

## IP15: ANALYTIC HIERARCHY PROCESS AND CONJOINT ANALYSIS: TWO APPROACHES TO INCLUDE PATIENTS' PREFERENCES FOR THERAPEUTIC PATHWAYS AND OUTCOMES INTO HEALTH ECONOMIC ANALYSIS

Andreas Gerber, Maarten IJzerman,  
Axel Mühlbacher

## The AMNOG Law

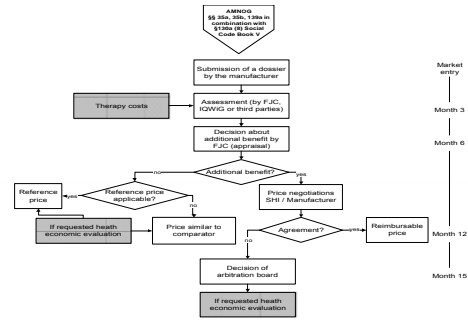


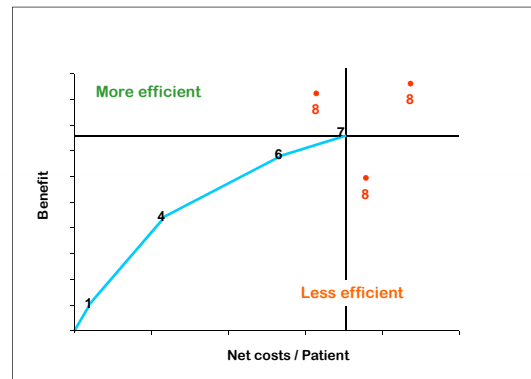
Figure 1: Timeline of the dossier assessment

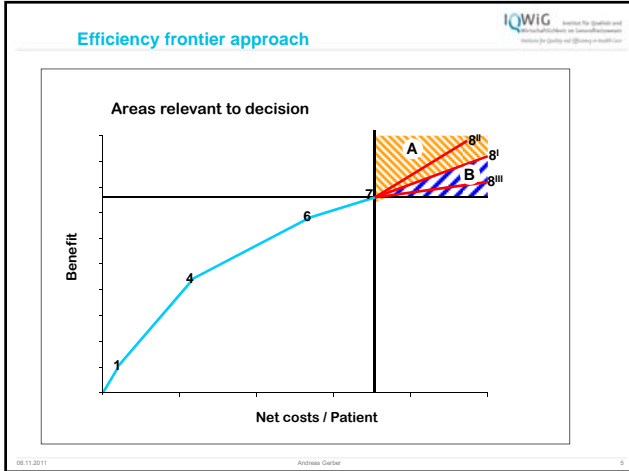
Legend: Figure 1 illustrates the timeline of the dossier assessment according to the new bill in effect January 1<sup>st</sup>, 2011. Boxes shaded display where and how IQWiG comes in with regard to health economic criteria in the decision making process on drug prices in Germany.

## The AMNOG Law

- German Social Code Book (SGB) V §35b  
Federal Joint Committee is to define an overall measure of benefit and harm („Maß des Gesamtnutzens“)

## Efficiency frontier approach





**Rationale: Why weighting?**

- Plot efficiency frontier for various patient-relevant outcomes on the basis of health economic evaluation
- Weighting of endpoint-specific efficiency frontiers to arrive at a reimbursable price
- Patients' preferences as a basis for the weighting process for they are experts in their specific disease area
- Elicitation of patients' preferences via
  - Analytic Hierarchy Process (AHP)
  - Conjoint Analyse (CA)

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- Background**
- The QALY has, to date, been the measure of economic benefit most used by decision-makers
  - Other stated preference approaches, such as conjoint analysis and analytic hierarchy process, have been regarded as methodologically superior, but relatively untried
  - IQWiG in Germany and the US (by and large) have rejected QALYs
  - This opens the door for more use, in practice, of alternative approaches
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**Introduction Conjoint Analysis**

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**MCDA and AHP**

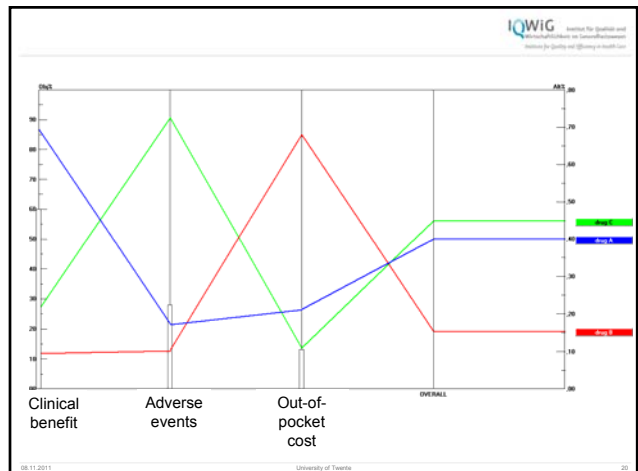
- MCDA methods utilize a decision matrix to provide a systematic analytical approach for integrating risk levels, uncertainty, and valuation, which enables evaluation and ranking of many alternatives. (Belton & Stewart, 2002)
  - MAUT, MAVT and AHP are the more complex MCDA techniques available
- The AHP structures a decision into a **hierarchy** of criteria, sub criteria and alternatives. By means of **pairwise comparisons** of two (sub) criteria or alternatives, it generates inconsistency ratios and weighting factors to prioritise the criteria and alternatives. **Sensitivity analysis** can be applied to test the robustness of the priorities. (Saaty, 1989)

See also: Sensitivity Analysis in MCDA models. Poster session. Tuesday, November, 8 2011 11-12 AM

**Eigenvalue: priorities**

	A	B	C	
A	1	3	5	
B	0.33	1	0.2	
C	0.2	5	1	
<b>SUMSCORE</b>	1.53	9	6.2	
<b>NORMALIZED SCORES</b>	0.65359477	0.33333333	0.80645161	
	0.21568627	0.11111111	0.03225806	
	0.13071895	0.55555556	0.16129032	
<b>AVERAGED</b>				0.59779324
				0.11968515
				0.28252161

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## Results Conjoint Analysis

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### Role of CA in HTA and CER: How IQWiG could use Conjoint Analysis

Prioritization

Weighting

Identification

$U_i =$

$W_1 *$   
 $W_2 *$   
 $W_3 *$

$v\_mortality$   
 $v\_morbidity$   
 $v\_qualityoflife$

$v\_mortality = \alpha + \beta * v\_mortality$   
 $v\_morbidity = \alpha + \beta * v\_morbidity$   
 $v\_qualityoflife = \alpha + \beta * v\_qualityoflife$

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### Identification: Attributes and Levels

Attribute	Level 1	Level 2	Level 4
duration of treatment	12 weeks	24 weeks	48 weeks
frequency of injecting interferon	Once in 2 weeks time	1 times a week	3 times a week
duration of fluc like symptoms after injection	one day after injection	two days after injection	tree days after injection
probability of getting gastrointestinal symptoms	25 out of 100 people (25%)	35 out of 100 people (35%)	45 out of 100 people (45%)
probability of getting psychiatric symptoms	35 out of 100 people (35%)	45 out of 100 people (45%)	55 out of 100 people (55%)
probability of getting skin problems or Alopecia	35 out of 100 people (35%)	45 out of 100 people (45%)	55 out of 100 people (55%)
probability of sustained virological response 6 month after treatment	45 out of 100 people (45%)	55 out of 100 people (55%)	65 out of 100 people (65%)

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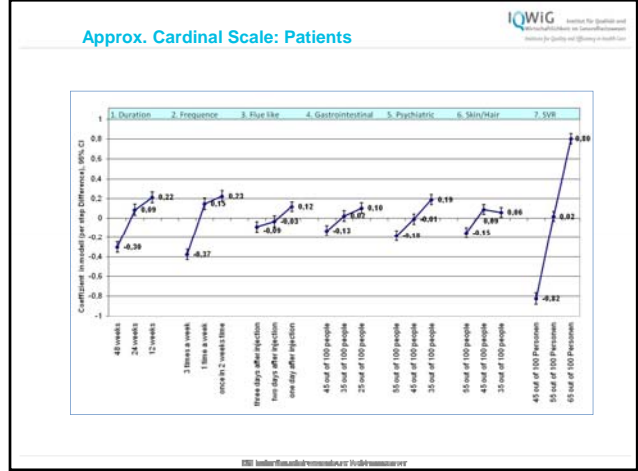
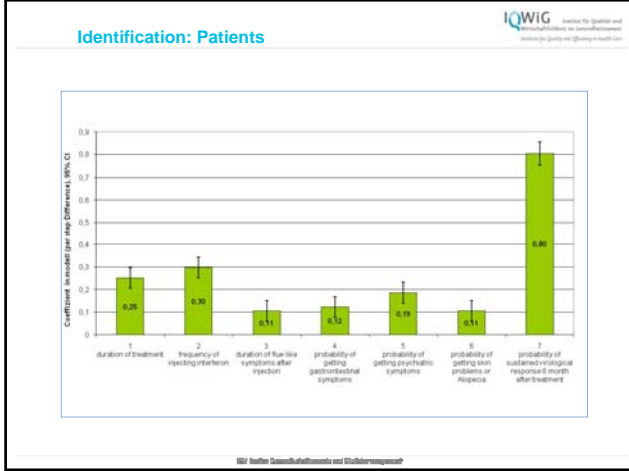
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### Identification: Patients

Attribut	coeff	Odds Ratio	se coeff	Sig	95% CI low	95% CI up	95% CI breite oneway	rel. Gew. in %
(1) duration of treatment	0,2503	1,284282	0,02342	< 0,001	0,2044	0,2962	0,0459	13
(2) frequency of injecting interferon	0,2966	1,345277	0,02337	< 0,001	0,2508	0,3424	0,0456	16
(3) duration of fluc like symptoms after injection	0,1052	1,110933	0,02323	< 0,001	0,0597	0,1507	0,0452	6
(4) probability of getting gastrointestinal symptoms	-0,1233	1,131224	0,02332	< 0,001	-0,0776	0,169	0,0453	7
(5) probability of getting psychiatric symptoms	0,1857	1,204061	0,02342	< 0,001	0,1398	0,2317	0,0459	10
(6) probability of getting skin problems or Alopecia	0,1055	1,111155	0,02627	< 0,001	0,0599	0,1511	0,0455	6
(7) probability of sustained virological response 6 month after treatment	0,8041	2,234684	0,02611	< 0,001	0,7529	0,8553	0,05115	43

Likelihood-ratio test of rho=0: chibar2(01) = 14.12 Prob = chibar2 = 0.000, Random-effects logistic regression, Number of obs = 5252, Log likelihood = -2852.7476, Prob > chi2 = 0.0000

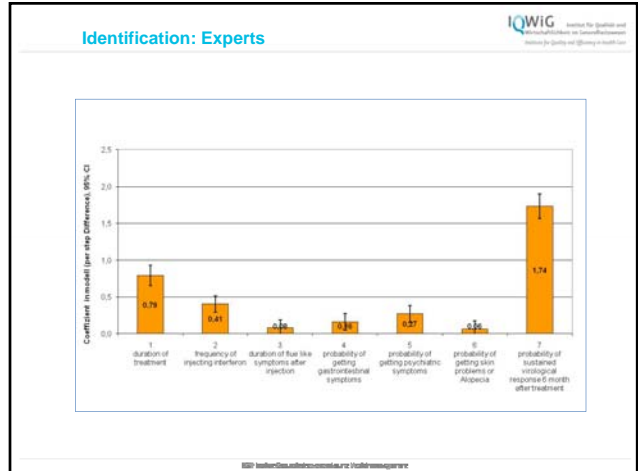
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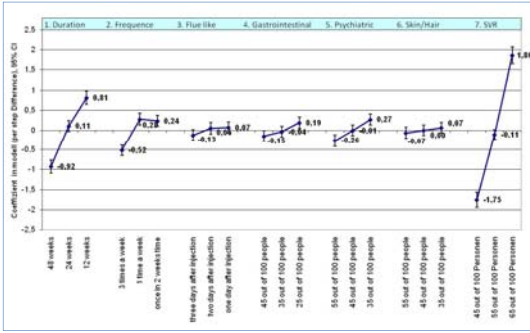
### Identification: Experts

Attribut	Coeff	Odds ratio	se coeff	sig	95% CI low	95% CI up	95% CI breite oneway	rel. Gew. in %
(1) duration of treatment	0.7918	2.207451	0.069329	< 0.001	0.6560	0.9277	0.1358817	23
(2) frequency of injecting interferon	0.4053	1.499740	0.056374	0.0000	0.2948	0.5158	0.1104905	12
(3) duration of flu like symptoms after injection	0.0786	1.081725	0.056094	0.1610	-0.0314	0.1885	0.1099418	2
(4) probability of getting gastrointestinal symptoms	0.1620	1.175813	0.058546	< 0.01	0.0472	0.2767	0.1147476	5
(5) probability of getting psychiatric symptoms	0.2702	1.310261	0.059416	< 0.001	0.1538	0.3867	0.1164531	8
(6) probability of getting skin problems or Alopecia	0.0622	1.064199	0.058534	0.2880	-0.0525	0.1769	0.1147253	2
(7) probability of sustained virological response 6 month after treatment	1.7362	5.675621	0.086153	< 0.001	1.5673	1.9050	0.168857	50

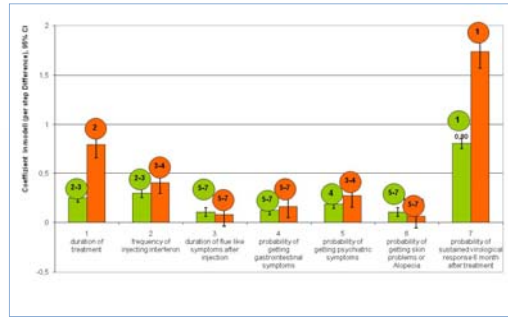
Likelihood-ratio test of rho=0:  $\chi^2(7) = 1076.62$ , Prob >  $\chi^2 = 1.000$ . Random-effects logistic regression. Number of obs = 1512. LR  $\chi^2(7) = 1076.62$ , Log likelihood = -509.20122, Prob >  $\chi^2 = 0.000$



### Approx. Cardinal Scale: Experts



### Expert judgment versus patient preferences



### Endpoint based utility assessment of therapy A: PegInterferon (high dose) + Ribavirin

Attribute	E <sub>0</sub>	E <sub>Min</sub>	E <sub>Max</sub>	Z <sub>nm</sub>	G <sub>nm</sub>	T <sub>nm</sub>
1) duration of treatment	48	48	48	0	0,2502	0
2) frequency of injecting interferon	1	1	3	0	0,2966	0
3) duration of flu like symptoms after injection	2	2	2	0	0,1502	0
4) probability of getting gastrointestinal symptoms	27,75	22,25	27,75	100	0,1233	-12,33
5) probability of getting psychiatric symptoms	30,75	29,75	32,50	36,36	0,1857	-6,75
6) probability of getting skin problems or Alopecia	32,67	26,67	32,67	100	0,105	-10,5
7) probability of sustained virological response 6 month after treatment	54	47	54	100	0,8041	80,41
Attribute-based utility assessment therapy A						50,83

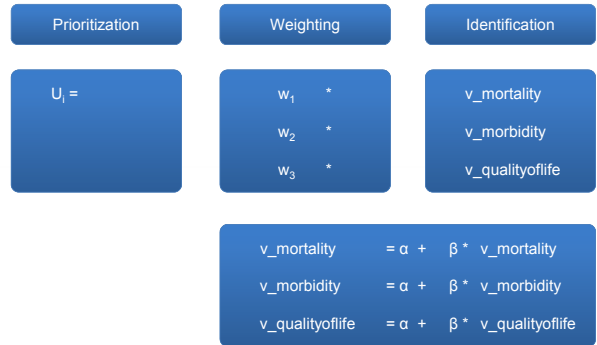
### Endpoint based utility assessment of therapy B: PegInterferon (low dose) + Ribavirin

Attribute	E <sub>0</sub>	E <sub>Min</sub>	E <sub>Max</sub>	Z <sub>nm</sub>	G <sub>nm</sub>	T <sub>nm</sub>
1) duration of treatment	48	48	48	0	0,2502	0
2) frequency of injecting interferon	1	1	3	0	0,2966	0
3) duration of flu like symptoms after injection	2	2	2	0	0,1502	0
4) probability of getting gastrointestinal symptoms	23,75	22,25	27,75	27,27	0,1233	-3,36
5) probability of getting psychiatric symptoms	29,75	29,75	32,50	0	0,1857	0
6) probability of getting skin problems or Alopecia	30,17	26,67	32,67	58,33	0,105	-6,12
7) probability of sustained virological response 6 month after treatment	47	47	54	0	0,8041	0
Attribute-based utility assessment therapy B						-9,48

**Endpoint based utility assessment of therapy C:  
Interferon + Ribavirin**

Attribute	$E_n$	$E_{Min}$	$E_{Max}$	$Z_{nm}$	$G_{nm}$	$T_{nm}$
1) duration of treatment	48	48	48	0	0,2502	0
2) frequency of injecting interferon	3	1	3	100	0,2966	-29,66
3) duration of flue like symptoms after injection	2	2	2	0	0,1502	0
4) probability of getting gastrointestinal symptoms	22,25	22,25	27,75	0	0,1233	0
5) probability of getting psychiatric symptoms	32,5	29,75	32,50	100	0,1857	-18,57
6) probability of getting skin problems or Alopecia	26,67	26,67	32,67	0	0,105	0
7) probability of sustained virological response 6 month after treatment	47	47	54	0	0,8041	0
<b>Attribute-based utility assessment therapy C</b>						<b>-48,23</b>

**Role of CA in HTA and CER:  
How IQWiG could use Conjoint Analysis**



**Results Analytic Hierarchy Process**

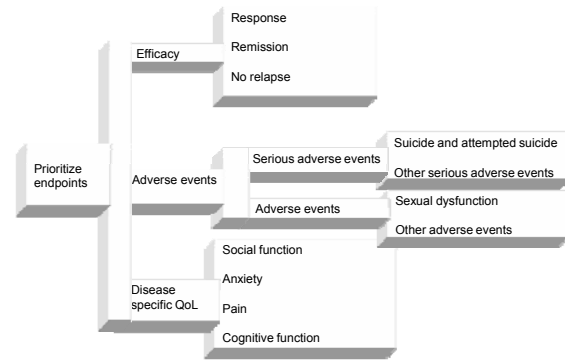
**Use of AHP in patient-centered healthcare**

1. Ranking (patient-relevant) outcome measures
  - Determination of most important outcome measure (for which to construct an efficiency frontier)
2. Weighting (patient-relevant) outcome measures
  - MCDA methods can be used to obtain relative weights for attributes and to estimate preference for treatment
3. Value based pricing, e.g. calculation of a ceiling price based on patient-weighted outcomes
  - estimation of the marginal value of an incremental improvement

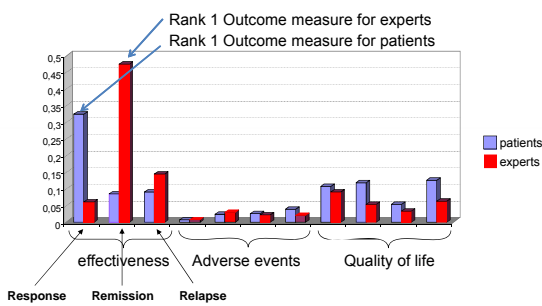
### Use of AHP to rank and weigh patient-relevant endpoints

- Objective: Ranking and weighting 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



### How patients and experts value patient relevant endpoints



### Treatment preference: integration of clinical evidence

	Duloxetine	Venlafaxine	Bupropion
Response	1.95 (1.61-2.36)	2.04 (1.74-2.38)	1.48 (1.20-1.82)
Remission	1.91 (1.56-2.34)	1.97 (1.64-2.35)	1.46 (1.18-1.82)
Discontinuation medication due to side effects	2.22 (1.55-3.19)	2.47 (1.81-3.37)	1.00 (0.61-1.65)

Pooled effect / clinical outcome (OR)

	Duloxetine	Venlafaxine	Bupropion
Response	,356	,373	,271
Remission	,358	,369	,273
Discontinuation medication due to side effects	,390	,434	,176

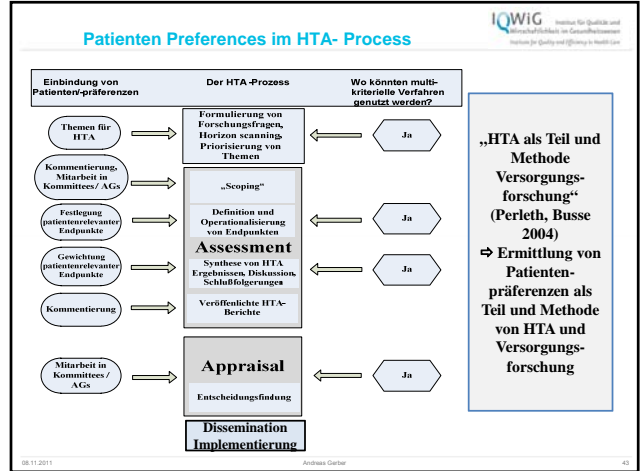
Weighted clinical outcome on linear scale

See also: Sensitivity Analysis in MCDA models. Poster session. Tuesday, November, 8 2011 11-12 AM

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**Conclusions**

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### Good quality standards

- Where do you think the two methods should be used?

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### Good quality standards

- What would you think one should include into a guideline for MCDA? Are there quality indicators you would suggest to be followed?
- What could we use from the checklist for conjoint applications, where would there be differences for MCDA / AHP?

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## Good quality standards

- Research question: Was a well-defined research question stated and is AHP an appropriate method for answering it.
- Were the criteria and the hierarchy supported by evidence.
- Was the construction of the questions and the tasks appropriate?
- Were the discussion rounds if done performed in a mode that all participants were to be heard.
- Were the preferences elicited credibly, eg inconsistency ratio?

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## Good quality standards

- Are the data complete?
- Was the data collection plan appropriate?
- Was overlap and potential dependency among criteria be taken into account/ into consideration?
- Was the validity of the results discussed? Were the limitations discussed, eg representativity?

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## Invitation to join



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Bildquelle: Wikipedia