COMPARISON OF DIFFERENT BENEFIT-RISK METHODS

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

3. Astra-Zeneca

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?

- Decision
  - Take A
    - Benefit
    - No Benefit
  - Take B
    - No Benefit

P

1-P
METHODS

MCDA
NNT
BRAT
PROACT
SMAA
Impact numbers
BRR
Benefit-risk methodology project
Work package 2 report: Applicability of current tools and processes for regulatory benefit-risk assessment

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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 measures
• 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)

1. Define decision context
2. Identify outcomes
3. Identify data sources
4. Customize framework
5. Assess outcome importance
6. Display & interpret key B-R metrics
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)

1. Define decision context
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Step 4: Customize framework

Application of the BRAT Framework to Case Studies: Observations and Insights
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STEP 2: IDENTIFY OUTCOMES

Benefit-risk balance

- Weight loss
- Waist circumference
- Cholesterol
- Triglycerides
- Diabetes
- Metabolic syndrome
- Blood pressure
- Systolic BP
- Diastolic BP
- Infection and infestation
- Upper respiratory tract infection
- Psychiatric disorder
- Anxiety
- Insomnia
- Mood alterations with depressive symptoms
- Dizziness
- Memory loss
- Hypoesthesia
- Sciatica
- Vascular disorders
- Hot flushes
- Gastrointestinal disorders
- Nausea
- Diarrhea
- Vomiting
- Skin and subcutaneous tissue disorder
- Pruritus
- Hyperhidrosis
- Tendinitis
- Muscle cramp
- Muscle spasm
- Musculoskeletal and connective tissue disorder
- Musculoskeletal and connective tissue disorder
- Influenza
- Asthenia/fatigue
- General disorders
- Joint sprain
- Confusion
- Fall
- Injury, poisoning and procedural complications
- Severe adverse events
- Death
- Overall Psychiatric disorder
- Severe depressive disorder
- Cardiac disorder
- Urinary disorder
- Road traffic accident
BRAT (Benefit Risk Action Team)

1. Define decision context
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**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)

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Decision

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Descriptive facts
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# Importance

How important are the following outcomes?

<table>
<thead>
<tr>
<th></th>
<th>1. Unimportant</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5. Very important</th>
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<tbody>
<tr>
<td>Weight loss</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
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<tr>
<td>Lowering cholesterol</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
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</tr>
<tr>
<td>Psychiatric events</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
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<tr>
<td>Dizziness</td>
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<tr>
<td>.....</td>
<td>○</td>
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<td>○</td>
<td>○</td>
<td>○</td>
</tr>
</tbody>
</table>
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

<table>
<thead>
<tr>
<th>Consequences</th>
<th>Acomplia A</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss more than 10%</td>
<td>25%</td>
<td>6%</td>
</tr>
<tr>
<td>Incidence of psychiatric disorders</td>
<td>20%</td>
<td>10%</td>
</tr>
<tr>
<td>Incidence of severe adverse events</td>
<td>2%</td>
<td>1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consequences</th>
<th>Acomplia B</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight loss more than 10%</td>
<td>25%–16%</td>
<td>6%</td>
</tr>
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</tr>
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</tbody>
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<table>
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<tr>
<th>Consequences</th>
<th>Acomplia C</th>
<th>Placebo</th>
</tr>
</thead>
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</tr>
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STOCHASTIC MULTICRITERIA ACCEPTABILITY ANALYSIS (SMAA)


- The OpenSource software, JSMAA. http://smaa.fi/jsmaa/
<table>
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</table>
Severe adverse events

Psychiatric events

Weight loss
Alternative 1 = Acomplia
Alternative 2 = Placebo
Value judgements?

Decision

Descriptive facts
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Thank you for your attention!