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Early-onset prostate cancer : Interplay of PRS & family history and rare pathogenic variants

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Introduction

1. Polygenic risk score (PRS) has been known to influence development of the prostate cancer over a life course.
2. PRS have recently been shown to have relative risks that depend on age, and genetic relative risks decrease with increasing age.
3. A recent study assessed the interplay of polygenic risk, rare pathogenic variants, and family history[1].

Objectives

We aimed to comprehensively assess the role of polygenic risk score (PRS):

- in the early-onset prostate cancer (PC) vs late-onset
- in the absence or presence of a family history of PC (FH)
- in the absence or presence of rare pathogenic variants (PV, across 5 PC susceptibility genes - HOXB13, BRCA2, ATM, CHEK2, BRCA1).

Methods

Results

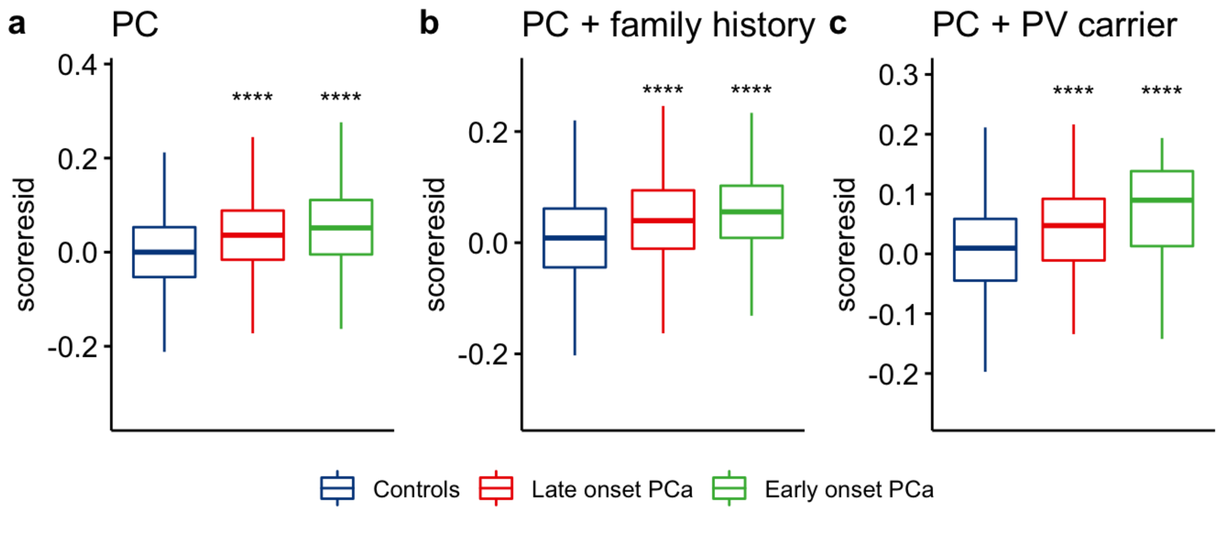

Figure 1: Boxplot of prostate cancer (PC) PRS for early-onset versus late-onset PC. PRS distribution across all PC cases (a), PC cases with PC family history (b), and PC cases with PV carrier (c)

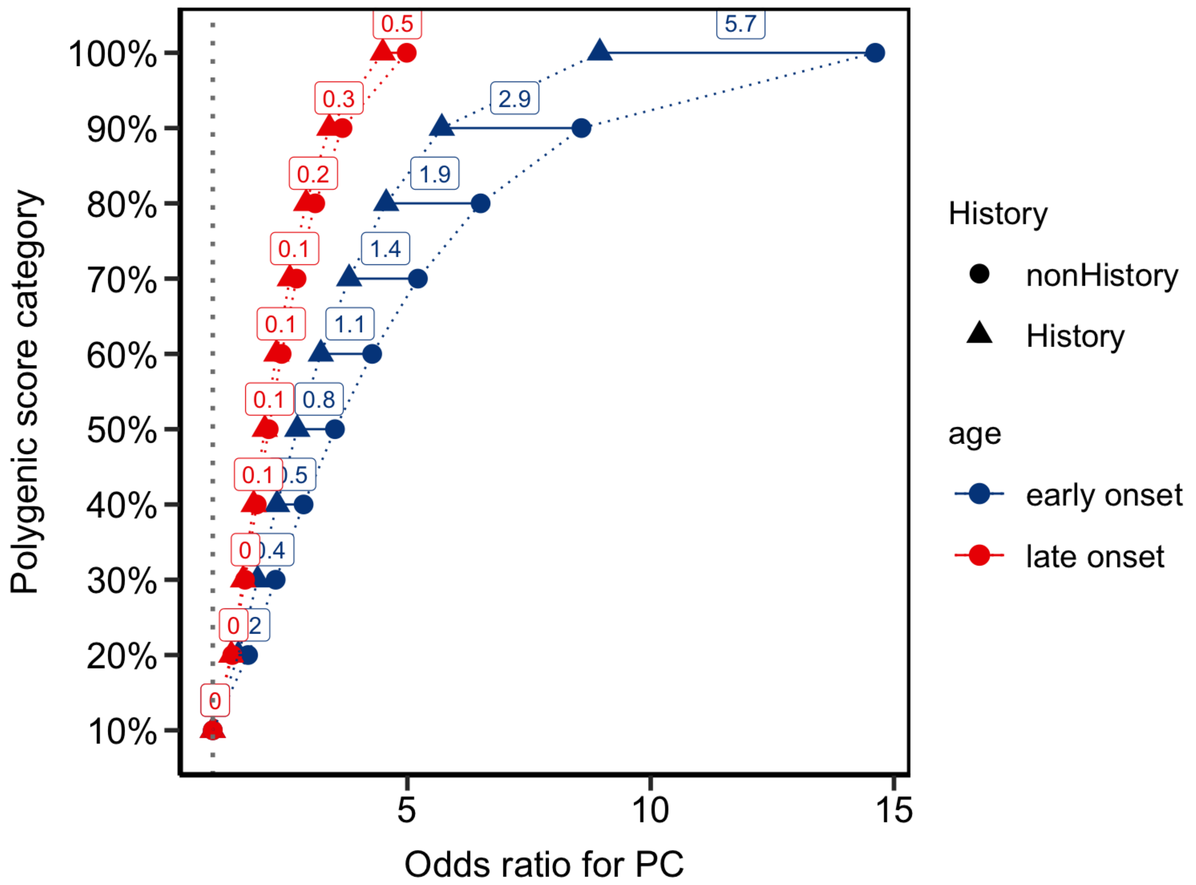

Figure 2: Risk estimates for early-onset versus late-onset CRC associated with PC PRS. Individuals stratified according to presence of family history.

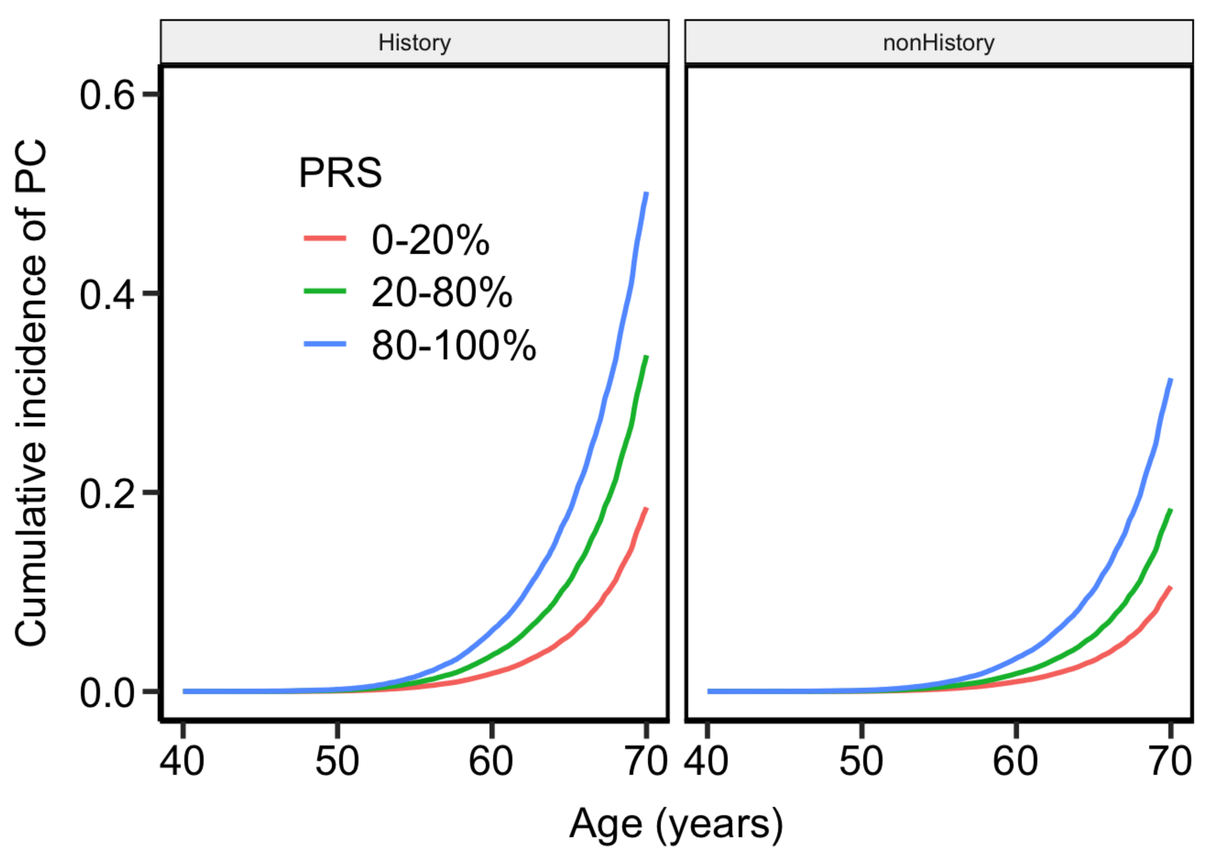

Figure 3: Absolute risk estimates of being diagnosed with PC across the age stratum by PRS percentile. Individuals stratified according to presence of family history.

References

1.
Hassanin, E. *et al.* Breast and prostate cancer risk: The interplay of polygenic risk, rare pathogenic germline variants, and family history. *Genet Med* **24,** 576–585 (2022).

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