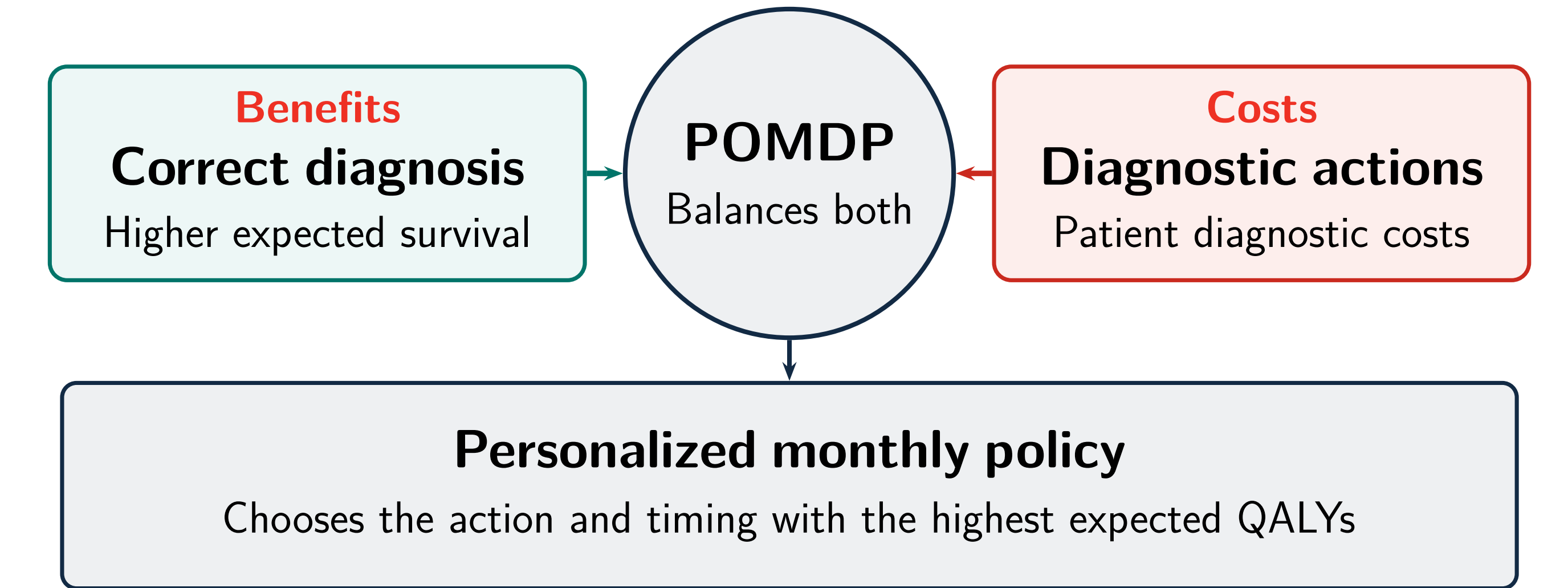


Introduction

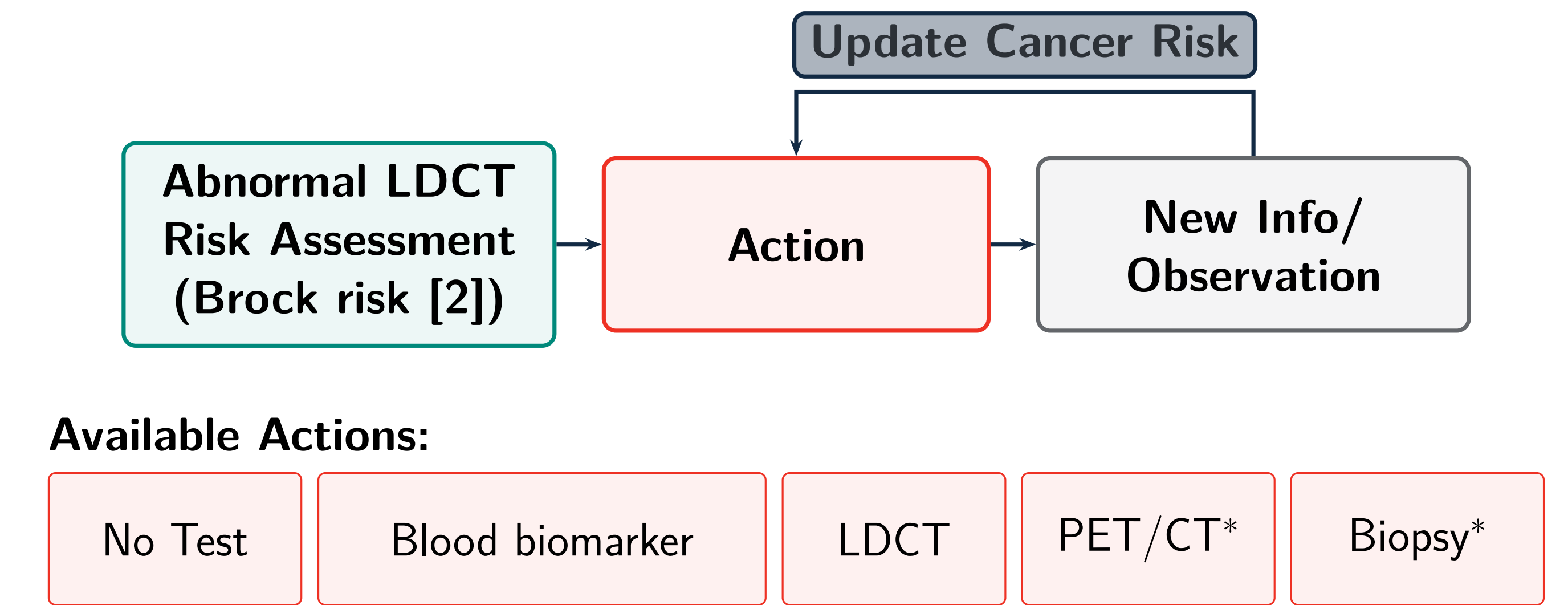
- Lung-RADS manage indeterminate pulmonary nodules (IPNs) based on nodule size and form recommending follow-up exams in **3 or 6** months [1].
- Brock risk score estimates initial risk from patient and nodule features,[2] but it is not utilized in practice.
- Fixed schedules may delay diagnosis or prompt unnecessary testing.

Objective

Develop a **personalized diagnostic strategy** for IPN using methods from Operations Research (partially observable Markov decision process, POMDP) and compare it against **Lung-RADS**.



Methods



*PET/CT and biopsy offer definitive diagnosis. If no cancer is detected, the person returns to regular screening.

Possible Observations from actions:

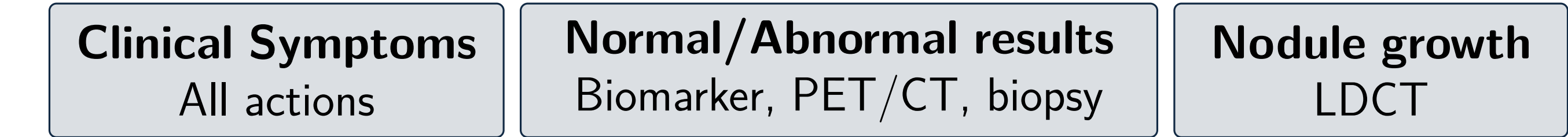


Figure 1. The 24-month risk-based follow-up protocol

Diagnostic Test Performance & Cost

Action	Sensitivity (Sens, %) by stage						Spec (%)	Cost
	IA	IB	II	IIIA	IIIB	IV		
No test	—	—	—	—	—	—	—	0
Biomarker	8.8	8.8	18.4	57.7	57.7	75.8	93.1	4 hrs
LDCT	8.8–56.6	10.3–64.1	11.2–64.5	41.6–75.9	68.3–87.1	95.7–99.4	97.0	5 hrs
PET/CT			89.0				78.0	12 hrs
Biopsy			90.0				100	24 hrs

Se, sensitivity; Spec, specificity; values are percentages. LDCT ranges span small-cell, squamous, adenocarcinoma, and other histologies at each stage. Diagnostic-performance sources: biomarker [3], LDCT [4], PET/CT [5], and biopsy [6].

Methods (cont.)

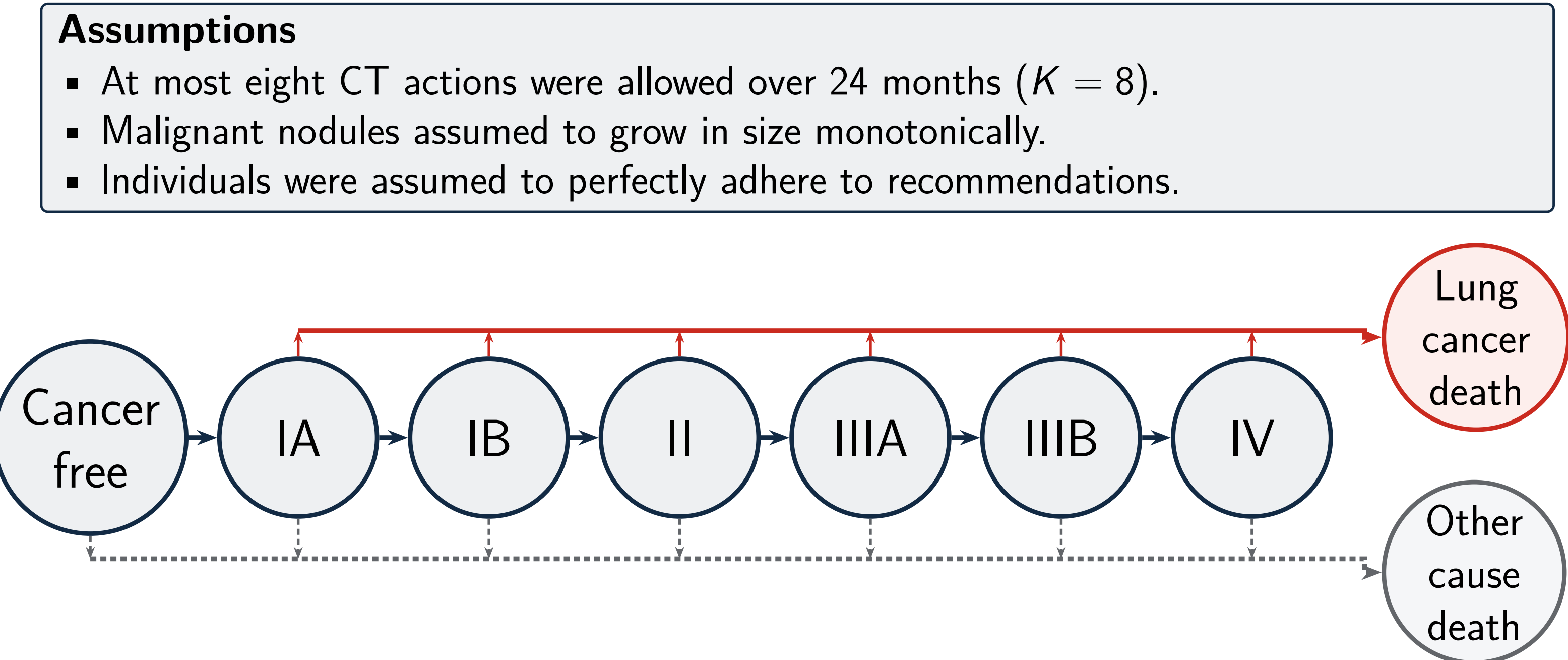


Figure 2. The CHRONOS-Lung Natural History Model offers sex-, histology-, and nodule attenuation-specific disease progression, with explicit modeling of nodule size.

Evaluation of strategies

- POMDP vs. Lung-RADS: 6 individuals (3 benign, 3 cancer) from the PanCan study.
- Each individual’s trajectory was simulated ×10,000 and managed under each strategy.
- Recorded cancer outcome defined truth, but was withheld from both policies.

Results

Table 1. Individual and nodule profiles at the time of abnormal screen

Case ID	Age/sex; BMI	Smoking; pack-yr	FHx/ Emph/COPD	Max diameter (mm); Attenuation; UL/Sp	No. of nodules	Brock Score
Benign						
Case 1	61/M; 29	Cur; 21	N/Y/N	3; solid; N/N	9	0.026%
Case 2	73/F; 26	Fmr; 15	N/Y/N	4; non-solid; Y/N	10	0.391%
Case 3	64/M; 20	Cur; 45	Y/Y/N	5; part-solid; N/N	5	0.706%
Cancer						
Case 4	68/F; 22	Cur; 60	Y/Y/N	5; non-solid; Y/N	2	2.124%
Case 5	64/F; 27	Fmr; 51	N/Y/Y	6; non-solid; Y/N	2	2.718%
Case 6	66/M; 27	Cur; 68	N/Y/Y	6; solid; Y/N	4	1.539%

BMI, body mass index (kg/m²); Cur/Fmr, currently/formerly smoking; FHx, family history of lung cancer; Emph, emphysema; UL, upper-lobe location; Sp, spiculation. Y/N indicates present/absent.

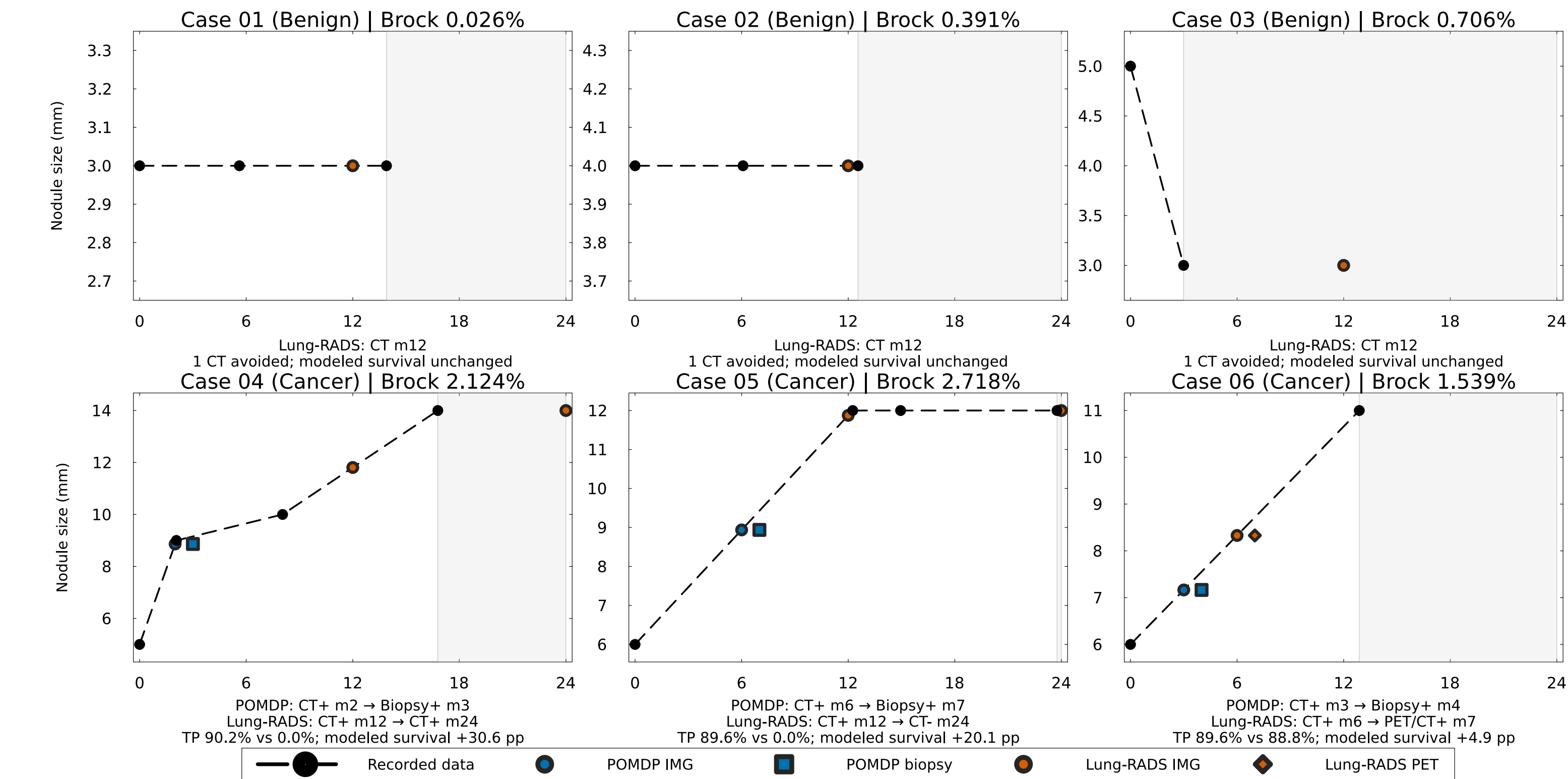


Figure 3. Patient-level POMDP and Lung-RADS comparisons. Dashed black lines show recorded trajectories. Marker color denotes policy: blue, POMDP; vermillion, Lung-RADS. Marker shape denotes action: circle, IMG; square, biopsy; diamond, PET.

Results (Cont.)

Table 2. Paired simulation outcomes and diagnostic-action counts

Case ID	Policy	Dx (%)	24-month Survival (%)	No. of actions			
				Bio	CT	PET	Bx
Benign							
Case 01	POMDP	0.0	97.1	0	0	0	0
	Lung-RADS	0.0	97.1	0	1	0	0
Case 02	POMDP	0.0	95.7	0	0	0	0
	Lung-RADS	0.0	95.7	0	1	0	0
Case 03	POMDP	0.0	96.5	0	0	0	0
	Lung-RADS	0.0	96.5	0	1	0	0
Cancer							
Case 04	POMDP	90.2	90.3	0	1	0	1
	Lung-RADS	0.0	59.7	0	2	0	0
Case 05	POMDP	89.6	87.3	0	1	0	1
	Lung-RADS	0.0	67.2	0	2	0	0
Case 06	POMDP	89.6	87.3	0	1	0	1
	Lung-RADS	88.8	82.4	0	1	1	0

Each case-policy row contains 10,000 paired replicates.

- **Benign:** The POMDP strategy required fewer interventions as compared to Lung-RADS; POMDP avoided one Lung-RADS CT per case; mimproved quality-of-life outcomes.
- **Cancer:** The POMDP strategy diagnosed the cancer cases faster and more frequently than Lung-RADS; modeled 24-month survival increased by up to 18.5% points. POMDP used one CT and one biopsy per case.

Discussion



How the model may help

- Uses the patient’s accumulated evidence rather than a fixed schedule alone.
- Supports earlier diagnosis when the estimated cancer risk is sufficiently high.
- May avoid unnecessary tests when the estimated cancer risk remains low.

Across these selected retrospective cases, the POMDP reduced surveillance for low-risk nodules and accelerated work-up for high-risk nodules, shortening the time to diagnosis in cancer cases.

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Artificial Intelligence (AI) Use Disclaimer

OpenAI Codex assisted with Julia simulation execution and figure generation, LaTeX editing, and language/layout refinement. The authors independently verified all data, computations, figures, and interpretations and retain responsibility for the content; AI did not replace clinical or independent scientific judgment.

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