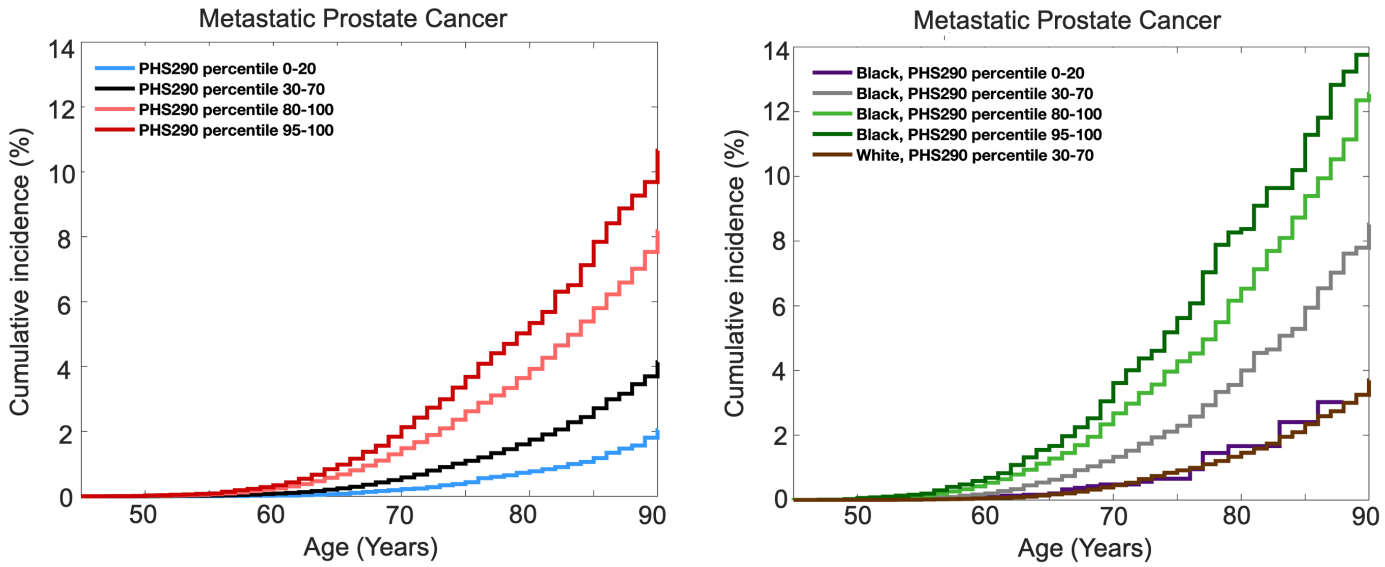
Genetic score to guide personalized prostate cancer detection

Prostate cancer is the #2 cause of cancer death among men in the U.S. Many more men live with metastatic prostate cancer, but their quality of life is dramatically impacted by cancer therapies. We can prevent these outcomes by detecting prostate cancer early and treating it before it spreads (metastasizes) to other parts of the body. However, not all men have the same risk of developing the disease. Our efforts to screen men for prostate cancer should focus on those at highest risk of potentially fatal disease. We have developed and tested genetic risk scores to identify those men at highest risk.



Cause-specific cumulative incidence of metastatic prostate cancer, stratified by a polygenic hazard score based on 290 common variants (PHS290). PHS290 percentile groups: 0-20th, 30-70th, 80-100th, and 95-100th. Left: all male participants in the Million Veterans Program study. Right: Participants with self-reported Black or African American race in various PHS290 strata, with average-genetic-risk Non-Hispanic White shown for comparison. Adapted from Pagadala et al., *JNCI* 2023.

- Select publications:
  - Pagadala et al., *Journal of the National Cancer Institute* 2023 https://pubmed.ncbi.nlm.nih.gov/36305680/
  - Huynh-Le et al., *Nature Communications* 2021 https://pubmed.ncbi.nlm.nih.gov/33623038/
  - Seibert et al., *British Medical Journal (BMJ)* 2018 https://pubmed.ncbi.nlm.nih.gov/29321194/
- Ongoing projects:
  - ProGRESS: The Prostate Cancer, Genetic Risk, and Equitable Screening Study. ProGRESS is a nationwide randomized clinical trial in the VA hospital system testing personalized prostate cancer screening using genetic tools developed and tested in the Seibert Lab. (Principal Investigator: Jason Vassy, MD from VA Boston and Harvard Medical School)
  - Germline Influence on Prostate Cancer Metastasis and Treatment Response. In collaboration with NRG Oncology and the Boutros Lab at UCLA, we are studying how inherited DNA (germline) influences the molecular and genetic features of prostate cancers. We are also investigating how inherited DNA impacts the development of prostate cancer metastasis and response to specific treatments.