
Visualizing Uncertainty among laypersons and experts

- PROTECT SYMPOSIUM
- 20 February 2015

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Contents

- **Background**
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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

WP6-WP5

A flowchart showing the structure of the WP6-WP5 Extension Studies. At the top is a light blue box labeled "WP6-WP5". Two dark blue arrows point downwards from this box to two separate light blue boxes below. The left box is labeled "Workstream 1" and describes testing B/R methods in a real-life setting, with Lead Billy Amzal (LASER) listed below it. The right box is labeled "Workstream 2" and describes validating visualisation tools, with Lead Andrea Beyer (Groningen) listed below it.

```
graph TD; A[WP6-WP5] --> B["Workstream 1  
Test how B/R methods adapt  
in a real-life setting"]; A --> C["Workstream 2  
Validate visualisation tools  
recommended by WP5 to the  
targeted audience"];
```

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

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

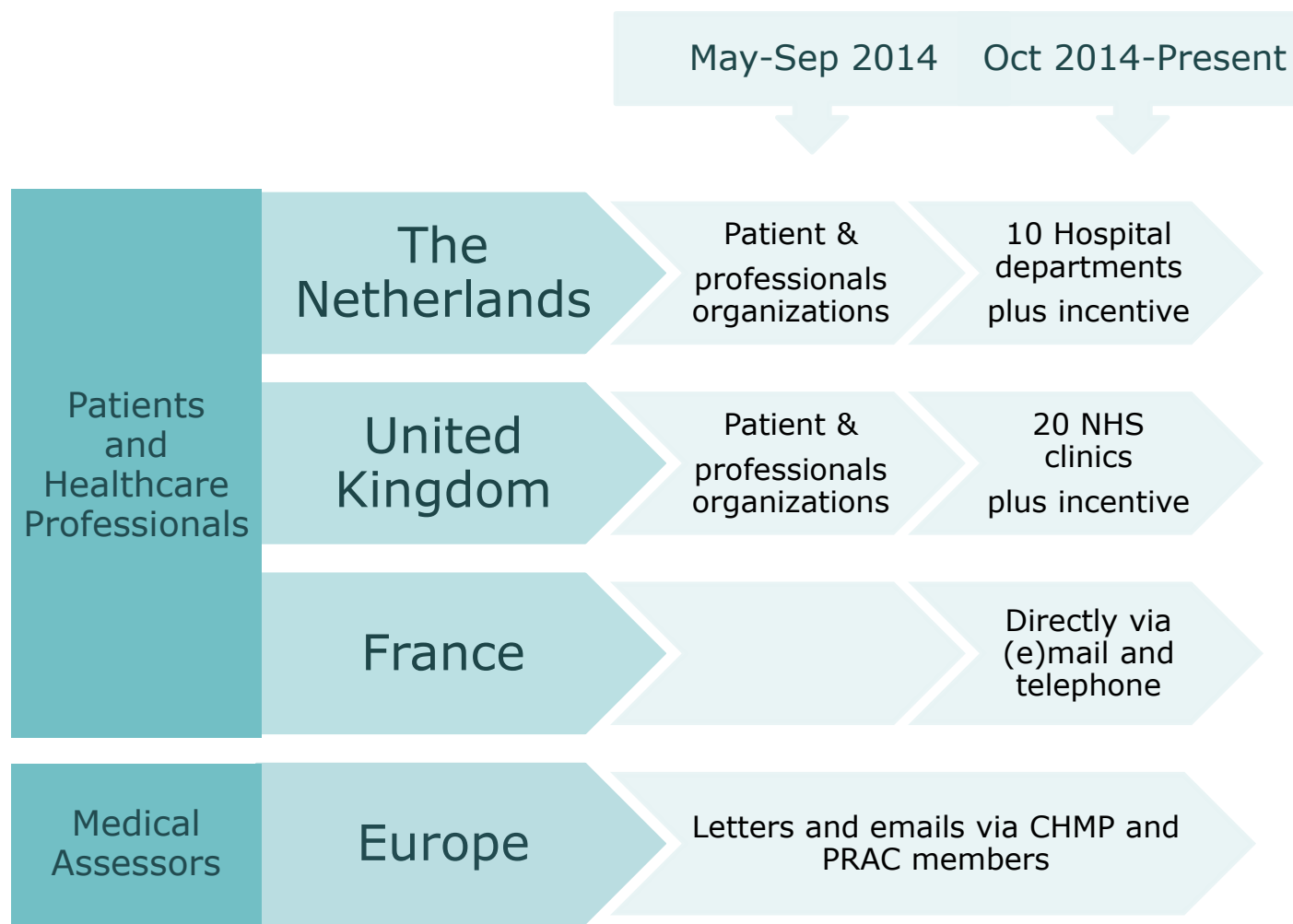
Breast Cancer:
300 per country

Total:
2700

Medical Assessors

Voluntary
enrollment

Study design - Recruitment methods



Study design – Focus groups (150 pts 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 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*



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.

[Change Setting...](#)

Examples of presentation formats

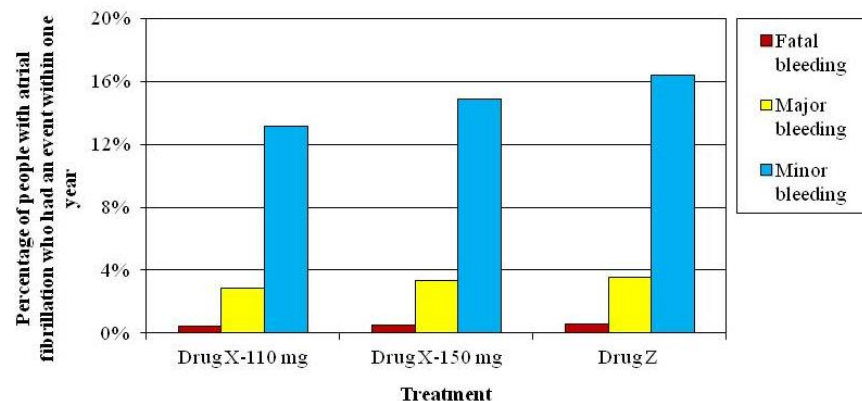
Drug Vignette (similar to EPAR):

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

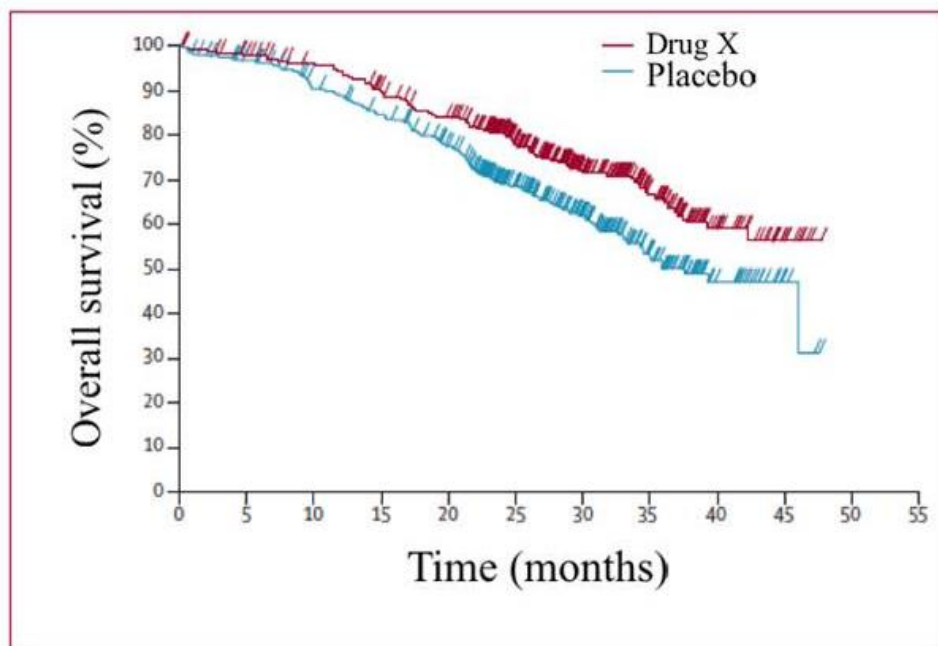
	Description	Drug X	Placebo
Benefits	Reduction in HbA1c levels	0.5%	0.2%
	Change in fasting plasma glucose levels (mean)	3.1 mg/dl reduction	1.6 mg/dl increase
Risks	Hospitalization for heart failure	3.5%	2.8%
	Pancreatitis	0.3%	0.3%
	Weight gain (mean)	0.6 kg	1.0 kg

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

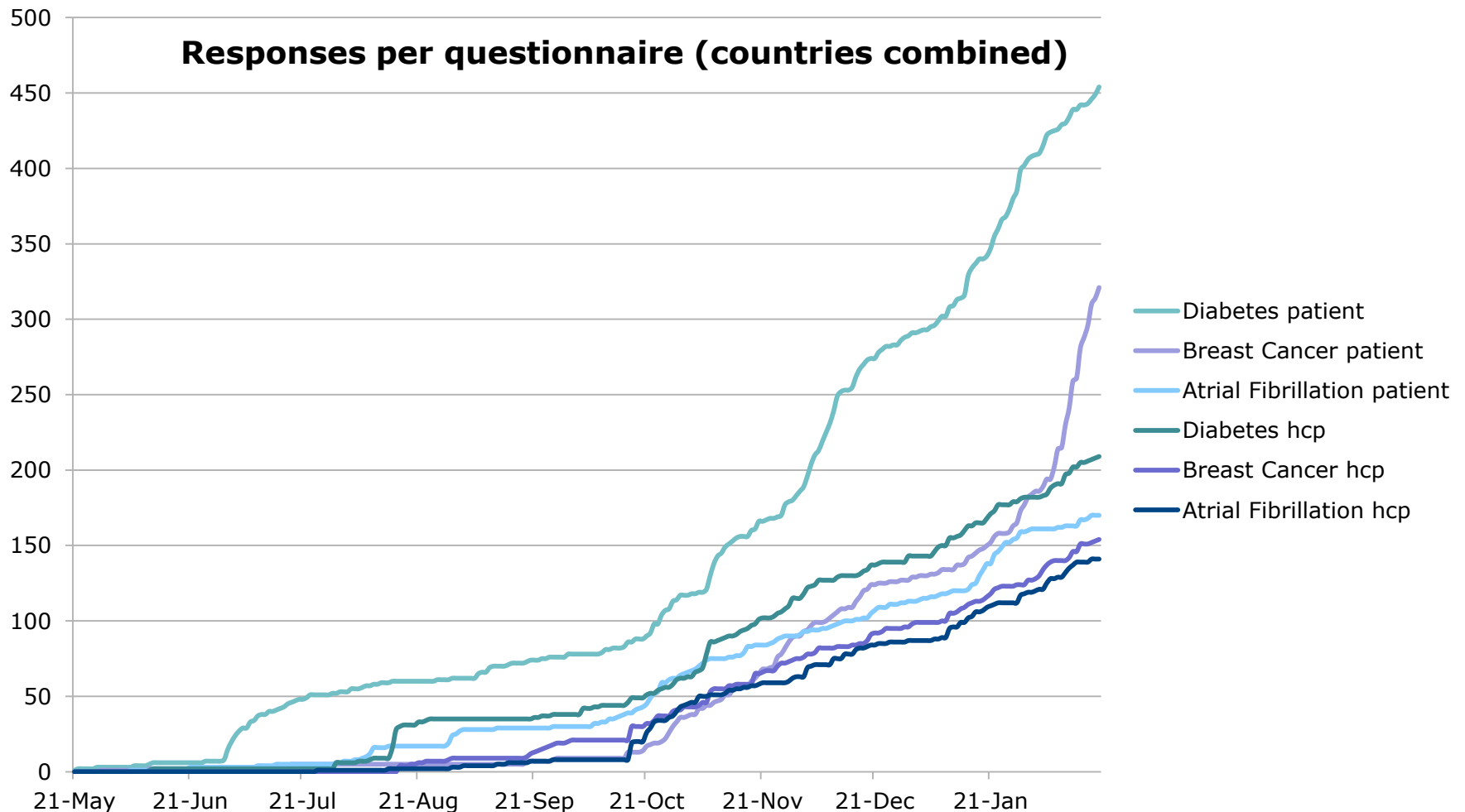
2. Which of the treatments had a better result, i.e. more reduction of HbA1c levels?

- ☐ Both equally good results
- ☐ Treatment with placebo
- ☐ Treatment with Drug X
- ☐ I don't know

3. What percentage of patients had major bleedings when taking Drug X-150 mg?

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

Recruitment efforts – Progress



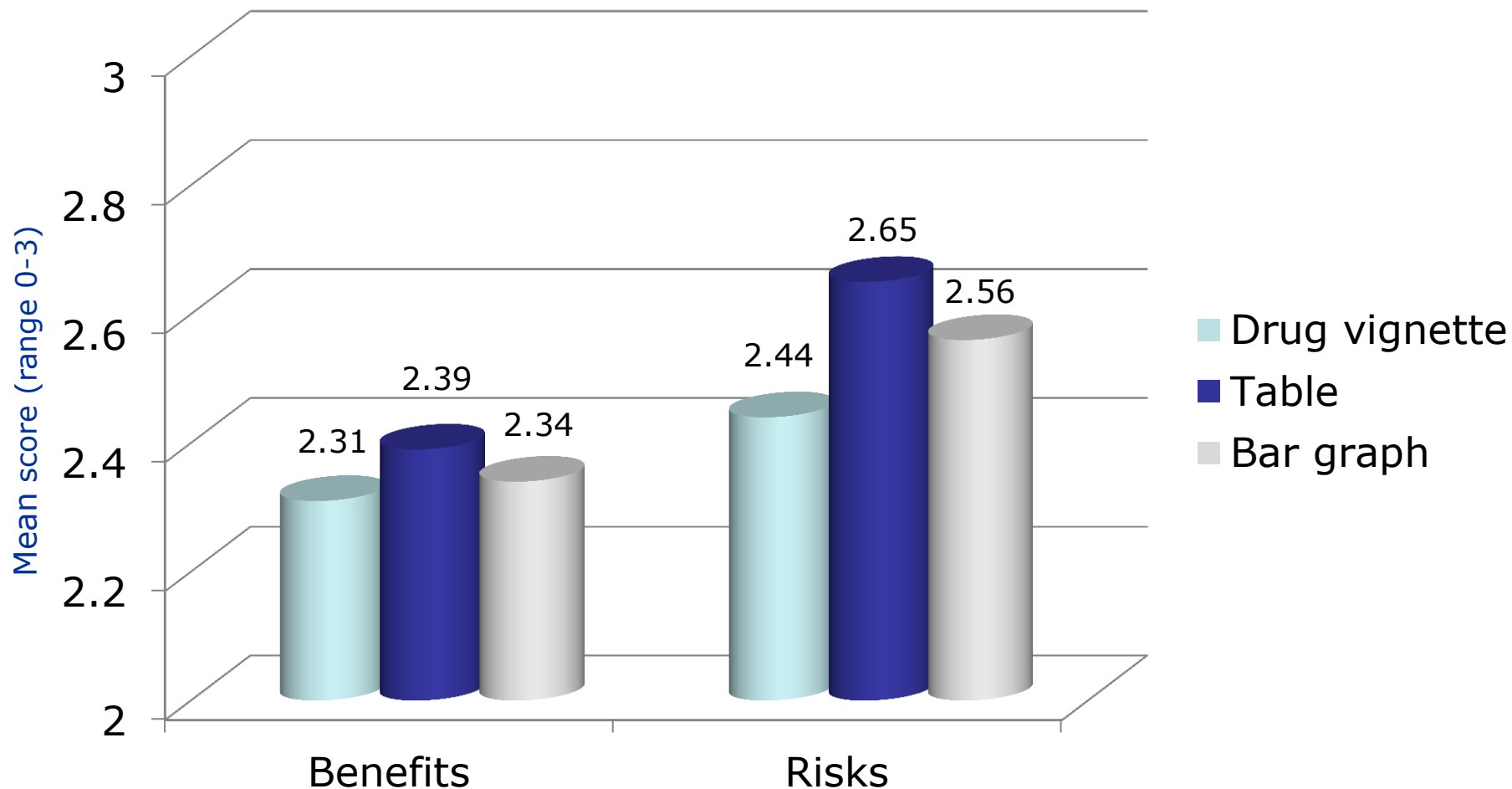
Demographics (countries combined)

	Diabetes	Atrial fibrillation	Breast cancer
	N= 419 Patients	N= 161 Patients	N= 190 Patients
Gender (male)	59%	69%	0%
Age (mean \pm sd)	60 \pm 12	64 \pm 9.9	57 \pm 11
Education			
< Associate degree	64%	62%	57%
\geq Associate degree	36%	38%	43%
Numeracy level (mean \pm sd)	1.9 \pm 1.0	2.1 \pm 1.0	1.8 \pm 1.1
- 0 questions correct	12%	9%	16%
- 1 question correct	21%	21%	20%
- 2 questions correct	30%	23%	32%
- 3 questions correct	37%	47%	32%

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%	48%	43%
Drug vignette – Risks	9%	6%	18%	67%
Table – Benefits	4%	8%	34%	54%
Table – Risks	6%	4%	10%	80%
Bar graph – Benefits	4%	7%	41%	48%
Bar graph – Risks	5%	8%	14%	73%

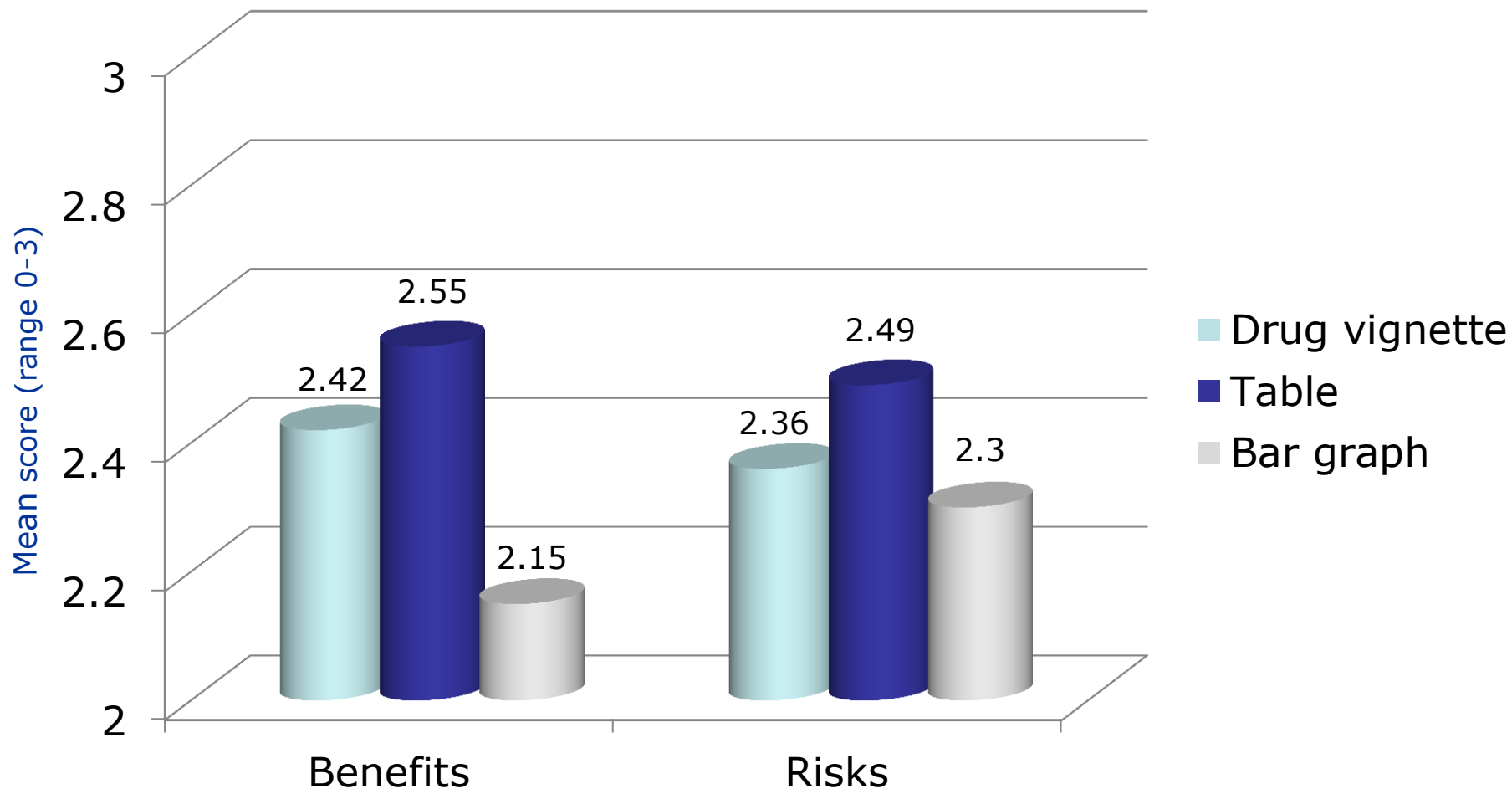
Comprehension – Benefits and Risks (DB)



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	7%	10%	18%	65%
Drug vignette – Risks	11%	7%	17%	65%
Table – Benefits	5%	6%	18%	71%
Table – Risks	4%	13%	12%	71%
Bar graph – Benefits	5%	9%	53%	33%
Bar graph – Risks	5%	7%	41%	47%

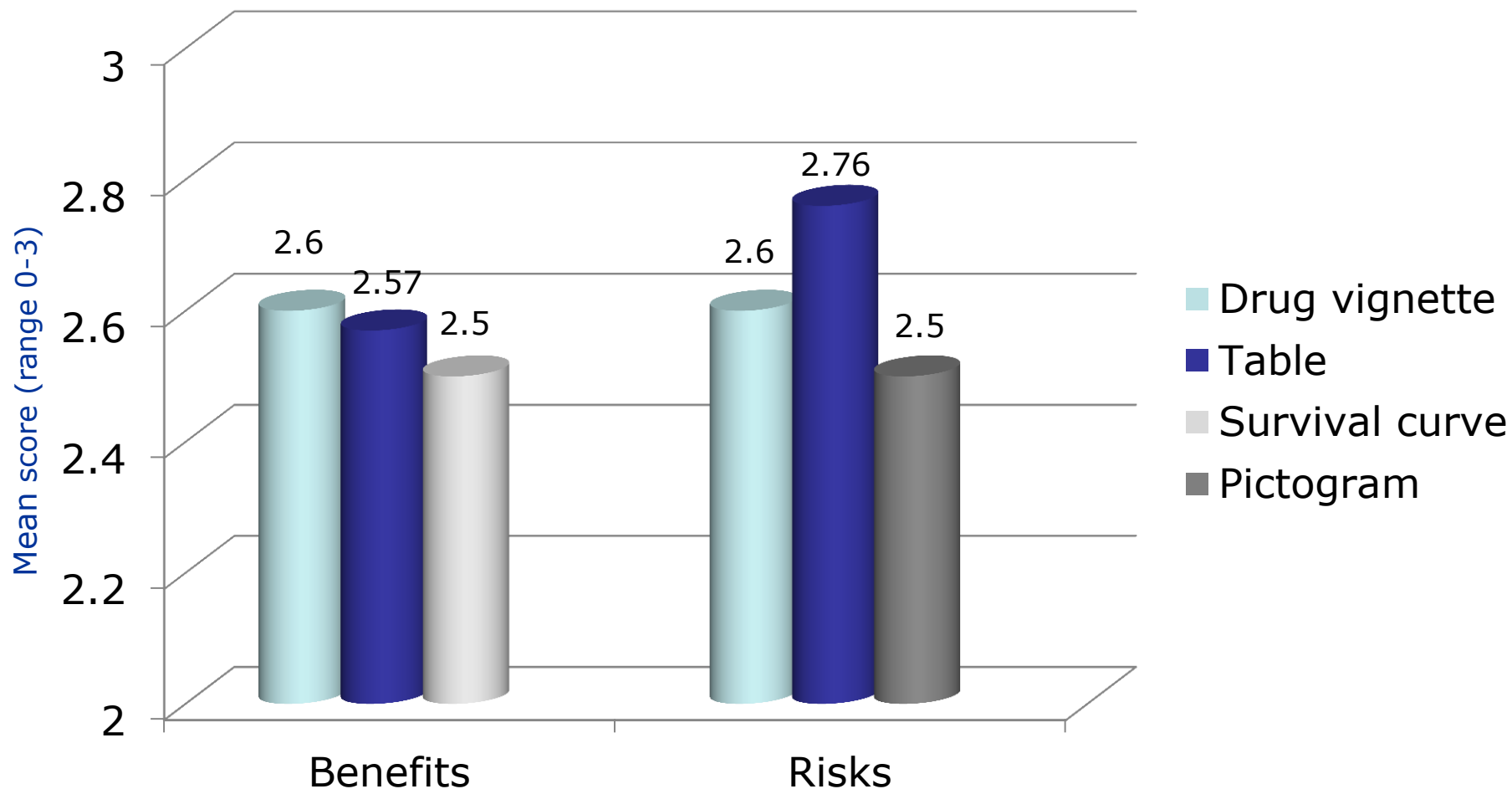
Comprehension – Benefits and Risks (AF)



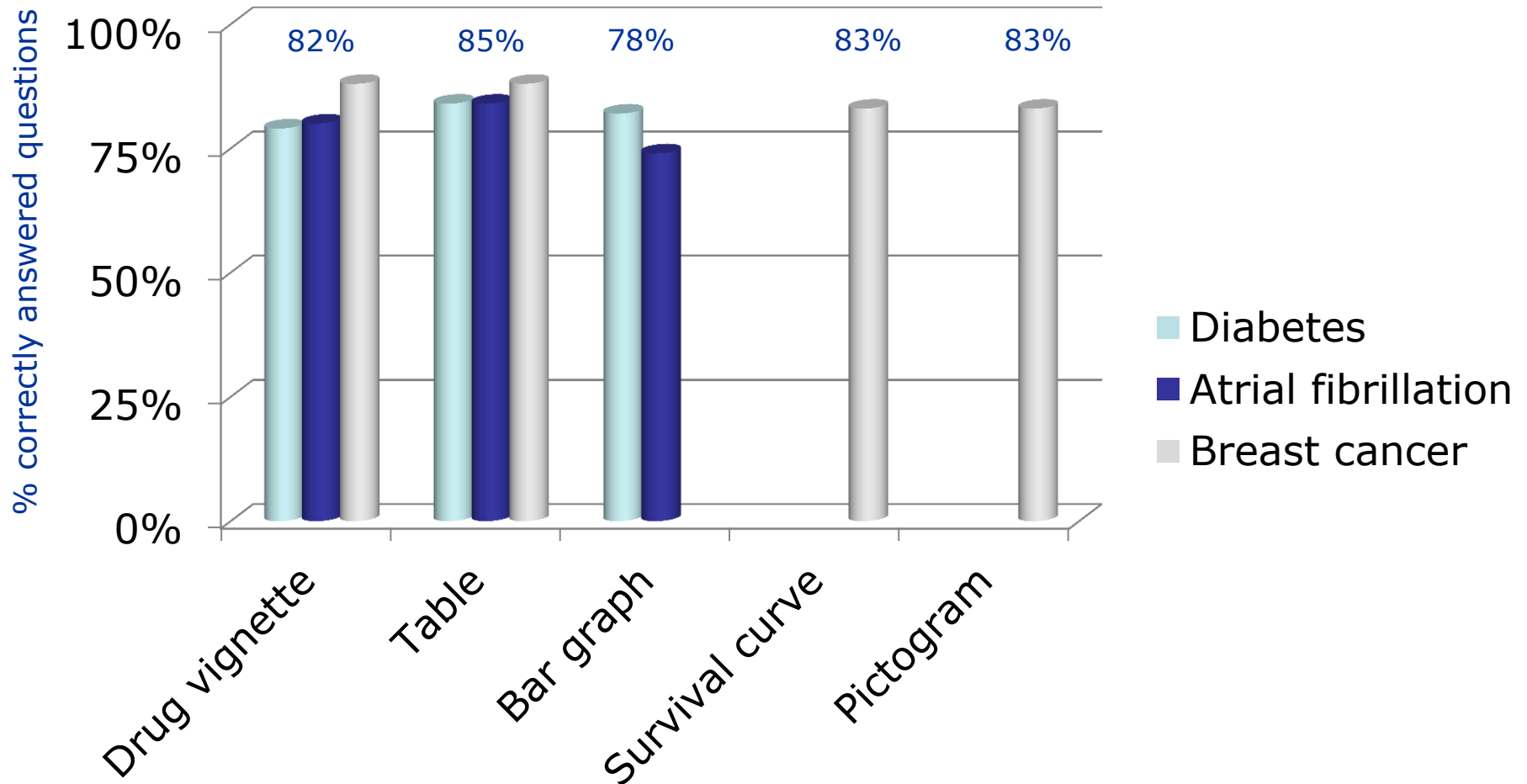
Comprehension – Benefit and Risks (BC)

	Percentage of patients with correct answers			
	0 questions correct	1 question correct	2 questions correct	3 questions correct
Drug vignette – Benefits	4%	7%	12%	77%
Drug vignette – Risks	5%	4%	15%	76%
Table – Benefits	2%	9%	19%	70%
Table – Risks	2%	4%	12%	82%
Survival curve – Benefits	6%	7%	18%	69%
Pictogram – Risks	4%	7%	24%	65%

Comprehension – Benefits and Risks (BC)



Overall comprehension – by presentation format



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

France

- LASER

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

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

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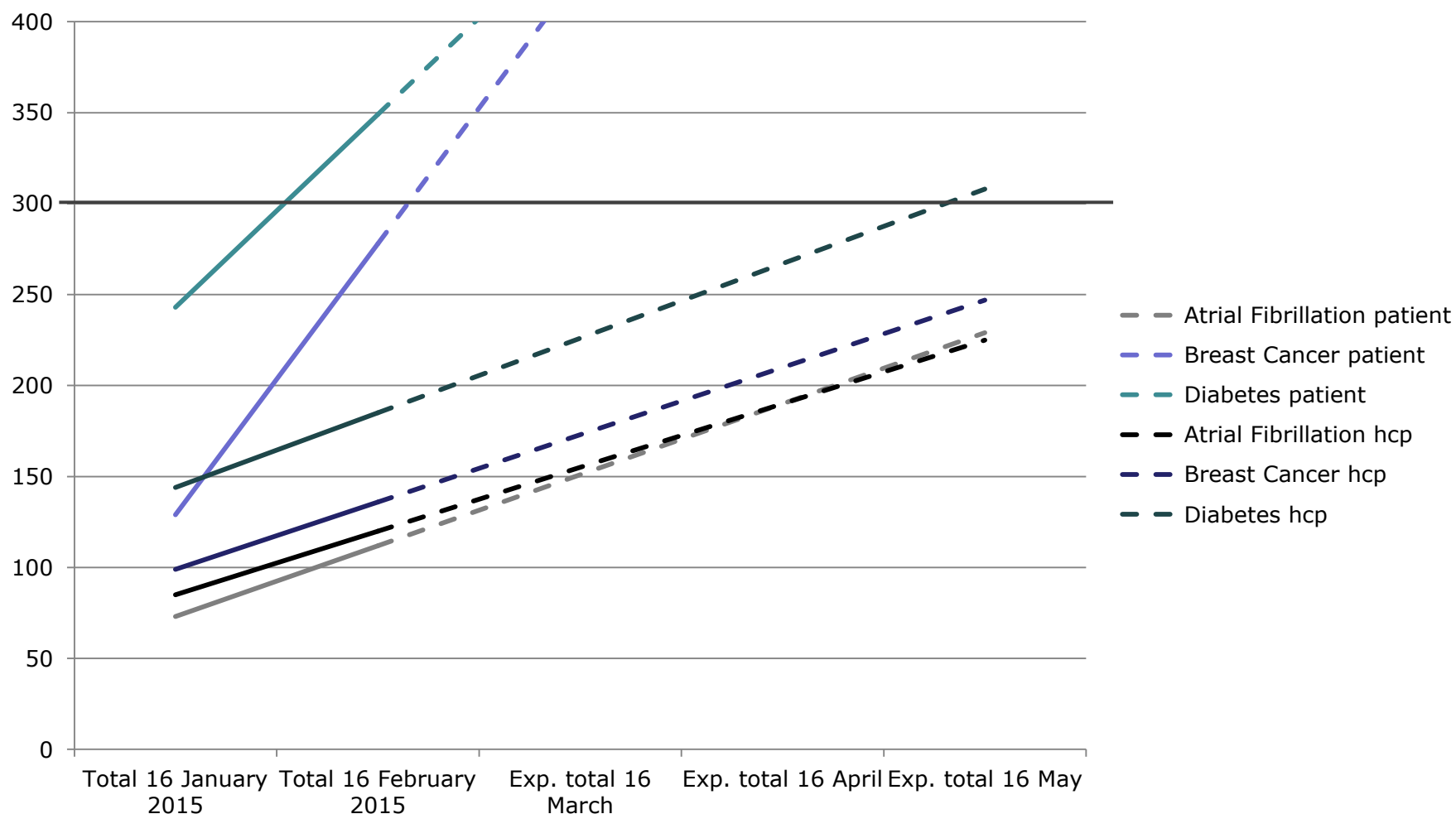
- University of Utrecht

- ♦ Marieke de Bruin



BACKUP SLIDES

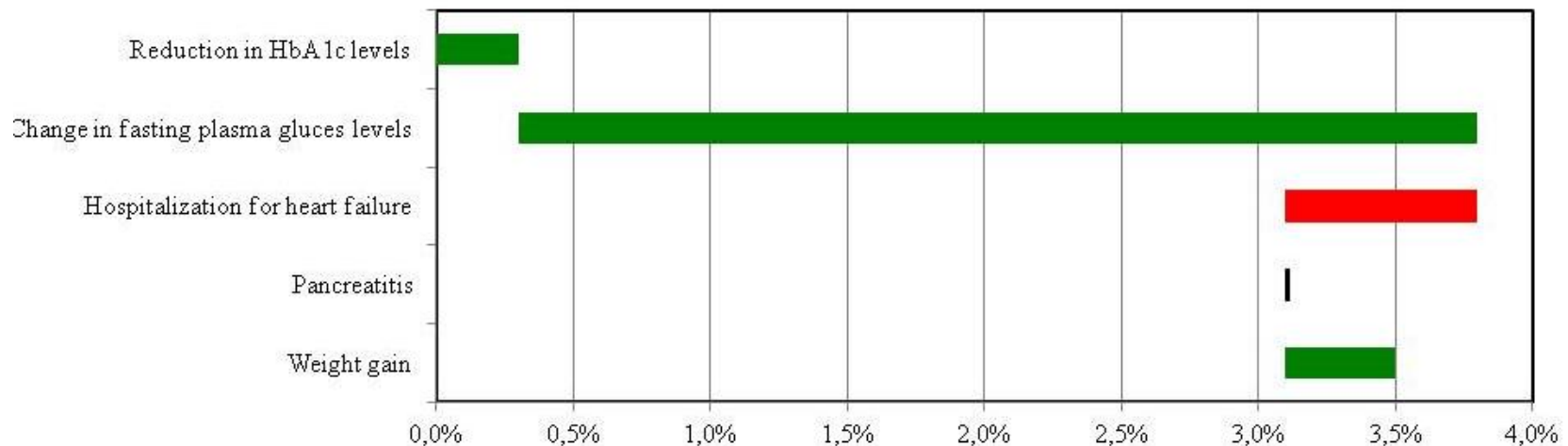
Recruitment efforts – Extending beyond PROTECT



Preliminary results – Demographics HCP's

	Diabetes	Atrial fibrillation	Breast cancer
	N= 183 HCP's	N= 123 HCP's	N= 135 HCP's
Gender (male)	30%	40%	26%
Age (mean \pm sd)	44 \pm 17	44 \pm 17	41 \pm 11
Education completed			
< Masters degree	27%	39%	30%
\geq Masters degree	73%	61%	70%
Numeracy level (mean \pm sd)	2.2 \pm 1.0	2.2 \pm 0.9	2.4 \pm 0.9
- 0 questions correct	9%	7%	4%
- 1 question correct	10%	10%	12%
- 2 questions correct	30%	34%	27%
- 3 questions correct	51%	49%	57%

Example of waterfall plot and comprehension questions

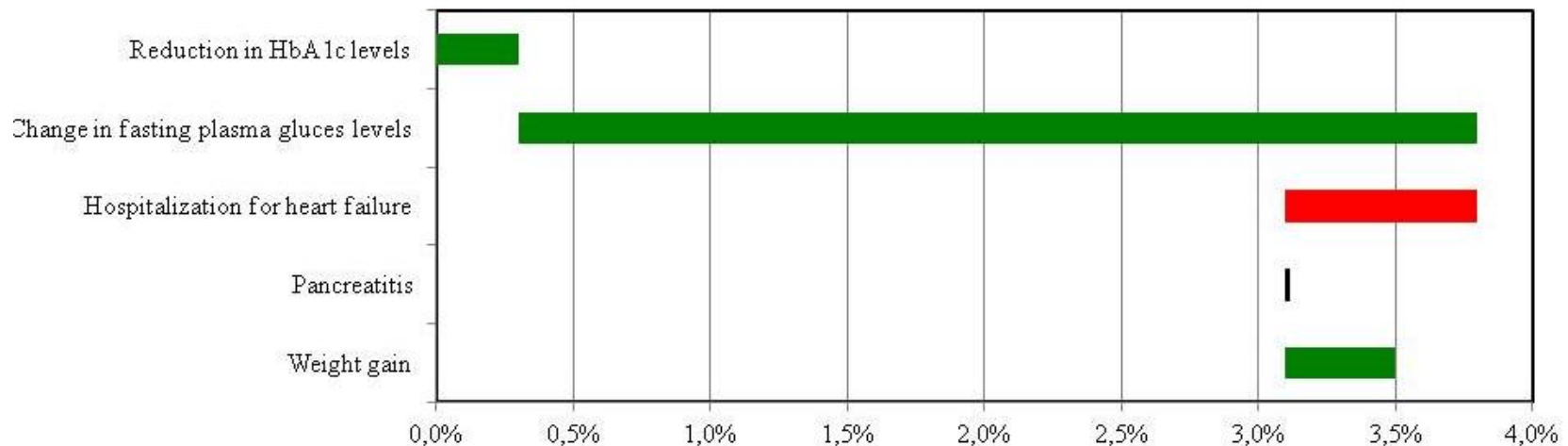


Favorable effects (benefits) and unfavorable effects (risks):
Drug X versus Placebo (standard therapy)

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

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

	Correct	Incorrect	Empty
Diabetes (n=183)			
Question 1	27%	56%	17%
Question 2	57%	21%	22%
Atrial fibrillation (n=123)			
Question 1	48%	28%	24%
Question 2	36%	42%	22%
Breast cancer (n=135)			
Question 1	25%	48%	27%
Question 2	64%	14%	22%

Preliminary results – Comprehension waterfall plot

