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predict prostate

An individualised pre-treatment prognostic model for survival in non-metastatic prostate cancer

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BACKGROUND

- Prognostic stratification is the cornerstone of management in non-metastatic prostate cancer (PCa)
- Existing prognostic models use inadequate surrogates for survival, stratify by broad groups and use heavily treated/screened cohorts.
- To address this unmet need for a modern personalised tool, we developed PREDICT: *Prostate* which contextualizes PCa-specific mortality (PCSM) against other mortality, and estimates treatment-impact on survival.

PATIENTS & METHODS

- The analytic cohort was composed of 10,089 men diagnosed with PCa between 2000 and 2010 in Eastern England from the UK National Cancer Registration and Analysis Service (Table 1).
- Data were randomly split 70:30 into development and validation cohorts
- Separate multivariable Cox models were built for 15-year PCSM and non-prostate cancer mortality(NPCM) with fractional polynomials used to fit continuous variables and baseline hazards.
- Biopsy characteristics were assessed within a sub-cohort
- Model performance was assessed by area under the ROC curve (AUC) and Chi-Square goodness-of-fit[1].
- A Singaporean cohort of 2,546 men represented an additional validation set of different ethnicity and geography. (Table 1)

Table 1: Baseline cohort characteristics amongst the UK and Singapore cohorts

	Eastern England	%	Singapore	%
Total Subjects	10,089	-	2,546	-
Time at risk (years)	82,944	-	12,316	-
Median f/u (years)	9.8	-	5.1	-
PCa Deaths within 10 yrs	1030	-	105	-
Non PCa deaths within 10yrs	2246	-	225	-
Total Deaths within 10yrs	3276	-	330	-
Age (mean)	69.9	-	66.1	-
PSA (mean)	18.4	-	15.7	-
Grade group:				
1	3328	33.0	1126	44.2
2	3017	29.9	723	28.4
3	1486	14.7	326	12.8
4	1032	10.2	170	6.7
5	1226	12.2	201	7.9
Clinical T-stage:				
1	5421	53.7	1625	63.8
2	3213	31.8	660	25.9
3	1378	13.7	244	9.6
4	77	0.8	17	0.7
Primary Treatment:				
Radical Prostatectomy	1419	14.1	1012	39.7
Radiotherapy	3495	34.6	823	32.3
ADT Monotherapy	3178	31.5	164	6.4
Conservative Management	1997	19.8	538	21.1
Missing/HIFU	0	0.0	9	0.4

RESULTS

Table 2: Hazard ratios, p values and coefficients of variables included in the PCSM and NPCM models. (FP = Fractional Polynomial, the function is displayed beneath)

	HR	95%CI	P	Coef.	SE
Prostate Cancer Specific Mortality					
Age FP (age/10)^3 -341.16	1.003	1.002-1.003	0.000	0.003	0.00
PSA FP ln((psa+1)/100)+1.6364	1.204	1.092-1.328	0.000	0.186	0.05
Grade group					
1	1.00	-	-	-	-
2	1.32	1.06-1.65	0.01	0.28	0.11
3	1.73	1.36-2.19	0.00	0.55	0.12
4	2.10	1.63-2.69	0.00	0.74	0.13
5	3.93	3.15-4.89	0.00	1.37	0.11
T stage					
1	1.00	-	-	-	-
2	1.18	1.01-1.37	0.04	0.16	0.08
3	1.49	1.23-1.80	0.00	0.40	0.10
4	1.88	1.14-3.13	0.01	0.63	0.26
Percentage positive cores (PPC)					
<50%	0.54	--	0.00	-0.62	--
≥50%	1.78	--	0.00	0.58	--
Primary Treatment					
AS	1.00	-	-	-	-
Radical	0.50	0.38-0.67	0.00	-0.68	0.14
ADT	2.48	1.92-3.20	0.00	0.91	0.13
Non Prostate Cancer Mortality					
Age FP age-69.87	1.13	1.12-1.14	0.00	0.12	0.00
Comorbidity Score					
1+	1.89	1.67-2.14	0.00	0.64	0.06

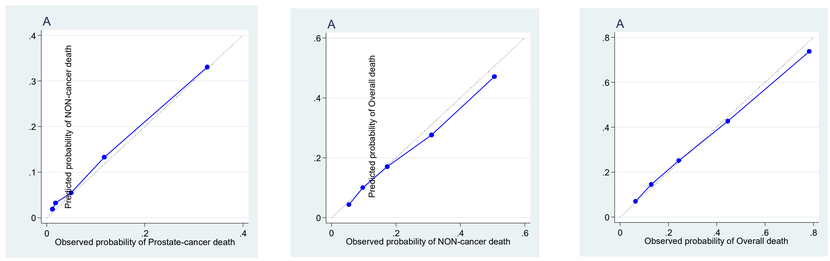

Figure 1: Calibration curves comparing observed and predicted PCa (left), non-prostate cancer (center) and overall deaths (right) at 10 years amongst the validation cohort.

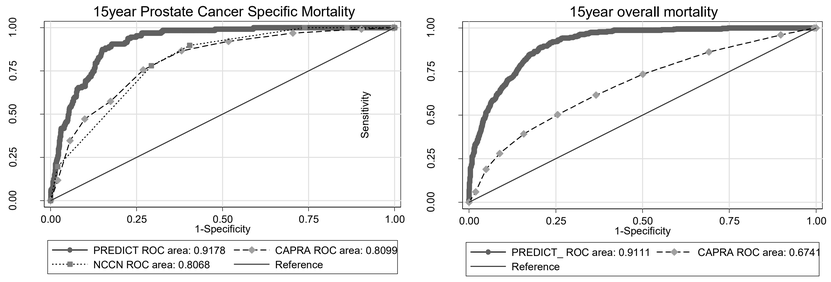

Figure 2: Area under the ROC curves for PCa-specific mortality (left) and overall mortality (right) within the Singaporean validation cohort. Comparisons are made between PREDICT , the UCSF-CAPRA Score[2] and the 2018-updated NCCN risk-stratification score.[3]

- An individualised model for 15-year PCSM was built combining age, PSA, histological grade group, percentage positive cores, stage and primary treatment which were each independent prognostic factors. Age and comorbidity were used to predict non-prostate cancer mortality (NPCM) (Table 2).
- UK validation cohort: calibration (Figure 1) and discrimination was good for both PCSM and overall mortality. AUC 0.83 (95%CI 0.80-0.85) and 0.83 (0.81-0.84) respectively.
- Singapore cohort: Calibration was excellent with <1% differences in actual and predicted deaths and AUC of 0.92 (95%CI 0.90-0.93) and 0.91 (95%CI 0.89-0.92) for PCSM and overall mortality respectively.
- Performance was better than existing pre-treatment prognostic models (Figure 2).
- An example clinical vignette with PREDICT: *Prostate* outputs is shown below.

Figure 3: Example PREDICT: *Prostate* outputs for a 68 year-old man with PSA 13.4ng/ml, Grade group 3 (GL4+3), cT2, 8/16 biopsy cores involved, no comorbidities. The impact of upfront radical treatment is shown through stacked mortality curves (A&B), bar charts (C) and actual numbers (D).

CONCLUSIONS

- PREDICT: *Prostate* is a new individualised prognostic model for use at the point of diagnosis; it has promising accuracy compared to existing tools .
- PREDICT provides accurate information on the potential benefit of treatment on survival as an aid to patient counselling and MDT decision-making.
- A freely available website is undergoing user-testing

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References

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