
**Models and methods for improving prostate cancer screening and
management with genetic information**

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(by courtesy)
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Abstract:

Prostate-specific antigen (PSA) screening is controversial because it can lead to overdiagnosis and overtreatment of prostate cancer when individuals have high PSA levels for reasons other than aggressive disease. It is thus important to ask the question how PSA screening can be improved. We have shown that accounting for genetic factors that impact constitutive, non-cancer PSA levels results in a test that ascertains more clinically relevant, aggressive disease. In parallel, we have shown that genetic factors for PSA can also be used to improve polygenic risk scores (PRS) for prostate cancer. Existing PRS are strongly predictive of prostate cancer risk, but they do not specifically predict aggressive disease because they were largely developed in men with PSA screen-detected, lower-risk disease. We demonstrate that removing PSA genetic factors from prostate cancer PRS makes the PRS more predictive of aggressive disease. We are now improving this prostate cancer PRS with a machine learning approach that incorporates PSA associations and functional information. We are also determining the clinical utility of incorporating genetically adjusted PSA levels and the PRS for aggressive prostate cancer into validated risk calculators for biopsy outcomes (higher grade disease) and prostate cancer active surveillance upgrading. These models will allow us to assess the benefit of incorporating genetic information into decisions about frequency of screening, escalation to prostate biopsy, and selection of active surveillance following diagnosis. Our ultimate goal is to reduce PSA screening harms while improving screening benefits and predicting risk of clinically important disease.

Reading List:

-PDF attached