Visualizing Uncertainty among laypersons and experts

- PROTECT SYMPOSIUM
- 20 February 2015

Andrea Beyer Phd
Contents

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• Study objectives
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Background

• Work Package 5 had several objectives:
  
  • 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.
WP6-WP5 Extension Studies

Workstream 1
Test how B/R methods adapt in a real-life setting

Lead Billy Amzal (LASER)

Workstream 2
Validate visualisation tools recommended by WP5 to the targeted audience

Lead Andrea Beyer (Groningen)
Workstream 2 - Research questions

Validation of Methods for Presentation of BR data

- Research Questions:
  - What graphical presentation methods are most useful for regulators/physicians in evaluating benefit-risk tradeoffs?
  - What graphical presentation methods are most useful for helping patients to understand benefits and risks of medicines?

Extension of Methodology to Elicit Patient Preferences

- Research Questions:
  - How comparable are the methods used in WP5 for eliciting preferences?
  - What are the differences in preferences for treatment outcomes among 3 stakeholders (patients, healthcare professionals, medical assessors)?
Study Objectives

The primary objective:

- measure the comprehension of benefit and risk data of medicinal products using several graphical presentation formats
  - What is the level of comprehension when benefit risk data are presented as text (as in EPAR)
  - Is there an change in comprehension when benefit risk data are presented graphically

The secondary objectives:

- impact of presentation format and order on perception of benefits and risks
- impact of mood states on comprehension of benefits and risks
- build decision models using elicited preferences and available clinical trial data

The exploratory objectives:

- explore differences between textual and graphical presentations
- compare *a priori* stated preference vs. preference elicited with two elicitation models
- build predictive models for the MACBETH value function curves
Study design – Study Population

- Patients
- Healthcare Professionals
- Medical Assessors

- Diabetes
- Atrial Fibrillation
- Breast Cancer
Study design – Countries

Patients and Healthcare Professionals

- United Kingdom
- The Netherlands
- France

Medical Assessors

- All European countries invited to participate via CHMP and PRAC
# Study design – Recruitment goals

<table>
<thead>
<tr>
<th>Patients</th>
<th>Healthcare Professionals</th>
<th>Medical Assessors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes: 300 per country</td>
<td>Diabetes: 300 per country</td>
<td>Voluntary enrollment</td>
</tr>
<tr>
<td>Atrial Fibrillation: 300 per country</td>
<td>Atrial Fibrillation: 300 per country</td>
<td></td>
</tr>
<tr>
<td>Breast Cancer: 300 per country</td>
<td>Breast Cancer: 300 per country</td>
<td></td>
</tr>
<tr>
<td>Total: 2700</td>
<td>Total: 2700</td>
<td></td>
</tr>
</tbody>
</table>

Patients: 300 per country for Diabetes, Atrial Fibrillation, and Breast Cancer, totaling 2700.

Healthcare Professionals: 300 per country for Diabetes, Atrial Fibrillation, and Breast Cancer, totaling 2700.

Medical Assessors: Voluntary enrollment.
Study design - Recruitment methods

- **The Netherlands**
  - Patients and Healthcare Professionals
  - Patient & professionals organizations
  - 10 Hospital departments plus incentive

- **United Kingdom**
  - Patient & professionals organizations
  - 20 NHS clinics plus incentive

- **France**
  - Directly via (e)mail and telephone

- **Europe**
  - Letters and emails via CHMP and PRAC members

May-Sep 2014 – Oct 2014-Present
# Study design – Focus groups

(150 pts per disease area)

<table>
<thead>
<tr>
<th>Disease Area</th>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Reduction HbA1c levels</td>
<td>Hospitalization for heart failure</td>
</tr>
<tr>
<td></td>
<td>Change in fasting plasma glucose levels</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Reduction ischemic stroke</td>
<td>Fatal bleeding</td>
</tr>
<tr>
<td></td>
<td>Reduction myocardial infarction</td>
<td>Major bleeding</td>
</tr>
<tr>
<td></td>
<td>Reduction pulmonary embolism</td>
<td>Minor bleeding</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>Overall survival</td>
<td>Gastrointestinal symptoms</td>
</tr>
<tr>
<td></td>
<td>Progression free survival</td>
<td>Cardiac disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peripheral neuropathy</td>
</tr>
</tbody>
</table>
Study design – data flow

Enrollment
- Informed consent
- Randomization

Part 1.a
- Drug Vignette > Table > Plot
- Drug Vignette > Plot > Table
- Table > Plot > Drug Vignette
- Plot > Table > Drug Vignette
- Comprehension questions
- Mood state

Part 1.b
- Perception
- Stated preferences

Part 2
- Demographics
- Disease characteristics
- Numeracy

Part 3
- Preference elicitation
- MACBETH
- Discrete Choice
Welcome to the VISUALize Study website and thank you for participating in this study. The data collected in this survey will help health authorities to improve the communication of benefits and risks of medicines. We will collect data on your understanding of benefit-risk data for medicines and your preferences for possible treatment outcomes related to your disease. Please choose the correct questionnaire from the options below to enter the site and begin the survey.

Which of the statements below describes you?

- I have been diagnosed with atrial fibrillation
- I have been diagnosed with breast cancer
- I have been diagnosed with diabetes
- I am a healthcare professional for pharmaceutical products in the area of atrial fibrillation
- I am a healthcare professional for pharmaceutical products in the area of breast cancer
- I am a healthcare professional for pharmaceutical products in the area of diabetes
- I am a medical assessor for pharmaceutical products in the area of atrial fibrillation
- I am a medical assessor for pharmaceutical products in the area of breast cancer
- I am a medical assessor for pharmaceutical products in the area of diabetes
- I am being treated for obesity

Start
Examples of presentation formats

**Drug Vignette (similar to EPAR):**
A study for the treatment of diabetes showed that HbA1c levels in patients who took Drug X, fell by 0.5% after 2 years, compared with a decrease of 0.2% in patients taking placebo. Furthermore, fasting plasma glucose levels decreased 3.1 mg/dl in the patients who took Drug X, whereas it increased 1.6 mg/dl in the patients taking placebo.

<table>
<thead>
<tr>
<th>Description</th>
<th>Drug X</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in HbA1c levels</td>
<td>0.5%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Change in fasting plasma glucose levels (mean)</td>
<td>3.1 mg/dl reduction</td>
<td>1.6 mg/dl increase</td>
</tr>
<tr>
<td>Hospitalization for heart failure</td>
<td>3.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Weight gain (mean)</td>
<td>0.6 kg</td>
<td>1.0 kg</td>
</tr>
</tbody>
</table>

**Abbreviated Effects Table**

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Drug X</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in HbA1c levels</td>
<td>0.5%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Change in fasting plasma glucose levels (mean)</td>
<td>3.1 mg/dl reduction</td>
<td>1.6 mg/dl increase</td>
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<tr>
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<td>3.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Weight gain (mean)</td>
<td>0.6 kg</td>
<td>1.0 kg</td>
</tr>
</tbody>
</table>

**Bar graphs**

Bar graphs showing the percentage of people with atrial fibrillation who had an event within one year for different treatments.
Examples of presentation formats

Survival curve

Pictograms

Diarrhea in breast cancer patients treated with Drug X
Example questions on benefits and risks

1. In the survival curves, how many treatment groups are there?
   - 2
   - 3
   - 1
   - I don’t know

2. Which of the treatments had a better result, i.e. more reduction of HbA1c levels?
   - Both equally good results
   - Treatment with placebo
   - Treatment with Drug X
   - I don’t know

3. What percentage of patients had major bleedings when taking Drug X-150 mg?
   - 3.3%
   - 14.9%
   - 2.9%
   - I don’t know
Recruitment efforts – Progress

Responses per questionnaire (countries combined)

- Diabetes patient
- Breast Cancer patient
- Atrial Fibrillation patient
- Diabetes hcp
- Breast Cancer hcp
- Atrial Fibrillation hcp
## Demographics (countries combined)

<table>
<thead>
<tr>
<th></th>
<th>Diabetes N= 419 Patients</th>
<th>Atrial fibrillation N= 161 Patients</th>
<th>Breast cancer N= 190 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>59%</td>
<td>69%</td>
<td>0%</td>
</tr>
<tr>
<td>Age (mean ± sd)</td>
<td>60 ± 12</td>
<td>64 ± 9.9</td>
<td>57 ± 11</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; Associate degree</td>
<td>64%</td>
<td>62%</td>
<td>57%</td>
</tr>
<tr>
<td>&gt; Associate degree</td>
<td>36%</td>
<td>38%</td>
<td>43%</td>
</tr>
<tr>
<td>Numeracy level (mean ± sd)</td>
<td>1.9 ± 1.0</td>
<td>2.1 ± 1.0</td>
<td>1.8 ± 1.1</td>
</tr>
<tr>
<td>- 0 questions correct</td>
<td>12%</td>
<td>9%</td>
<td>16%</td>
</tr>
<tr>
<td>- 1 question correct</td>
<td>21%</td>
<td>21%</td>
<td>20%</td>
</tr>
<tr>
<td>- 2 questions correct</td>
<td>30%</td>
<td>23%</td>
<td>32%</td>
</tr>
<tr>
<td>- 3 questions correct</td>
<td>37%</td>
<td>47%</td>
<td>32%</td>
</tr>
</tbody>
</table>
## Comprehension – Benefit and Risks (DB)

<table>
<thead>
<tr>
<th></th>
<th>Percentage of patients with correct answers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 questions correct</td>
</tr>
<tr>
<td><strong>Drug vignette – Benefits</strong></td>
<td>3%</td>
</tr>
<tr>
<td><strong>Drug vignette – Risks</strong></td>
<td>9%</td>
</tr>
<tr>
<td><strong>Table – Benefits</strong></td>
<td>4%</td>
</tr>
<tr>
<td><strong>Table – Risks</strong></td>
<td>6%</td>
</tr>
<tr>
<td><strong>Bar graph – Benefits</strong></td>
<td>4%</td>
</tr>
<tr>
<td><strong>Bar graph – Risks</strong></td>
<td>5%</td>
</tr>
</tbody>
</table>
Comprehension – Benefits and Risks (DB)

```
<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.31</td>
<td>2.65</td>
</tr>
<tr>
<td>2.34</td>
<td>2.56</td>
</tr>
<tr>
<td>2.39</td>
<td></td>
</tr>
</tbody>
</table>
```

Mean score (range 0-3)
## Comprehension – Benefit and Risks (AF)

### Table – Percentage of patients with correct answers

<table>
<thead>
<tr>
<th></th>
<th>0 questions correct</th>
<th>1 question correct</th>
<th>2 questions correct</th>
<th>3 questions correct</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug vignette – Benefits</strong></td>
<td>7%</td>
<td>10%</td>
<td>18%</td>
<td>65%</td>
</tr>
<tr>
<td><strong>Drug vignette – Risks</strong></td>
<td>11%</td>
<td>7%</td>
<td>17%</td>
<td>65%</td>
</tr>
<tr>
<td><strong>Table – Benefits</strong></td>
<td>5%</td>
<td>6%</td>
<td>18%</td>
<td>71%</td>
</tr>
<tr>
<td><strong>Table – Risks</strong></td>
<td>4%</td>
<td>13%</td>
<td>12%</td>
<td>71%</td>
</tr>
<tr>
<td><strong>Bar graph – Benefits</strong></td>
<td>5%</td>
<td>9%</td>
<td>53%</td>
<td>33%</td>
</tr>
<tr>
<td><strong>Bar graph – Risks</strong></td>
<td>5%</td>
<td>7%</td>
<td>41%</td>
<td>47%</td>
</tr>
</tbody>
</table>
Comprehension – Benefits and Risks (AF)

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Risks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.42</td>
<td>2.36</td>
</tr>
<tr>
<td>2.55</td>
<td>2.49</td>
</tr>
<tr>
<td>2.15</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Mean score (range 0-3)
**Comprehension – Benefit and Risks (BC)**

<table>
<thead>
<tr>
<th></th>
<th>Percentage of patients with correct answers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 questions correct</td>
</tr>
<tr>
<td><strong>Drug vignette – Benefits</strong></td>
<td>4%</td>
</tr>
<tr>
<td><strong>Drug vignette – Risks</strong></td>
<td>5%</td>
</tr>
<tr>
<td><strong>Table – Benefits</strong></td>
<td>2%</td>
</tr>
<tr>
<td><strong>Table – Risks</strong></td>
<td>2%</td>
</tr>
<tr>
<td><strong>Survival curve – Benefits</strong></td>
<td>6%</td>
</tr>
<tr>
<td><strong>Pictogram – Risks</strong></td>
<td>4%</td>
</tr>
</tbody>
</table>
Comprehension – Benefits and Risks (BC)

![Bar chart showing mean scores for benefits and risks across different formats: drug vignette, table, survival curve, pictogram. Scores range from 2.5 to 2.76.](chart.png)
PROTECT

Overall comprehension – by presentation format

% correctly answered questions

Drug vignette | Table | Bar graph | Survival curve | Pictogram
---|---|---|---|---
82% | 85% | 78% | 83% | 83%

Diabetes
Atrial fibrillation
Breast cancer
Summary

- Analyses of the results for perception, preferences ongoing
- Continue to recruit until April 2015
  - ~100 completed questionnaires per week
- Direct clinic recruitment most effective
  - Incentives helpful but not key
- Education level may be less indicative of understanding; level of numeracy
- Comprehension appears high for text presentation but is higher when data are provided in a table
## Participating Organisations and Health Centers

### Europe
- European Heart Network
- AGE platform Europe
- European Patient’s Forum
- European Society of Endocrinology
- Pharmaceutical Group of the EU
- European Society of Oncology Pharmacists
- EUPATI

### United Kingdom
- Diabetes UK
- Breast Cancer Care
- Atrial Fibrillation Association
- British Heart Foundation
- NICR:
  - Chelsea and Westminster Hospital NHS Foundation Trust
  - Royal Brompton Hospital Trust
  - Imperial College Healthcare NHS Trust
  - Primary Care North West London (Brent CCG)
  - North West London Hospitals NHS Trust
  - Ealing Hospital NHS Trust
  - Central London Community Healthcare Trust
  - Hillingdon Hospitals NHS Trust
  - Basildon & Thurrock University Foundation NHS Trust
  - East and North Hertfordshire NHS Trust, Mount Vernon Hospital
  - West Middlesex University Hospital NHS Trust
  - Royal Cornwall Hospitals NHS Trust
  - Plymouth Community Healthcare, Mount Gould Hospital
  - Royal Devon & Exeter Hospital
  - Plymouth Hospitals NHS Trust
  - Southern Health NHS Foundation Trust
  - South Devon Healthcare NHS Foundation
  - Yeovil District Hospital Foundation Trust
  - Rotherham NHS Foundation Trust
  - Florence Road and Bramley Road Surgeries

### The Netherlands
- Hart en Vaatgroep
- ikVS
- Diabetesfonds
- Diabetesvereniging Nederland
- EADV
- Borstkankervereniging Nederland
- Pink Ribbon
- NPCF
- Amazones

### Hospitals:
- University Medical Center Groningen
- Maastricht University Medical Center
- Erasmus Medical Center Rotterdam
- University Medical Center Utrecht
- Radboud University Medical Center
- Academic Medical Center Amsterdam
- Isala Hospital Zwolle
- Medical Center Leeuwarden
Acknowledgements

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    • Xavier Kurz
    • Lucia Caporuscio
  – Laser
    • Billy Amzal
    • Witold Wiecek
    • Helene Karcher
    • Constance Charveriat
  – Sanofi
    • Laurence Mazuranok
  – University of Utrecht
    • Marieke de Bruin
BACKUP SLIDES
Recruitment efforts – Extending beyond PROTECT

Atrial Fibrillation patient
Breast Cancer patient
Diabetes patient
Atrial Fibrillation hcp
Breast Cancer hcp
Diabetes hcp
## Preliminary results – Demographics HCP’s

<table>
<thead>
<tr>
<th></th>
<th>Diabetes</th>
<th>Atrial fibrillation</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 183 HCP’s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (male)</td>
<td>30%</td>
<td>40%</td>
<td>26%</td>
</tr>
<tr>
<td>Age (mean ± sd)</td>
<td>44 ± 17</td>
<td>44 ± 17</td>
<td>41 ± 11</td>
</tr>
<tr>
<td>Education completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; Masters degree</td>
<td>27%</td>
<td>39%</td>
<td>30%</td>
</tr>
<tr>
<td>&gt; Masters degree</td>
<td>73%</td>
<td>61%</td>
<td>70%</td>
</tr>
<tr>
<td>Numeracy level (mean ± sd)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- 0 questions correct</td>
<td>9%</td>
<td>7%</td>
<td>4%</td>
</tr>
<tr>
<td>- 1 question correct</td>
<td>10%</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>- 2 questions correct</td>
<td>30%</td>
<td>34%</td>
<td>27%</td>
</tr>
<tr>
<td>- 3 questions correct</td>
<td>51%</td>
<td>49%</td>
<td>57%</td>
</tr>
</tbody>
</table>
Favorable effects (benefits) and unfavorable effects (risks): Drug X versus Placebo (standard therapy)

1. What was the difference in risk of getting hospitalized for heart failure for patients taking Drug X compared with patients taking Placebo?
   ____ %

2. Which treatment group had a higher risk of gaining weight?
   ______
Example of waterfall plot and comprehension questions

Favorable effects (benefits) and unfavorable effects (risks):
Drug X versus Placebo (standard therapy)

1. What was the difference in risk of getting hospitalized for heart failure for patients taking Drug X compared with patients taking Placebo?
   \[0.7\%\]

2. Which treatment group had a higher risk of gaining weight?
   Placebo
## Preliminary results – Comprehension waterfall plot

<table>
<thead>
<tr>
<th></th>
<th>Correct</th>
<th>Incorrect</th>
<th>Empty</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes (n=183)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Question 1</td>
<td>27%</td>
<td>56%</td>
<td>17%</td>
</tr>
<tr>
<td>Question 2</td>
<td>57%</td>
<td>21%</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Atrial fibrillation (n=123)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Question 1</td>
<td>48%</td>
<td>28%</td>
<td>24%</td>
</tr>
<tr>
<td>Question 2</td>
<td>36%</td>
<td>42%</td>
<td>22%</td>
</tr>
<tr>
<td><strong>Breast cancer (n=135)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Question 1</td>
<td>25%</td>
<td>48%</td>
<td>27%</td>
</tr>
<tr>
<td>Question 2</td>
<td>64%</td>
<td>14%</td>
<td>22%</td>
</tr>
</tbody>
</table>
Preliminary results – Comprehension waterfall plot

Correct
Incorrect
Empty

0%
20%
40%
60%
80%
100%

Diabetes - Q1
Diabetes - Q2
Atrial fibrillation - Q1
Atrial fibrillation - Q2
Breast cancer - Q1
Breast cancer - Q2