Center for Translational Molecular Medicine

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Using SMAA to assess the cost effectiveness of health care interventions: a case study in infertility treatment

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Introduction

- In cost-effectiveness analysis (CEA), two or more medical interventions are evaluated in terms of their
  - Costs (e.g. hospitalization costs)
  - Effects (e.g. mean survival time)
- Using a fixed substitution rate λ, the consequences of each alternative are combined in a single outcome measure, called the net monetary benefit (NMB = λ*e - c)
- Decision support is provided by plotting for each possible value of λ the probability that an alternative has the highest NMB

=> Cost-effectiveness acceptability curves (CEACs)

Example: treatment and control

Treatment

Cost (x $1,000)	Effect (life years)	Probability
90	5	1/3
110	4	1/3
110	6	1/3

Control

Cost (x $1,000)	Effect (life years)	Probability
100	5	1

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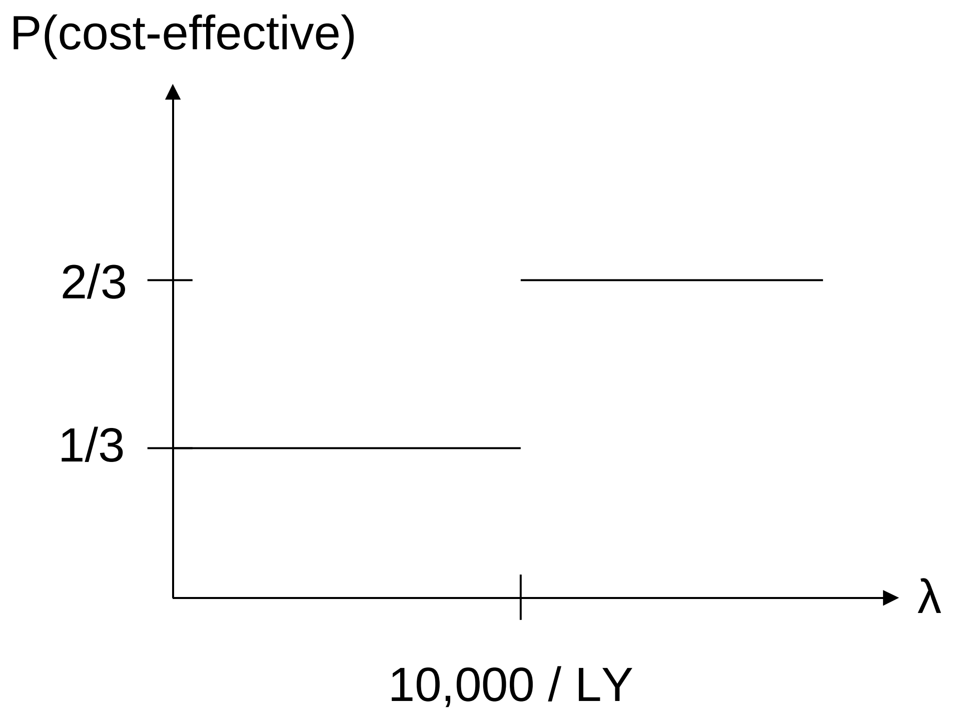
Example cont'd: CEAC treatment



Cost-effectiveness acceptability curves and their limitations

- CEACs only provide a partial picture of the uncertainty surrounding the decision problem:
  - it shows the probability of making the correct decision when a certain alternative is selected
  - it does NOT provide any information about the alternative's probability distribution over the other ranks when making a wrong decision
- Ignoring information about ranks other than the first one can make it difficult to identify good compromise solutions:
  - extreme alternatives look similar to those with good acceptabilities for the best ranks only

SMAA-CEA

- To overcome the limitations associated with the CEAC, we have developed SMAA-CEA as a new method for representing decision uncertainty in CEA
- SMAA-CEA is based on stochastic multi-criteria acceptability analysis (SMAA), a family of methods for aiding multi-criteria group decision making
- These methods are based on exploring the weight space in order to describe the preferences that make each alternative the most preferred one, or that would give a certain rank for a specific alternative
- SMAA has successfully been applied in various real-life decision aiding contexts, including cargo harbor environmental impact assessment, elevator planning, and drug benefit-risk analysis

Preliminaries

- Consider *n* health care interventions that are to be evaluated with respect to their costs (*c*) and effects (*e*)
- It is assumed that the decision maker's preference structure can be represented by the NMB function

$$\mathrm{NMB}(e, c, \lambda) = \lambda e - c$$

- The costs and effects of the different alternatives are uncertain and represented by the random vectors **C** = $[C_1, \ldots, C_n]^T$ and **E** = $[E_1, \ldots, E_n]^T$

Preliminaries cont'd

- For given realizations **c** of **C** and **e** of **E**, the alternatives are ranked in descending order by means of a ranking function

$$\text{rank}(i,\mathbf{c},\mathbf{e},\lambda) = 1 + \sum_{\text{k}=1}^{\text{n}} I(\text{NMB}(e_k, c_k, \lambda) > \text{NMB}(e_i, c_i, \lambda))$$

- Define, based on this ranking function, the sets of favorable cost and effect measurements as

$$M_i^r(\lambda) = \{(c,e) \in R^n \times R^n : \text{rank}(i,\mathbf{c},\mathbf{e},\lambda) = r\}$$

- Any realization (*c*,*e*) in $M_i^r(\lambda)$ results in such values for the different alternatives that alternative *i* obtains rank *r*

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Rank acceptability indices

- The *rank acceptability index* $b_i^r(\lambda)$ describes, for a given value of λ, the share of all possible realizations of **C** and **E** for which alternative *i* is ranked at place *r*
- It is computed as a multidimensional integral over the consequence space as

$$b_i^r(\lambda) = \int\int_{(c,e)\in M_i^r(\lambda)} f_{CE}(\mathbf{c},\mathbf{e})d\mathbf{c}d\mathbf{e}$$

- By definition, an alternative's rank acceptability indices are within the interval [0,1]
  - 0 indicates that the alternative will never indicate rank *r*
  - 1 indicates that the alternative will obtain rank *r* for certain

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Cumulative rank acceptability indices

- Favorable alternatives are those with high acceptability indices for the best ranks and low acceptability indices for the worst ranks
- This information can be obtained from the *cumulative rank acceptability indices*

$$t_i^k(\lambda) = \sum_{r=1}^{k} b_i^r(\lambda)$$

- $t_i^k(\lambda)$ describes the fraction of all possible realizations of **C** and **E** for which alternative *i* is assigned at any of the *k* best ranks
  - $t_i^1(\lambda) = b_i^1(\lambda)$
  - $t_i^n(\lambda) = 1$

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Case study in IVF treatment selection

- To illustrate the use of the SMAA-CEA descriptive indices, we consider a previously published cost-effectiveness decision problem relating to infertility treatment (Fiddelers et al., 2009)
- The objective of the original study was to compare the cost-effectiveness of seven IVF strategies based on a maximum of three consecutive IVF cycles and different combinations of embryo transfer policies per cycle
- For this purpose, an elaborate Markov cycle tree was developed, taking into account
  - canceled cycles,
  - availability of only one embryo (resulting in a so-called compulsory single embryo transfer),
  - declining pregnancy rates in subsequent cycles,
  - the possibility of having frozen embryo transfers when a patient did not achieve a pregnancy after fresh embryo transfer or had a miscarriage / stillborn child, and
  - treatment dropouts due to cycle cancellation or fertilization failure

Case study in IVF treatment selection cont'd

- Effects were quantified in terms of the mean live birth probability for a couple starting IVF treatment
- Costs were analyzed from a societal perspective and included
  - the cost of IVF treatment,
  - the cost of a singleton and twin pregnancy,
  - the cost of delivery, and
  - the cost of the period from birth until sex weeks after birth
- Uncertainty was accounted for by specifying probability distributions for the model parameters

Results of the probabilistic cost-effectiveness analysis

Strategy	Mean effect	Mean Cost	ICER	Dominated by
1. 3 x eSET	0.374	14,154		
2. eSET + 2 x STP	0.458	15,157		1-5
3. eSET + STP + DET	0.470	15,609		5
4. eSET + 2 x DET	0.490	16,423		5
5. 3 x STP	0.523	15,498	9,002	
6. STP + 2 x DET	0.552	16,567	38,488	
7. 3 x DET	0.575	11,700	46,560	

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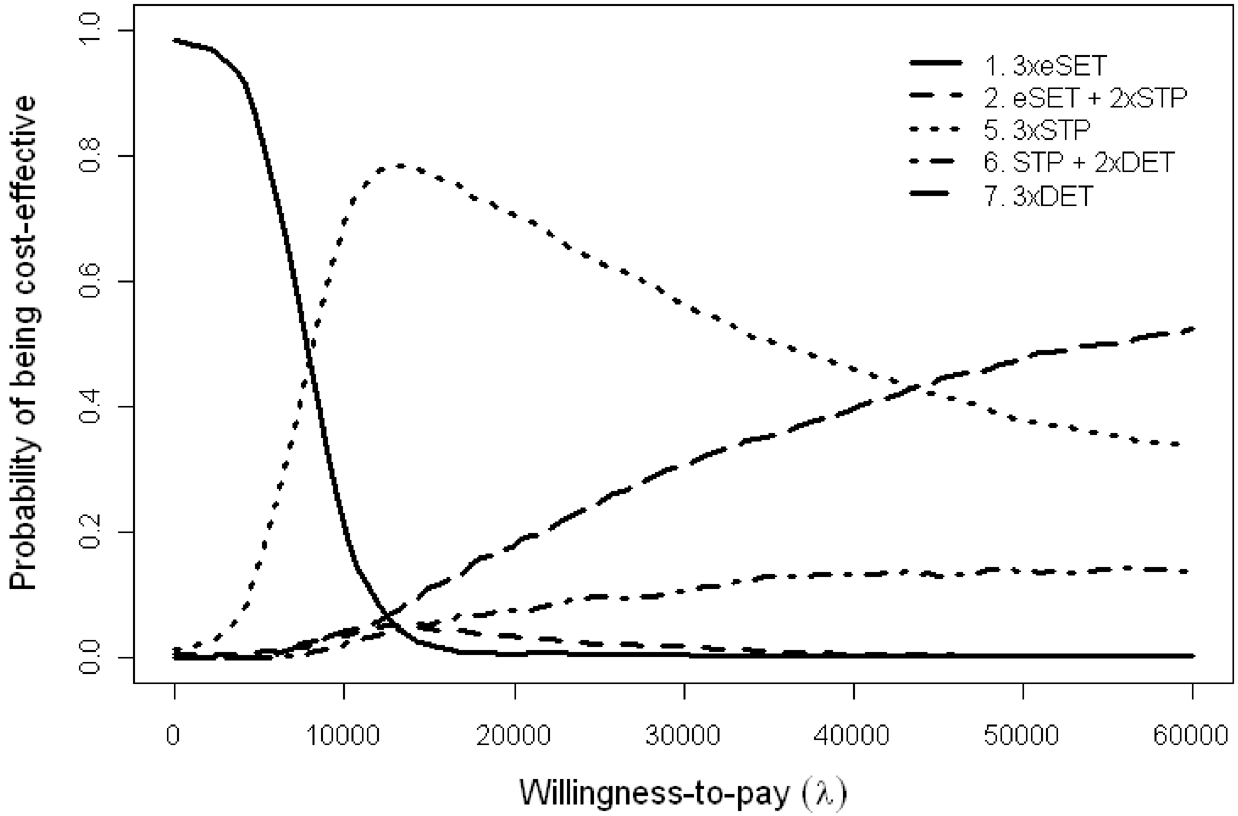
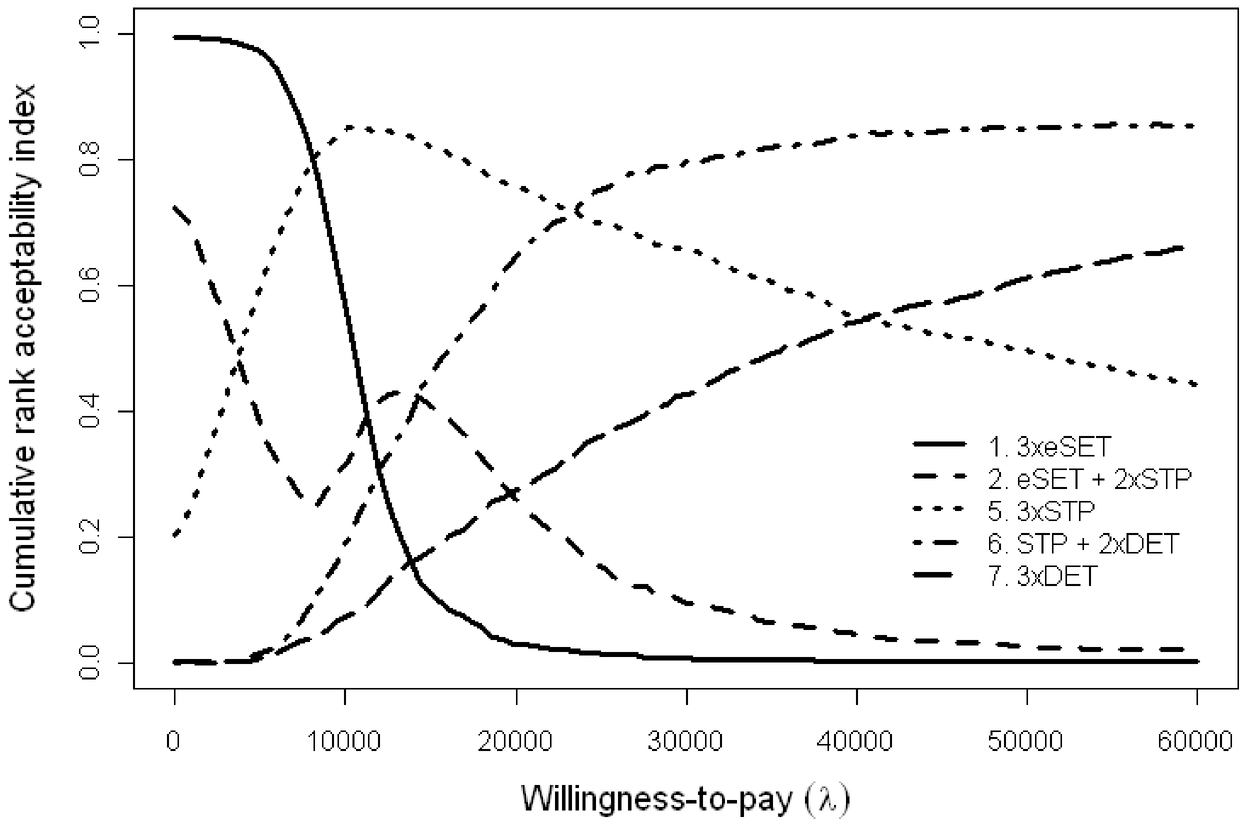
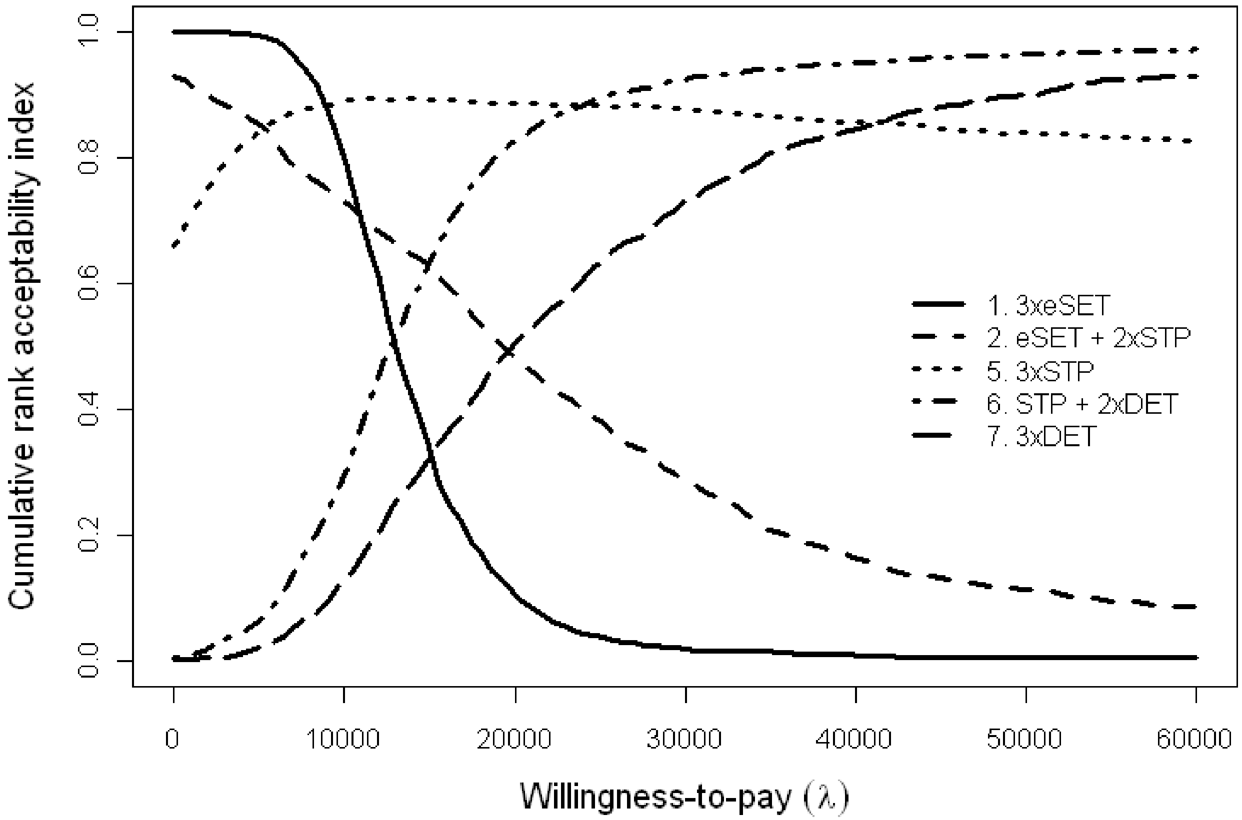
Cost-effectiveness acceptability curves



Cumulative rank acceptability curves for ranks 1 and 2



Cumulative rank acceptability curves for ranks 1, 2, and 3



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Discussion

- When the value of λ is established a priori of the CEA, the general concensus is that a decision maker should select the alternative with the highest expected NMB

  => The rank acceptability indices can be used to provide a complete picture of the uncertainty surrounding the treatment selection decision

- In many real-life decision problems, the value of λ is not exactly known by the decision maker

  => The cumulative rank acceptability indices can be used to identify compromise alternatives that have reasonable cost-effectiveness profiles across wide λ ranges

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Conclusion

- By describing an intervention’s rank distribution, the SMAA-CEA descriptive indices provide a complete picture of the uncertainty surrounding the cost-effectiveness decision problem
- We therefore believe that the (cumulative) rank acceptability curves will be a useful extension of the CEAC, which only provides information on the probability that a given intervention is the optimal one

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