ARCC
Canadian Centre for Applied Research in Cancer Control

BC Cancer Agency
CARE & RESEARCH
An agency of the Provincial Health Services Authority

UBC
UNIVERSITY OF TORONTO

Canadian Cancer Society
Société canadienne du cancer

Advancing Health Economics, Services, Policy and Ethics

COLORECTAL CANCER SCREENING & RETURN OF SECONDARY FINDINGS: A VALUE FRAMEWORK ANALYSIS

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Value for money

Canada & UK (Reference Case)

- Maximize health gains s/t limited budget
- $\Delta C / \Delta QALY < \lambda$,
- QALY=quality adjusted life year
- λ is cost of displacing QALYs
- Health system perspective

USA Second Panel (Reference Case)

- Max. health gains, $\Delta C / \Delta QALY < \lambda$
- Health system & Societal perspectives

Estimating a QALY

Mobility
I have no problems in walking about
I have some problems in walking about
I am confined to bed

Self-Care
I have no problems with self-care
I have some problems washing or dressing myself

QALY = 0.639

Pain/Discomfort
I have no pain or discomfort
I have moderate pain or discomfort
I have extreme pain or discomfort

Anxiety/Depression
I am not anxious or depressed
I am moderately anxious or depressed
I am extremely anxious or depressed

Value of precision medicine (PM)

*The value of PM will depend on what **information** patients will receive and the benefit patients and providers ascribe to information*

*Decision-makers need **quantification and valuation of all health and non-health effects** of interventions, and to summarize those effects in a single quantitative measure*

Marshall DA, et al. Estimating Preferences for Complex Health Technologies: Lessons Learned and Implications for Personalized Medicine. Value In Health 2017: 20(1) 32-39

Neumann P, et al. Cost-effectiveness in health and medicine: 2nd Edition. 2017. New York: Oxford University Press.

Preference-based utility = value

Personal utility

- The utility of individuals and/or families for genomic information (Grosse et al, 2010)
  - Enhances sense of control, informs self-identity Foster et al, 2009)
  - Resolved uncertainty (Regier et al, 2009)

Valuation of personal utility

- Discrete choice experiment (DCE)
- Attribute-based measure of value
- Random utility theory

Secondary findings (SF)

Next generation sequencing & SFs

- Information on diseases not related to current diagnosis
  - E.g., Test for Lynch syndrome, find risk for Long QT syndrome (treatable) and Alzheimer's (effective treatment not available).

- ACMG recommends returning SFs with effective medical treatment
- CCMG does not because of high cost and potential psychological harm

Aim: What is the predicted uptake and willingness to pay of different strategies for returning secondary findings?

Attribute	Option A	Option B	No information
Disease risk More diseases will be identified if the lifetime risk is lower	Diseases with a 5% lifetime risk or higher	Diseases with a 90% lifetime risk or higher	No information
Disease treatability	Recommended effective medical treatment only	Recommended effective lifestyle change only	No information
Disease severity Health consequences of the diseases you may develop	Very severe health consequences	Severe health consequences	No information
Carrier status Disease risk not affecting you but could affect your family	Does not provide information on carrier status	Information on whether your family members could be affected	No information
Cost to you	$1500	$750	$0
Your preference	**Option A ☐**	**Option B ☐**	**No information ☐**

Regier DA, Peacock SJ, Pataky R, van der Hoek K, Jarvik G, Veenstra DA. Societal preferences for the return of incidental findings from clinical genomic sequencing: a discrete choice experiment. *CMAJ* 2015; 187(6): E190-E197.

Personal utility for SFs

Table 3: Willingness to pay and predicted uptake for scenarios related to return of incidental findings

Senario no.	New policy scenario	Prevailing policy senario	Average incremental willingness to pay, $ (95% CI)*	Predicted uptake of new policy scenarios, % (95% CI)
1	Return results only for disorders with: • Recommended effective medical treatment • Severe health consequences • ≥ 80% lifetime risk	Information on incidental findings is not returned	445 (322–567)	66 (63–71)
2	Return results only for disorders with: • Recommended effective medical treatment and lifestyle change • Severe health consequences • ≥ 80% lifetime risk	Information on incidental findings is not returned	641 (520–762)	73 (69–77)
3	Patient's choice between 2 options — Return results only for disorders with: • Any treatability level • Severe health consequences • ≥ 80% lifetime risk Or return results only for disorders with: • Recommended effective medical treatment • Severe health consequences • ≥ 80% lifetime risk	Recommended effective medical treatment only; severe health consequences; ≥ 80% lifetime risk	280 (248– 313)	• Medical and nonmedical treatment 27 (24–29) • Medical treatment only 49 (45–52) • Total uptake 76 (72–79)

Note: CI = confidence interval.
*Willingness to pay was derived from the estimates of the mixed logit statistical model using the compensating variation formula. All estimates are in 2013 Canadian dollars.

Value for money: SFs

ΔC/ ΔQALY for returning SFs (Bennette et al 2015)

- $44,800 (cardiomyopathy), $115,020 (colorectal cancer), $133,400 per QALY (population screening)

Decision uncertainty

- λ=$100,000
- 85% (cardiomyopathy), 28% (colorectal cancer), 10% generally healthy

Limitations

- Upstream cost/consequences not examined
- No allowance for personal utility

Bennette CS, et al: The cost-effectiveness of returning incidental findings from next-generation genomic sequencing. *Genetics in medicine:* 2015, **17**(7):587-595.

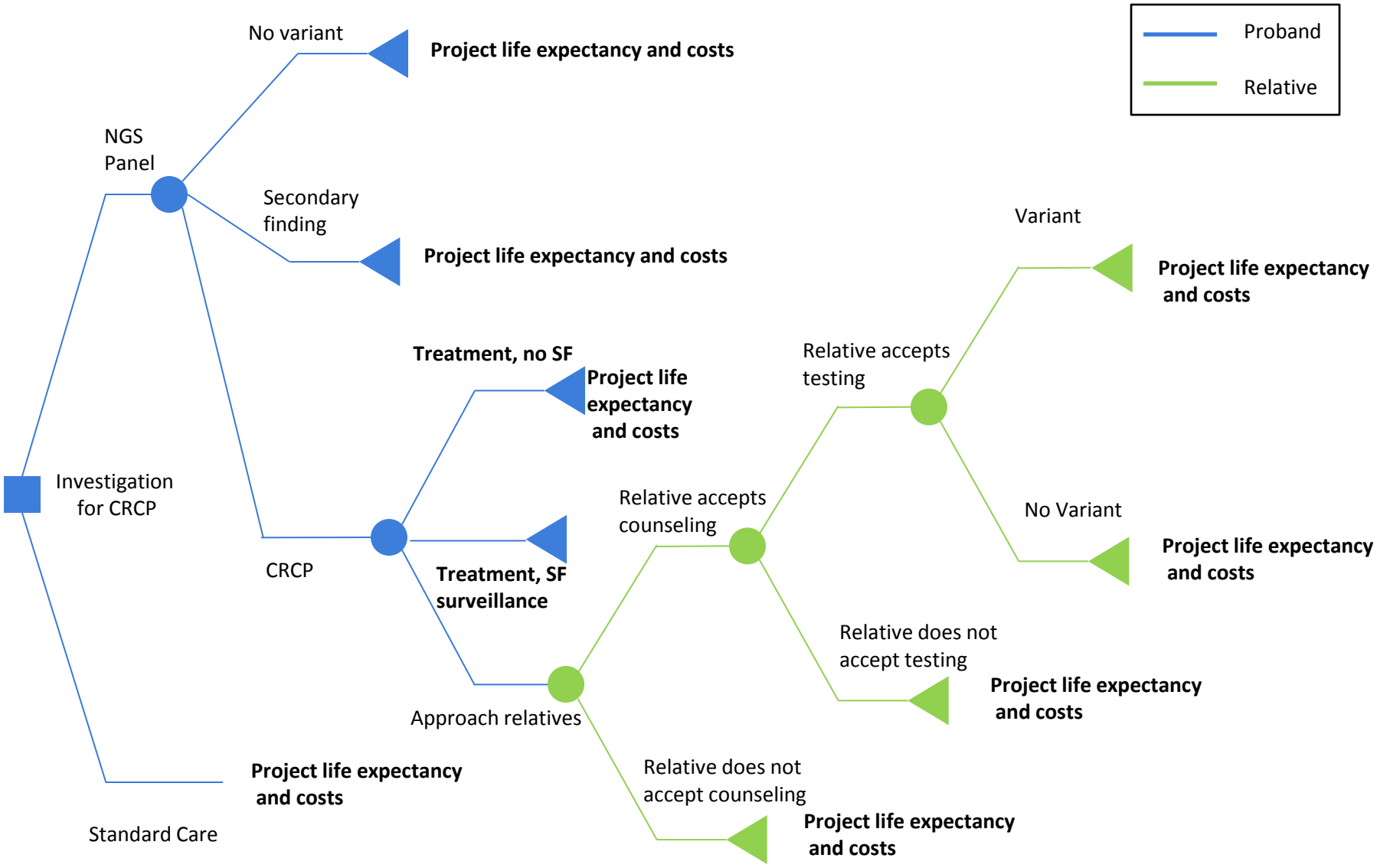
Research Question(s)

Cost-effectiveness of NGS for the diagnosis colorectal cancer & polyposis (CRCP) syndromes and the return of SFs

$$ICER = \Delta C / \Delta QALYs < \lambda$$

What is the net-benefit when allowance is made for personal utility?

$$V\text{-}NMB = \xi + \lambda * \Delta QALYs - \Delta C$$



Data requirements: Because of quantitative complexity and data availability, 7 SFs are modeled (95% of all SFs). For each SF, prevalence estimates are needed. Decision models estimating cost/QALYs for each SF are also required in addition to cost and consequences for NGS for CRCP.

Cost-effectiveness - results

	Δ COST	ΔQALY	ICER ($/QALY)	V-NMB†
Colorectal Cancer Polyposis Syndromes	$5,827	0.128	$45,521	$7,614
Hereditary Breast and Ovarian Cancer	-$5,918	0.126	Dominates‡	$19,359
Familial hypercholesterolemia	$2,791	0.777	$3,594	$75,550
Hypertrophic and dilated cardiomyopathy	$15,945	0.567	$28,119	$41,396
Arrhythmogenic right ventricular cardiomyopathy	$45,981	0.162	$283,460	($29,140)
Malignant hyperthermia susceptibility	-$211	0.007	Dominates	$1,552
Long QT Syndromes	$24,256	0.094	$258,800	($14,215)
Other, rare conditions (combined)	$72,238	0.00	N/A	($71,597)
Total (SFs excluding CRCP)	***$3,274***	***0.007***	***$467,714***	($1,932)
Total (all conditions)	***$9,100***	***0.133***	***$68,421***	$4,843

QALY: Quality-adjusted life year; **ICER:** Incremental Cost-Effectiveness Ratio; **SF:** Secondary Finding; **CRCP:** Colorectal Cancer Polyposis Syndrome

† - calculation of Net Monetary Benefit includes a frequency-weighted estimate of the value of knowing

‡ - Dominates: is less costly, more effective than comparator (IHC)

Decision uncertainty

Reference case

- λ=100,000 per QALY
- The probability that CRCP/ SFs is cost-effective was 72%

Personal utility and net benefit

- λ = $100,000 per QALY and ξ=$641
- V-NMB was $12,529 (CR: -$3,890;$22,579).
- The probability that CRCP/ SFs is cost-effective was 82%
- 95% cost-effective if NGS = $3200

Discussion

Methodological

- Guidelines for technology assessment do not endorse personal utility
- This may lead to over(under) investment in precision medicine technologies
- Value frameworks allow us to broaden the evaluative space (and go beyond QALYs)

Applied

- Upstream & downstream considerations are critical
- Absent of personal utility, decision uncertainty is substantial
- PM amplifies complex decisions; data requirements supporting decision-making are signficant

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Cancer Care Ontario
Action Cancer Ontario

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