

Susan Talbot

**IN SICKNESS AND IN HEALTH, AND FOR THE
GREATER GOOD
INVOLVING PATIENTS AND THE PUBLIC IN BENEFIT-
RISK DECISION-MAKING**

PPI Team members

Authors	Organisation
Kimberley Hockley (PPI team leader) Deborah Ashby (Co-leader of WP5) Subhakanta Das Christine Hallgreen Shahrul Mt-Isa Richard Nicholas Ed Waddingham	Imperial College London
Susan Talbot	Amgen
Isabelle Stoeckert	Bayer
Georgy Genov	European Medicines Agency
Yasemin Dil Jo Groves Rebecca Johnson Alison Lightbourne Jeremiah Mwangi Rachel Seal-Jones	International Alliance of Patients' Organizations
Adam Elmachetoub	Massachusetts Institute of Technology
Craig Allen Andrew Thomson	Medicines and Healthcare products Regulatory Agency
Emanuel Lohrmann Alain Micaleff (Co-leader of WP5)	MerckSerono SA
Richard Nixon	Novartis
Joanne Treacy Lesley Wise	Takeda

The licensing challenge

- Task of regulators: to make good and defensible decisions on best available evidence
 - Which medicine(s) for which indication(s) for which patient population(s)?
- It is increasingly important to be able to justify and explain these decisions to patients and the public—and also meaningfully involve them
- **Can formal approaches of benefit-risk decision-making be used to elicit preferences from patients and the public for use in a regulatory setting?**

Challenges with formalised preference elicitation and benefit-risk assessment

- Whose preferences?
- How much involvement?
- Which favourable and unfavourable effects?
- Which methodology or methodologies?
- How to communicate?

Whose preferences?

Patient and public:

Clinical trial participants, patients and potential patients, disabled people, parents and guardians, people who use health and/or social care services, carers, members of the public, and the organisations who represent the interests of these consumers.

Source: NHS INVOLVE

How much involvement?

Consultation

Health professionals elicit the patient and public perspective to inform the decision making process



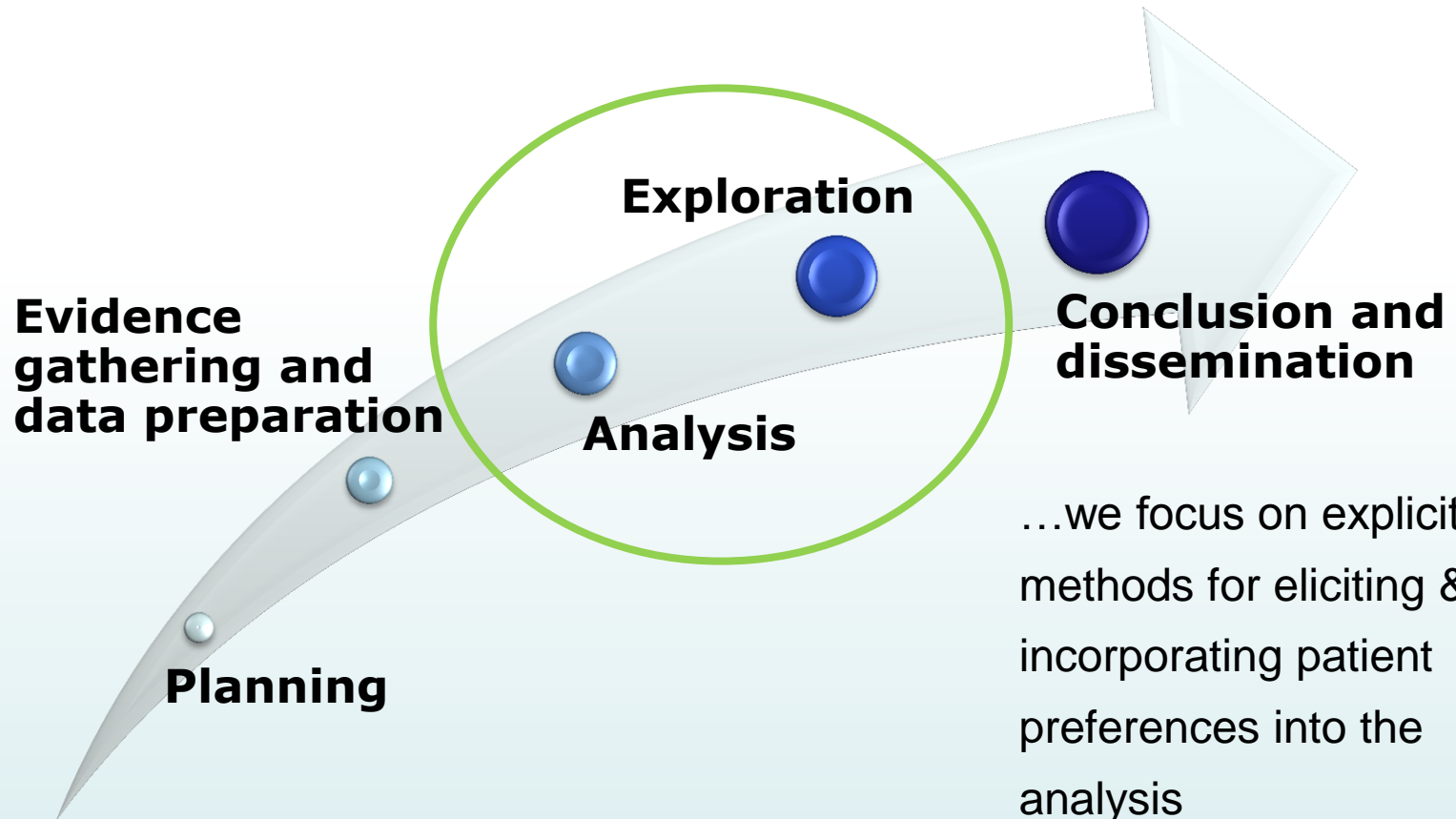
Collaboration

Health professionals and patients and the public form an active partnership and jointly participate in decision making



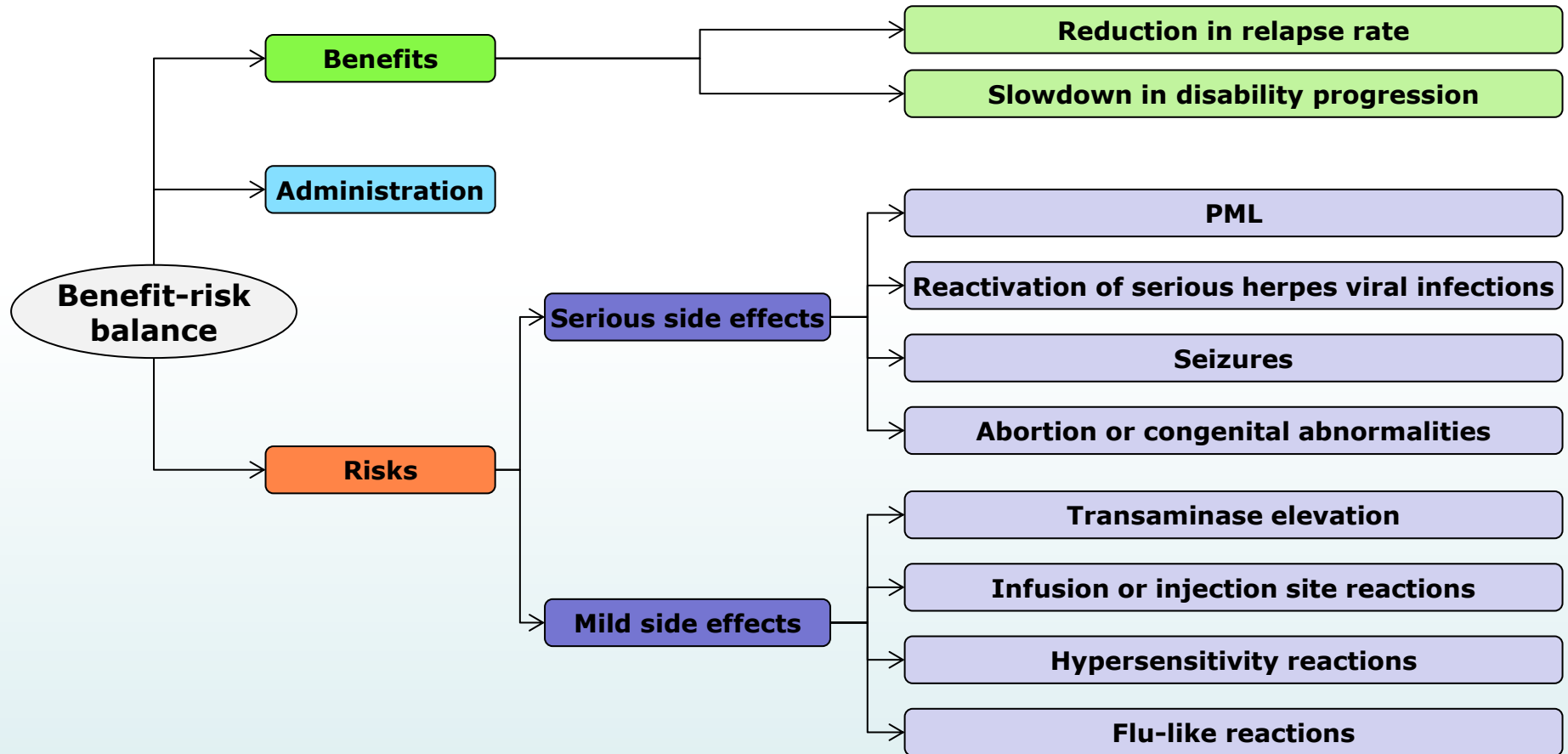
At what stage can PPI occur

There is scope for patients and the public to be involved throughout the BR assessment process...



Which favourable and unfavourable effects?

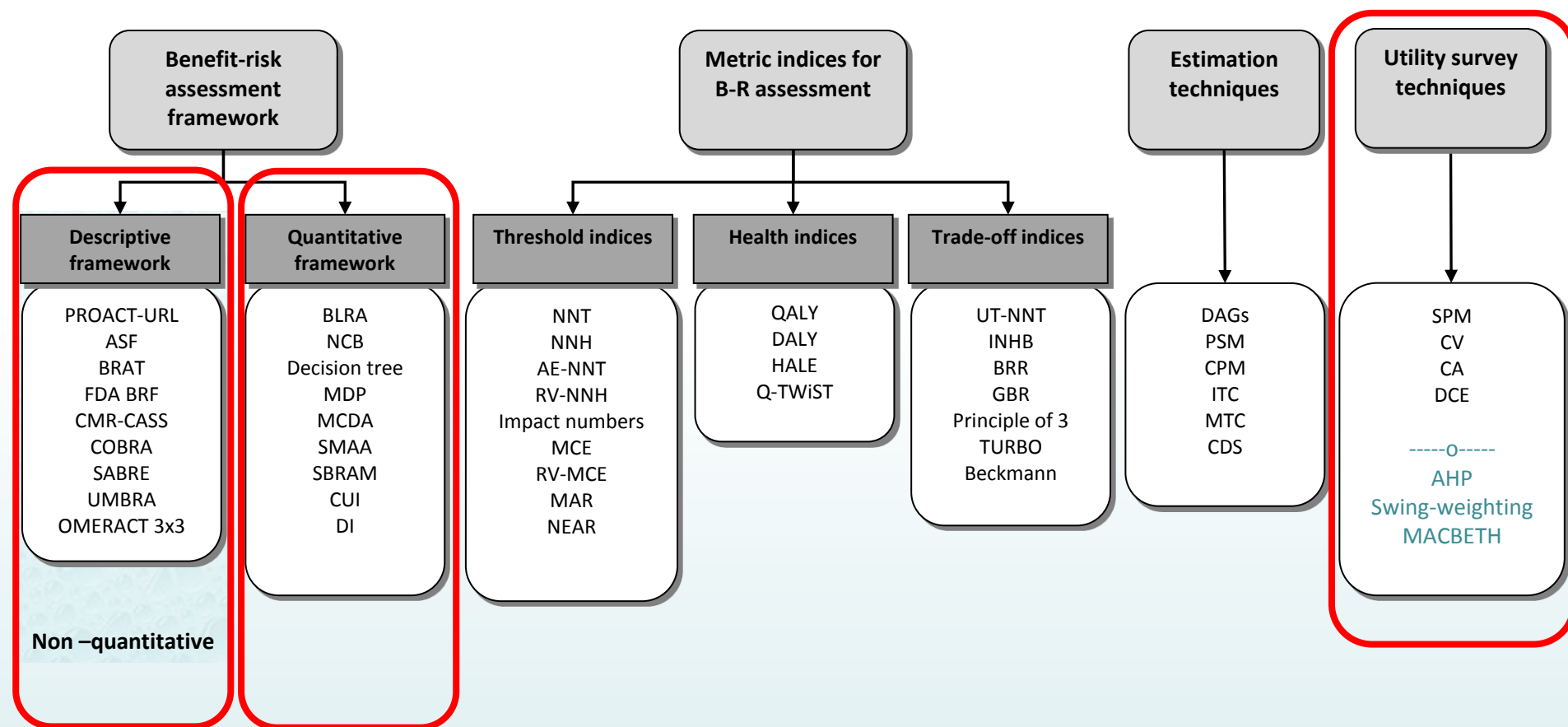
- Which outcome measures to use?



Challenges when selecting favourable and unfavourable effects

- Limitations on the number of outcomes
- Aggregated scores, e.g. EDSS, QoL
- Ranges of severities, e.g. transaminase elevation
- Surrogate measures, e.g. 10% weight loss

Methodologies available

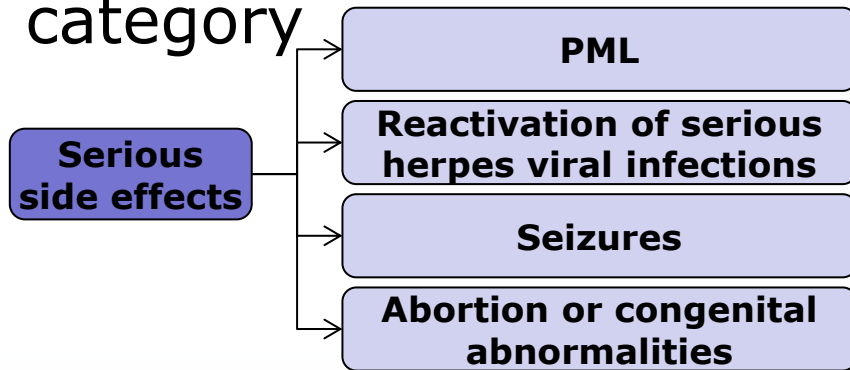


Which methodology or methodologies?

- Testing the elicitation of patient preferences through two case studies:
 - Rimonabant
 - ♦ DCE (Discrete Choice Experiment)
 - Natalizumab
 - ♦ Swing-weighting (in MCDA)
 - ♦ MACBETH (Measuring Attractiveness by a Categorical Based Evaluation Technique)
 - ♦ AHP (Analytic Hierarchy Process)
 - ♦ DCE (Discrete Choice Experiment)

Swing-weighting

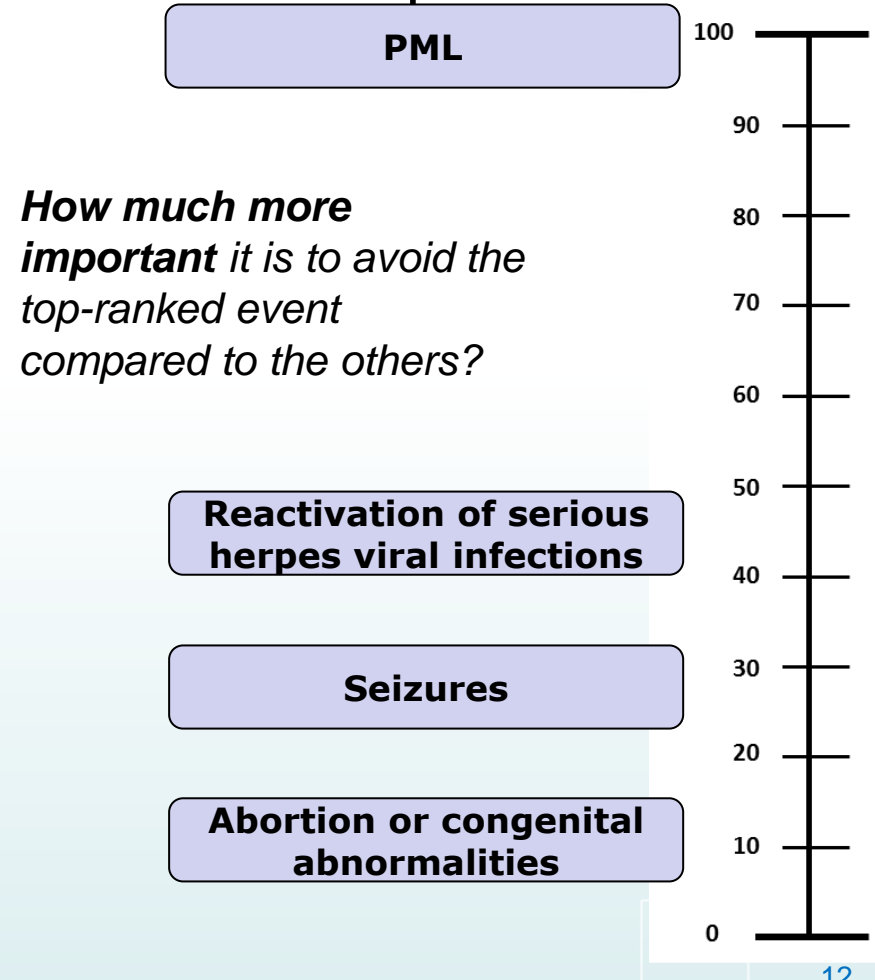
1. For each outcome category



1. Rank outcomes

Outcome	Rank
PML	1
Reactivation of serious herpes viral infections	2
Seizures	3
Abortion or congenital abnormalities	4

2. Relative importance



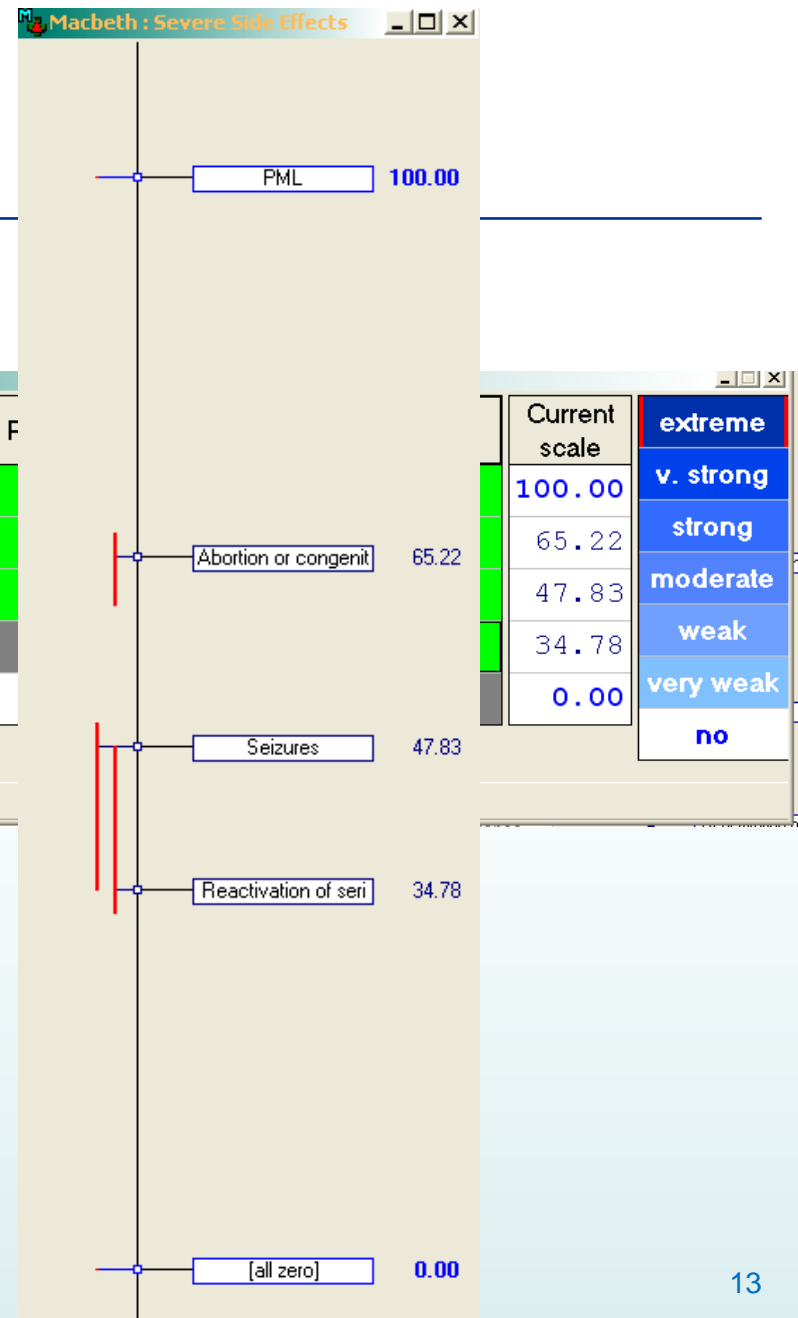
MACBETH

	PML	Abortion or congenit	Seizures	F
PML	no	extreme	extreme	
Abortion or congenit		no	strong	
Seizures			no	
Reactivation of seri				
[all zero]				

Consistent judgements



Fine
tuning...



AHP


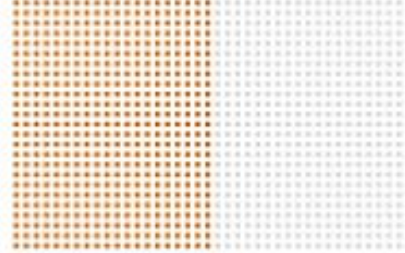


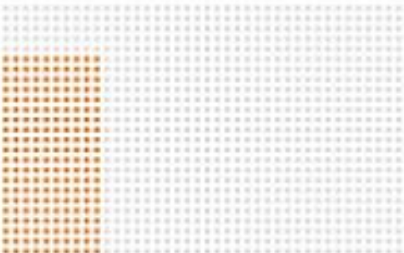

- *Which of the two mild to moderate risks would you prefer to avoid? (Please tick one)*

<input type="checkbox"/>	Flu-like reactions
<input type="checkbox"/>	Mild allergic reactions
<input type="checkbox"/>	They are equally important to avoid

- *If you did not tick "They are equally important to avoid", how much more important is it to avoid the risk you selected compared to the other risk? (Please tick one)*

<input type="checkbox"/>	Extremely more
<input type="checkbox"/>	Very strongly more
<input type="checkbox"/>	Strongly more
<input type="checkbox"/>	Moderately more

Discrete choice experiments





Mild allergic reactions	0 patients out of 1000 	500 patients out of 1000 
Serious allergic reactions	0 patients out of 1000 	0 patients out of 1000 
Depression	200 patients out of 1000 	100 patients out of 1000 
Which would you prefer? (Please tick one)	<input type="checkbox"/> Treatment A	<input type="checkbox"/> Treatment B

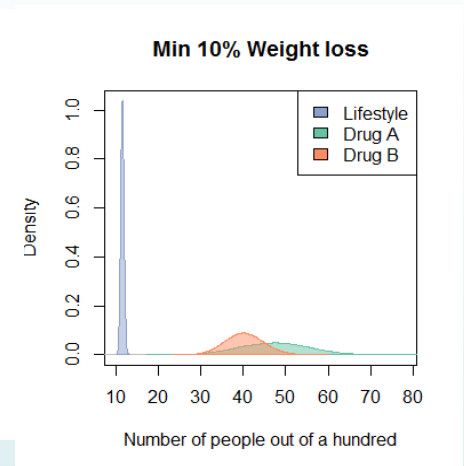
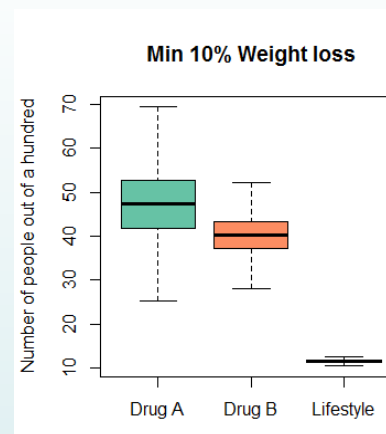
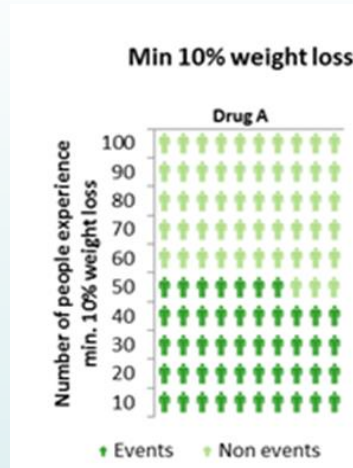
Comparative overview of elicitation methods

	Swing-weighting	MACBETH	AHP	DCE
Responses	Quantitative	Qualitative	Qualitative or quantitative	Qualitative
How is consistency measured?	Method ensures consistency	Inconsistencies must be resolved	Computes a consistency score	Reflected in uncertainty of estimates
Weight calculation	Direct	Linear optimisation (plus tuning)	Principal eigenvector	Regression
Can be given out as a paper questionnaire?	No	No	Yes	Yes

How to communicate?

- Communicating benefits and risks through text
 - “This is not patient worded.”
 - Frequency, severity, duration, reversibility, vignettes, impact on quality of life
- Communicating through visualisations

Magnitude	Expect about on event per	Min. 10% weight loss
1 in 1	 Person	
1 in 2	 Couple	Drug A Drug B
1 in 5	 Family	
1 in 10	 Extended family	Lifestyle



Progress

- The questionnaires (n=500) are currently being handed out at the MS Clinic
- Delays attributable to:
 - a) Difficulties accessing patients and the public
 - ♦ Unsuccessful recruiting online through patient organisations
 - b) Internal debates within the PPI team regarding the inclusion, exclusion and lay definitions of favourable and unfavourable clinical outcome measures
 - c) A lot of paperwork and approval processes
 - ♦ Imperial College London Sponsorship
 - ♦ Insurance (public liability and no fault)
 - ♦ Peer Review Certification
 - ♦ NHS Research Ethics Committee Approval
 - ♦ Imperial College NHS Trust Research and Development Approval
 - ♦ Imperial College Healthcare NHS Trust Feasibility Approval
- Preference elicitation activities will end 30th April 2015

Conclusions

- Eliciting patient preferences in regulatory assessment could add value and lead to more clinically relevant decisions
 - Political legitimacy, transparency, trust, communicability
- Many different formal methods of benefit-risk assessment can be used to elicit patient preferences
 - Each methodology has its own unique features, strengths and weaknesses: further exploration necessary
- Benefit-risk assessment methodologies support decision-making and are not intended to replace medical or regulatory expertise
- There isn't a right or wrong or one-size-fits-all answer