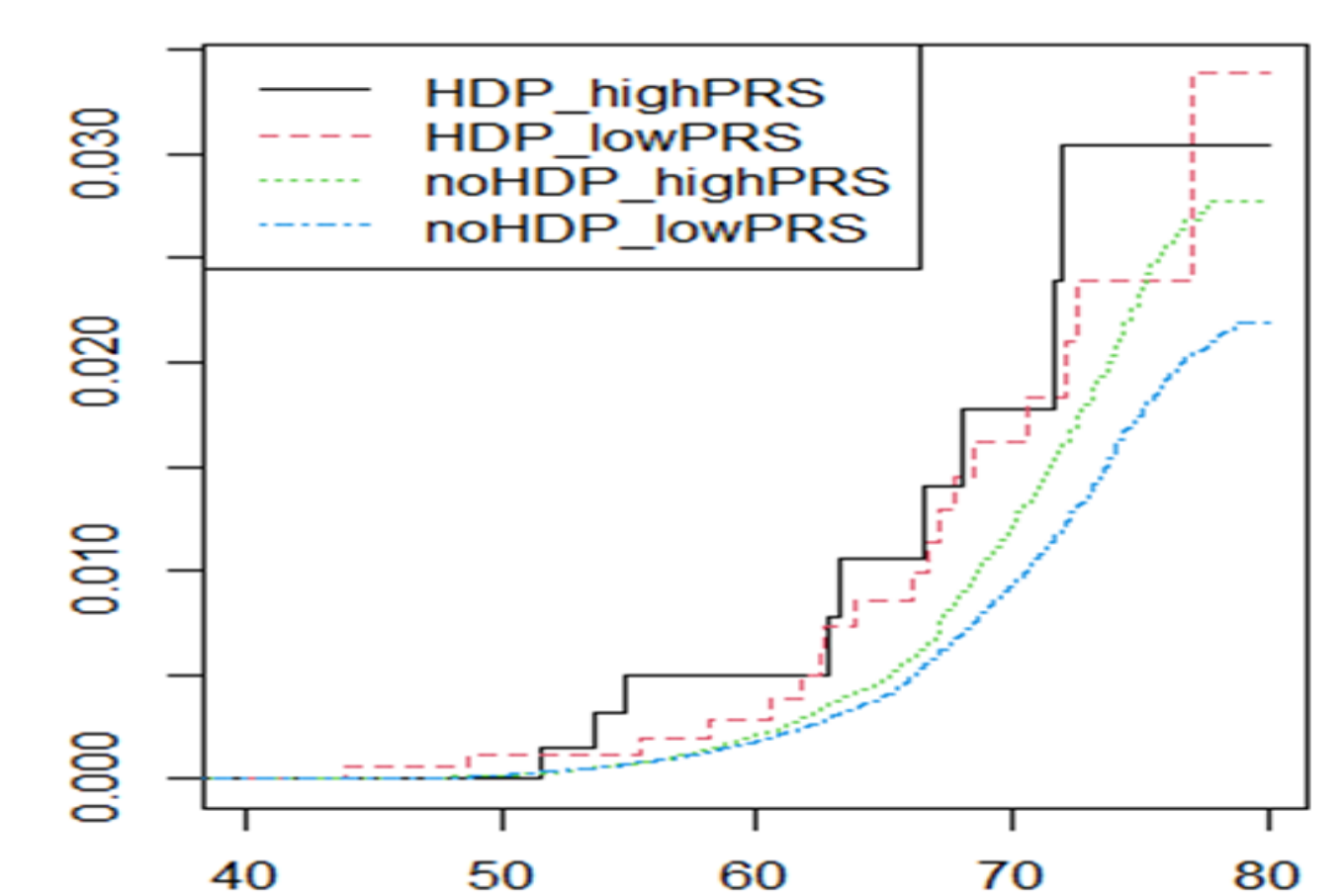
Figure 3. Survival analysis according to polygenic risk score for HDP and the history of HDP by Cox regression analyses

Coronary artery disease



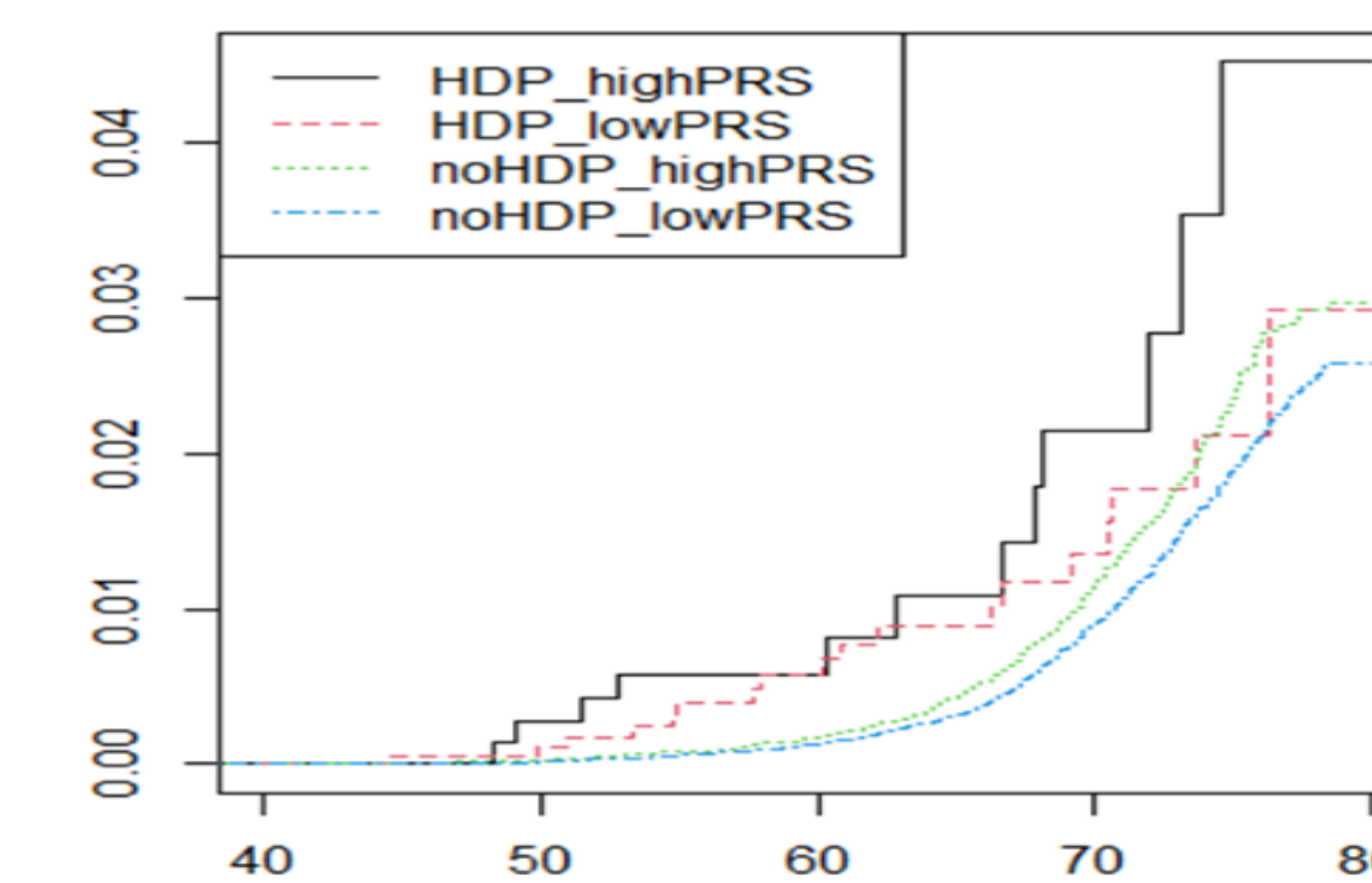
High PRS: HR 1.09 (1.015-1.162, $p^2 = 0.017$)
*p, After adjustment for age, BMI, smoking, prevalent hypertension/DM/dyslipidemia, HDP

Myocardial infarction



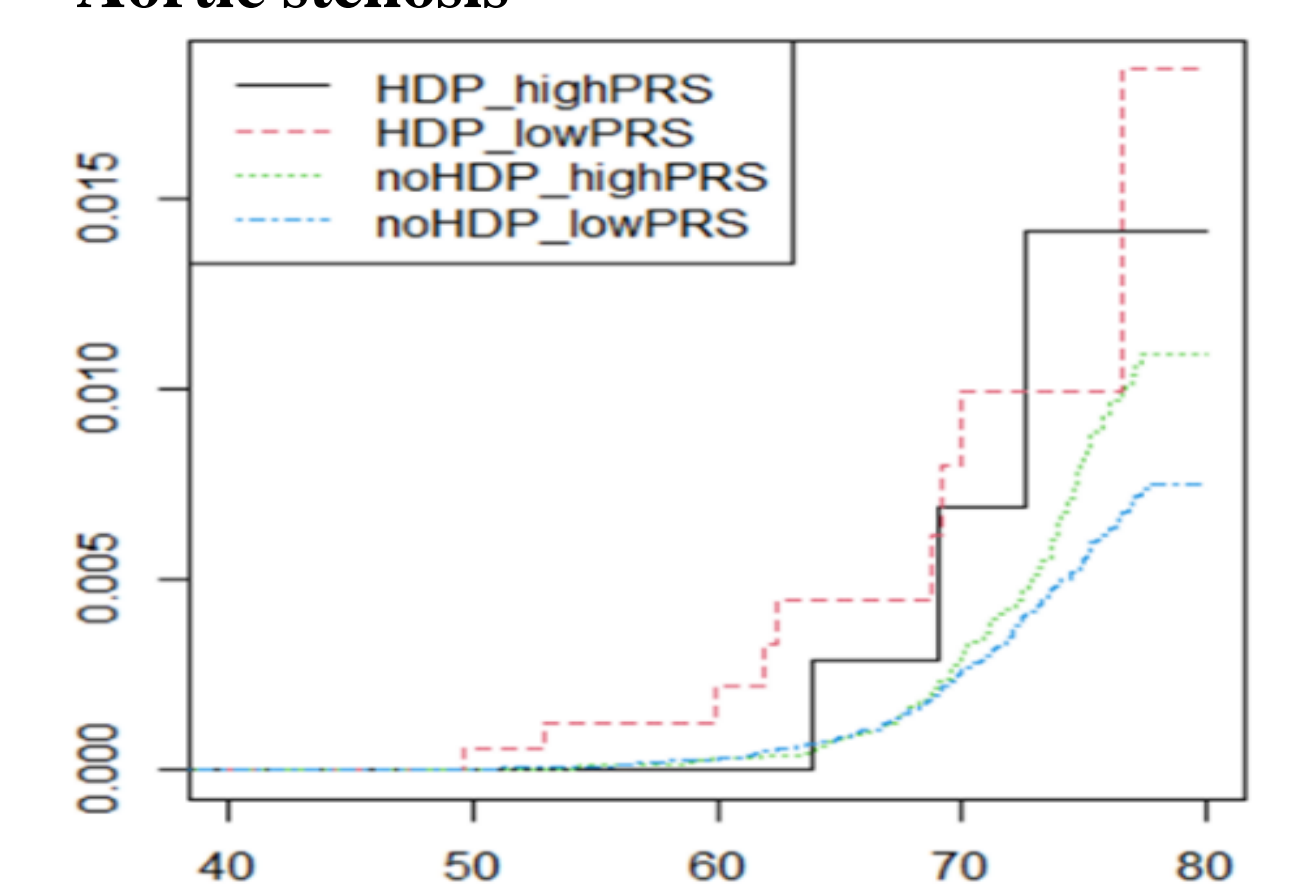
High PRS: HR 1.23 (1.107-1.372, $p^2 < 0.001$)
*p, After adjustment for age, BMI, smoking, prevalent hypertension/DM/dyslipidemia, HDP

Heart failure



High PRS: HR 1.18 (1.0586-1.308, $p^2 = 0.002$)
*p, After adjustment for age, BMI, smoking, prevalent hypertension/DM/dyslipidemia, HDP

Aortic stenosis



High PRS: HR 1.23 (1.011-1.486, $p^2 = 0.038$)
*p, After adjustment for age, BMI, smoking, prevalent hypertension/DM/dyslipidemia, HDP

Figure 1. Risk of HDP according to polygenic risk score

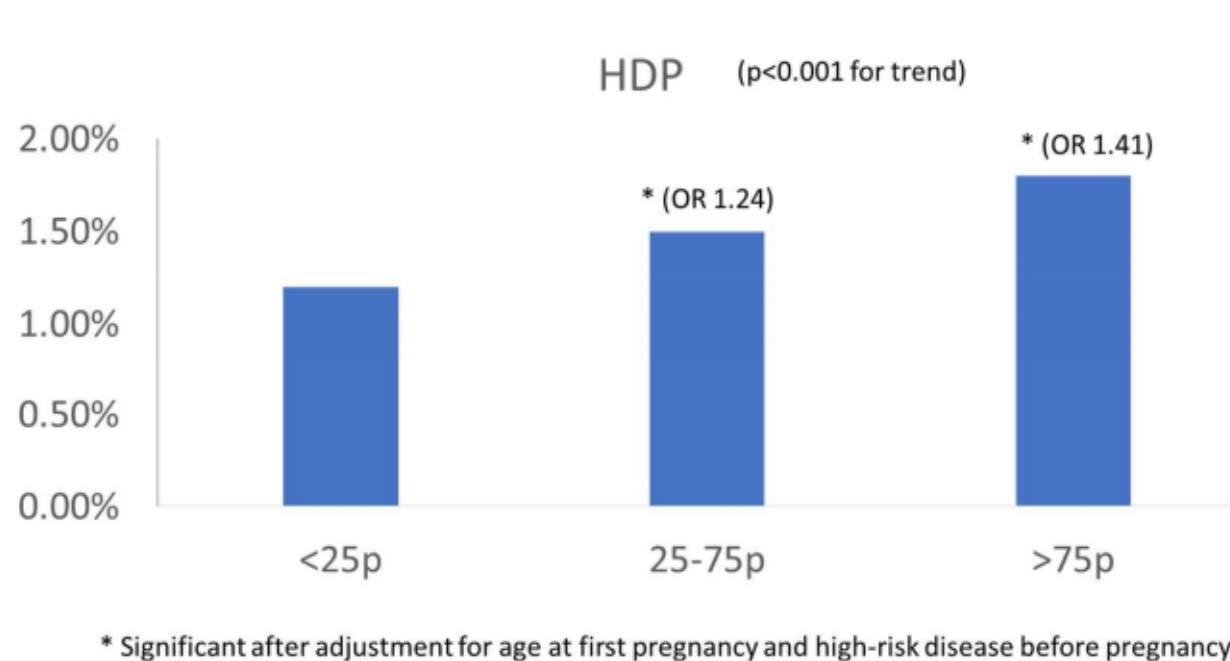
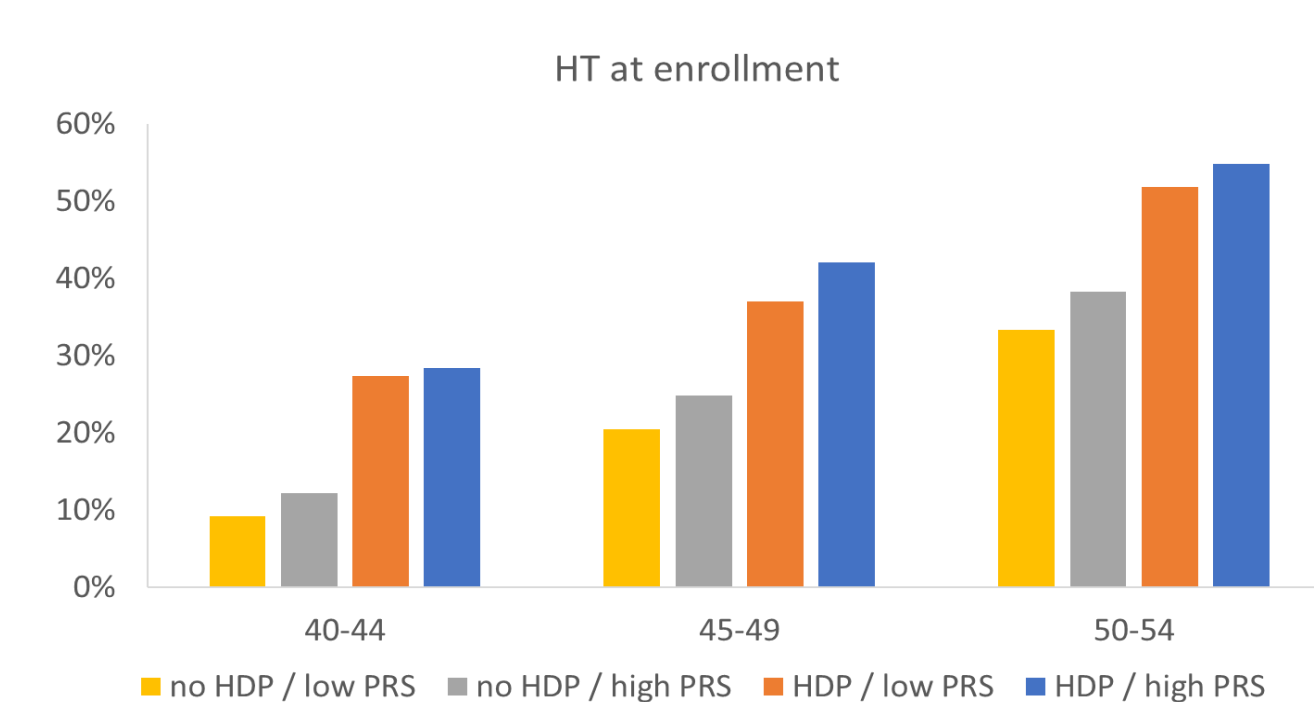


Figure 2. Prevalent Hypertension by the history of HDP and HDP-PRS score



Conclusion

- This study provides evidence on the informative value of HDP-PRS in the prediction of long-term cardiovascular outcomes later in life.
- The application of PRS information for risk assessment and medical interventions needs to be evaluated in further studies.

Figure 4. Hazard ratio of each cardiovascular outcomes by Cox regression analyses

