COMPARISON OF DIFFERENT BENEFIT-RISK METHODS

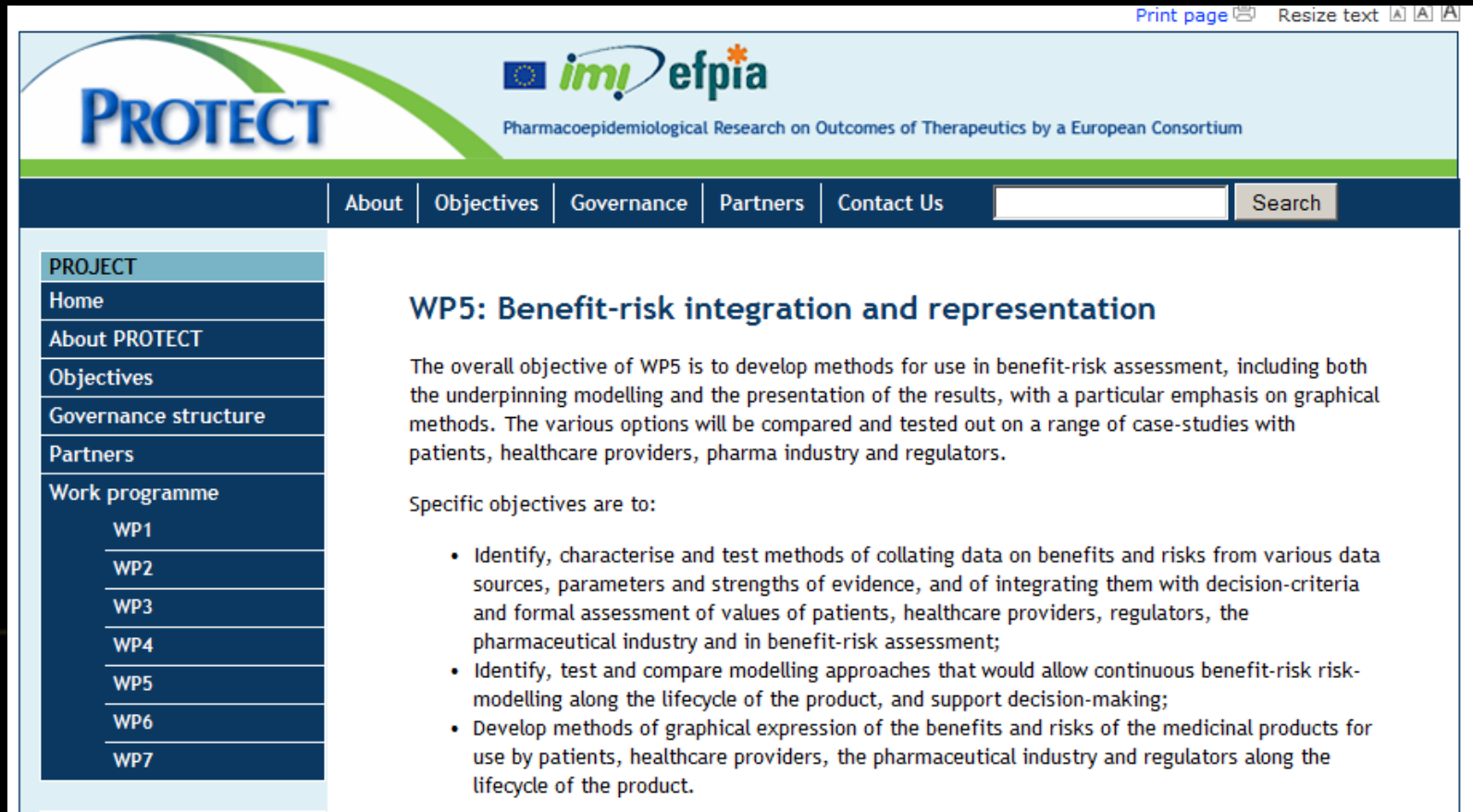
Johan Bring

Statisticon AB

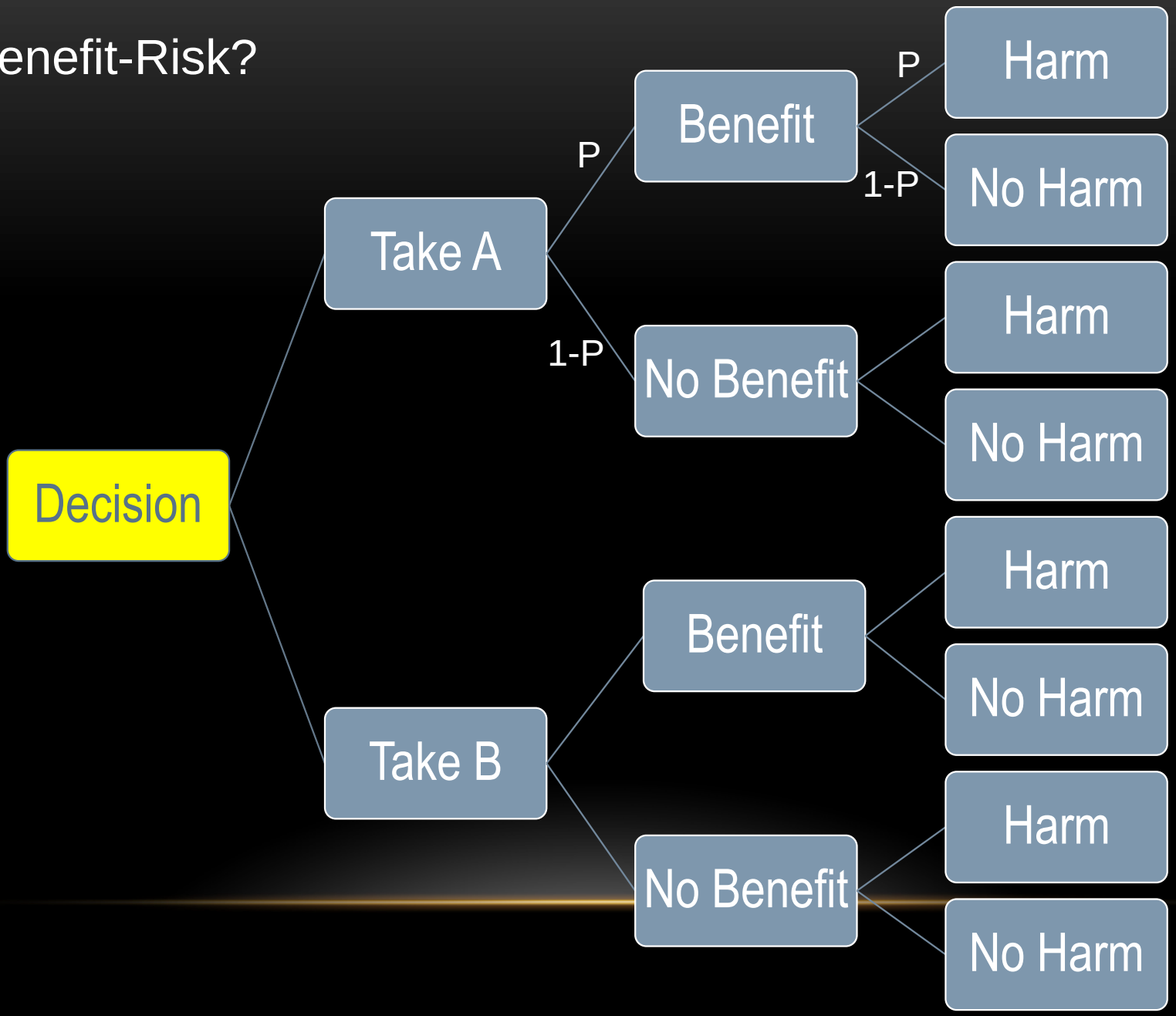
1. Consultant at Statisticon

2. Teach at the university programme:
Decision, Risk and Policy Analysis

3. Astra-Zeneca



Benefit-Risk?



METHODS

MCDA

NNT

BRAT

Impact numbers

PROACT

SMAA

BRR

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 August 2010
EMA/549682/2010 - Revision 1
Human Medicines Development and Evaluation

Benefit-risk methodology project

Work package 2 report: Applicability of current tools and processes for regulatory benefit-risk assessment

Volume 13 • Number 5 • 2010
VALUE IN HEALTH

A Review of Quantitative Risk–Benefit Methodologies for Assessing Drug Safety and Efficacy—Report of the ISPOR Risk–Benefit Management Working Group

Jeff J. Guo, PhD,[1] Swapnil Pandey, MS,[2] John Doyle, PhD,[3,4] Boyang Bian, MS,[1] Yvonne Lis, PhD,[4] Dennis W. Raisch, PhD[5]

[1]University of Cincinnati Health Academic Center, College of Pharmacy, Cincinnati, OH, USA; [2]Kendle International Inc., Cincinnati, OH, USA; [3]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA; [4]Centre for Socioeconomic Research, Welsh School of Pharmacy, Cardiff, UK; [5]University of New Mexico, College of Pharmacy, Albuquerque, NM, USA

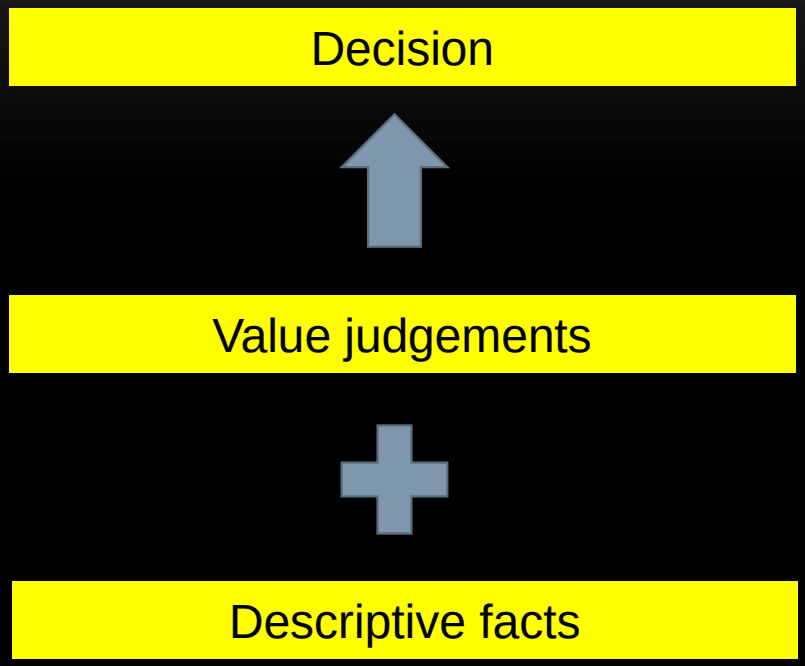
12 METHODS

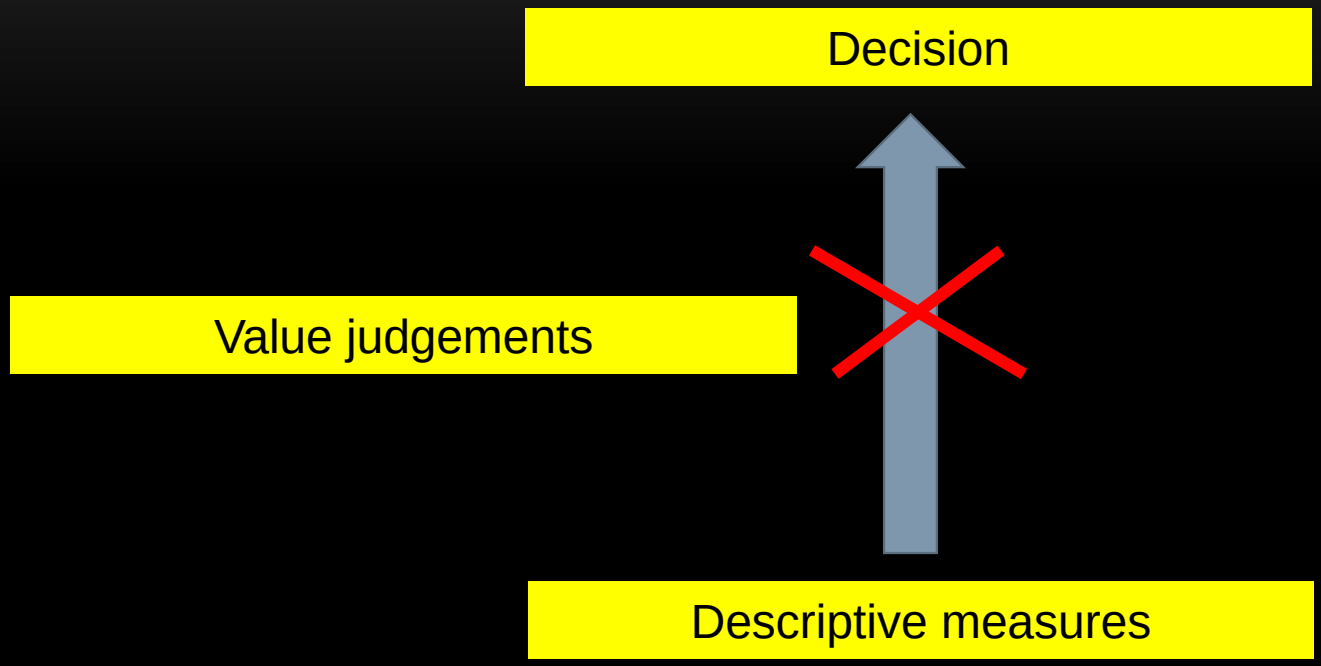
- QFRBA
- BLRA
- Q-TWIST
- NNT/NNH
- RV-NNT
- MCE
- INHB
- RBAT
- PSM
- MCDA
- RBC
- SPM

BRR=NNT/NNH

- NNT = average number of patients that would have to be treated in order to receive one beneficial effect.

- NNH = average number of patients that would have to be treated in order to receive one harmful effect.


Decision
Value judgements
Descriptive facts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- **Descriptive measures:** E.g. NNT, NNH, BRR, Impact numbers.
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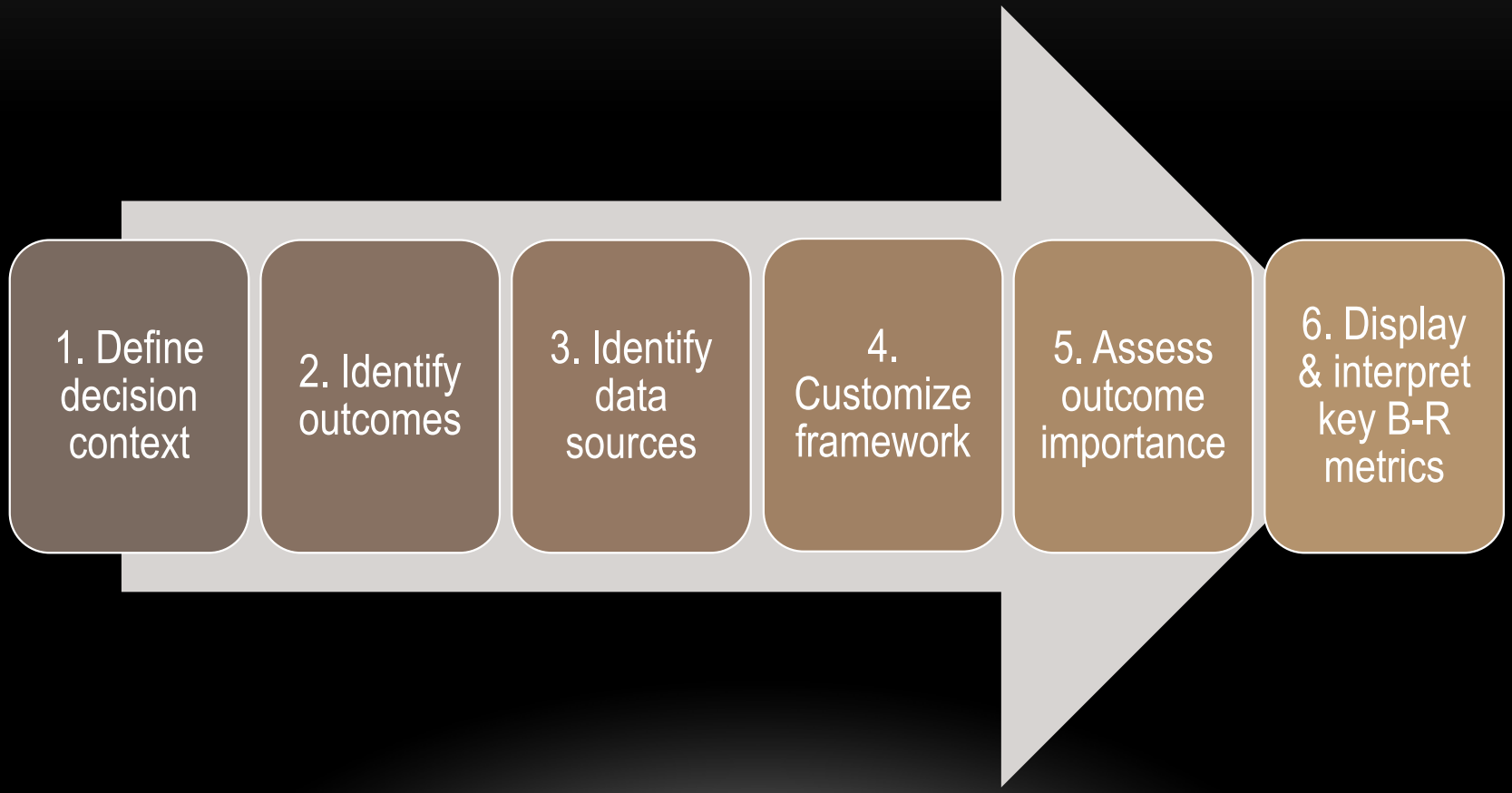
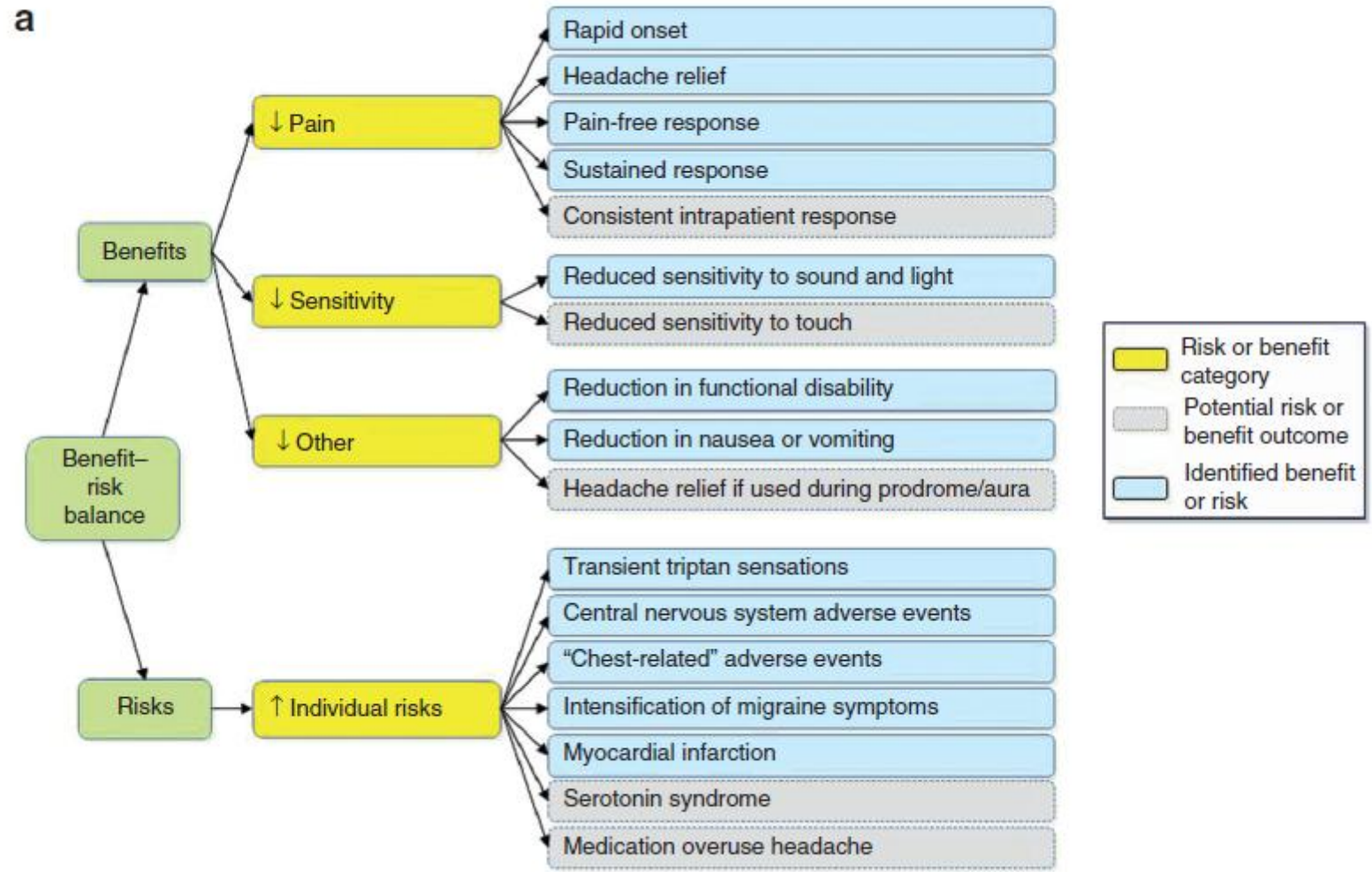
BRAT (Benefit Risk Action Team)



Application of the BRAT Framework to Case Studies: Observations and Insights

Levitan et al. *Clinical Pharmacology & Therapeutics* **89**, 217-224 (February 2011)



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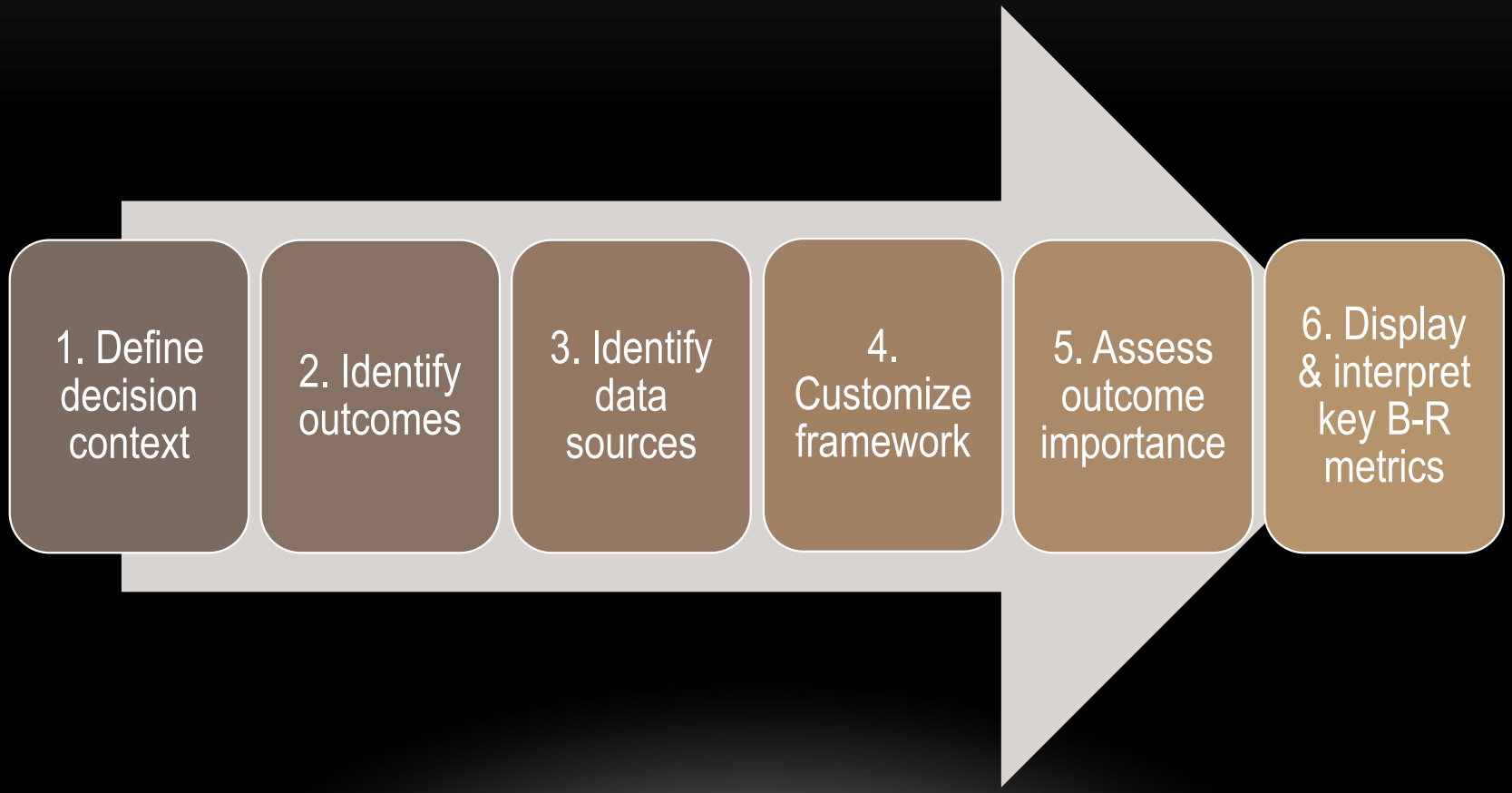
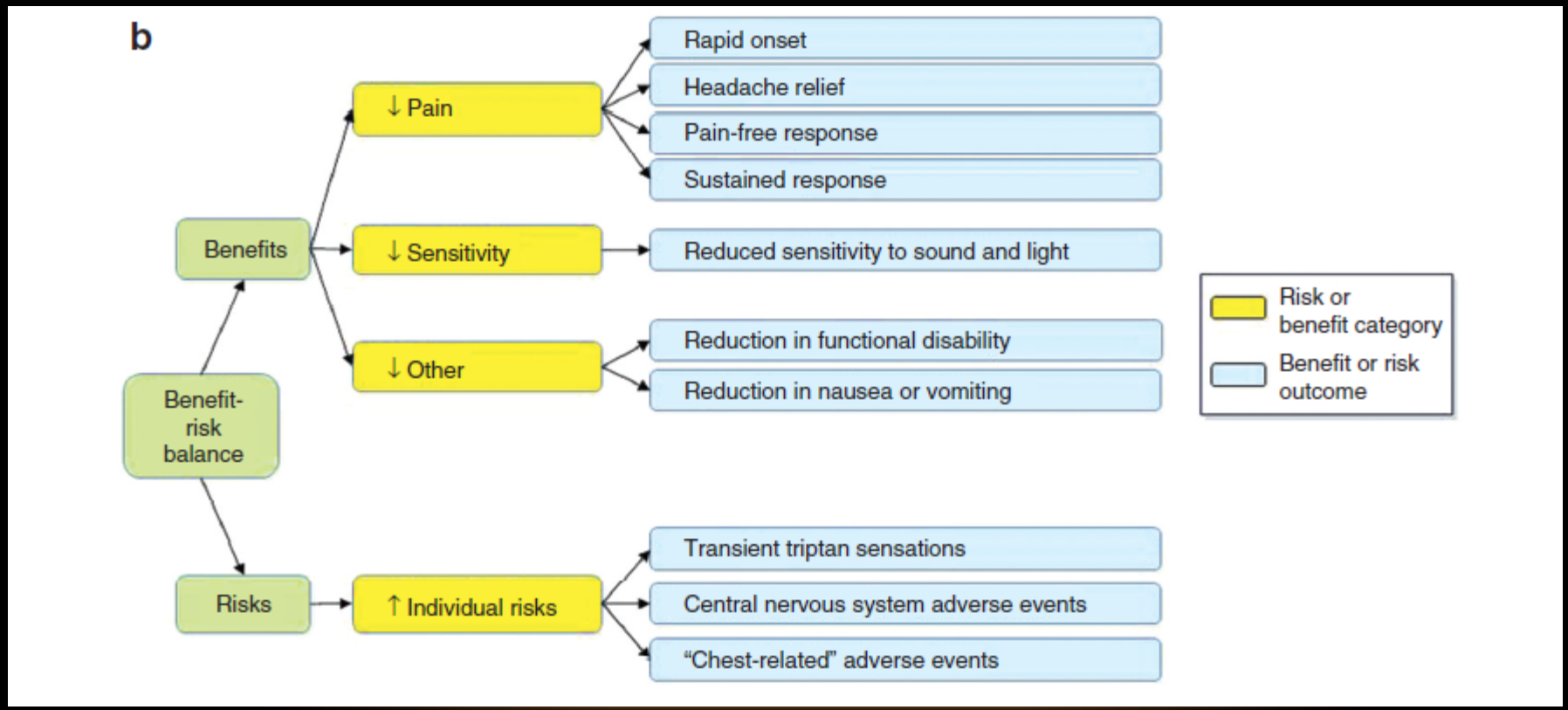


Step 4: Customize framework



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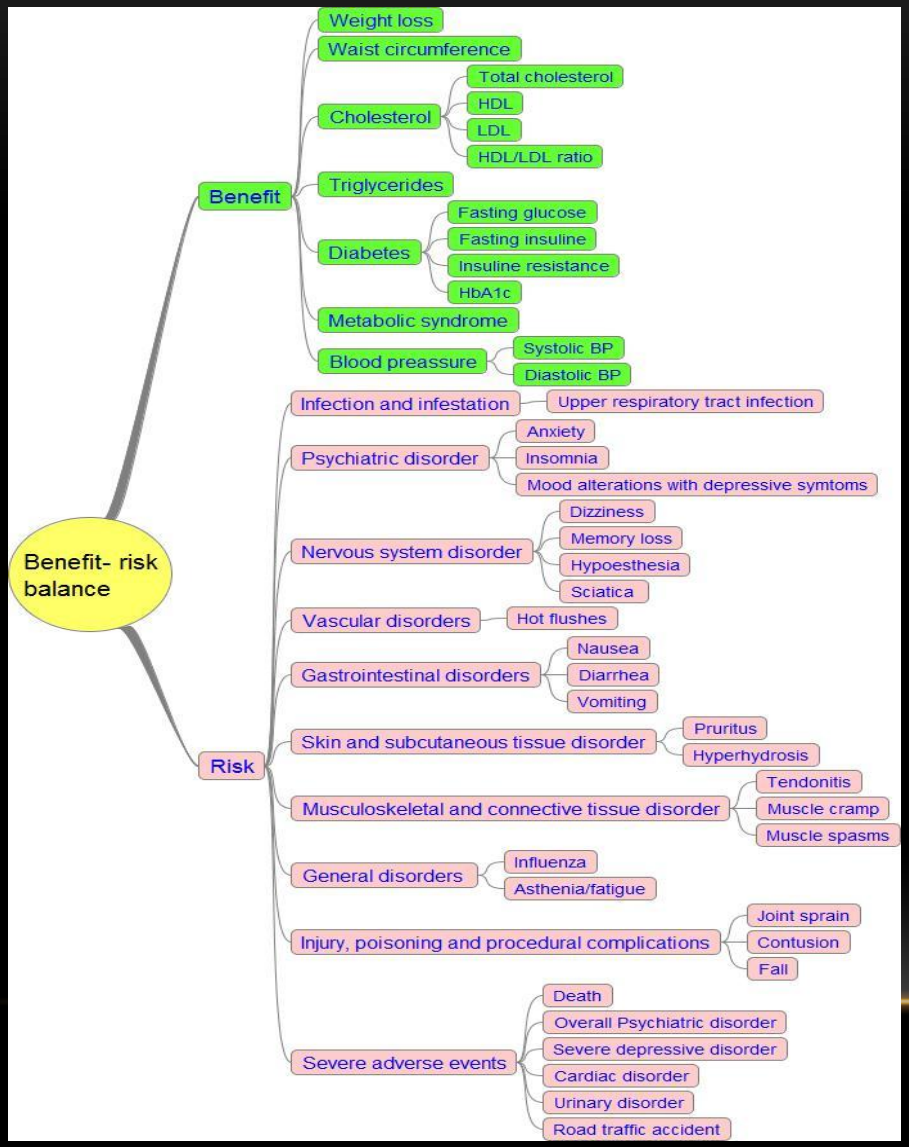
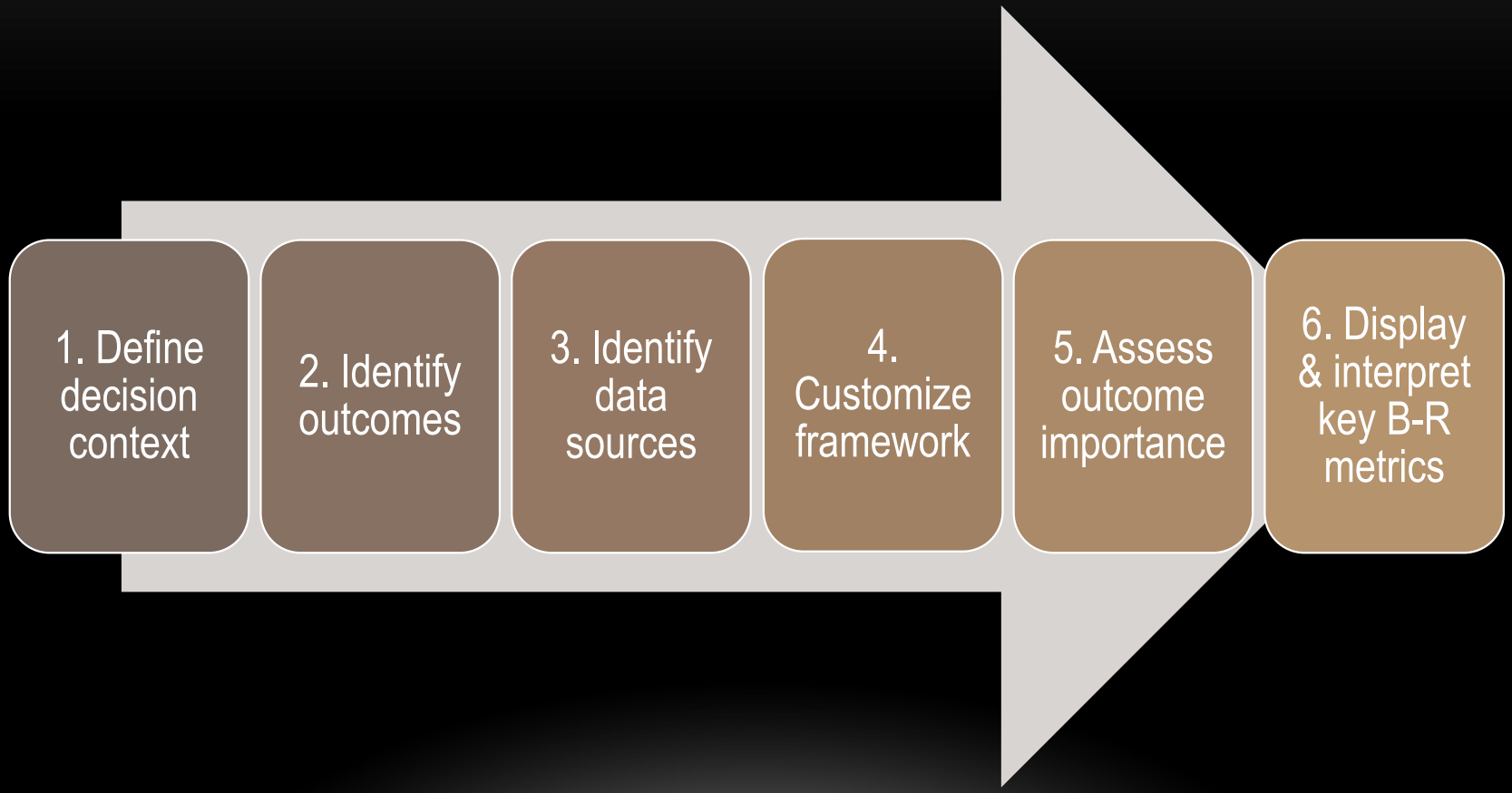
STEP 2: IDENTIFY OUTCOMES



BRAT (Benefit Risk Action Team)



Step 5. Assess importance of outcome

Numerous methods exist for assessing the relative importance or weight of outcomes in the value tree. Although the BRAT Framework does not advocate a particular method of importance weighting, it does facilitate the inclusion of outcome weighting information to support decisions. Importance weights are not included in this report,

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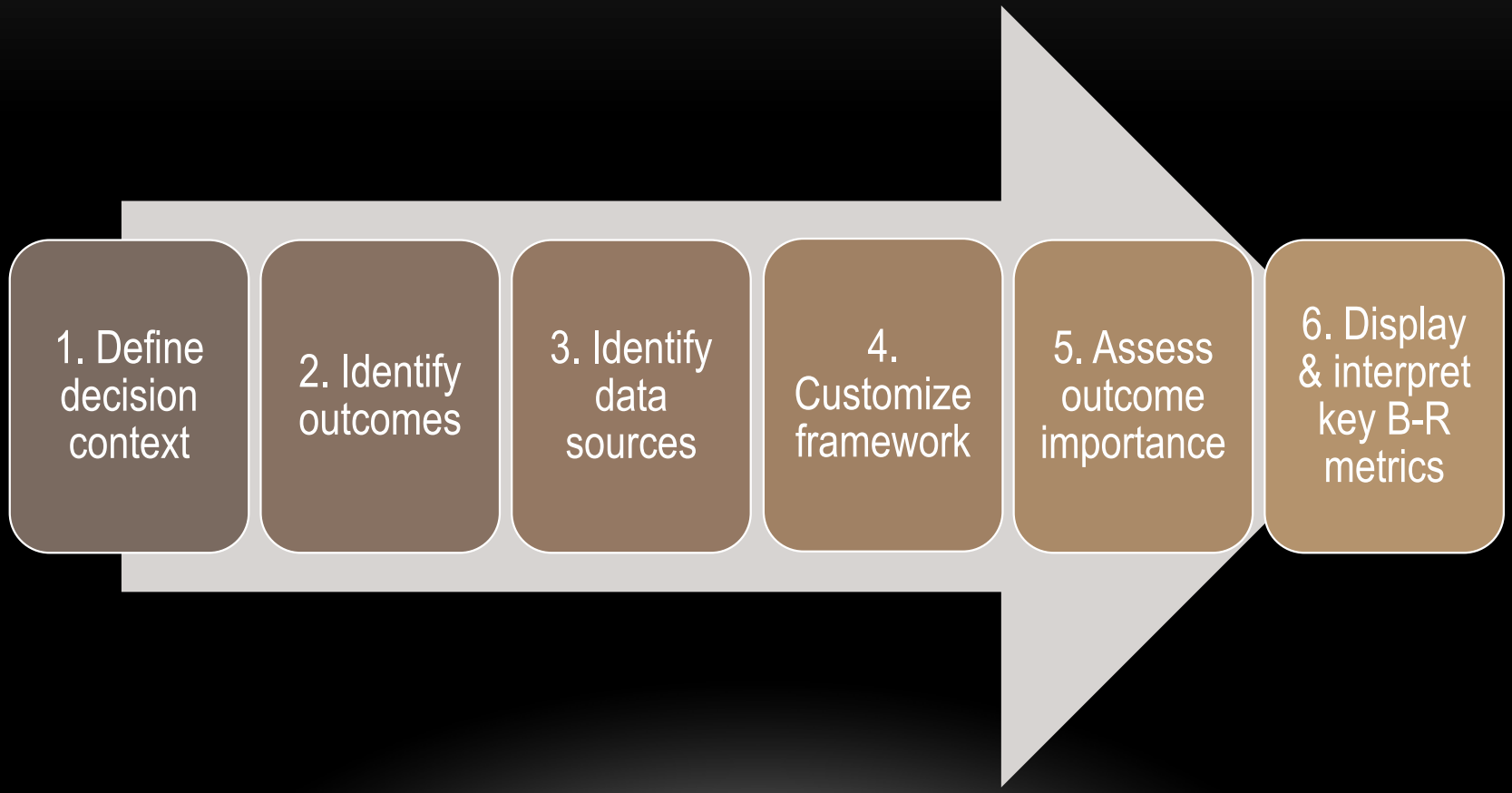
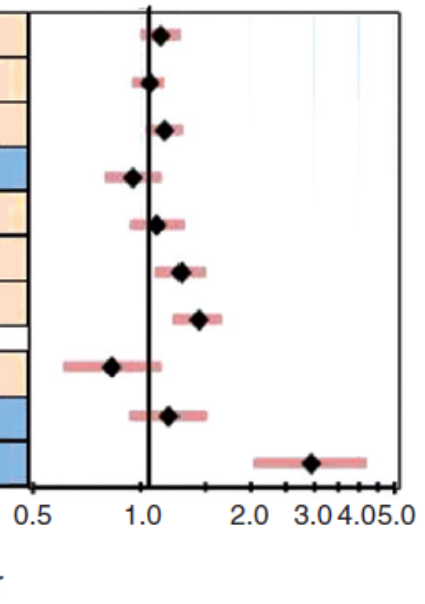
BRAT (Benefit Risk Action Team)



		Outcome	Study drug risk (/1,000 pts)	Comparator risk (/1,000 pts)	Odds ratio (95% CI)
Benefits	↓ Pain	Rapid onset	271	248	1.13 (1.00,1.27)
		Headache relief	643	633	1.04 (0.94,1.15)
		Pain-free response	383	349	1.16 (1.03,1.30)
		Sustained response	285	295	0.95 (0.80,1.14)
	↓ Sensitivity	Reduced sensitivity to sound and light	530	505	1.10 (0.94,1.30)
	↓ Other	Reduction in functional disability	540	480	1.28 (1.09,1.49)
		Reduction in nausea or vomiting	604	517	1.43 (1.22,1.67)
Risks	↑ Individual risks	Transient triptans sensations	43	52	0.83 (0.61,1.14)
		CNS AEs	53	45	1.18 (0.92,1.51)
		"Chest-related" AEs	58	21	2.93 (2.04,4.20)



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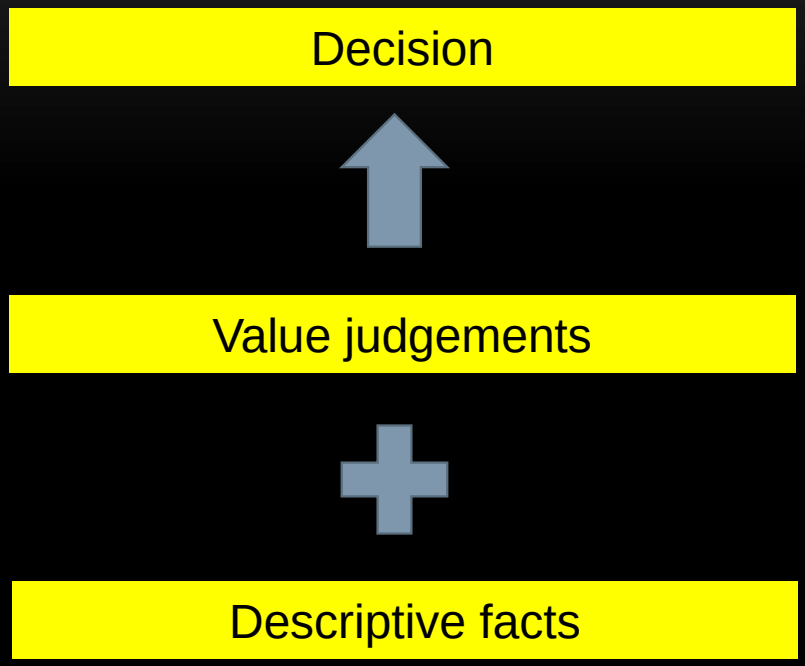
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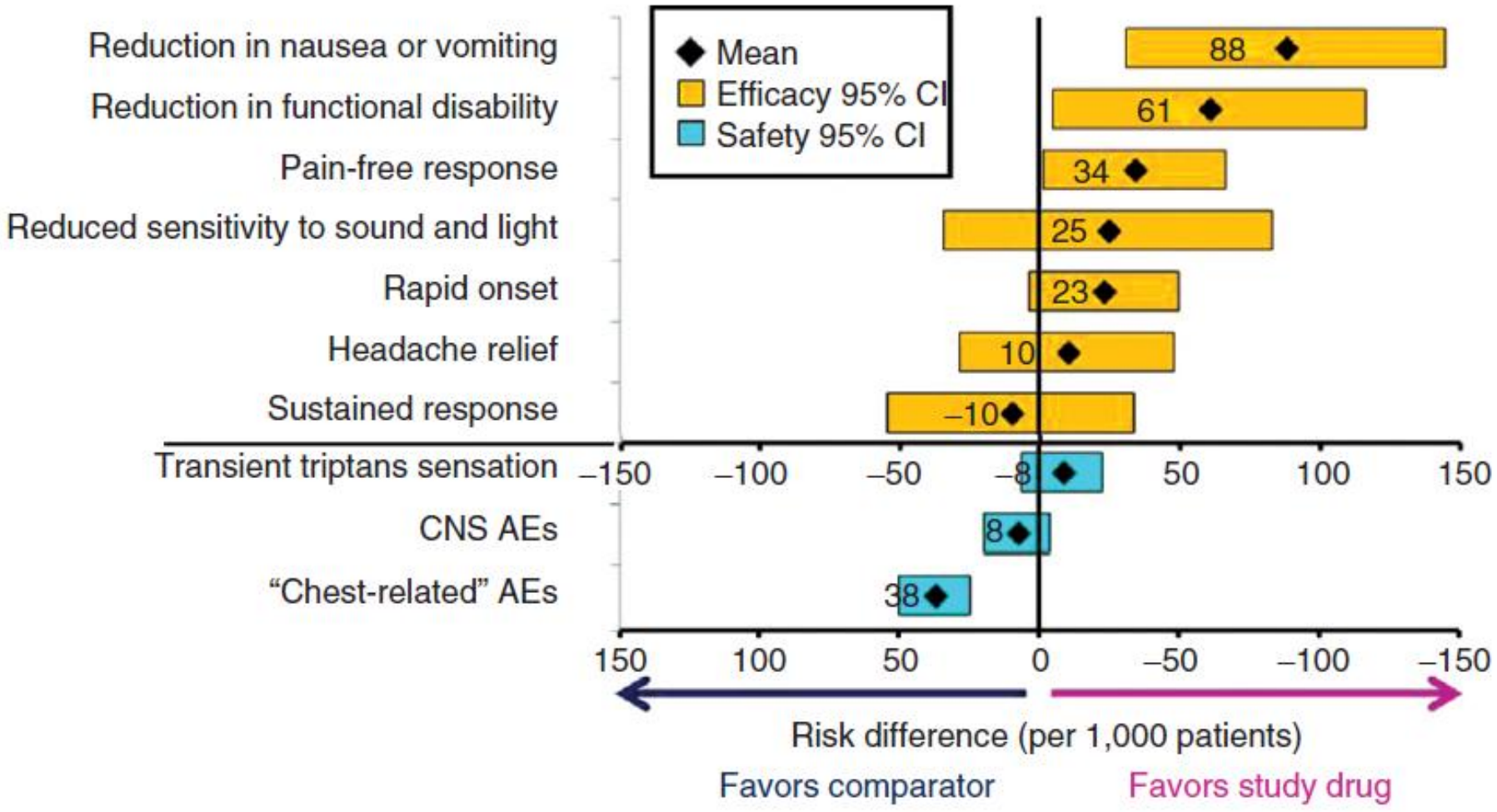

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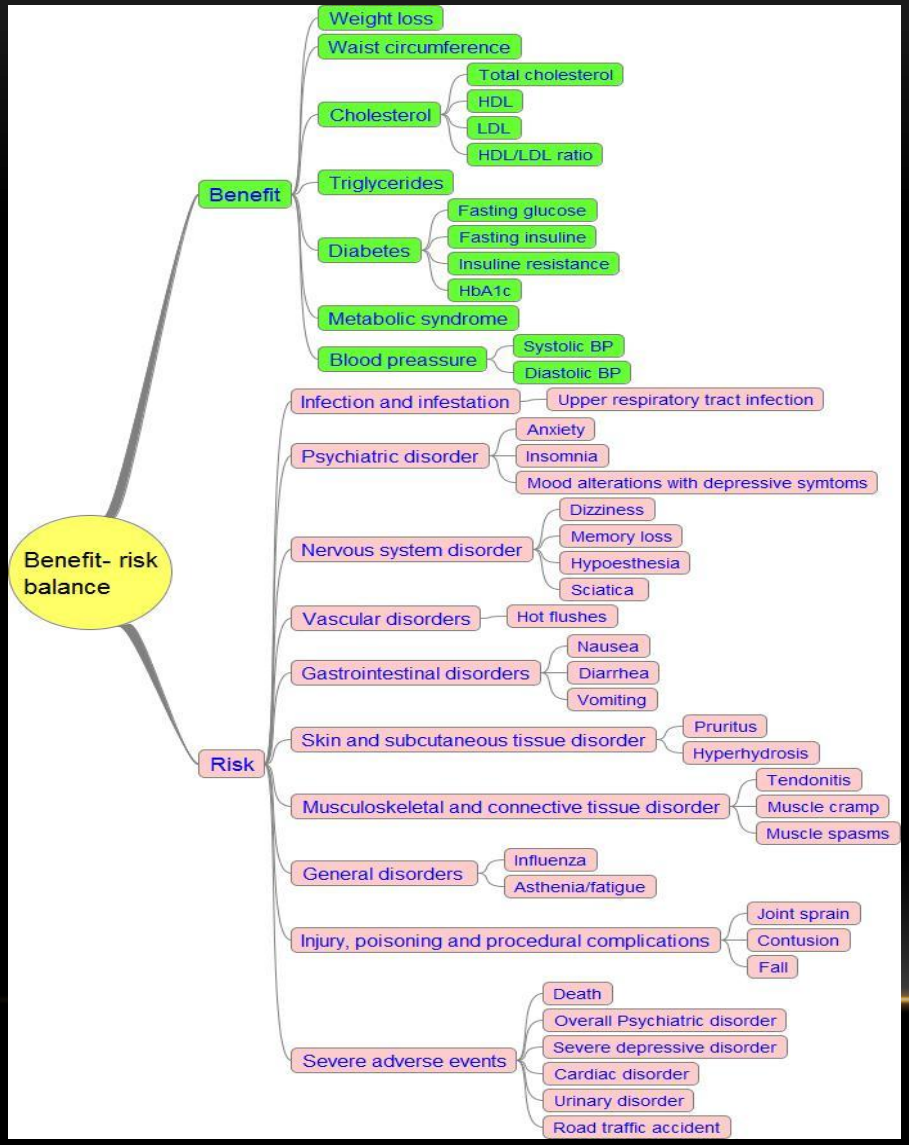
Importance

How important are the following outcomes?

	1. Unimportant	2	3	4	5. Very important
Weight loss	○	○	○	○	○
Lowering cholesterol	○	○	○	○	○
Psychiatric events	○	○	○	○	○
Dizzines	○	○	○	○	○
.....	○	○	○	○	○

STEP 5: ASSES OUTCOME IMPORTANCE



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PROACT
HYPOTHETICAL TRADEOFFS

Consequences	Acomplia A	Placebo
Weight loss more than 10%	25%	6%
Incidence of psychiatric disorders	20%	10%
Incidence of severe adverse events	2%	1%

Consequences	Acomplia B	Placebo
Weight loss more than 10%	~~25%~~ 16%	6%
Incidence of psychiatric disorders	20%	10%
Incidence of severe adverse events	~~2%~~ 1%	1%

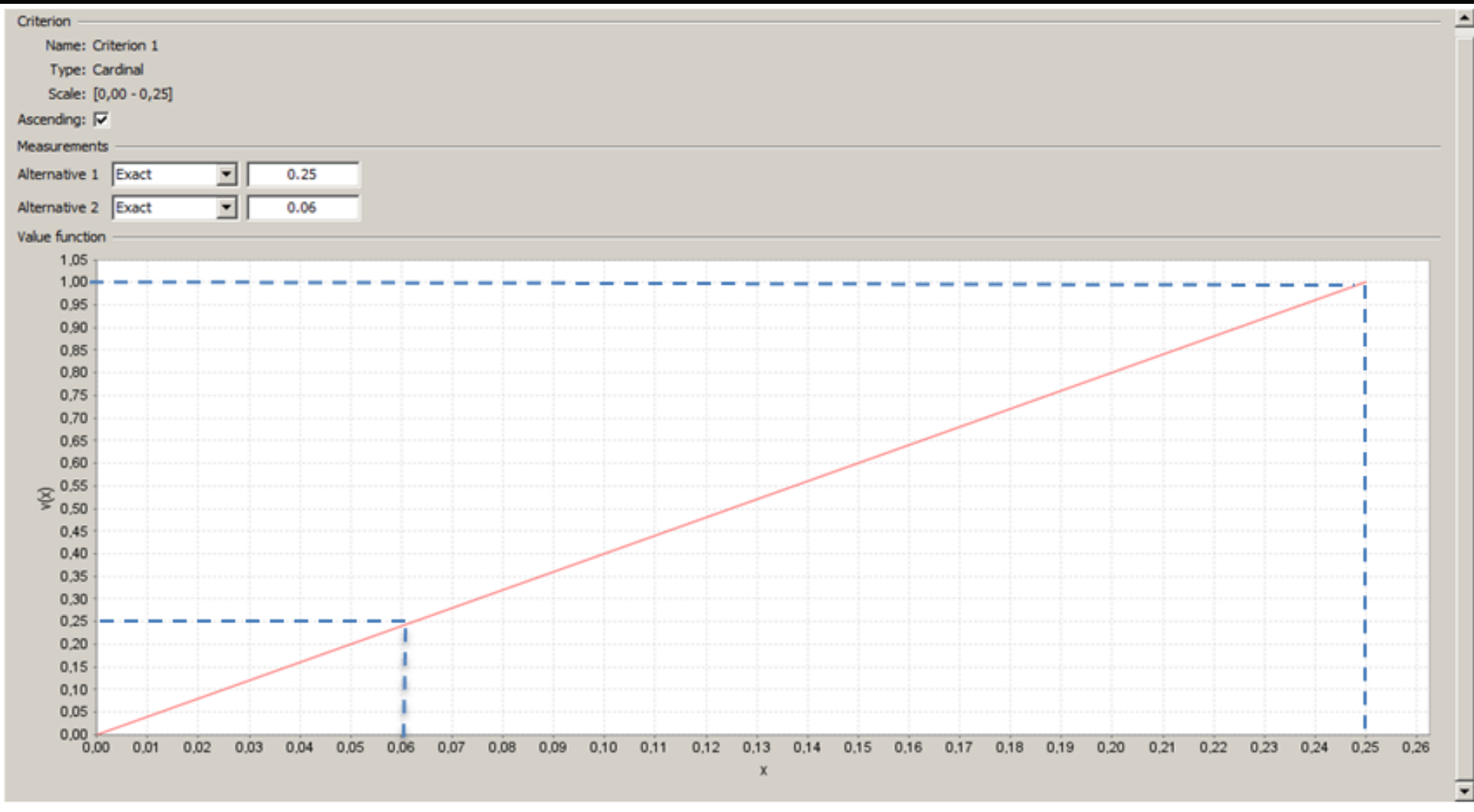
Consequences	Acomplia C	Placebo
Weight loss more than 10%	~~25%~~ ~~16%~~ 6%	6%
Incidence of psychiatric disorders	~~20%~~ 15%	10%
Incidence of severe adverse events	~~2%~~ 1%	1%

STOCHASTIC MULTICRITERIA ACCEPTABILITY ANALYSIS (SMAA)

- Tervonen et al (2011), ’A stochastic multicriteria model for evidence-based decision making in drug benefit-risk analysis.’ *Stat Med,* May 30;30(12):1419-28.

- The OpenSource software, JSMAA. http://smaa.fi/jsmaa/

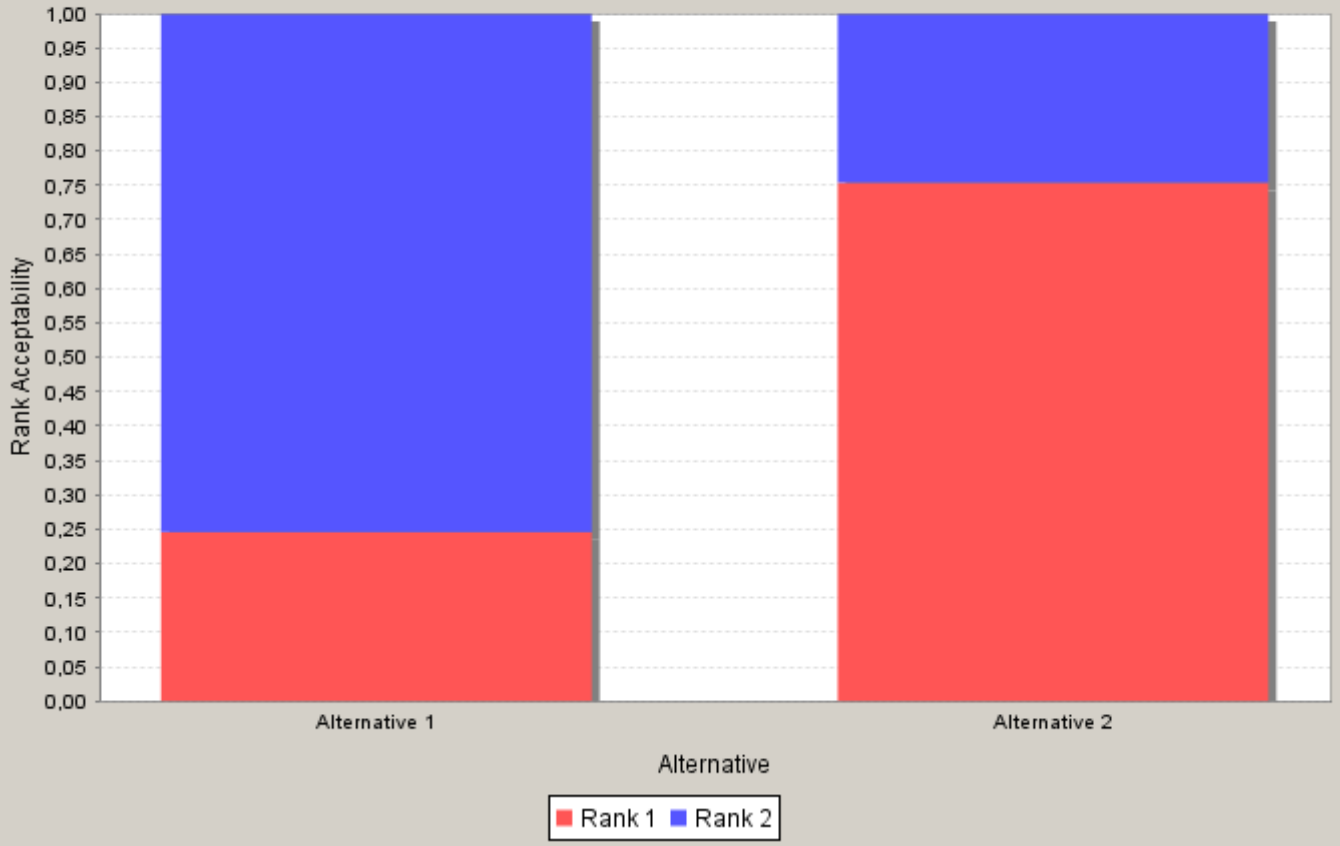
Consequences	Acomplia	Placebo
Weight loss more than 10%	25%	6%
Incidence of psychiatric disorders	20%	10%
Incidence of severe adverse events	2%	1%




Severe adverse events
Psychiatric events
Weight loss

Rank acceptability indices

Alternative	Rank 1	Rank 2
Alternative 1	0,25	0,75
Alternative 2	0,75	0,25



Alterntive 1 = Acomplia
Alterntive 2 = Placebo

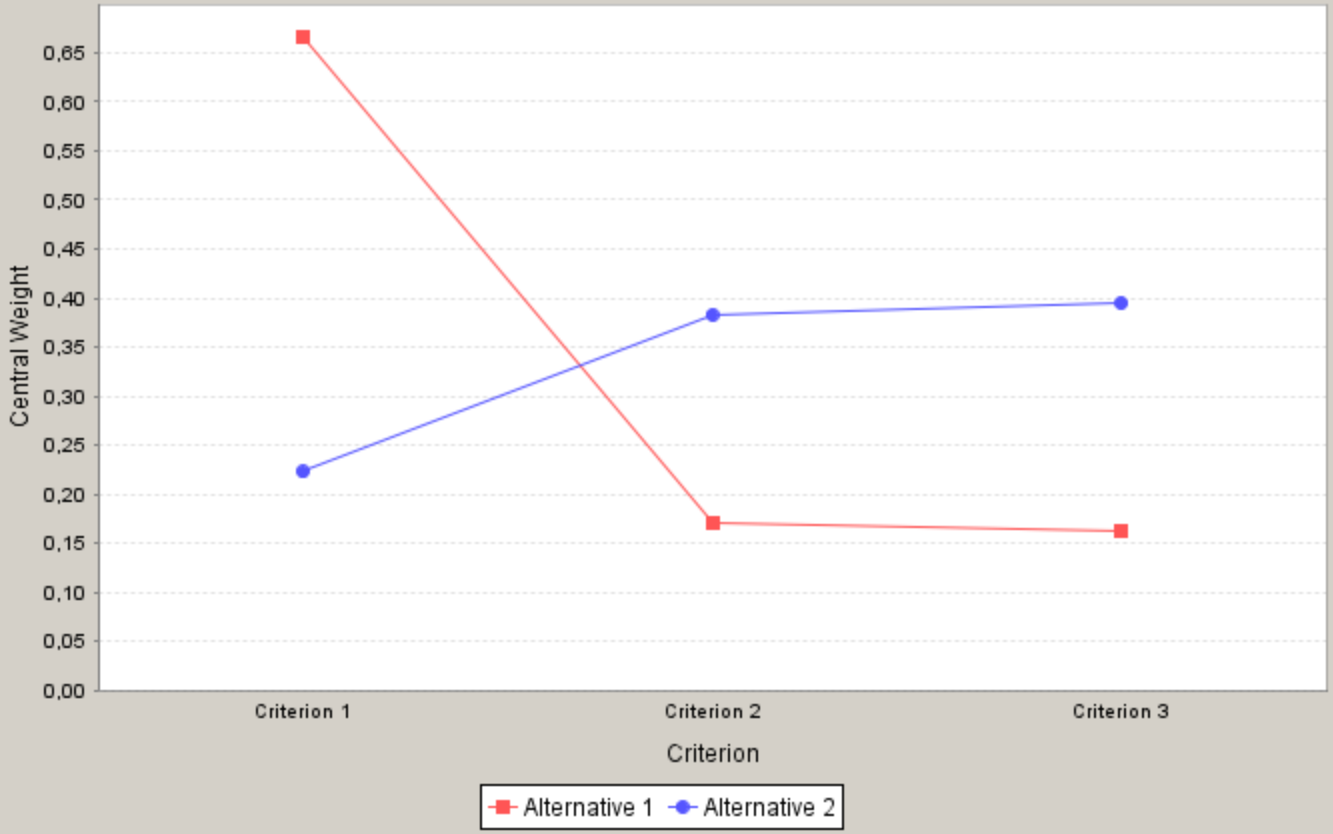
JSMAA v0.8.5 - Unsaved model*

File Edit Criteria Alternatives Results

SMAA-2 Model
- Alternatives
  - Alternative 1
  - Alternative 2
- Criteria
  - Criterion 1
  - Criterion 2
  - Criterion 3
- Preferences
- Results
  - RankAcc
  - CW

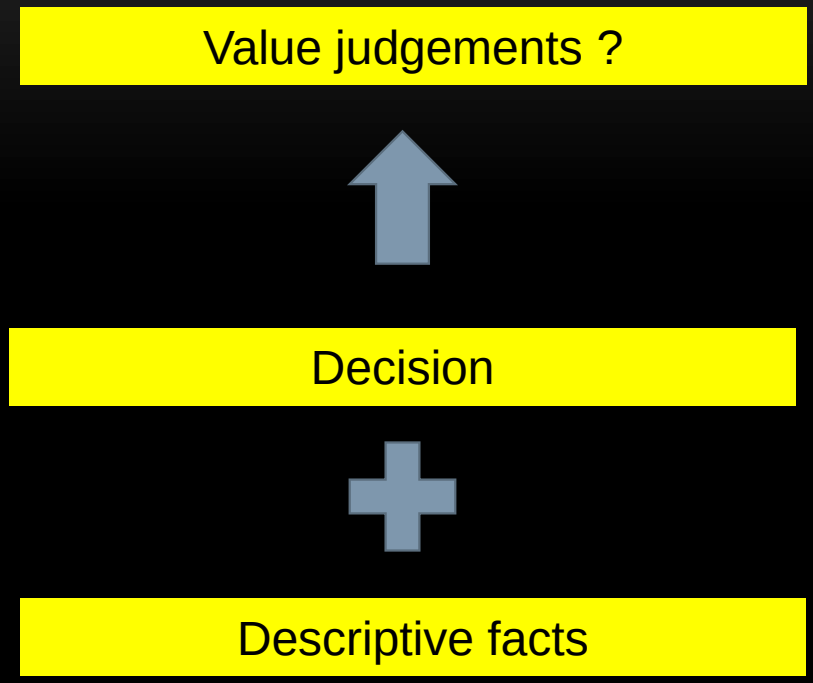
Central weight vectors

Alternative	CF	Criterion 1	Criterion 2	Criterion 3
Alternative 1	1,00	0,67	0,17	0,16
Alternative 2	1,00	0,22	0,38	0,39



Export figure dataset as GNUPlot script

Done!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Thank you for you attention!