

Visualizing Uncertainty Among Laypersons and Experts



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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 a 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

Patients

Diabetes:
300 per country

Atrial Fibrillation:
300 per country

Breast Cancer:
300 per country

Total:
2700

Healthcare Professionals

Diabetes:
300 per country

Atrial Fibrillation:
300 per country

Breast Cancer:
300 per country

Total:
2700

Medical Assessors

Voluntary
enrollment

Study design – Selected outcomes by patient focus groups (150 patients per disease area)

Disease Area	Benefits	Risks
Diabetes	Reduction HbA1c levels	Hospitalization for heart failure
	Change in fasting plasma glucose levels	Pancreatitis
		Weight gain
Atrial fibrillation	Reduction ischemic stroke	Fatal bleeding
	Reduction myocardial infarction	Major bleeding
	Reduction pulmonary embolism	Minor bleeding
Breast cancer	Overall survival	Gastrointestinal symptoms
	Progression free survival	Cardiac disorders
		Peripheral neuropathy

Study design – Data flow

Enrollment

- Informed consent
- Randomization

Part 1a

- Drug Vignette > Table > Plot
- Drug Vignette > Plot > Table
- Table > Plot > Drug Vignette
- Plot > Table > Drug Vignette
- Comprehension questions
- Mood state

Part 1b

- Perception
- Stated preferences

Part 2

- Demographics
- Disease characteristics
- Numeracy

Part 3

- Preference elicitation
 - *MACBETH*
 - *Discrete Choice*



Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium



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](#)

Extended Battery Life is activated.

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Examples of presentation formats

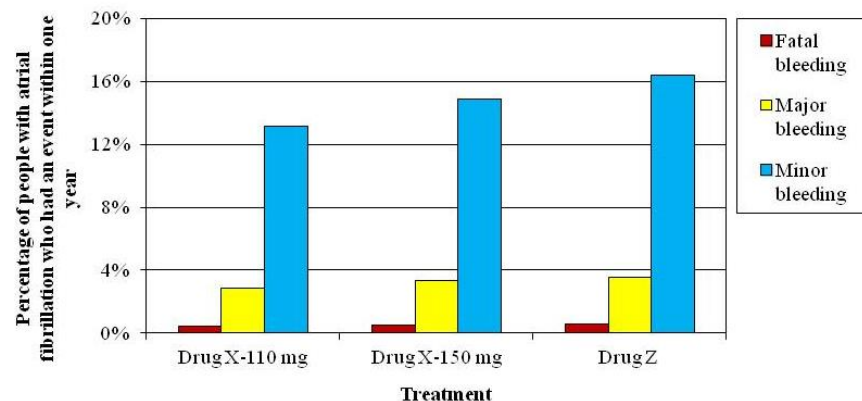
Drug Vignette (similar to EPAR):

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.

Abbreviated Effects Table

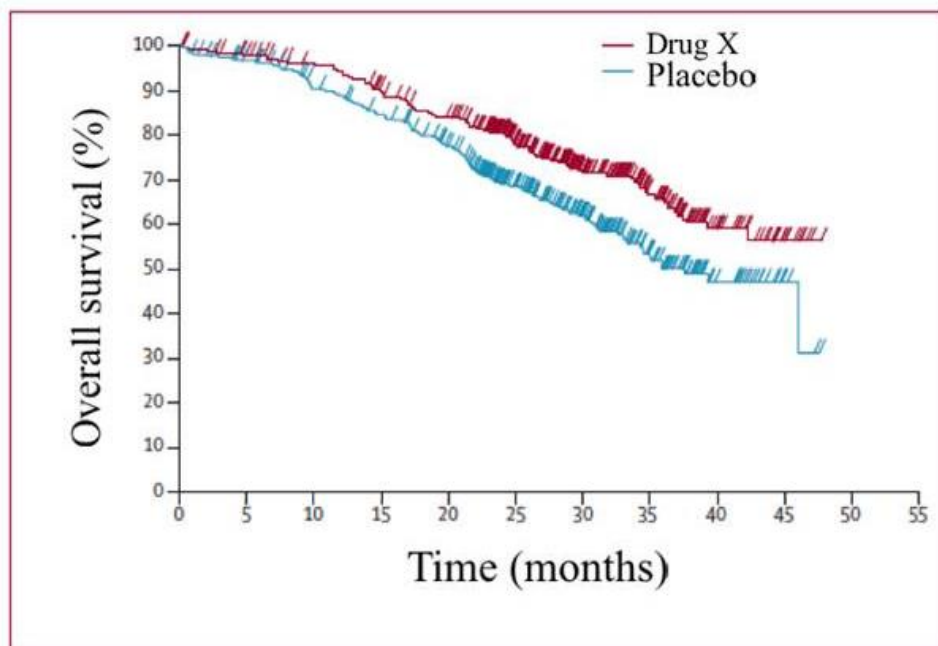
	Description	Drug X	Placebo
Benefits	Reduction in HbA1c levels	0.5%	0.2%
	Change in fasting plasma glucose levels (mean)	3.1 mg/dl reduction	1.6 mg/dl increase
Risks	Hospitalization for heart failure	3.5%	2.8%
	Pancreatitis	0.3%	0.3%
	Weight gain (mean)	0.6 kg	1.0 kg

Bar graphs



Examples of presentation formats

Survival curve



Pictograms

Diarrhea in breast cancer patients treated with Drug X



■ Patients with diarrhea

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 bleeding when taking Drug X-150 mg?

- ☐ 3.3%
- ☐ 14.9%
- ☐ 2.9%
- ☐ I don't know

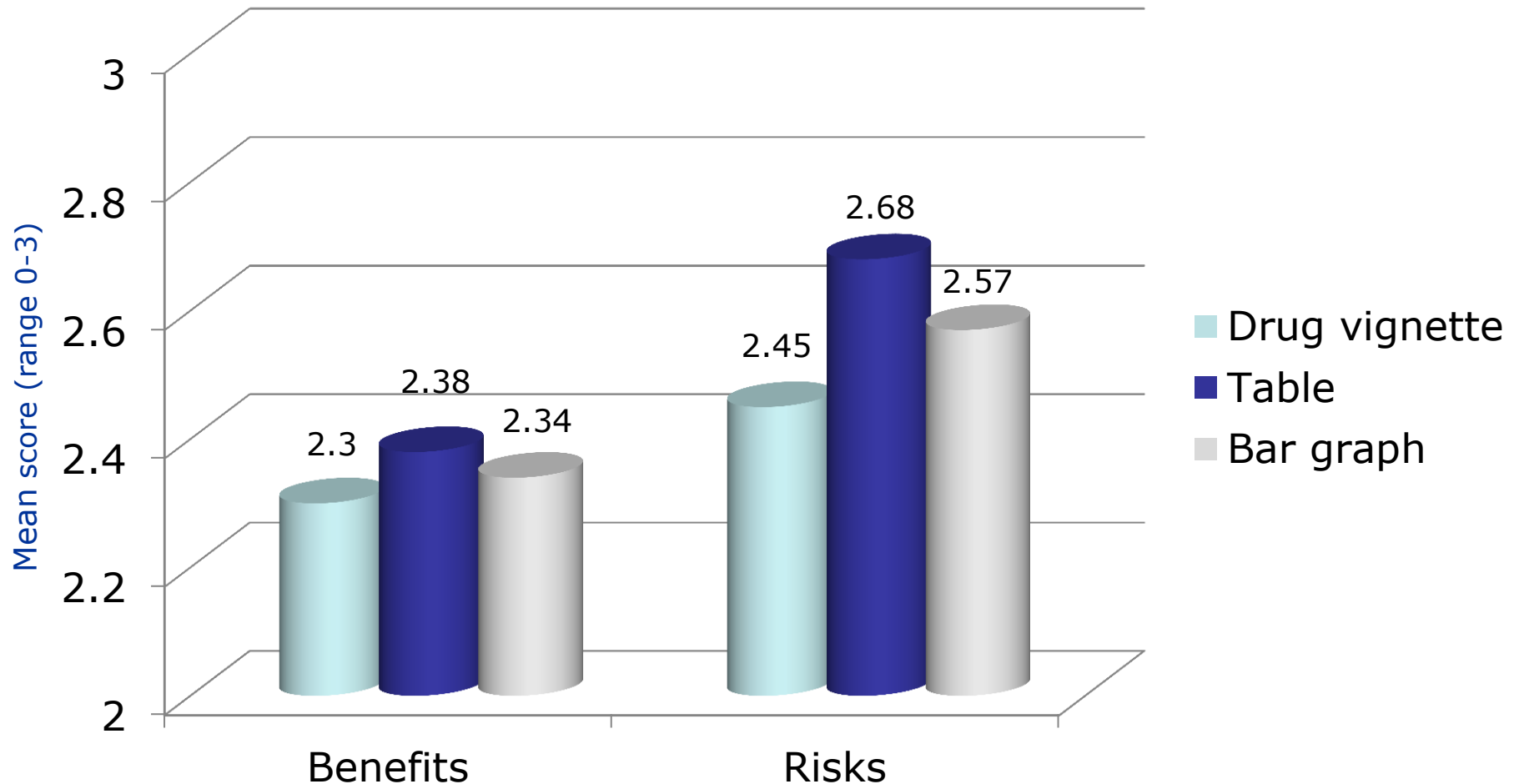
Demographics (countries combined)

	Diabetes	Atrial fibrillation	Breast cancer
	N= 531 Patients	N= 189 Patients	N= 448 Patients
Gender (male)	58%	73%	1%
Age (mean $\pm$ sd)	60 $\pm$ 11	65 $\pm$ 10	58 $\pm$ 10
Education			
< Associate degree	65%	64%	65%
$\geq$ Associate degree	35%	36%	35%
Numeracy level			
- 0 questions correct	28%	23%	25%
- 1 question correct	16%	18%	17%
- 2 questions correct	24%	20%	26%
- 3 questions correct	31%	39%	31%

Comprehension – Benefit and Risks (DB)

	Percentage of patients with correct answers			
	0 questions correct	1 question correct	2 questions correct	3 questions correct
Drug vignette – Benefits	3%	6%	49%	42%
Drug vignette – Risks	8%	7%	17%	68%
Table – Benefits	5%	7%	35%	53%
Table – Risks	6%	3%	10%	82%
Bar graph – Benefits	4%	7%	41%	49%
Bar graph – Risks	5%	7%	15%	73%

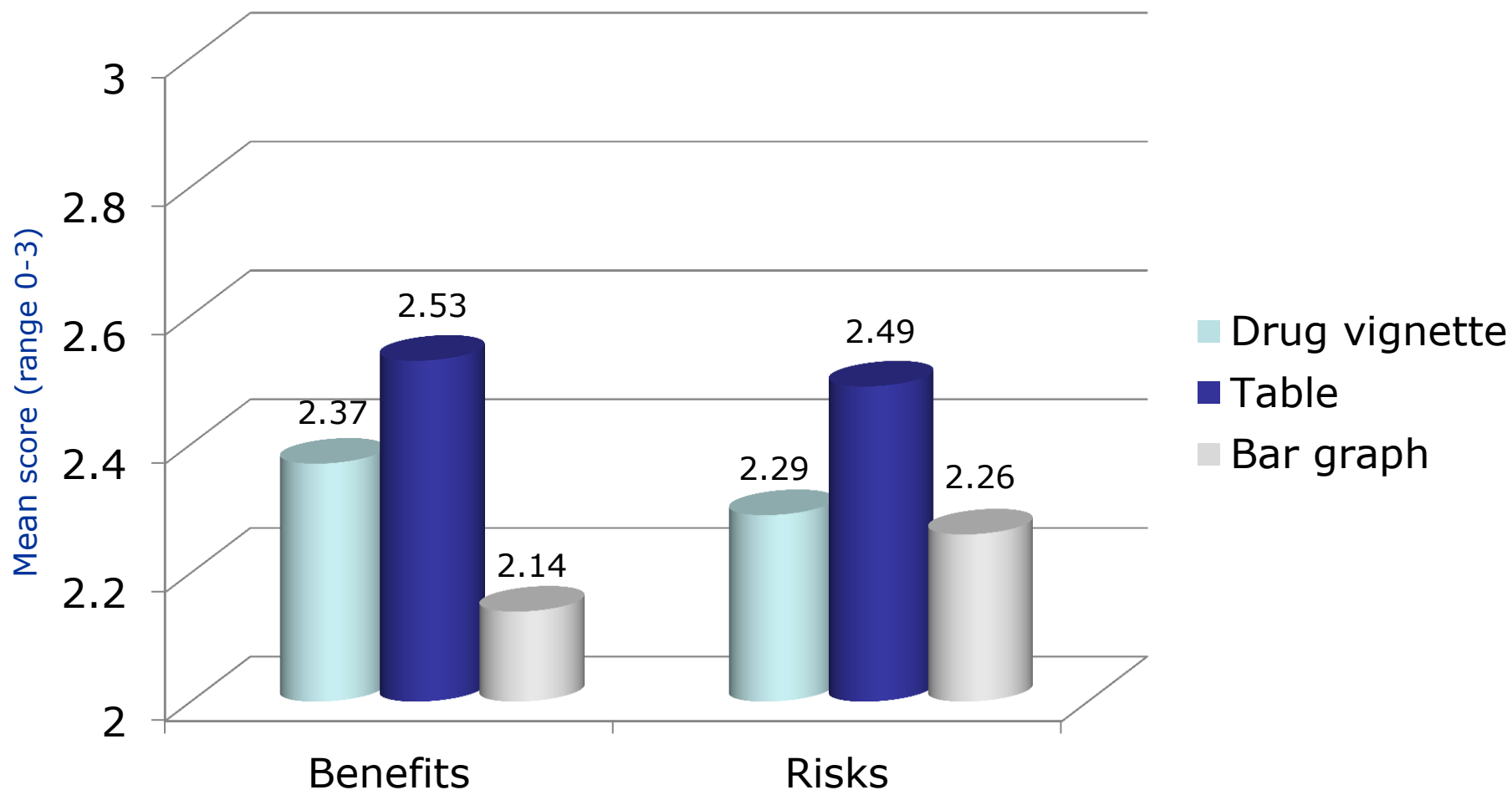
Comprehension – Benefits and Risks (DB)



Comprehension – Benefit and Risks (AF)

	Percentage of patients with correct answers			
	0 questions correct	1 question correct	2 questions correct	3 questions correct
Drug vignette – Benefits	9%	10%	16%	65%
Drug vignette – Risks	14%	7%	16%	64%
Table – Benefits	6%	6%	18%	70%
Table – Risks	5%	12%	10%	72%
Bar graph – Benefits	5%	10%	51%	34%
Bar graph – Risks	6%	9%	38%	47%

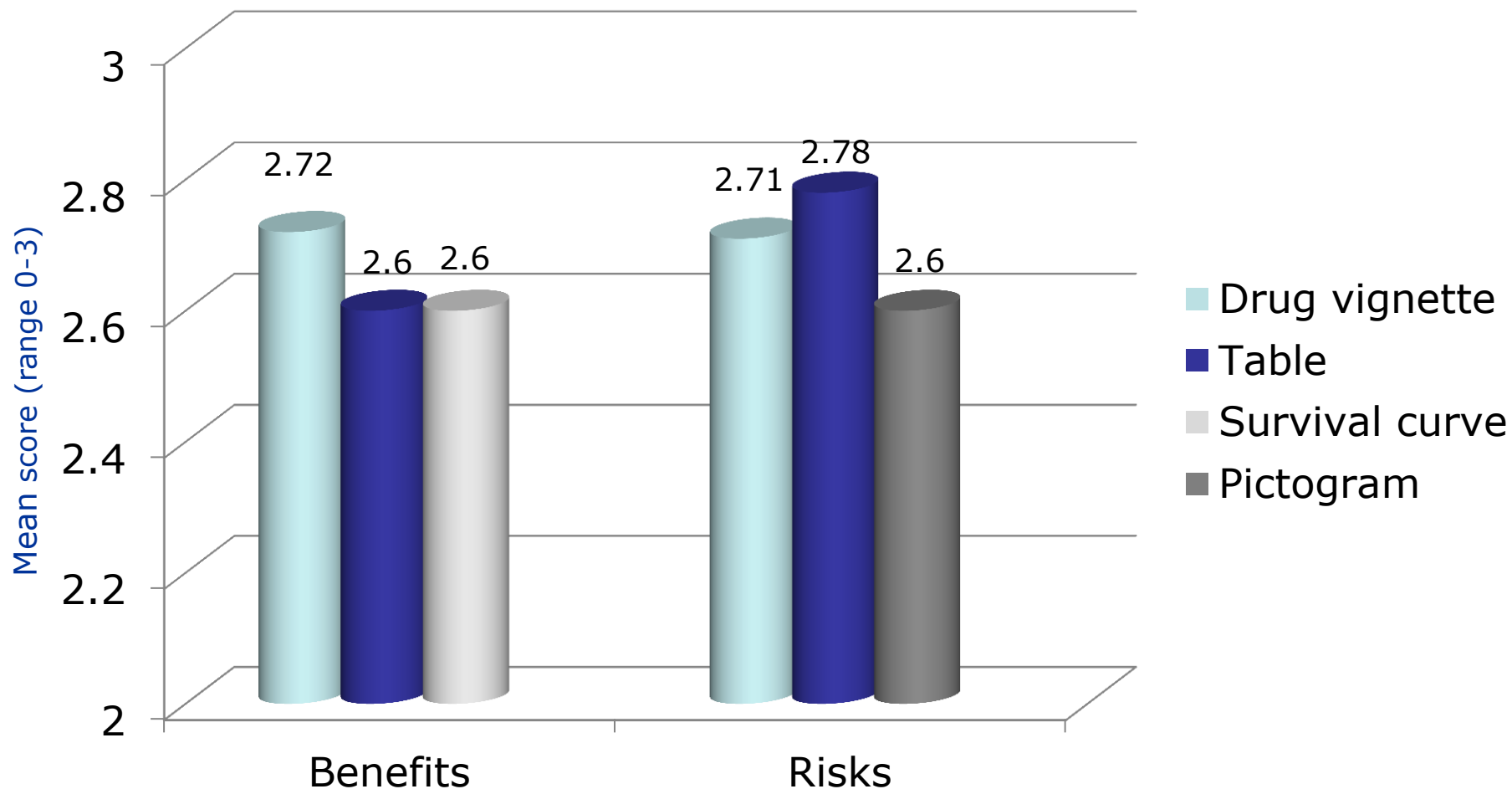
Comprehension – Benefits and Risks (AF)



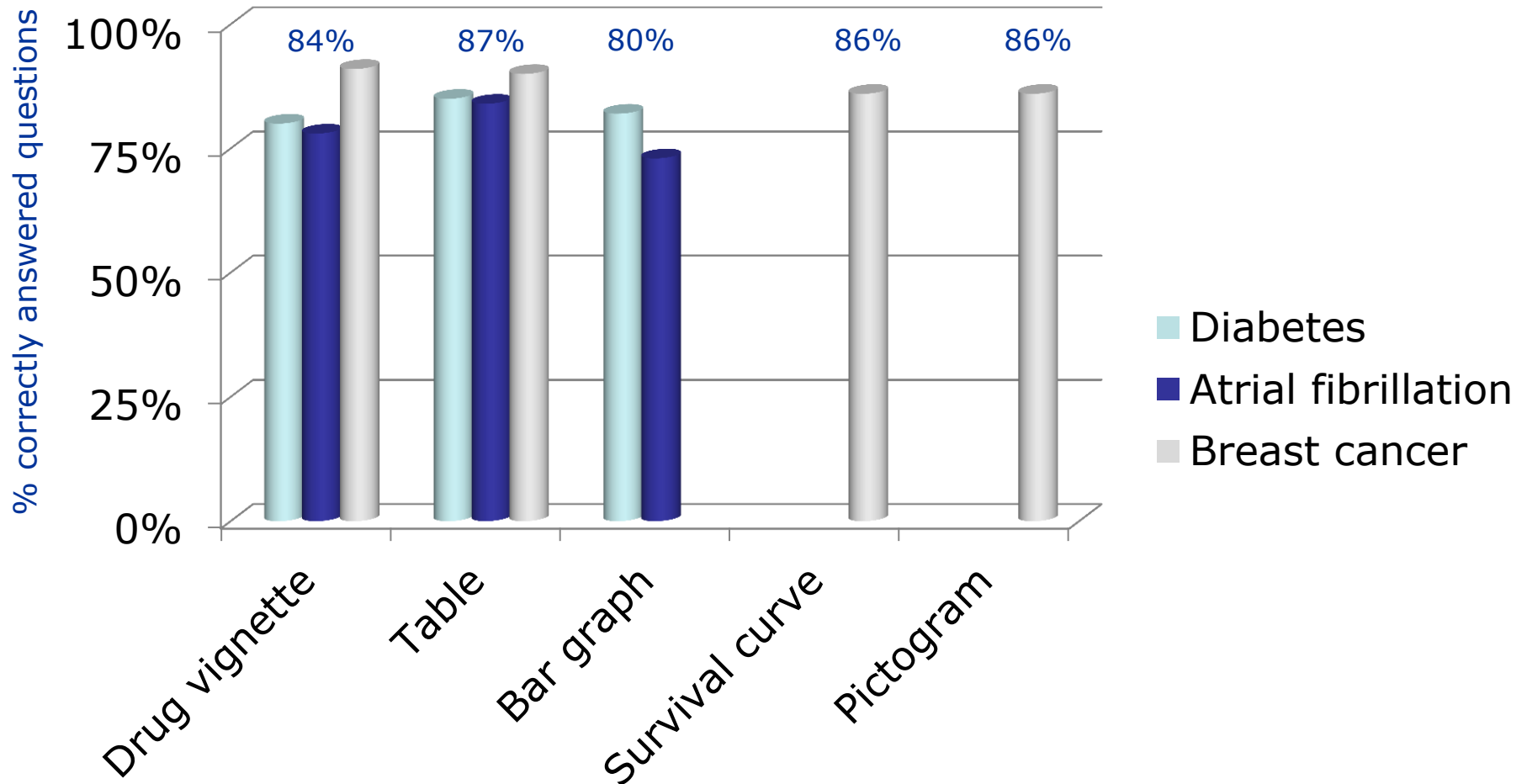
Comprehension – Benefit and Risks (BC)

	Percentage of patients with correct answers			
	0 questions correct	1 question correct	2 questions correct	3 questions correct
Drug vignette – Benefits	3%	3%	11%	82%
Drug vignette – Risks	4%	3%	12%	82%
Table – Benefits	2%	6%	20%	72%
Table – Risks	2%	3%	10%	86%
Survival curve – Benefits	4%	5%	18%	72%
Pictogram – Risks	3%	5%	23%	69%

Comprehension – Benefits and Risks (BC)



Overall comprehension – by presentation format



Analysis of preference: Discrete Choice Experiment

Attribute	Low Level	High Level
Change in HbA1c levels	-2%	+2%
Change in fasting plasma glucose levels	-30mg/dl	+30mg/dl
Patients getting cardiac disorders	0%	10%
Patients getting pancreatitis	0%	4%
Change in weight	-1.5 kg	+0.5kg

Discrete Choice Experiment

Atrial fibrillation

- All 6 attributes had explanatory power, significant at 1%

Order	Patients	Experts
1	Stroke	Fatal bleeding
2	Fatal bleeding	Stroke
3	Major bleeding	Major bleeding
4	Myocardial infarction	Minor bleeding
5	Minor bleeding	Myocardial infarction
6	Pulmonary embolism	Pulmonary embolism

Discrete Choice Experiment

Breast cancer

- Peripheral neuropathy was not significant at the 1% level in the expert model.
All other attributes had explanatory power, significant at 1%
- The order of importance was equal for patients and experts

Order	Patients and Experts
1	Percentage of patients dying within 30 months
2	Months being progression free
3	Diarrhoea
4	Constipation
5	Left ventricular dysfunction
6	Peripheral neuropathy (patients only)

Discrete Choice Experiment

Diabetes

- All 5 attributes had explanatory power, significant at 0.5%

Order	Patients	Experts
1	Cardiac disorders	Cardiac disorders
2	Pancreatitis	Change in HbA1c levels
3	Change in HbA1c levels	Pancreatitis
4	Change in fasting plasma glucose levels	Change in weight
5	Change in weight	Change in fasting plasma glucose levels

Summary

- Table better for comprehension than other graphical formats but not same for BC pts
- Presentation order matters!
 - Favorable effects first and understanding the data → positive perception of the drug both for safety and willingness to take it
- Mood states may be relevant but our results are variable...no real pattern observed
- DCE - Some differences noted between experts and patients most notable is the AF difference

Summary

- The table format was most often selected as easiest to understand and most helpful in making a decision re what drug to treat their disease (patients) or to prescribe (experts).
- For confidence, textual presentation is no different from table or non-stacked bar chart; but it is different from stacked bar charts, survival and pictograms and bar chart with Rx on X axis.

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

France

- LASER

The Netherlands

- Hart en Vaatgroep
- ikVS
- Diabetesfonds
- Diabetesvereniging Nederland
- EADV
- Borstkankervereniging Nederland
- Pink Ribbon
- NPCF
- Amazones
- Certe
- 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

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
 - Ashford and St Peter's Hospitals NHS Foundation Trust
 - Brighton and Sussex University Hospitals NHS Trust
 - University Hospital of North Midland Staffordshire NHS Trust, Royal Stoke
- Open Door Surgery
- Mayfield Surgery
- Mitcham Family Practice
- Park Group Practice
- Elm Lodge Surgery
- Hurley Clinic
- Hetherington Group Practice
- Upper Norwood Group Practice
- The Merton Medical Practice
- Royal Arsenal Medical Centre
- Paxton Green
- Francis Grove
- South West London GP Surgeries
- Kernow CCG
- Royal Brompton Hospital Trust
- Brent CCG
- Imperial College Healthcare NHS Trust
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