Isaac Newton Institute for Mathematical Sciences

Design of Experiments in Healthcare

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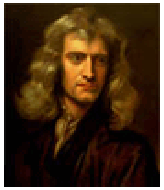

The Usefulness of Bayesian Optimal Designs for Discrete Choice Experiments

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Outline

1. Motivating example from healthcare
   - Multinomial logit model and Bayesian D-optimality
2. Design comparison study
   - Bayesian versus utility-neutral

Healthcare system preference study

- To measure people's preferences for changes in the healthcare system due to care payment system effects
- Four types of respondents:
  1. Individual care providers
  2. Provider organizations' executives
  3. Policy makers
  4. Healthcare experts
- In Europe, US, Canada, Australia and New Zealand
- Led by the Center for Health Services and Nursing Research of the Catholic University of Leuven

11 healthcare system performance domains

1. Clinical effectiveness and patient safety
2. Best practice of service use
3. Care equity
4. Care coordination, teamwork and continuity
5. Patient centeredness
6. Timeliness
7. ST cost containment and budget safety
8. LT cost containment and budget safety
9. Provider wellness
10. Innovation
11. Gaming the system

Choice set with partial profiles

Change to your current healthcare system performance due to payment system effects	
Situation A	Situation B
Improved level of care equity (avoiding care variation between patients with equal needs)	Current level of care equity (avoiding care variation between patients with equal needs)
Current level of care coordination, teamwork and continuity	Deteriorated level of care coordination, teamwork and continuity
Improved level of timeliness (avoiding waiting and delays)	Deteriorated level of timeliness (avoiding waiting and delays)
Deteriorated level of patient centeredness (respecting preferences and values)	Improved level of patient centeredness (respecting preferences and values)
Deteriorated level of short term cost containment and budget safety	Current level of short term cost containment and budget safety

Prior beliefs about attributes

RANK	PERFORMANCE DOMAIN
1	Clinical effectiveness and patient safety
2	Best practice of service use
	LT cost containment and budget safety
3	Gaming the system
	Care equity
	Care coordination, teamwork and continuity
4	Timeliness
	Patient centeredness
	Innovation
	Provider wellness
	ST cost containment and budget safety

Prior beliefs about attribute levels

RANK	OUTCOME IN A PERFORMANCE DOMAIN
1	Positive
	V
2	No change or neutral
	V
	V
3	Negative

People are loss averse!

Multinomial logit model

- Based on the random utility model

$$U_{js} = \mathbf{x}'_{js}\boldsymbol{\beta} + \varepsilon_{js}$$

  - □ U_{js} is the utility that a respondent attaches to alternative *j* in choice set *s*
  - □ $\mathbf{x}_{js}$ is a *k* x 1 vector containing the attribute levels of alternative *j* in choice set *s*
  - □ $\boldsymbol{\beta}$ is a *k* x 1 vector of parameter values or *part-worths*
  - □ ε_{js} is the IID Gumbel error term

Multinomial logit model

- Multinomial / conditional logit probability that a respondent chooses alternative *j* in choice set *s*:

$$p_{js}\begin{pmatrix}\text{option } j \text{ chosen} \\ \text{in choice set } s\end{pmatrix} = \frac{e^{\mathbf{x}'_{js}\boldsymbol{\beta}}}{\sum_{t=1}^{J} e^{\mathbf{x}'_{ts}\boldsymbol{\beta}}}$$

Information matrix **M**

- Optimal choice designs maximize a function of

$$\mathbf{M}(\mathbf{X},\boldsymbol{\beta}) = \sum_{s=1}^{S} \mathbf{X}_s' \left(\mathbf{P}_s(\boldsymbol{\beta}) - \mathbf{p}_s(\boldsymbol{\beta}) \mathbf{p}_s'(\boldsymbol{\beta}) \right) \mathbf{X}_s$$

To maximize the information in **M**, we need values for the parameter vector **β**. However, **β** is unknown and the objective of the experiment is to find **β**!
→ CIRCULAR PROBLEM

Bayesian D-optimality

- For most design situations, the best approach is a Bayesian design strategy in which we specify a prior parameter distribution $\pi(\boldsymbol{\beta})$ and then find the best design on average over this distribution
- The Bayesian D-optimal design has the largest average D-criterion value
- Methodology introduced in the choice design literature by Sándor and Wedel (2001)

Bayesian D-optimality

- The Bayesian D-optimal design maximizes

$$D_B(\mathbf{X}) = \int_{\Re^k} \log\left|\mathbf{M}(\mathbf{X},\boldsymbol{\beta})\right| \pi(\boldsymbol{\beta}) d\boldsymbol{\beta}$$

  - In our computations, we assume $\pi(\boldsymbol{\beta}) = N(\boldsymbol{\beta} \mid \boldsymbol{\beta}_0, \boldsymbol{\Sigma}_0)$
  - We solve the integral using the fast quadrature scheme proposed by Gotwalt, Jones and Steinberg (2009)

Reflection on the prior mean

RANK	PERFORMANCE DOMAIN	-
1	Clinical effectiveness and patient safety	-0.6
2	Best practice of service use	-0.4
	LT cost containment and budget safety	-0.4
3	Gaming the system	-0.35
	Care equity	-0.35
	Care coordination, teamwork and continuity	-0.35
4	Timeliness	-0.3
	Patient centeredness	-0.3
	Innovation	-0.3
	Provider wellness	-0.3
	ST cost containment and budget safety	-0.3

Reflection on the prior mean

RANK	PERFORMANCE DOMAIN	-	N	+
1	Clinical effectiveness and patient safety	-0.6	0.1	0.5
2	Best practice of service use	-0.4	0.05	0.35
	LT cost containment and budget safety	-0.4	0.05	0.35
3	Gaming the system	-0.35	0.05	0.3
	Care equity	-0.35	0.05	0.3
	Care coordination, teamwork and continuity	-0.35	0.05	0.3
4	Timeliness	-0.3	0.05	0.25
	Patient centeredness	-0.3	0.05	0.25
	Innovation	-0.3	0.05	0.25
	Provider wellness	-0.3	0.05	0.25
	ST cost containment and budget safety	-0.3	0.05	0.25

Prior mean

$$\boldsymbol{\beta}_0 = [-0.6, 0.1\ \ , -0.4, 0.05, -0.4, 0.05, -0.35, 0.05, -0.35, 0.05, -0.35, 0.05,$$

$$-\ 0.3, 0.05, -0.3, 0.05, -0.3, 0.05, -0.3\ \ , 0.05, -0.3\ \ , 0.05]'$$

Reflection on the prior variance

RANK	PERFORMANCE DOMAIN	N	+
1	Clinical effectiveness and patient safety	0.1	0.5
2	Best practice of service use	0.05	0.35
	LT cost containment and budget safety	0.05	0.35
3	Gaming the system	0.05	0.3
	Care equity	0.05	0.3
	Care coordination, teamwork and continuity	0.05	0.3
4	Timeliness	0.05	0.25
	Patient centeredness	0.05	0.25
	Innovation	0.05	0.25
	Provider wellness	0.05	0.25
	ST cost containment and budget safety	0.05	0.25

Reflection on the prior variance

RANK	PERFORMANCE DOMAIN	N	+	Std.
1	Clinical effectiveness and patient safety	0.1	0.5	0.3
2	Best practice of service use	0.05	0.35	0.25
	LT cost containment and budget safety	0.05	0.35	0.25
3	Gaming the system	0.05	0.3	0.2
	Care equity	0.05	0.3	0.2
	Care coordination, teamwork and continuity	0.05	0.3	0.2
4	Timeliness	0.05	0.25	0.15
	Patient centeredness	0.05	0.25	0.15
	Innovation	0.05	0.25	0.15
	Provider wellness	0.05	0.25	0.15
	ST cost containment and budget safety	0.05	0.25	0.15

Prior variance

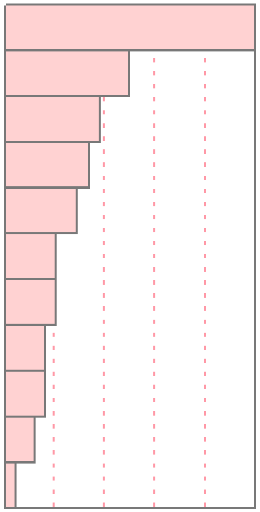
$$\Sigma_0 = \begin{bmatrix}
0.09 & -0.05 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & 0.09 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & 0.06 & -0.03 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & 0.06 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & 0.06 & -0.03 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & 0.06 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & 0.04 & -0.02 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & 0.04 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & 0.04 & -0.02 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & 0.04 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & 0.04 & -0.02 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & 0.04 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & 0.02 & -0.01 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & & 0.02 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & & & 0.02 & -0.01 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & & & & 0.02 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & & & & & 0.02 & -0.01 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & & & & & & 0.02 & 0 & 0 & 0 & 0 \\
 & & & & & & & & & & & & & & & & & & 0.02 & -0.01 & 0 & 0 \\
 & & & & & & & & & & & & & & & & & & & 0.02 & 0 & 0 \\
 & & & & & & & & & & & & & & & & & & & & 0.02 & -0.01 \\
 & & & & & & & & & & & & & & & & & & & & & 0.02
\end{bmatrix}$$

Bayesian D-optimal design

- Partial profile design consisting of 3 surveys or blocks of 18 choice sets each
- Brief data analysis results from 547 respondents:

Effect Likelihood Ratio Tests

Source	L-R ChiSquare	DF	Prob>ChiSq
effect_safety	993.705	2	<.0001*
providerwellness	500.745	2	<.0001*
LTCost	377.611	2	<.0001*
under_overuse	342.350	2	<.0001*
coordination	288.016	2	<.0001*
innovation	206.305	2	<.0001*
patientcenter	201.577	2	<.0001*
gaming	165.635	2	<.0001*
timeliness	159.013	2	<.0001*
equity	118.336	2	<.0001*
STCost	48.433	2	<.0001*



Design comparison study

- Is it worth the effort generating a Bayesian D-optimal design?
- Producing a utility-neutral optimal design would be easier and less computationally demanding
- Does design matter???
- **YES, IT DOES!!!**
- Cfr. our discussion paper in Applied Stochastic Models in Business and Industry (2011)

Bayesian D-optimal design

	Bayesian design					
Choice set	Attributes					
	1	2	3	4	5	6
1	1	2	2	2	1	2
1	2	1	1	1	2	1
2	2	2	1	1	1	2
2	1	1	2	2	2	1
3	1	2	2	1	2	1
3	2	1	1	2	1	2
4	1	2	1	2	2	1
4	2	1	2	1	1	2
5	1	2	2	2	1	2
5	2	1	2	1	2	2
6	1	1	1	2	2	2
6	2	2	2	1	1	1
7	2	1	2	2	1	1
7	1	2	1	1	2	2
8	1	1	2	1	1	2
8	2	2	1	2	2	1

$N\left(\boldsymbol{\beta} \mid \boldsymbol{\beta}_0, 0.4^2 \times \mathbf{I_6}\right)$ with

$\boldsymbol{\beta}_0 = \left[-0.8, -0.4, -0.8, -0.4, -0.8, -0.8\right]'$

Utility-neutral optimal design

	2^{6-2} factorial					
Choice set	Attributes 1	2	3	4	5	6
1	1	2	2	1	1	2
1	2	1	1	2	2	1
2	1	2	2	2	1	1
2	2	1	1	1	2	2
3	2	1	2	2	1	2
3	1	2	1	1	2	1
4	1	1	1	2	1	2
4	2	2	2	1	2	1
5	1	2	1	2	2	2
5	2	1	2	1	1	1
6	2	2	1	2	1	1
6	1	1	2	1	2	2
7	1	1	2	2	2	1
7	2	2	1	1	1	2
8	1	1	1	1	1	1
8	2	2	2	2	2	2

Orthogonally blocked 2^{6-2} fractional factorial design with implied prior mean

$$\boldsymbol{\beta}_Z = [0,0,0,0,0,0]'$$

Simulation study

- Starting from the true parameter

$$\boldsymbol{\beta}_t = [-0.8, 0, -0.8, 0, -0.8, 0]'$$

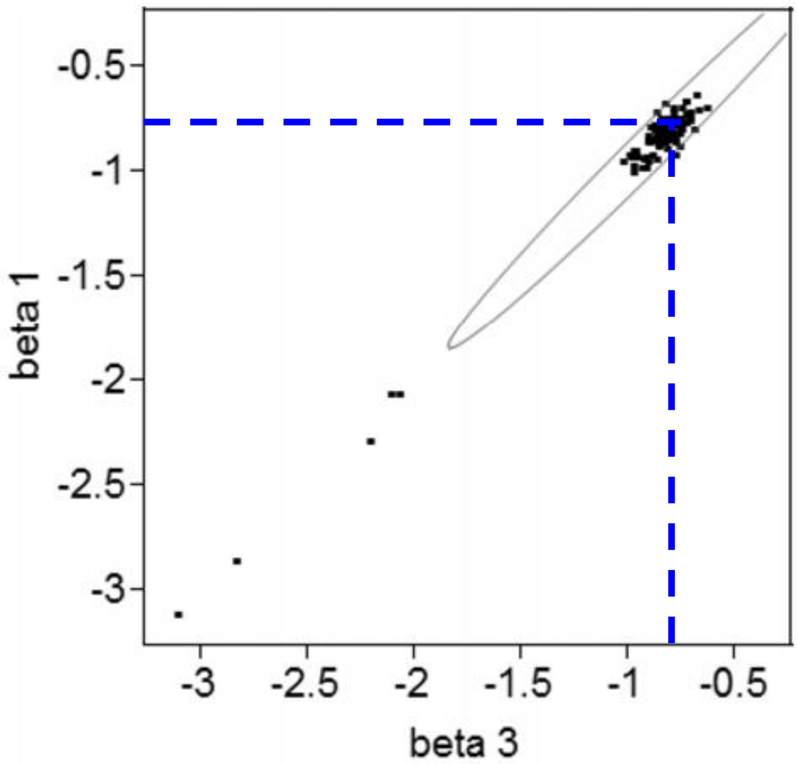
→ prior mean values of Bayesian design

→ prior mean values of utility-neutral design

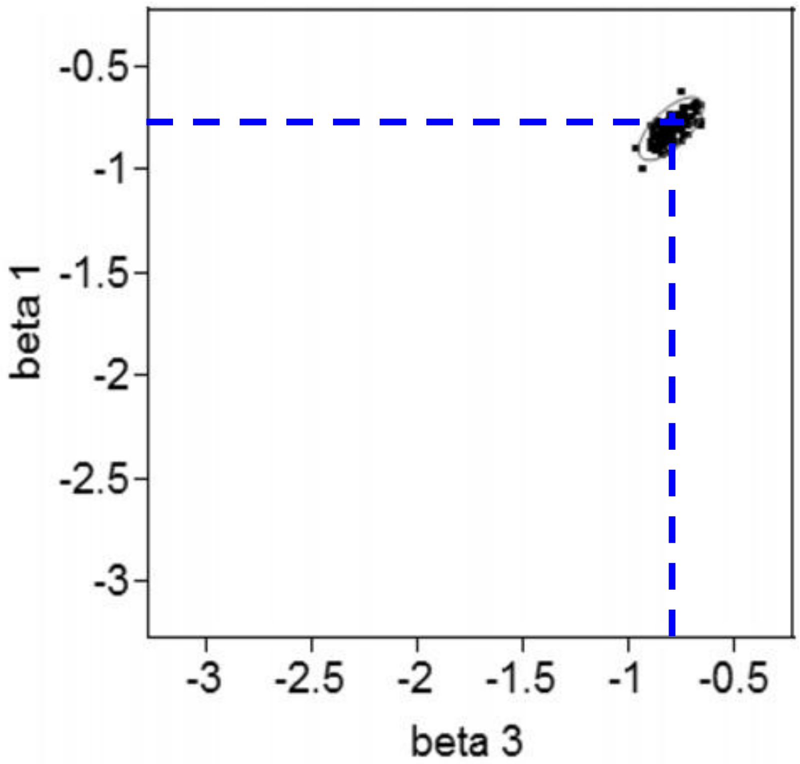
- For each design, we simulated 100 datasets with choices from 200 respondents
- We estimated the parameter values for each dataset

Estimates for $\boldsymbol{\beta}_{t1} = \boldsymbol{\beta}_{t3} = -0.8$

Utility-neutral design

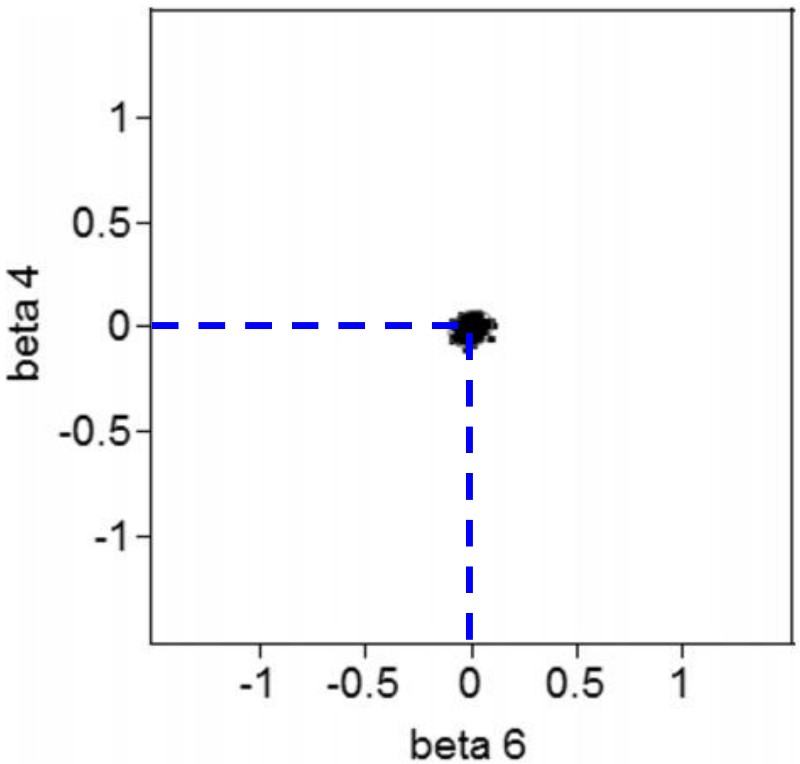


Bayesian design

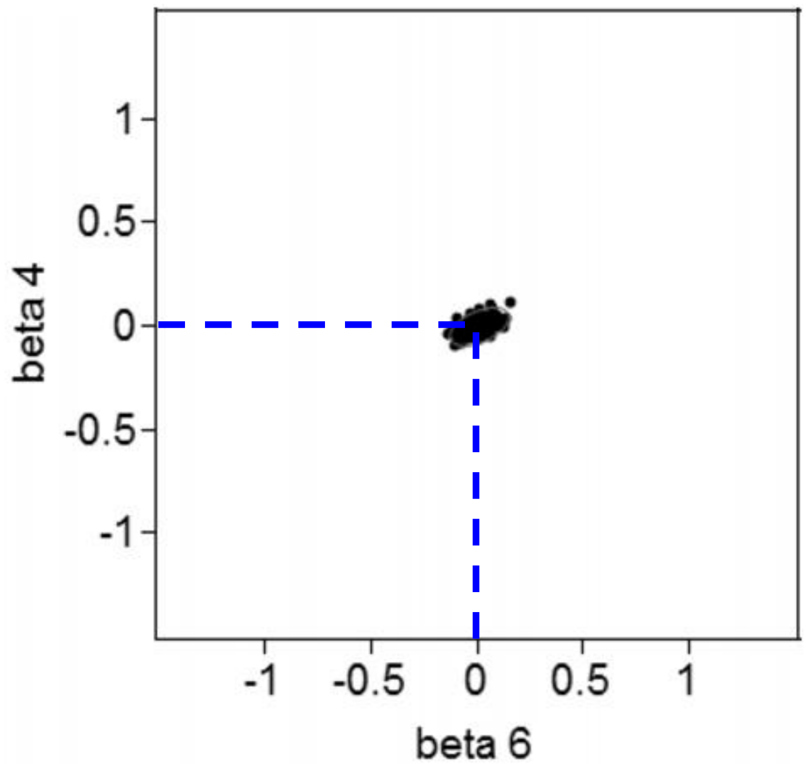


Estimates for $\boldsymbol{\beta}_{t4} = \boldsymbol{\beta}_{t6} = 0$

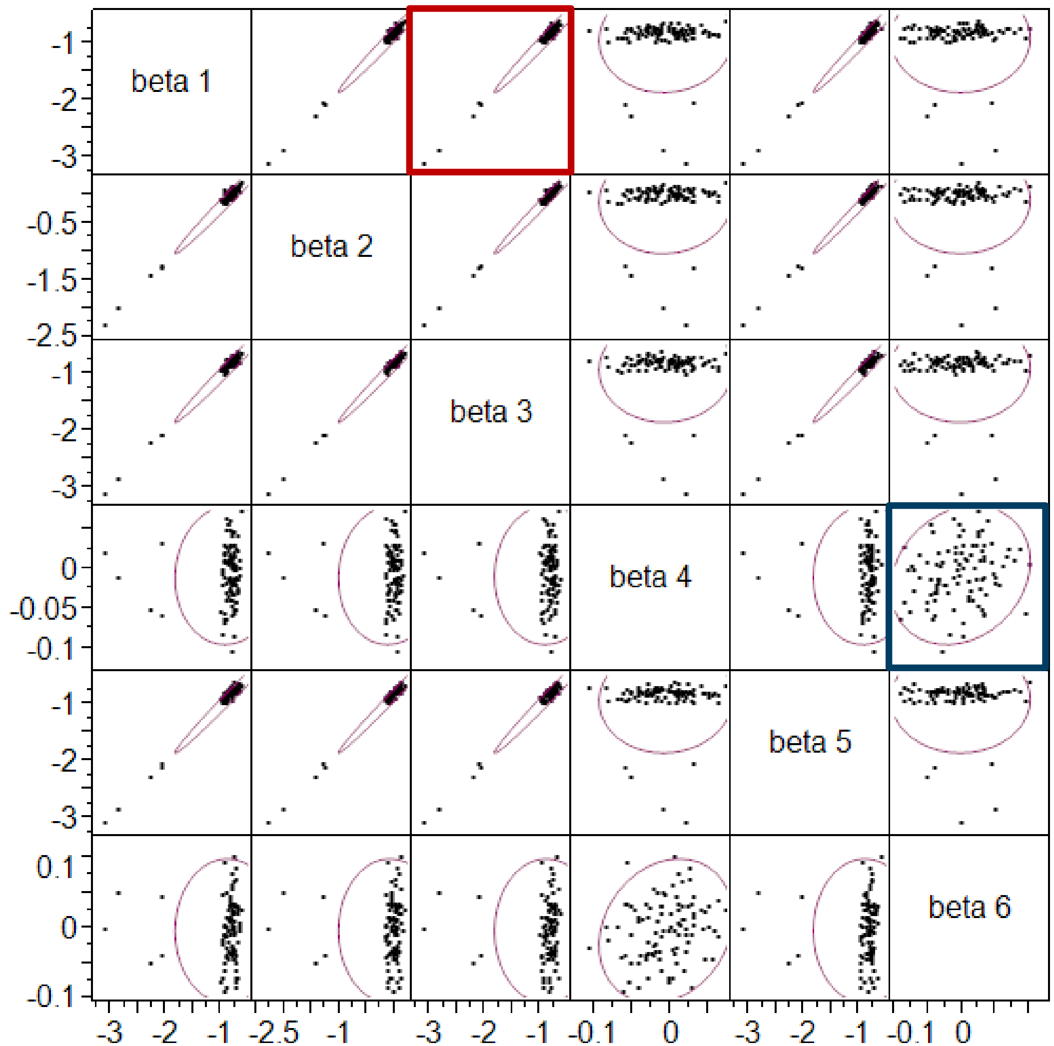
Utility-neutral design



Bayesian design



Utility-neutral design estimates



Variance-covariance matrix

Utility-neutral design

	$\hat{\beta}_{t1}$	$\hat{\beta}_{t2}$	$\hat{\beta}_{t3}$	$\hat{\beta}_{t4}$	$\hat{\beta}_{t5}$	$\hat{\beta}_{t6}$
$\hat{\beta}_{t1}$	0.14869	0.14565	0.14550	0.00059	0.14600	0.00003
$\hat{\beta}_{t2}$	0.14565	0.14551	0.14432	0.00063	0.14472	-0.00003
$\hat{\beta}_{t3}$	0.14550	0.14432	0.14530	0.00030	0.14418	0.00008
$\hat{\beta}_{t4}$	0.00059	0.00063	0.00030	0.00130	0.00047	0.00030
$\hat{\beta}_{t5}$	0.14600	0.14472	0.14418	0.00047	0.14590	-0.00001
$\hat{\beta}_{t6}$	0.00003	-0.00003	0.00008	0.00030	-0.00001	0.00178

Variance-covariance matrix

Bayesian design

	$\hat{\beta}_{t1}$	$\hat{\beta}_{t2}$	$\hat{\beta}_{t3}$	$\hat{\beta}_{t4}$	$\hat{\beta}_{t5}$	$\hat{\beta}_{t6}$
$\hat{\beta}_{t1}$	0.00389	0.00159	0.00260	0.00119	0.00324	0.00275
$\hat{\beta}_{t2}$	0.00159	0.00222	0.00171	0.00083	0.00131	0.00150
$\hat{\beta}_{t3}$	0.00260	0.00171	0.00386	0.00112	0.00323	0.00253
$\hat{\beta}_{t4}$	0.00119	0.00083	0.00112	0.00142	0.00069	0.00108
$\hat{\beta}_{t5}$	0.00324	0.00131	0.00323	0.00069	0.00496	0.00310
$\hat{\beta}_{t6}$	0.00275	0.00150	0.00253	0.00108	0.00310	0.00329

Mean estimates

	Utility-neutral
$E\left(\hat{\beta}_{t1}\right)$	**-0.90793**
$E\left(\hat{\beta}_{t2}\right)$	**-0.09679**
$E\left(\hat{\beta}_{t3}\right)$	**-0.90846**
$E\left(\hat{\beta}_{t4}\right)$	**-0.00685**
$E\left(\hat{\beta}_{t5}\right)$	**-0.90988**
$E\left(\hat{\beta}_{t6}\right)$	**-0.00318**

Mean estimates

	Utility-neutral	Bayesian
$E\left(\hat{\beta}_{t1}\right)$	**-0.90793**	-0.80266
$E\left(\hat{\beta}_{t2}\right)$	**-0.09679**	0.00022
$E\left(\hat{\beta}_{t3}\right)$	**-0.90846**	-0.80376
$E\left(\hat{\beta}_{t4}\right)$	-0.00685	-0.00327
$E\left(\hat{\beta}_{t5}\right)$	**-0.90988**	-0.80328
$E\left(\hat{\beta}_{t6}\right)$	-0.00318	0.01100

Problem with utility-neutral design

	2^{6-2} factorial					
Choice set	Attributes					
	1	2	3	4	5	6
1	1	2	2	1	1	2
1	2	1	1	2	2	1
2	1	2	2	2	1	1
2	2	1	1	1	2	2
3	2	1	2	2	1	2
3	1	2	1	1	2	1
4	1	1	1	2	1	2
4	2	2	2	1	2	1
5	1	2	1	2	2	2
5	2	1	2	1	1	1
6	2	2	1	2	1	1
6	1	1	2	1	2	2
7	1	1	2	2	2	1
7	2	2	1	1	1	2
8	1	1	1	1	1	1
8	2	2	2	2	2	2

$$\boldsymbol{\beta}_t = [-0.8, 0, -0.8, 0, -0.8, 0]'$$

$$p_1\left(\begin{array}{c}\text{profile 1 chosen}\\ \text{in choice set 4 or 8}\end{array}\right) = \frac{e^{-2.4}}{e^{-2.4}+e^{2.4}} = \mathbf{0.0082}$$

$$p_2\left(\begin{array}{c}\text{profile 2 chosen}\\ \text{in choice set 4 or 8}\end{array}\right) = \frac{e^{2.4}}{e^{-2.4}+e^{2.4}} = \mathbf{0.9918}$$

Separation problem

- Probability that all 200 respondents choose profile 2 in choice sets 4 and 8 is $(0.9918)^{400}$ = **0.0377!**
- So, in 3.77% of the simulated datasets, choice sets 4 and 8 are not informative
- In these cases, a separation problem occurs and the maximum likelihood estimates do not exist

Conclusion

- Utility-neutral designs consist of choice sets with dominating profiles which can lead to separation problems
- Also Bayesian D-optimal designs may contain dominating profiles in certain instances, especially in instances involving only a few attributes, but their occurrence can be limited by a proper choice for the prior distribution

?