

Calibration of a Diabetes Microsimulation Model Improves Mortality Prediction in Prostate Cancer Survivors:

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Abstract:

Background: Older men with advanced prostate cancer (PC) have high rates of type 2 diabetes (T2DM) and cardiovascular disease (CVD), compounded by androgen deprivation therapy (ADT). Microsimulation models can predict long-term tradeoffs of T2DM treatments, but available models were developed in populations without cancer. The UKPDS Outcomes model 2 (OM2), the most widely applied T2DM microsimulation model, has been validated in US T2DM populations, but not in PC survivors, whose competing mortality and CV risk differ from general T2DM populations. Accurate risk prediction is critical for T2DM clinical decision making in advanced PC survivors. To improve T2DM mortality prediction in this population, we compared UKPDS OM2 mortality prediction against observed mortality in PC survivors and recalibrated UKPDS OM2 equations.

Methods: Men ≥ 66 years with locally advanced (NCCN high risk, very high risk or regional N1M0) and metastatic PC with DM were identified from 2009-2015 US Surveillance, Epidemiology, and End Results (SEER) data linked to Medicare. OM2 inputs were constructed from claims; missing biometric variables unavailable in claims were imputed from NHANES with predictive means matching. Observed 8-year overall mortality was estimated by Kaplan-Meier and compared with predictions from published OM2 equations. Stage-specific baseline mortality hazards were then scaled iteratively until predicted curves converged with observed, with fit summarized by observed expected (O/E) ratios.

Results: Among 3,460 survivors, median age was 75 years (interquartile range 71-79), and 50% had preexisting CVD; 1,641 (47%) had high-risk localized PC, 1,113 (32%) had very high-risk localized or regional (N1M0) PC, and 706 (20%) had metastatic PC. As initial treatment, 26% underwent prostatectomy, 30% received RT with ADT, 26% ADT alone, and 7% RT alone, and 11% had either missing or no recorded therapy. Observed 8-year mortality was 51% (95% confidence interval [CI] 48%-54%) for high-risk localized, 62% (95% CI 58%-66%) for very high-risk localized or regional PC, and 91% (95% CI 88%-94%) for metastatic PC. Uncalibrated OM2 underestimated 8-year mortality for later stage PC, predicting 53% (95% CI 51%-54%) for very high-risk localized/regional (O/E 1.2) and 59% (95% CI 57%-61%) for metastatic PC (O/E 1.6), but was similar for high-risk localized PC, predicting 50% (95% CI 49%-51%). After calibration, O/E ratios were 1.0 with mean absolute error under 2 percentage points across 8 years of follow-up.

Conclusions: A widely used DM model substantially underestimated mortality in older men with very high-risk localized or regional and metastatic PC, while accurately predicting mortality in high-risk localized PC. Stage-specific calibration improved accuracy, highlighting the need to adapt T2DM models in cancer survivors. This calibrated model will be updated with contemporary data and used to conduct simulated clinical trials to determine custom DM strategies that optimize quantity and quality of life across PC stage and ADT exposure.

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