Cost-Effectiveness Analysis of Contemporary Advanced Prostate Cancer Management:
A Markov Model for the Canadian Context

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Introduction

- Recent treatments for advanced PCa: second-gen antiandrogens (SGAA)
- Four SGAAs: abiraterone (abi), apalutamide (apa), darolutamide (daro), & enzalutamide (enza)
- SGAAs are effective but lead to resistance:
  - lack of evidence supporting rechallenge
  - necessary to choose timing for SGAAs
- Existing CEAs compare single states:
  - Saad et al. (2022), Yoo et al. (2023), Sathianathen et al. (2024) compare SGAAs in mCSPC
  - no comparison of treatment sequences

Objective

Find the most effective and cost-effective advanced PCa treatment sequences in the Canadian health-economic context, focusing on timing of second-gen antiandrogen use.

We focus on Canadian health costs, clinical guidelines, and cost-effectiveness thresholds.

Methods

- 3 starting health states:
  - nmCSPC: onto nmCRPC, mCRPC, progressed mCRPC, death
  - low-risk/volume mCSPC: onto mCRPC, prog. mCRPC, death
  - high-risk/volume mCSPC: onto mCRPC, prog. mCRPC, death
- Combine patient outcome data from many trials:
  - AFFIRM, ARAMIS, ARANOTE, ARASENS, COU-AA-301, COU-AA-302, EMBARK, ENZAMET, FIRSTANA, GETUG-AFU-15, PEACE-1, PRESIDE, PREVAIL, PROSELICA, SPARTAN, STAMPEDE, TITAN, & TROPIC
  - Statistical challenge: we develop new parameter estimation algorithm to model transitions probabilities for counterfactual treatment sequences
- Using Canadian guidelines: 62 allowable treatment sequences
  - e.g. (abiraterone+ADT in mCSPC, docetaxel+ADT in mCRPC)
  - define early SGAA use = before mCRPC, late use = in mCRPC
- Markov model: 200,000 simulated patients

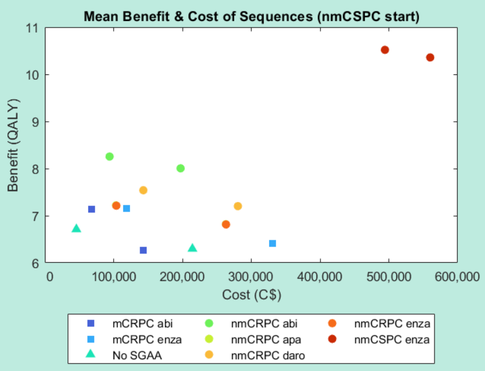
Results

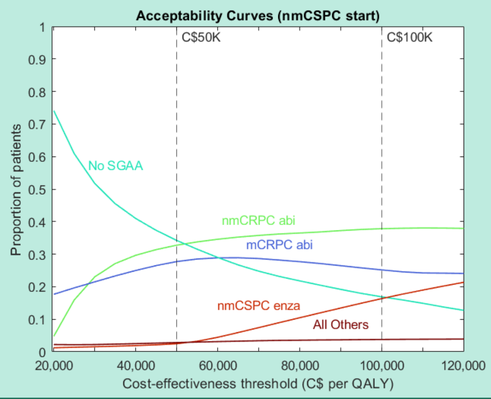
- SGAA timing:
  - Most effective: early SGAA use
  - Most cost-effective: early SGAA use
- Individual drugs:
  - Most effective:
    - enzalutamide for nmCSPC, low-risk mCSPC
    - apalutamide for high-risk mCSPC
  - Most cost-effective: abiraterone

Explanation

- SGAAs effective, but expensive:
  - early use: high benefit & cost
  - For thresholds of C$ 50K+ per QALY (or LY), early SGAA use is worth the cost
- Abiraterone cost-effectiveness: comparable outcomes with generic price (~C$920 vs C$3400 /mo)

nmCSPC

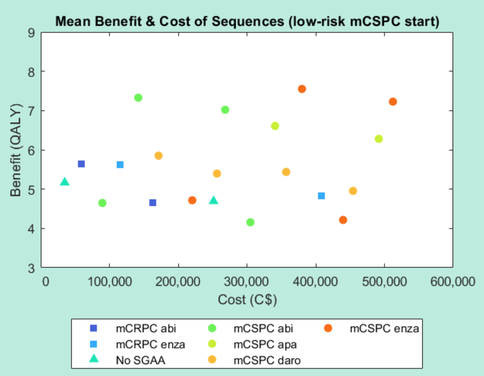


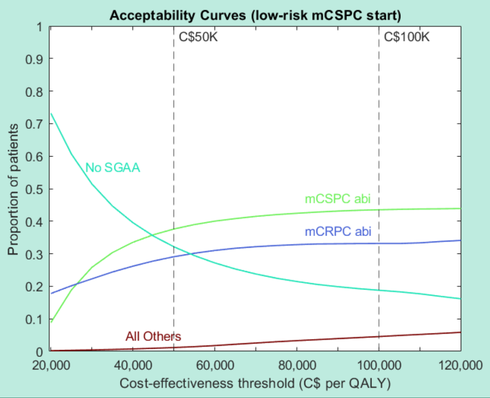


Best mean outcomes for nmCSPC

Outcome	Benefit (QALY)	Cost (C$)	NHB* (QALY)	Treatment Sequence** (nmCSPC, nmCRPC, mCRPC)
Benefit	**10.55**	495,406	N/A	(**enza**, doce, doce)
NHB* @ WTP of C$50K per QALY	8.26	94,438	**6.37**	(ADT, **abi**, doce)
NHB* @ WTP of C$100K per QALY	8.26	94,438	**7.31**	(ADT, **abi**, doce)

low-risk mCSPC



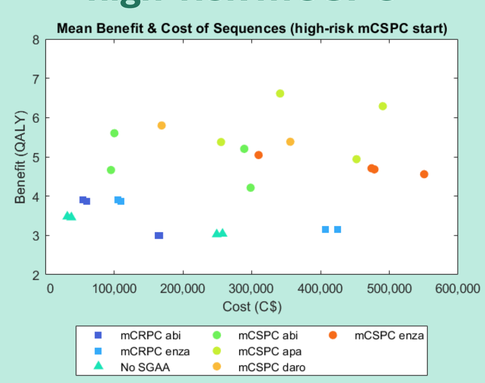


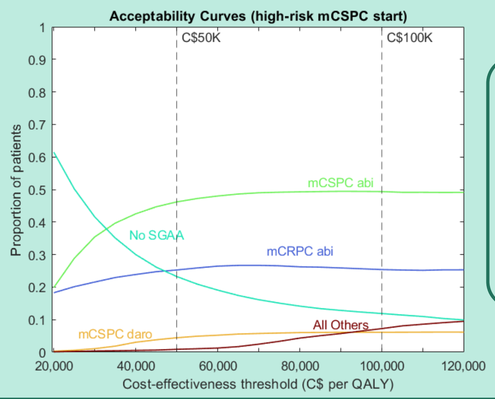
Best mean outcomes for low-risk mCSPC

Outcome	Benefit (QALY)	Cost (C$)	NHB* (QALY)	Treatment Sequence** (mCSPC, mCRPC)
Benefit	**7.55**	380,237	N/A	(**enza**, doce)
NHB* @ WTP of C$50K per QALY	7.32	141,717	**4.49**	(**abi**, doce)
NHB* @ WTP of C$100K per QALY	7.32	141,717	**5.90**	(**abi**, doce)

*NHB= Net Health Benefit **all treatments include ADT; doce = docetaxel

high-risk mCSPC





Best mean outcomes for high-risk mCSPC

Outcome	Benefit (QALY)	Cost (C$)	NHB* (QALY)	Treatment Sequence** (mCSPC, mCRPC)
Benefit	**6.61**	341,307	N/A	(**apa**, doce)
NHB* @ WTP of C$50K per QALY	5.60	100,448	**3.59**	(**abi**, doce)
NHB* @ WTP of C$100K per QALY	5.60	100,448	**4.60**	(**abi**, doce)

*NHB= Net Health Benefit **all treatments include ADT ; doce = docetaxel

Legend:
- ● early SGAA
- ■ late SGAA
- ▲ no SGAA

Highlights:
1) Early SGAA use is high benefit & cost
2) Enza & apa most effective
3) Abi least expensive SGAA

Highlights:
1) As funding rises (CET aka WTP ↑), early SGAA use becomes more cost-effective
2) Early abi most cost-effective

Conclusion

- Implications for clinicians and payers:
  - SGAA use in nmCSPC most effective
  - Early SGAA use is most cost-effective
  - Most early SGAA use cost-effective (net benefit > 0)
  - Abiraterone most cost-effective if generic
- Sensitivity analysis: if all SGAA cost ~C$920 /mo
  - apalutamide, darolutamide, & enzalutamide become most cost-effective

Contribution

We find the most effective and cost-effective contemporary treatment sequences for advanced PCa in the Canadian context.

We develop and demonstrate a novel parameter estimation algorithm to adapt trial data to treatment sequence analysis.

We provide predictions for future cost-effectiveness after FINITE trial (nmCSPC abi) and enzalutamide patent expiry.

References:

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