The role of HRQL in clinical decision-making in surgical trials in oncology

JM Blazeby[1,2], K Avery[1], MAG Sprangers[3],

H Pikhart[4], P Fayers[5,6], JL Donovan[1]

[1]University of Bristol & United Bristol Healthcare Trust, Bristol UK

[3]Academic Medical Centre, Amsterdam, NL

[4]University College, London, UK

[5]University of Aberdeen, UK & [6]Faculty of Medicine, Trondheim, Norway

HRQL, RCTs & decision-making

Goodwin *et al* 2003 *JNCI*;**95:**263-81

5/46 trials in breast cancer

Efficace *et al* 2003 *JCO;***21:**3502-3511

6/24 trials in prostate cancer

HRQL, RCTs & decision-making

Poorly designed studies

HRQL instruments too crude

HRQL secondary importance

Clinicians do not understand HRQL

Patients want more detailed information

Informed consent essential

Hypothesis

HRQL important endpoint in surgical trials in oncology

HRQL in surgical oncology trials

Systematic review:

1. RCT in surgical oncology with HRQL
2. Determine the contribution of HRQL to surgical decision-making

Methods

2005 Medline & Cochrane Trials Register

1. RCTs with adults
2. Full papers > 1966 (English)
3. Self report HRQL: 2 domains with documented psychometric properties
4. Surgical procedures under GA & surgical versus non surgical procedures

Excluded

Surgical trials under local anaesthetic

Endoscopic interventions

Surgery +/- adjuvant/neoadjuvant treatment

Screening trials

Preventative studies

Trials of pre-malignant conditions

HRQL & decision-making

1. HRQL reported by investigators as influencing clinical decision
2. HRQL reported by investigators as influencing informed consent
3. HRQL was assessed robustly according to predefined criteria

Results

1188 abstracts in Medline

883 abstracts in Cochrane

39 citations in 33 RCTs in surgical oncology

Mostly breast and gastrointestinal cancer

23 compared different types of surgery

10 surgery *vs.* non surgical treatment

33 RCTs in surgical oncology

23 final treatment recommendation

10 without treatment decision

18/23 influenced by HRQL

8 HRQL better & equivalent clinical

5 clinical better & equivalent HRQL

3 both clinical & HRQL better

2 both clinical & HRQL equivalent

5/23 not influenced by HRQL

2 clinical better (no HRQL discussion)

1 clinical & HRQL worse
Weeks *JAMA* 2002

1 clinical equivalent & HRQL worse
de Boer *JCO* 2004

1 clinical better & HRQL worse
Imamura *Pancreas* 2004

10/33 without treatment decision

5 completely inconclusive

5 HRQL useful for informed consent

Trials with robust HRQL design

12 with robust HRQL design

- 7 influenced decisions / consent
- 5 HRQL did not influence decision

5 robust HRQL, but no influence

1 clinical & HRQL worse
Weeks *JAMA 02*

1 clinical equivalent & HRQL worse
de Boer *JCO* 04

1 clinical better, no HRQL discussion
Furst *Dis Colon Rectum* 2002

2 clinical equivalent & HRQL better
Seiler *BJS* 2005 & Poulson *Eur Surg Oncol* 97

‘Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus’

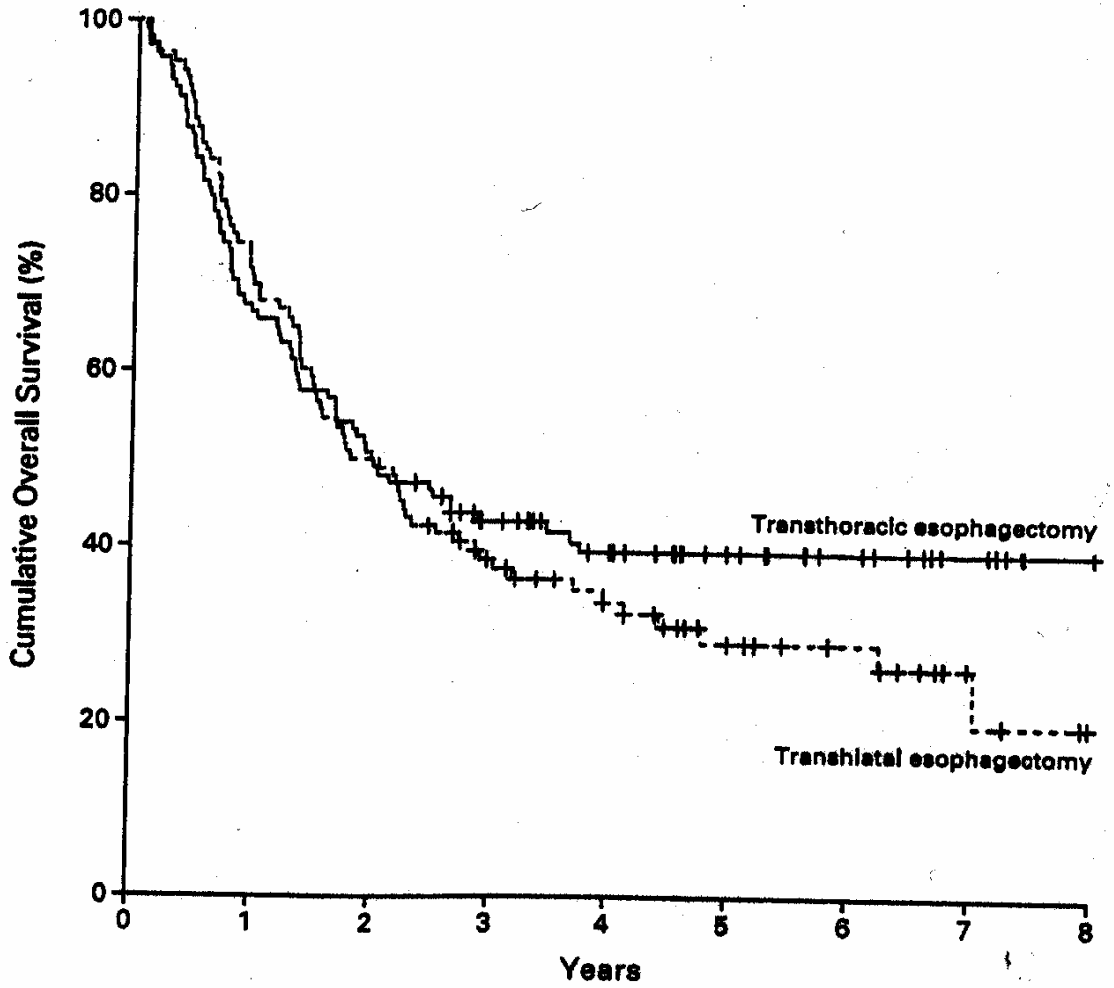
Hulscher, van Sandick, de Boer *et al*

New Eng J Medicine 2002; *347: 1662-9*

Clinical outcomes

	Transhiatal n=106	Transthoracic n=114
Morbidity (%)		
Respiratory	29 (27)	65 (57)*
Leakage	15 (14)	18 (16)
ICU stay (range)	2 (0-38)	6 (0-79)*
Hospital stay (range)	15 (4-63)	19 (7-154)*
Mortality (%)	2 (2)	5 (4)

* $P < 0.001$



No. at Risk								
Transhiatal esophagectomy	106	74	53	35	25	16	11	4
Transthoracic esophagectomy	114	76	57	42	31	20	14	7

Figure 2. Kaplan–Meier Curves Showing Overall Survival among Patients Randomly Assigned to Transhiatal Esophagectomy or Transthoracic Esophagectomy with Extended en Bloc Lymphadenectomy.

Survival after surgery

P = 0.12

One year after surgery 35% have died

Two years after surgery 55% have died

Median survival 1.4 & 1.7 years

Subgroup analyses

- Survival better after transthoracic surgery for patients with tumours of the oesophagogastric junction

‘Quality of life after transhiatal compared with extended transthoracic resection for adenocarcinoma of the esophagus’

de Boer, van Lanschot, van Sandick *et al*

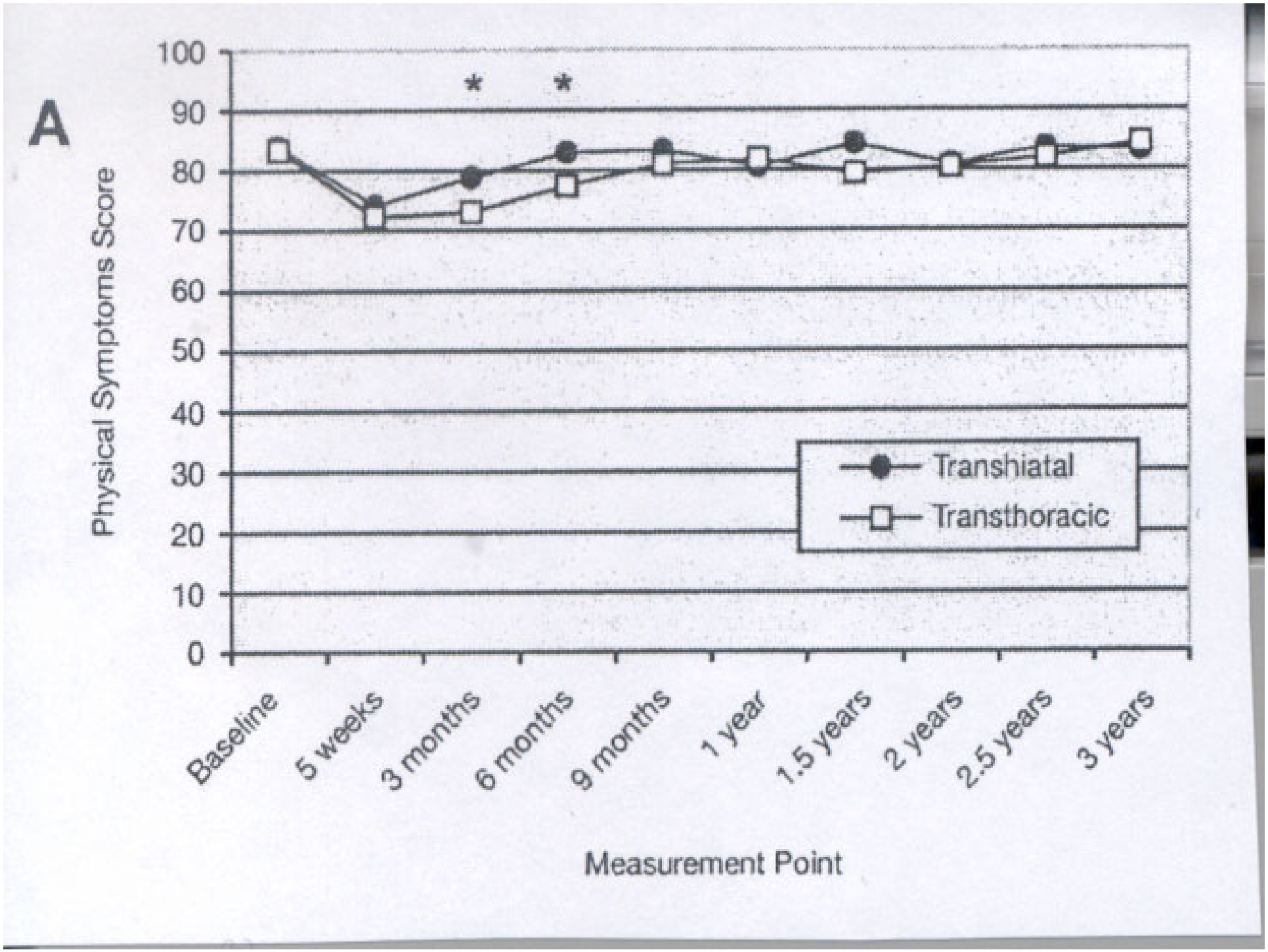
JCO 2004; *22: 4202-4208*

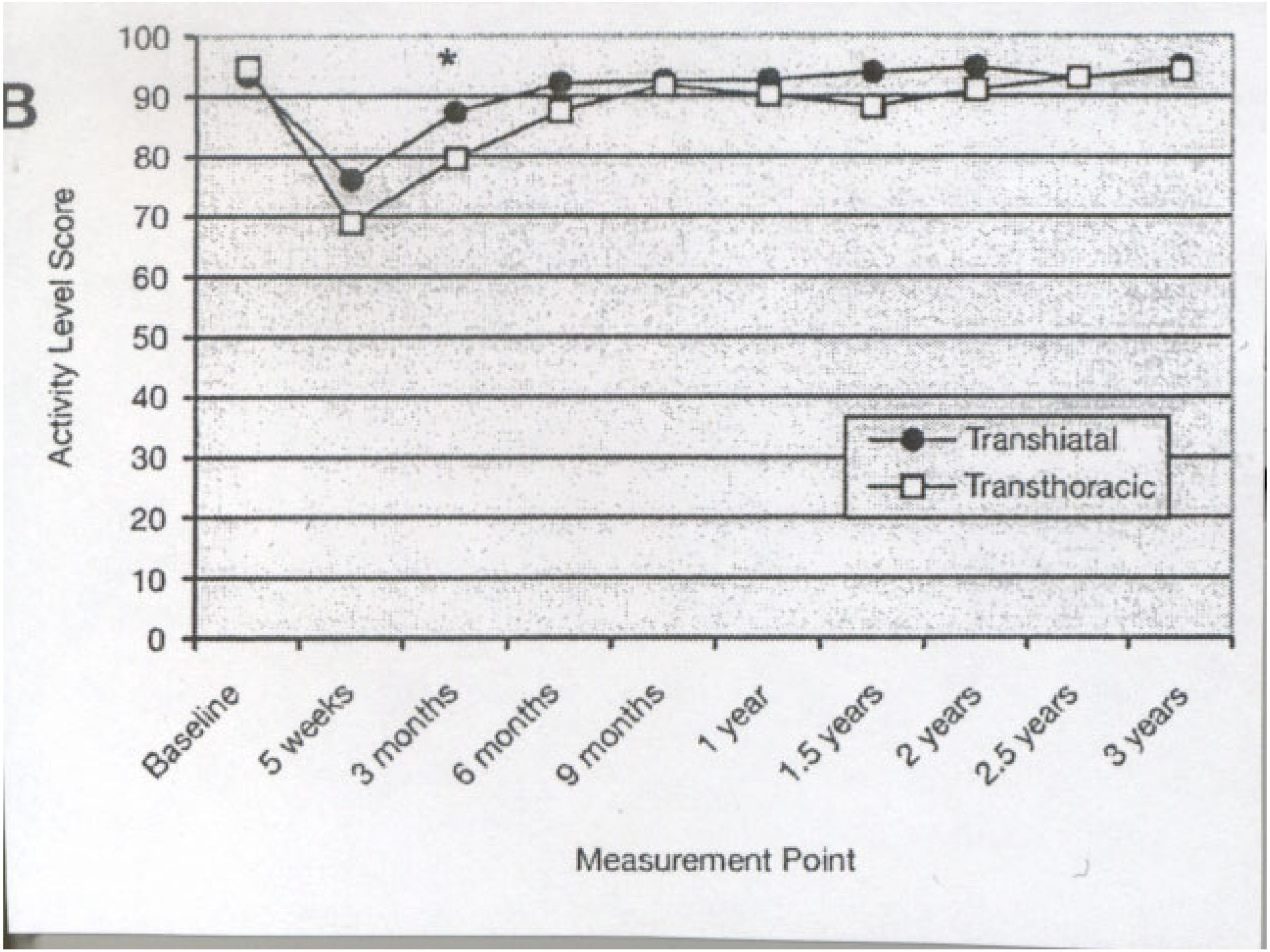
HRQL design – sets the standard

Hypothesis – effects of operation on QL
Rational for instrument – RSCL and SF20
Method of administration – postal, 1follow up
Baseline compliance reported
Timing documented
Missing data documented
Clinical significance addressed
Presentation of results in general

Missing data

	0	**1.5**	**3**	**6**	**9**	**12**	**1.5**	**2**	**2.5**	**3**
Eligible	199	192	188	160	139	132	113	98	87	76
Returned	189	161	155	141	126	125	100	82	66	61
% eligible	95	84	82	88	91	95	88	84	76	80
Dead	0	7	11	39	60	67	86	101	112	123
Random	10	14	13	10	7	3	8	9	14	12
Too ill	0	17	20	9	6	4	5	7	7	3


A
Physical Symptoms Score
100
90
80
70
60
50
40
30
20
10
0
*
*
Transhiatal
Transthoracic
Baseline
5 weeks
3 months
6 months
9 months
1 year
1.5 years
2 years
2.5 years
3 years
Measurement Point


B
Activity Level Score
100
90
80
70
60
50
40
30
20
10
0
*
Transhiatal
Transthoracic
Baseline
5 weeks
3 months
6 months
9 months
1 year
1.5 years
2 years
2.5 years
3 years
Measurement Point

HRQL impact in clinical decision

HRQL worse in 1st yr in recommended treatment

Treatment recommendation based upon clinical data in subgroup analyses

35% die in 1st year & 65% by the 2nd year

HRQL during early post operative phase important

Summary

33 RCT in surgical oncology

18 influenced decisions

5 informed consent

23 influenced decisions or consent

Only 7 of these had robust HRQL design

Thoughts

HRQL is relevant in surgical trials

Robust trial design & hypotheses

Publish clinical & HRQL together

Research is needed to explore how HRQL influences decisions