

Quality of life in clinical trials in GI cancer

Jane M Blazeby MD FRCS (Gen. Surg)

Bristol Royal Infirmary &

Bristol University

Bristol UK

Quality of life in clinical trials

What is the added value of quality of life?

Future projects - Quality of life & GI groups

Added value of quality of life?

Randomised controlled trials, $n > 50$

Oesophageal & gastric cancer

Self completion, multi-dimensional
quality of life assessment

RCT & QL & oesophageal or gastric cancer

Author	Year	Journal	Intervention
Glimelius	1997	Ann. Oncol	ELF vs. best care
Webb	1997	JCO	ECF vs. FAMTX
Dallal	2001	Gastroint. En.	Metal stent vs. thermal
Tebbutt	2002	Ann. Oncol	5FU vs. 5FU+MMC
Ross	2002	JCO	ECF vs. MCF
de Boer	2004	JCO	THO vs. TTO
Homs	2004	Lancet	Metal stent vs. brachy.
Shenfine	2005	HTA report	Metal stent vs. plastic

RCT & QL & oesophageal or gastric cancer

Author	Year	Journal	Baseline compliance
Glimelius	1997	Ann. Oncol	>90%
Webb	1997	JCO	64%
Dallal	2001	Gastroint. En.	100%
Tebbutt	2002	Ann. Oncol	Not reported
Ross	2002	JCO	64%
de Boer	2004	JCO	95%
Homs	2004	Lancet	>90%
Shenfine	2005	HTA report	>85%

✓

✓

✓

✓

RCT & QL & oesophageal or gastric cancer

Author	Year	N	QOL measure	Follow up
Glimelius	1997	61	QLQ-C30	>90%
Dallal	2001	65	C30/OES, HAD, SF36	> 90%
de Boer	2004	199	Rotterdam & SF20	95%
Homs	2004	209	QLQ-C30 & OES18	>90%

Advanced gastric cancer

61 patients

```
graph TD; A[61 patients] --> B[ELF]; A --> C[Best care]; B --> D["45% maintain QOL*  
Survival 8 months**"]; C --> E["20% maintain QOL  
Survival 5 months"];
```

ELF

Best care

45% maintain QOL*
Survival 8 months**

20% maintain QOL
Survival 5 months

* $p < 0.05$

** $p = 0.12$

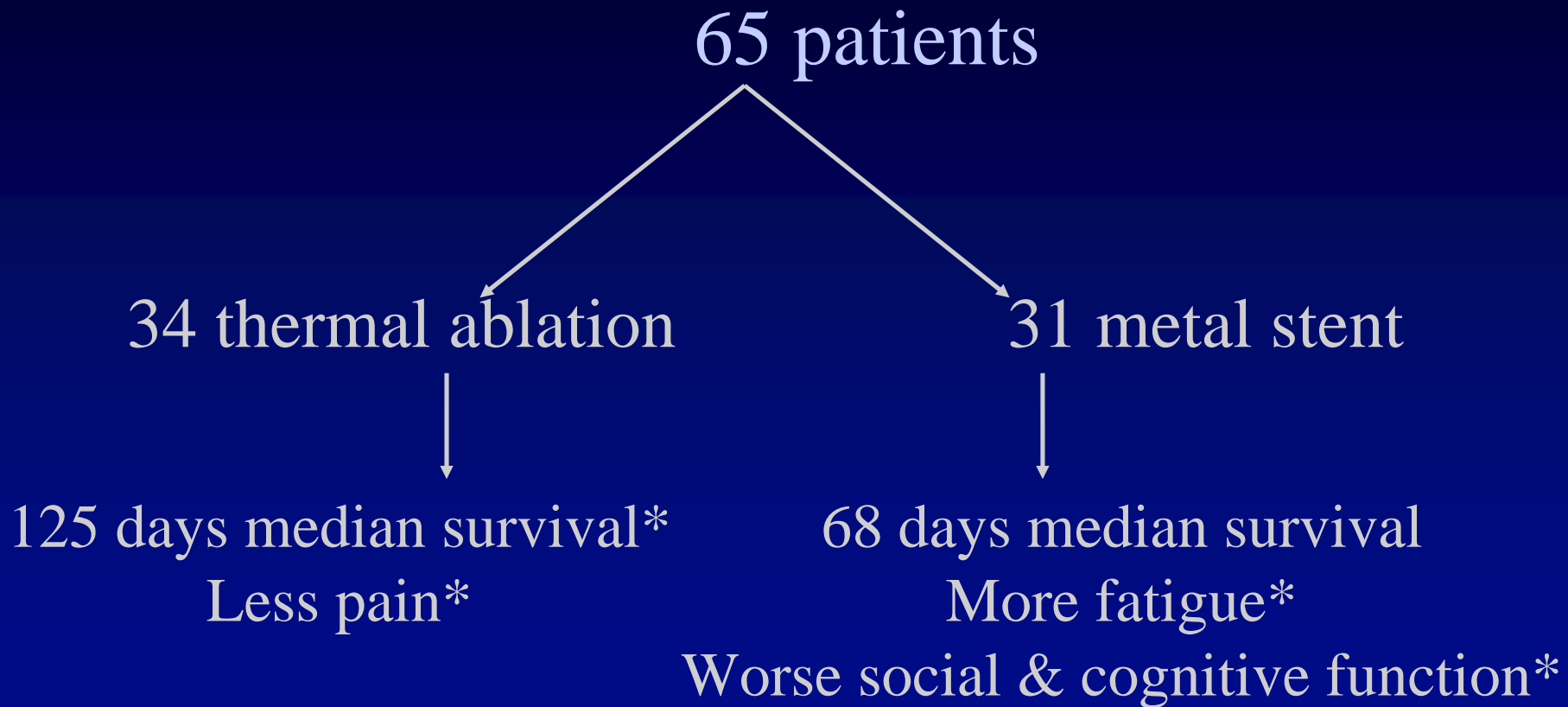
Glimelius et al Ann. Oncol. 1997

Added value of QOL?

- Survival analyses not significantly different, but secondary analyses show some benefit
- QOL data show that ELF not detrimental
- Added value - ELF in may benefit patients

Glimelius et al *Ann. Oncol.* 1997

Advanced oesophageal cancer or medically unfit



*p < 0.05

Dallal et al *Gastrointest. Endosc.* 2001

Added value of QL?

- QOL supports survival data that better palliation with thermal ablative therapy
- Caution in interpretation very small study

Dallal et al *Gastrointest. Endosc.* 2001

Transhiatal or transthoracic esophagectomy for oesophageal cancer

220 patients

```
graph TD; A[220 patients] --> B[Transhiatal]; A --> C[Transthoracic]; B --> D[Fewer pulmonary complications*]; B --> E[Less ITU stay*]; C --> F[More morbidity]; C --> G[Trend to better survival];
```

Transhiatal

Fewer pulmonary complications*
Less ITU stay*

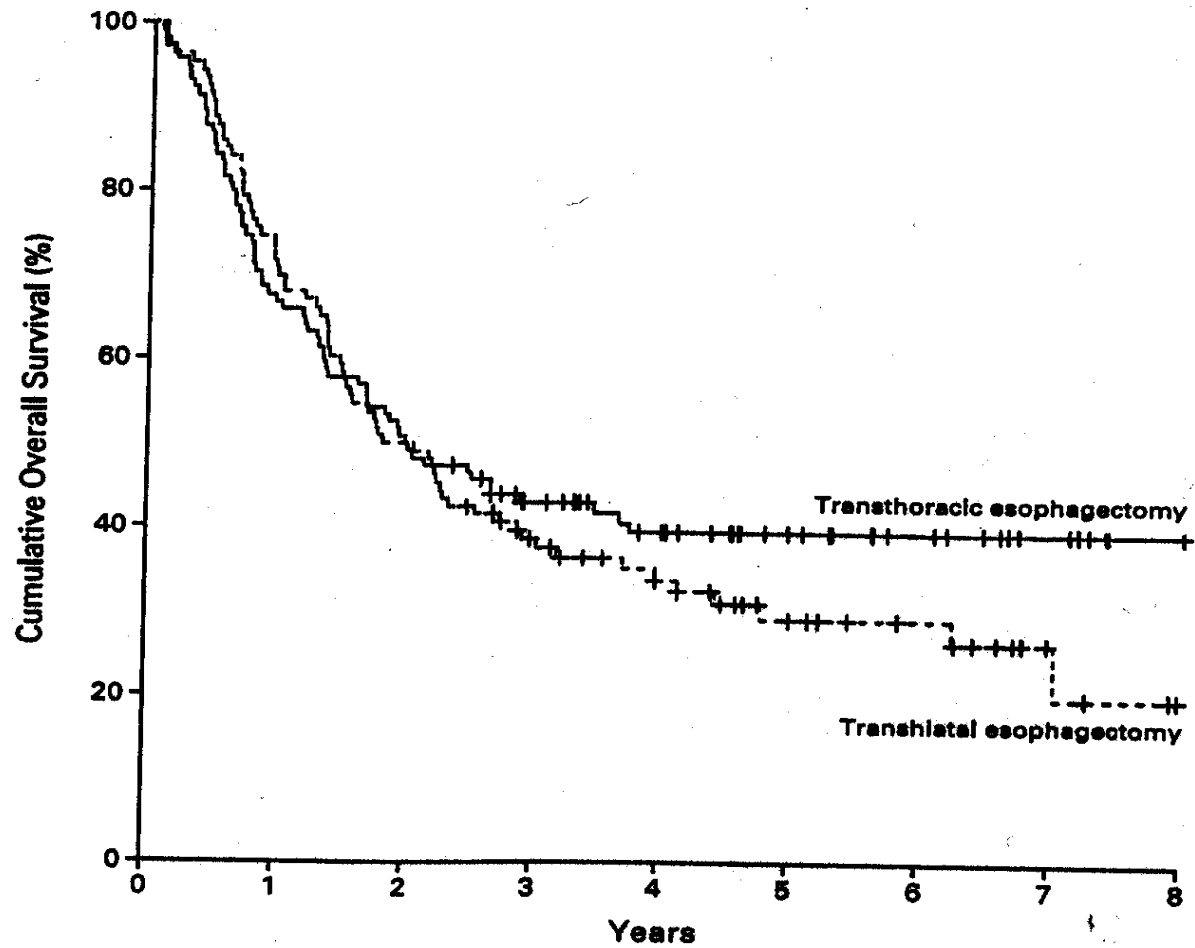
*p < 0.05

Transthoracic

More morbidity
Trend to better survival

Hulscher NEJM 2002

De Boer et al JCO 2004



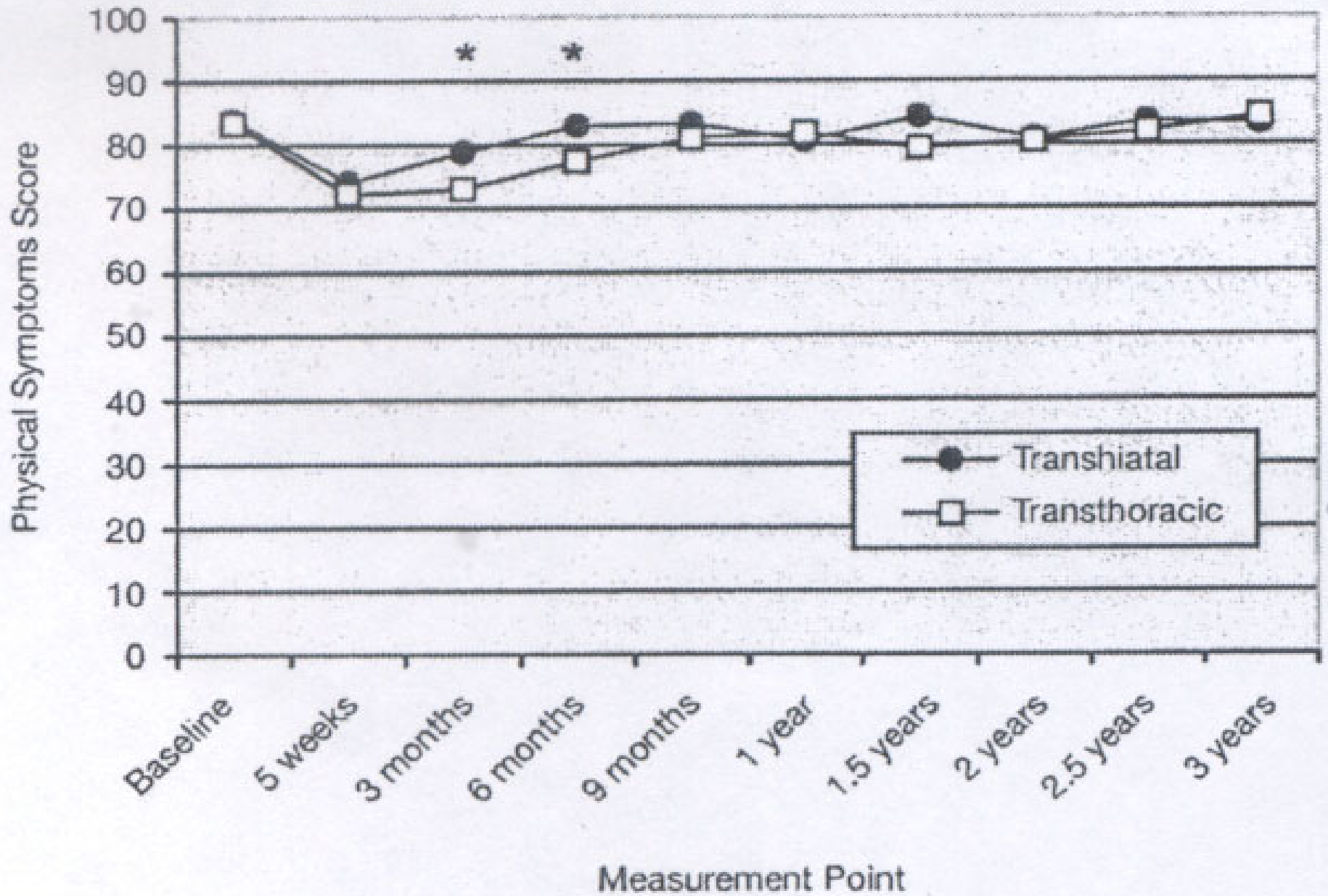
No. AT Risk								
Transhiatal esophagectomy	106	74	53	35	25	16	11	4
Transthoracic esophagectomy	114	76	57	42	31	20	14	7

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

QOL compliance

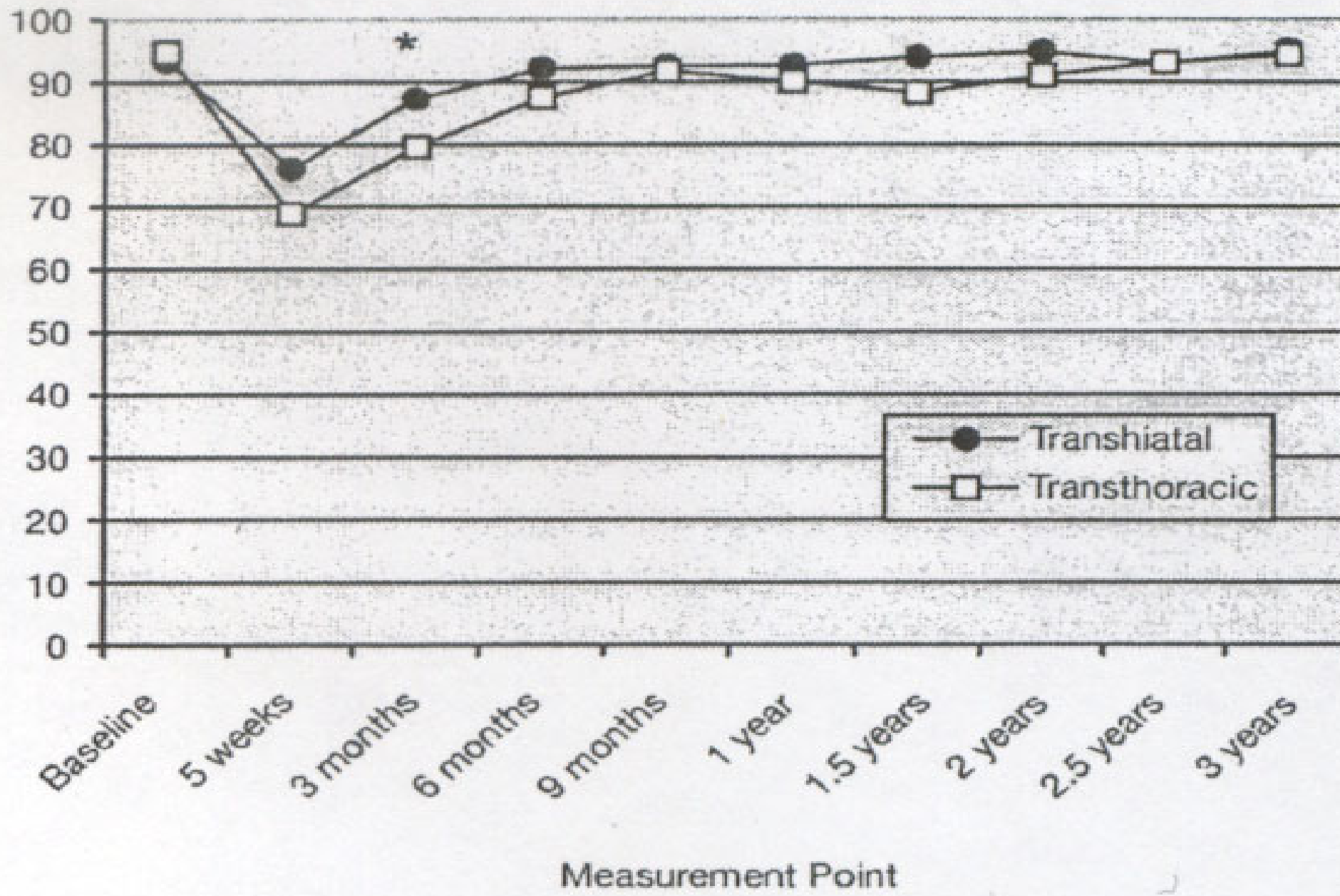
Time	0	1.5	3	6	9	12	1.5	2	2.5	3
Eligible	199	192	188	160	139	132	113	98	87	76
Dead	0	7	11	39	60	67	86	101	112	123
Returned	189	161	155	141	126	125	100	82	66	61
% eligible	95	84	82	88	91	95	88	84	76	80
Random	10	14	13	10	7	3	8	9	14	12
Too ill	0	17	20	9	6	4	5	7	7	3

A



B

Activity Level Score



Added value of QOL

- ? survival differences
- Early post op. QOL benefits for transhiatal
- Informs clinical decision-making

Hulscher NEJM 2002

De Boer et al JCO 2004

Single dose brachytherapy vs. metal stent placement

209 patients

```
graph TD; A[209 patients] --> B[Brachytherapy]; A --> C[Metal stent]; B --> D[Lasting relief of dysphagia]; C --> E[More morbidity]; C --> F[Similar survival];
```

Brachytherapy

Lasting relief of dysphagia

Metal stent

More morbidity
Similar survival

Homs Lancet 2004

Compliance

> 90%

6 trained nurses

Home visits

Single dose brachytherapy vs. metal stent placement

209 patients

```
graph TD; A[209 patients] --> B[Brachytherapy]; A --> C[Metal stent]; B --> D[Better QOL]; B --> E[Dysphagia, cognitive function]; C --> F[More morbidity]; C --> G[Similar survival];
```

Brachytherapy

Metal stent

Better QOL

More morbidity

Dysphagia, cognitive function

Similar survival

*p < 0.001

Homs Lancet 2004

Added value of QL?

- QOL scores show better palliation with brachytherapy than metal stents
- QOL valuable – but expensive outcome (home visits)

Homs Lancet 2004

Conclude

Few high quality trials with QOL in oesophageal & gastric cancer

QOL is of added value – where no clear survival benefit

Design studies with QOL research question and ensure compliance



Updating the EORTC QLQ-CR38

JM Blazeby, Bristol UK

T Conroy, Nancy, France

M Guren, Norway

M Koller, Germany

P King, Bristol, UK

O Sezer, Germany

M Sprangers, The Netherlands

Why update?

EORTC QLQ-CR38 Eur. J Can. 1999

Changes in treatments

Missing data

Stoma items not comparable

Never fully validated

EORTC QLQ-CR38

Urinary symptoms

Body image

Chemotherapy scale

Gastrointestinal symptoms – non stoma

Gastro intestinal symptoms – stoma

Sexual function

Sexual male

Sexual female

Single items: health in future, weight loss,
sexual enjoyment

Updating the QLQ-CR38

The literature

Interviews with professionals n=11

Surgeons, nurses, oncologists

Interviews with patients n=79

25 UK, 24 Germany, 30 France

The Literature

Three validated questionnaires

Fact C

Patient generated tool rectal ca.

Colorectal module (UK)

New QOL issues

Incontinence stool/gas/mucus

Social issues related to incontinence

Anal irritation

QLQ-CR29

Urinary symptoms

Pain scale

Faecal incontinence scale

Gastro intestinal function scale

Stoma specific issues

Male sex scale

Female sex scale

Body image

Single items: bloating, sore anal skin, dry mouth, anxiety about weight, thin hair, taste, worry about future health.

QLQ-CR29

Report to MDC October 2004 (3 reviewers)

Responded to reviewers March 2005

Translated into French, German & Norwegian

Pilot testing new translations (French completed)

QLQ-CR29 - next steps

Pilot test Norwegian and German

Further patient interviews

Patients

Neoadjuvant chemoradiation

Adjuvant chemotherapy

New chemotherapeutic agents

Survivors?

QLQ-CR29 - next steps

International questionnaire
validation study with QLG & GI group

Based at data centre

Funding?