CISNET Bladder Model Characteristics: Key Similarities and Differences*   **Date: 2025/03/26**

	Kystis	COBRAS	SCOUT
Model characteristics			
Model type	Continuous Time Discrete Event Simulation	Continuous Time Discrete Event Simulation	Discrete Time State-Transition
Population model	Yes	Yes	Yes
Model individuals (microsimulation)	Yes	Yes	Yes
Model of organ	Yes	No	No
Lesion risk			
Mechanism	Non-Homogenous Poisson Point Process	Random-Intercept Zero-Inflated Poisson Model	Non-Homogeneous Markov Model
Demographic risk factors	Age, sex, race, birth-year	Age, sex, race, birth-year	Age, sex, race, birth-year
Modifiable risk factors:			
Smoking	Yes	Yes	Yes
Occupational/environmental toxins	Yes	Yes	No
Genetic risk factors	Lynch Syndrome	No	No
Comorbidities	No	No	CKD, Diabetes Mellitus, Hypertension
Varies randomly across individuals	Yes	Yes	Yes
Multiple lesions possible	Yes	Yes	Yes
Lesion attributes			
Transitional cell carcinoma	Lesions of low invasive potential (Ta, T1, T2+, Tis)	PUNLMP, Ta, T1-4, Tis	Ta, T1-4, Tis
Grade	Low/High (Ta and T1)	Low/High (Ta only)	Low/High (Ta only)
Non-transitional cell carcinoma	Yes	Yes	No
Morphology/configuration	Flat, Sessile, Pedunculated	Not explicitly modeled	No
Size	Cell number and surface area on bladder	Lesion diameter and volume	No
Location within bladder	Mapped to 678 unit areas/tiles on a bladder	No	No
Lesion growth model			
Mechanism	Generalized logistic (Verhulst)	Gompertzian	Not applicable
Size modeled as continuous	Yes	Yes	Not applicable
Vary randomly across individuals	Yes	Yes	Not applicable
Vary randomly across lesions	Yes	Yes	Not applicable
Transitions among lesions			
Initial lesion	Ta-LG, Ta-HG, Tis, T1-HG (for non urothelial neoplasm)	Ta-LG, Ta-HG, Tis	Ta-LG, Ta-HG/Tis
Allowable transitions	For both LG and HG lesions, Ta → T1 → T2/T3 → Metastasis, and similar for Tis	Ta-LG → Ta-HG → T1 → T2 → T3 → Metastasis	Ta-LG → Ta-HG/Tis → T1 → T2 → T3 → non-Metastasis T4 → Metastasis
Mechanism	Stochastic function of lesion size	Stochastic function of lesion size	Age-dependent Stochastic matrix

Vary systematically by	Lesion stage and grade	Lesion stage and grade	Lesion stage and grade
Vary randomly across individuals	Yes	Yes	Yes
Vary randomly across same-size lesions within individuals	Yes	Yes	Yes
Nodal metastases explicitly modeled	No	Yes	No
Metastasis process explicitly modeled	Yes	Yes	Yes
Mortality			
Cancer deaths	Can occur if MIBC (T2/T3) or metastasis (T4) occur	Can only occur if metastasis occurs	Can only occur if metastasis occurs
Other deaths	Same as general population	Same as general population	Risk of all-cause and cardiovascular deaths stratified by CKD stages
Transitions to Clinical Disease			
Mechanism	Stochastic function of lesion size	Time-to-event distribution	Age-dependent Stochastic matrix
Symptoms modeled explicitly	Microscopic or macroscopic hematuria, voiding symptoms	No (only diagnosis modeled)	Microscopic or macroscopic hematuria (detectable state)
Vary systematically by	Sex, race, lesion T-stage	Sex, race, lesion T-stage	Sex, race, lesion T-stage, lesion grade
Vary randomly across individuals	Yes	Yes	Yes
Vary randomly across same-size lesions within individuals	Yes	Yes	Yes
Post-Tx Recurrence & Progression			
Recurrence mechanisms:			
Incomplete TUR/regrowth	Yes	No	No
New lesions	Yes	Yes	Yes
Missed lesions	Yes	Yes	Yes
Vary systematically by	Lesion histology, grade, T-stage, lesion size, treatment	Lesion histology, grade, T-stage, lesion size, concomitant Tis, treatment	Lesion grade, T-stage, treatment
Progression mechanisms:			
Transitions among preclinical new and missed lesions	Yes	Yes	Yes
Transitions among regrown lesions	Yes	No	No
Understaged lesions	Yes	Yes	Yes
Vary systematically by	Lesion histology, grade, T-stage, lesion size, treatment	Lesion histology, grade, T-stage, lesion size, concomitant CIS, treatment	Lesion grade, T-stage, treatment
Development			
Software	R	R	Python
Uncertainty	Stochastic	Stochastic	Stochastic
Calibration	Bayesian	Bayesian	Bayesian

* CKD: Chronic Kidney Disease; COBRAS: The Cancer of the Bladder in R Analytic Simulator; HG: High Grade; Kystis: Greek word for "bladder"; LG: Low Grade; MIBC: Muscle-Invasive Bladder Cancer; PUNLMP: Papillary Urothelial Neoplasm of Low Malignant Potential; SCOUT: Simulation of Cancers of the Urinary Tract Model; T1-T4: Tumor stages indicating invasion into lamina propria (T1), muscle (T2), perivesical tissue (T3), and nearby organs (T4); Ta: Non-invasive papillary carcinoma; Tis: Carcinoma in situ; TUR: Transurethral Resection.