



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# Evaluating methods to capture stakeholder preferences

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MACBETH: A Non-numerical Method for Eliciting Preferences

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EMA/UMCG Collaboration

An agency of the European Union





# Acknowledgements

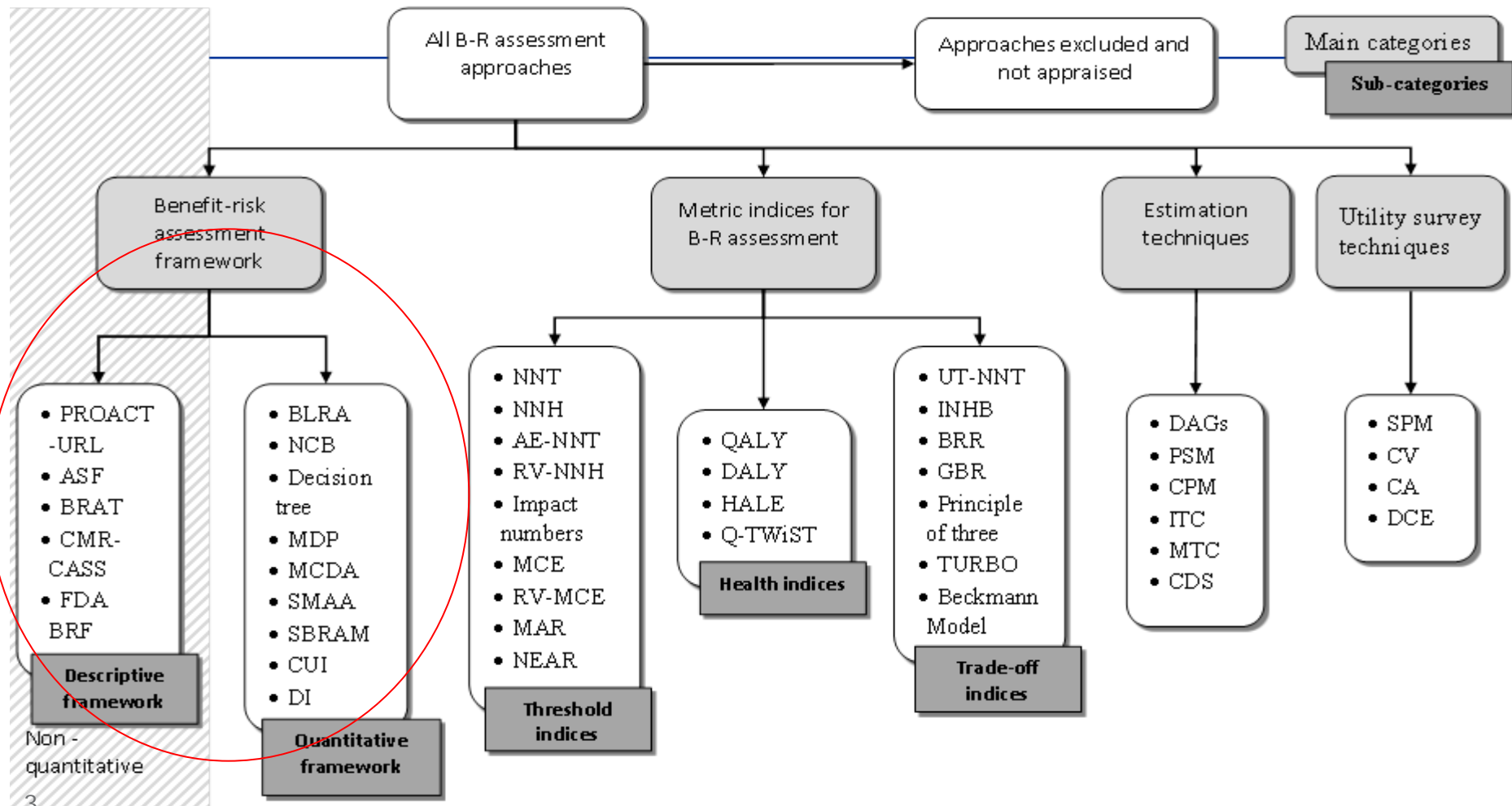
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IMI-PROTECT WP5

Prof. Carlos Bana e Costa



# WP5- Benefit-Risk Methodologies





# Example Effects Table: Raptiva

	Name	Description	Fixed Upper	Fixed Lower	Units	Raptiva	Placebo
Favourable Effects	PASI75	Percentage of patients achieving 75% reduction in baseline PASI <sup>1</sup> at week 12.	60.0	0.0	%	29.5	2.7
	PASI50	Percentage of patients achieving 50% reduction in baseline PASI <sup>1</sup> at week 12.	60.0	0.0	%	54.9	16.7
	PGA	Percentage of patients achieving Physician's Global Assessment <sup>2</sup> clear/almost clear at week12.	40.0	0.0	%	295	5.1
	OLS	Percentage of patients with Overall Lesion Severity rating of minimal or clear at FT (day 84).	40.0	0.0	%	32.1	2.9
	DLQI	Dermatology Life Quality Index <sup>3</sup> . Mean percentage of patients showing an improvement.	10.0	0.0	Change score	5.8	2.1
Unfavourable Effects	AEs	Percentage of patients exhibiting injection site reactions, mild to moderate dose-related acute flu like symptoms.	50.0	20.0	%/100ptyrs	41.0	24.0
	Severe infections	Proportion of patients experiencing infections serious enough to require hospitalisation.	3.00	0.00	%/100ptyrs	2.83	1.4
	Severe Thrombocytopenia	Number of cases exhibiting severe (grade 3 and above) thrombocytopenia <sup>4</sup> .	10	0	number	9	0
	Psoriasis Severe Forms	Percentage of patients developing severe forms of psoriasis (erythrodermic, pustular).	4.0	0.0	%	3.2	1.4
	Hypersensitivity Reactions	Percentage of patients exhibiting hypersensitivity reactions, arthralgia, psoriatic arthritis, flares, back pain asthenia, ALT and Ph. Alk increase.	10.0	0.0	%	5.0	0
	Interstitial Lung Disease	Number of cases of interstitial lung disease.	20	0	number	18	0
	Inflammatory Polyradiculopathy	Number of cases of inflammatory polyradiculopathy.	5	0	Data	4	0
	SAEs	Number of cases of haemolytic anemia.	25	0	number	24	0
	PML	Number of cases of progressive multifocal leukoencephalopathy.	5	0	number	3	0
	Aseptic Meningitis	Number of cases of aseptic meningitis.	30	0	number	29	0



# VALue and Utilities among European Patients: The VALUE Study

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## Objective:

- to evaluate the use of the MACBETH (**M**easuring **A**ttractiveness through a **C**ategorical **B**ased **E**valuation) software for the elicitation of patient preferences
  - determine value functions for treatment outcomes
  - assess weights between treatment outcomes (trade-offs)

## Design

- Web-based study among Multiple Sclerosis (MS) patients using select number of treatment outcomes
- Supported by the UK MS Society whose members (patients) were invited to participate



# Example of treatment outcomes and levels in MS Study

<b>Treatment Outcomes</b>	<b>Levels</b>
Number of relapses during next 5 years	No relapse
	1 relapse
	2 relapses
	3 relapses
	4 relapses
Time (from today) until your disease worsens	8 years
	5 years
	3 years
	1 year
Chance of dying from liver failure within 10 years	None would die
	5 patients out of 1000
	20 patients out of 1000
	50 patients out of 1000
Chance of dying or severe disability from PML within 10 years	None would die
	5 patients out of 1000
	20 patients out of 1000
	50 patients out of 1000
Chance of dying from leukemia within 10 years	None would die
	5 patients out of 1000
	20 patients out of 1000
	50 patients out of 1000

Question number:

1 2 3 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

What is the difference in attractiveness between:

**“having no relapses in the next 5 years compared to 1 relapse in the next 5 years?”**

- extreme
- very strong
- strong
- moderate
- weak
- Very weak
- no

Question number:

1 2 3 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

What is the difference in attractiveness between:

**'having 1relapse in the next 5 years compared to 2 relapses in the next 5 years?**

- extreme
- very strong
- strong
- moderate
- weak
- Very weak
- no



Question number:

1 2 3 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

What is the difference in attractiveness between:

**'having 2 relapses in the next 5 years compared to 3 relapses in the next 5 years?'**

- extreme
- very strong
- strong
- moderate
- weak
- Very weak
- no

Question number:

1 2 3 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

What is the difference in attractiveness between:

**'having 3 relapses in the next 5 years compared to 4 relapses in the next 5 years?'**

- extreme
- very strong
- strong
- moderate
- weak
- Very weak
- no



Define Criteria

Define Scales

Weight Criteria

Define Options

Evaluate Options

Analyze Results

- Add Reference
- Edit Reference
- Delete Reference
- Get Goal
- Get Neutral
- Get Scale
- Edit Scale
- Propose Scale

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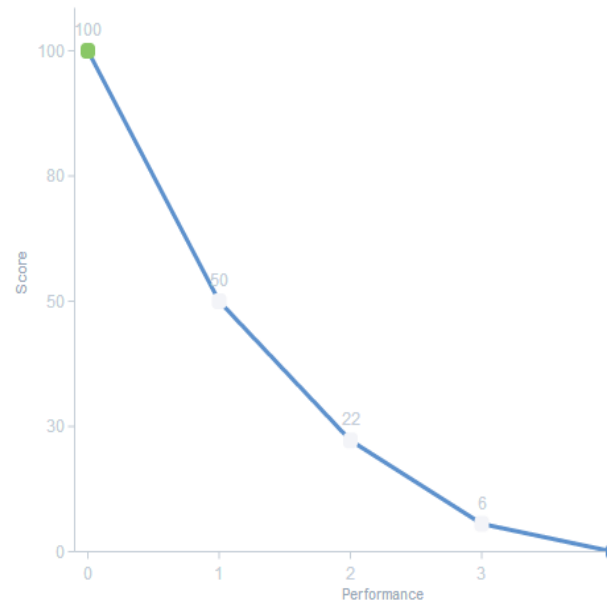
### Judgements matrix

Judgements of comparison between each pair of

	1	2	3	4
0	Extreme	Extreme	Extreme	Extreme
1		Very Strong	Very Strong	Extreme
2			Moderate	Strong
3				Very Weak

### Value Function

Local impacts and scores for both references and options on the selected criterion

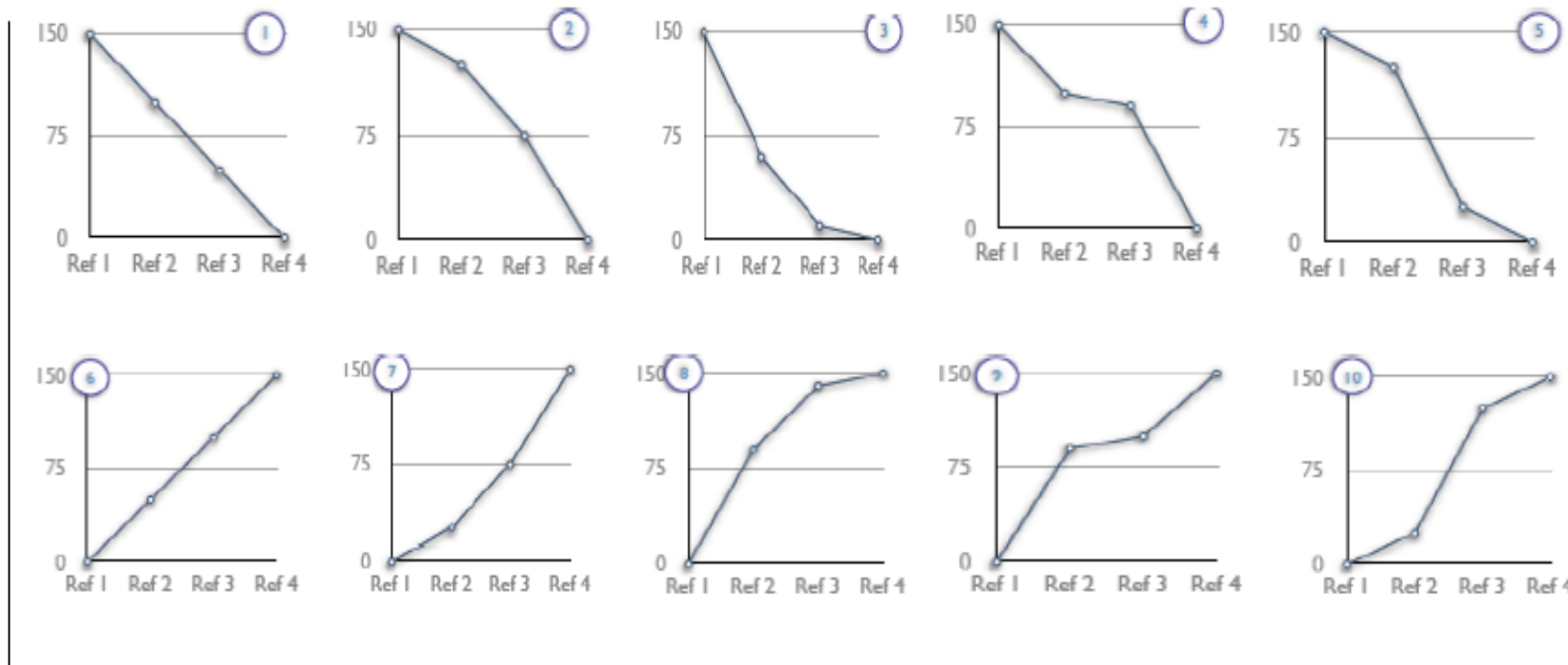


### Mathematical expression

$$Y = \begin{cases} -50 * x + 100 & \leq 0 < x < 1 \\ -27.78 * x + 77.78 & \leq 1 < x < 2 \\ -16.66 * x + 55.54 & \leq 2 < x < 3 \\ -5.56 * x + 22.24 & \leq 3 < x < 4 \end{cases}$$



# Value Function Profiles



Value functions will fit one of these 10 profiles

Question number:

1 2 3 4 5 **6** 7 8 9 10

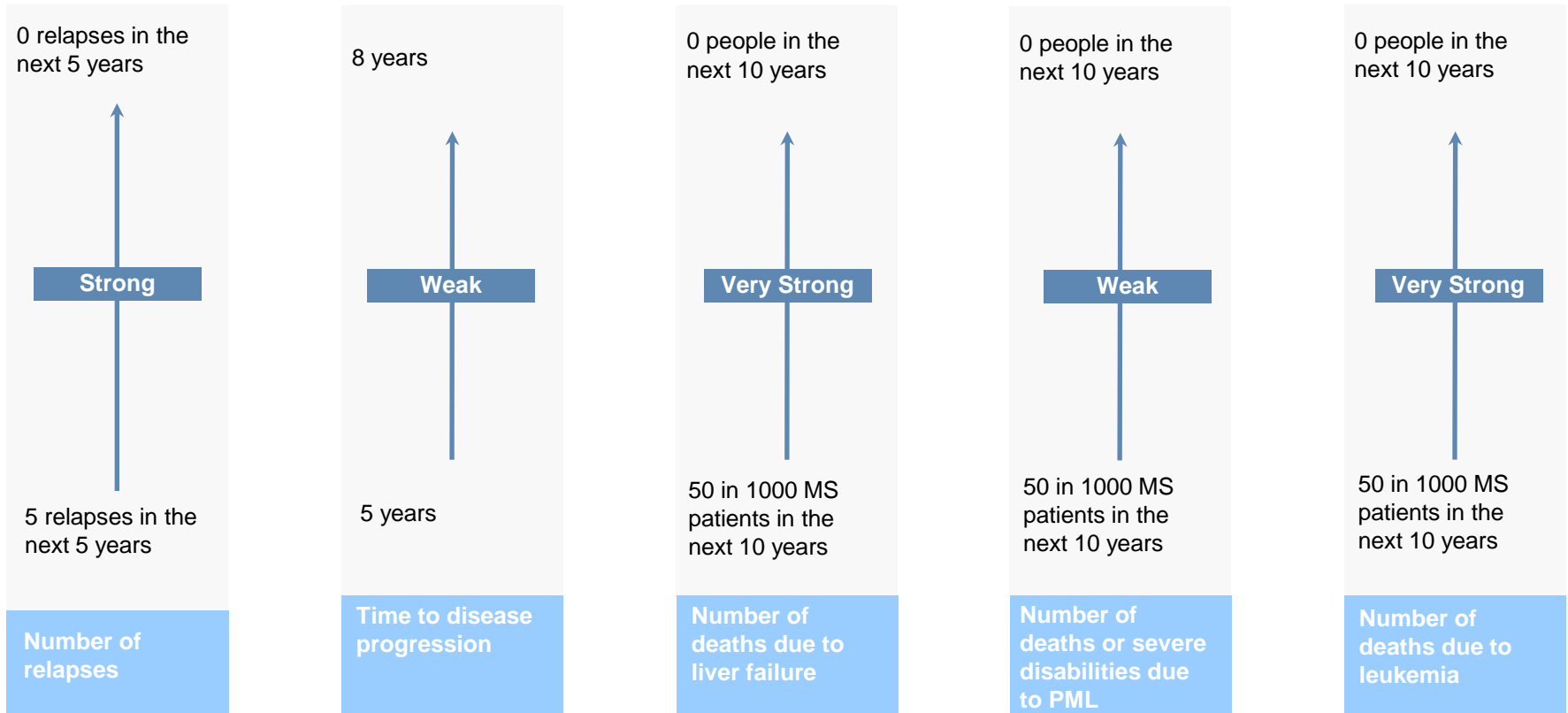
Previous

Next

Pause

Quit

If you confirm all these judgments, please press next to proceed.



Question number:

1 2 3 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

How desirable is this improvement ?

0 relapses in the next 5 years

5 relapses in the next 5 years

- extreme
- very strong
- strong
- moderate
- weak
- Very weak
- no

Number of relapses

8 years

5 years

Time to disease progression

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to liver failure

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths or severe disabilities due

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to leukemia

Question number:

1 2 3 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

How desirable is this improvement ?

0 relapses in the next 5 years

5 relapses in the next 5 years

Number of relapses

8 years

5 years

Time to disease progression

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to liver failure

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths or severe disabilities due

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to leukemia

**Strong**

- extreme
- very strong
- strong
- moderate
- weak
- Very weak
- no

Question number:

1 2 **3** 4 5 6 7 8 9 10

Previous

Next

Pause

Quit

How desirable is this improvement ?

0 relapses in the next 5 years

5 relapses in the next 5 years

Strong

Number of relapses

8 years

5 years

Weak

Time to disease progression

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to liver failure

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths or severe disabilities due

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to leukemia

extreme

very strong

strong

moderate

weak

Very weak

no



Question number:

1 2 3 **4** 5 6 7 8 9 10

Previous

Next

Pause

Quit

How desirable is this improvement ?

0 relapses in the next 5 years

Strong

5 relapses in the next 5 years

Number of relapses

8 years

Weak

5 years

Time to disease progression

0 people in the next 10 years

Very Strong

50 in 1000 MS patients in the next 10 years

Number of deaths due to liver failure

0 people in the next 10 years

extreme

very strong

strong

moderate

weak

Very weak

no

50 in 1000 MS patients in the next 10 years

Number of deaths or severe disabilities due to PML

0 people in the next 10 years

50 in 1000 MS patients in the next 10 years

Number of deaths due to leukaemia

Question number:

1 2 3 4 **5** 6 7 8 9 10

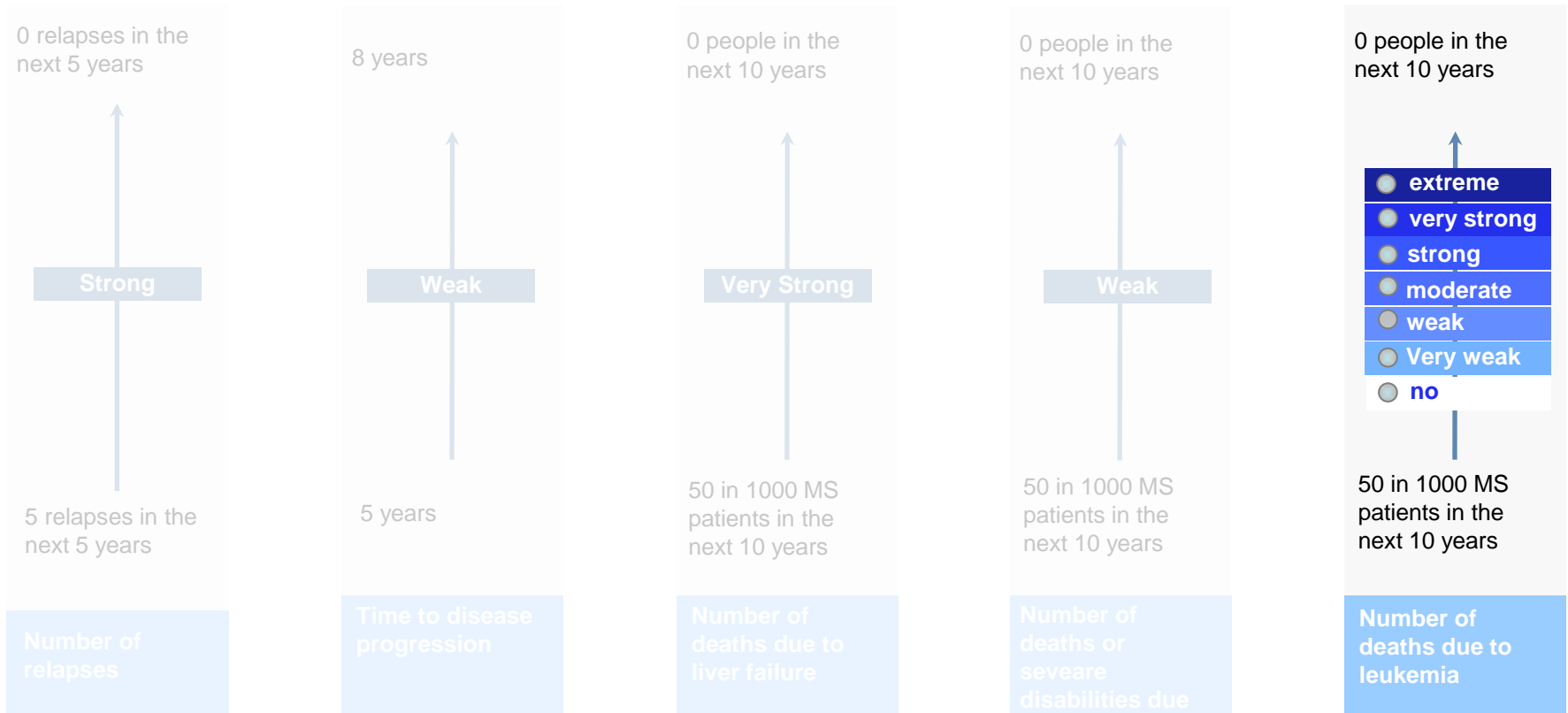
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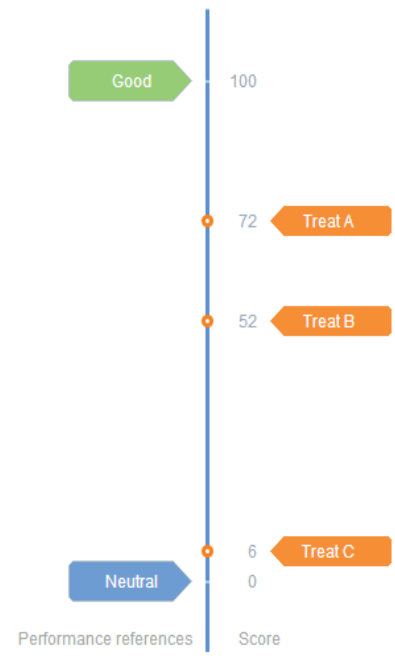
Quit

How desirable is this improvement ?



Global Results  
Table of global and partial scores for each option in each criteria

	Number of relapses	Time to disease prog	Disease progr...	Total
Good	100	100	100	100
Treat A	50	92	86	72
Treat B	6	89	100	52
Treat C	-6	11	29	6
Neutral	0	0	0	0
Weights	46%	38%	15%	



Results

Global results  
Tabela de pontuações globais e parciais para cada opção em cada fator de avaliação

Analysis

Profile Analysis  
Pontuações das opções em todos os fatores. Selecione a opção pretendida para ver o seu perfil. A seleção de duas opções permite ver a comparação entre as duas

Sensitivity Analysis  
Análise da sensibilidade dos resultados a variações nos pesos dos fatores



# Regression analysis of factors predictive of differences in preferences (value)

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- Disease severity
- Time since diagnosis
- Gender
- Age



## Main Results of the VALUE Study

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- Patients found the qualitative elicitation approach easy to follow and respond
- Majority of the patients had non-linear value functions for all treatment outcomes
- Preferences were predicted by severity of disease; ability to walk
  - Patients who could not walk indicated risk seeking profiles compared to other patients
- Data can be used to build decision models for actual treatments



# IMI-PROTECT PROJECT: Visualization and Preferences

Comprehension/  
Perception

Drug Vignette: Textual presentation  
of benefit-risk data from EPARs

Comprehension/  
Perception

Visual presentation of benefit and  
risks using tabular and other  
graphical formats

Elicitation of  
preferences for  
treatment  
outcomes

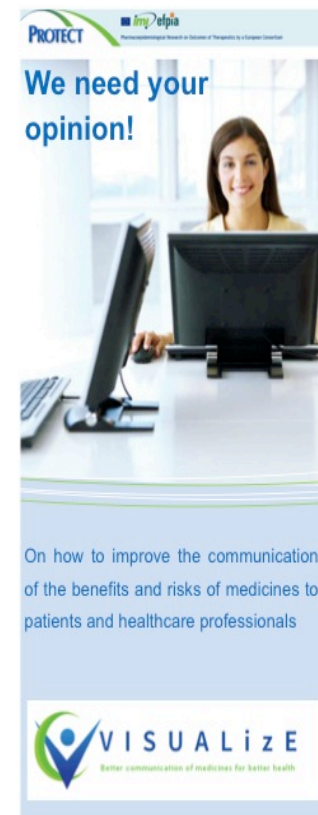
Discrete Choice  
Experiment

MCDA -  
MACBETH



# Visualizing Uncertainty Among Laypersons and Experts (VISUALize)

- Target for the study:  
patients, healthcare professionals and regulators
- 3 disease areas: atrial fibrillation, breast cancer, diabetes
- 3 countries: UK, France, the Netherlands









# Seeking support from Organizations

## **Patients**

European Heart Network

International Diabetes Federation

International Diabetes Trust

Europadonna

## **Healthcare Professionals**

European Association for the Study of  
Diabetes

European Society of Endocrinology

European Society of Medical Oncology

European Society of Cardiology

European Specialist Nurses  
Organization

Pharmaceutical Group of the European  
Union

European Association of Hospital  
Pharmacists

European Society of Oncology  
Pharmacists



## What are we asking them?

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- To liaise with their members (if membership-based)
- List of the appropriate organizations and their contact details
- To announce the study on the organization website
- To send an email to members with a link to the study website
- To liaise with us whenever their members have questions or need clarification



# What are we asking from other organizations?

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Details of any relevant patient or healthcare professional conferences where the study could be announced

Willing to host an announcement for the study on your organization's website

Contact information:

Project Lead: [a.r.m.beyer@umcg.nl](mailto:a.r.m.beyer@umcg.nl)

Project Manager: [t.hoekstra@umcg.nl](mailto:t.hoekstra@umcg.nl)