

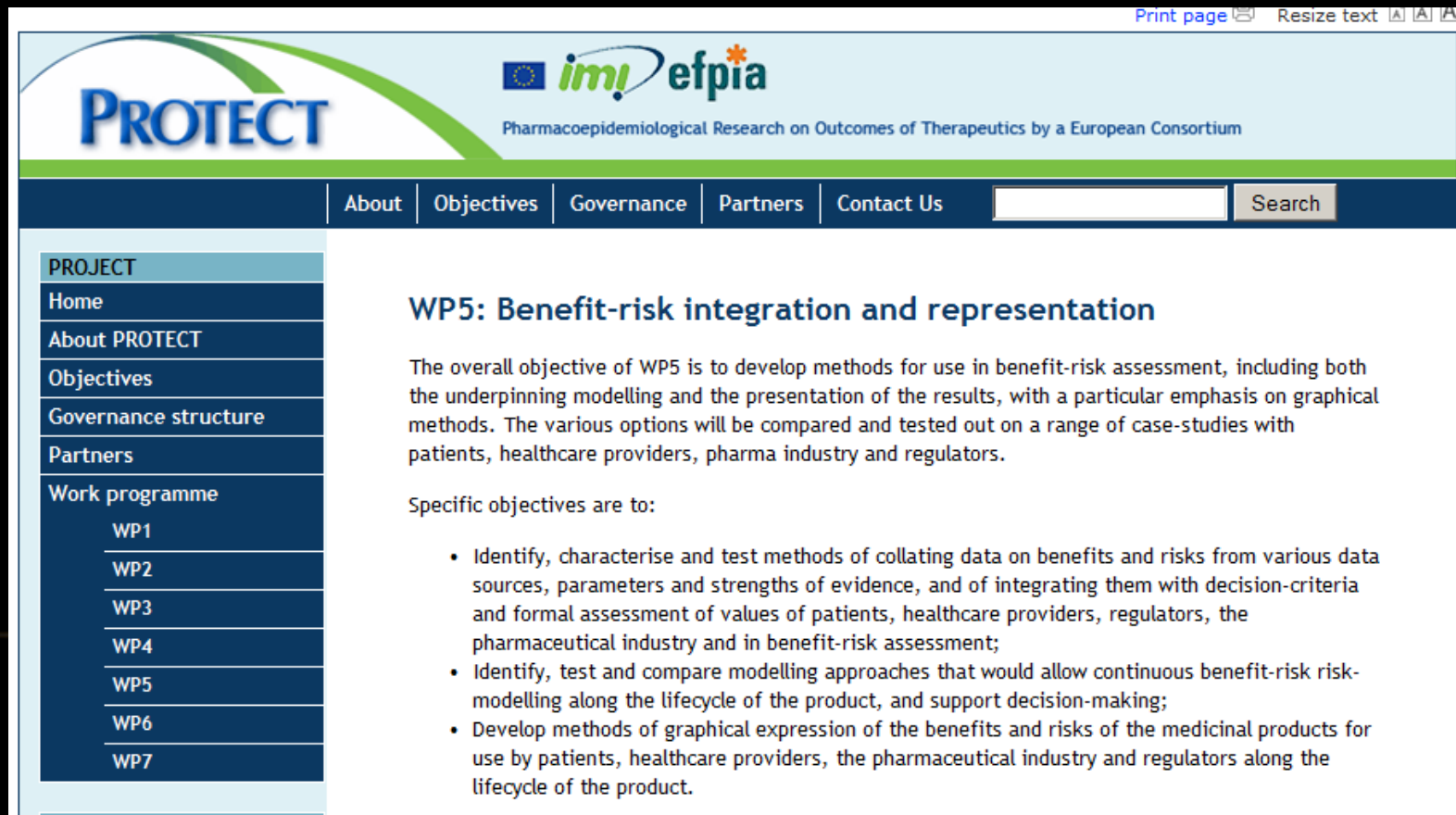
# COMPARISON OF DIFFERENT BENEFIT-RISK METHODS

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, the IMI and EFPIA logos, and the text "Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium". The navigation bar includes links for About, Objectives, Governance, Partners, and Contact Us, along with a search box. The left sidebar lists the project structure: PROJECT, Home, About PROTECT, Objectives, Governance structure, Partners, and Work programme (WP1 to WP7). The main content area displays the title "WP5: Benefit-risk integration and representation" and a paragraph describing the overall objective of WP5. Below this, it lists specific objectives.

Print page  Resize text  

**PROTECT**

IMI EFPIA

Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

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**PROJECT**

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

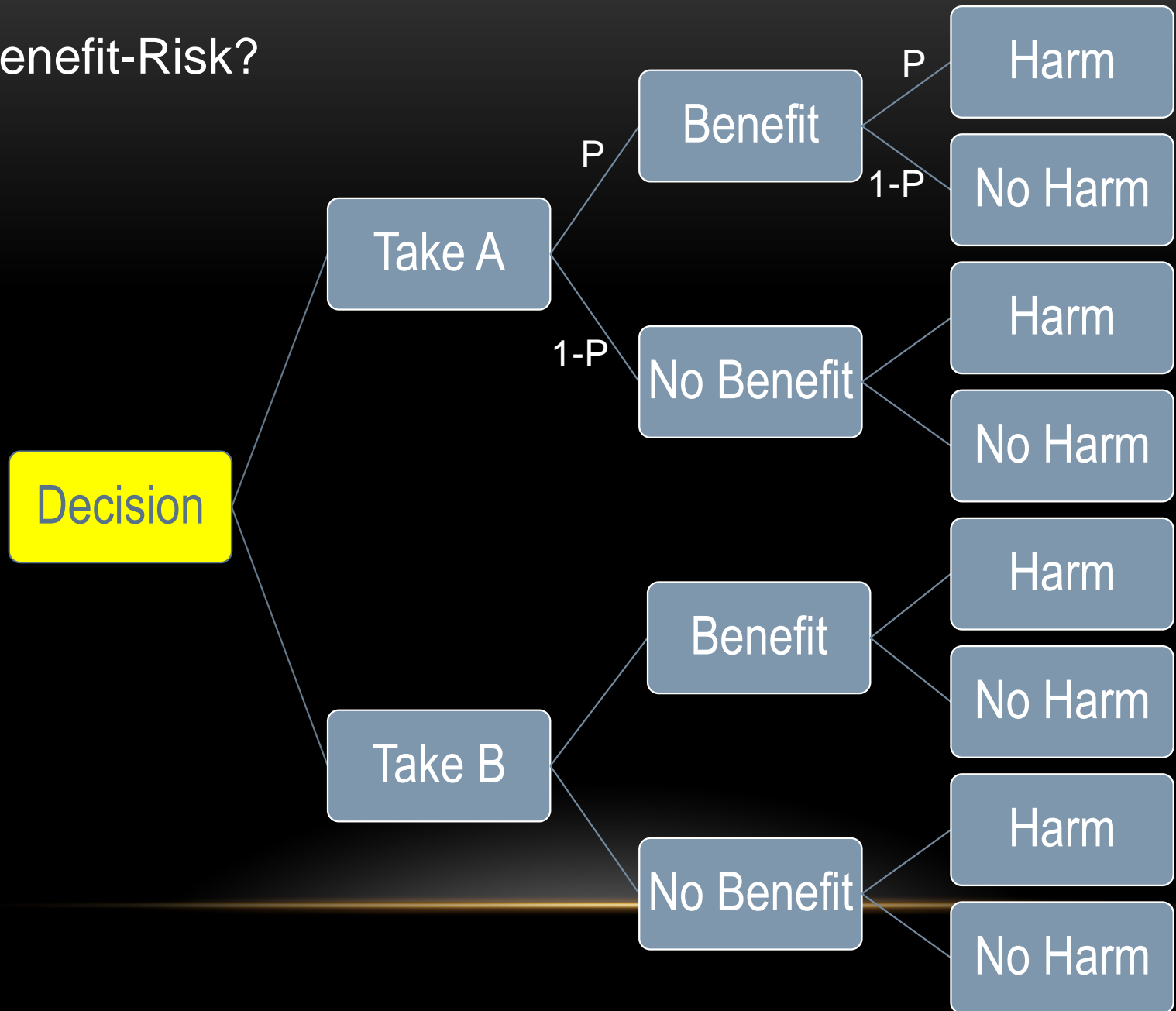
## WP5: Benefit-risk integration and representation

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**

**Impact  
numbers**

**PROACT**

**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**

# **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,<sup>1</sup> Swapnil Pandey, MS,<sup>2</sup> John Doyle, PhD,<sup>3,4</sup> Boyang Bian, MS,<sup>1</sup> Yvonne Lis, PhD,<sup>4</sup>  
Dennis W. Raisch, PhD<sup>5</sup>

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

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

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

- 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.



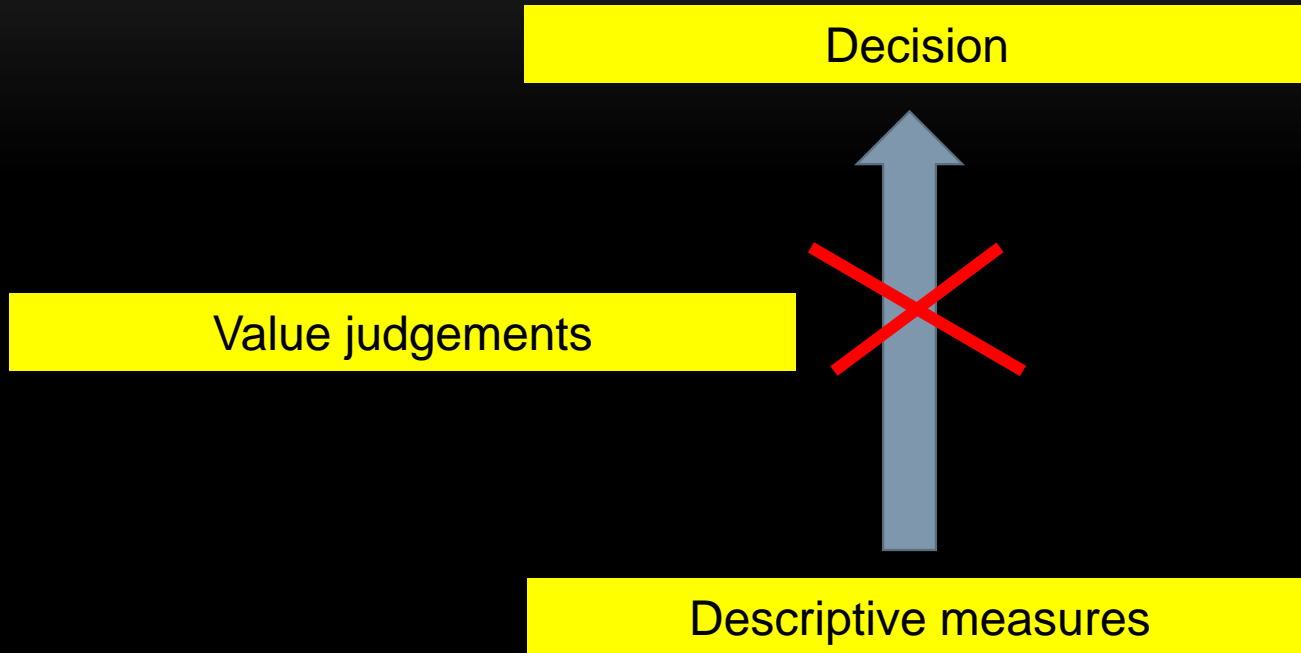
Decision



Value judgements

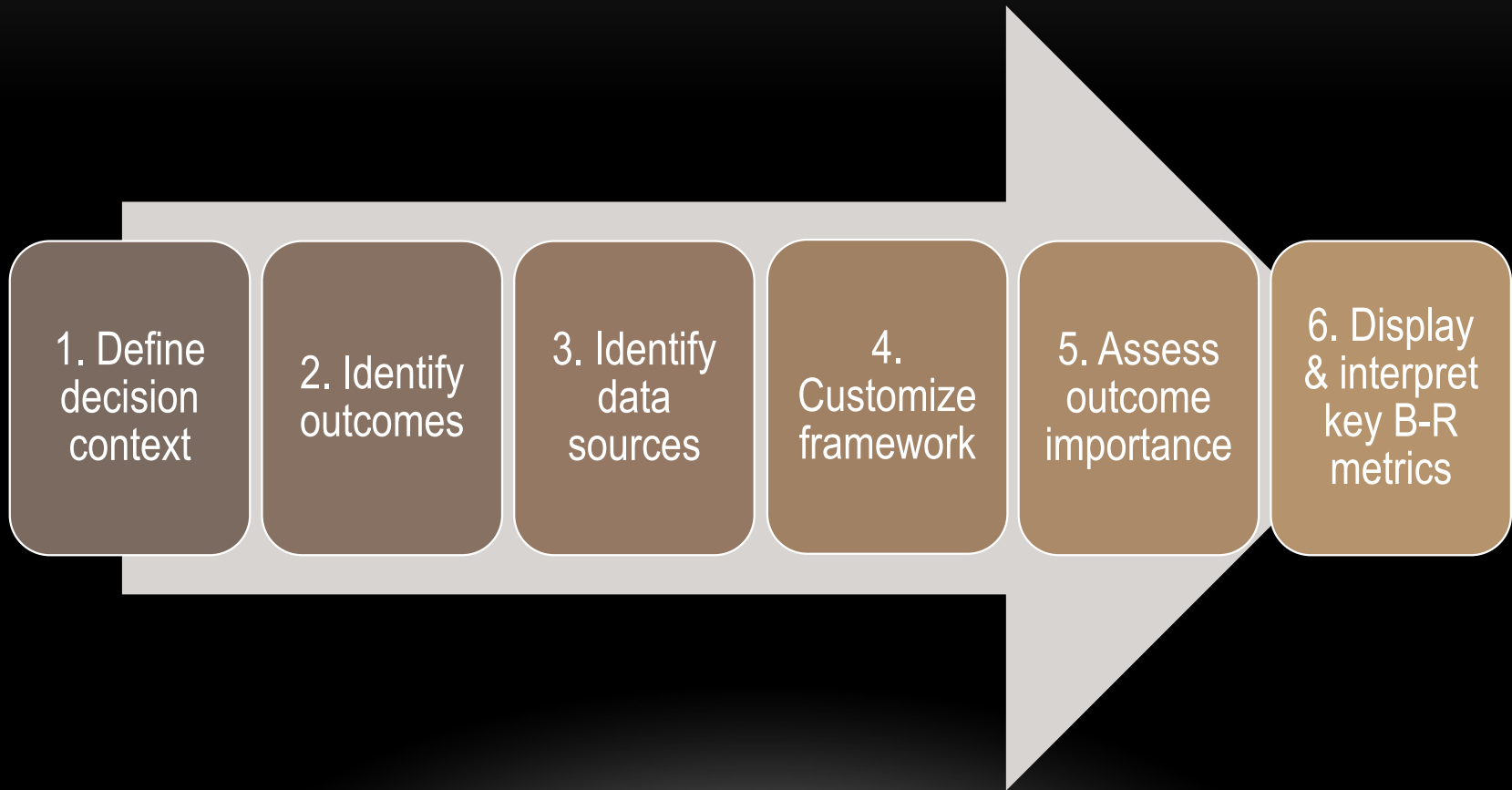


Descriptive facts



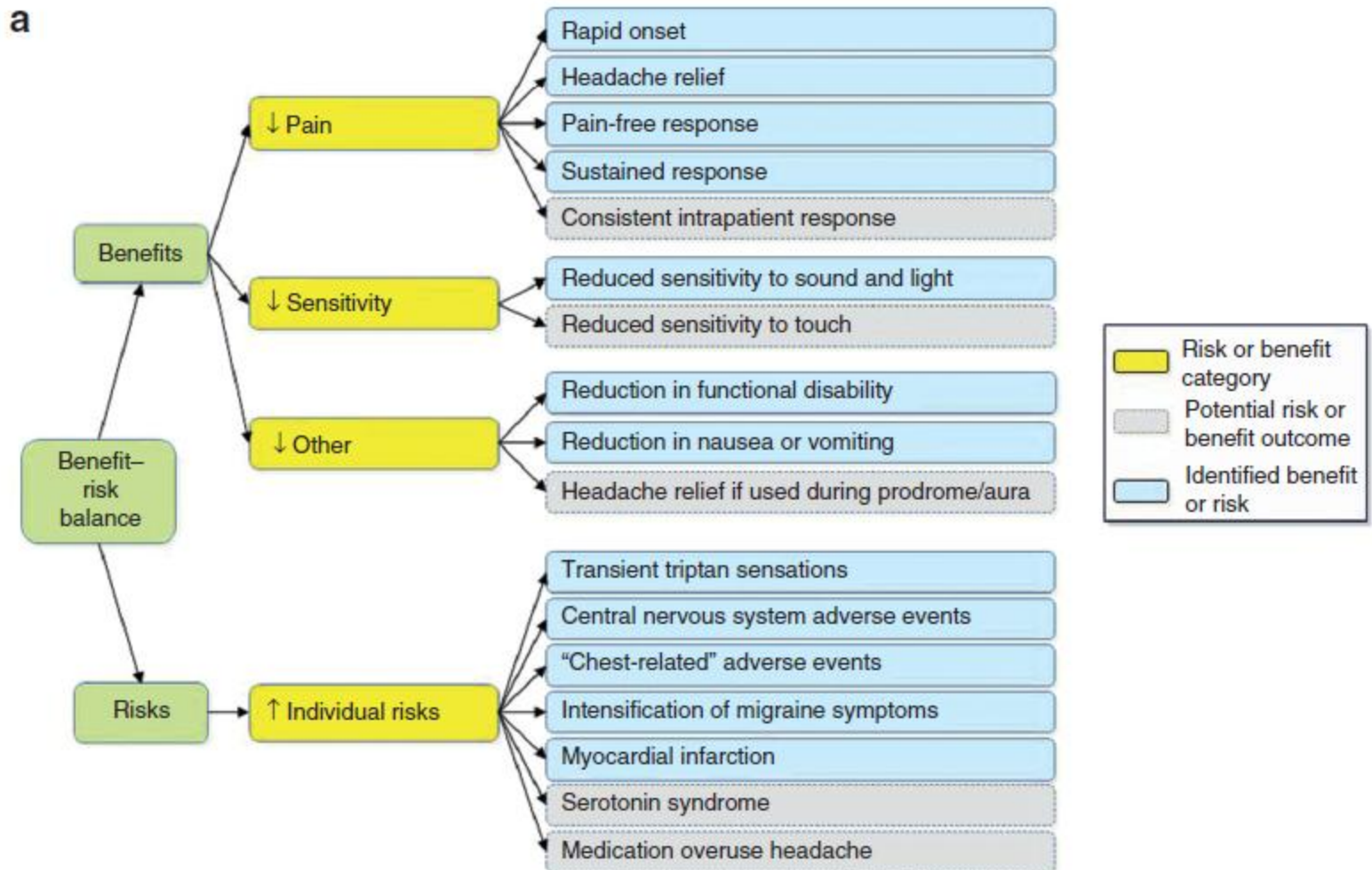
- **Descriptive measures:** E.g. NNT, NNH, BRR, Impact numbers.
- **Descriptive and partly normative:** E.g. BRAT, SMAA
- **Descriptive and normative:** E.g, MCDA, PROACT

# BRAT (Benefit Risk Action Team)

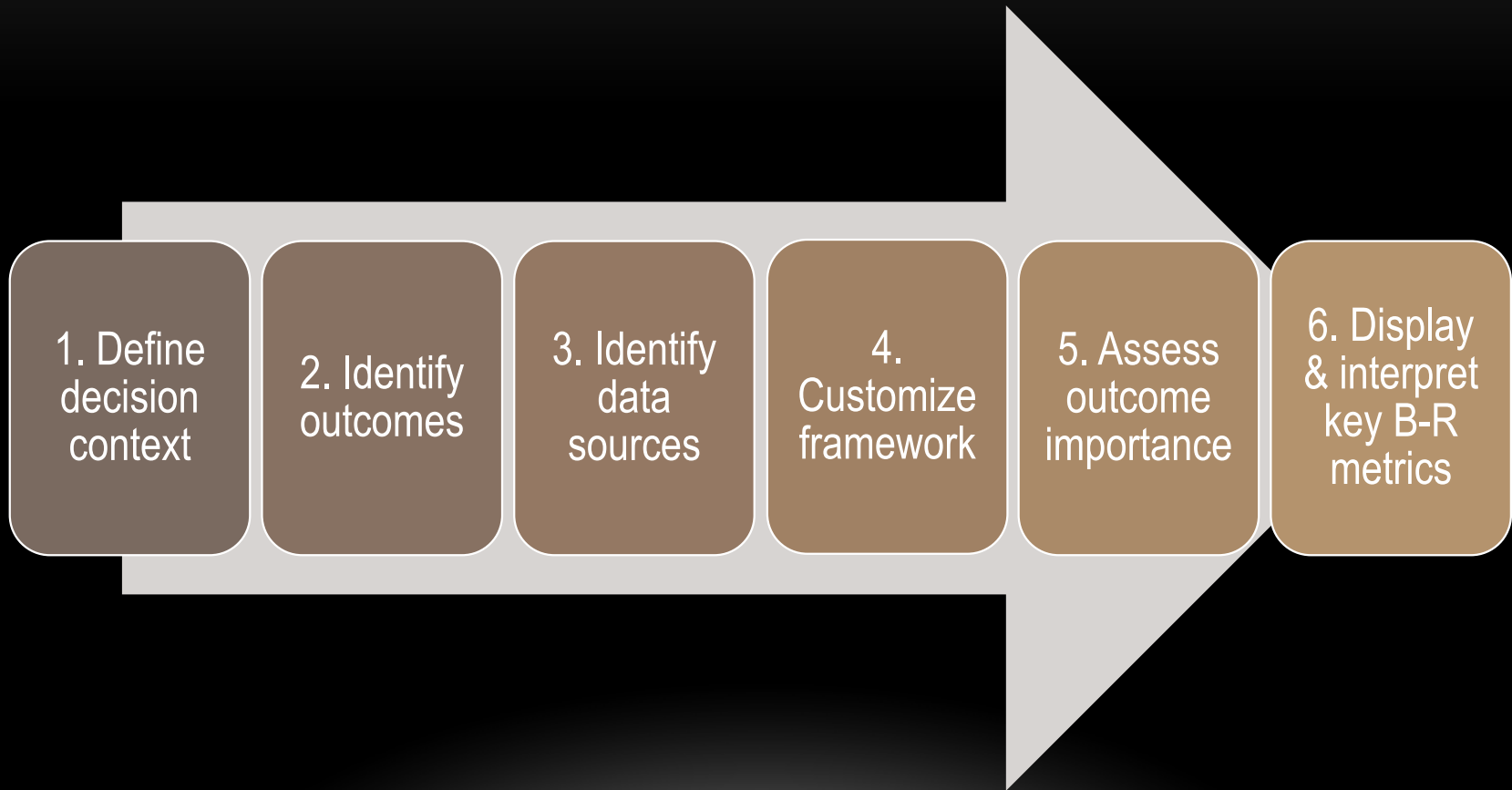


# Application of the BRAT Framework to Case Studies: Observations and Insights

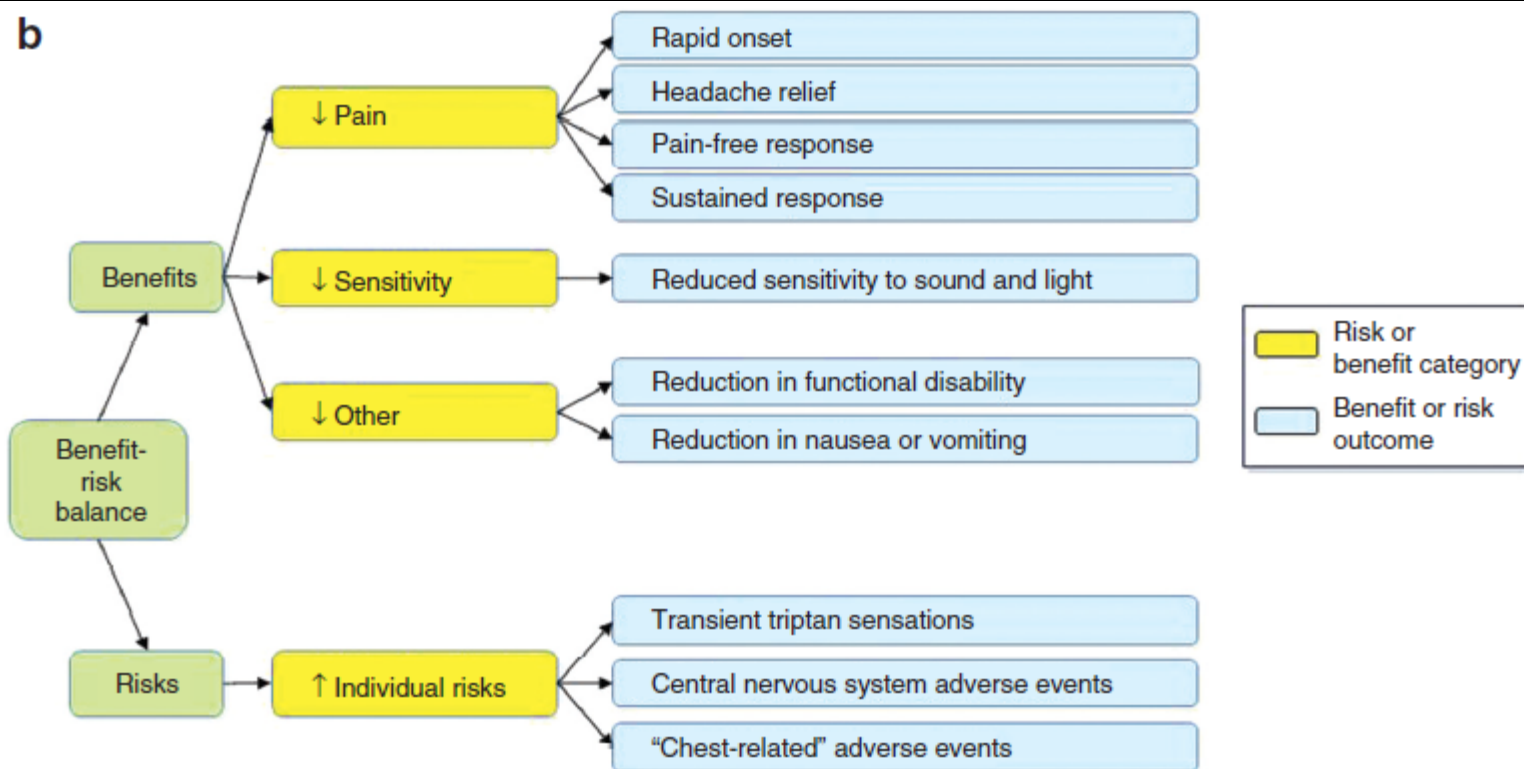
Levitan et al. *Clinical Pharmacology & Therapeutics* 89, 217-224 (February 2011)



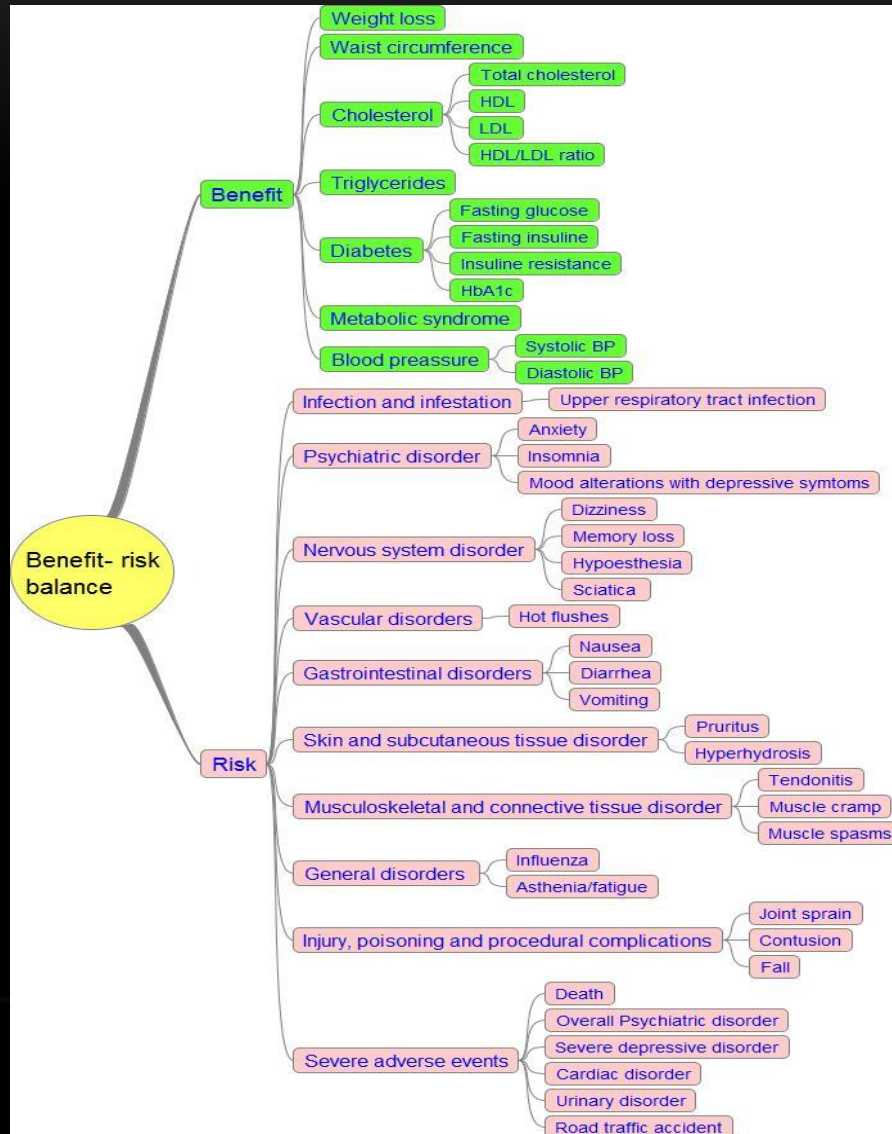
# BRAT (Benefit Risk Action Team)



## Step 4: Customize framework

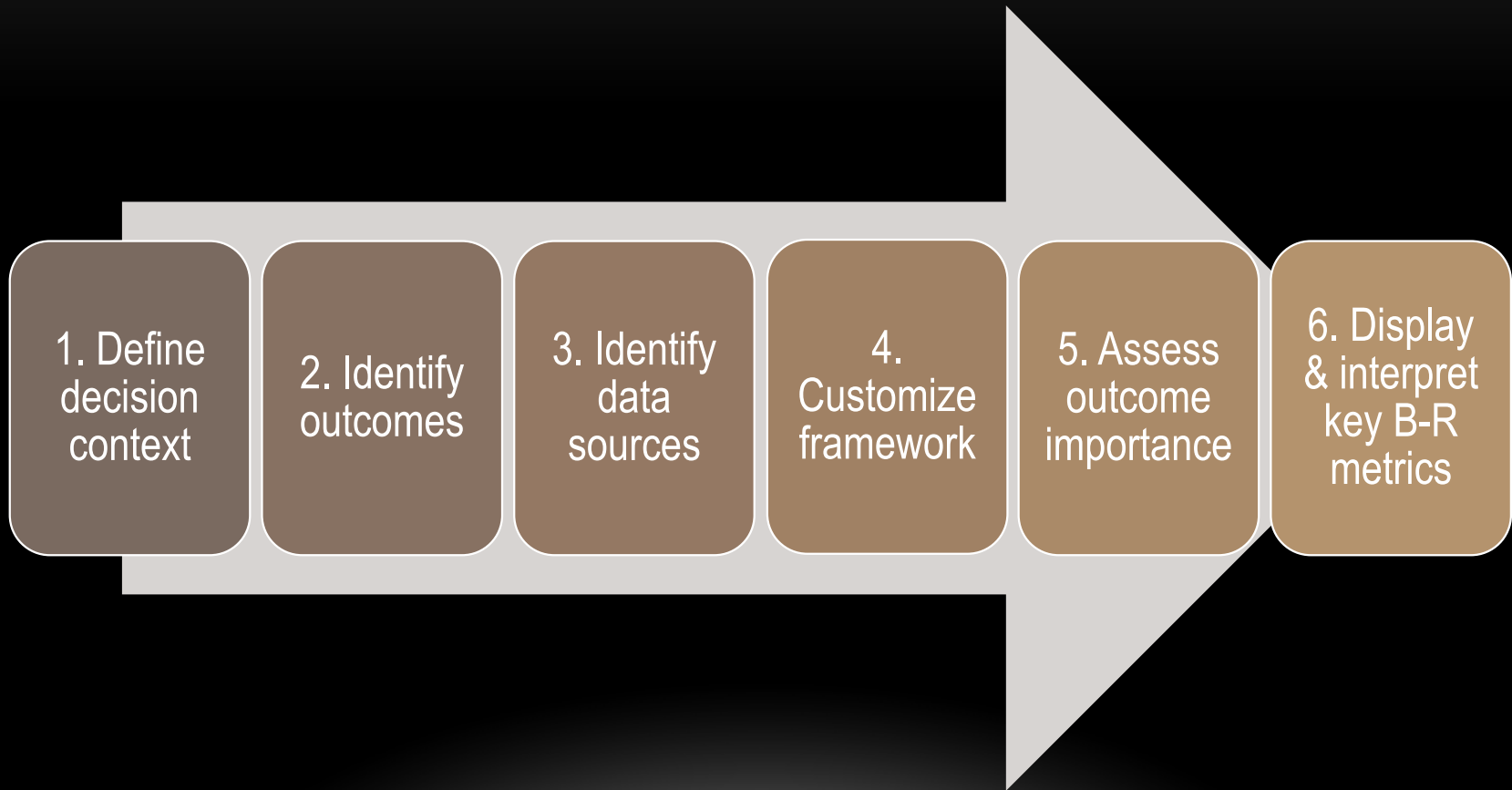


# STEP 2: IDENTIFY OUTCOMES





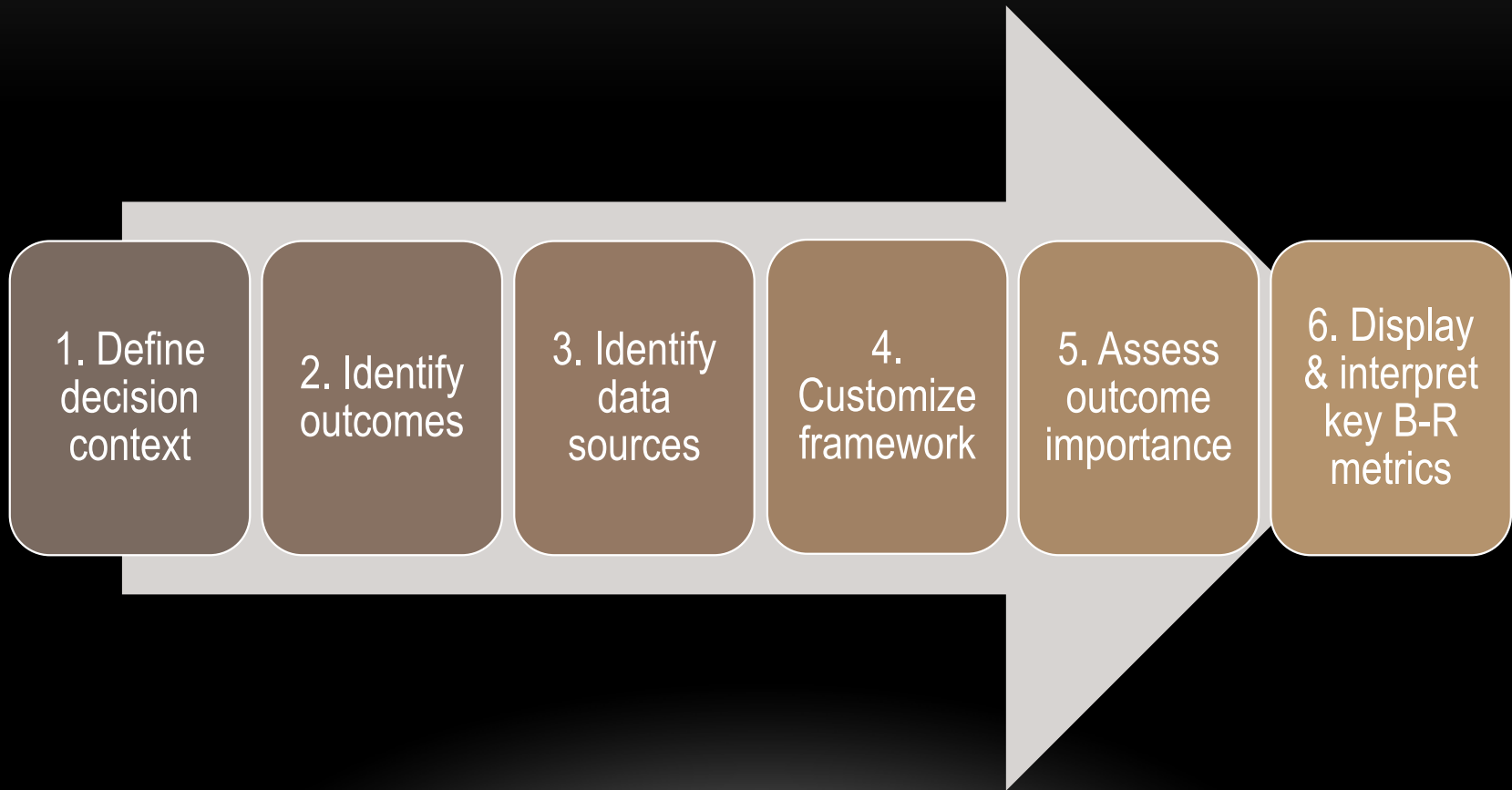
# BRAT (Benefit Risk Action Team)

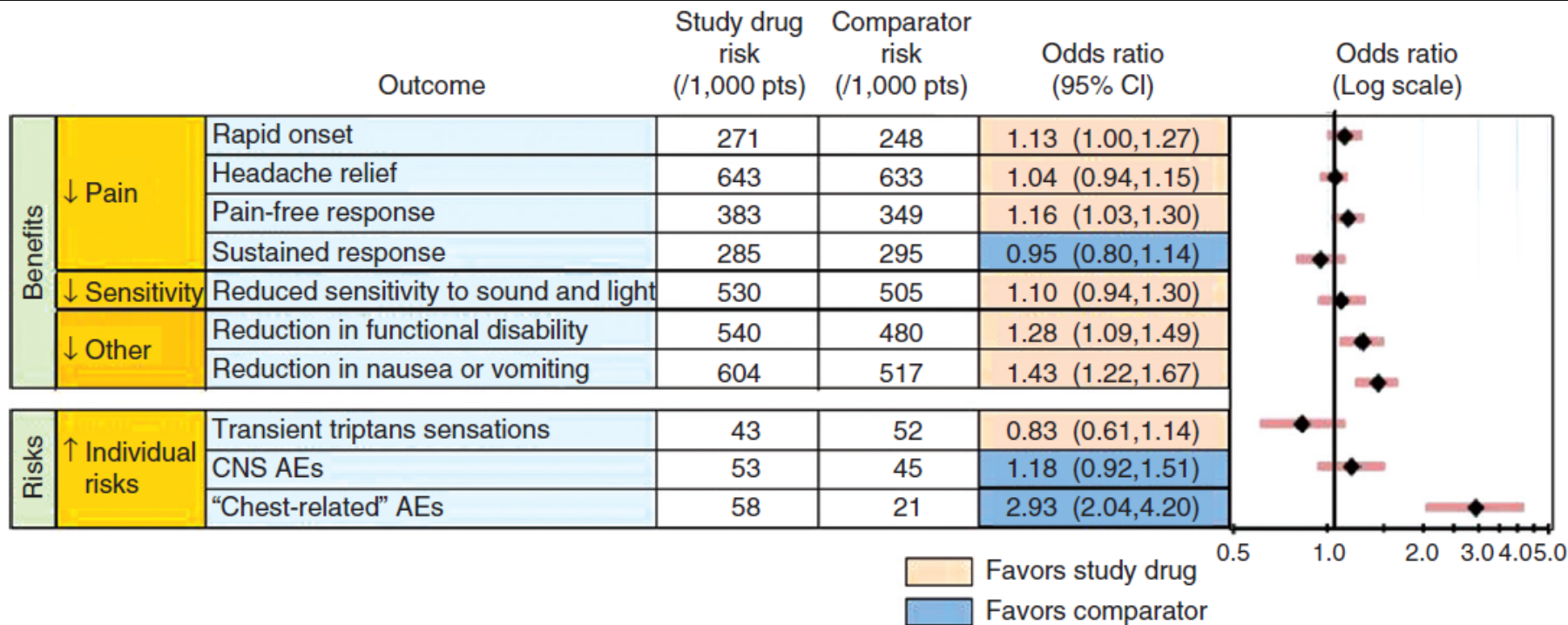


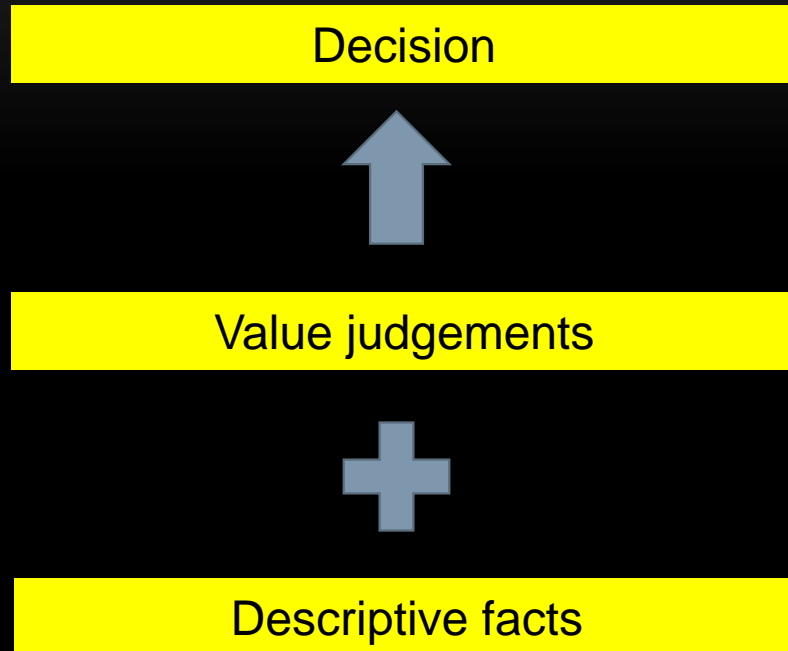
## **Step 5. Assess importance of outcome**

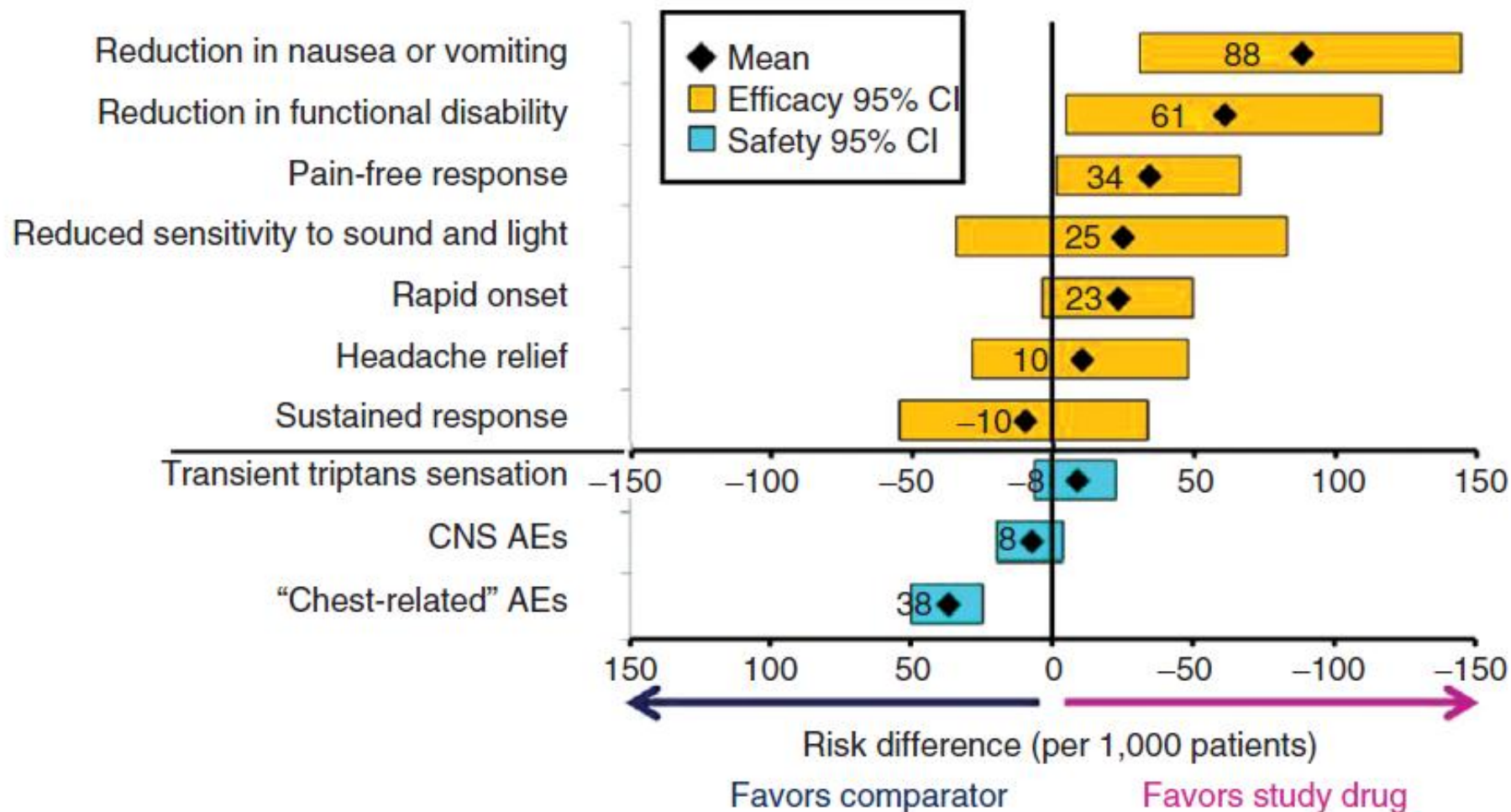
Numerous methods exist for assessing the relative importance or weight of outcomes in the value tree. Although the BRAT Framework does not advocate a particular method of importance weighting, it does facilitate the inclusion of outcome weighting information to support decisions. Importance weights are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

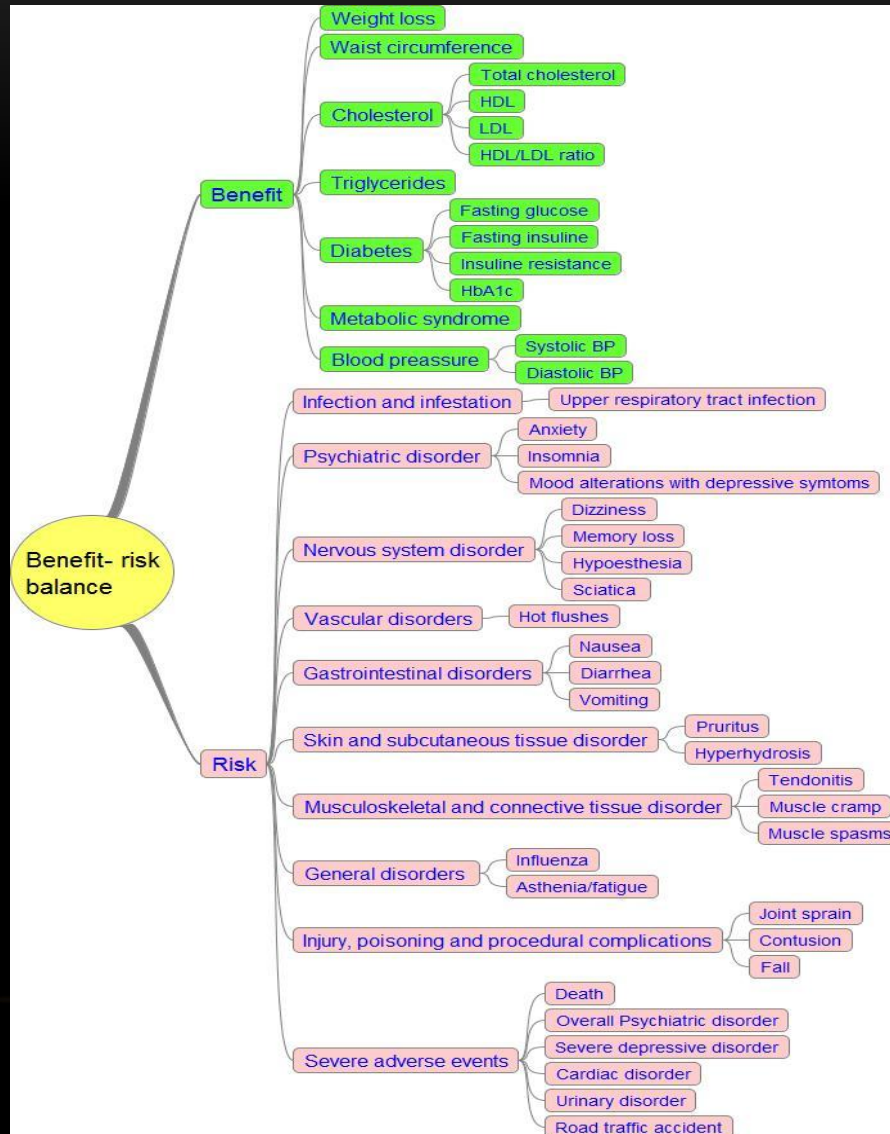
# Importance

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%

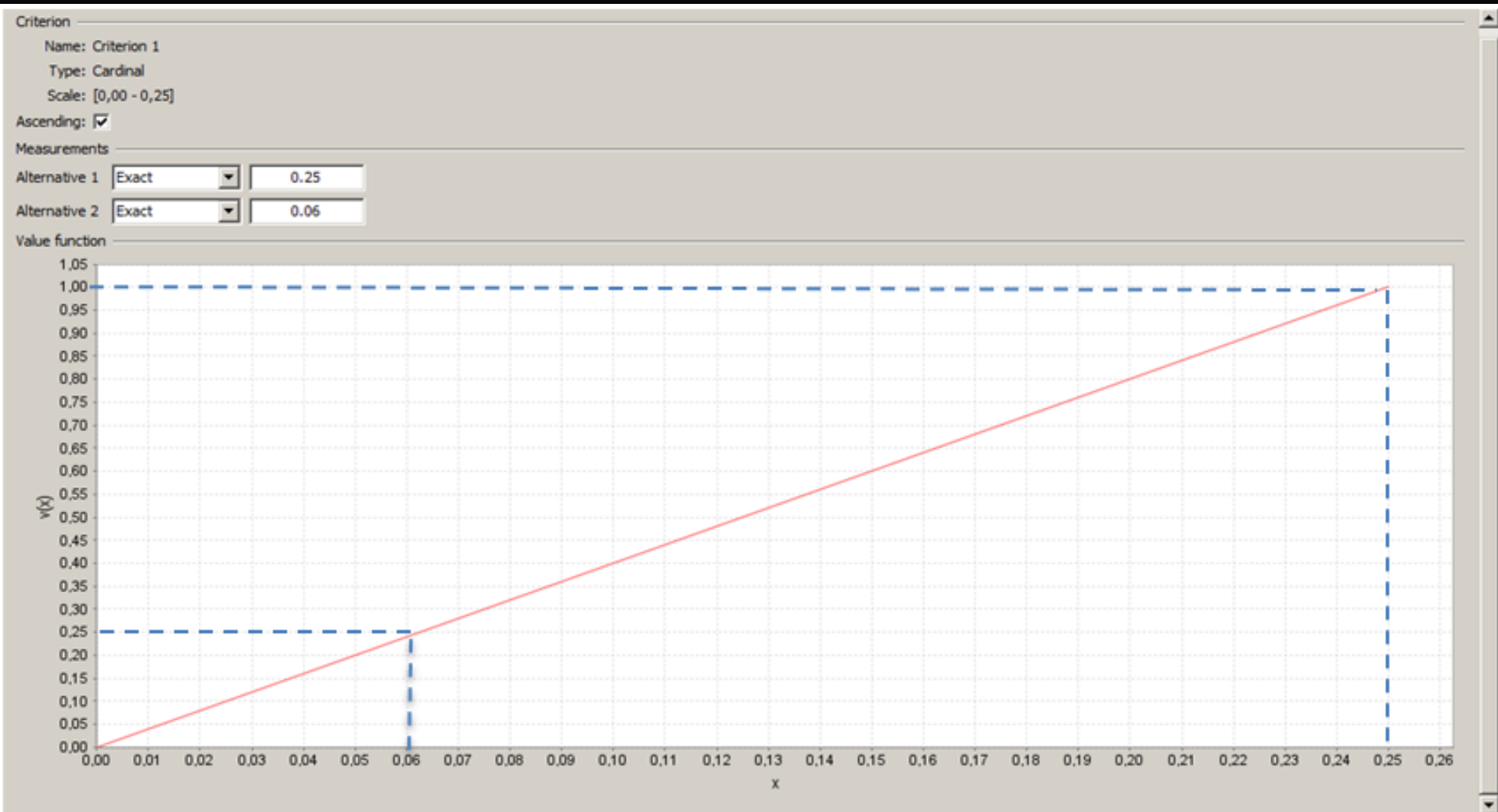
Consequences	Acomplia B	Placebo
Weight loss more than 10%	<del>25%</del> 16%	6%
Incidence of psychiatric disorders	20%	10%
Incidence of severe adverse events	<del>2%</del> 1%	1%

Consequences	Acomplia C	Placebo
Weight loss more than 10%	<del>25%</del> <del>16%</del> 6%	6%
Incidence of psychiatric disorders	<del>20%</del> 15%	10%
Incidence of severe adverse events	<del>2%</del> 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



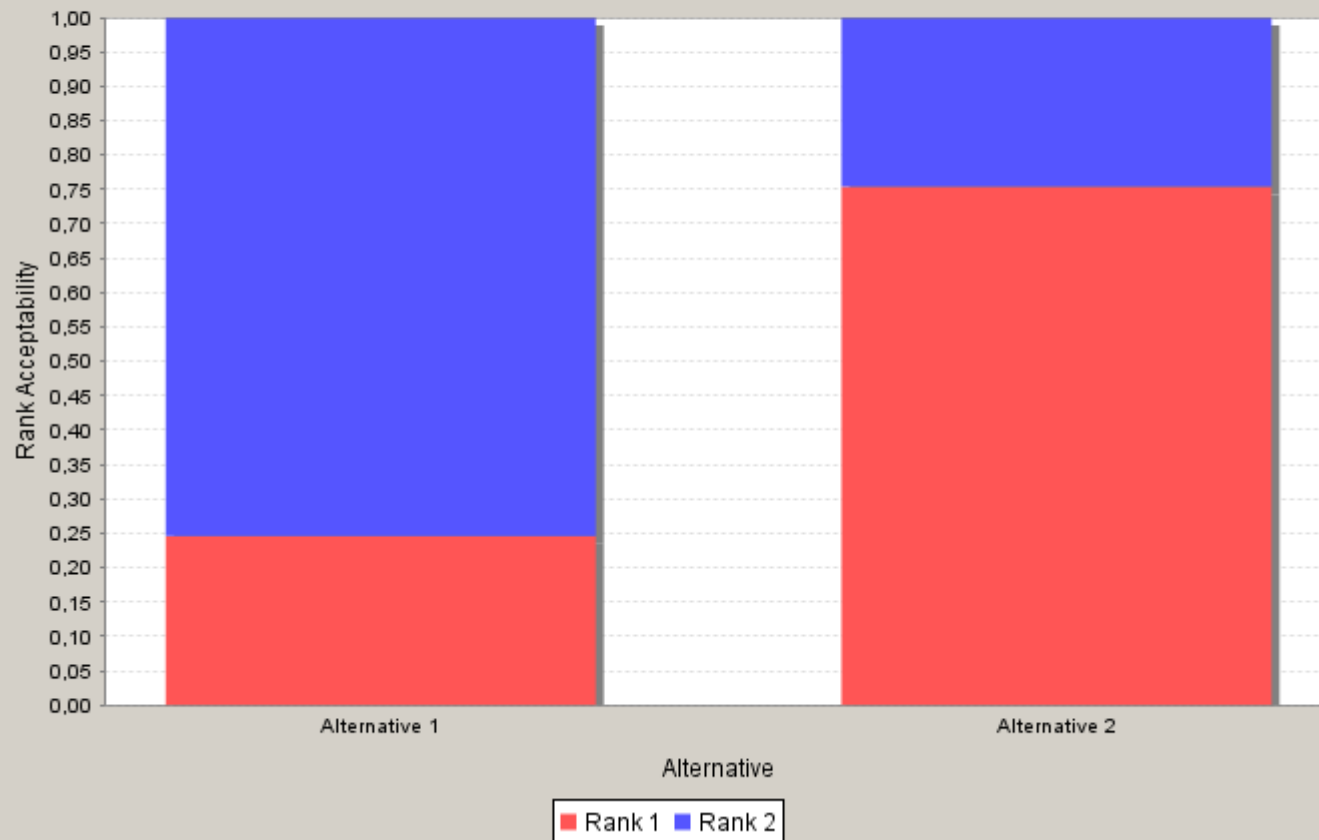
Psychiatric events



Weight loss



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



**Alterntive 1 = Acomplia**  
**Alterntive 2 = Placebo**

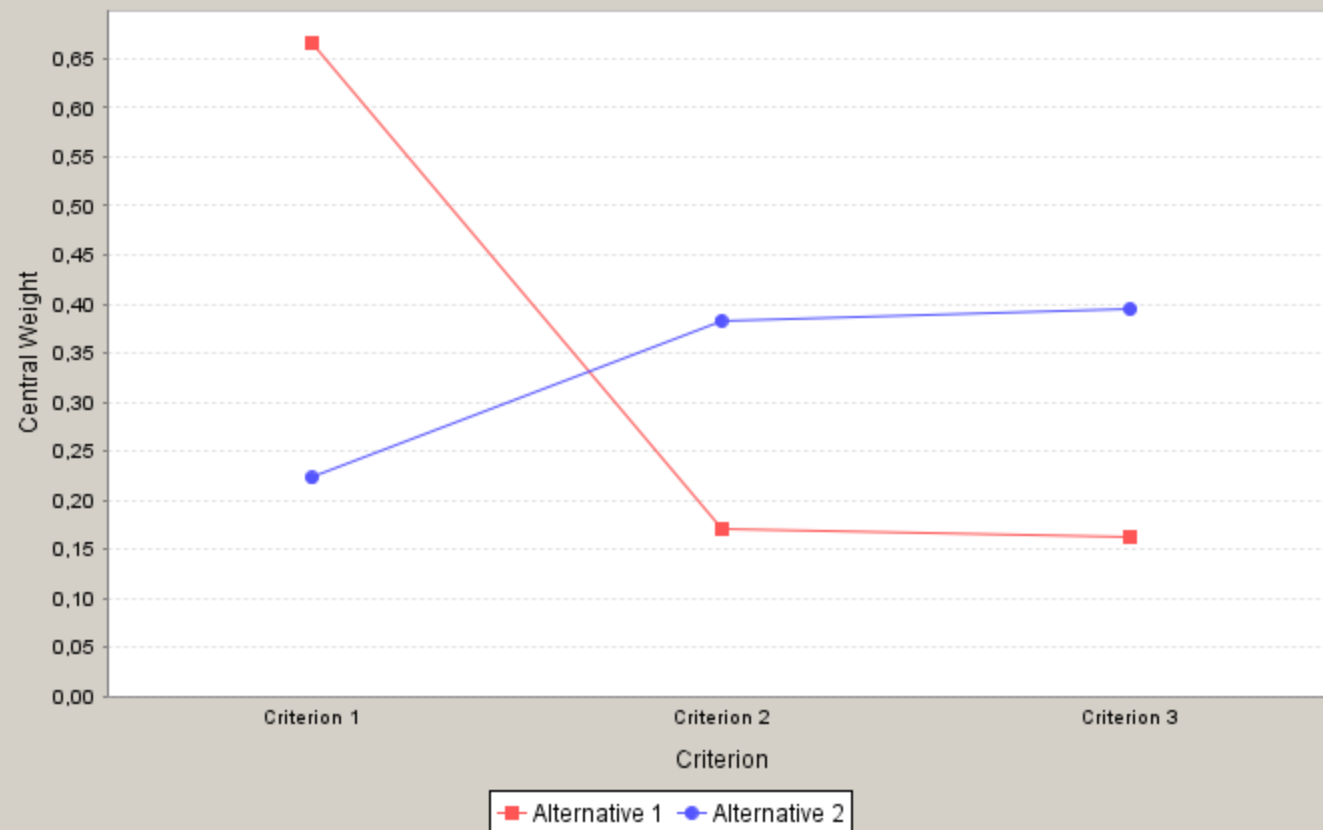


## SMAA-2 Model

- 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!