

Cost-Effectiveness of a Microarray-Based Gene Expression Test for Identifying Primary Tumor in Patients with Cancer of Unknown Primary

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Cancer of unknown primary (CUP)

- Up to 4% of metastatic cancer patients are not readily classified in the course of the initial diagnostic work up
- Further clinical and pathologic investigation including immunohistochemical (IHC) analysis
- Current success rate of exhaustive diagnostic work-up varies from 20% to 25%
- 5000-7000 CUP cases annually diagnosed in Canada
- Have small clinically undetectable (i.e., occult) primary tumour sites

Cancer of unknown primary (CUP)

- No consensus of defined treatment guidelines
- Broad-spectrum empiric chemotherapeutic regimens
- No site-specific therapeutic regimens
- Median survival of 8-12 months
- More impaired HRQoL compared to patients with known primary cancers with metastases
- Cost of diagnostic work up could reach up to \$130,000 CAD per patient

Gene expression-profiling techniques for tumour classification

- Identify a primary tumour site continues to be the most important goal in the clinical management of CUP
- Histogenetic information is maintained during metastasis process
- Gene profiling from a biopsy specimen of a metastatic tumour reflects the histogenetic make-up of the primary tumour site
- Identification of the primary tumour site

The Tissue of Origin (TOO) test

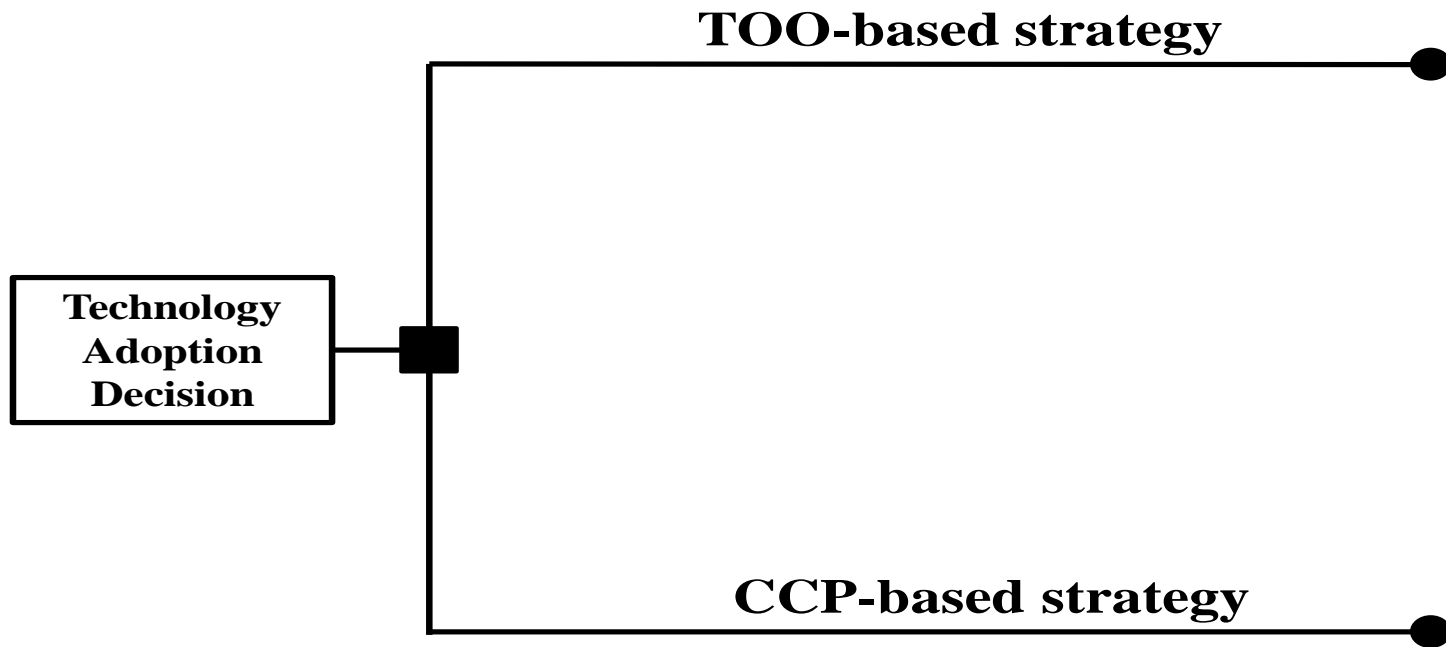
PATHOLOGIST'S INTERPRETATION			TISSUE OF ORIGIN ANALYSIS			
MOST LIKELY TISSUE OF ORIGIN:			TISSUE TYPE	SS	≤ 5	100
BREAST			Breast	68.9		
			Ovarian	18.3		
			Colorectal	2.7		
			Gastric	1.9		
DEGREE OF CONFIDENCE:			Pancreas	1.3		
HIGH			Non-Small Cell Lung	1.1		
			Kidney	1.1		
			Sarcoma	1.0		
			Bladder	0.7		
			Non-Hodgkin Lymphoma	0.6		
			Prostate	0.6		
TISSUES RULED OUT:			Hepatocellular	0.5		
Colorectal	Gastric	Pancreas	Melanoma	0.5		
Non-Small Cell Lung	Kidney	Sarcoma	Thyroid	0.5		
Bladder	Non-Hodgkin Lymphoma	Prostate	Testicular Germ Cell	0.3		
Hepatocellular	Melanoma	Thyroid				
Testicular Germ Cell						
PATHOLOGIST'S COMMENTS:						
The Tissue of Origin Test classified this tissue as Breast with a high degree of confidence. While an origin of Ovarian cannot be ruled out, it is highly unlikely that the origin for this tissue is Ovarian. All other tissues have been ruled out with > 99% confidence.						

Specimen preparation: The specimen was macro-dissected.

Obstacles to incorporating the test in Canadian clinical practice

- Clinical impact of the test in “real life” clinical practice ?
- Testing may cost \$4,400 CAD per patient !
- Resource constrained health care system ?
- A comprehensive health economic evaluation of this approach in the Canadian setting is required

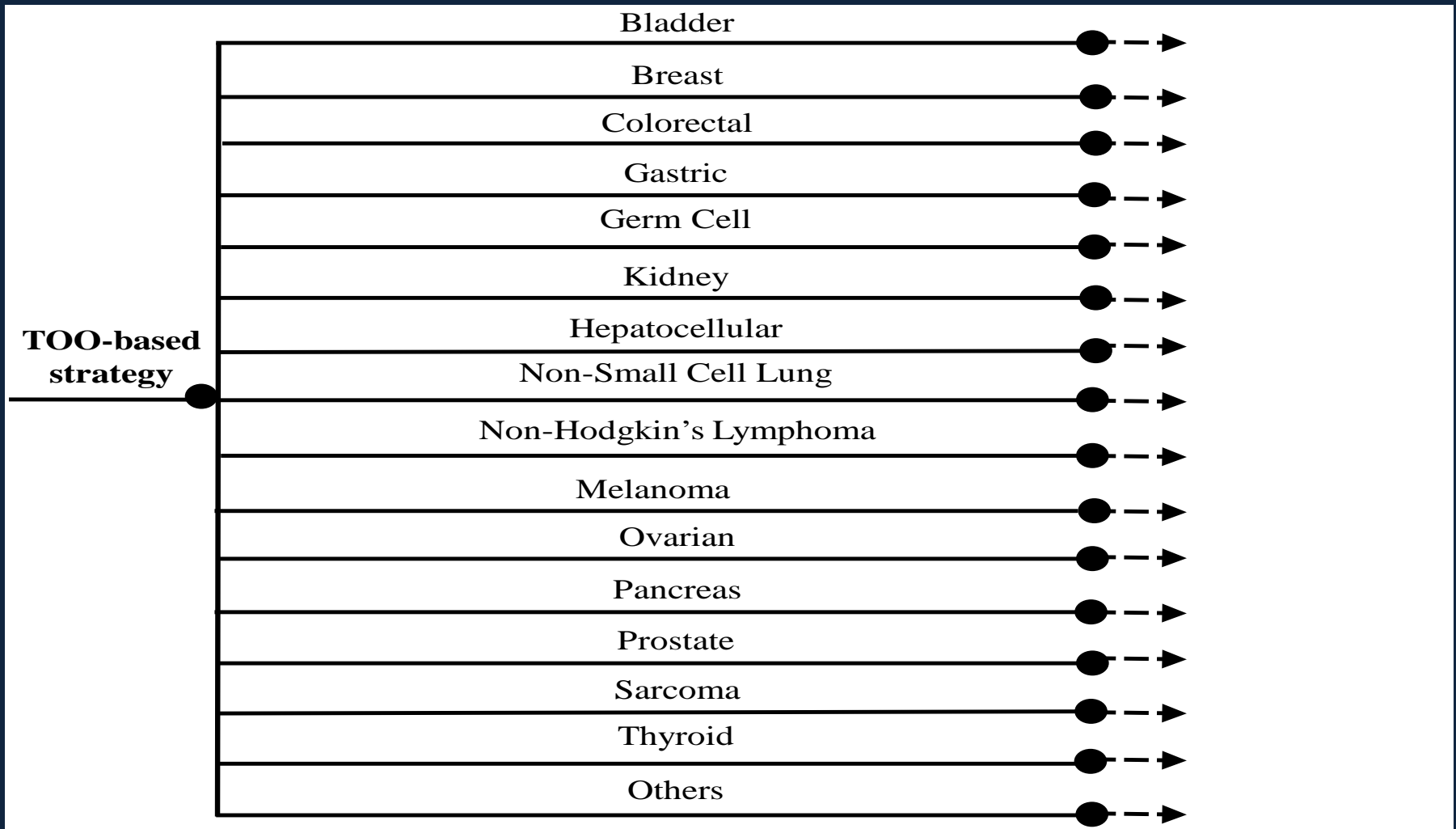
Decision model for cancer of unknown primary



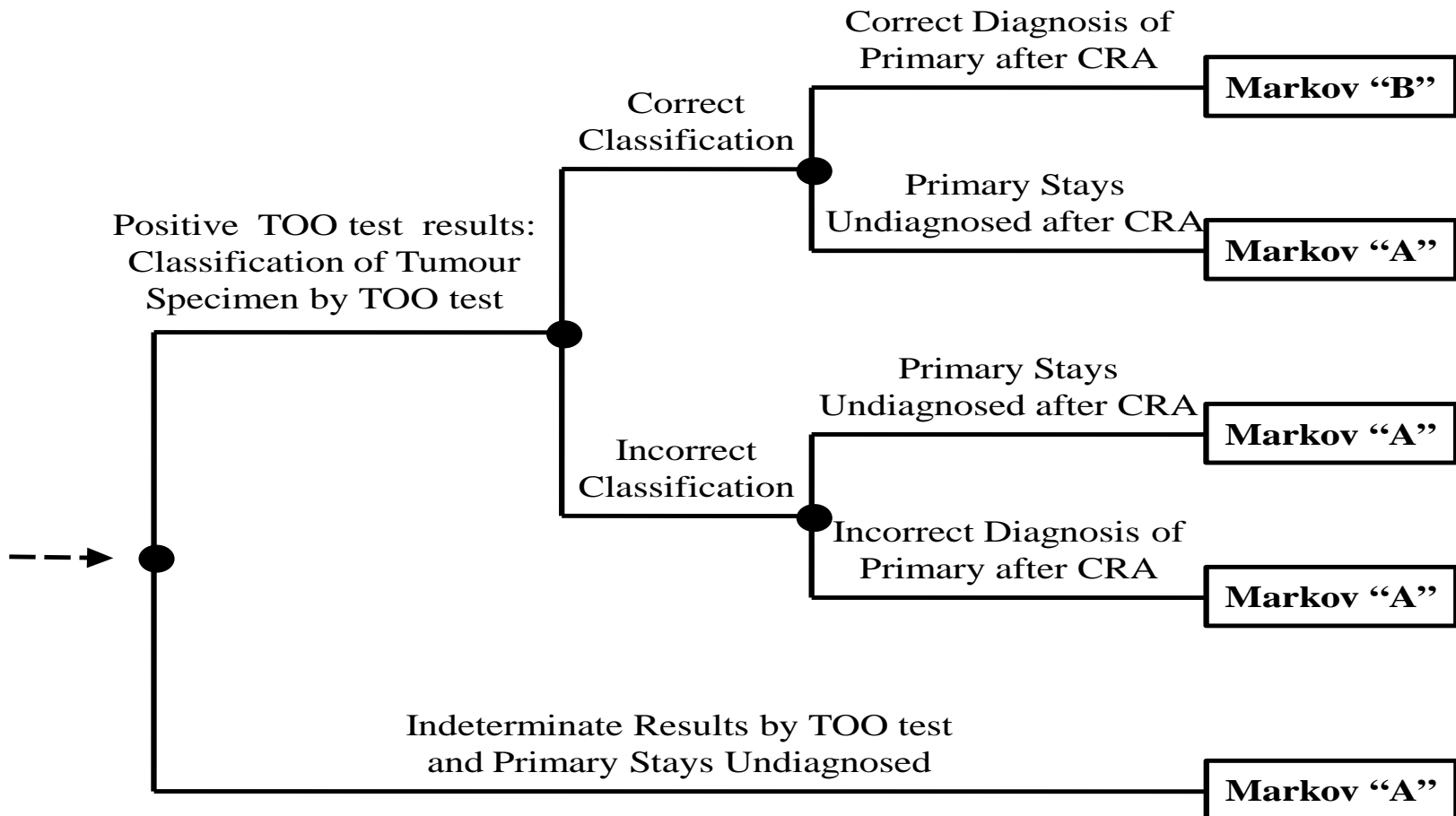
Decision model for cancer of unknown primary



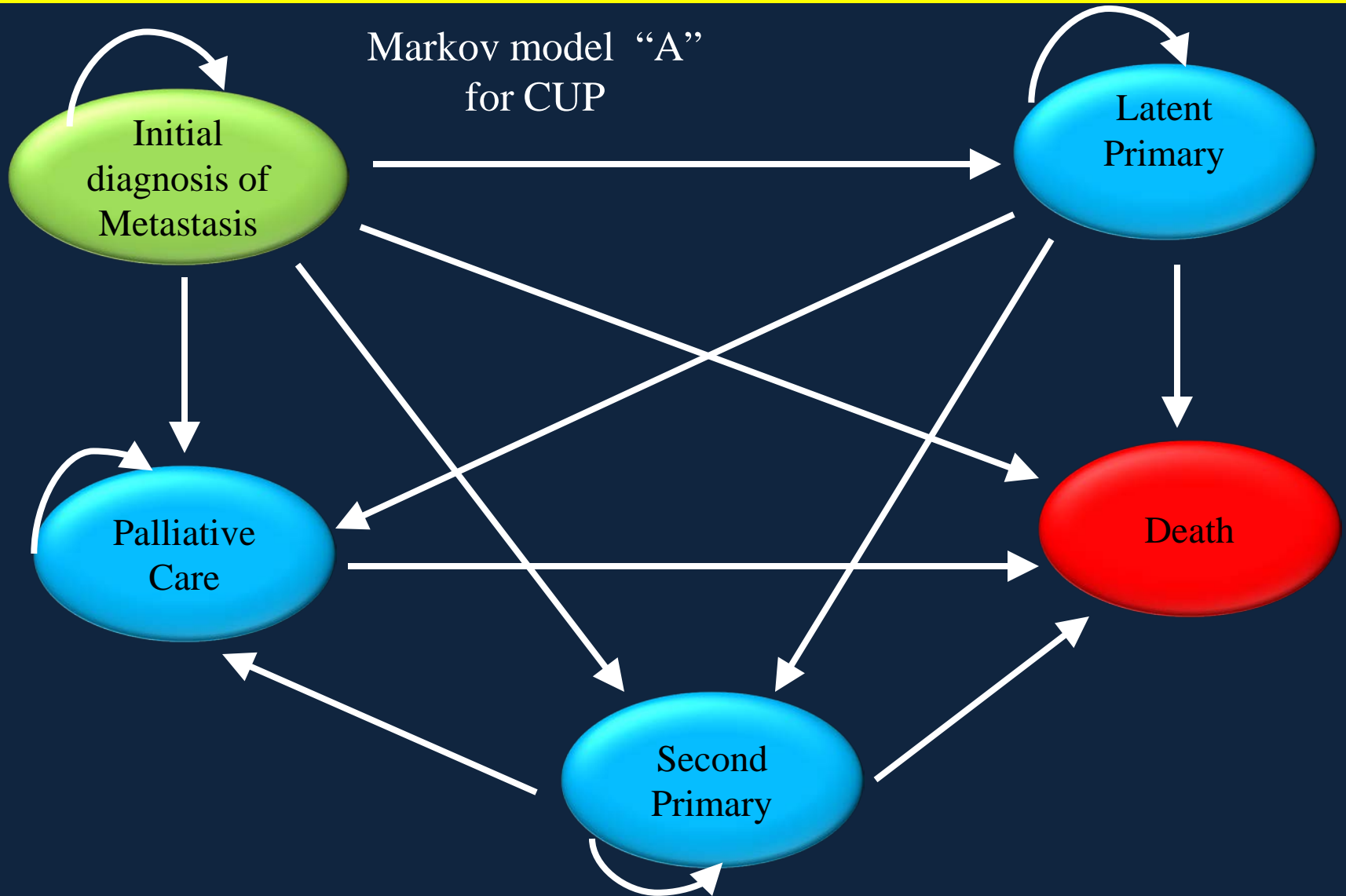
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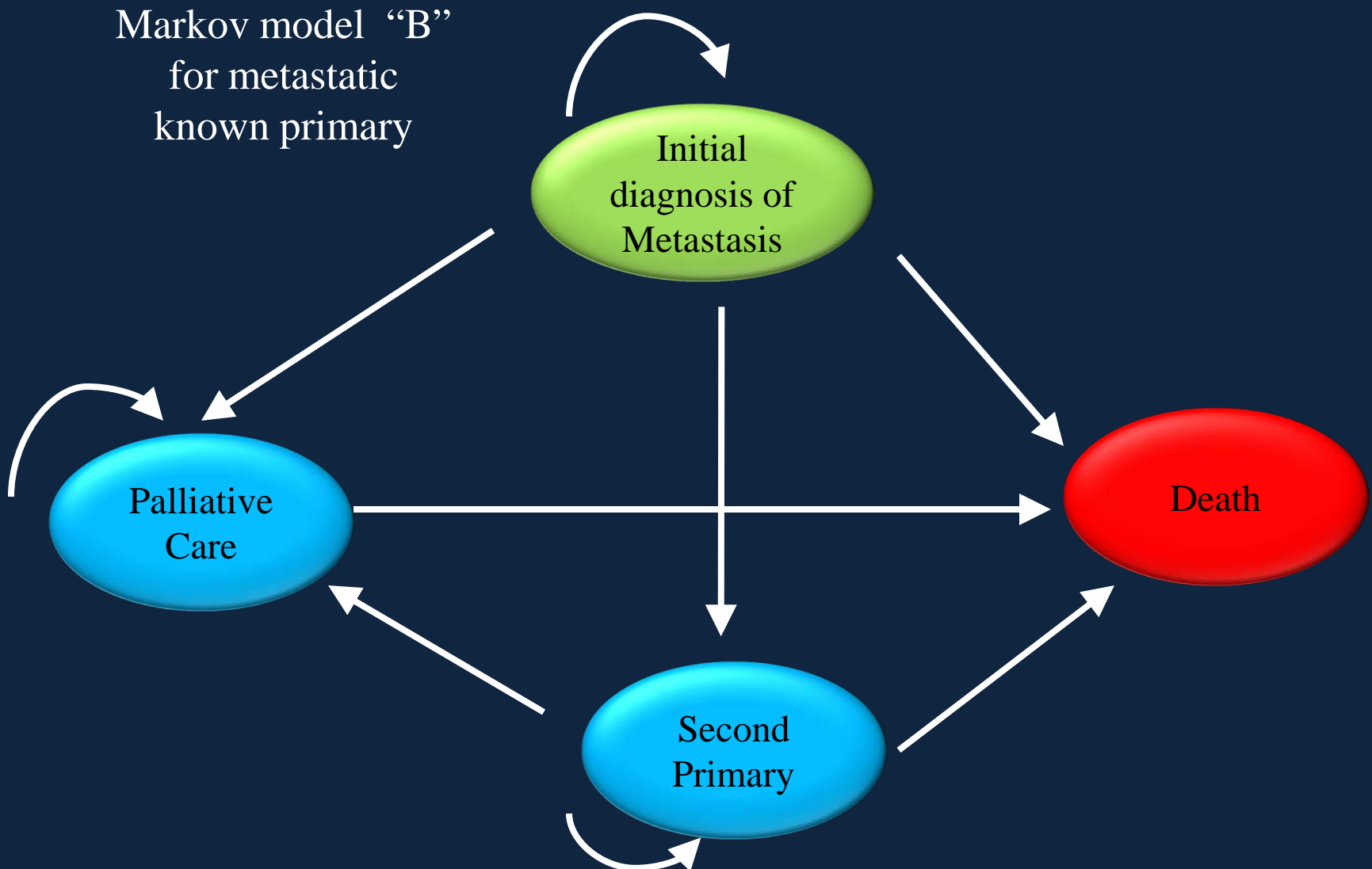
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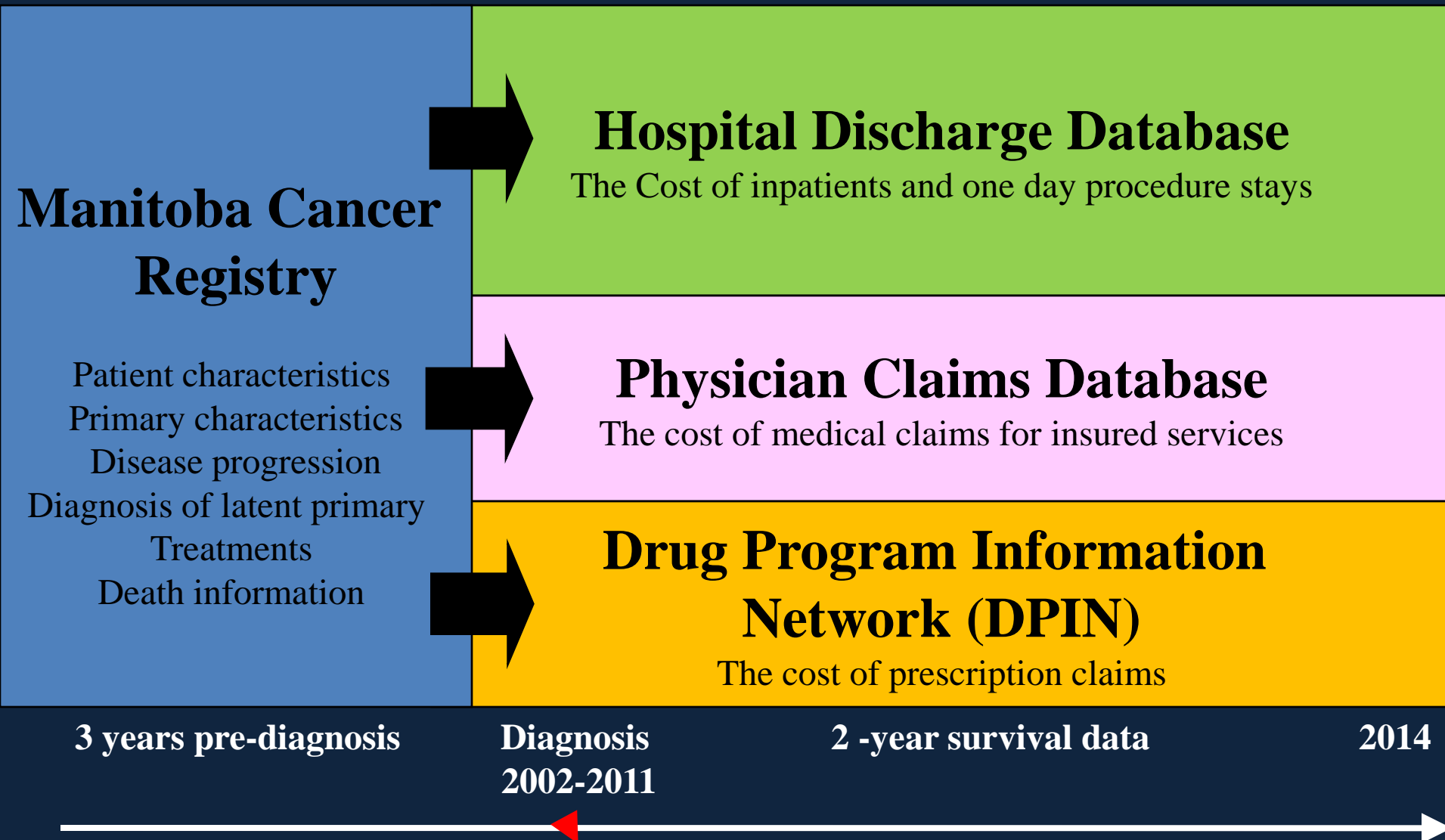
Decision model for cancer of unknown primary



Decision model for cancer of unknown primary



Canadian clinical practice data sources



Canadian clinical practice data sources

- Metastatic cancer cohorts (2002-2011):
 - 1) 1214 patients diagnosed initially with CUP :
 - 809 patients initially diagnosed with CUP and had no change detected with their diagnosis later
 - 405 patients initially diagnosed with CUP and had their latent primary subsequently detected
 - 2) 9314 initially diagnosed with known primary and had no change detected with their primary diagnosis later
 - 3) 2417 patients initially diagnosed with a given known primary and had a latent primary detected later

TOO data sources

Validation and reproducibility of TOO test for tumor identification in formalin-fixed, paraffin-embedded specimens

Tumour specimens	Validation study design	Results by reference diagnosis group
462 specimens of metastatic or poorly differentiated or undifferentiated primary tumours (Pallie et al., 2011)	TOO classification vs. reference diagnosis	Agreement Non-agreement Indeterminate

Utilities

Psycho-Oncology

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Psychiatric manifestations, personality traits and health-related quality of life in cancer of unknown primary site

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Abstract

Objective: Psychiatric manifestations and personality traits are known to influence cancer patients. We aimed to assess psychological distress symptoms, psychosocial factors and health-related quality of life (HRQoL) in cancer of unknown primary site (CUP) and to test whether these parameters differ between CUP and Metastatic (MKPC) or Non-Metastatic Known Primary Cancers (N-MKPC) after controlling for demographics and clinical variables.

Methods: In this cross-sectional study, we recruited 50 CUP, 264 N-MKPC and 52 MKPC participants. We assessed depressive symptoms (Center for Epidemiologic Studies-Depression [CES-D]), psychological distress symptoms (Symptom Distress Checklist-90 Revised), sense of coherence (SOC), ego defense mechanisms (Life Style Index) and HRQoL (World Health Organization Quality of Life Instrument, Short Form).

Baseline Outcomes

Strategy	Effectiveness		Incremental Effectiveness		Cost	Incremental Cost	ICER	
	LY	QALY	LY	QALY			Per LY gained	Per QALY gained
CCP	1.13	0.63	0.28	0.24	\$17,802	\$10,807	\$37,774	\$44,151
TOO test	1.42	0.87			\$28,609			

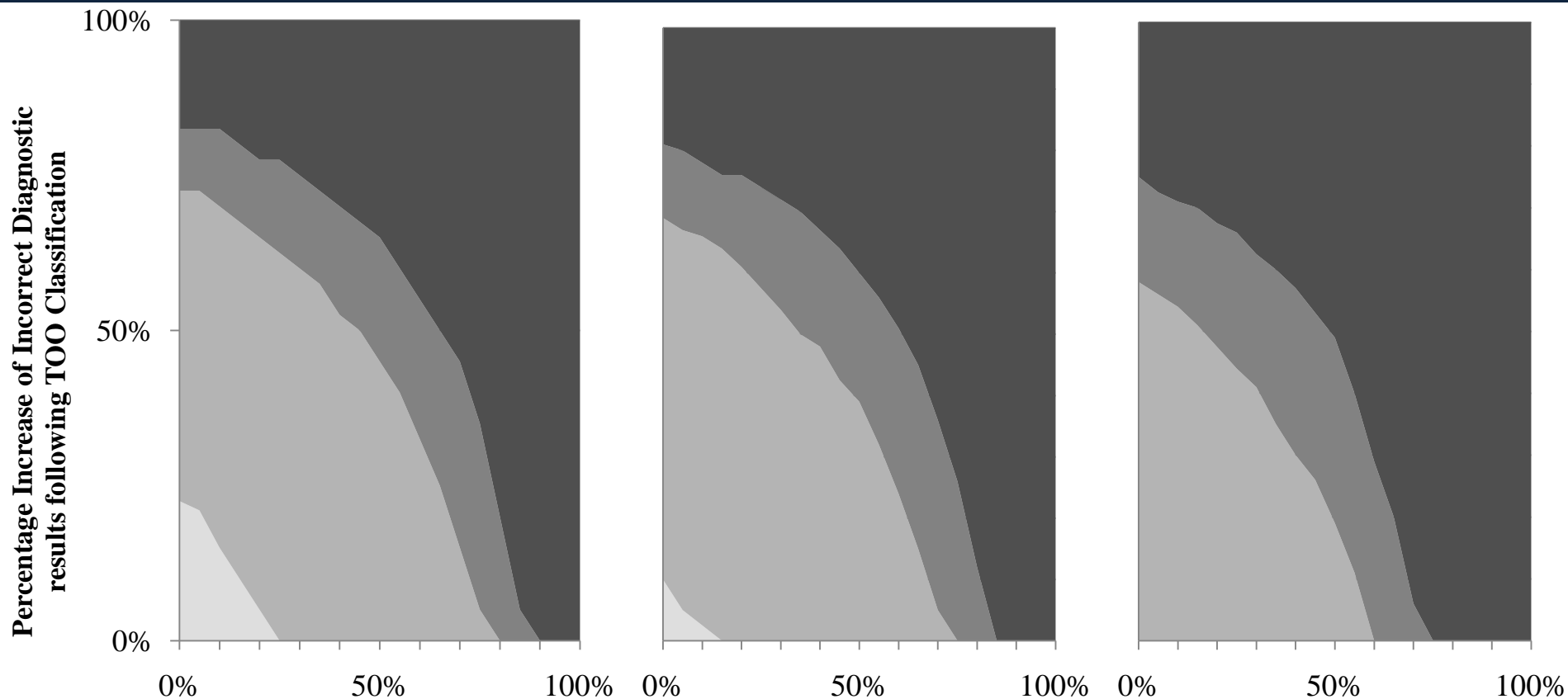
Sensitivity analyses on TOO test related parameters

Percentage Decrease of Baseline Survival Following Correct Primary Diagnosis

0%

-10%

-30%



Percentage Decrease of Baseline TOO Accuracy

ICER ≤ \$50,000 per QALY gained

\$50,000 < ICER ≤ \$100,000 per QALY

\$100,000 < ICER ≤ \$150,000 per QALY

ICER > \$150,000 per QALY

Implications and recommendations

- ICERS were within ranges of a number of cancer technologies that have recently been approved in Canada
- The TOO-based strategy appears to provide good value for money in this patient population
- Results were most sensitive to accuracy of the test, its interpretation and patient survival following correct diagnosis
- Field evaluation of the TOO test has a large societal impact and should be initiated in Canada to ensure its clinical utility and cost-effectiveness