

Using Customized PRO Profiles to Evaluate Expected Patient Quality of Life Outcomes

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BACKGROUND

- Clinical trials (CTs) routinely collect Patient Reported Outcome (PRO) scores; CT PROs remain underutilized.
- A model-based approach for CT PRO data could characterize expected outcomes given key demographic and clinical characteristics (profiles).
- Estimated expected outcomes would facilitate clinician/patient treatment discussions & increases patient-centricity.

OBJECTIVES

- Demonstrate the value of a multivariate model for estimating expected outcomes within a trial
- Illustrate how model can be used to project to expected outcomes in clinical care

METHODS

- Phase 3 trial of patients with prostate cancer randomized to either Hypofractionated 3D-CRT/MRT (experimental arm) or Conventionally Fractionated 3D-CRT/MRT (comparator arm).¹
- Relevant variables:**
 - PRO: Expanded Prostate cancer Index Composite (EPIC) urinary domain scores.
 - Predictors: baseline EPIC urinary score, treatment arm, age, race, clinical T-stage, and Gleason score.
- Analytic Steps:**
 - 1). Fit a longitudinal regression model (i.e., MMRM) to EPIC scores at 6, 12, 24, and 60-months post-baseline, including relevant clinical and demographic predictors;
 - 2). Identify a patient profile of interest for estimating expected outcomes;
 - 3). Estimate expected outcomes ($\hat{y}$) at 6 months;
 - 4). Compare expected outcomes to observed outcomes for a patient in the trial data who matches the identified profile.

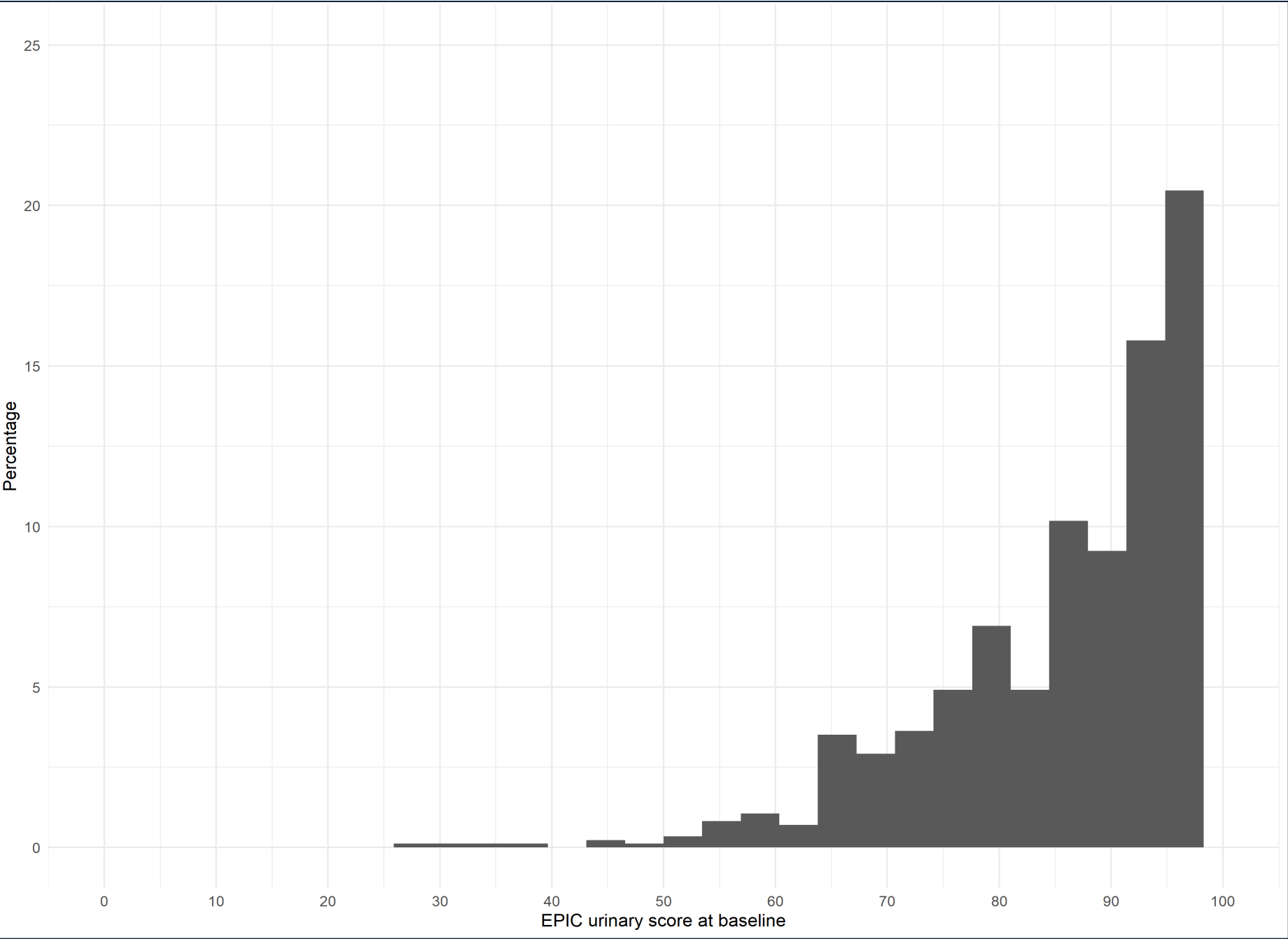
RESULTS: CONFIRMING TREATMENT EFFICACY

- The study included 550 patients in the experimental arm and 542 patients in the comparator arm (mean age: 66.6 years).
- The difference in EPIC urinary scores between treatment arms at 6 and 12 months were computed, with higher scores reflecting greater symptom severity.
- The model estimated a difference of 2.12 points (p=0.009) at 6 months and 2.16 points (p=0.013) at 12 months, favoring the experimental arm (**Table 1**).

Table 1. Comparison of EPIC Urinary Scores at 6 and 12 Months

Time	Experimental	Comparator	95% CI	P-Value
6 months	77.8	79.9	-2.12 (-0.53, -3.70)	p=0.009
12 months	77.2	79.4	-2.16 (-0.44, -3.87)	p=0.013

Figure 1. Histogram of Baseline EPIC Urinary Scores



RESULTS: EXPECTED PROFILE-SPECIFIC PRO OUTCOMES AT FOLLOW-UP

- A patient profile with clinical T-stage, Gleason Score, and baseline EPIC score reflecting higher baseline disease severity (i.e., higher EPIC score) was selected to illustrate the approach. Demographic variables for the profile were also selected.
- Estimated expected outcome for the selected profile for 6-month EPIC scores was 94.2 with 95% confidence interval of (92.94, 95.75).
- In observed trial data, a patient matching the selected profile reported EPIC score at 6 months of 93.8.
- The estimated expected outcome suggests that such a profile can be expected to achieve a one category decrease on two of the 12 domain items (i.e., a decrease in symptom severity).
- Consistent with theory, expected outcome differed from observed score by only 0.53%, demonstrating accuracy expected outcome estimates.

Table 2. Patient Profile: Clinical and Demographic Characteristics

Treatment arm	Conventionally Fractionated 3D-CRT/MRT (comparator arm)
Age	57
Race	White
Clinical T-stage	T2
Gleason Score	6
EPIC Urinary Score at Baseline	97.9
Results	
Expected EPIC urinary score at 6 months (estimate and 95% CI based on Statistical Model)	94.2 (92.94, 95.75)
Observed EPIC urinary score at 6 months (from clinical trial PRO scores)	93.8

CONCLUSIONS

- Precision:** Expected PRO outcomes can be precisely estimated for patients with a given profile using a multivariate model.
 - Estimates projected from trial to real world may exhibit decrements in precision.
- Communication:** Enable clinicians to discuss likely treatment outcomes for patients with a given profile; improves patient-centricity in treatment and fosters transparency.
- Generality:** Illustration based on patient profile with n=1; expected outcomes for subpopulations of interest can be characterized via profiles of n > 1.

ACKNOWLEDGMENT

This manuscript was prepared using data from dataset CDR0000481119 from the NCTN Data Archive of the National Cancer Institute's (NCI's) National Clinical Trials Network (NCTN). Data were originally collected from clinical trial NCT number 00331773: "Radiation Therapy in Treating Patients With Stage II Prostate Cancer." All analyses and conclusions in this manuscript are the sole responsibility of the authors and do not necessarily reflect the opinions or views of the clinical trial investigators, the NCTN, or the NCI.

REFERENCES

- Lee WR, Dignam JJ, Amin MB, et al. Randomized Phase III Noninferiority Study Comparing Two Radiotherapy Fractionation Schedules in Patients With Low-Risk Prostate Cancer. J Clin Oncol. Jul 10 2016;34(20):2325-32. doi:10.1200/jco.2016.67.0448.
- Steyerberg EW. Clinical prediction models. Springer; 2019.
- R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing; 2021.