Supplementary Information

Cost-effectiveness and carbon footprint of cystoscopic surveillance schedules in non-muscle-invasive bladder cancer

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Contents. Supplementary Methods S1–S3; Supplementary Tables S1–S3; Supplementary Figs. S1–S6; CHEERS 2022 checklist and carbon-accounting reporting note. Bracketed reference numbers refer to the main-text reference list. Section numbers refer to the main manuscript (1 Introduction, 2 Results, 3 Discussion, 4 Methods).

Supplementary Methods

S1. Model structure and transitions

We used a configuration-driven state-transition (Markov) cohort model with monthly cycles over a 15-year horizon (180 cycles) and a half-cycle correction (Supplementary Fig. S1). The seven modelled states were: no evidence of disease under surveillance; occult (undetected) recurrence; detected-and-treated recurrence; muscle-invasive progression (MIBC); post-radical-cystectomy; and two absorbing death states (bladder-cancer death and other-cause death).

Recurrence moves a patient from the surveillance state into the occult state and is removed only by detection, either at a scheduled cystoscopy (per-examination sensitivity applied to the occult compartment) or by interval symptomatic presentation. Time spent in the occult state defines detection delay. Occult disease progresses to MIBC at an elevated untreated hazard, and treated disease at a lower hazard. On entry to MIBC a fixed one-time proportion undergo radical cystectomy; the remainder receive non-cystectomy management. Competing transitions were combined by a standard competing-risk formulation. Annual rates were converted to monthly transition probabilities by $p = 1 - \exp(-r\,\Delta t)$, and cumulative 5-year probabilities to monthly hazards by $r = -\ln(1-p)/60$.

S2. Population, comparators and outcomes

The target population was adults with newly diagnosed non-muscle-invasive bladder cancer (NMIBC; Ta, T1 or carcinoma in situ) entering surveillance after initial transurethral resection of bladder tumour (TURBT), at a representative entry age of 70 years, stratified into European Association of Urology (EAU) low, intermediate and high-risk groups with cohort weights 0.35, 0.40 and 0.25.

The reference comparator was the EAU risk-stratified guideline schedule: low risk, cystoscopy at 3 and 12 months then annually to 5 years; intermediate risk, 3 months then 6-monthly to 2 years, annually to 5 years and 2-yearly thereafter; high risk, 3-monthly for 2 years, 6-monthly to 5 years, then annually. Conventional alternatives were fixed 3-, 6- and 12-monthly cystoscopy and an adaptive schedule lengthening intervals after consecutive negative examinations. Sub-guideline de-escalated schedules (high-risk surveillance unchanged) were, for low risk: a single 3-month cystoscopy then discharge; a minimal two-examination schedule; and a sparse three-examination schedule; and, for intermediate risk, an extended-interval schedule (cystoscopy at 3, 12, 24, 48, 72, 96 and 120 months).

Primary outcomes were discounted cost (United States Medicare 2021, payer perspective), quality-adjusted life-years (QALYs) and carbon footprint (kg CO_2e). Secondary outcomes were cysto-

scopies, TURBTs and cystectomies per patient, mean detection delay, cumulative progression and bladder-cancer death. Costs and QALYs were discounted at 3% per year; carbon was undiscounted, with a 3% discounted-carbon scenario. Decision metrics were the incremental cost-effectiveness ratio, net monetary benefit at willingness-to-pay thresholds of US$20,000, US$50,000 and US$100,000 per QALY, and a carbon-inclusive societal cost at a social cost of carbon of US$100 per tonne CO_2e. Reporting emissions alongside costs and monetising them within a societal cost correspond, respectively, to the parallel and integrated approaches described by Williams et al. [11].

S3. Parameters, uncertainty and reproducibility

All parameters carry a complete provenance block (citation, resolvable identifier, exact locus, verbatim quote, population-match flag, unit and rate conversion, and confidence rating) and were clinician-verified before the reported analysis; key values and sources are in Supplementary Table S2.

The probabilistic sensitivity analysis (5,000 iterations, fixed seed) sampled each uncertain input from a provenance-derived distribution (beta for probabilities and utilities, gamma for costs, log-normal for carbon factors), with dispersion taken from each parameter's reported confidence interval or standard-deviation band; a documented 20% coefficient of variation was used for the few single-point unit costs and for the single-point cystectomy carbon factor. Risk-stratified hazards were sampled independently per risk group. On each iteration the complete parameter set was drawn and the five conventional schedules were re-run on that single sampled set, yielding cost-effectiveness acceptability curves and 95% credible intervals for per-strategy and incremental outcomes (Supplementary Table S1); the sub-guideline de-escalation schedules were evaluated deterministically only.

Reporting follows the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 statement [29]. The complete model, parameter provenance record and analysis code are provided as a reproducibility archive, reproduce every table and figure from a single command with a fixed random seed, and are also available from the corresponding author on request. No patient-level data were analysed.

Supplementary Tables

Supplementary Table S1. Per-strategy 15-year outcomes with 95% credible intervals from the 5,000-iteration parameter-level probabilistic sensitivity analysis of the 5 conventional schedules. Credible intervals are 2.5th to 97.5th percentiles of the forward-propagated parameter uncertainty, not sampling standard errors. Note the contrast between the wide, heavily overlapping quality-adjusted life-year (QALY) intervals and the cost and carbon intervals, which separate between the guideline and the most intensive schedule.

Schedule	Cost, US$ (95% CrI)	QALYs (95% CrI)	kg CO_2e (95% CrI)
EAU guideline	22,547 (15,085 to 34,392)	8.512 (5.484 to 10.151)	275 (213 to 344)
12-monthly	23,432 (15,848 to 35,330)	8.510 (5.436 to 10.161)	343 (265 to 429)
Adaptive	28,656 (20,162 to 41,179)	8.504 (5.371 to 10.172)	393 (310 to 486)
6-monthly	33,208 (23,699 to 46,532)	8.495 (5.311 to 10.180)	435 (347 to 540)
3-monthly	51,227 (37,005 to 68,923)	8.458 (5.144 to 10.199)	509 (407 to 647)

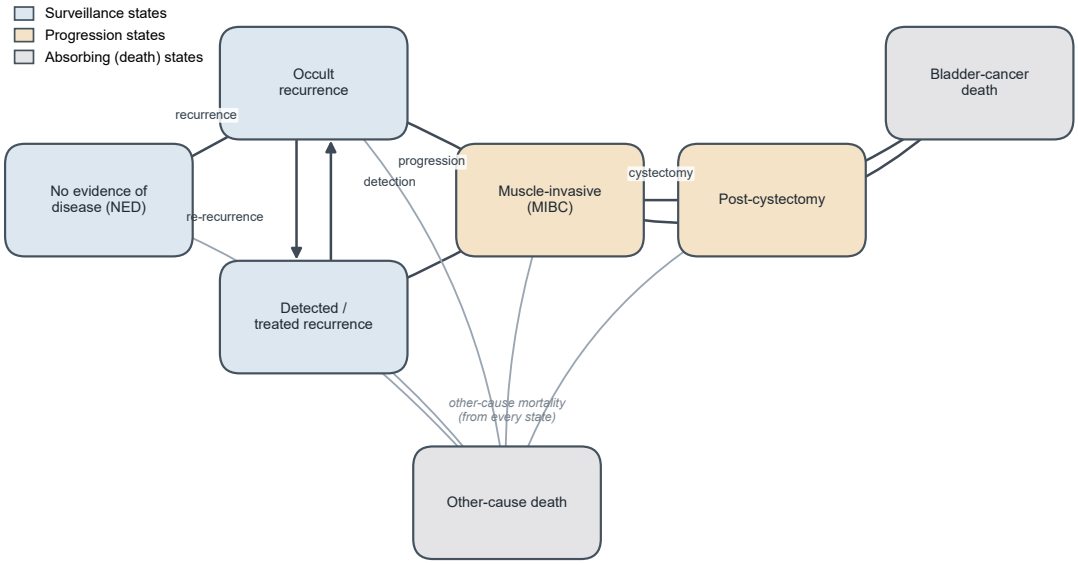
Supplementary Table S3. Carbon composition by schedule under the top-down (76 kg CO_2e per intravesical-instillation visit) and bottom-up (approximately 6 kg CO_2e) instillation carbon factors. The treatment cascade retains the large majority of surveillance emissions under both factors, so the conclusion that emissions reside in the cascade rather than in the cystoscope is not an artefact of the top-down proxy.

Instillation factor	Schedule	Total	Cascade	Scope	Cystectomy	Cascade share
			kg CO_2e			
Top-down (76 kg)	EAU guideline	277	269	6.2	2.1	97%
Top-down (76 kg)	12-monthly	346	337	6.5	2.1	98%
Top-down (76 kg)	Adaptive	398	386	9.9	2.0	97%
Top-down (76 kg)	6-monthly	441	425	13.2	2.0	97%
Top-down (76 kg)	3-monthly	515	487	26.5	1.9	94%
Bottom-up (∼6 kg)	EAU guideline	187	178	6.2	2.1	96%
Bottom-up (∼6 kg)	12-monthly	232	224	6.5	2.1	96%
Bottom-up (∼6 kg)	Adaptive	268	256	9.9	2.0	96%
Bottom-up (∼6 kg)	6-monthly	297	282	13.2	2.0	95%
Bottom-up (∼6 kg)	3-monthly	351	323	26.5	1.9	92%

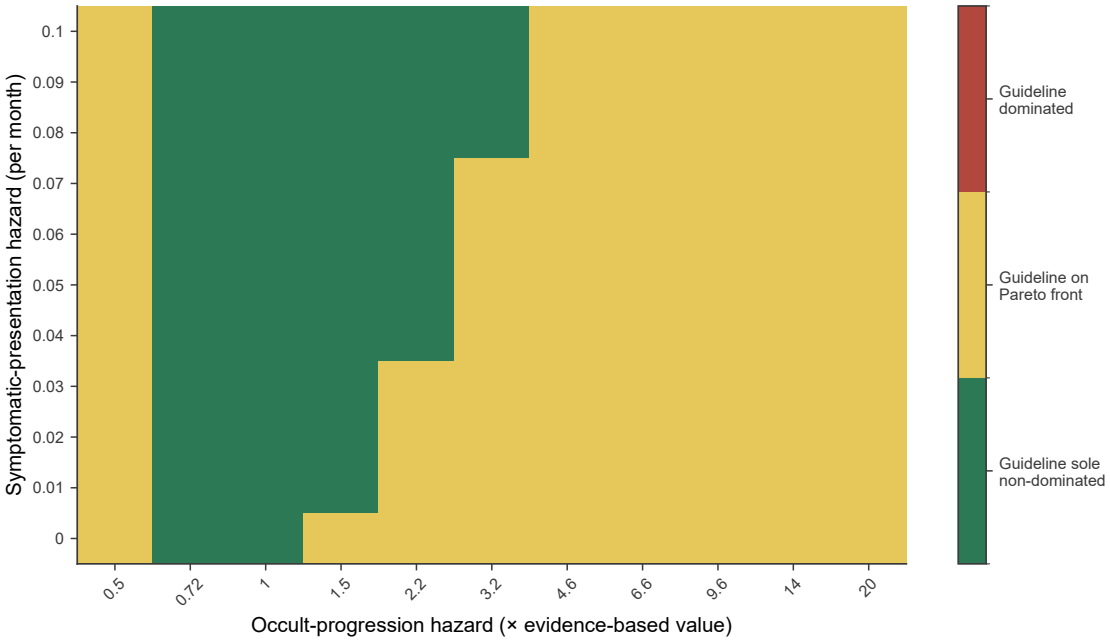
Supplementary Table S2. Key model parameters, base-case values and sources. Bracketed numbers refer to the main-text reference list. Full provenance for every parameter, including exact locus, verbatim source quote, unit conversion and confidence rating, is in the reproducibility archive (`PARAMETERS_PROVENANCE.md`).

Parameter	Base value	Source
5-year recurrence (low / intermediate / high)	31% / 62% / 68%	EORTC [16]; CUETO [17]
5-year occult-to-MIBC progression, untreated (low / int. / high)	0.93% / 4.9% / 9.6%	EAU risk groups [2]
5-year progression, adequately BCG-treated (int. / high)	3.3% / 5.3%	Lobo 2022 [18]
Cystoscopy sensitivity, per examination (white light)	0.71	Russo 2021 [19]
Interval symptomatic-presentation hazard	0.03 per month	Structural, anchored to Fujita 2021 [15]
Radical cystectomy on MIBC entry (one-time)	18.9%	Williams 2017 [20]
MIBC mortality	0.033 per month	Martini 2019 [21]
Post-cystectomy mortality	0.0028 per month	Abdollah 2011 [22]
Other-cause mortality (age 70)	0.0018 per month	US life tables 2021 [23]
Utilities: surveillance / recurrent / MIBC	0.85 / 0.80 / 0.78	Smith 2022 [24]
Utility: post-cystectomy	0.57	Cooper 2023 [25]
Disutility per cystoscopy	0.002 QALY	Heijnsdijk 2018 [10]
Cost: cystoscopy / TURBT / intravesical course / cystectomy	US$835 / 3,383 / 1,440 / 15,324	Creswell 2023 [26]
Cost: ongoing MIBC care	US$10,817 per month	Squires 2025 [27]
Carbon: cystoscopy, reusable / single-use	0.53 / 2.40 kg CO_2e	Abdulrasheed 2024 [5]
Carbon: TURBT pathway	131.8 kg CO_2e	John 2025 [8]
Carbon: radical cystectomy	208 kg CO_2e	Rutten 2025 [9]
Carbon: intravesical-instillation visit (top-down proxy)	76 kg CO_2e	Tennison 2021 [4]
Social cost of carbon (base / range tested)	US$100 (US$0–340) per tonne CO_2e	US EPA 2023 [28]

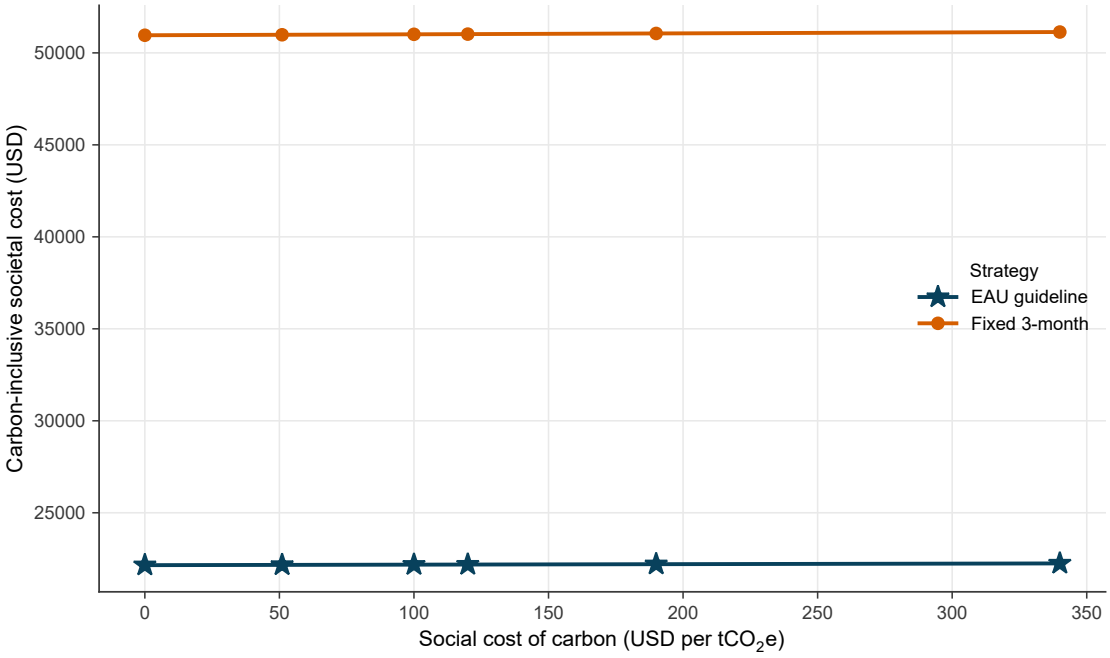
Supplementary Figures



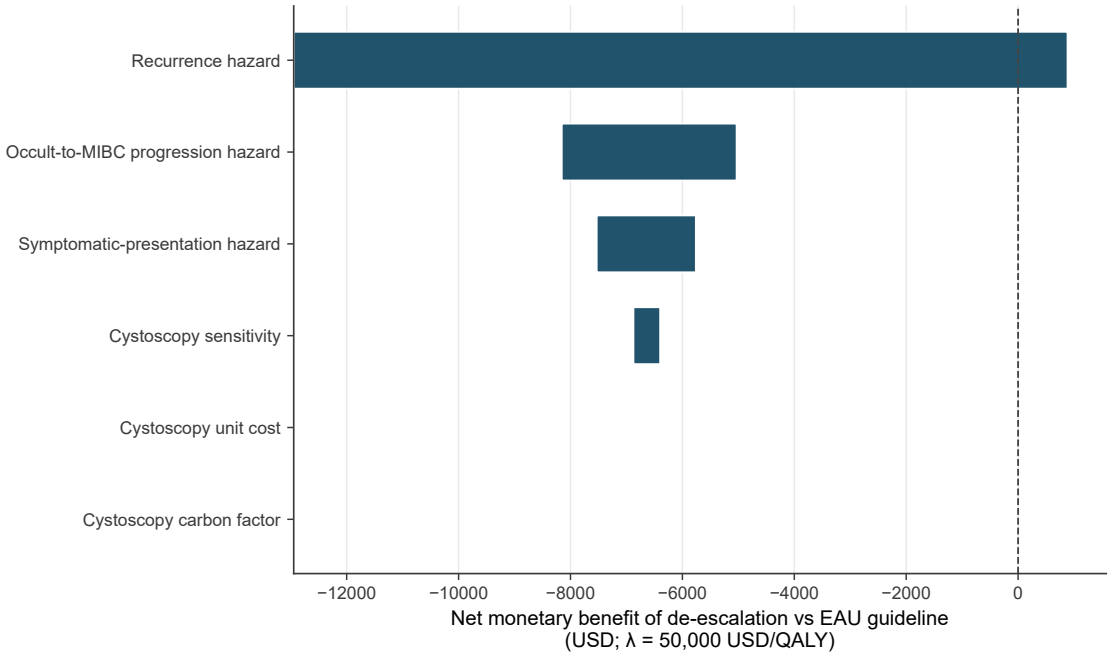
Supplementary Fig. S1. State-transition structure of the model. Surveillance states (no evidence of disease, occult recurrence, detected and treated recurrence) feed progression to muscle-invasive disease and post-cystectomy; all states may transition to other-cause death.



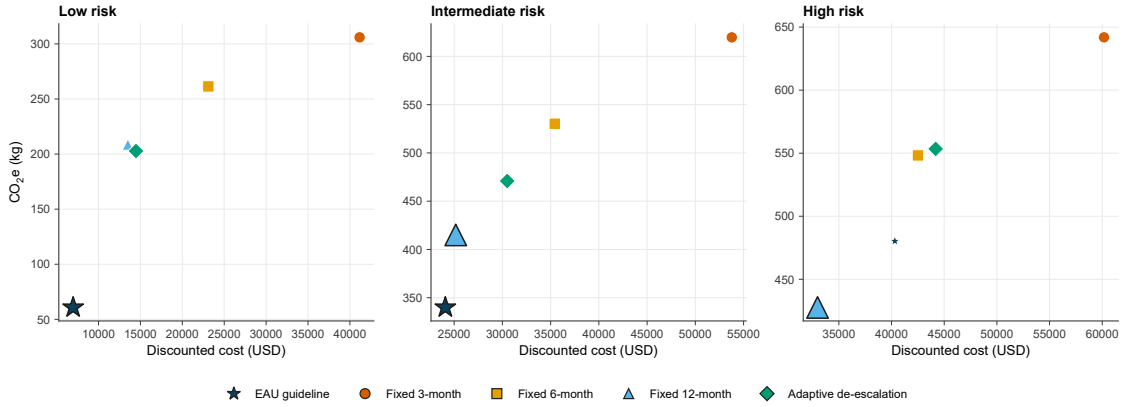
Supplementary Fig. S2. Threshold map of the guideline schedule's frontier status across the occult-progression hazard (as a multiple of its evidence-based value) and the interval symptomatic-presentation hazard. The region in which the guideline is the sole non-dominated strategy is bounded by rising occult progression (approximately 2.19 times base) and widens as the symptomatic-presentation hazard rises; at the base occult-progression hazard the guideline remains sole non-dominated at every symptomatic hazard tested, including its complete absence.



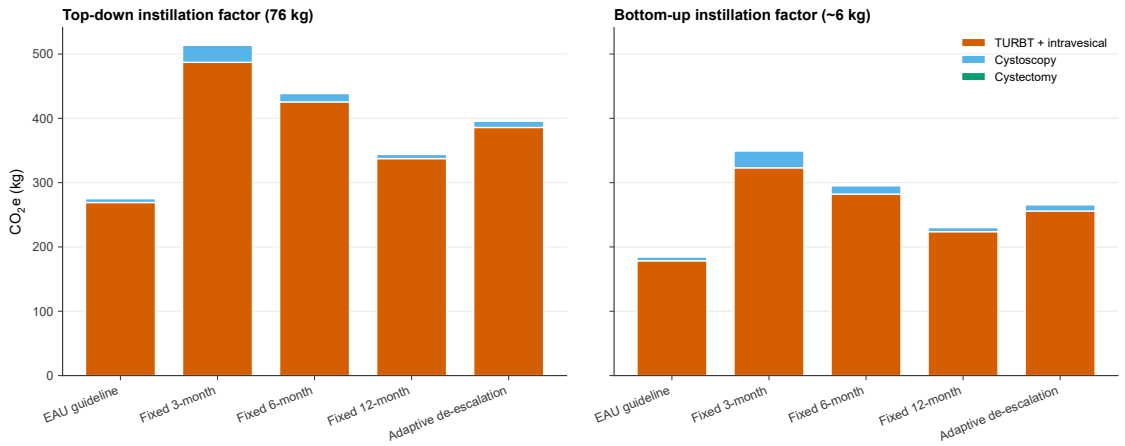
Supplementary Fig. S3. Carbon-inclusive societal cost versus the social cost of carbon. The guideline schedule remains the minimum-societal-cost strategy across the full US$0–340 per tonne CO_2e range tested.



Supplementary Fig. S4. One-way (deterministic) sensitivity analysis of the net monetary benefit of the adaptive de-escalation schedule versus the guideline. Bars span each varied parameter's evidence-based low-to-high range.



Supplementary Fig. S5. Per-risk-group cost and carbon results. Cohort-weighted per-group results reconcile exactly to the pooled base case.



Supplementary Fig. S6. Carbon composition under the top-down (76 kg CO_2e) versus bottom-up (approximately 6 kg CO_2e) instillation-visit factor. The treatment cascade dominates surveillance carbon under both factors.

Supplementary Note: CHEERS 2022 checklist

Consolidated Health Economic Evaluation Reporting Standards 2022 [29]. Section numbers refer to the main manuscript, which follows the journal's Introduction / Results / Discussion / Methods order.

#	CHEERS 2022 item	Where addressed	Status
1	Title identifies the study as an economic evaluation	Title names cost-effectiveness and carbon footprint and the surveillance schedules compared; the keywords and Section 4 identify the design as a decision-analytic model	Addressed
2	Structured abstract	Abstract. The journal requires an unstructured abstract, so the background, methods, cost, QALY and carbon results are given in continuous prose rather than under subheadings	Partly, by journal requirement
3	Background and objectives	Section 1	Addressed
4	Health economic analysis plan	Sections 4.3 and 4.5–4.8: pre-specified comparators, outcomes, decision metrics, scenarios and release gate	Addressed
5	Study population	Section 4.2	Addressed
6	Setting and location	Section 4.2: United States, Medicare 2021	Addressed
7	Comparators	Section 4.3	Addressed
8	Perspective	Section 4.4: health-care payer plus environmental perspective, with optional carbon monetisation	Addressed
9	Time horizon	Section 4.4: 15 years, 180 monthly cycles, with the truncation and its consequences stated	Addressed
10	Discount rate	Section 4.4: 3% per year for costs and QALYs; carbon undiscounted with a 3% variant	Addressed
11	Selection of outcomes	Section 4.5	Addressed
12	Measurement of outcomes	Sections 4.1 and 4.5: model-derived state occupancy	Addressed
13	Valuation of outcomes	Section 4.8 and Supplementary Table S2: utility sources and per-examination disutility	Addressed
14	Measurement and valuation of resources and costs	Section 4.8 and Supplementary Table S2	Addressed
15	Currency, price date, conversion	Section 4.2: US$ 2021 (Medicare)	Addressed
16	Rationale and description of model	Section 4.1 and Supplementary Fig. S1	Addressed
17	Analytics and assumptions	Sections 4.1 and 4.8, and the limitations paragraphs of Section 3	Addressed
18	Characterising heterogeneity	Section 4.2 (risk stratification) and Section 2.5 (per-risk-group analysis)	Addressed
19	Characterising distributional effects	Section 3: distributional and equity effects were not modelled	Addressed as not modelled
20	Characterising uncertainty	Section 4.7; Sections 2.4–2.5	Addressed
21	Engagement with patients and others affected by the study	Section 3: no patient or public involvement informed the analysis	Addressed as not performed

#	CHEERS 2022 item	Where addressed	Status
22	Study parameters	Section 4.8, Supplementary Table S2 and the provenance record in the reproducibility archive	Addressed
23	Summary of main results	Sections 2.1–2.5, Tables 1–3, Figs. 1–4	Addressed
24	Effect of uncertainty	Sections 2.4–2.5: credible intervals, acceptability curves, threshold and scenario analyses	Addressed
25	Effect of engagement with patients and others	Section 3: no engagement was conducted, so no engagement effect was assessed	Addressed as not applicable
26	Findings, limitations, generalisability, current knowledge	Section 3	Addressed
27	Source of funding	Additional information: no external funding	Addressed
28	Conflicts of interest	Additional information: none declared	Addressed

Supplementary Note: carbon-accounting reporting

- **System boundary and method.** Bottom-up process life-cycle factors for cystoscopy, TURBT and radical cystectomy; a top-down national-average outpatient-attendance proxy for the intravesical-instillation visit, disclosed as a data limitation and tested with a bottom-up replacement (Supplementary Table S3, Supplementary Fig. S6).
- **Functional unit.** kg CO_2e per patient over the 15-year surveillance pathway. Per-procedure factors are in Supplementary Table S2. No emission factor was available for ongoing muscle-invasive care, which is therefore outside the inventory boundary.
- **Reusable versus single-use cystoscopes.** Retained as an explicit scenario (approximately 11% increase in surveillance carbon), reported in Section 2.2.
- **Carbon valuation.** Social cost of carbon US$100 per tonne CO_2e in the base carbon-inclusive decision metric, with the official US EPA range (US$0–340 per tonne CO_2e) tested in sensitivity analysis. This is the integrated approach of Williams et al. [11]; emissions are additionally reported in parallel with costs throughout.