

**ARCC**

Canadian Centre  
for Applied Research  
in Cancer Control

# NEXT GENERATION GENOMIC SEQUENCING AND THE DISCLOSURE OF INCIDENTAL FINDINGS

Regier DA, Pataky R, van der Hoek K,  
Hoch J, Veenstra D, Peacock SJ

ARCC Conference Vancouver Canada  
May 24, 2013

# Background

- Next generation genomic sequencing is increasingly used
- Potential of incidental findings
  - Risk for diseases not related to patients current diagnosis
- Varying types of incidental findings
  - E.g., medically actionable, lifetime risk of acquiring the condition, consequences on health status

# ACMG Recommendations

- Published list of incidental findings that should be returned by lab
  - Verifiable and amenable to medical intervention
- The working group suggests:
  - *Pre and post-test counselling should be provided*
  - *Does not favor offering the patient a preference as to whether or not to receive the minimum list*
  - *Patients have the right to decline clinical sequencing*

# A role for the patient

- Personal utility for genetic testing
  - Value beyond clinical utility (Foster, 2009; Regier et al, 2009)
    - No clear, direct implications for patient care
    - Value of knowing
    - Value of genetic tests are best judged by affected individual or by society (Regier et al, 2009; Townsend et al, 2012)

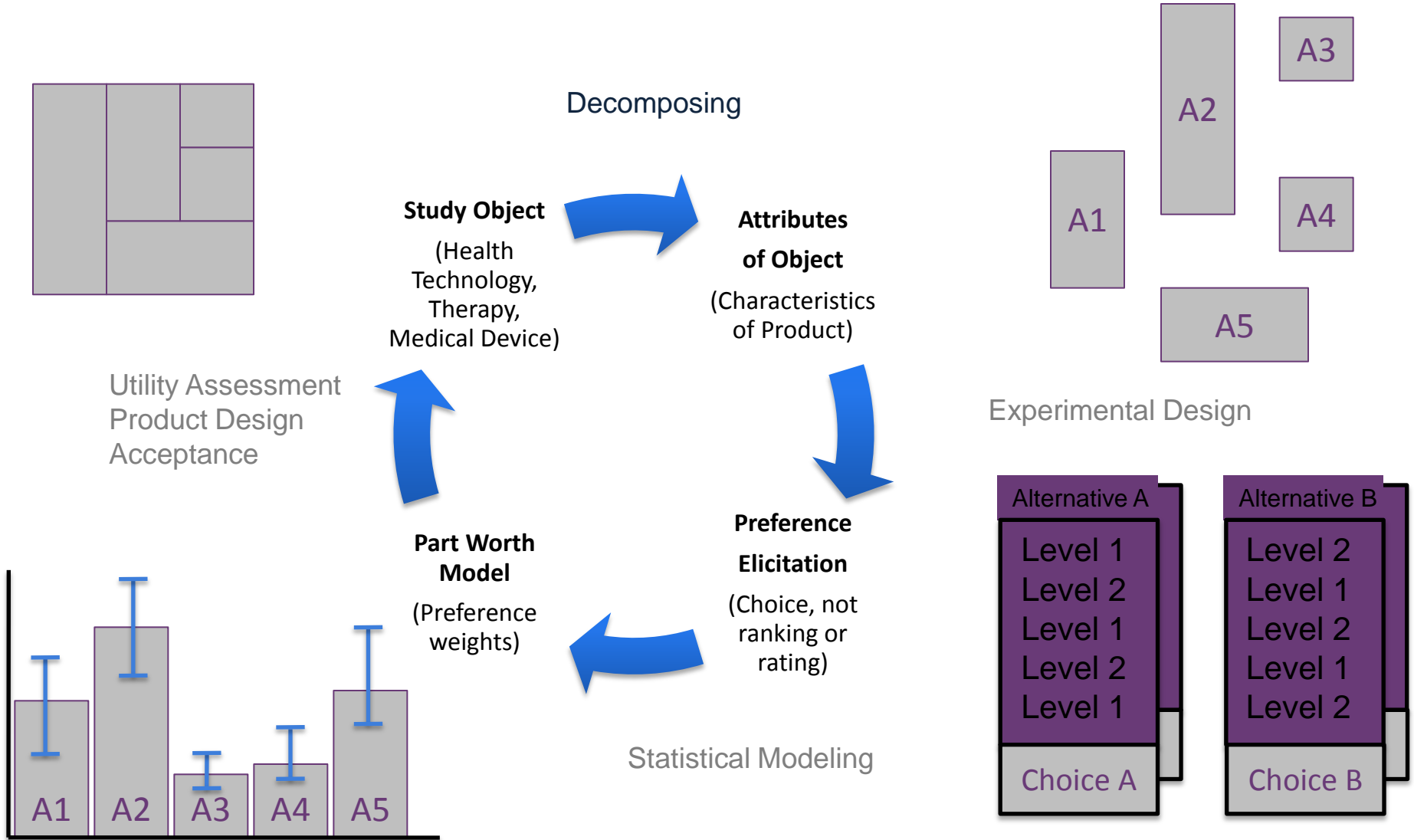
# Objective/Sample

- Objective
  - Estimate personal utility for the return incidental findings
  - Discrete choice experiment method
- Respondent Sample
  - General public in Canada
  - Pilot study

# Discrete Choice Experiments

- ***Attribute* based measure of value** (Thurstone, 1927; Lancaster, 1966)
  - A good can be described by attributes
  - Attributes are defined by levels
- **Utility for attribute levels can be estimated** (McFadden, 1978)
- **Monetary equivalence of utility via willingness to pay** (Small and Rosen, 1979)

# Method: Discrete Choice Experiment



# Study Approach

- Define Attributes/levels
  - Cognitive interviews (n=6)/focus groups (n=12)
- Experimental design
  - D-efficient design
- Statistical Analysis
  - Error components Mixed Logit Model
- Welfare Analysis
  - Willingness to pay (via compensating variation)

# Cognitive interviews/Focus Groups

- **Desire to know** *(Benette et al, 2013, Genetics in Medicine)*
  - *I'd want to know everything. I'd want no sugar coating at all*
  - *If it can be treated, I'd want to know, but if it's something that they may not be able to treat or if it's like a 50/50 chance then not really*
  - *I think you could go nuts treating all these little possibilities....I would go crazy*
  - *Essentially how it's going to affect my independence and how much pain I'm going to have*

# Choice task example

	Option A	Option B	No information
<b>Disease Risk</b> <i>More disease will be identified if the lifetime risk is lower</i>	Diseases with a <b>80% lifetime risk or higher</b>	Diseases with a <b>90% lifetime risk or higher</b>	No information
<b>Disease Treatability</b>	Recommended effective medical treatment and lifestyle change	No effective medical treatment or lifestyle change recommended	No information
<b>Disease Severity</b> <i>Health consequences of the disease you may develop</i>	Very severe health consequences	Severe health consequences	No information
<b>Carrier Status</b> <i>Disease risk not affecting you but can affect your family</i>	Does not provide information on carrier status	Information on if your family members could be affected	No information
<b>Cost to you</b>	\$1000	\$425	\$ 0
	Option A <input type="checkbox"/>	Option B <input type="checkbox"/>	No Information <input type="checkbox"/>

# Demographics of panel

<b>Sample Size, N=100</b>	<b>Mean or %</b>
Age	46 years (range: 19-82)
Gender	49% were female
Western Canada	32%
Central Canada	40%
Eastern Canada	28%
Number of Adults in Family	2.23 (range 1-6)
Number of Children	1.46 (range 0-5)
Elementary only	2%
High school only	34%
College degree	50%
Post-graduate	12%
Median Income	\$50,000 to 59,999
Average time to completion	12 minutes

# Results: discrete choice experiment

Attribute	Attribute level	Estimate (se)	P-val
Risk threshold	90 or greater risk	0.53 (0.11)	0.00
	80 or greater risk	0.61 (0.09)	0.00
	40 or greater risk	0.81 (0.12)	0.00
	5 or greater risk (reference)	--	
Treatment options of the identified disease(s)	Lifestyle only (reference)	--	
	Medical only	0.07 (0.06)	0.04
	Medical and Lifestyle	0.14 (0.062)	0.01
	None	-0.23 (0.07)	0.00
Quality of life consequences	Mild (reference)	--	
	Moderate	0.21 (0.09)	0.00
	Severe	0.30 (0.08)	0.00
	Very Severe	0.26 (0.09)	0.00
Reproductive Risk	Is given	0.07 (0.03)	0.03
Cost to you	Cost	-0.0006 (0.00008)	0.00

# Welfare analysis

- Estimated if 'cost to you' attribute included

Marginal utility of income

$$CV = \frac{1}{\lambda} \left[ \ln \sum_J e^{V_j^0} - \ln \sum_J e^{V_j^1} \right]$$

Utility, 'new' practice

Utility, 'current' practice

The diagram illustrates the components of the Cost of Valuation (CV) formula. A blue arrow points from the text 'Marginal utility of income' to the parameter  $\lambda$  in the denominator of the formula. Another blue arrow points from the text 'Utility, 'new' practice' to the first term of the formula,  $\ln \sum_J e^{V_j^0}$ . A third blue arrow points from the text 'Utility, 'current' practice' to the second term of the formula,  $\ln \sum_J e^{V_j^1}$ .

- Scenarios for WTP

- 80% or higher risk, medical treatment, severe qol consequences, v. no return of incidental findings
- 80% or higher risk, no medical treatment, severe qol consequence v. no return of incidental findings

	<b>Willingness to pay</b>	<b>95% CI</b>
Scenario 1 (IFs with medical treatment , 80% or greater risk, severe QOL)	\$1,071	738– 1,394
Scenario 2 (IFs with no treatment, 80% or greater risk, severe QOL)	\$509	125-894
Current practice → return all information	\$209	82-336

	<b>Uptake of option</b>	<b>95% CI</b>
Scenario 1	89%	0.87-0.91
Scenario 2	40%	0.37 – 0.43

# Discussion

- Respondents, on average, valued receiving information on incidental findings
- Value of knowing extended to diseases with no known medical treatment
- Uptake of information varied substantially between treatable and non-treatable diseases
- Does return of information provide good 'value for money'?
- How did task complexity affect responses?

# Acknowledgements

- DCE research funded by the Canadian Centre for Applied Research in Cancer Control (ARCC)
- Qualitative research funded by the National Institutes of Health, National Human Genome Research Institute



Canadian  
Cancer  
Society

Société  
canadienne  
du cancer



**Cancer Care Ontario**  
**Action Cancer Ontario**

# References

Foster MW, Mulvihill JJ, Sharp RR. Evaluating the utility of personal genomic information. *Genet Med*. Aug 2009;11(8):570-574.

McFadden D. Conditional Logit Analysis of Qualitative Choice Behavior. In P.Z., ed. *Frontiers in Econometrics*. New York: Academic Press.

Regier DA, Friedman JM, Makela N, Ryan M, Marra CA. Valuing the benefit of diagnostic testing for genetic causes of idiopathic developmental disability: willingness to pay from families of affected children. *Clin Genet*. Jun 2009;75(6):514-521.

Thurstone, LL. A law of comparative judgement. *Psychological Review*. 1927; 21:721-35

Townsend A, Adam S, Birch PH, Lohn Z, Rousseau F, Friedman JM. "I want to know what's in Pandora's box": Comparing stakeholder perspectives on incidental findings in clinical whole genomic sequencing. *Am J Med Genet A*. Oct 2012;158A(10):2519-2525