

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

The screenshot shows the PROTECT website. The header features the PROTECT logo on the left and the IMI and efpia logos on the right, with the text "Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium" below them. A navigation bar contains links for "About", "Objectives", "Governance", "Partners", and "Contact Us", along with a search box. A left sidebar lists the project structure: "PROJECT", "Home", "About PROTECT", "Objectives", "Governance structure", "Partners", and "Work programme". Under "Work programme", a list of work packages (WP1 to WP7) is shown, with WP5 highlighted. The main content area is titled "WP5: Benefit-risk integration and representation". It contains a paragraph describing the overall objective of WP5 and a list of specific objectives.

Print page Resize text

PROTECT

IMI efpia
Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

About Objectives Governance Partners Contact Us Search

PROJECT

- Home
- About PROTECT
- Objectives
- Governance structure
- Partners
- Work programme
 - WP1
 - WP2
 - WP3
 - WP4
 - WP5**
 - WP6
 - WP7

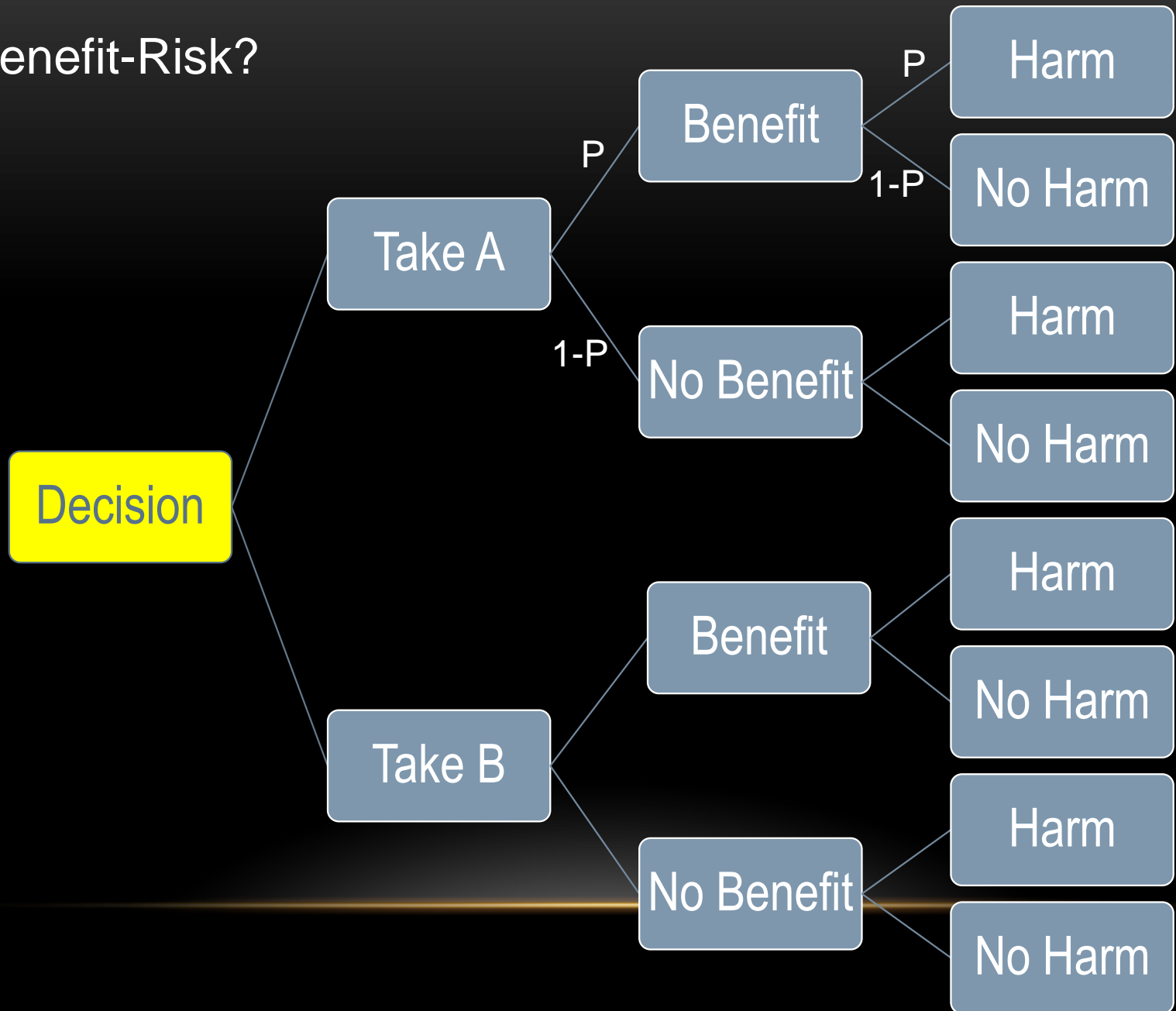
WP5: Benefit-risk integration and representation

The overall objective of WP5 is to develop methods for use in benefit-risk assessment, including both the underpinning modelling and the presentation of the results, with a particular emphasis on graphical methods. The various options will be compared and tested out on a range of case-studies with patients, healthcare providers, pharma industry and regulators.

Specific objectives are to:

- Identify, characterise and test methods of collating data on benefits and risks from various data sources, parameters and strengths of evidence, and of integrating them with decision-criteria and formal assessment of values of patients, healthcare providers, regulators, the pharmaceutical industry and in benefit-risk assessment;
- Identify, test and compare modelling approaches that would allow continuous benefit-risk risk-modelling along the lifecycle of the product, and support decision-making;
- Develop methods of graphical expression of the benefits and risks of the medicinal products for use by patients, healthcare providers, the pharmaceutical industry and regulators along the lifecycle of the product.

Benefit-Risk?



METHODS

MCDA

NNT

BRAT

SMAA

PROACT

BRR

Impact
numbers



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

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, PhD⁵

¹University of Cincinnati Health Academic Center, College of Pharmacy, Cincinnati, OH, USA; ²Kendle International Inc., Cincinnati, OH, USA;

³Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA; ⁴Centre for Socioeconomic Research, Welsh School of Pharmacy, Cardiff, UK; ⁵University 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

$$\text{BRR} = \text{NNT} / \text{NNH}$$

- 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.

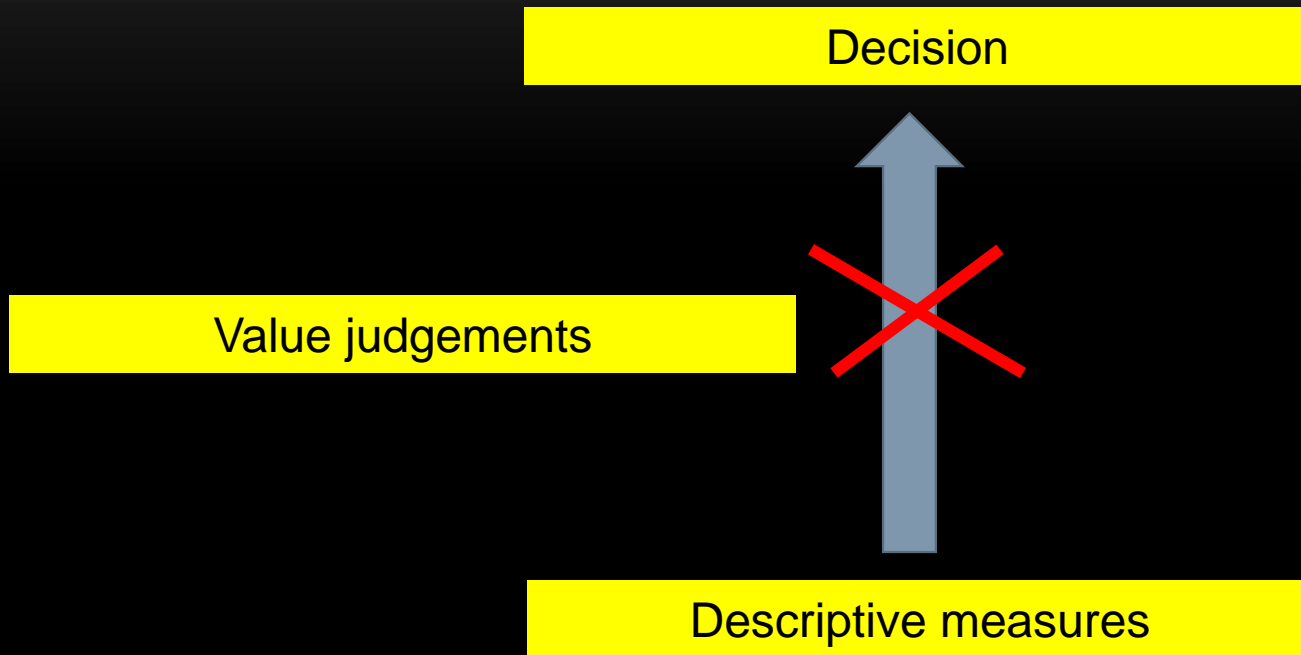
Decision



Value judgements

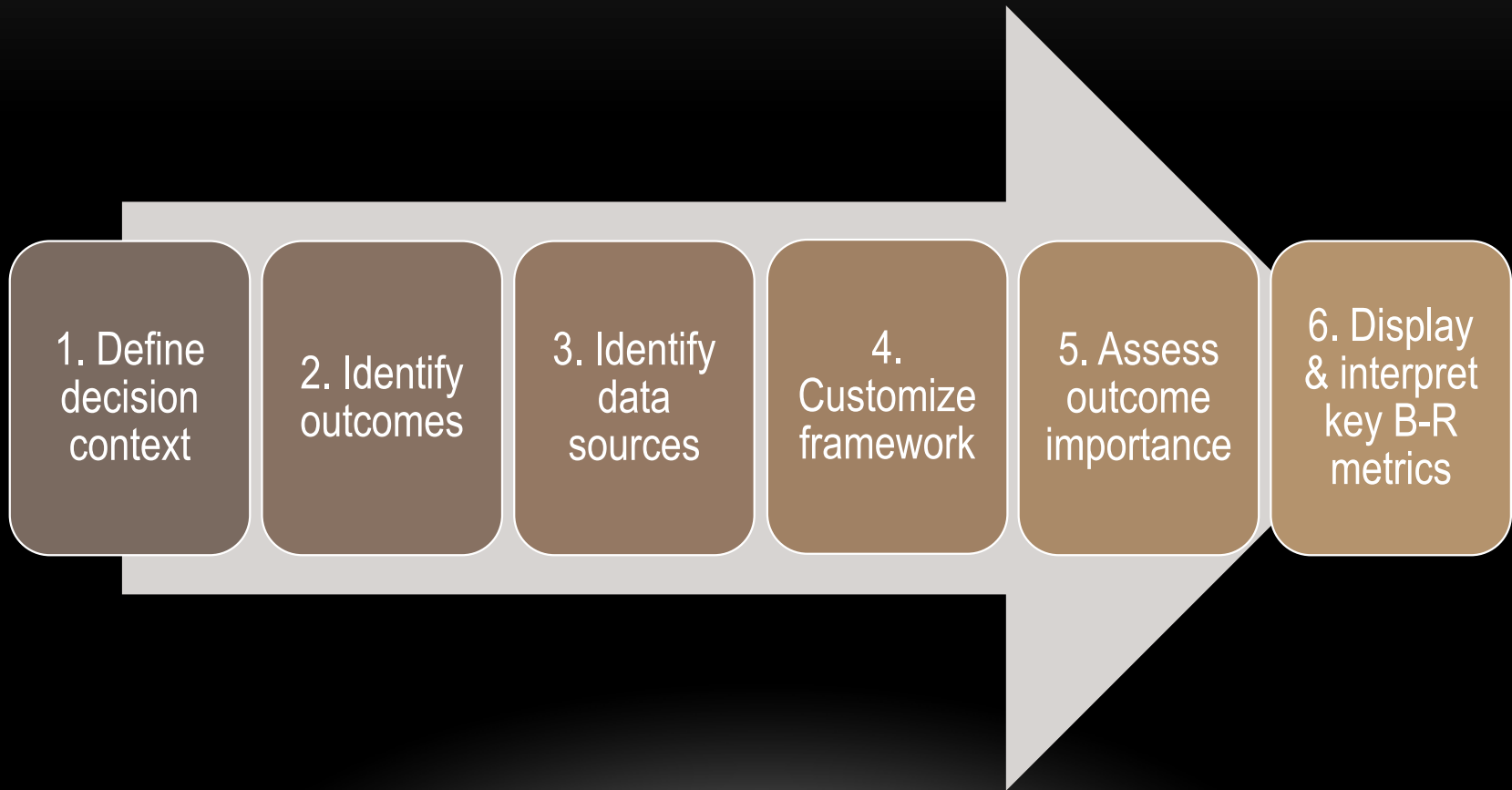


Descriptive facts



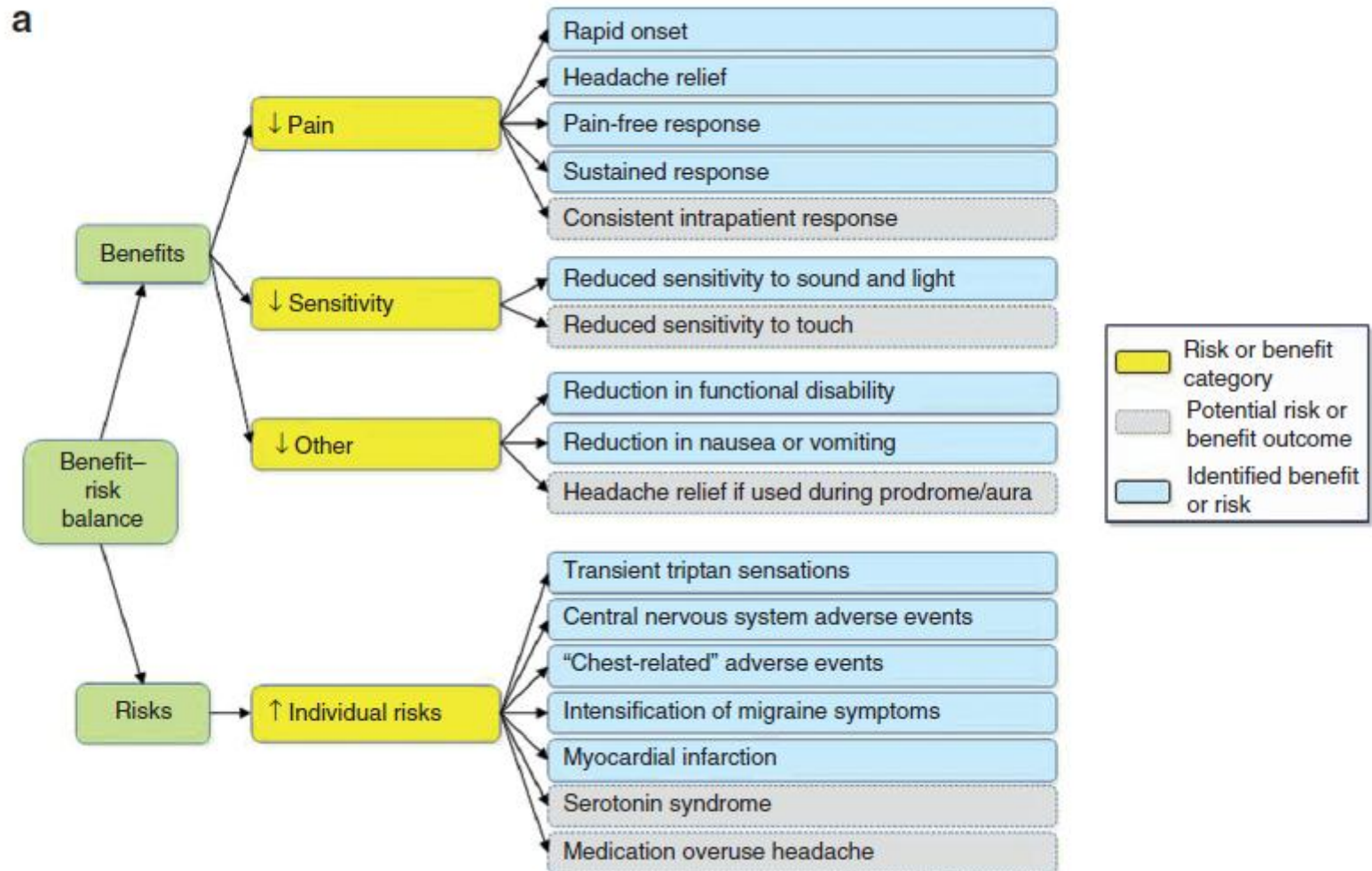
- **Descriptive measures:** E.g. NNT, NNH, BRR, Impact numbers.
- **Descriptive and partly normative:** E.g. BRAT, SMAA
- **Descriptive and normative:** E.g, MCDA, PROACT

BRAT (Benefit Risk Action Team)

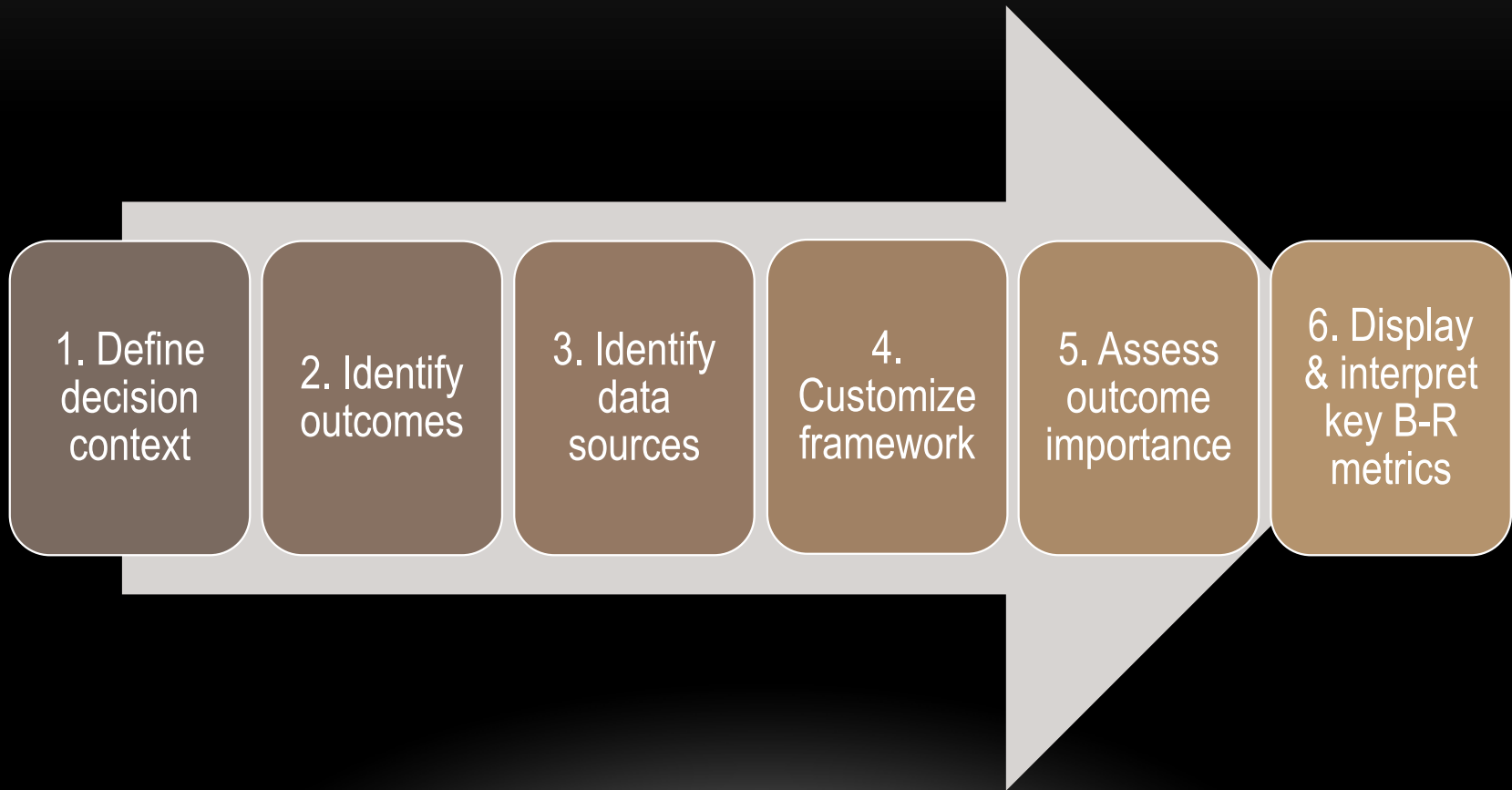


Application of the BRAT Framework to Case Studies: Observations and Insights

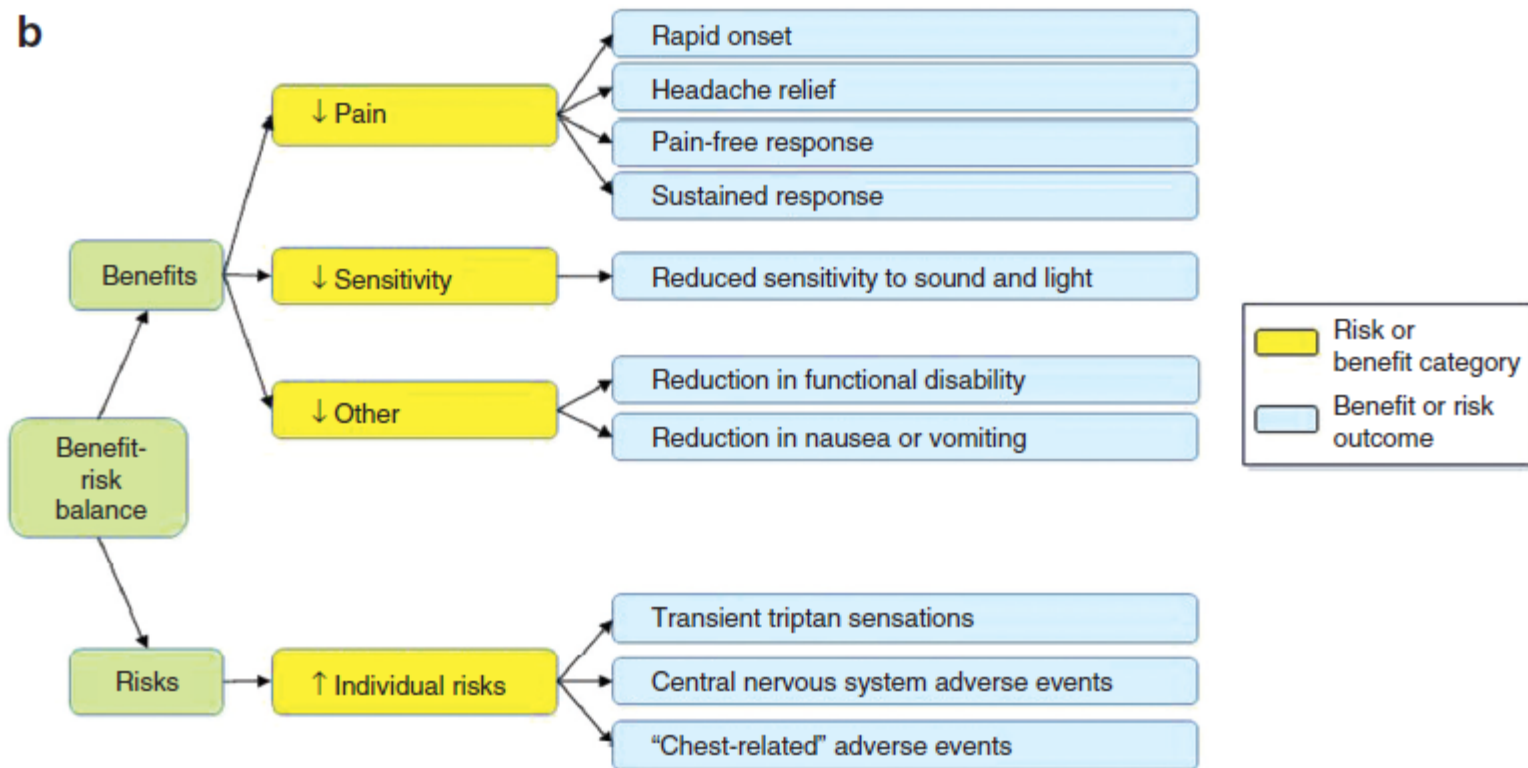
Levitan et al. *Clinical Pharmacology & Therapeutics* 89, 217-224 (February 2011)



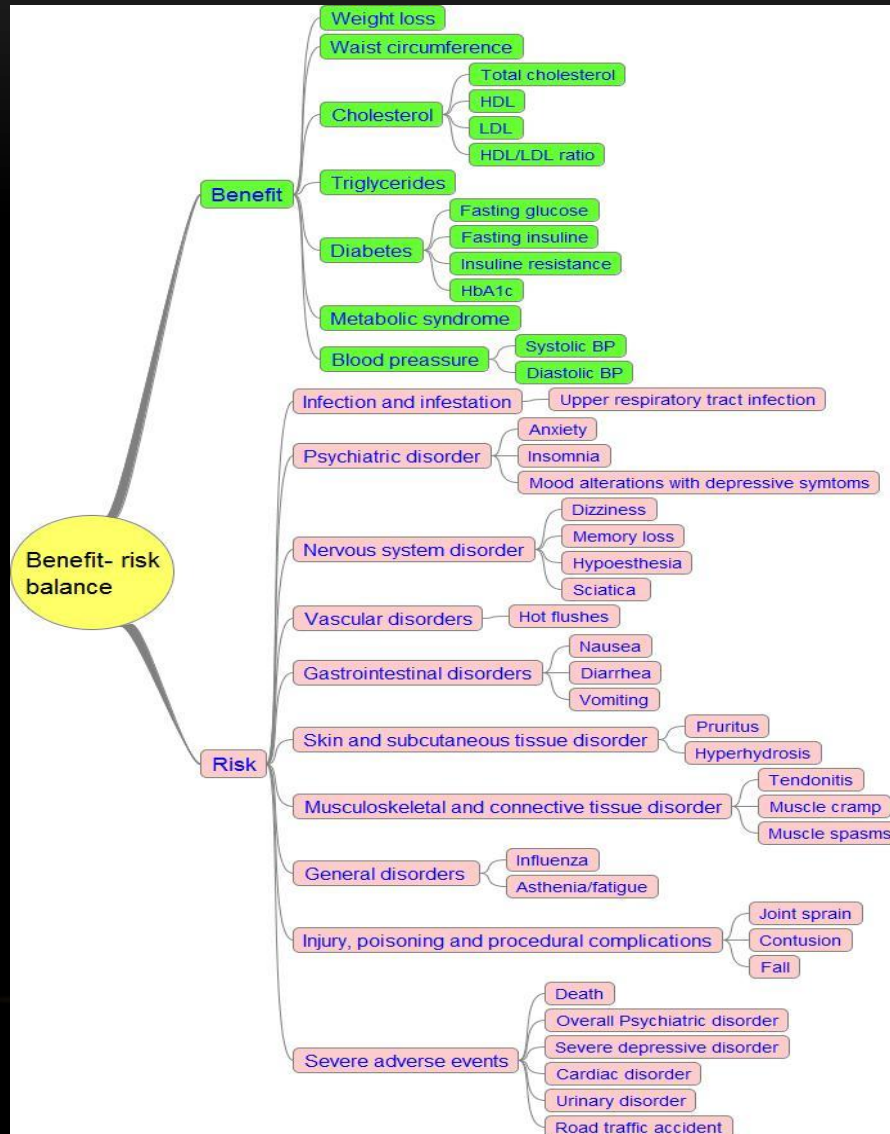
BRAT (Benefit Risk Action Team)



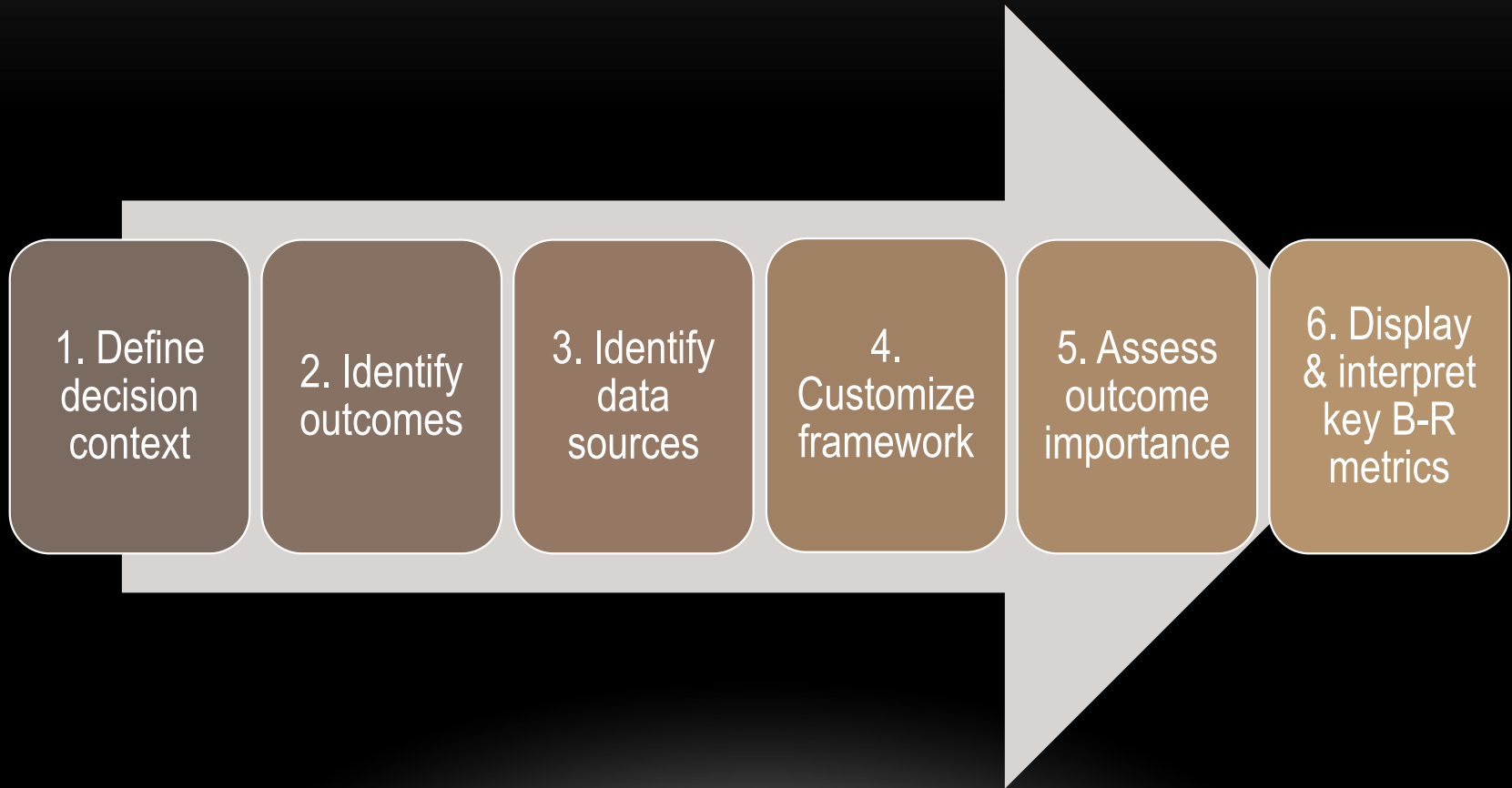
Step 4: Customize framework



STEP 2: IDENTIFY OUTCOMES



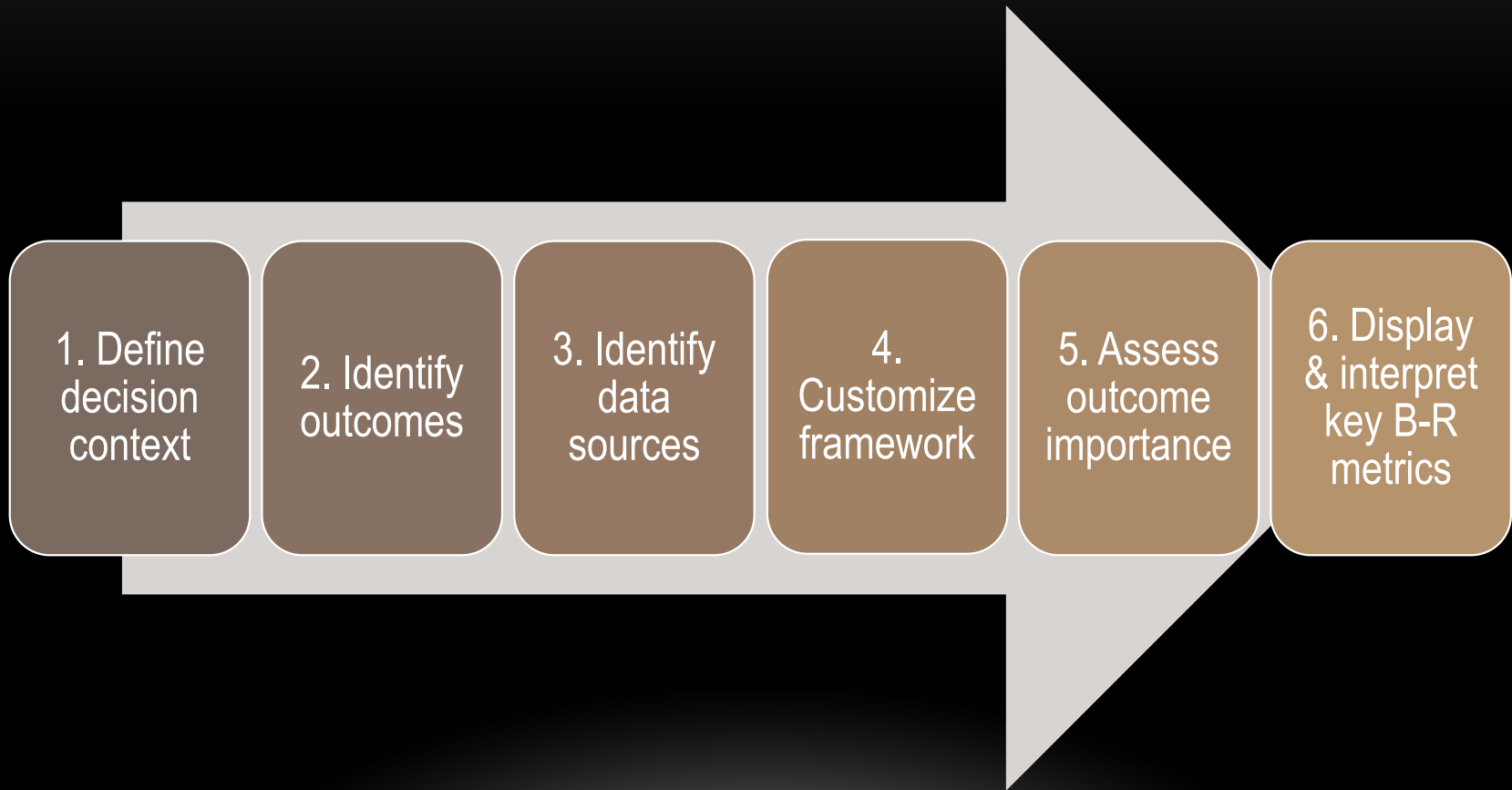
BRAT (Benefit Risk Action Team)

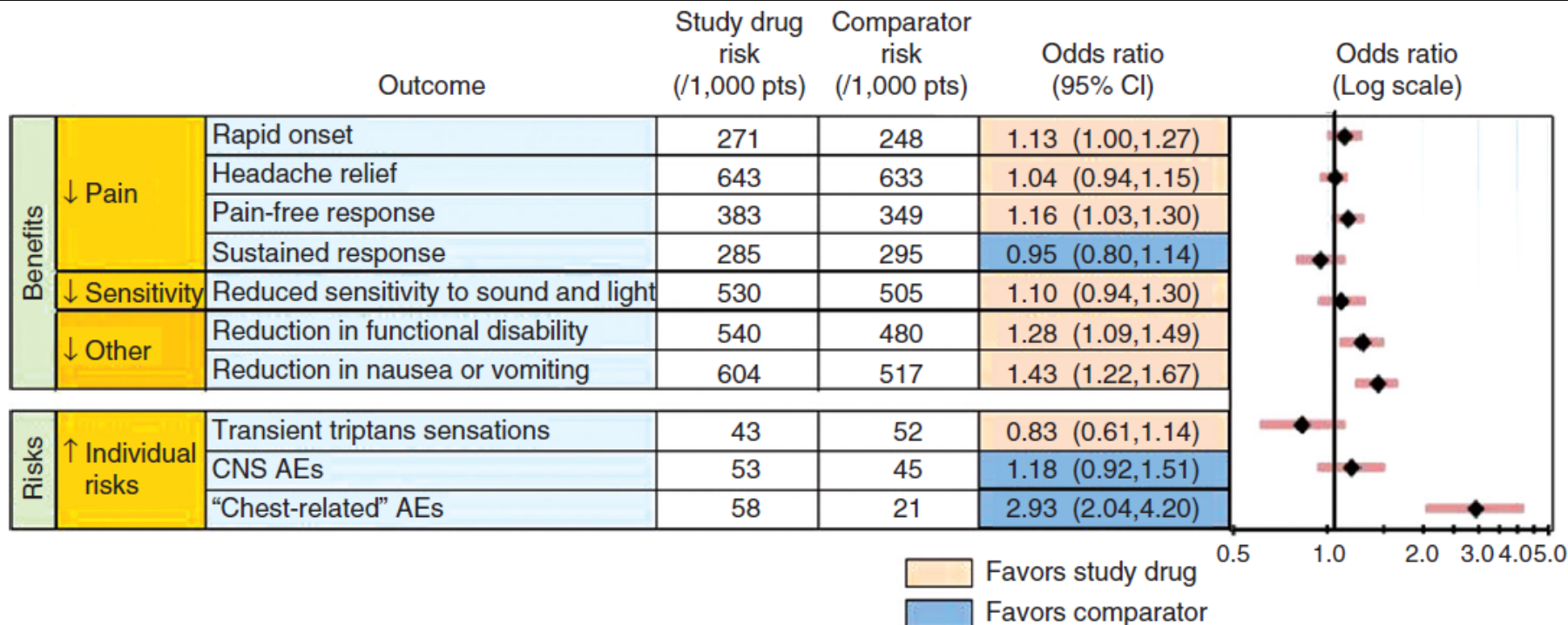


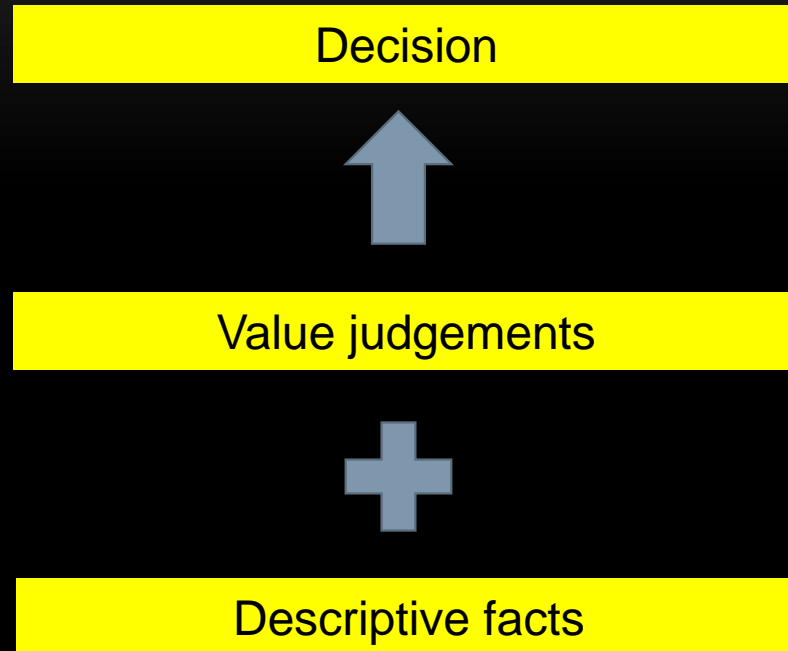
Step 5. Assess importance of outcome

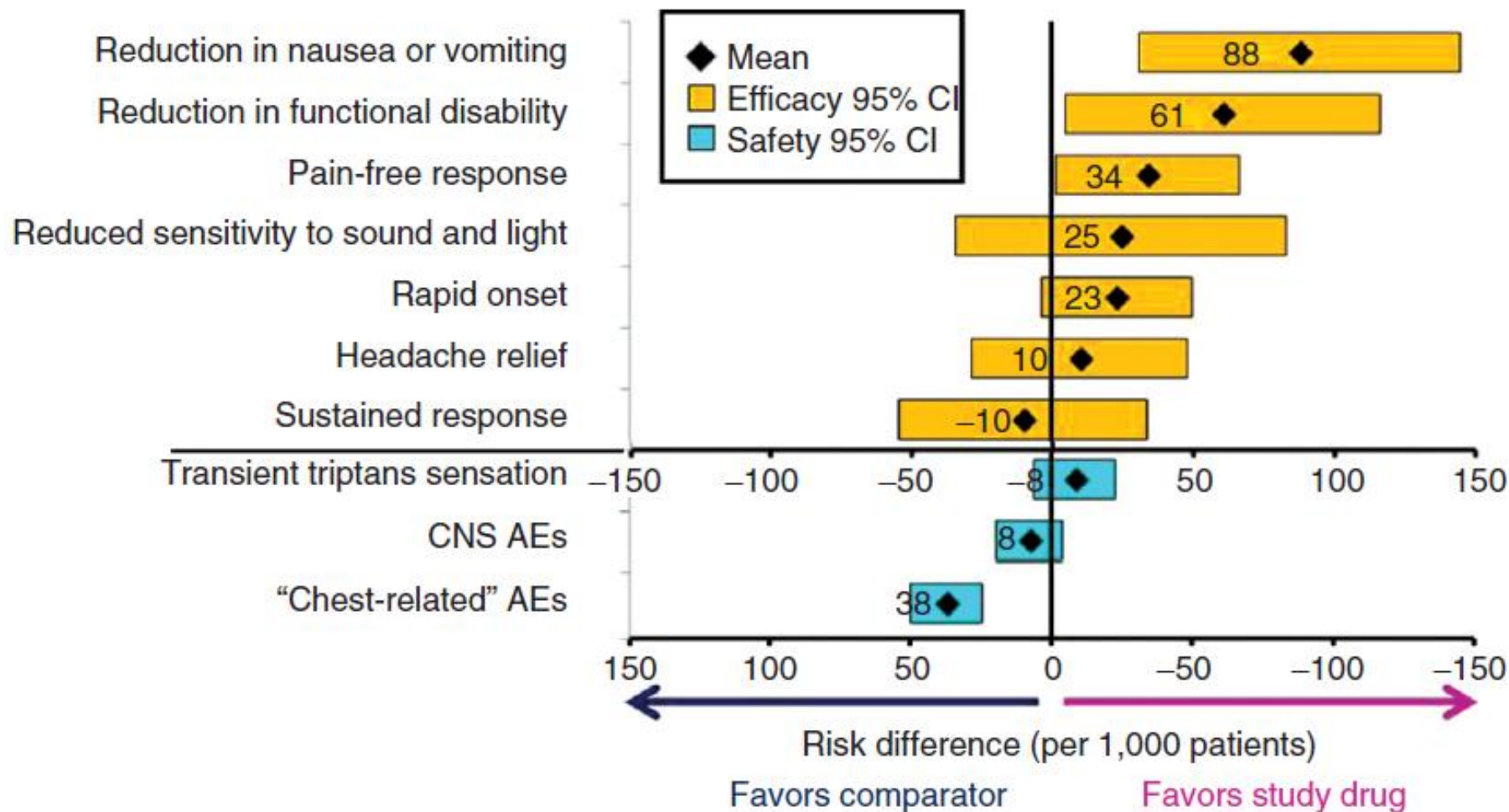
Numerous methods exist for assessing the relative importance or weight of outcomes in the value tree. Although the BRAT Framework does not advocate a particular method of importance weighting, it does facilitate the inclusion of outcome weighting information to support decisions. Importance weights are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

BRAT (Benefit Risk Action Team)









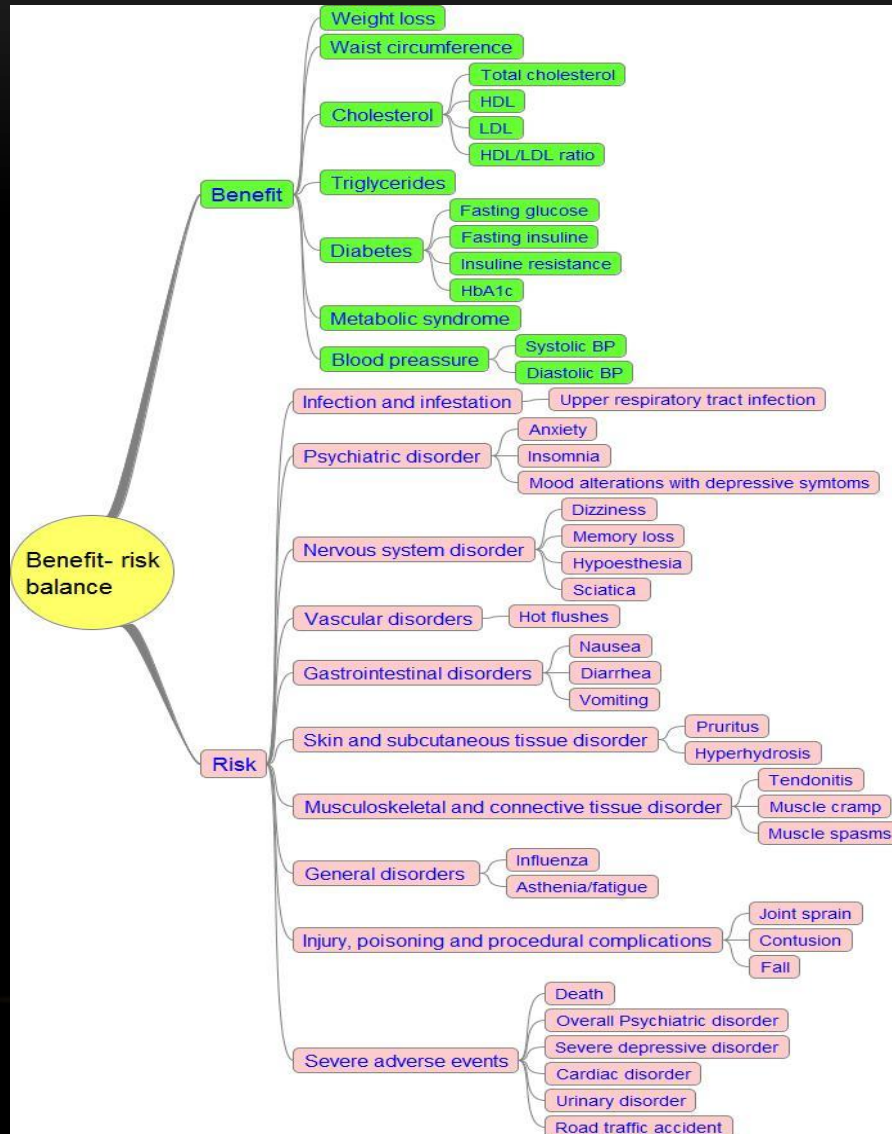
- **Descriptive measures:** E.g. NNT, NNH, BRR, Impact numbers.
- **Descriptive and partly normative:** E.g. BRAT, SMAA
- **Descriptive and normative:** E.g, MCDA, PROACT

Importance

How important are the following outcomes?

	1. Unimportant	2	3	4	5. Very important
Weight loss	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Lowering cholesterol	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Psychiatric events	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Dizzines	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
.....	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

STEP 5: ASSES OUTCOME IMPORTANCE



- **Descriptive measures:** E.g. NNT, NNH, BRR, Impact numbers.
- **Descriptive and partly normative:** E.g. BRAT, SMAA
- **Descriptive and normative:** E.g, MCDA, PROACT

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%

Criterion

Name: Criterion 1

Type: Cardinal

Scale: [0,00 - 0,25]

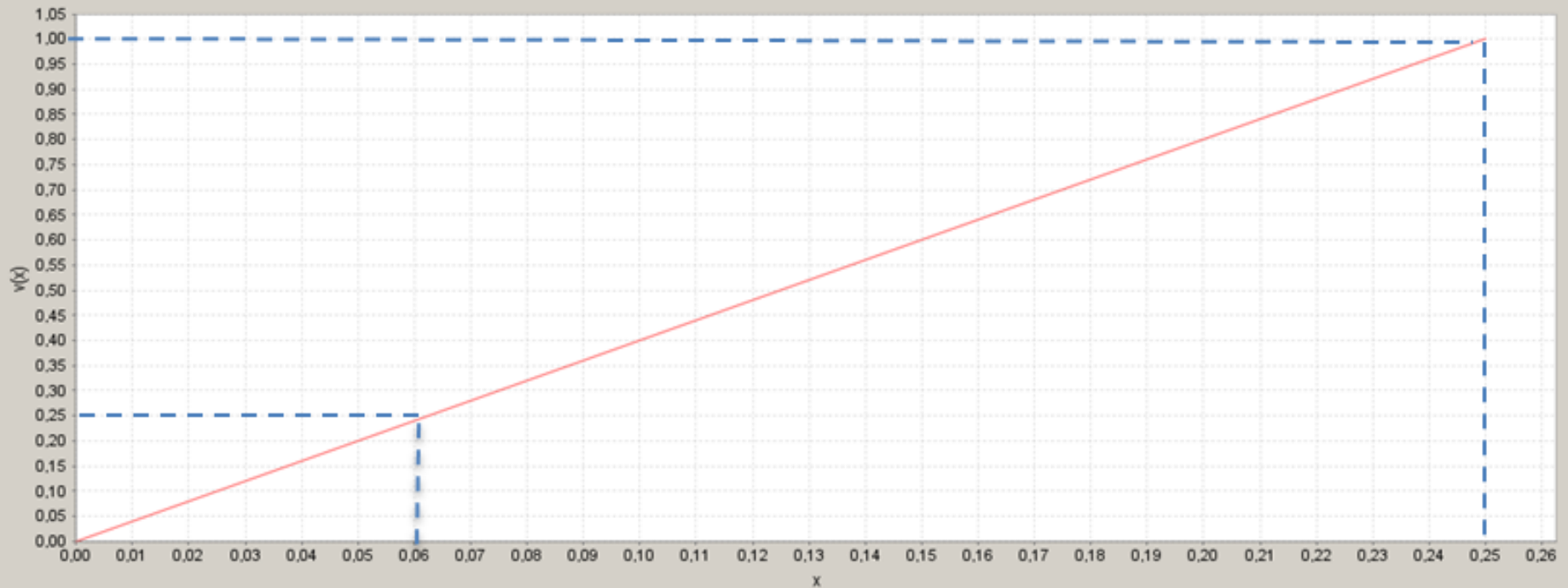
Ascending: ☒

Measurements

Alternative 1

Alternative 2

Value function



Severe adverse events



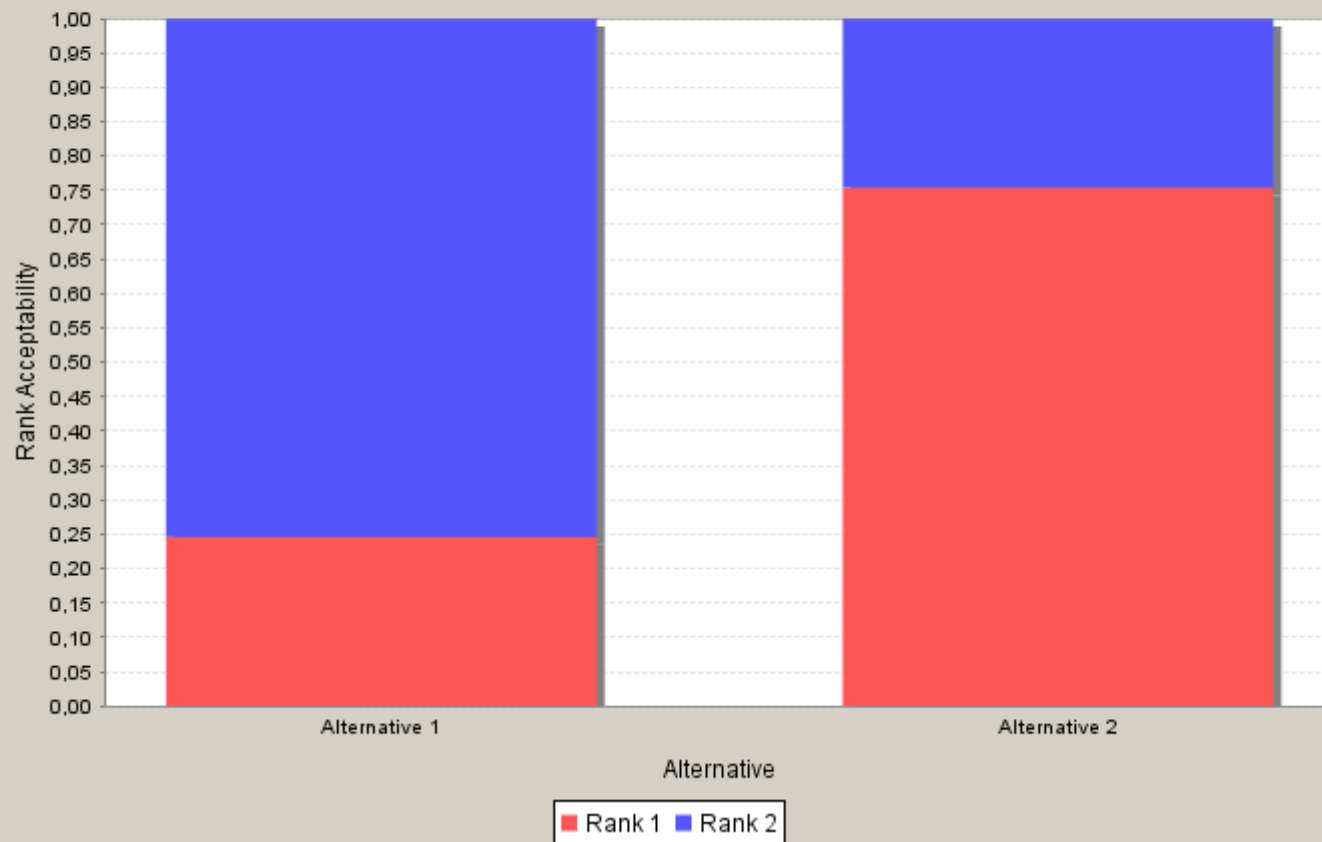
Psychiatric events



Weight loss



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



Alterntive 1 = Acomplia
Alterntive 2 = Placebo


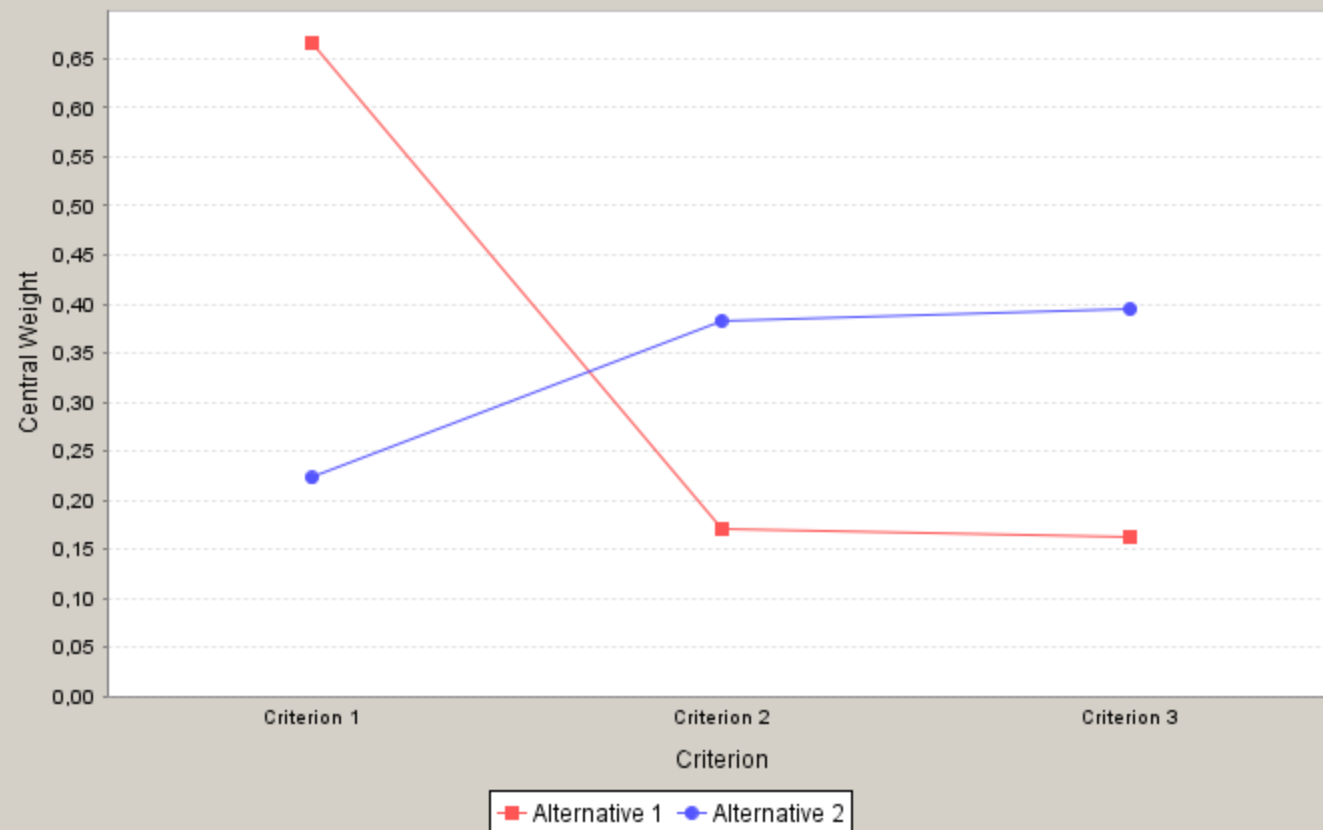


SMAA-2 Model

- 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

Value judgements ?



Decision



Descriptive facts

- **Descriptive measures:** E.g. NNT, NNH, BRR, Impact numbers.
- **Descriptive and partly normative:** E.g. BRAT, SMAA
- **Descriptive and normative:** E.g, MCDA, PROACT

Thank you for you attention!