



**Ramon Schaefer and Michael Schlander:**

**Is NICE in the UK More “Innovation-Friendly”  
Than IQWiG/GBA in Germany?**



Session OS26 Country-Specific and Regional HTA – Country Focus – Tuesday, June 20, 2017 – 16:30 – 18:00



*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

1. Background & Research Question
2. Material & Methods
3. Results
  - ↪ GBA
  - ↪ NICE
  - ↪ Cancer Drug Appraisals
  - ↪ Matched Pairs Comparison
4. Conclusions



*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

# 1

## Background & Research Question



## What are Technology Assessments for?

A broad range of expectations (and fears) ...

“issuing guidance to  
potential users”

“containing costs”

“restricting use”

“prioritizing for  
further evaluation”

“alerting users to  
future possibilities”



## XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017: Is NICE More “Innovation-Friendly” Than IQWiG/GBA?

### Perceptions of HTA Outcomes

**Are Cancer Drugs Less Likely to be Recommended for Listing by the Pharmaceutical Benefits Advisory Committee in Australia?**  
Patrick J. Kelly<sup>1</sup>, Glenn Salkeld<sup>1</sup> and Martin R. Stockley<sup>1</sup>

EUROPEAN JOURNAL OF CANCER 45 (2009) 1188–1192

available at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.ejconline.com](http://www.ejconline.com)

**Public funding of new cancer drugs: Is NICE getting nastier?**

Anne R. Mason\*, Michael F. Drummond

Centre for Health Economics, Alcuin A Block, University of York, Heslington, York YO10 5DD, UK

**ARTICLE INFO**

Article history:  
Received 6 November 2008  
Received in revised form 25 November 2008

**ABSTRACT**

Background: Decision-making processes that determine cancer drug availability vary internationally. The National Institute for Health and Clinical Excellence (NICE) assesses clinical and cost-effectiveness, but recent restrictions on the availability of cancer drugs suggest that NICE may be getting tougher.

#### ARZNEIMITTELNUTZENBEWERTUNG

# Für Patienten folgenreich

Als Konsequenz des Arzneimittelmarktneuordnungsgesetzes (AMNOG) stehen einige Medikamente für Diabetiker in Deutschland nicht mehr zur Verfügung.

Deutsches Ärzteblatt – Perspektiven der Diabetologie 2/2015: 17-19.

on of cancer drugs and  
2008 were classified as  
after a change in NICE's  
sons for its restrictions  
proportion of 'negative'  
ngs were similar when  
explained by the new  
ge is the shift from an  
e of value-for-money.  
td. All rights reserved.



## Health Economic Evaluation Principles



### The Logic of Cost-Effectiveness – Questions Asked:

1.



#### Safety

- ▮ Does it harm?  
(controlled conditions)

2.



#### Efficacy

- ▮ *Can it work?*  
(controlled conditions)

3.



#### Effectiveness

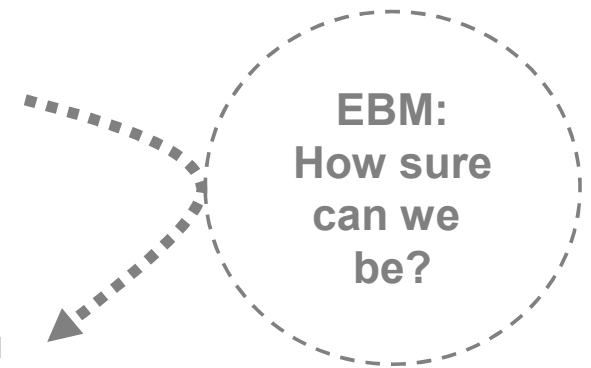
- ▮ Does it work and is it safe?<sup>1</sup>  
(normal practice)

4.



#### Efficiency

- ▮ Do its benefits outweigh its costs?  
(*United Kingdom: “Is it cost-effective”?*)





*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Assessment and Appraisal Criteria



(Single) Technology Appraisals are primarily based on:

➤ **Clinical evidence**

Sources of evidence should be integrated into a systematic review; RCTs are considered to be most appropriate for measures of relative treatment effect

➤ **Economic evidence**

NICE has to take account of the overall resources available to the NHS and determine cost effectiveness (ICER per QALY gained)

### Assessment:

➤ **Assessment** by the Evidence Review Group (ERG)

- ERG reviews manufacturer submission and produces the ERG report
- ERG reports on the clinical and cost effectiveness of the technology in line with NICE's methods of technology appraisal





## XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017: Is NICE More “Innovation-Friendly” Than IQWiG/GBA?

# Assessment and Appraisal Criteria



## Appraisal:

- Appraisal of the evidence while considering clinical effectiveness, health-related factors, cost effectiveness and non-health-factors
- Decisions/ recommendations refer primarily to the most plausible ICER (*“the ICER is a necessary, but [...] not the sole, basis for decision-making”*)
- NICE considers that it is most appropriate to use an ICER range:
  - “Below a most plausible ICER of £20,000 per QALY gained, the decision to **recommend the use of a technology is normally based on the cost-effectiveness estimate** and the acceptability of a technology as an effective use of NHS resources.”
  - “As the ICER of an intervention increases in the range of £20,000 to £30,000 per QALY gained, the Committee's judgement about the acceptability of the technology as an effective use of NHS resources will make **explicit reference to relevant factors** (*i.e., innovative nature of a technology*).”
  - “Above a most plausible ICER of £30,000 per QALY gained, the Committee will need to identify an **increasingly stronger case** for supporting the technology as an effective use of NHS resources, with regard to the factors.”





## Early Benefit Assessments in Germany



### The Logic of Comparative Effectiveness – AMNOG:

1.



#### Safety

- ▢ Does it harm?  
(controlled conditions)

2.



#### Efficacy

- ▢ *Can it work?*<sup>1</sup>  
(controlled conditions)

3.



#### Effectiveness

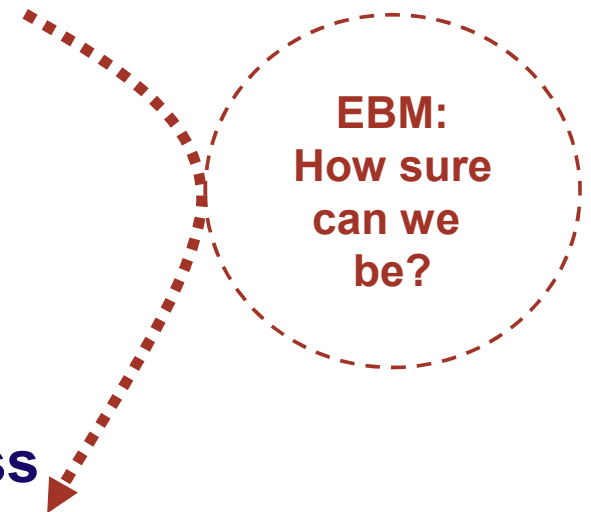
- ▢ Does it work and is it safe?  
(normal practice)

4.



#### Comparative Effectiveness

- ▢ Does it outperform current standard therapy?  
(*Germany: “Is it more effective”?*)





## Assessment and Appraisal Criteria



### Assessment by IQWiG<sup>1</sup> & Appraisal by GBA<sup>2</sup>

- ↪ Both agencies focus on comparative effectiveness, based on a rigorous application of principles of evidence-based medicine (EBM)
- ↪ Focusing on clinical evidence, primarily on **patient-relevant outcomes**:
  - ↪ Mortality
  - ↪ Morbidity
  - ↪ Health-related Quality of Life (HRQoL),
  - ↪ and, *additionally*, (serious) adverse events.
- ↪ Clinical evidence submitted in terms of **RCTs** or **systematic reviews of RCTs** are considered to be most appropriate to measure clinical effectiveness



## Research Questions

- ▮ **Are Different Methodological Choices Associated with Different HTA Outcomes?**
- ▮ **Can We Confirm Widely-Held Perceptions re. HTA Outcomes by NICE versus IQWiG/GBA?**
  - ▮ Descriptive analysis of Early Benefit Assessments
  - ▮ Descriptive analysis of NICE Single Technology Appraisals
  - ▮ Can we confirm that HTA agencies follow their own criteria?
- ▮ **How Do HTA Outcomes by NICE and IQWiG Compare with each other?**
  - ▮ Identification and analysis of matched condition / intervention pairs
  - ▮ Exploration of variables potentially explaining any differences



*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

# 2

## Materials & Methods



## Note on Terminology

### GBA/IQWiG:

Both agencies use the German word “*Patientenpopulation*”;

For patient groups within a technology’s indication GBA and IQWiG use the wording “*Subpopulation*” or “(Patienten-)*Subgruppe*”

### NICE:

NICE uses the wording “(patient) population”;

For patient groups within a technology’s indication NICE uses the wording “patient (sub)groups”, as well as the description of “treatment options” and “decisions”



## *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

# Materials and Methods

## Data source:

Publicly available and completed benefit assessment documents from official websites<sup>1,2</sup>

## Data excluded:

### NICE

Multi Technology Appraisals (MTAs);  
*early* terminated STAs

### GBA

expired / re-assessed appraisals;  
not (*yet*) completed appraisals

## Data included:

### NICE

Single Technology Appraisal (STA)  
Guidance;  
*if required (e.g., missing data),*  
Evidence Review Group (ERG) Reports

### GBA

GBA appraisals  
(resolution texts of GBA decisions);  
IQWiG assessments  
(health benefit dossiers)



## Materials and Methods

### Data extracted:

#### NICE

- ↪ therapeutic area;
- ↪ benefit assessment results;
- ↪ study population/treatment options;
- ↪ clinical evidence (use of RCTs);
- ↪ annual drug acquisition costs;
- ↪ cost effectiveness (ICER per QALY);
- ↪ end-of-life criteria

#### GBA

- ↪ therapeutic area;
- ↪ benefit assessment results;
- ↪ study population/subgroups;
- ↪ clinical evidence (use of RCTs);
- ↪ annual treatment costs;
- ↪ patient-relevant endpoints (mortality, morbidity, HRQoL)

### Matched pair analysis:

- ↪ For a valid comparison, we used matched condition-intervention pairs, which were defined as health technologies with similar indications.
- ↪ We did not differentiate by patient subpopulations because of the often imprecise match of patient (sub)group definitions by NICE and GBA/IQWiG.





# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Materials and Methods

### Flowchart

of all NICE single  
technology  
appraisal guidance,

GBA appraisals  
and  
IQWiG benefit  
assessments,

as well as of all  
matched condition-  
intervention pairs.

**NICE completed 115 TAs**  
by April 30, 2015

- STAs (n=88)
- MTAs (n=14)
- Terminated Appraisals (n=10)

**88 STAs subdivided into**  
**125 patient groups**

- 67 technologies/  
99 patient groups were  
recommended
- 21 technologies/  
26 patient groups were  
not recommended

**G-BA completed**  
**112 EBAs**  
by April 30, 2015

- Expired/ re-assessed  
appraisals  
(n=7)

**105 EBAs subdivided into**  
**226 subgroups**

- 64 technologies/  
90 subgroups  
with added benefit
- 41 technologies/  
136 subgroups  
without added benefit

**IQWiG completed**  
**120 dossiers**  
by April 30, 2015

- Expired (n=7) / not  
completed appraisals  
by G-BA (n=8)

**105 dossiers subdivided**  
**into 240 subgroups**

- 53 technologies/  
75 subgroups  
with added benefit
- 52 technologies/  
165 subgroups  
without added benefit

**37 matched condition-intervention pairs**

#### NICE

- 29 technologies/ 48 groups  
were recommended
- 8 technologies/ 22 groups  
were not recommended

#### G-BA

- 21 technologies/ 43 subgroups  
with added benefit
- 16 technologies/ 42 subgroups  
without added benefit



# 3

## Results

- ↵ NICE
- ↵ GBA
- ↵ Cancer Drug Appraisals
- ↵ Matched Pairs Comparison



## *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

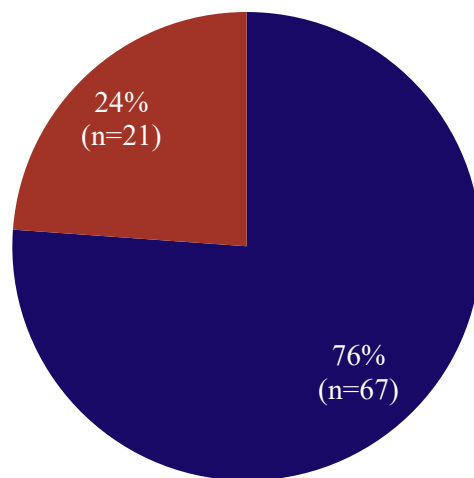
### Results

### NICE STA Guidance

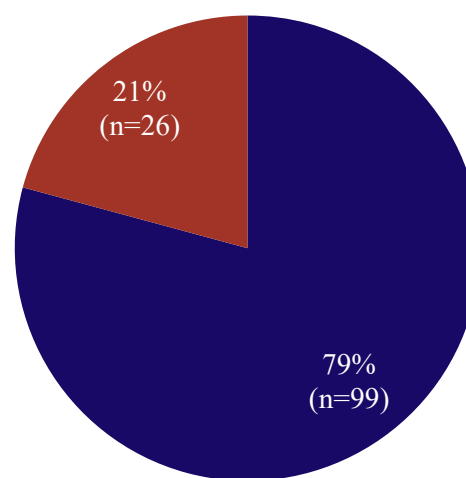
January 2011 – April 2015



Single Technology Appraisal  
guidance  
(n=88)



Single Technology Appraisal  
guidance by patient groups  
(n=125)



■ not recommended

■ recommended



# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Single Technology Appraisals: NICE

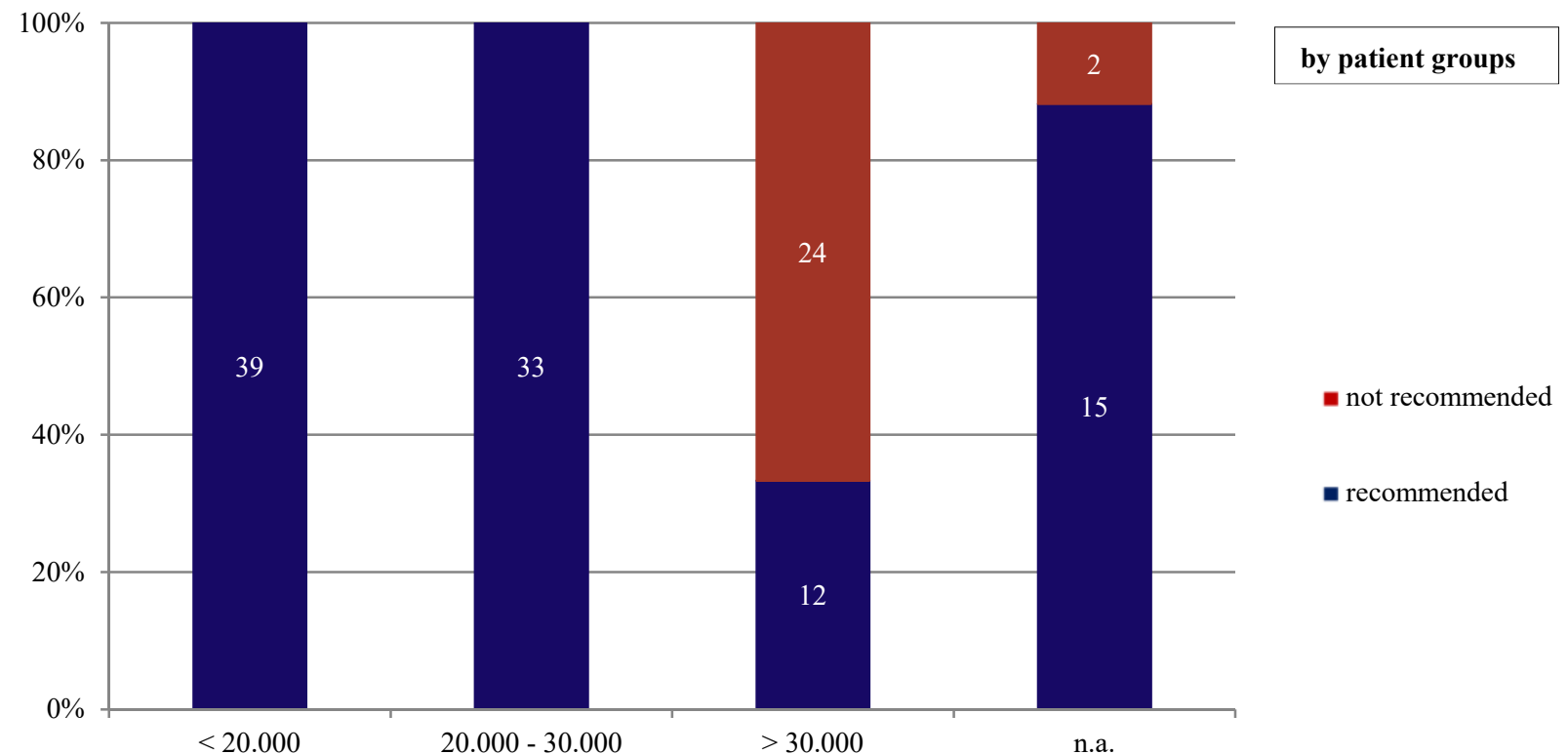


January 2011 – April 2015 (n=88 STAs / 125 patient groups)

Benefit recommendations  
by NICE are correlated with,

(i) the most plausible ICER  
( $p < 0.01$ , chi-square test)  
→ ICERs above 30,000  
GBP increase the  
probability of rejection  
significantly

(ii) submitted evidence by  
manufacturer: availability of  
RCTs ( $p < 0.05$ , chi-square  
test).



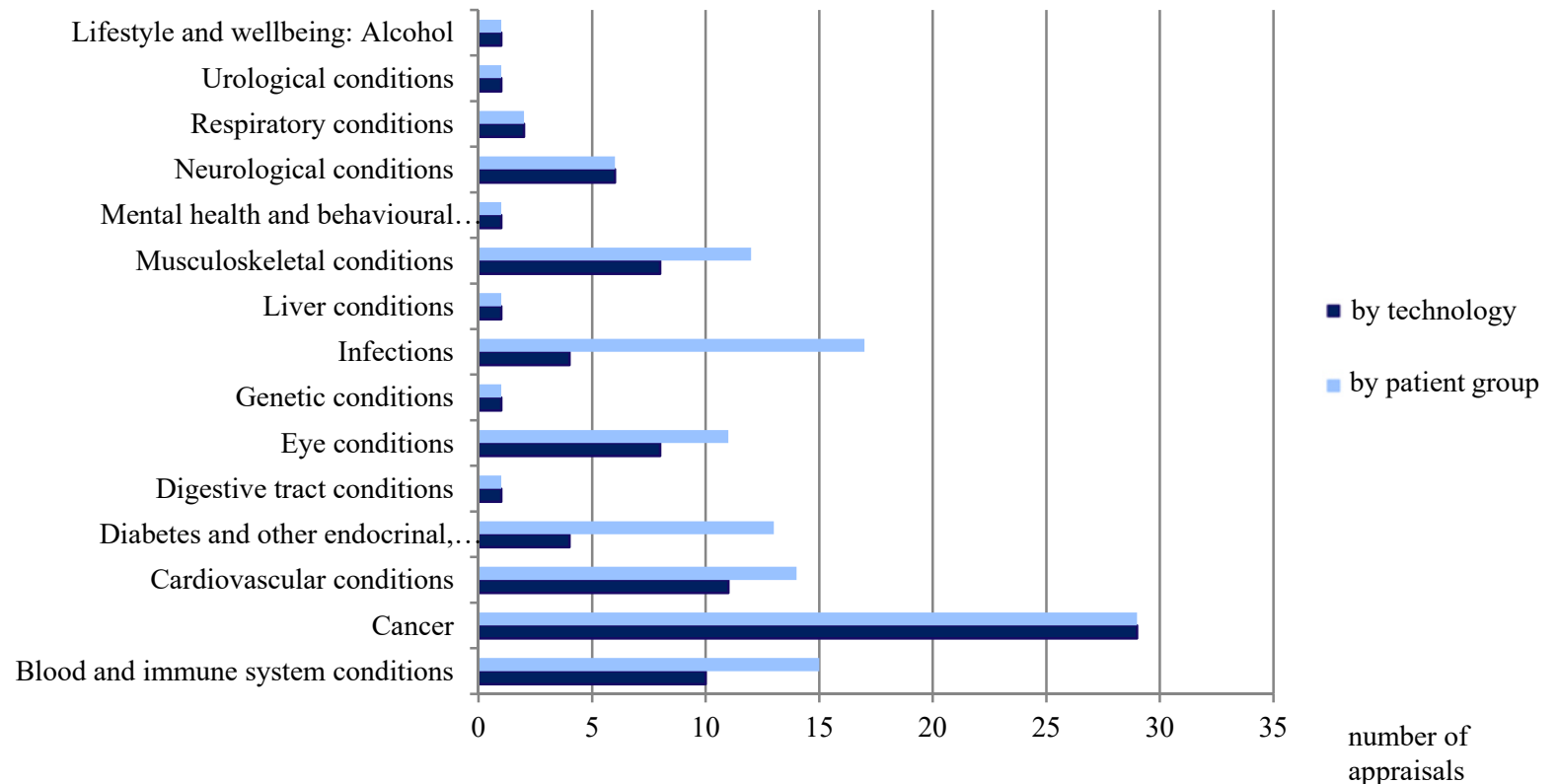


## Results

### Single Technology Appraisals: NICE



January 2011 – April 2015 (n=88 STAs / 125 patient groups)





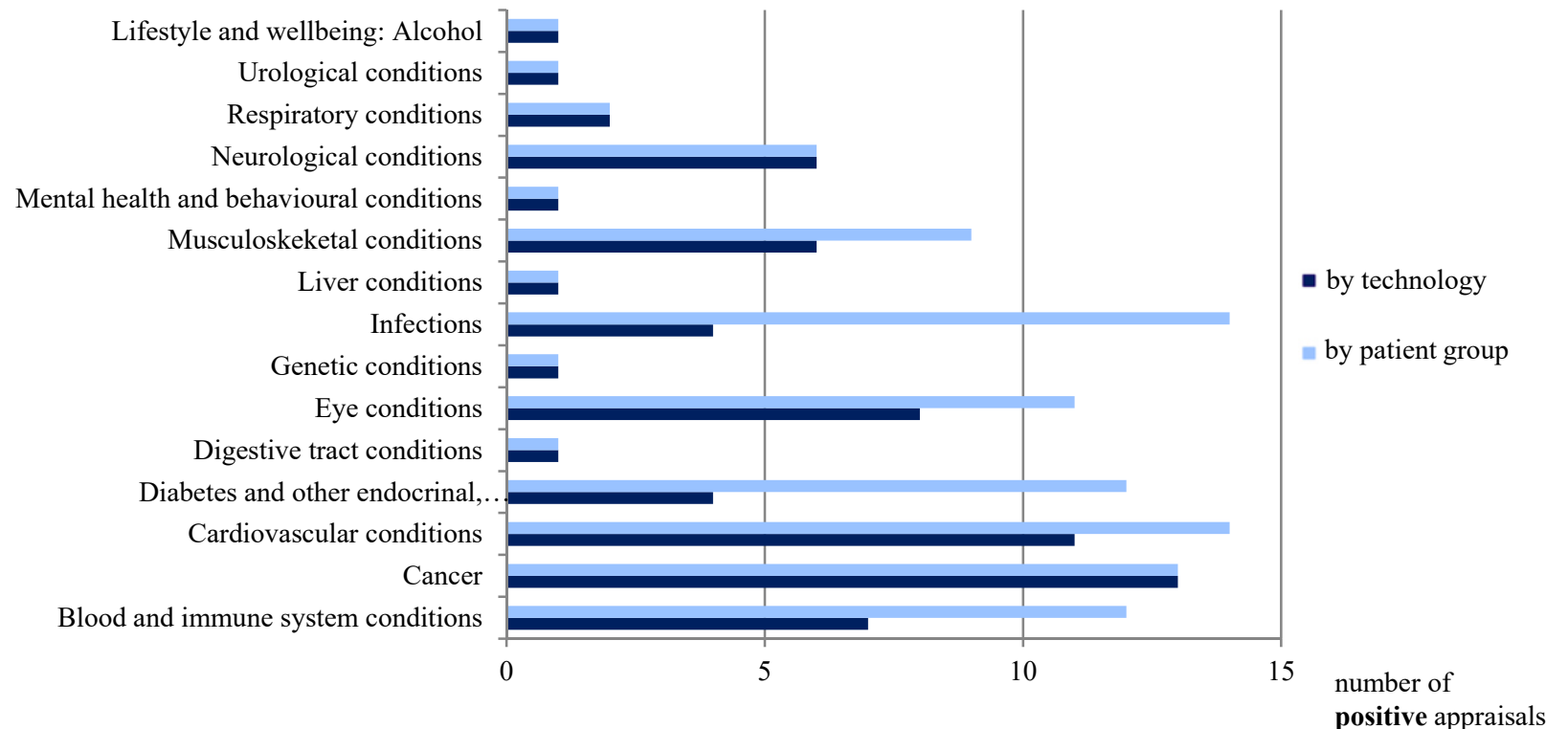
# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Positive STAs: NICE



January 2011 – April 2015 (n=88 STAs / 125 patient groups)





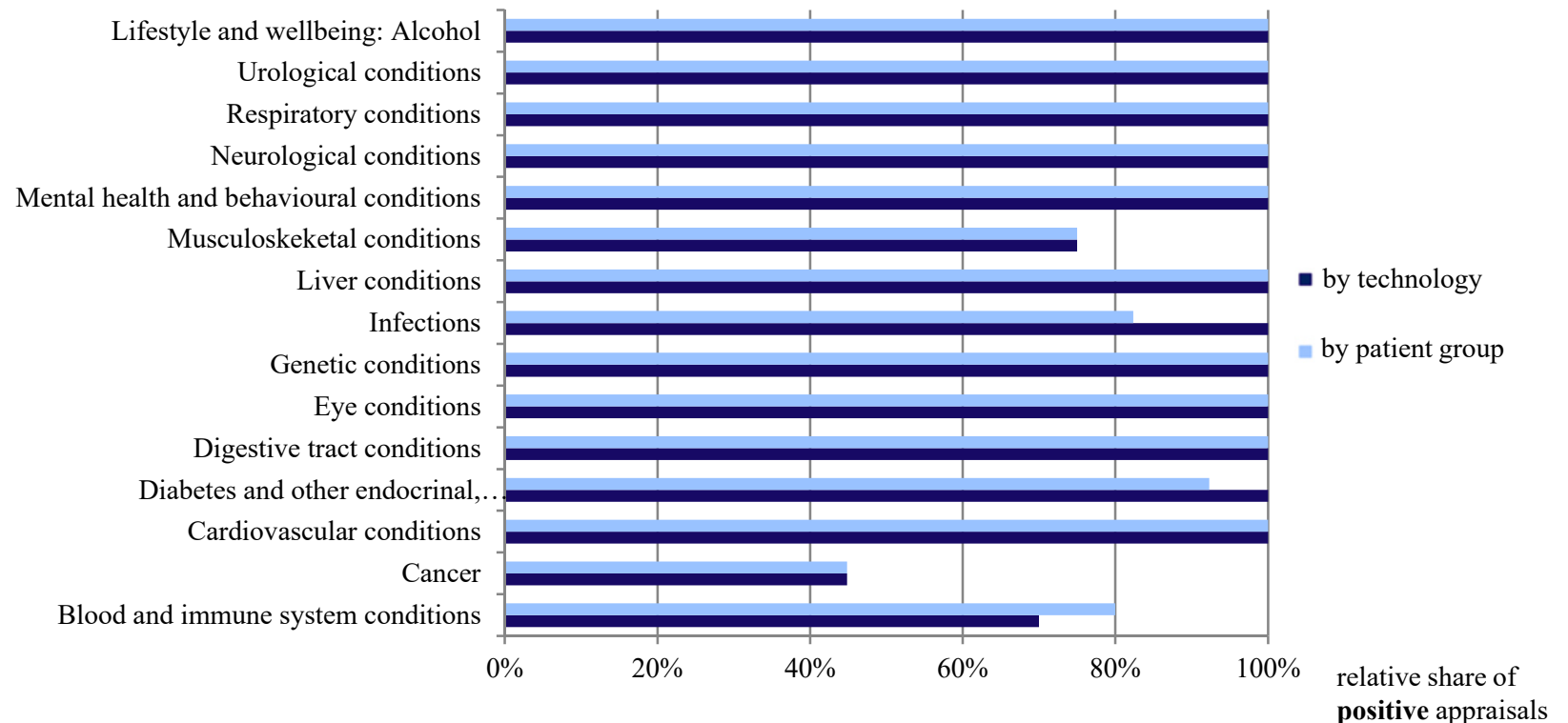
# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Positive STAs: NICE



January 2011 – April 2015 (n=88 STAs / 125 patient groups)





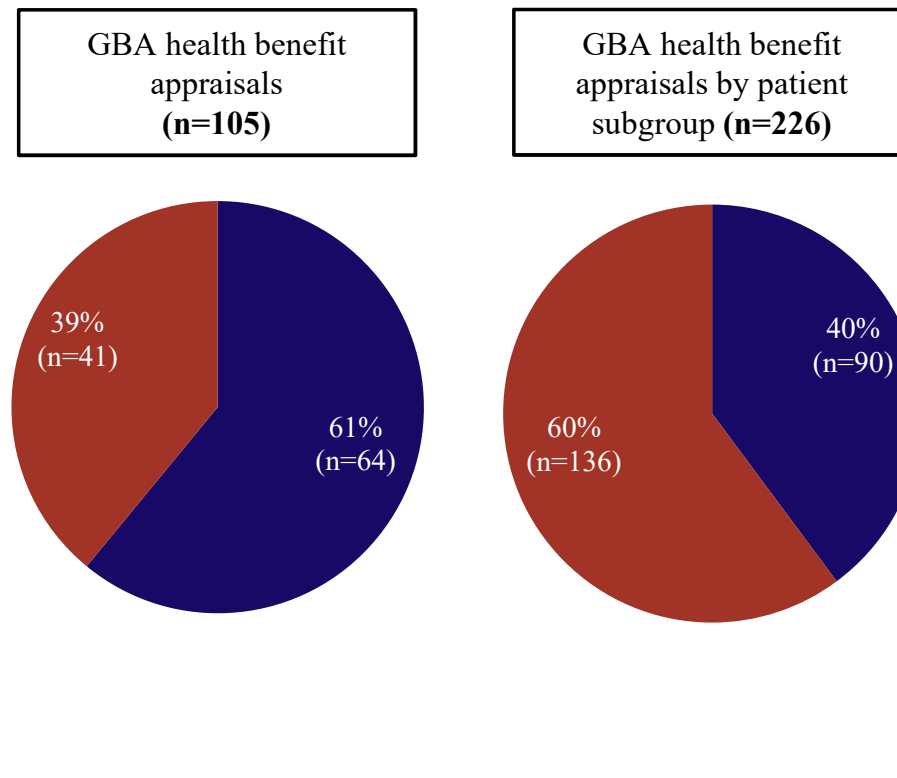


# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### GBA Appraisals

January 2011 – April 2015



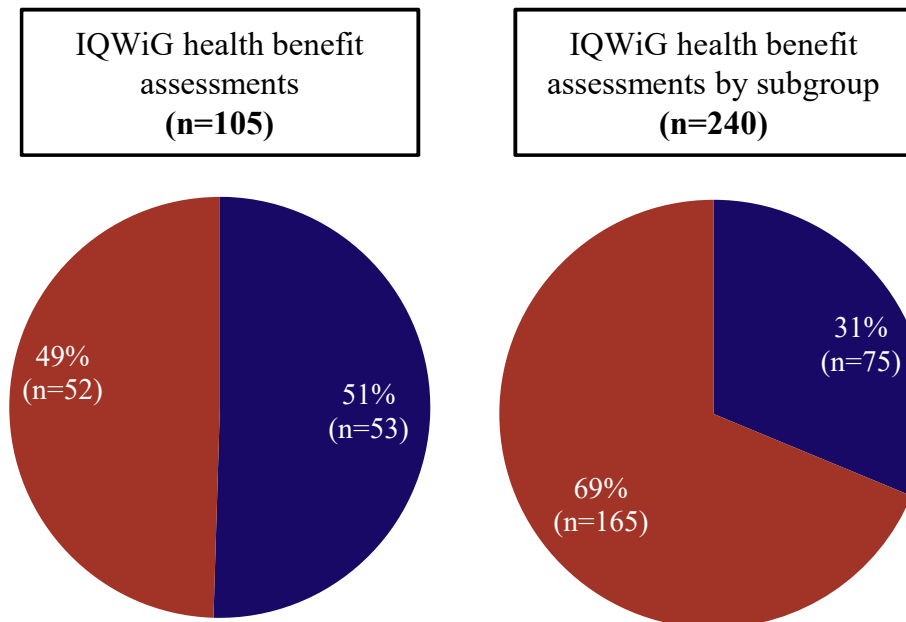


## *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

### Results

### IQWiG Assessments

January 2011 – April 2015



■ no added benefit

■ added benefit



## Results

### Early Benefit Appraisals: GBA

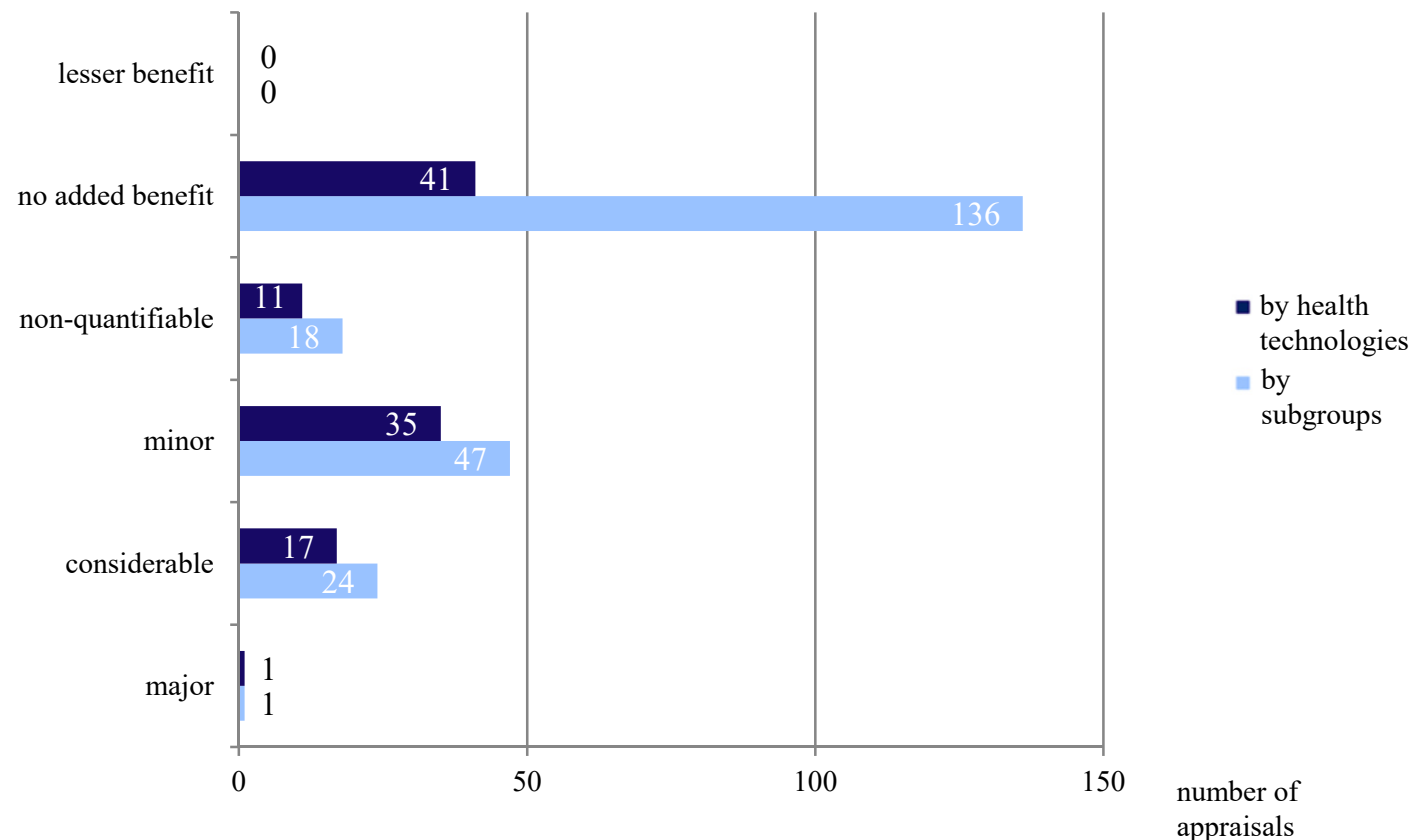
January 2011 – April 2015 (n=105 EBAs / 226 subgroups)



Added benefit by GBA (and also IQWiG) is correlated with,

(i) significant superiority in patient relevant-outcomes compared to the appropriate comparative therapy ( $p < 0.01$ , chi-square test);

(ii) submitted evidence by manufacturer: availability of RCTs ( $p < 0.01$ , chi-square test).



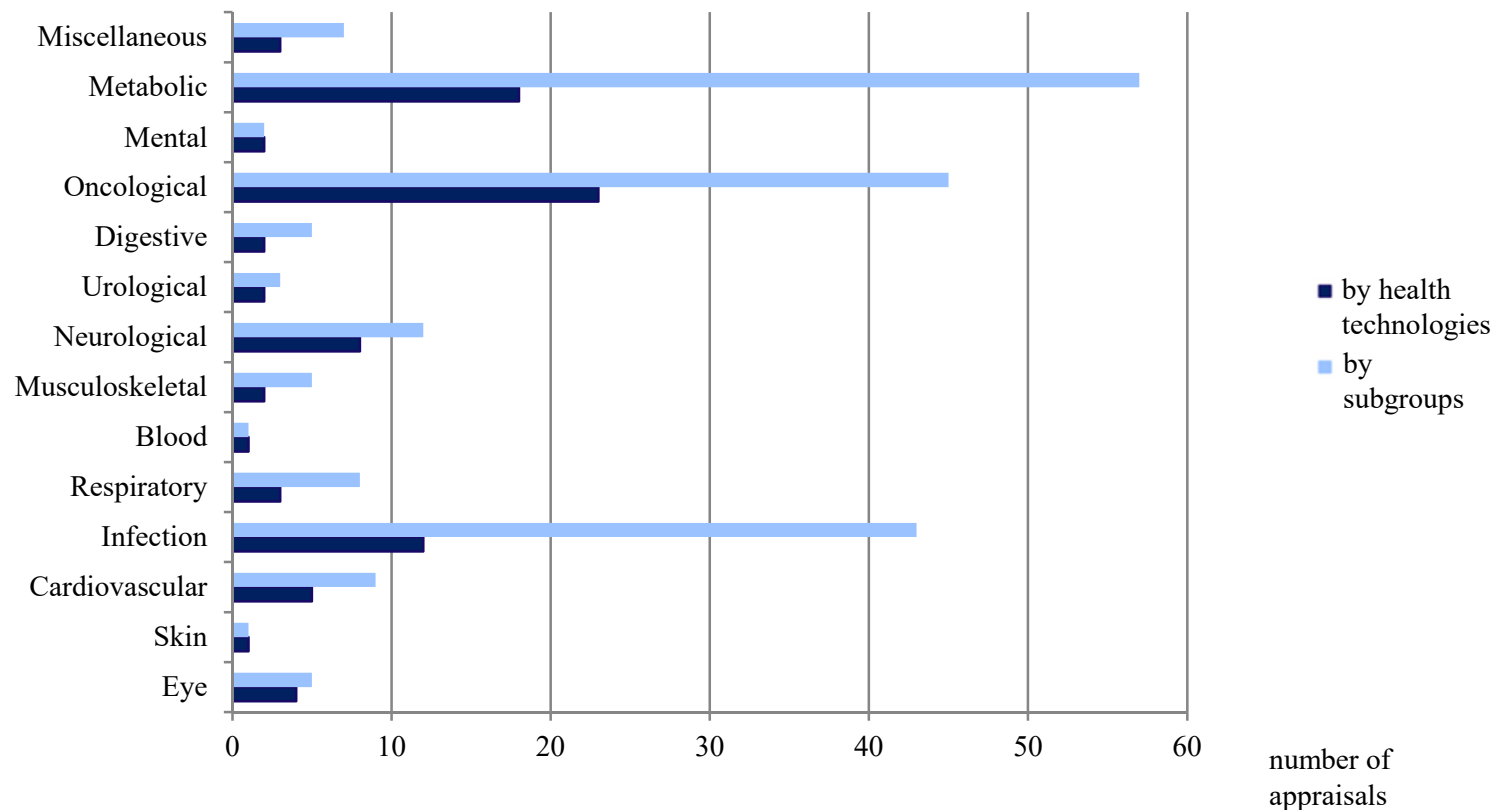


# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Early Benefit Appraisals: GBA

January 2011 – April 2015 (n=105 EBAs / 226 subgroups)



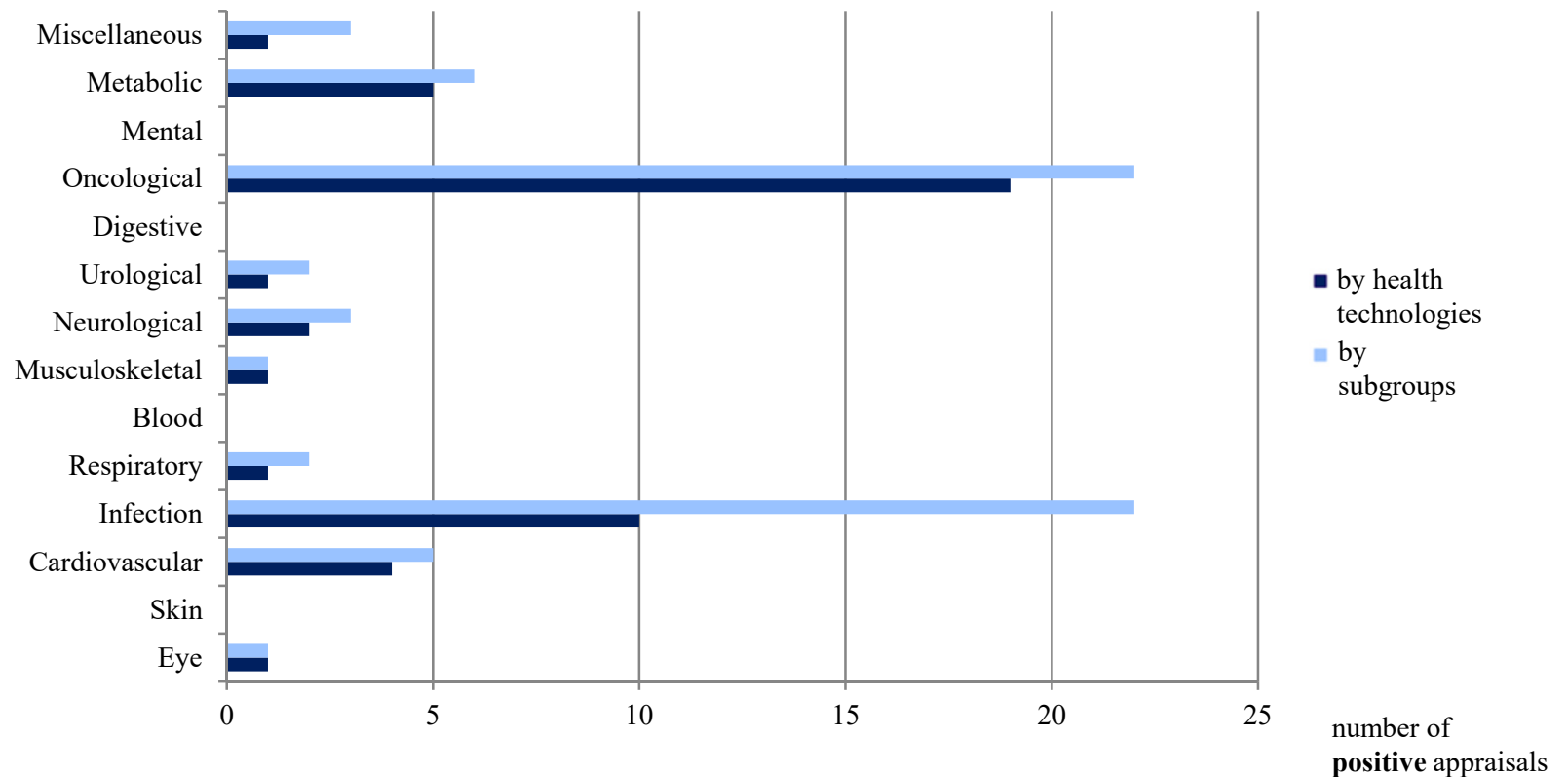


# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Positive Benefit Appraisals: GBA

January 2011 – April 2015 (n=105 EBAs / 226 subgroups)

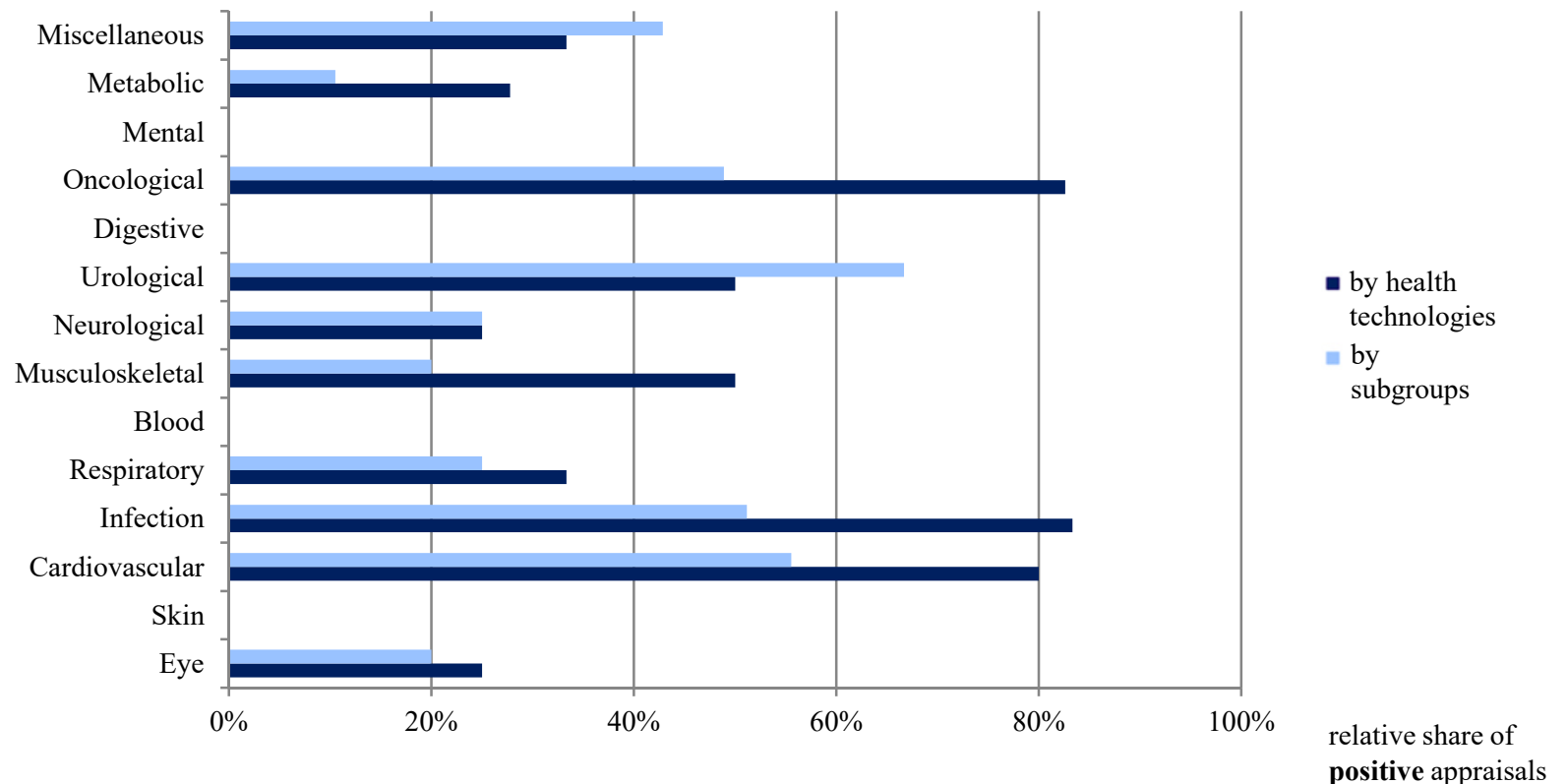




## Results

### Positive Benefit Appraisals: GBA

January 2011 – April 2015 (n=105 EBAs / 226 subgroups)





# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Cancer Drug Appraisals: NICE



January 2011 – April 2015 (n=37 STAs / 40 patient groups)

Therapeutic Area: 'Topic Area'			Health technologies	Health technologies by subgroups	Benefit decisions by subgroups		ICER/QALY (threshold in GBP)
					recommended	not recommended	
Onco-logical diseases	Cancer	29	29	1	52.5%		< 20.000
				4			20.000 - 30.000
				6			> 30.000
				2			n.a.
	Blood and immune system conditions	8	11	2		< 20.000	
				3		20.000 - 30.000	
				3	3	> 30.000	
						n.a.	





# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

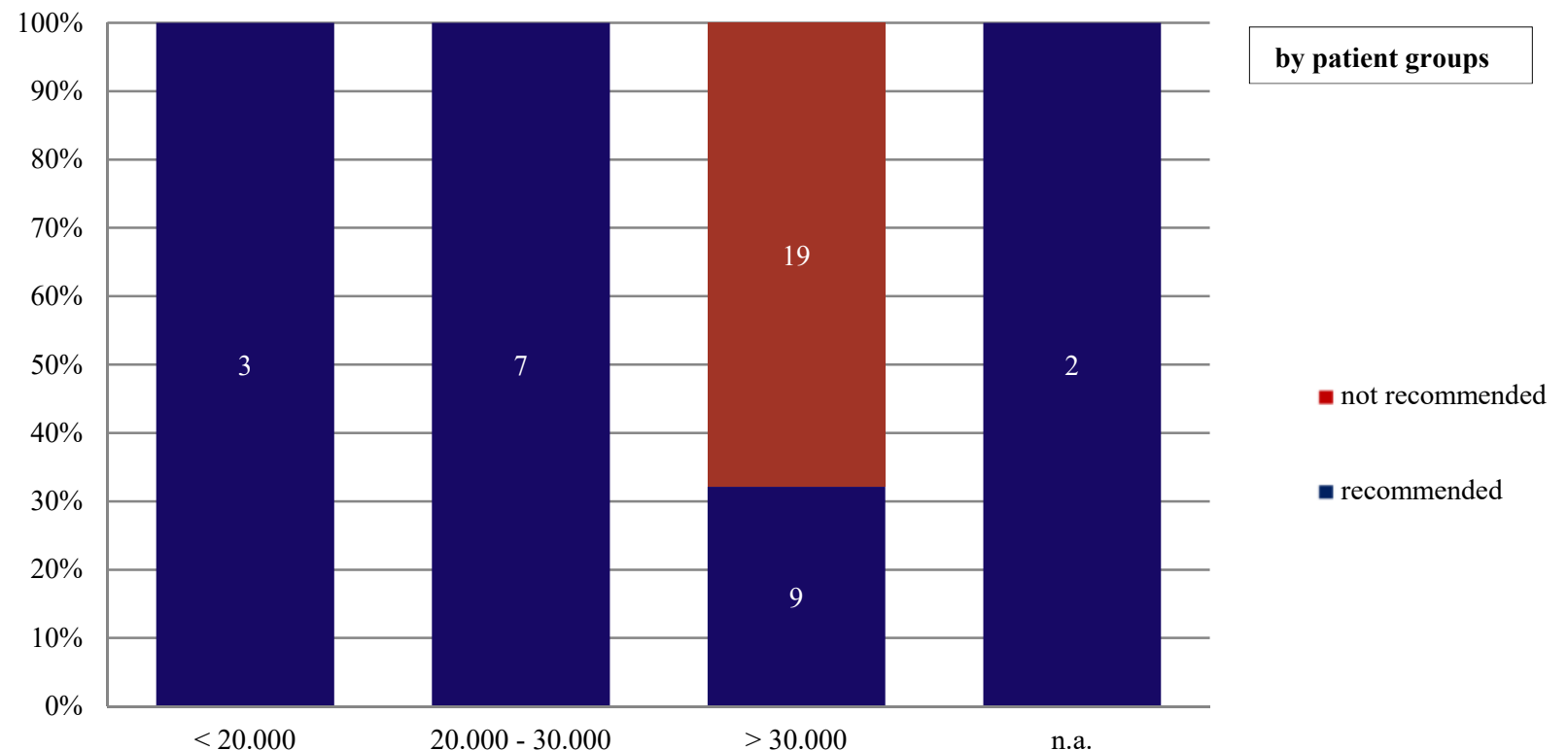
### Cancer Drug Appraisals: NICE



January 2011 – April 2015 (n=37 STAs / 40 patient groups)

Benefit recommendations  
for cancer drugs with an  
ICER > 20,000 GBP are  
correlated with

end-of-life considerations  
( $p < 0.01$ , Fisher-Yates test).





# XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017: Is NICE More “Innovation-Friendly” Than IQWiG/GBA?

## Results

### Cancer Drug Appraisals: IQWiG/GBA



January 2011 – April 2015 (n=32 EBAs / 56 subgroups)

Therapeutic area	Number of health technologies by therapeutic area	Number of health technologies by subgroup	Extent of the assessed added benefit (by subgroup)				Probability of the assessed added benefit	
			Major	Considerable	Minor	Non-quantifiable	No added benefit	Lesser benefit
Oncological Diseases	23	45	8	4	3		23	Proof Indication Hint [Proof]
<i>[Orphan Drug]</i>	9	11	2	2	7			
<b>Total</b>	<b>32</b>	<b>56</b>	<b>13</b>	<b>10</b>	<b>10</b>		<b>23</b>	
in %			23%	18%	18%		41%	
in % (in total)				59%			41%	



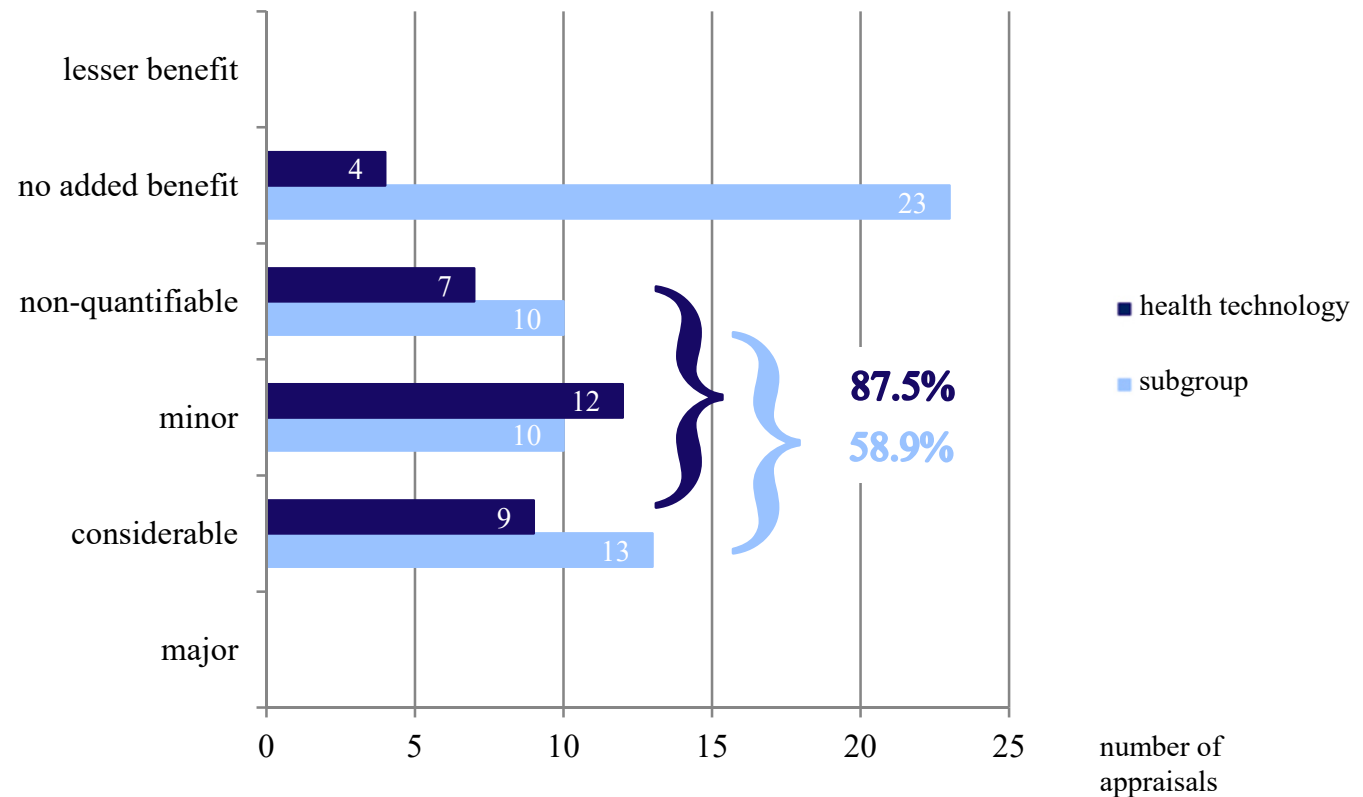
# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Results

### Cancer Drug Appraisals: IQWiG/GBA



January 2011 – April 2015 (n=32 EBAs / 56 subgroups)





# *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## **Results: Matched Pair Analysis**

## **NICE and GBA New Technology Appraisals**

**Pairwise Comparison, January 2011 – April 2015 (n=37)**

Therapeutic Area: Conditions and Diseases	Quantity	G-BA Appraisal:		NICE Guidance:	
		Additional Benefit		Recommendation	
		+	-	+	-
Respiratory	1	1		1	
Eye	3	1	2	3	
Hematological/Oncological	3	2	1	1	2
Cardiovascular	3	3		3	
Infections	4	3	1	4	
Neurological	4		4	4	
Oncological	14	11	3	8	6
Alcohol	1		1	1	
Metabolic	3		3	3	
Urological	1		1	1	
Total	37	21	16	29	8
Relative share (%)		57%	43%	78%	22%
Total: oncological conditions	17	13	4	9	8
Relative share (%)		76%	24%	53%	47%



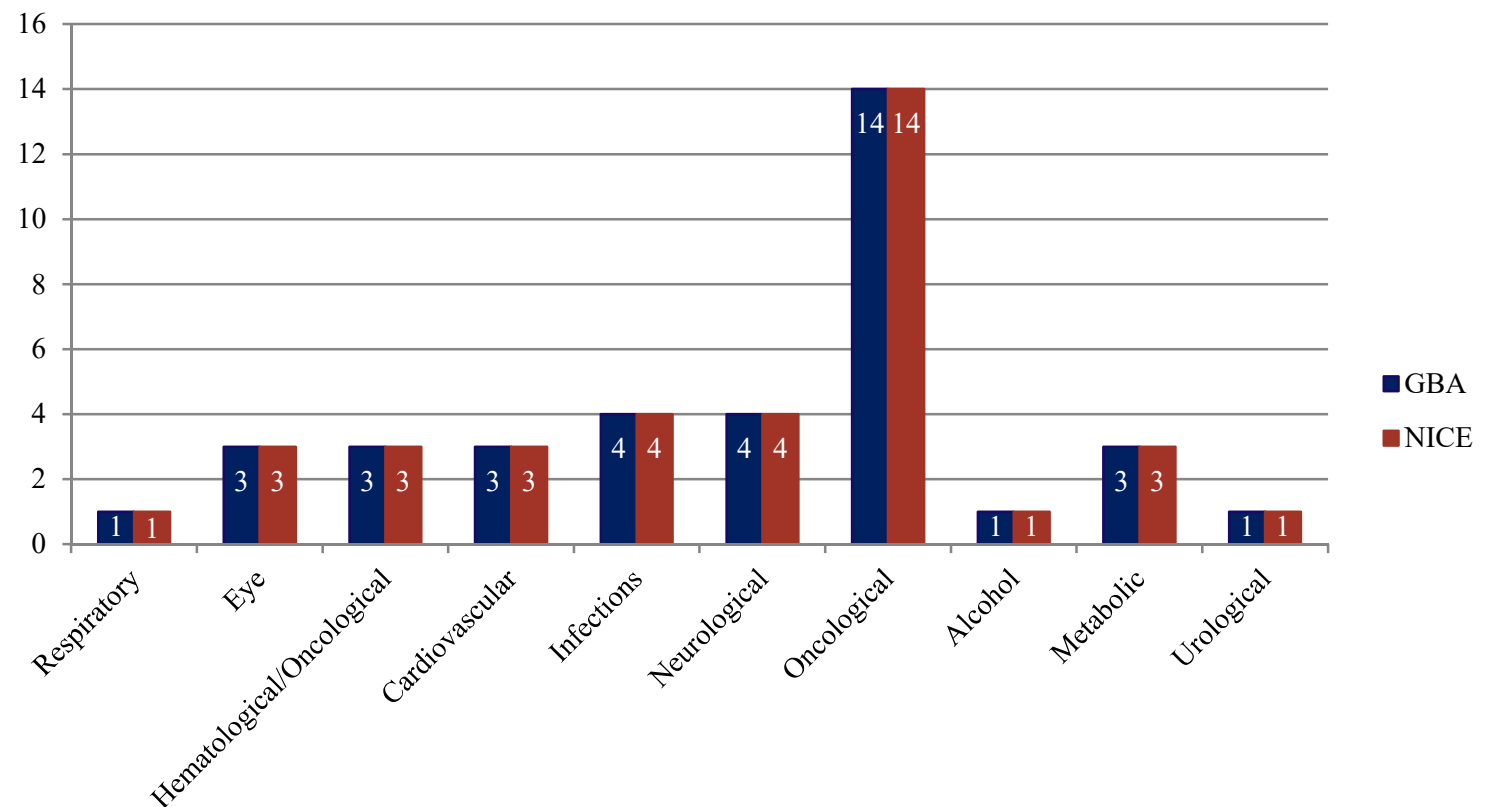
## *XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:* **Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

### **Results: Matched Pair Analysis**

### **NICE and GBA New Technology Appraisals**

**Pairwise Comparison, January 2011 – April 2015 (n=37)**

number of appraisals  
(by technology)



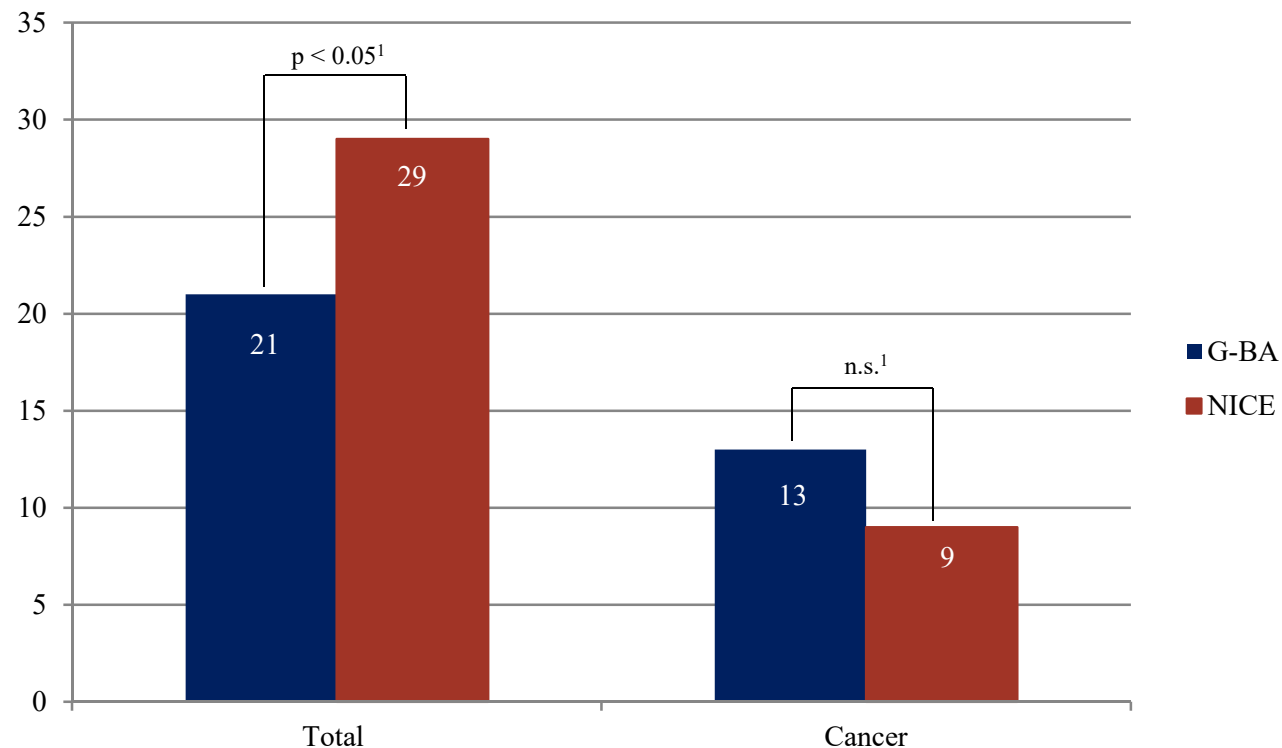


## Results: Matched Pair Analysis

### NICE and GBA New Technology Appraisals

Pairwise Comparison, January 2011 – April 2015 (n=37)

number of **positive**  
appraisals  
(by technology)



<sup>1</sup>two-tailed chi-square test

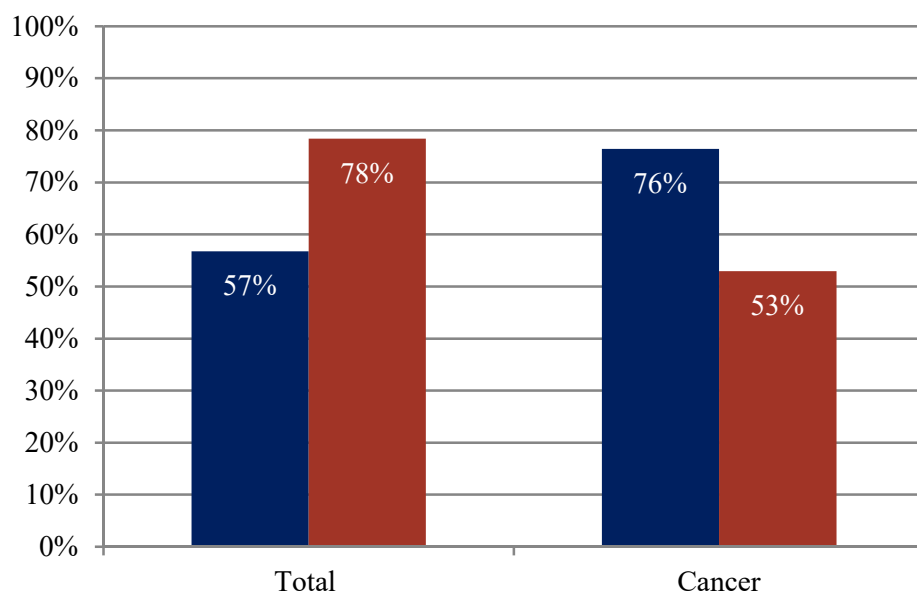


## Results: Overview of Positive Appraisals

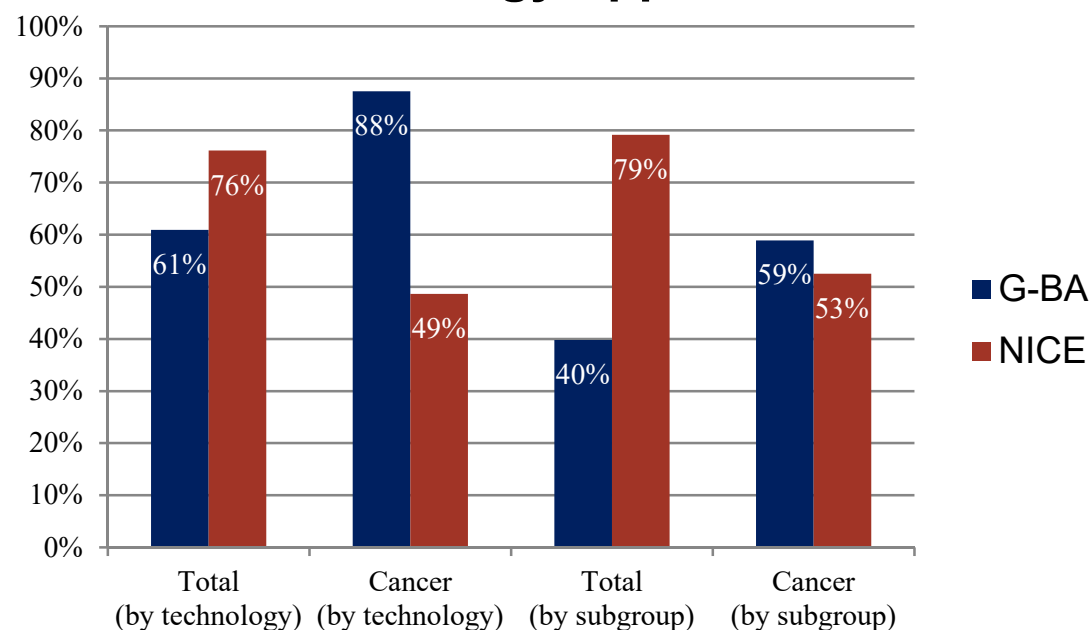
### NICE and GBA New Technology Appraisals

January 2011 – April 2015

**Matched Pairs**



**All Technology Appraisals**







*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

# 4

## Conclusions



*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

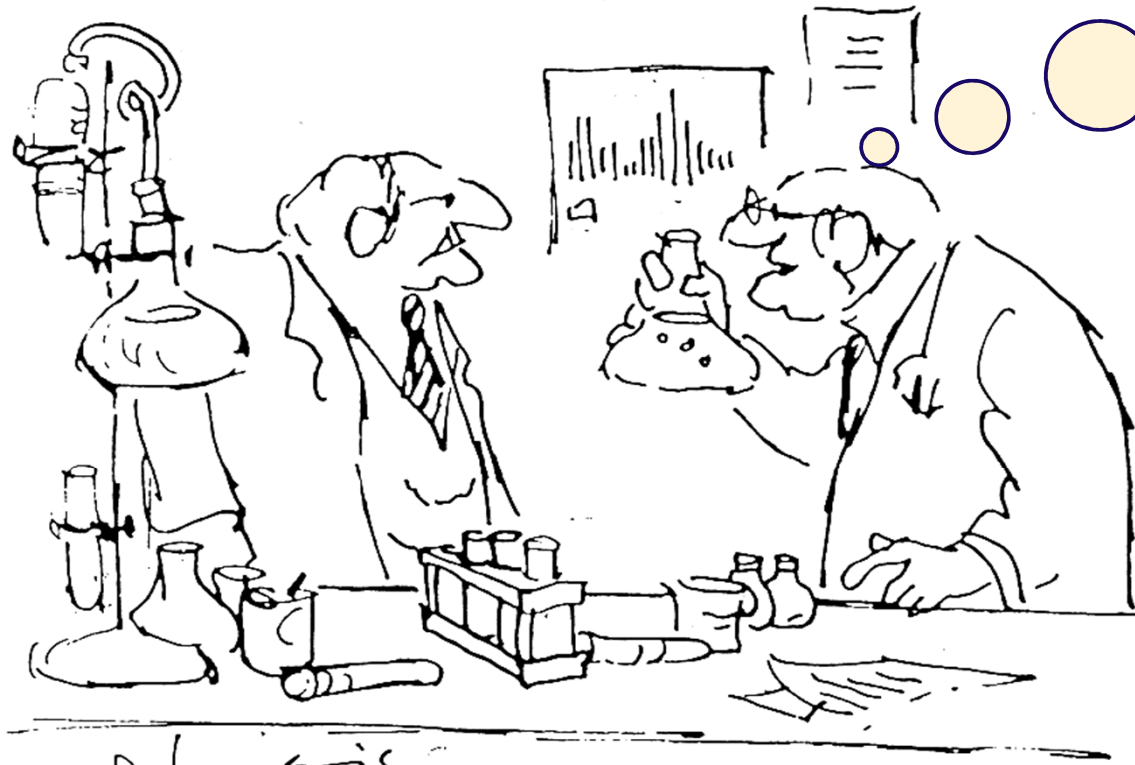
## Summary & Conclusions

- HTA agencies have adopted different methodological approaches, which – at least in part – reflect different value judgments.
- NICE in England, as well as GBA and IQWiG in Germany, may be regarded as exemplars for implementation of the **logic of cost effectiveness** and of **evidence-based medicine**, respectively.
- Apart from well-defined exceptions (orphans, end-of-life treatments), both agencies follow their official criteria in a consistent manner.
- NICE evaluates new interventions more friendly than GBA/IQWiG.**
- Our analysis confirms the perception that **cancer** drugs are relatively less likely to be recommended by NICE, whereas GBA/IQWiG appear less likely to recommend drugs for **metabolic** and **CNS** disorders.
- Apparently, different (value judgments and) methodological choices indeed lead to different HTA outcomes.**



*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Discussion



**“It may well  
bring about  
immortality**

**–**

**but it will  
take forever  
to test it.”**



*XIV HTAi 2017 Annual Meeting – Rome, Italy – June 17-21, 2017:*  
**Is NICE More “Innovation-Friendly” Than IQWiG/GBA?**

## Thank You for Your Attention!

**Ramon Schaefer**, M.A., B.Sc.

Professor **Michael Schlander**, M.D., Ph.D., M.B.A.

### Contact

[www.innoval-hc.com](http://www.innoval-hc.com)

[www.michaelschlander.com](http://www.michaelschlander.com)

[michael.schlander@dkfz.de](mailto:michael.schlander@dkfz.de)

[michael.schlander@innoval-hc.com](mailto:michael.schlander@innoval-hc.com)

**INNOVAL<sup>HC</sup>**  
Institute for Innovation & Valuation  
in Health Care

### DKFZ

Im Neuenheimer Feld 581 (TP4)  
D-69120 Heidelberg

Phone: +49 (0) 6221 42 1911

### InnoVal<sup>HC</sup>

An der Ringkirche 4  
D-65197 Wiesbaden

+49 (0) 611 4080 789 10

