Prostate Cancer
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POD-1
The impact of ethnicity on prostate cancer mortality in Canada

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Introduction: The purported increased risk of early and aggressive prostate cancer has led to the classification of men of African descent as high-risk, with subsequent recommendations of more aggressive screening practices in these men. However, the underlying data for these recommendations lack high-quality evidence, leaving the validity of these conclusions uncertain. Recent data suggest that adjusting for non-biologic differences, including socioeconomic status and access to healthcare, may account for the disparities seen.[1] Data from the Canadian healthcare system is uniquely suited to study the impact of ethnicity on prostate cancer mortality due to its diverse population and universal healthcare model.

Methods: Using Statistics Canada's Canadian Census Health and Environment Cohort, we identified all men diagnosed with prostate cancer from 1992–2010. Cox proportional-hazards models were used to calculate hazard ratios (HR), predicting the association between the survival time of those with prostate cancer and ethnicity, controlling for age, immigration status, education, and province/territory.

Results: A total of 51 530 cases of prostate cancer were identified, with 21 785 total deaths and 7925 deaths caused by prostate cancer (Table 1). On multivariate analysis South Asian (HR 0.53, confidence interval [CI] 0.36–0.76, p=0.0006) and East Asian (HR 0.62, 95% CI 0.49–0.78, p≤0.0001) men had lower risks of prostate cancer-specific mortality compared to non-visible minority men. No increased risk of prostate cancer mortality was seen in black Canadian men (HR 0.83, 95% CI 0.67–1.02, p=0.068) (Table 2).

Conclusions: In our Canadian cohort, black ethnicity does not confer increased risks of prostate cancer mortality, while South- and East-Asian men appear to have protective factors. Our study highlights the need for caution when

POD-1. Table 1. Baseline characteristics of men with prostate cancer who died of any cause or of prostate cancer in the CanCHEC between 1992 and 2010

	Diagnosed with prostate cancer (n=51 530)		Died from any cause (n=21 785)		Died from prostate cancer (n=7925)	
				p<0.0001		p<0.0001
Minority group*						
Non-visible minority	48 680	94.5%	21 045	96.6%	7 675	96.9%
Black	1 080	2.1%	235	1.1%	95	1.2%
South Asian	510	1.0%	125	0.6%	30	0.4%
East Asian	725	1.4%	215	1.0%	70	0.9%
Southeast Asian, Filipino	210	0.4%	55	0.3%	15	0.2%
West Asian, Arabs	325	0.6%	110	0.5%	35	0.4%
Immigrant status						
Not an immigrant	38 725	75.2%	16 695	76.6%	6 130	77.4%
Immigrant status	12 805	24.8%	5 095	23.4%	1 795	22.6%
Age categories						
25–34	755	1.5%	25	0.1%	20	0.3%
35–44	5 545	10.8%	325	1.5%	185	2.3%
45–54	12 635	24.5%	1 740	8.0%	750	9.5%
55–64	16 185	31.4%	6 105	28.0%	2 225	28.1%
65+	16 415	31.9%	13 590	62.4%	4 750	59.9%
Education categories						
No high school	22 440	43.5%	12 235	56.2%	4 420	55.8%
High school	16 835	32.7%	6 210	28.5%	2 270	28.6%
Postsecondary	4 905	9.5%	1 495	6.9%	575	7.3%
University degree	7 350	14.3%	1 845	8.5%	660	8.3%

Percentage of men of each cohort who died of any cause or of prostate cancer is shown. Men must have been 25 years of age or older at time of census to be included. All counts have been weighted and rounded to a base 5, and percentages are based on weighted, rounded counts. *As self-reported on the 1991 long-form census. Categorical grouping required to ensure sample size adheres to Statistics Canada's Research Data Centre confidentiality and reporting guidelines.

POD-1. Table 2. Multivariate analysis of prostate cancer-specific mortality in men diagnosed with prostate cancer between 1992 and 2010 in the 1991 CanCHEC

	HR (95% CI)	p
Minority categories *ref=non-visible minority		
Black	0.83 (0.67–1.02)	0.07
South Asian	0.53 (0.36–0.76)	<0.001
East Asian	0.62 (0.49–0.79)	<0.0001
Southeast Asian, Filipino	0.68 (0.42–1.11)	0.12
West Asian, Arabs	1.03 (0.74–1.43)	0.88
Immigrant status ref=non-immigrant		
Immigrant	0.87 (0.83-0.92)	<0.0001
Age categories ref=25–34		
35–44	1.35 (0.84–2.18)	0.21
45–54	2.45 (1.55–3.88)	0.0001
55–64	6.20 (3.93–9.77)	<0.0001
65+	21.45 (13.61–33.81)	<0.0001
Education ref=no high school		
High school	0.83 (0.79–0.87)	<0.0001
Postsecondary	0.78 (0.71–0.85)	<0.0001
University degree	0.60 (0.55–0.65)	<0.0001

*As self-reported on the 1991 long-form census. Categorical grouping required to ensure sample size adheres to Statistics Canada's Research Data Centre confidentiality and reporting guidelines.

drawing conclusions from observational studies and the potential importance of addressing socioeconomic and cultural barriers to healthcare.

Reference

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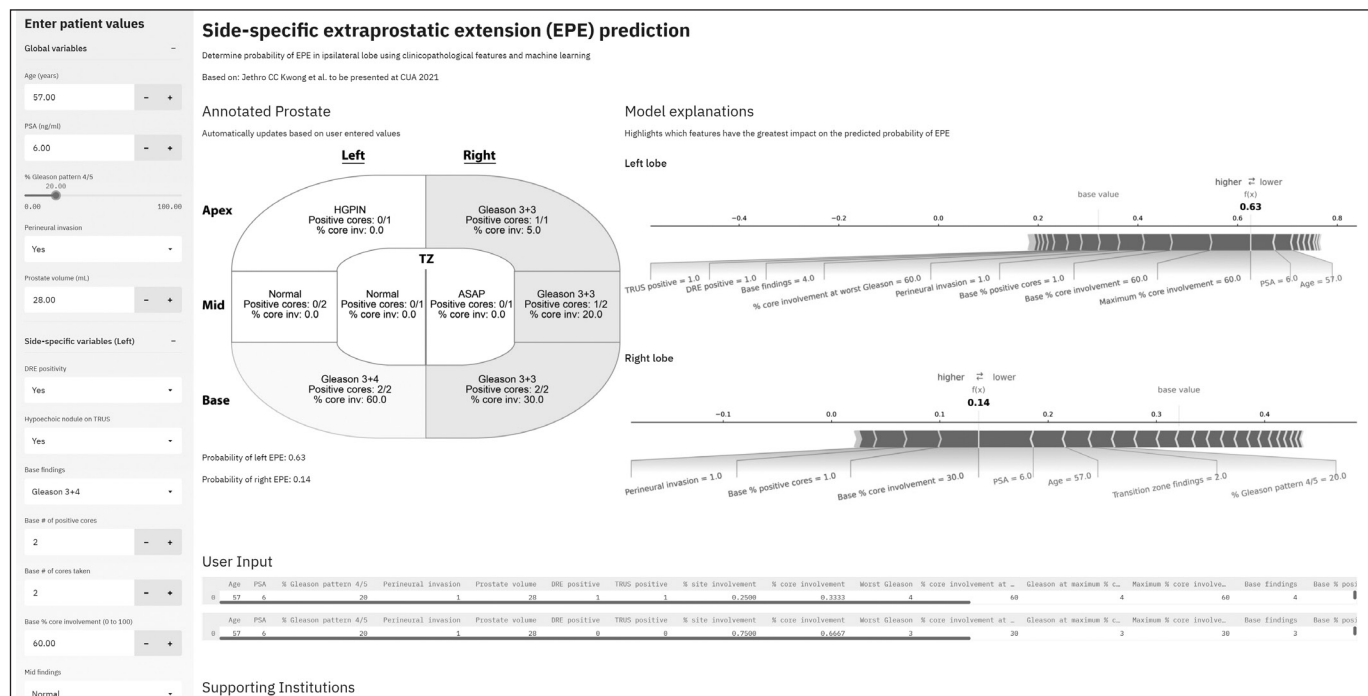
MP-1

End-to-end deployment of an explainable machine learning model to predict risk of side-specific extraprostatic extension in men with prostate cancer

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Introduction: Current machine learning (ML) models are limited by poor interpretability, precluding their routine use in planning nerve-sparing at radical prostatectomy (RP). We aimed to develop an intuitive web application that leverages explainable ML to provide accurate, interpretable, and personalized predictions for side-specific extraprostatic extension (ssEPE).

Methods: A retrospective sample of 900 prostatic lobes (450 patients) from RP specimens at Credit Valley Hospital, Mississauga between 2010 and 2020 was used for model development. Features included patient demographic, clinical, and site-specific data from prostate biopsy. A 10-fold, stratified, cross-validation method was used to train a gradient-boosted model and optimize hyperparameters. External validation was performed using a cohort of 122 lobes (61 patients) from RP specimens at Mississauga Hospital, Mississauga between 2016 and 2020. Discriminative capability was quantified by area under receiver-operating-characteristic (AUROC) and precision-recall curve (AUPRC). Shapley Additive exPlanations were used to interpret the model's predictions.

MP-1. Fig. 1. ssEPE prostate map.

Results: The incidence of ssEPE in the development and validation cohorts were 30.7 and 41.8%, respectively. Our ML model achieved a mean AUROC and AUPRC of 0.80 and 0.69, respectively, in the development set. AUROC was 0.79 in the validation cohort. This model was used to build a web application in which de-identified patient data is used to generate an individualized ssEPE prostate map with annotated explanations to highlight which features had the greatest impact on model predictions (Fig. 1) *(www.ssepe.ml)*.

Conclusions: We have developed a user-friendly application that enables physicians without prior ML experience to assess ssEPE risk and understand the factors driving these predictions to aid surgical planning and patient counselling. Further assessment of the applicability of this model is warranted.

MP-2
Magnetic resonance imaging-ultrasound fusion-targeted prostate biopsies: Finding prostate cancer in patients with previously negative biopsies and elevated PSA

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Introduction: Patients with negative transrectal ultrasound (TRUS) prostate biopsies but continued prostate-specific antigen (PSA) elevation are at risk of harboring clinically significant prostate cancer (csPCa). Such patients commonly receive prostatic magnetic resonance imaging (MRI) to identify index lesions suspicious for csPCa. We report our experience with MRI-ultrasound (US) fusion biopsies in this cohort with previously negative TRUS biopsies.

Methods: In this prospective study from our institution, we included 122 patients displaying a total of 178 index lesions identified on prostatic MRI. All men had clinical suspicion of PCa, a minimum of one prior negative TRUS biopsy, and persistent PSA elevation. Index lesions on multiparametric MRI were reviewed using PI-RADS v2 scoring system. Lesions classified as PIRADS ≥3 received targeted MRI-US fusion biopsy. Biopsy-naive patients and those on active surveillance were excluded. The primary outcome was detection rate of csPCa, defined as ISUP grade group ≥2. Multivariant analysis was used to determine predictors of csPCa on fusion biopsy.

Results: Prior to fusion biopsy, patients had mean PSA 11.53, mean 17.9 negative core biopsies per patient. MRI-US fusion biopsy resulted in diagnosis of PCa in 54/122 (44.3%) patients. Clinically significant PCa was found in 8 (12.5%), 14 (21.2%), 26 (50.0%) of PIRADS 3, 4, and 5 lesions, respectively. The location of csPCa was within the peripheral zone (61.9%), anterior zone (50.0%), and transitional zone (38.1%). Clinical management following newly diagnosed csPCa identified 4.8%, 57.1%, and 38.1% receiving active surveillance, radiation treatment, and radical prostatectomy, respectively. Predictors of csPCa of fusion biopsy included age, PSA, and anterior index lesion location.

Conclusions: MRI-US fusion targeted biopsy yields high detection rates for csPCa in men with previously negative TRUS biopsies and persistent elevated PSA. Missed csPCa is often found within the anterior zone.

MP-2. Table 1. Demographics in patients with persistent PSA elevation and previously negative TRUS prostate biopsy now undergoing MRI-US fusion prostate biopsy

N	122
Median age (years) (range)	65 (44–80)
Mean PSA (ng/ml)	11.53±6.26
Mean PSA density (ng/ml/cc)	0.22±0.16
Mean prostate volume (cm3)	71.3±43.8
Mean interval between MRI and fusion Bx (days)	128±132
Mean number of cores per lesion	2.7±1.1
Mean number of cores per patient prior to fusion Bx	17.9±8.6

MP-2. Table 2. Prostate cancer detection by PI-RADS score and lesion location in patients undergoing MRI-US fusion prostate biopsy

% positive MRI-US fusion Bx	44.3%
% negative MRI-US fusion Bx	55.7%
Overall PCa detection (GG ≥1)	54 (44.3%)
csPCa detection (GG ≥2)	42 (34.4%)
Lesions detected by PI-RADS score	
PI-RADS 3	61
PI-RADS 4	65
PI-RADS 5	52
% csPCa by lesion score	
PI-RADS 3	8 (12.5%)
PI-RADS 4	14 (21.2%)
PI-RADS 5	26 (50.0%)
% csPCa by lesion zone	
Peripheral	26 (61.9%)
Transition	16 (38.1%)
Central	4 (9.5%)
% csPCa by lesion location	
Anterior	21 (50.0%)
Midgland	17 (40.5%)
Posterior	8 (19.0%)

MP-2. Table 3. Clinical outcomes of patients following detection of csPCa on MRI-US fusion biopsy

csPCa detection (GG ≥2)	42/122 (34.4%)
Active surveillance	2/42 (4.8%)
Radiation treatment	24/42 (57.1%)
Radical prostatectomy	16/42 (38.1%)

MP-2. Table 4. Multivariate analysis of factors prognostic for csPCa following MRI-US fusion biopsy in patients with prior negative TRUS biopsy

Feature	Exp(B) (95% CI)	p
Age	1.127 (1.052–1.208)	0.001
PSA	1.087 (1.002–1.178)	0.044
Prostate volume on MRI	0.980 (0.970–0.990)	0.000
mpMRI to fusion (days)	0.995 (0.992–0.999)	0.049
PI-RADs lesions		
3	Reference	0.195
4	0.536 (0.199–1.444)	0.218
5	1.246 (0.447–3.472)	0.674
Index tumor location		
Midgland	1.400 (0.494–3.969)	0.527
Anterior	3.636 (1.093–12.093)	0.035
Posterior	Reference	0.078
Index tumor zone		
Central	0.483 (0.117–1.997)	0.315
Transitional	0.188 (0.071–0.495)	0.001
Peripheral	Reference	0.003

MP-3
Molecular determinants associated with long-term response to apalutamide (APA) in non-metastatic castration-resistant prostate cancer (nmCRPC)

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Introduction: SPARTAN, a phase 3 placebo (PBO)-controlled study in patients (pts) with nmCRPC, showed that APA plus androgen deprivation therapy (ADT) significantly improves metastasis-free survival compared with PBO + ADT. This exploratory analysis investigated potential biological signatures of pts with long-term responses to APA and PBO.

Methods: The biomarker cohort of SPARTAN was characterized as long-term responders (LTR) or early progressors (EP) based on time to metastasis and separated into quartiles for APA and PBO groups. Pts progressing in the first quartile (APA, 21; PBO, 17), with shortest time to metastatic event, were classified as EP, those progressing in the last quartile (APA, 39; PBO, 20) as LTR. Gene expression profiles were generated from 233 archival primary prostate tumors. Predefined gene signatures indicative of cancer biology were compared between LTR and EP groups within the APA and PBO arms using two sample t-tests. Signatures associated with LTR and EP were identified using $p<0.05$.

Results: Median time to metastatic progression was 40.5 months in APA pts and 22 months in PBO pts in the LTR group, and 7.3 and 3.6 months in APA and PBO pts, respectively, in the EP group. Signatures were categorized into three general mechanistic classes, i.e., immune regulation, tumor vascularization, and hormone dependence. LTR on APA was associated with increased T cell activity reflected by T cell activation, stimulation, and antigen presentation, low proliferative capacity ($p=0.0435$), and increased hormonal dependence ($p=0.0485$). High proliferative, hormone-non-responsive tumors were associated with early progression on treatment with PBO.

Conclusions: Although this data requires confirmation in larger studies, the molecular determinants associated with LTR may have utility in selecting pts with nmCRPC who may derive the most benefit from APA and other androgen signaling inhibitors.

MP-4
Quality of care during active surveillance in low-risk prostate cancer patients: A population-based approach

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Introduction: Active surveillance (AS) is now recognized worldwide as the preferred management strategy for most low-risk prostate cancer (PCa) to minimize risks of overtreatment. Despite increasing use of AS worldwide, wide variability of care during followup has been observed, and these variations in quality of care have not been well-described. Furthermore, choosing appropriate quality indicators is a point of ongoing debate. We measured quality of AS care using structure proces-outcome-based quality indicators (QIs) using Canadian administrative databases.

Methods: We developed 20 quality indicators (QIs) to measure quality of AS at the population level. Quality indicators were identified using a literature search from current guidelines on AS, and further refined through a modified Delphi process. Selected AS-specific QIs (n=20) were used to measure quality of AS care among low-risk PCa from 2002–2014 using population-level cancer registry databases. We assessed adherence to clinical guidelines using QIs and compared with healthcare system-related characteristics.

Results: This cohort study included 31 102 low-risk PCa men with a mean (standard deviation [SD]) age at diagnosis of 65.0 (8.8) years who are included in the Ontario Cancer Registry. The mean (interquartile range) prostate-specific antigen (PSA) level at diagnosis was 6.2 (4.7–8.6) ng/mL and the mean positive core was 2.6 (SD 1.9). A total of 25 126 men (79%) were primarily managed by a urologist. Overall use of initial AS was 40.8% in 31 102 eligible men with low-risk disease. Most (82.3%) patients underwent at least eight or more core diagnostic biopsy. Just over half (51.9%) of low-volume patients (defined as ≤3 positive cores and <50% of max. percent core) went on AS and 75.9% had regular followup with urologist as per guidelines. Only 48.1% of patients on AS underwent confirmatory biopsy within 6–12 months from diagnosis, and 82.3% patients had a biopsy prior to receiving definitive therapy. A total of 89.4% of patients who eventually received definitive therapy did so after upgrade in clinical stage or Gleason score. Specific to outcomes indicators, 45.6% of patients discontinued AS within five years from diagnosis, and the 5- and 10-year metastases-free survival rates were 98.5% and 95.4%, respectively. Five- and 10-year PCa-specific survival rates were 99.6% and 98.3%, respectively. Overall survival at 10 years was 90.9%, with median followup of nine years.

Conclusions: This study establishes a foundation on which to build quality of care assessment to monitor the quality of AS patients at population level. In this Canadian, population-based cohort study based on OCR database, although the use of AS increased, considerable quality of AS care variation appeared with QIs related to process of care and outcome of AS care.

MP-5
Type of androgen deprivation therapy and the risk of cardiovascular diseases in patients with prostate cancer with or without pre-existing cardiovascular risk

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Introduction: We sought to evaluate the association between GnRH agonists vs. GnRH antagonist (degarelix) and the risk of cardiovascular disease (CVD) in patients with prostate cancer with or without prior CVD.

Methods: Using administrative databases from the province of Quebec in Canada, we identified patients initiating androgen deprivation therapy (ADT) between January 2012 and June 2016. Two groups of patients were defined based on the type of first ADT prescribed: GnRH agonists and degarelix groups. To be included, patients had to be new users of ADT. The end of followup was the date of the first CVD (myocardial infarction [MI], stroke, ischemic heart disease [IHD], arrythmia, and heart failure [HF]), switch of GnRH group, death or December 13, 2016. The inverse probability of treatment weighting (IPTW) based on propensity score was used to reduce the effect of potential confounding. IPTW-Cox proportional hazard model for competing risk was used to evaluate the association between the exposure to GnRH agonist or antagonist, and the risk of CVD.

Results: This study cohort consists of 10 785 patients: 10 201 initiating GnRH agonists and 584 initiating dgarelix. Mean age was 75 years old, similar between groups. A total of 3304 (32.4%) and 236 (40.4%) men had CVD in the year prior to ADT initiation, in GnRH agonists and antagonist groups, respectively. A decreased risk of MI, stroke, and HF was observed in the degarelix group, yet the hazard ratios (HR) were not significant (HR 0.63; 95% confidence interval [CI] 0.37–1.07; HR 0.76, 95% CI 0.42–1.37; and HR 0.64, 95% CI 0.41–1.00, respectively). An increased risk of arrhythmia was observed (HR 1.46. 95% CI 1.18–1.81) in the degarelix group when compared to the GnRH agonist group.

Conclusions: Degarelix was found to be associated with the risk of developing arrythmia compared to GnRH agonists in patients with prostate cancer regardless of pre-existing cardiovascular risk. Yet, it might be associated with a decreased risk for other CVDs in this population.