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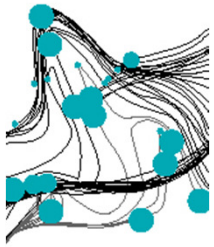
Recent advances in incorporating stakeholders' perspectives in Health Technology Assessment

Maarten J. IJzerman, PhD
Professor and chair,
department Health Technology & Services Research
m.j.ijzerman@utwente.nl

NIHA forum, Singapore
July, 1 2013



Making decisions in a complex healthcare system

- Decisions are complex and involve multiple criteria
  - Both, licensing (approval) and reimbursement decisions
- The appraisal process is usually a responsibility of expert committees
- These committees make a recommendation based on an implicit value judgment
- Evidence exists for some criteria but not for others
  - Primary endpoints chosen in clinical trials may not be the most relevant endpoints for patients and other stakeholders
- Previous studies have attempted to analyze decision criteria and weights (Koopmanschap, 2010; Devlin, 2004; Phillips, 2011)
  - ICER, budget impact, burden of disease and uncertainty

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Latest news

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- European patient organisations concerned about CVZ ...

22-07-2012
- Gene therapy: EGAN protests against rejection of ma ...

17-04-2012
- EGAN signs MoU with ENHA and EPF

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17-09-2012

European patient organisations concerned about CVZ advice regarding Pompe and Fabry

EURORIDS, EPF and EGAN have expressed their concern about the advice of the Dutch Health Care Insurance Board (CVZ), to no longer reimburse the orphan medication.

The decision of CVZ may have a significant adverse impact on the estimated 30 million adults and childeren living with rare diseases in the European Union.
Read the letter here.

<< Return to overview

Upcoming events

17-09-2013
- 16th International Fragile X and Other Early-Onset ...

Directly to
- Biomedinvo4all
- GRIP
- EUPATI
- GENCODYS
- GenGuide
- PatientPartner
- Eurordis

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A patient's perspective (Tysabri / Natalizumab)

- *I have had MS since 1970. I'm an RN, DSN, ASAC, HIV-educated counselor and an MPS. I've been on Tysabri for 4 years.*
- *I am 63 years old. I am not worried about PML and it doesn't bother me. I've started going through the survey and all those 1 in 1000, 2 in 1000--yes I know. I've been on it for 4 years and it's supposed to be like 1 in 600.*
- *I'm now driving again. I used to drive 350 miles a day to see patients and then I was told I couldn't drive anymore and I'm back to driving now. So life is good.*
- *I was without it for 5 months when I had a skin cancer and it was the most miserable 5 months of my life. Do anything but don't take my Tysabri away.*

By courtesy of F. Reed Johnson

Natalizumab (Tysabri®) background

- FDA approved 2004 for multiple sclerosis
- Withdrawn 2005 after 3 cases of progressive multifocal leukoencephalopathy (PML)
- Re-approved in 2006 with restrictions
- Approved in 2007 for Crohn's disease in US only
- Patient benefit-risk preference studies submitted to MS and Crohn's FDA advisory committees

Patient centered healthcare systems

Comparative Effectiveness Research

"…The purpose of CER is to assist consumers, clinicians, purchasers and policy makers to make informed decisions that will improve health care at both the individual and population levels."

Institute of Medicine, 2009

Patient Centered-Outcomes Research

"… helps people and their caregivers communicate and make informed health care decisions, allowing their voices to be heard in assessing the value of health care options.."

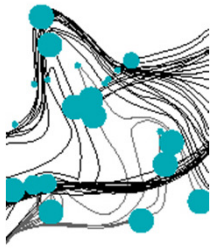
Patient Centered Outcomes Research Institute (PCORI)

The patient voice in Health Technology Assessment

Why including patients in HTA?

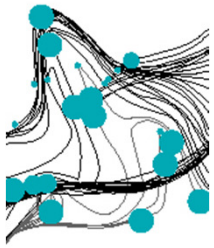
- To improve the quality of the decision made by regulatory agencies
  - The experience to live with a (chronic) disease can spread light and for instance explain why technologies that appear effective in clinical trials prove not to be in real life
- To improve transparency and openness and thus legitimacy of the decision
  - Democratic arguments would support the idea that people directly affected by policies be involved

Facey *et al.* Int. J. Techn Assessment Healthcare, 2010



What prevents us from using patient perspectives?

- Patients' perspectives are seen as anecdotal, biased views
- Patients may not be informed about benefits, risks and costs preventing them from making appropriate decisions
- It is difficult to obtain the patient view reliably, e.g. strong influence of few dominant patients prevents generalizability
- It is not clear how to tackle preference heterogeneity, e.g. different preferences in subgroups (there are no average patients)

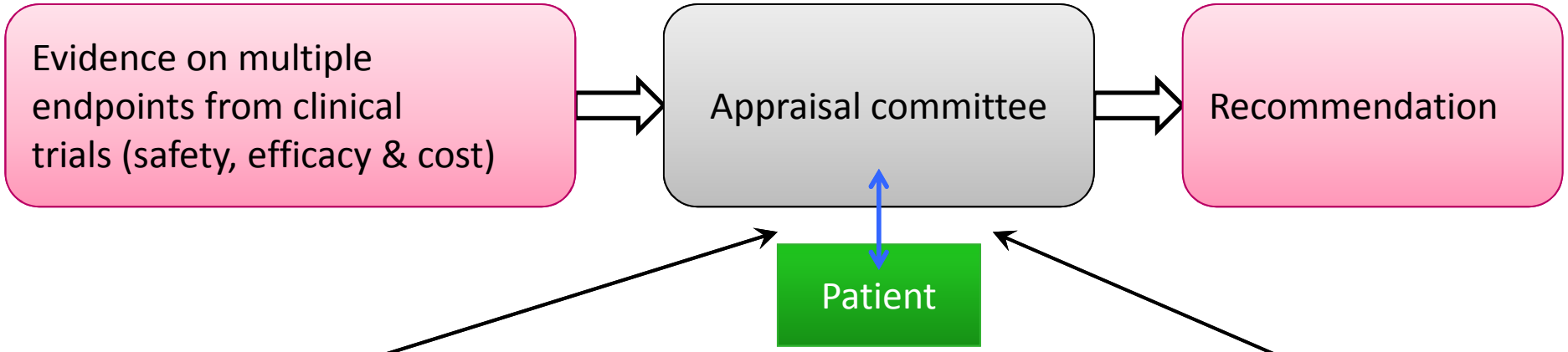


Public engagement. Three levels of involving patients.

- In *public communication*, information is conveyed from the sponsors of the initiative to the public.
- In *public consultation*, information is conveyed from members of the public to the sponsors of the initiative, following a process *initiated by* the sponsor.
  - Significantly, no *formal* dialogue exists between individual members of the public and the sponsors. The information elicited from the public is believed to represent currently held opinions on the topic in question.
- In *public participation*, information is exchanged between members of the public and the sponsors. That is, there is some degree of dialogue in the process.

Rowe, G. and L. Frewer, *A Typolicy of Public Engagement Mechanisms.* Science, Technology & Human Values, 2005. **30**(2): p. 251-290.

Patient preferences in regulatory decision making

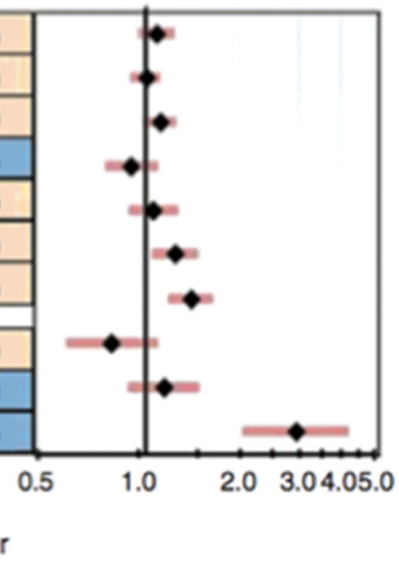


Use of patient preference data in four stages of HTA

- Identification of topics (horizon scanning)
  - Prioritizing topics for HTA using patient preference data (needs)
- Assessment of the evidence
  - Patient preference data as an additional piece of evidence
  - Appraisal committee may use them in making recommendations
- Deliberation
  - Direct patient involvement in appraisal committees
  - Empowering patients to actually take part in the discussion using preference data
- Communication and dissemination
  - Communicate what is important to patients

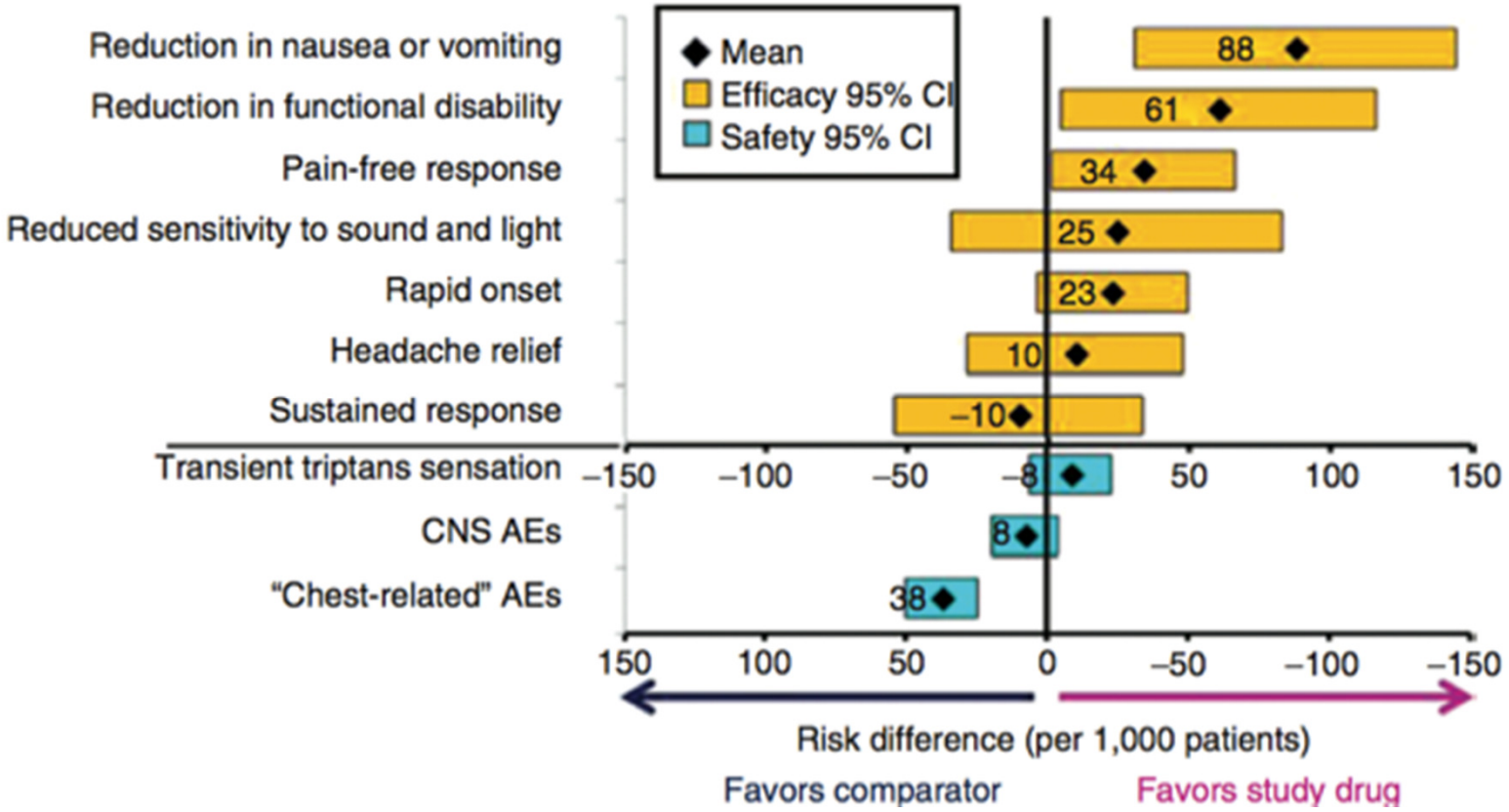
A benefit-risk assessment

		Outcome	Study drug risk (/1,000 pts)	Comparator risk (/1,000 pts)	Odds ratio (95% CI)
Benefits	↓ Pain	Rapid onset	271	248	1.13 (1.00,1.27)
		Headache relief	643	633	1.04 (0.94,1.15)
		Pain-free response	383	349	1.16 (1.03,1.30)
		Sustained response	285	295	0.95 (0.80,1.14)
	↓ Sensitivity	Reduced sensitivity to sound and light	530	505	1.10 (0.94,1.30)
	↓ Other	Reduction in functional disability	540	480	1.28 (1.09,1.49)
		Reduction in nausea or vomiting	604	517	1.43 (1.22,1.67)
Risks	↑ Individual risks	Transient triptans sensations	43	52	0.83 (0.61,1.14)
		CNS AEs	53	45	1.18 (0.92,1.51)
		"Chest-related" AEs	58	21	2.93 (2.04,4.20)



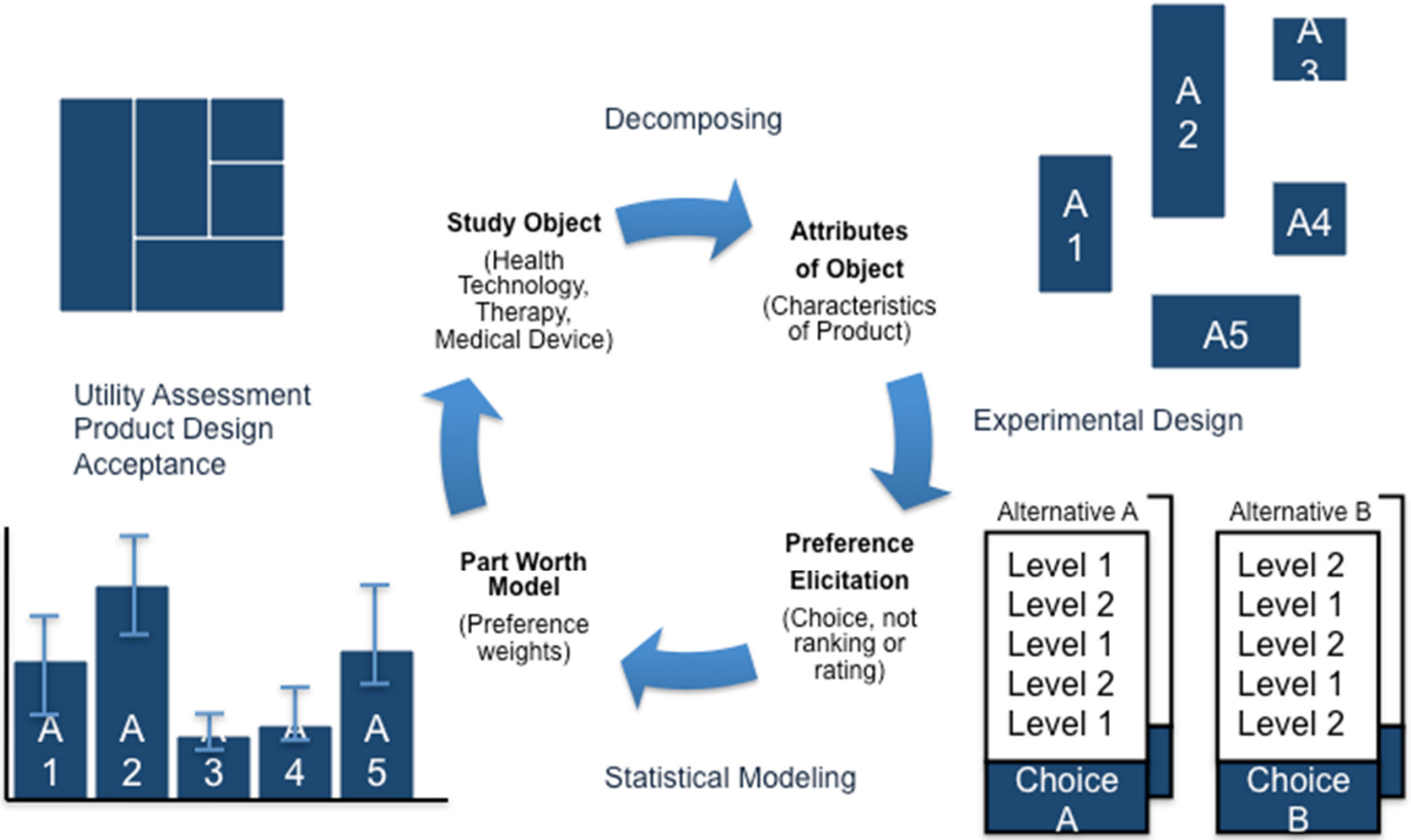
Levitan B (2011) A Concise Display of Multiple End Points for Benefit–Risk Assessment, Clinical Pharmacology & Therapeutics (2011) 89 1, 56–59. doi:10.1038/clpt.2010.251

A benefit-risk assessment (2)



Levitan B (2011) A Concise Display of Multiple End Points for Benefit–Risk Assessment, Clinical Pharmacology & Therapeutics (2011) 89 1, 56–59. doi:10.1038/clpt.2010.251

Conjoint analysis, discrete-choice experiments



Health State Utility (QALY) vs. Stated Preference Utility

- Clinical outcomes
- Duration

- Clinical Outcomes
- Duration
- Treatment factors
  - Side Effects/Tolerability
  - Dosage Method/Frequency
  - Cost
- Process factors
  - Health-Care Setting
  - Physician interactions
- Personal factors
  - Age, gender, education
  - Health history
  - Financial circumstances

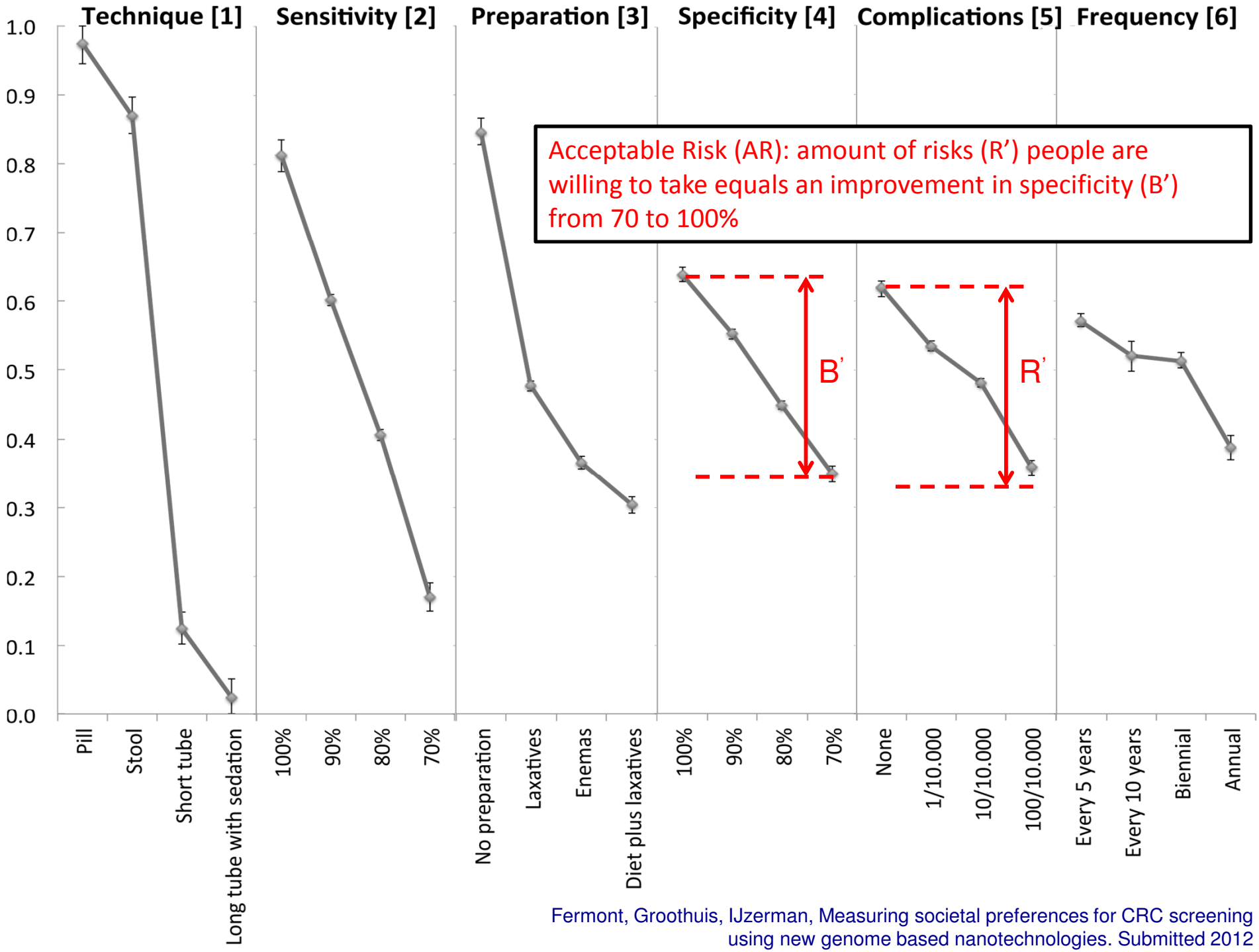
Imagine that you can choose how you will be screened for colorectal cancer. Please look at the screeningtests below and select the test you prefer by clicking the button below this test.

How do you need to prepare?	Before the test you need to take laxatives which cause diarrhoea to empty your colon.	Before the test you need to take enemas which cause diarrhoea to empty your colon.	For 3 days you need to alter your diet and medication. Before the test you need to take laxatives which cause diarrhoea to empty your colon.
How is the test done?	A short flexible tube with a small camera is inserted through the anus into the last part of the colon. This test is done at a hospital.	A long flexible tube with a small camera is inserted through the anus into the full colon. During the examination you will be sedated. This test is done at a hospital.	You need to swallow a pill that leaves your body through faeces after several hours. Your test results are wirelessly sent to your physician. This test is done at home.
How many out of 10 people <u>with</u> cancer, would the test correctly identify?	7 out of 10 	8 out of 10 	9 out of 10 
How many out of 10 people <u>without</u> cancer, would the test correctly identify?	7 out of 10 	10 out of 10 	9 out of 10 
How many out of 10.000 people who take this test have a complication?	None	10 out of 10.000	10 out of 10.000
How often do you need to take the test?	Every 5 years	Every year	Every 10 years
	○	○	○

If you could choose between the test you chose or not to be screened for colorectal cancer, what would you prefer?

- ○ I would still prefer the test I chose above
- ○ I would prefer not to be screened

Fermont, Groothuis, IJzerman, Measuring societal preferences for CRC screening using new genome based nanotechnologies. Submitted 2012



Fermont, Groothuis, IJzerman, Measuring societal preferences for CRC screening using new genome based nanotechnologies. Submitted 2012

A conjoint analysis study trading pregnancy rate for patient centredness

Table III Willingness to trade off pregnancy rate for decreased travel time and increased patient-centredness.

Attribute	Level	Patients' trade-off percentage[a] (95% CI)[b]	Physicians' trade-off percentage[a] (95% CI)[b]
Travel time to clinic	90 min	0	0
	45 min	3.1% (2.8; 3.6)	2.7%[c] (2.5; 3.5)
	15 min	5.2% (4.7; 6.0)	4.5% (4.1; 5.8)
Physician's attitude to patient	Unfriendly and uninterested	0	0
	Friendly, but distant	7.9% (7.4; 8.8)	5.7% (4.8; 6.5)†
	Friendly and interested	9.8% (9.2; 10.9)	6.3% (4.9; 6.7)‡
Information on treatment	Contradictory information	0	0
	Only general information	5.6% (5.1; 6.3)	3.4% (2.5; 4.0)†
	Clear and customized information	9.6%[d] (9.0; 10.8)	5.5% (4.1; 5.8)‡
Continuity of physician	Seeing a different physician almost every visit	0	0
	Having one lead physician	3.2% (2.8; 3.7)	2.1% (1.5; 2.8)*
	Always seeing your own physician	4.0% (3.5; 4.7)	2.6% (2.0; 3.2)†

Patients ($n = 925$) and physicians ($n = 227$).

[a]Willingness to trade-off ongoing pregnancy rate (WT_{preg}) is calculated by dividing the attribute's coefficients (Table II) by the continuous coefficient of pregnancy rate.

[b]Non-parametric 95% CI is based on bootstrapping with 2000 replications.

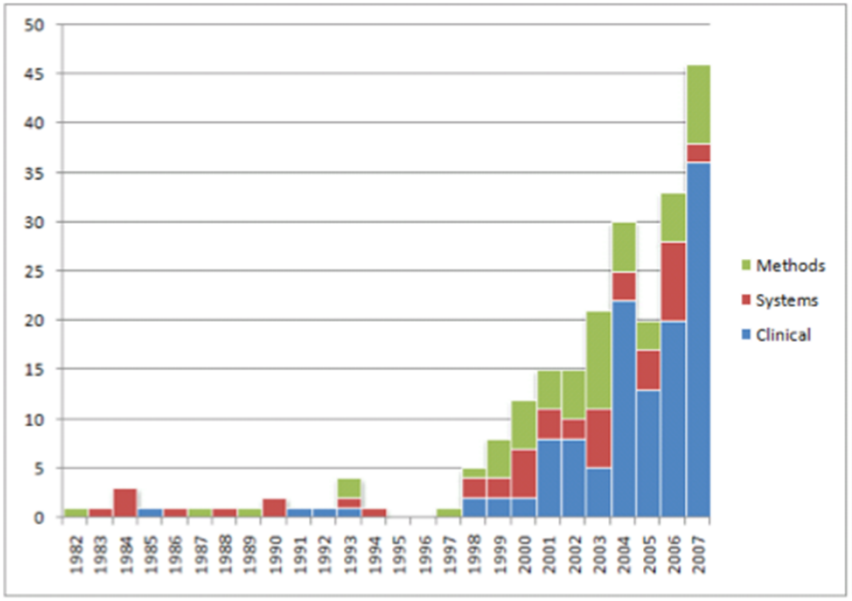
[c]For a 45-min decrease in travel time, physicians recommend to trade-off 2.7% in pregnancy rate ($45 \times 0.02/0.33$).

[d]Patients are willing to sacrifice 9.6% in pregnancy rate for receiving clear and customized instead of contradictory information ($2.77/0.29 = 9.6$).

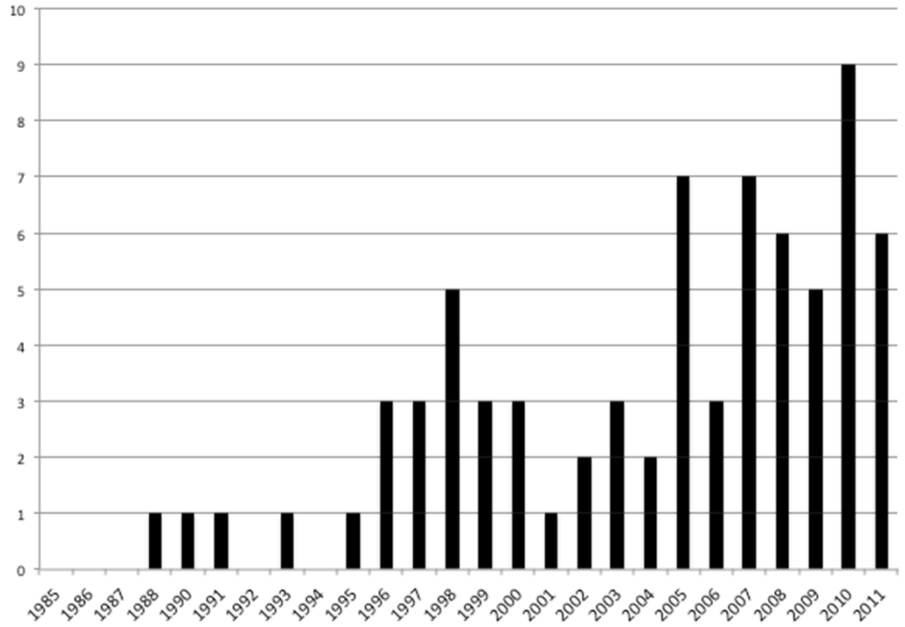
*$P < 0.05$ difference physicians versus patients; †$P < 0.01$ difference physicians versus patients; ‡$P < 0.001$ difference physicians versus patients.

van Empel IWH et al. Physicians underestimate the importance of patient-centredness to patients: a discrete choice experiment in fertility care. Hum. Reprod. 2011 Mar;26(3):584–93.

Rapid growth of studies (1982-2011)…

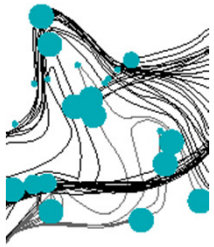


Conjoint analysis.
Marshall et al, 2009



MCDA and AHP methods
Hummel&IJzerman, 2011

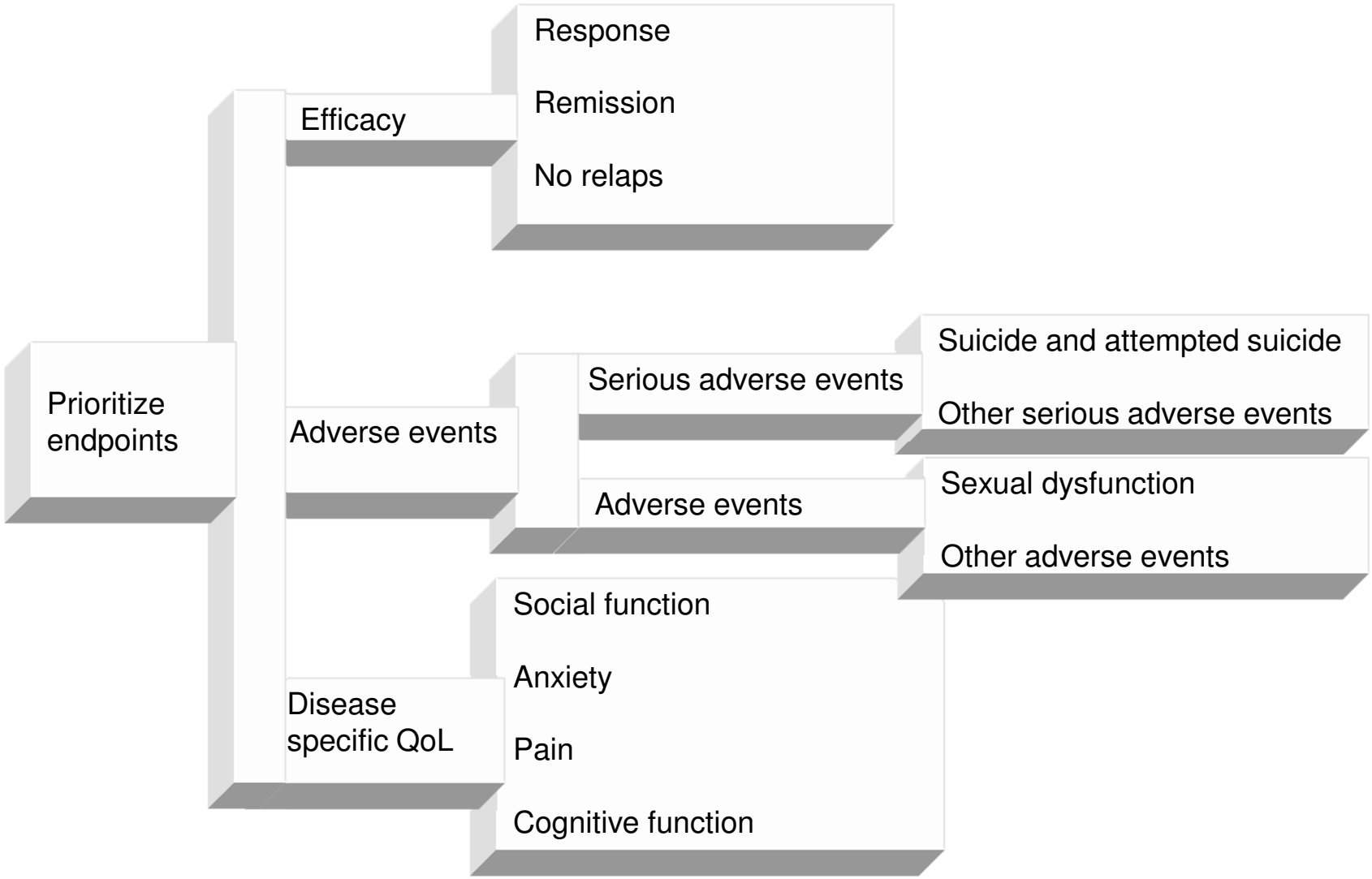
But the formal use of preference data in HTA is limited



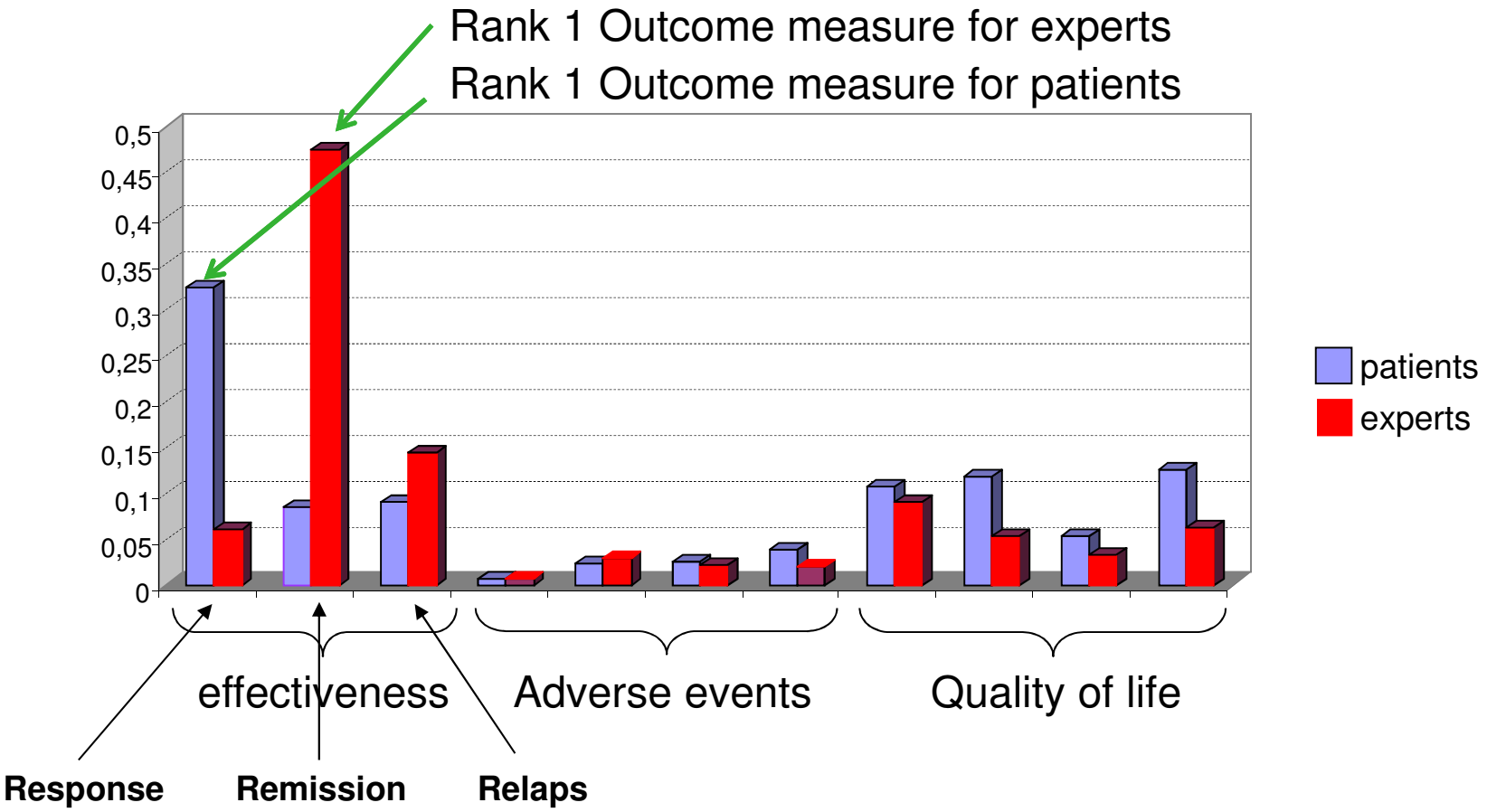
IQWiG's guidance on patient-relevant endpoints

- Objective: Ranking and weighing of patient-relevant endpoints for use of anti-depressants
- Based on benefits assessment by IQWIG
  - Reports: A05-20A (SNRIs duloxetine, venlafaxine) and A05-20C (Bupropion, Mirtazapin, Reboxitin)
  - Both commissioned by the G-BA
- Approach
  - Definition of decision tree with IQWIG team
  - Selection of representatives
  - Panel session with experts (n=7) and patients (n=12)
    - Panel scores obtained after discussion

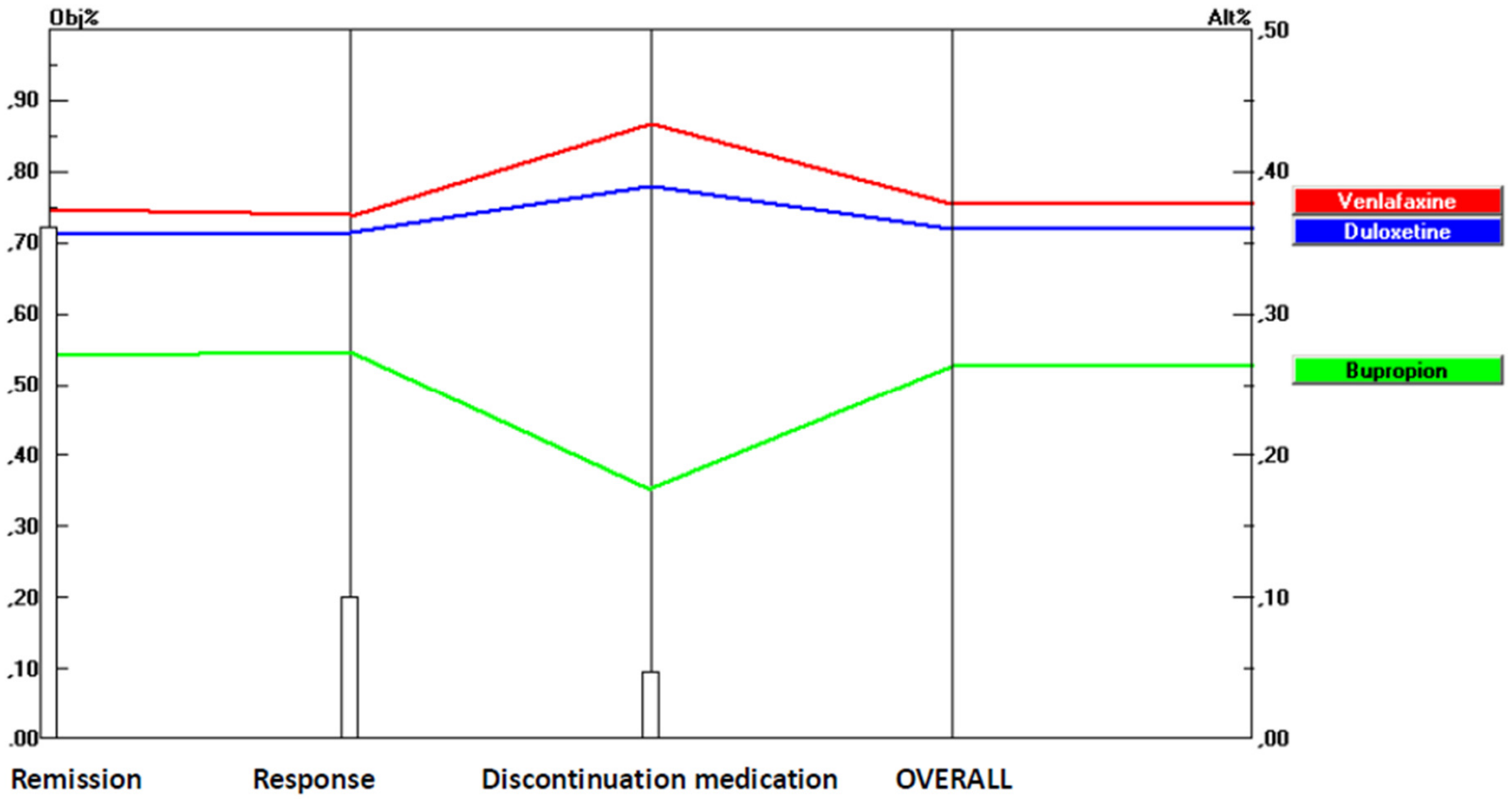
Danner, Hummel *et al.* Int. J. Techn. Assessm. Healthcare. 2011

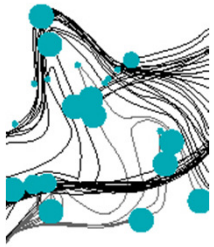

Prioritize endpoints
Efficacy
Response
Remission
No relaps
Adverse events
Serious adverse events
Suicide and attempted suicide
Other serious adverse events
Adverse events
Sexual dysfunction
Other adverse events
Disease specific QoL
Social function
Anxiety
Pain
Cognitive function

How patients and experts value patient relevant endpoints



Patient weighted performance of three antidepressants





The patient perspective in licensing (B/R assessment)

- Any decision about the availability of medicines today should involve the views of the consumer, that is, the patient. (Breckenridge, Drug Discoveries Today, 2011)

- Fifty years after thalidomide, there is still an important role for drug regulators but the time has come to bring patients fully into the decision process – as equal partners (Eichler, Abadie et al, Br. J. Pharmacology, 2012)

- "There is only one authority—that is the patient. We will be doing [DCE measures of patient-preference weights] in 10 years." Hans-Georg Eichler. DIA, Washington DC, June 2012

FDA (CDRH) 2012

- When assessing such data in a PMA application or *de novo* petition, FDA realizes that some patients are willing to take on a very high risk to achieve a small benefit, whereas others are more risk averse. Therefore, FDA would consider evidence relating to patients' perspective of what constitutes a meaningful benefit when determining if the device is effective, as some set of patients may value a benefit more than others. It should also be noted that if, for a certain device, the probable risks outweigh the probable benefits for all reasonable patients, FDA would consider use of such a device to be inherently unreasonable.

EMA roadmap 2015:
Public awareness of transparency and openness

- The Agency strives to make its opinions on the balance of benefits and risks as consistent and transparent as possible. A three-year project on benefit-risk methodology was begun in early 2009, aiming to identify decision-making models that can be used in the Agency's work.

- Current work with EMA is on the added value of patient preference data to the work of the patient and consumer working party (PCWP), directly related to the CHMP

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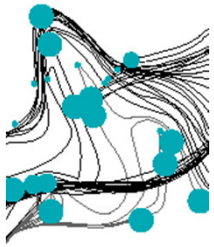

Concluding remarks: where are we now

- Political climate is changing and the role of patient preferences is gaining interest
- Patient preferences may be used
  - As additional evidence in technology appraisal (consultation)
  - To empower patients and to stimulate participatory decision making
- There are different quantitative methods to elicit patient preferences
  - They make decision trade-offs more explicit and transparent
  - Methods papers exist but application guidance in HTA is absent
- Regulators currently explore use of patient preference data
  - Issues of validity, bias, and responsibility