Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Current Prostate Cancer Genetic Risk Scores Add Limited Predictive Value for Black Men: a prospective cohort study in the UK Biobank and Our Future Health

Callum Webb
University of Exeter
Ge Chen
University of Exeter
Luke C. Pilling
University of Exeter
Jiaqi Li
University of Exeter
Ella Daniels
University of Exeter
Samuel W. D. Merriel
University of Manchester
Sarah E. R. Bailey
University of Exeter
Tanimola Martins
University of Exeter
Leigh Jackson
University of Exeter
Harry D. Green
H.D.Green@exeter.ac.uk

University of Exeter

Research Article

Keywords: Genetic Risk Score, Polygenic Score, Prostate Cancer, Disparities, Ethnicity, Screening, Prediction, UK Biobank, Our Future Health, Genomics

Posted Date: November 11th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11373780/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Current Prostate Cancer Genetic Risk Scores Add Limited Predictive Value for Black Men: a prospective cohort study in the UK Biobank and Our Future Health

Callum Webb[1], Ge Chen[1,2], Luke C Pilling[1], Jiaqi Li[1], Ella Daniels[1,3], Samuel W.D. Merriel[4], Sarah E. R. Bailey[2], Tanimola Martins[2,5], Leigh Jackson[1], Harry D. Green[1]*

[1] Department of Clinical and Biomedical Sciences, University of Exeter, Exeter, UK

[2] Department of Health and Community Sciences, University of Exeter, Exeter, UK

[3] BSW Hospitals Group, Royal United Hospital, Bath, UK

[4] Centre for Primary Care and Health Services Research, University of Manchester, Manchester, UK

[5] Department of Public Health and Sport Sciences, University of Exeter, Exeter, UK

*Corresponding author: Harry D. Green (H.D.Green@exeter.ac.uk)

2026-10-14

Abstract

Background

Genetic risk scores could support risk-stratified prostate cancer screening, but their predictive performance may be limited in Black men, who are at greater risk and are underrepresented in genetic studies. We evaluated whether currently available genetic risk scores predict incident prostate cancer equitably in the UK, on fixed prediction horizons of 2-, 5-, and 10-years.

Methods

Male participants with imputed genetic data were included from the UK Biobank and Our Future Health cohorts. Logistic regression models combining genetic risk scores with age and/or family history were used to predict diagnosis within 2, 5, and 10 years of either the assessment centre visit or participants' 40th, 50th, or 60th birthday. Performance was evaluated using the area under the receiver operating characteristic curve, odds ratios per standard deviation increase in genetic risk score, risk stratification by model decile, and net benefit analysis. Primary analyses compared Black and White men based on self-reported ethnicity.

Results

Adding the 269-variant multiethnic score to age in an integrated risk model improved discrimination in White men across all prediction horizons, increasing AUC by 8.69-11.23%. In Black men, improvement was significant only over 10 years, increasing the AUC by 1.83%. Age alone was a stronger discriminative predictor in Black men, so models

combining age and genetic risk had similar AUC between groups. For the best-performing GRS, 10-year odds ratios per standard deviation were 2.18 [2.13 - 2.23] in White men and 1.62 [1.40 - 1.88] in Black men. These GRS showed comparable case/control discrimination and association with diagnosis in age-specific screening scenarios in the Our Future Health cohort. Net benefit analysis revealed that the useful range of absolute risk thresholds is wider, and that optimal sensitivity and specificity is typically achieved at higher thresholds, in Black men.

Conclusions

Models combining age and genetic risk can achieve similar overall discrimination in Black and White men, but current GRS contribute little beyond age alone in Black men. Absolute risk thresholds may need to be higher in Black men to prevent overdiagnosis. Greater representation of underrepresented groups in Genome-Wide Association Studies is needed to improve GRS performance for Black men.

Keywords: Genetic Risk Score, Polygenic Score, Prostate Cancer, Disparities, Ethnicity, Screening, Prediction, UK Biobank, Our Future Health, Genomics

Background

Prostate cancer (PrCa) is a highly polygenic disease, with 451 common single-nucleotide polymorphisms (SNPs) having been identified as risk variants in Genome-Wide Association Studies (GWAS) (1,2). These variants can be accumulated as Genetic Risk Scores (GRS), where each included variant's effect size is used to calculate an individual's relative predisposition to PrCa, based on the risk variants they carry. Population-level analysis suggests that GRS can predict PrCa risk (1–4), but there are concerns that their discriminatory performance may be stronger for individuals genetically similar to European reference cohorts (hereafter EUR-like participants) compared to those genetically similar to African reference cohorts (hereafter AFR-like participants) (5,6). In the UK context, this suggests that Black men, who are at a significantly elevated risk of PrCa compared to White men (7), could benefit less from GRS implementation in primary care pathways and in PrCa screening programmes, exacerbating current health inequities.

The latest PrCa GRS, developed by Conti *et al.* (2021) and later Wang *et al.* (2023), were derived from large multi-ethnic GWAS meta-analyses (1,2). To develop their 451-SNP PrCa GRS (GRS_{451}), Wang *et al.* (2023) included 19,391 cases and 61,608 controls of AFR-like participants in their GWAS meta-analysis, plus 122,188 cases and 604,640 controls of EUR-like participants, making it the PrCa GWAS with the greatest number of AFR-like participants to-date (2). Although it outperforms the earlier 269-SNP score (GRS_{269}), which included 10,368 AFR cases and 10,986 AFR controls (1), its association with PrCa remains weaker in AFR-like (OR per SD (MADCaP): 1.78 [1.67 - 1.90]) than EUR-like populations (OR

per SD (MGB): 2.21 [2.08 - 2.34]) (2). These findings suggest that greater representation of AFR-like populations in GWAS discovery cohorts could further improve risk prediction for Black men in the UK.

Population-level polygenic risk scoring is a national priority in NHS England's most recent 10-year health plan and in the 2026 National Cancer Plan for England, but whether this would work equitably for Black men is unclear. Available evidence indicates weak associations between PrCa GRS and PrCa risk in AFR-like than in EUR-like men. For example, GRS_{269} showed a stronger association with PrCa diagnosis in EUR-like than AFR-like UK Biobank participants (OR per SD: 2.04 vs. 1.35) (8). Similarly, a population-aware GRS derived from the same variants discriminated PrCa cases and controls more effectively in White than Black men (AUC: 0.70 vs. 0.63), although this difference disappeared after incorporating age into the prediction model (9). However, this study did not compare the integrated risk models to age-only models, so it is not clear whether the GRS added predictive value above age alone. Furthermore, both studies investigated anytime PrCa case-control status as their primary endpoint, meaning that participants had variable durations of follow-up, and it was not possible to assess the integrated model's potential to detect incident PrCa.

Using anytime case/control status as the primary outcome is typical of most PrCa GRS evaluation studies, but fails to generate the evidence that would be needed to consider the clinical application of GRS. Lifetime risk is not only non-specific but is also influenced by the age of the cases and controls in the cohort, inter-patient variability in the length of follow-up, and other factors. Other studies evaluate GRS-based prediction of incident

PrCa within 2, 5, or 10 years of a specified index date (start of observation window), but either do not compute analyses in Black men (10–13) do not compare performance of subpopulation-specific GRS weights against “cross-ancestry” weights (6); or do not use the latest trans-ancestry scores (14). Therefore, it is not known which currently available GRS is most suitable for Black men living in the UK, at what age GRS-based screening would be most useful, and how far into the future these models can faithfully predict PrCa diagnosis in Black men.

The present study addresses these aspects by evaluating the ability of PrCa GRS published between 2018 and 2025 to predict 2-, 5-, and 10-year incident PrCa diagnosis in Black men living in the UK compared to White men, on both an absolute and relative risk scale.

Methods

Throughout this manuscript, we used the terms “genetic similarity” and “EUR/AFR/EAS/SAS/CSA/MID/AMR-like” to describe genetic similarity groups based on guidance from the National Academies of Sciences, Engineering, and Medicine’s 2023 consensus report on using population descriptors in Genetics and Genomics Research.

Participants

Male participants from the UK Biobank (field 31, “Sex”) and Our Future Health (field “DEMOG_SEX_1_1” and “DEMOG_SEX_2_1”) with linked imputed genotype data (UKB field 22828, “Imputation from genotype” ; OFH field “imputed_bgen”) were included in this study.

For UKB analyses, the index date was defined as the initial assessment center date (2006-2010). Recruitment to OFH began in 2021 and is ongoing, resulting in limited follow-up data. As a result, index dates were fixed at participants’ 40th, 50th, and 60th birthdays (with the day set to the 16th of the birth month), or 31 December 2013, which at the time of analysis, marks 10 years prior to the latest cancer registry records in the dataset. For each scenario using 40th/50th/60th birthdays as index dates, any participant that was not old enough to have lived to the relevant index age was excluded from the analysis. Additionally, any control who was not old enough to have lived through the entire prediction horizon or died of any cause other than PrCa before the end of the prediction horizon was excluded from the OFH analysis. As this study aims to evaluate tools for

predicting incident rather than prevalent PrCa, we excluded any participant with a PrCa diagnosis prior to the index date in both datasets.

Prostate cancer phenotype definition

PrCa cases were defined as at least one record of "malignant neoplasm of prostate" using International Classification of Diseases (ICD) diagnosis codes (ICD9: 185; ICD10: C61) in the Cancer Register (UKB fields 40013 and 40006; OFH field SITE_ICD10_O2 in nhse_eng_canreg_pattumour), or those with these codes in the Hospital Episode Statistics (HES) (UKB fields 41271 and 41270; OFH "diag" fields in "nhse_eng_inpat" and "nhse_eng_outpat"), provided that a record was confirmed in the Death Register (UKB fields 40001 and 40002; OFH field S_COD_CODE_X/S_UNDERLYING_COD_ICD10 in nhse_engwal_deaths).

Since stage and grade of cancer is not available in the UKB, actionable and severe PrCa diagnoses were defined as follows:

- Actionable: a record of radiotherapy (Office of Population Censuses and Surveys Classification of Interventions and Procedures (OPCS-4) codes X65, X67, X68, X69, or Y91), prostatectomy (OPCS-4 code M61), or anti-androgen treatment (OPCS-4 codes X74.1, X38.3, S52.5, S52.6, or X37.6) administration within 2 years of diagnosis, or any of the Severe criteria.

- Severe: a record of death from any cancer (ICD10 code C* as the primary or secondary cause of death), or chemotherapy administration (OPCS-4 codes X70, X71, X72, X73, or X74) within 2 years of diagnosis.

Controls were defined as any male participant who did not fit the PrCa case criteria above, and also had no record of any of the PrCa-suggestive codes in Supplementary Table 1 in their HES, Cancer Register, Death Register, or Operative Procedures (UKB field 41272; OFH fields “OPERTN_XX” in nhse_eng_inpat and nhse_eng_outpat or “OPCS4_CODE” in nhse_eng_canreg_treat) records.

Ethnicity and Genetic Similarity

Self-reported ethnicity (UKB field 21000; OFH field “DEMOG_ETHNICITY_1_1”) was the primary grouping factor used in this work. White participants were defined as those who selected “White”, “British”, “Irish”, or “Any other White background” in UKB, or “White - English / Welsh / Scottish / Northern Irish / British”, “White Irish”, “White Gypsy or Irish Traveller”, “White Polish”, or “Any other White background” in OFH. Black participants were defined as those who selected “African”, “Caribbean”, “Any other Black background”, or “Black or Black British” in UKB, or “Black or Black British - African”, “Black or Black British - Caribbean”, or “Any other Black / African / Caribbean background” in OFH.

Additionally, genetic similarity to the European (EUR) and African (AFR) Human Genome Diversity Project + 1,000 Genomes (HGDP + 1KG) reference populations was used as a sensitivity analysis. Genetic similarity is inferred from principal component analysis, where

participant genetic principal components are projected into the principal component space of the reference panel and clustered based on the original population labels used in the reference panel. This variable is defined in the UKB (field 30079, "Genomic ancestry") as generated by the Pan-UKB Project (15). In Our Future Health, genetic similarity groups are provided as ancestry calls (OFH table "ofh_imputed_sample_ancestry.v6.tsv"), from which EUR was defined as "NW_WALES", "SW_WALES", "N_ENG_S_SCOT", "NI_N_SCOT", "C_S_UK", "FINLAND", "IRELAND", "PORTUGAL_SPAIN", "SE_EUROPE", "N_EUROPE", "E_EUROPE", or "CW_EUROPE"; and AFR as "N_AFRICA", "E_AFRICA", "W_AFRICA", "C_S_AFRICA".

Genetic Risk Scores

Genetic Risk Score variant lists and per-allele weights were derived from the following studies: Conti *et al.* (2021), supplementary table 4 (1); Wang *et al.* (2023), supplementary table 4 (2); the BARCODE1 Pilot study (16), Polygenic Score (PGS) catalog entry PGP000726; and the Genomics Ltd "Standard PRS for prostate cancer" (17), UKB field 26267. Since the Conti *et al.* and Wang *et al.* scores provide both overall ("multiethnic") and subpopulation-specific SNP effect sizes for EUR-like, AFR-like, East Asian-like (EAS-like), and Hispanic-like (HIS-like) groups, separate GRS calculations were performed for each set of per-allele weights. Although UKB participants were included in the GWAS meta-analysis that informed the SNPs and effect sizes included in the Wang *et al.* score (2), this was limited to EUR-like participants, meaning that the overfitting risk is lower when evaluating discriminative performance of this GRS in AFR-like or Black UKB participants.

Each participant's Genetic Risk Score (GRS_p) was calculated using PLINK2, using imputed genotype data and the additive formula:

$$\mathrm{GRS}_p = \frac{\sum_{i \in \mathrm{score}} G_{ip} \times \beta_i}{2N_p}$$

Where (G_{ip}) is the participant's number of effect alleles at variant i, (β_i) is the natural log of the Odds Ratio for PrCa diagnosis corresponding to the effect allele at variant i, and (N_p) is the number of non-missing score formula variants for the participant.

Prior to inclusion in prediction models, each GRS column was scaled to population standard deviation units, standardised to the global population of men in the cohort (mean = 0, SD = 1).

Covariates

In UKB analyses, age is defined as the participant's age at the initial assessment centre visit. In OFH analyses, age was only used as a covariate when 31 December 2013 was set as the index date, and is defined as the participant's age at that date. In both cohorts, family history was defined as a recorded family history of i) PrCa in illnesses of father (UKB field 20107; OFH field "FATHER_DIAG_CANCER_1_M"), ii) breast cancer (BC) in illnesses of mother (UKB field 20110; OFH field "MOTHER_DIAG_CANCER_1_M"), or iii) PrCa or BC in illnesses of siblings (UKB field 20111; OFH field "SIBLING_DIAG_CANCER_1_M"), due to shared monogenic risk patterns between PrCa and BC.

Statistical Analysis

All statistical analysis was performed in R version 4.4.0 (“Puppy Cup”) on the DNAnexus-based UK Biobank Research Analysis Platform (UKB-RAP) and Our Future Health Trusted Research Environment (OFH-TRE). For all statistical tests, p values were adjusted within test families using the Benjamini-Hochberg (False Discovery Rate, FDR) method (18). Results are presented as Mean [95% Confidence Interval, CI] unless stated otherwise. For ROC curves, 95% confidence intervals are calculated using the DeLong method.

The association between GRS, age, and/or family history with 2, 5, and 10-year risk of PrCa diagnosis was primarily assessed using logistic regression models and a corresponding Receiver Operating Characteristic (ROC) curve was used to assess discrimination. Odds Ratio of PrCa per standard deviation increase in GRS (OR per 1SD) was derived from the GRS coefficient in these models. Association of integrated risk models (IRMs) with PrCa diagnosis was also evaluated by stratifying absolute model-predicted risks into deciles and comparing the odds ratio of PrCa diagnosis for a specified decile to the median quintile [40-60%], both on a global and subpopulation-specific scale. Within-subpopulation AUC comparisons between models were made using paired DeLong tests, and AUC comparisons between populations for the same model were made using unpaired DeLong tests, unless stated otherwise.

Algorithmic fairness metrics (sensitivity, specificity, positive predictive value, negative predictive value, treatment equality, and accuracy) at set model-predicted absolute risk thresholds were evaluated within-sample using the R package epi.tests. Thresholds were

determined using net benefit decision curves, where net benefit was calculated using the standard equation defined in (19):

$$\text{Net Benefit} = \frac{\text{TP}}{N} - \left(\frac{\text{FP}}{N} \times \frac{p_t}{1 - p_t}\right)$$

where N is the total number of participants, p_t is the absolute risk threshold used to define predicted cases, TP is the number of true positives at the risk threshold, and FP is the number of false positives at the risk threshold.

Net benefit analysis is used to place the benefit (proportion of the population who are correctly identified as cases and would benefit from intervention) and harm (the proportion of the population who receive unnecessary intervention) on the same scale, where p_t / (1 - p_t) functions as the exchange rate between benefit and harm.

From net benefit analysis, the lowest useful threshold was defined as the lowest threshold at which the net benefit curve for the model exceeded the net benefit of referring all participants (where all PrCa cases are true positives and all controls are false positives) or referring no participants (where TP and FP are 0, therefore net benefit = 0), while the highest useful threshold was defined as the highest threshold at which the net benefit curve for the model exceeded the net benefit of referring all participants and referring no participants. These thresholds, as well as the Youden's J threshold, were then used as cutoffs for the purpose of calculating algorithmic fairness metrics.

Results

Following phenotype definitions and control exclusions, 195354 White men (13155 cases, 182199 controls) and 3056 Black men (284 cases, 2772 controls) were included in the UKB arm of this study (Table 1).

Table 1: PrCa incident case and control counts by population and observation window

Population	Total	Controls	Cases	Diagnosed within 2y	Diagnosed within 5y	Diagnosed within 10y
UK Biobank						
Black	3056	2772	284 (9.3%)	43 (1.4%)	88 (2.9%)	204 (6.7%)
White	195354	182199	13155 (6.7%)	1398 (0.7%)	3963 (2.0%)	9311 (4.8%)
Our Future Health, screening at 31/12/2013						
Black	4196	4086	110 (2.6%)	10 (0.2%)	49 (1.2%)	110 (2.6%)
White	268715	261097	7618 (2.8%)	968 (0.4%)	3107 (1.2%)	7605 (2.8%)
Our Future Health, screening at age 40						
Black	3232	3101	131 (4.1%)	<10	<10	10 (0.3%)
White	239148	228826	10322 (4.3%)	<10	24 (0.0%)	169 (0.1%)
Our Future Health, screening at age 50						
Black	2051	1930	121 (5.9%)	<10	17 (0.8%)	58 (2.8%)
White	200958	190804	10154 (5.1%)	154 (0.1%)	555 (0.3%)	2113 (1.1%)
Our Future Health, screening at age 60						
Black	921	858	63 (6.8%)	15 (1.6%)	34 (3.7%)	53 (5.8%)
White	139561	131520	8041 (5.8%)	847 (0.6%)	2350 (1.7%)	5188 (3.7%)

2, 5, and 10 years refers to time elapsed since the index date. “Screening” refers to a simulated date from which the observation window starts, and is set either to 31st December 2013 (10 years before the latest cancer registry update) or the date of participants’ 40th, 50th, and 60th birthdays.

GRS performance in UK Biobank

GRS_{269} with "multiethnic" per-allele weightings (GRS269-Multi) was selected as the initial score formula for UKB analyses, as it is the most recent large GWAS meta-analysis that did not include UKB participants in its training data (1). Summary forest plots of GRS Receiver Operating Characteristic Area Under the Curve (ROC AUC) results following logistic regression, on 2-, 5-, and 10-year prediction horizons, are shown in Figure 1.

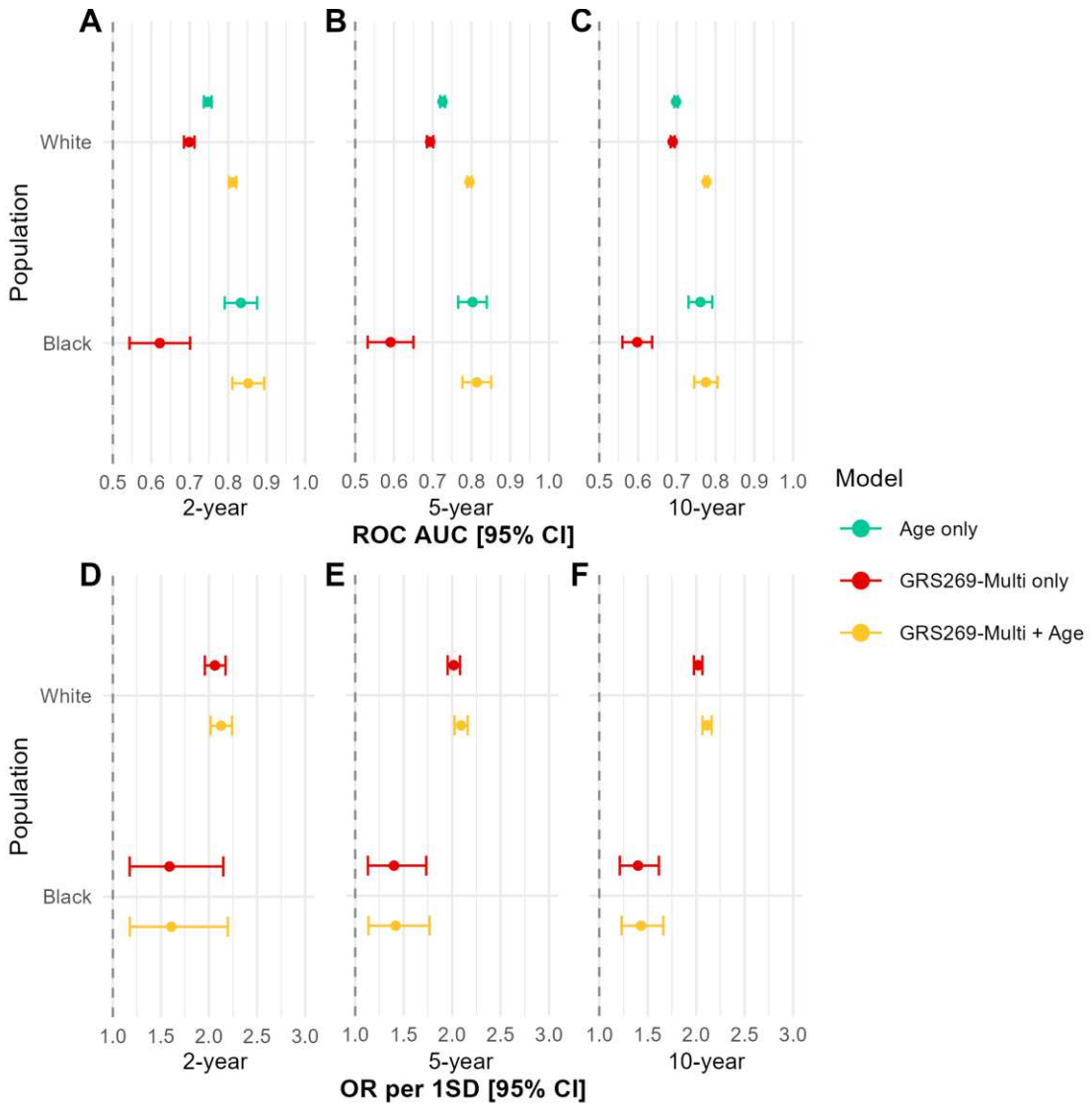


Figure 1: Forest plots summarising ROC AUC and OR per SD increase in GRS from logistic regression models combining GRS_{269}-Multi and age to predict incident PrCa diagnosis. Results are shown for prediction horizons of 2, 5, and 10 years following the assessment centre visit. OR per 1SD refers to the Odds Ratio of PrCa diagnosis in the prediction window per SD increase in GRS, standardised to the global population of men in the cohort. GRS_{269}-Multi refers to the Conti *et al.* (2021) GRS with "Multiethnic" per-allele weights. Figure generated in R version 4.6.0 (2026-04-24 ucrt) ("Because it was There").

In general, ROC AUC estimates decreased with longer prediction horizons. In White men, the addition of GRS_{269}-Multi to Age in an integrated risk model (IRM) significantly improved case/control discrimination compared to age alone across all prediction horizons (ΔAUC: 0.065 - 0.078, adjusted p value (p_{adj}): < 5.00e-08). Further addition of family history to these models significantly improved discrimination, but made a small difference to the point estimate (ΔAUC: 0.002 - 0.003, p_{adj}: ≤ 2.74e-04) (Supplementary Figure 1).

In Black men, the addition of GRS_{269}-Multi to Age in an IRM did not significantly improve case/control discrimination on a 2-year (ΔAUC: 0.019, p_{adj}: 0.08) or 5-year prediction horizon (ΔAUC: 0.011, p_{adj}: 0.13), but did significantly improve discrimination over 10 years (ΔAUC: 0.014, p_{adj}: 0.02). Across all prediction horizons, Age alone discriminated PrCa case/control status more effectively in Black men than in White men (ΔAUC: 0.063 - 0.086, p_{adj}: ≤ 6.22e-04), whereas GRS_{269}-Multi alone discriminated case/control status more effectively in White men than in Black men on a 5-year (ΔAUC: -0.102, p_{adj}: 4.13e-03) and 10-year prediction horizon (ΔAUC: -0.092, p_{adj}: 1.18e-04), but not on a 2-year prediction horizon (ΔAUC: -0.076, p_{adj}: 0.12). The AUC of IRMs combining GRS_{269}-Multi and Age were

not significantly different between White and Black men for any prediction horizon (p_{adj} > 0.05 for all) (Supplementary table 5), though the OR of PrCa diagnosis per SD increase in GRS associated with these models was generally lower in Black men (10-year OR per SD: 1.43 [1.23 - 1.66]) than in White men (10-year OR per SD: 2.11 [2.07 - 2.16]). Addition of family history to any model in Black men did not significantly increase AUC (p_{adj} > 0.05 for all) (Supplementary Figure 1; Supplementary Table 5).

These findings were almost identical when testing in EUR and AFR men as a sensitivity analysis (Supplementary Figure 1).

These analyses were repeated for Actionable and Severe PrCa as the outcome (Supplementary Figure 2). Fewer than 10 cases of Severe PrCa were diagnosed among Black men in 10 years, compromising the ability to meaningfully compare discriminative performance. 77 cases of Actionable PrCa occurred in Black men over 10 years. As with overall PrCa, GRS_{269}-Multi alone was a better predictor of 10-year PrCa diagnosis in White men than in Black men (ΔAUC: -0.088, p_{adj} = 0.01) and AUC did not significantly differ between groups with a GRS + age IRM (ΔAUC: -0.048, p_{adj} = 0.14), though addition of GRS_{269}-Multi to age in an IRM did not significantly increase AUC above age alone for Black men (ΔAUC: 0.025, p_{adj} = 0.16) (Supplementary table 5; Supplementary table 6). 10-year OR per SD increase in GRS_{269}-Multi was comparable with overall PrCa in White men (2.13 [2.06 - 2.21; GRS_{269}-Multi + Age model]) and Black men (1.49 [1.19 - 1.88; GRS_{269}-Multi + Age model]) (Supplementary table 3).

Having established that GRS_{269}-Multi performs optimally when combined with Age in an integrated risk model across all prediction horizons, and that these analyses are best powered to detect differences on a 10-year prediction horizon due to increased case numbers, we then investigated whether participants assigned to higher or lower risk deciles by these models had significantly higher or lower odds of PrCa diagnosis, respectively, compared to the median quintile [40-60%]. To do this, we calculated the OR of 10-year PrCa diagnosis by GRS + Age IRM decile relative to the median group [40-60%] (Figure 2).

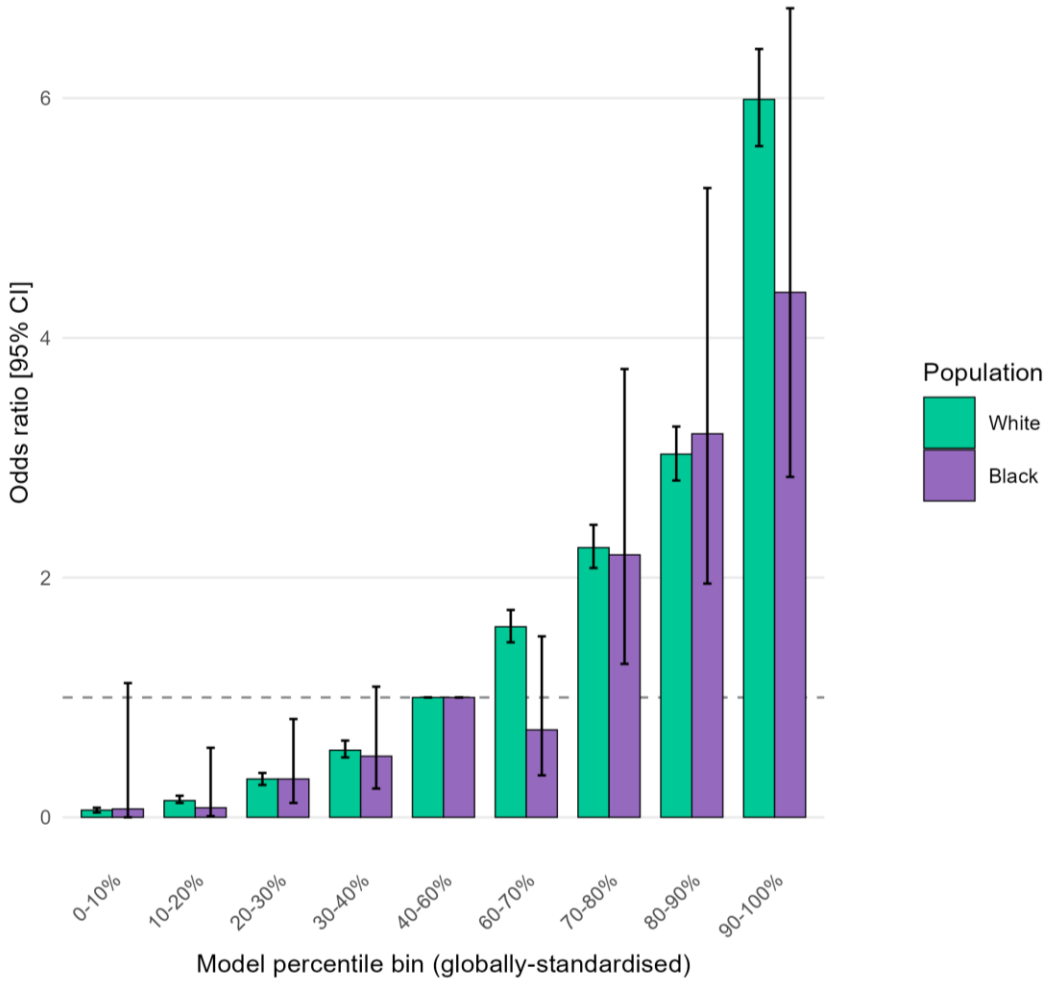


Figure 2: Odds Ratio of PrCa diagnosis by Age + GRS_{269}-Multi IRM decile and ethnicity, relative to the median quintile (40-60%). Results are shown for a 10-year prediction horizon following the UK Biobank assessment centre visit. Decile bins were standardised by the global population of men in the cohort. Figure generated in R version 4.6.0 (2026-04-24 ucrt) ("Because it was There").

Using the median quintile as the reference group, the top decile of the Age + GRS_{269}-Multi IRM had a significantly increased 10-year OR of PrCa diagnosis of 5.99 [5.60 - 6.41, p < 5.00e-08] for White men and 4.38 [2.84 - 6.75, p = 1.47e-12] for Black men. In the bottom decile, 10-year odds of PrCa diagnosis was significantly lower than that of the median quintile in White men (0.06 [0.04 - 0.08, p = 1.64e-165] but results were inconclusive for Black men (0.07 [0.00 - 1.12, p = 3.20e-03]) (Figure 2), due to small numbers of Black men having an IRM score in the bottom decile when standardising to the global population of men in the cohort. A sensitivity analysis using subpopulation-standardised decile bins revealed that Black men in the top IRM decile had a 10-year OR compared to the median quintile for Black men (5.43 [3.44 - 8.57, p = 4.29e-14]) that was comparable with that of White men compared with the median quintile for White men (5.90 [5.51 - 6.31, p < 5.00e-08]) (Supplementary Figure 3). Similarly, the bottom IRM decile had a significantly lower 10-year OR when comparing to subpopulation-specific median quintiles in Black men (0.03 [0.00 - 0.51, p = 5.02e-06]) and White men (0.06 [0.04 - 0.08, p = 1.39e-168]) (Supplementary Figure 3).

Head-to-head analyses were then performed on a 10-year prediction horizon for other PrCa GRS (Figure 3). The GRS most strongly associated with 10-year PrCa diagnosis was

the Genomics Ltd GRS in both White men (OR per SD: 2.18 [2.13 - 2.23; GRS + Age model]) and Black men (OR per SD: 1.62 [1.40 - 1.88; GRS + Age model]). The second-most strongly associated GRS were GRS_{269}-Multi in White men (OR per SD: 2.11 [2.07 - 2.16; GRS + Age model]) and GRS_{451} using AFR-specific per-allele weights (hereafter GRS_{451}-AFR) in Black men (OR per SD: 1.57 [1.35 - 1.82; GRS + Age model]), performing similarly to the Genomics Ltd GRS. In Black men, no GRS + Age model significantly improved ROC AUC beyond GRS_{269}-Multi + Age ($p > 0.05$ for all comparisons) (Supplementary table 6).

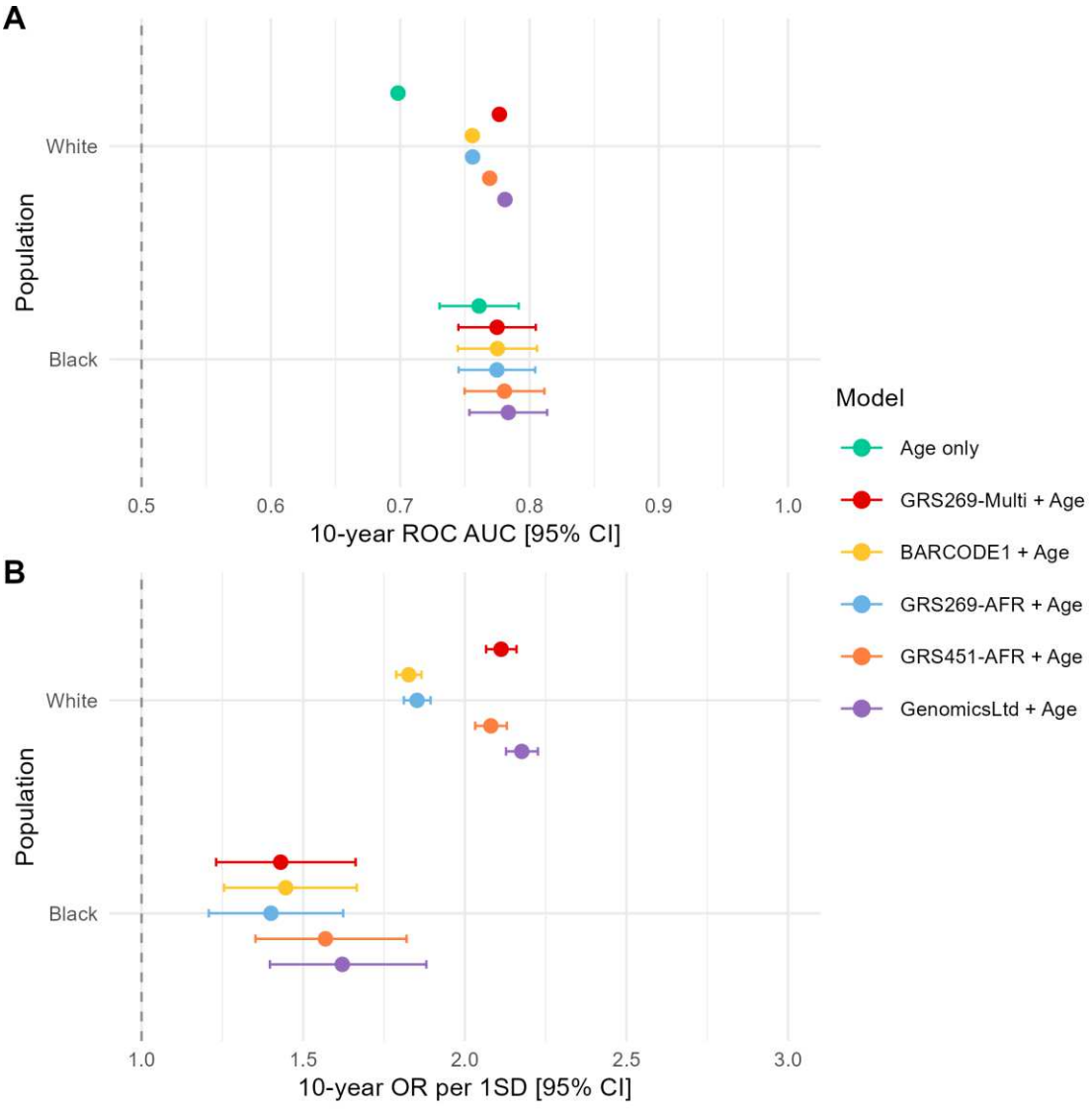


Figure 3: Head-to-head comparison of GRS_{269}-Multi and BARCODE1, GRS_{269}-AFR, GRS_{451}-AFR, and Genomics Ltd's "Standard PRS for Prostate Cancer" as predictors of incident PrCa diagnosis. OR per 1SD refers to the Odds Ratio of PrCa diagnosis in the 10-year prediction window per SD increase in GRS, standardised to the global population of men in the cohort. GRS_{269}-AFR and GRS_{451}-AFR refer to the 269-SNP GRS from Conti *et al.* (2021) and the 451-SNP GRS from Wang *et al.* (2023), calculated using per-allele weights specific to the AFR-like participants in these studies. Figure generated in R version 4.6.0 (2026-04-24 ucrt) ("Because it was There").

GRS performance in Our Future Health

At the time of writing, the Genomics Ltd "Standard PRS for Prostate Cancer" is not available in the OFH dataset. As a result, the second best-performing GRS - GRS269-Multi for White men and GRS451-AFR for Black men - were then tested as predictors of incident PrCa diagnosis in OFH (Figure 4).

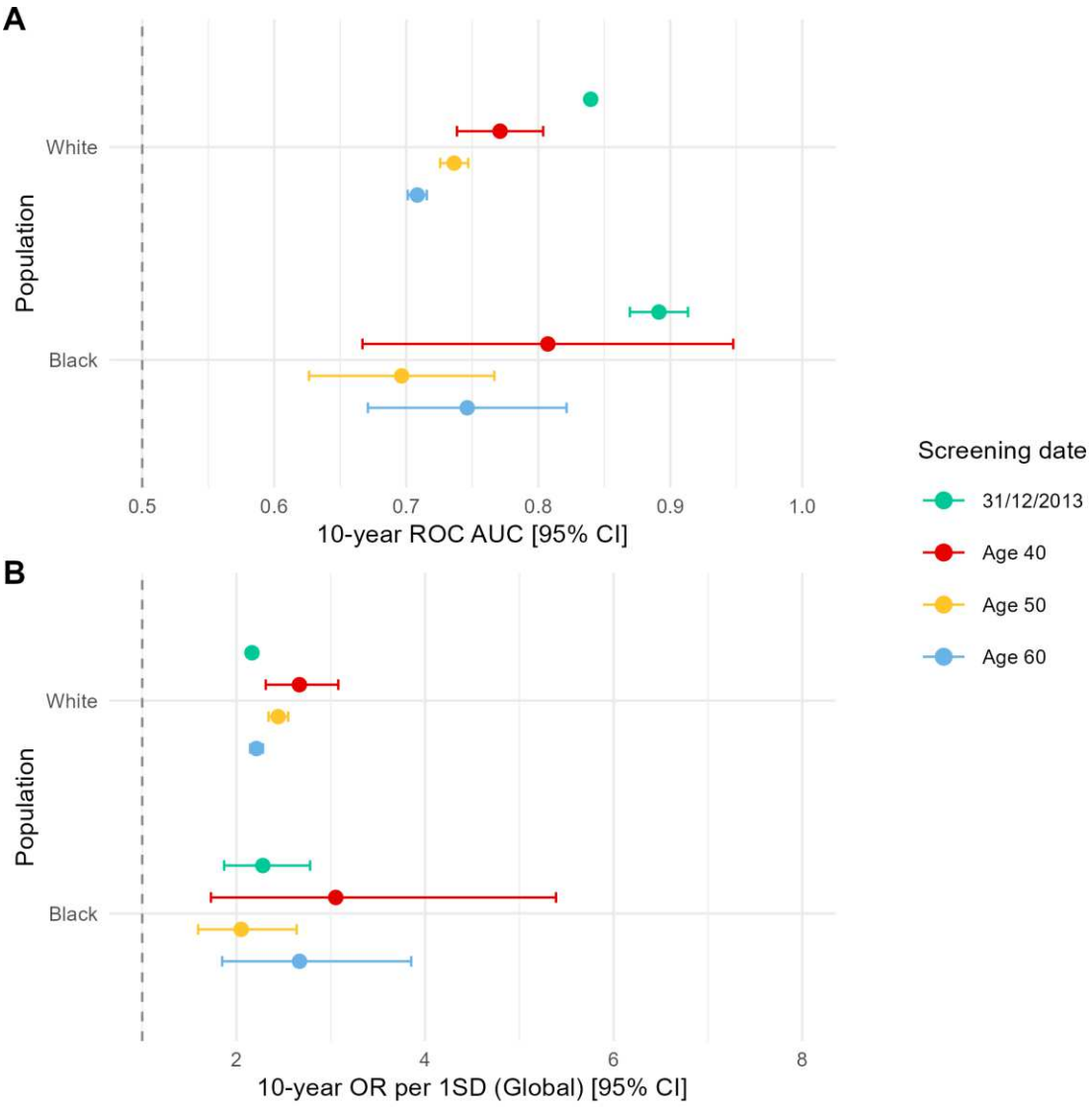
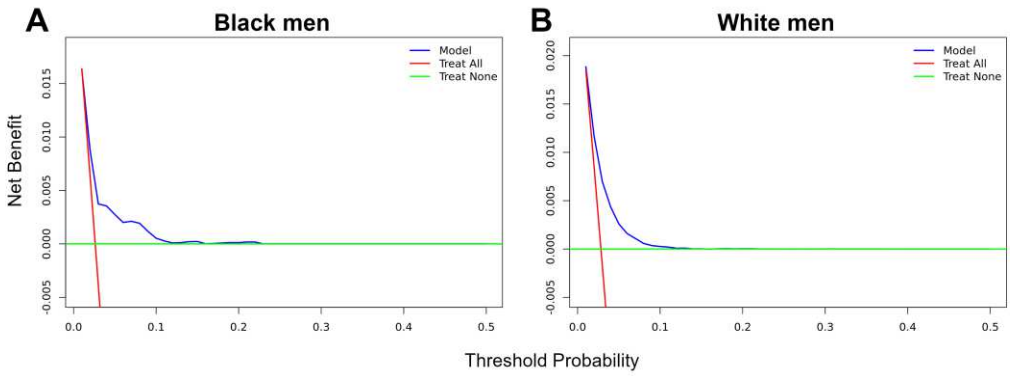


Figure 4: Comparison of second best-performing GRS between White and Black men across screening dates in the Our Future Health cohort. GRS_{269}-Multi and GRS_{451}-AFR were the second best-performing GRS for White and Black men, respectively. OR per 1SD (Global) refers to the Odds Ratio of PrCa diagnosis in the 10-year prediction window per SD increase in GRS, standardised to the global population of men in the cohort. Figure generated in R version 4.6.0 (2026-04-24 ucrt) ("Because it was There").

Among the age-specific index dates, GRS performance was highest when screening was simulated at age 40, as measured by ROC AUC (White men: 0.771 [0.738 - 0.804]; Black men: 0.807 [0.667 - 0.948]) and OR per 1SD (White men: 2.67 [2.31 - 3.08]; Black men: 3.05 [1.73 - 5.39]). The greatest disparity in GRS discriminative performance between White and Black men was observed when screening at 50 years of age, with a suggestive difference in ROC AUC (White men: 0.736 [0.726 - 0.747]; Black men: 0.697 [0.626 - 0.767]), though this difference was not significant (ΔAUC: 0.040, p_{adj}: 0.44).

For the models summarised in Figure 4, we then sought to determine algorithmic fairness metrics (sensitivity, specificity, PPV, NPV, Treatment Equality, and Accuracy). For this, a model-predicted absolute risk threshold needs to be determined. As well as set thresholds of 1%, 2%, 3%, 4%, 5%, and 10% absolute risk, additional thresholds were derived from net benefit analysis and the Youden's J method. Net benefit decision curves were plotted in order to determine the range of absolute risk thresholds at which referring participants for further investigation based on model predictions confers a net benefit over referring all or referring none. Representative net benefit curves are shown for an index date of 31/12/2013 in Figure 5.



377

378 **Figure 5: Representative Net Benefit Curves for Black and White Men**. Curves were
379 plotted using logistic regression models predicting 10-year PrCa diagnosis using
380 31/12/2013 as the index date, with GRS_{451}-AFR as a predictor for Black men and the GRS_{269}-
381 Multi as a predictor for White men, using age at 31/12/2013 as a covariate. The "Model"
382 line (Blue) represents the net benefit of referring participants for further investigation
383 based on model predictions. The "Treat All" line (Red) represents the net benefit of
384 referring all participants for further investigation. The "Treat None" line (Green) represents
385 the net benefit of referring no participants for further investigation. Figure generated in R
386 version 4.6.0 (2026-04-24 ucrt) ("Because it was There").

387 The useful range of absolute risk thresholds was generally wider for Black men. When
388 screening at 31/12/2013, the model provided net benefit over referring all and referring
389 none between thresholds 1.0% - 38.0%. When screening at ages 50 and 60, no highest
390 useful threshold was found between 1 - 50%, suggesting that referring according to the
391 model still provides some net benefit over referring none or referring all in Black men even
392 at high thresholds. For White men, this range is smaller when screening at age 50 (1.0% -

23.0%) and at 31/12/2013 (1.0% - 20.0%). In the age-specific scenarios, the Youden's J threshold was typically higher for Black men (age 50: 7.0%; age 60: 41.0%) than for White men (age 50: 2.0%; age 60: 8.0%). At the fixed screening date 31/12/2013, an IRM combining GRS and age yielded the same Youden's J threshold for White men and Black men (2.0%), producing similar algorithmic fairness results (Supplementary table 8).

Discussion

This study is the first to assess the utility of the latest PrCa GRS as predictors of future PrCa diagnosis in two cohorts of Black men in the UK, using both "multiethnic" and AFR-specific weights from the latest trans-ancestry GWAS (1,2). Our core finding that currently available PrCa GRS minimally improve 10-year case/control discrimination beyond age alone in Black men (Figures 1 and 3) is supported by a previous study from Tanha *et al.* (2025). In this study, the authors found that the ROC AUC for 5-year incident PrCa diagnosis was ~0.81 for AFR-like men and ~0.79 for EUR-like men using an IRM of GRS_{269} + Age, compared to ~0.79 for AFR-like men and ~0.71 for EUR-like men using age alone in the UK Biobank (6), a result we replicate (Supplementary figure 1). Why age alone is a stronger predictor of PrCa risk in Black men than in White men is unknown, but could be influenced by the lower median age at baseline of AFR-like vs EUR-like men (50 vs 58, respectively) (6). We build on this work by stratifying based on self-reported ethnicity as well as genetic similarity to reference populations, by extending the prediction horizon to 10 years to achieve greater statistical power, and by implementing best-performing GRS in age-specific screening scenarios in the Our Future Health cohort.

We also find that the association between GRS_{269} and PrCa diagnosis is stronger in White men (OR per SD: 2.11 [2.07 - 2.16]) compared to Black men (OR per SD: 1.43 [1.23 - 1.66]) in the UK Biobank, consistent with previous findings from Judd *et al.* (2025) (EUR OR per SD = 2.04 [2.00-2.09]; AFR OR per SD = 1.35 [1.16-1.58]) (8), with small differences expected due to their use of all-time PrCa case/control status and within-subpopulation z-

transformation of GRS_{269}. In addition to this, we also find that GRS_{451}-AFR, which was developed by meta-analysing a large cohort including 19,391 AFR-like cases and 61,608 AFR-like controls (2), has a suggestively higher association with PrCa diagnosis in Black men (OR per SD: 1.57 [1.35 - 1.82]) than GRS_{269}-Multi and GRS_{269}-AFR (Figure 3). Since the GWAS meta-analysis that produced GRS_{269} included 10,368 AFR-like cases and 10,986 AFR-like controls, this supports the hypothesis that greater representation of Black/AFR-like men in large GWAS meta-analyses of prostate cancer will help to further identify AFR-specific variants and to reduce the disparity in GRS predictive performance. Interestingly, GRS_{451}-AFR produced a similar OR per SD (2.08 [2.03 - 2.13; GRS + Age model]) to GRS_{269}-Multi in White men, suggesting that using per-allele effect sizes derived from a mismatched genetic similarity population makes little difference provided that the included SNPs are largely similar.

At the time of writing, there is no national, population-wide PrCa screening programme in the UK. In an attempt to simulate what an age-based PrCa screening programme incorporating GRS would look like, and to normalise age between White and Black men, we carried forward the best-performing publicly available GRS from the UK Biobank analyses into the Our Future Health cohort and applied these as predictors of prostate cancer diagnosis between ages 40-50, 50-60, and 60-70; or at an arbitrary date in the past (31/12/2013) where we had sufficient follow-up to determine PrCa outcomes. We found that the GRS produced the greatest ROC AUC and OR per SD when used as a predictor of 10-year PrCa status at age 40 (Figure 4), though large confidence intervals for Black men make this result unstable. In all age-specific scenarios, there was no difference in ROC

AUC or OR per SD between White and Black men, suggesting that these GRS could be used equitably if applied in this context.

When using these models to predict absolute 10-year risk of prostate cancer diagnosis, it is unclear where the "high-risk" threshold should be placed for the purpose of prioritising individuals for further screening, testing, or referral, and depends on the relative benefit of identifying a true case of prostate cancer against the harms of unncessary interventions for healthy individuals. Net benefit analysis suggested that, across all screening scenarios, the range of thresholds at which referring individuals according to GRS model predictions is beneficial the same as, or wider, for Black men than for White men (Figure 5). Additionally, the absolute risk threshold that produces optimal sensitivity/specificity was either the same as that for White men or higher across all scenarios for Black men (Supplementary table 8). For example, we find that in our scenario of screening at age 50 that the Youden's J threshold is higher for Black men (7.0%) than for White men (2.0%) to achieve similar sensitivity (0.57 vs 0.53) and specificity (0.74 vs 0.79). These results suggest that absolute risk thresholds for referral would be set higher for Black men to account for their increased background risk of prostate cancer diagnosis, in order to prevent overtesting and/or overdiagnosis.

Limitations

This study has several limitations. Firstly, since OFH is a research programme with recruitment beginning in 2021 and that is ongoing, most of the PrCa cases included in this analysis were prevalent, rather than incident cases. Using a date in the past before the

assessment centre date as the index date confers a survivor bias, since all participants must have survived until the date at which they joined the study. Therefore, these PrCa cases are likely to be less severe than the incident cases identified in the UK Biobank. This carries important implications for screening, since the identification of benign or indolent prostate cancer cases may exacerbate the overdiagnosis issue rather than address it. This is also a limitation of the UKB arm of the study, as the UKB does not yet provide stage, grade, or Gleason score of a tumour in the cancer registry records. As a proxy, we checked for follow-up events relating to chemotherapy, radiotherapy, hormone therapy, prostatectomy, or death, but we lacked sufficient cases of severe PrCa in Black men to meaningfully compare GRS performance in this context. From the evidence available to us, we did find that the association of GRS_{269}-Multi with overall 10-year PrCa (1.43 [1.23 - 1.66; GRS_{269}-Multi + Age model]). and actionable 10-year PrCa (1.49 [1.19 - 1.88; GRS_{269}-Multi + Age model]) were similar in Black men (Supplementary Figure 2).

Furthermore, there are disparities in phenotype definitions between the UKB and OFH arms of this study. This is due to the closure of the UK Biobank in April 2026, meaning that results could not be updated beyond this point. In the UKB analyses, controls who died before the end of the prediction horizon of a non-PrCa cause were not excluded but were excluded in OFH, and control exclusion criteria included several OPCS-4 codes that were later removed from the control exclusion criteria for OFH analyses (Supplementary Table 1). This is unlikely to change results due to the large numbers of controls in both datasets, but this inconsistency merits mentioning.

Conclusions

Integration of currently available PrCa GRS with age in an IRM achieves similar discrimination of PrCa case/control status in both Black and White men within 2, 5, and 10-years of follow up, but the added benefit of GRS is minimal compared to age-only models in Black men. Enrichment of GWAS meta analysis cohorts with additional cases and controls of AFR-like men appears to strengthen case/control discrimination and association of the resulting GRS with PrCa diagnosis. For equitable clinical risk prediction in primary care, age of the patient must be accounted for, and the discrepancy in association strength between GRS and prostate cancer risk between White and Black men should be considered. Further improvements in GRS performance for Black men will likely be mediated through increased representation in genetic research studies.

List of abbreviations

AFR/AFR-like Genetic Similarity to African Reference Populations

AUC Area Under the Curve

BC Breast Cancer

CI Confidence Interval

EAS/EAS-like Genetic Similarity to East Asian Reference Populations

EUR/EUR-like Genetic Similarity to European Reference Populations

FDR False Discovery Rate

FHx Family History

GRS Genetic Risk Score

GRS_{269} Genetic Risk Score based on 269 variants from Conti *et al.* (2021)

GRS_{269}-AFR Genetic Risk Score based on 269 variants from Conti *et al.* (2021) using per-allele effect sizes estimated in African ancestry populations

GRS_{269}-Multi Genetic Risk Score based on 269 variants from Conti *et al.* (2021) using per-allele effect sizes estimated for all ancestry populations

GRS_{451} Genetic Risk Score based on 451 variants from Wang *et al.* (2023)

GRS_{451}-AFR Genetic Risk Score based on 451 variants from Wang *et al.* (2023) using per-allele effect sizes estimated in African ancestry populations

GRS_{451}-Multi Genetic Risk Score based on 451 variants from Wang *et al.* (2023) using per-allele effect sizes estimated for all ancestry populations

GWAS Genome-Wide Association Study

HIS/HIS-like Genetic Similarity to Hispanic Reference Populations

HGDP Human Genome Diversity Project

ICD International Classification of Diseases

IRM Integrated Risk Model

NPV Negative Predictive Value

$\mathbf{p_{adj}}$ p-value adjusted using the Benjamini-Hochberg False Discovery Rate (FDR) method

PPV Positive Predictive Value

PrCa Prostate Cancer

PGS Polygenic Score

OFH Our Future Health

OFH-TRE Our Future Health Trusted Research Environment

OPCS Office of Population Censuses and Surveys Classification of Interventions and Procedures

OR Odds Ratio

ROC Receiver Operating Characteristic

SD Standard Deviation

SNP Single Nucleotide Polymorphism

TE Treatment Equality

UKB UK Biobank

UKB-RAP UK Biobank Research Analysis Platform

1KG 1000 Genomes Project

Declarations

Ethics approval and consent to participate

This research utilised de-identified data held by the UK Biobank and Our Future Health resources, carried out under study IDs 103356 and OFHS260023, respectively. UK Biobank protocols were approved by the National Research Ethics Committee. Ethics approval for the UK Biobank study was obtained from the North West Centre for Research Ethics Committee (11/NW/0382). Ethics approval for the Our Future Health study was obtained from the East of England Cambridge East Research Ethics Committee (21/EE/0016). Written informed consent was obtained from all participants. The study was performed in accordance with the Declaration of Helsinki. The responsibility for the interpretation of the information supplied by UK Biobank and Our Future Health is the authors' alone.

Consent for publication

Not applicable.

Availability of data and materials

This research has been conducted using the UK Biobank and Our Future Health resources under study IDs 103356 and OFHS260023, respectively. Information on how to access these datasets can be found at https://www.ukbiobank.ac.uk/use-our-data/apply-for-access/ and https://ourfuturehealth.org.uk/researchers/.

This work uses data that has been provided by patients and collected by the NHS as part of their care and support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHS England. Access to the data was facilitated by the NHS England Data Access Request Service.

All code used to generate results for this study can be found on the author's GitHub repository: https://github.com/ExeterGenetics/Prostate_Cancer_GRS_analysis. Code searching was carried out using scripts developed in-house, stored in the GitHub repositories ukbextractR (https://github.com/ExeterGenetics/ukbextractR) and ukbrapR (https://github.com/lcpilling/ukbrapR).

Competing interests

The authors declare that they have no competing interests.

Funding

This work was supported by Prostate Cancer UK through an award (Ref: RWE25-ST2-002). The funders had no role in the study conceptualisation, study design, data collection, analysis, interpretation, manuscript preparation, or the decision to submit the manuscript for publication.

Authors' contributions

HG, LJ, TM, SM, and SB generated the initial hypothesis. CW, HG, LJ, TM, SB, and GC designed the study, with CW, HG, LJ, and GC defining phenotypes for prostate cancer case

inclusion and control exclusion. CW carried out data preparation and analysis. All authors reviewed the results and contributed to their interpretation. CW wrote the first draft of the manuscript. LP, HG, and JL wrote scripts for reading healthcare records and calculating participant GRS. All authors commented on the final manuscript. All authors take the responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Corresponding author

Correspondence should be addressed to Harry Green (H.D.Green@exeter.ac.uk).

Acknowledgements

The authors thank Prostate Cancer UK for funding and supporting this research, as well as all staff and research participants who have donated their data to the UK Biobank and Our Future Health research programmes. The authors also thank the Royal Arch Freemasons Devonshire for their generous donations, which supported this work.

References

1. Conti DV, Darst BF, Moss LC, Saunders EJ, Sheng X, Chou A, et al. Trans-ancestry genome-wide association meta-analysis of prostate cancer identifies new susceptibility loci and informs genetic risk prediction. Nat Genet. 2021 Jan;53(1):65–75. doi:10.1038/s41588-020-00748-0 PubMed PMID: 33398198; PubMed Central PMCID: PMC8148035.

2. Wang A, Shen J, Rodriguez AA, Saunders EJ, Chen F, Janivara R, et al. Characterizing prostate cancer risk through multi-ancestry genome-wide discovery of 187 novel risk variants. Nat Genet. 2023 Dec;55(12):2065–74. doi:10.1038/s41588-023-01534-4 PubMed PMID: 37945903; PubMed Central PMCID: PMC10841479.

3. Chen F, Sheng X, Wang A, Xu Y, Hughley R, Xiong W, et al. Integrating Pathogenic Variants, Polygenic Risk Score, and Family History for Prostate Cancer Risk Estimation in Men of African Ancestry. European Urology. 2026 May 1;89(5):416–25. doi:10.1016/j.eururo.2025.09.4161

4. Odole I, Andrews C, Agalliu I, Rohan T, Fernandez PW, Irusen H, et al. Association of Family History and Polygenic Risk Scores With Prostate Cancer in Africa. JCO Glob Oncol. 2026 Mar 1;12(3):e2500431. doi:10.1200/GO-25-00431

5. Kim MS, Naidoo D, Hazra U, Quiver MH, Chen WC, Simonti CN, et al. Testing the generalizability of ancestry-specific polygenic risk scores to predict prostate cancer in sub-Saharan Africa. Genome Biol. 2022 Sep 13;23(1):194. doi:10.1186/s13059-022-02766-z

6. Tanha HM, Law MH, Ingold N, Ly P, Olsen CM, Pandeya N, et al. Polygenic risk scores for prostate cancer: Comparative evaluations in UK and Australian cohorts. HGG Adv. 2025 Jul 7;6(4):100477. doi:10.1016/j.xhgg.2025.100477 PubMed PMID: 40629691; PubMed Central PMCID: PMC12304678.

7. Ben-Shlomo Y, Evans S, Ibrahim F, Patel B, Anson K, Chinegwundoh F, et al. The Risk of Prostate Cancer amongst Black Men in the United Kingdom: The PROCESS Cohort Study. European Urology. 2008 Jan 1;53(1):99–105. doi:10.1016/j.eururo.2007.02.047

8. Judd J, Spence JP, Pritchard JK, Kachuri L, Witte JS. Investigating the role of neighborhood socioeconomic status and germline genetics on prostate cancer risk. HGG Adv. 2025 Aug 8;6(4):100492. doi:10.1016/j.xhgg.2025.100492 PubMed PMID: 40783788; PubMed Central PMCID: PMC12536654.

9. Shah Y, Kulm S, Nauseef JT, Chen Z, Elemento O, Kensler KH, et al. Benchmarking multi-ancestry prostate cancer polygenic risk scores in a real-world cohort. PLoS Comput Biol. 2024 Apr 10;20(4):e1011990. doi:10.1371/journal.pcbi.1011990 PubMed PMID: 38598551; PubMed Central PMCID: PMC11034641.

10. Green HD, Merriel SWD, Oram RA, Ruth KS, Tyrrell J, Jones SE, et al. Applying a genetic risk score for prostate cancer to men with lower urinary tract symptoms in primary care to predict prostate cancer diagnosis: a cohort study in the UK Biobank. Br J Cancer. 2022 Nov;127(8):1534–9. doi:10.1038/s41416-022-01918-z PubMed PMID: 35978138; PubMed Central PMCID: PMC9553867.

11. Dite GS, Spaeth E, Murphy NM, Allman R. Development and validation of a simple prostate cancer risk prediction model based on age, family history, and polygenic risk. The Prostate. 2023;83(10):962–9. doi:https://doi.org/10.1002/pros.24537

12. Nyberg T, Brook MN, Ficorella L, Lee A, Dennis J, Yang X, et al. CanRisk-Prostate: A Comprehensive, Externally Validated Risk Model for the Prediction of Future Prostate Cancer. J Clin Oncol. 2023 Feb 10;41(5):1092–104. doi:10.1200/JCO.22.01453 PubMed PMID: 36493335; PubMed Central PMCID: PMC9928632.

13. Zhu M, Zhu X, Han Y, Ma Z, Ji C, Wang T, et al. Polygenic risk scores for pan-cancer risk prediction in the Chinese population: A population-based cohort study based on the China Kadoorie Biobank. PLoS Med. 2025 Feb 28;22(2):e1004534. doi:10.1371/journal.pmed.1004534 PubMed PMID: 40019942; PubMed Central PMCID: PMC11870365.

14. Liu X, Duan H, Liu S, Zhang Y, Ji Y, Zhang Y, et al. Preliminary effects of risk-adapted PSA screening for prostate cancer after integrating PRS-specific and age-specific variation. Front Genet. 2024 Aug 1;15:1387588. doi:10.3389/fgene.2024.1387588 PubMed PMID: 39149591; PubMed Central PMCID: PMC11324495.

15. Karczewski KJ, Gupta R, Kanai M, Lu W, Tsuo K, Wang Y, et al. Pan-UK Biobank genome-wide association analyses enhance discovery and resolution of ancestry-enriched effects. Nat Genet. 2025 Oct;57(10):2408–17. doi:10.1038/s41588-025-02335-7

16. Benafif S, Ni Raghallaigh H, McGrowder E, Saunders EJ, Brook MN, Saya S, et al. The BARCODE1 Pilot: a feasibility study of using germline single nucleotide polymorphisms to target prostate cancer screening. BJU International. 2022;129(3):325–36. doi:10.1111/bju.15535

17. Thompson DJ, Wells D, Selzam S, Peneva I, Moore R, Sharp K, et al. UK Biobank release and systematic evaluation of optimised polygenic risk scores for 53 diseases and quantitative traits. medRxiv. 2022 Jan 1;2022.06.16.22276246. doi:10.1101/2022.06.16.22276246

18. Benjamini Y, Hochberg Y. Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society: Series B (Methodological). 1995;57(1):289–300. doi:https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

19. Vickers AJ, Calster BV, Steyerberg EW. Net benefit approaches to the evaluation of prediction models, molecular markers, and diagnostic tests [Internet]. 2016 Jan 25. doi:10.1136/bmj.i6

Supplementary Figure Legends

Supplementary Figure 1: ROC AUC and OR of PrCa diagnosis per SD increase in GRS from logistic regression models combining GRS_{269}, Age, and Family History (FHx) to predict incident PrCa diagnosis. Results shown for self-reported ethnicity groups ("White", "Black") and genetic similarity groups ("EUR", "AFR")

Supplementary Figure 2: ROC AUC and OR of Actionable PrCa diagnosis per SD increase in GRS from logistic regression models combining GRS_{269}, Age, and Family History to predict incident PrCa diagnosis. Results shown for self-reported ethnicity groups ("White", "Black") and genetic similarity groups ("EUR", "AFR")

Supplementary Figure 3: Odds Ratio of PrCa diagnosis by Age-only / Age + GRS_{269}-Multi IRM decile; and ethnicity, relative to the median quintile (40-60%). Results are shown for a 10-year prediction horizon following the UK Biobank assessment centre visit. Decile bins were standardised A) within subpopulation groups; and B) within the global population of men in the cohort. Figure generated in R version 4.6.0 (2026-04-24 ucrt) ("Because it was There").

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- multipanelfiguresupplementary1.png
- multipanelfiguresupplementary2.png
- multipanelsupplementaryfigure3.png
- supplementarytables.xlsx