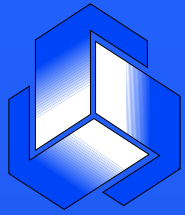


Is baseline quality of life a prognostic factor?

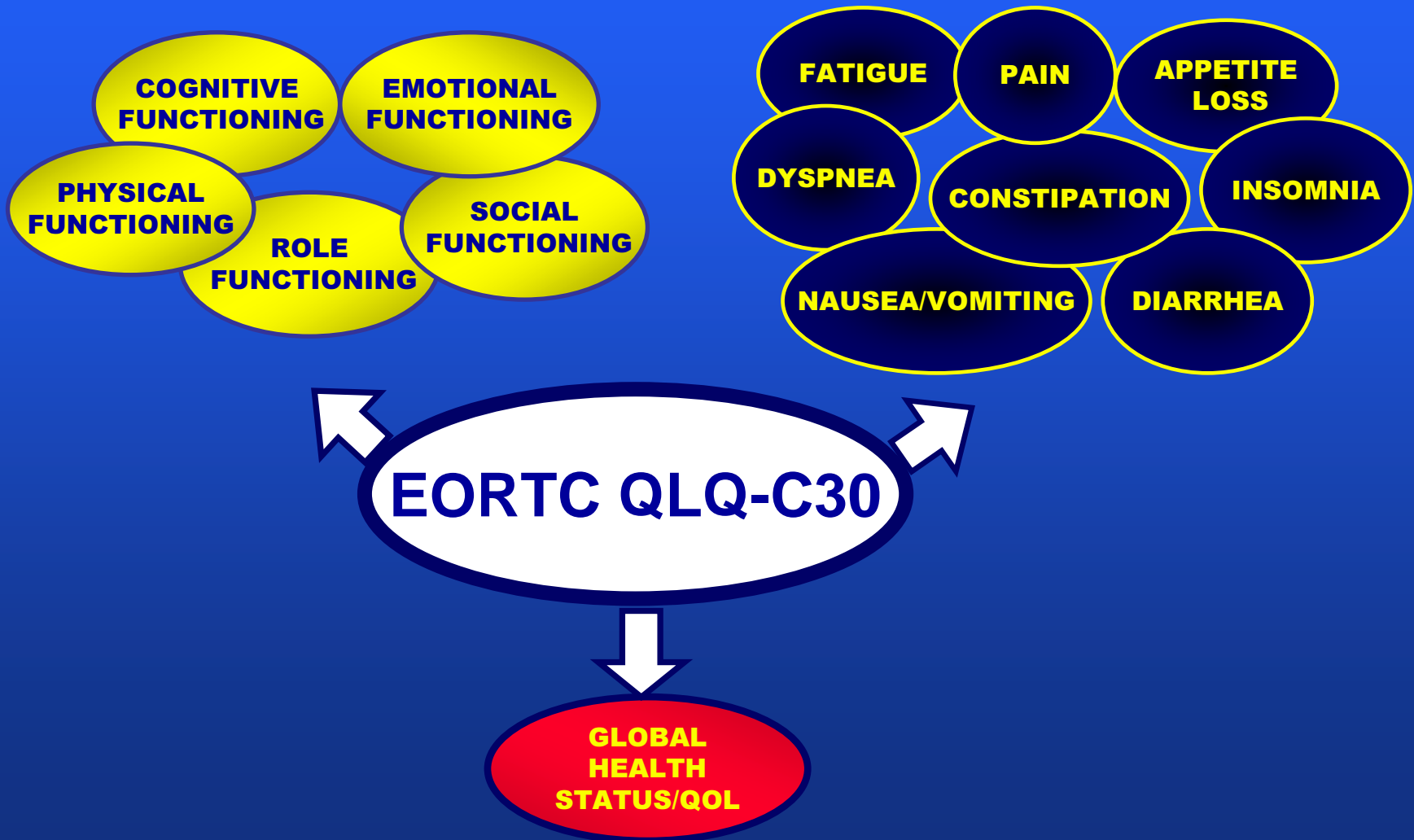
Fabio Efficace, PhD

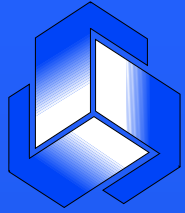
**Andrew Bottomley, PhD, Corneel Coens, MSc,
Laurence Collette, MSc, Richard Sylvester, Sc.D**

**EORTC Data Center
Quality of Life and Biostatistics Units
Brussels**



QUALITY OF LIFE (QOL) PARAMETERS





BACKGROUND

A number of recent studies have shown that baseline QOL parameters independently predict duration of survival

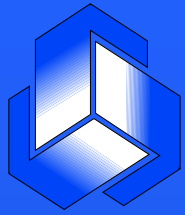
Examples:

- Lung
- Breast
- Colorectal
- Multiple myeloma
- Bladder
- Gastric
- Head & Neck

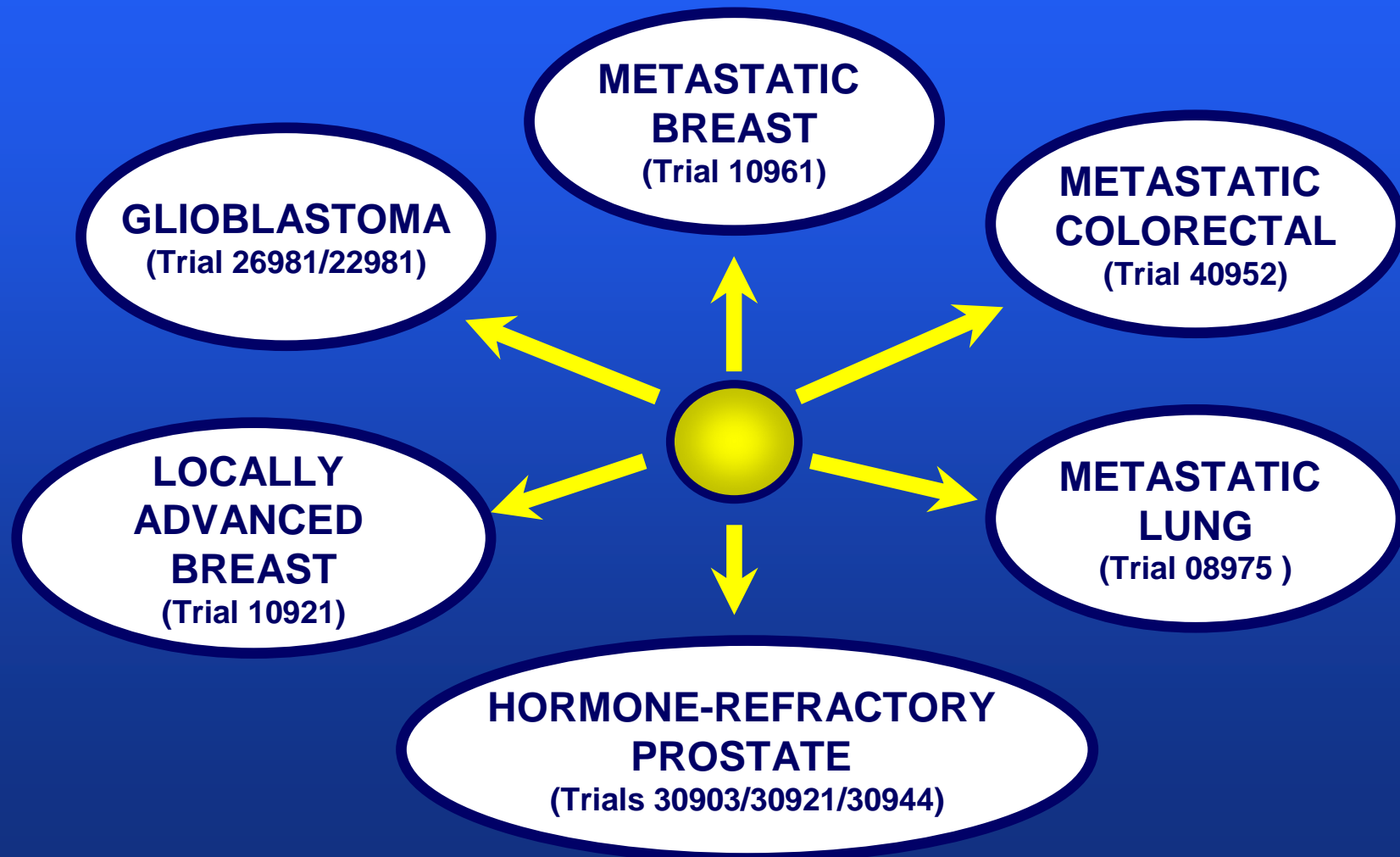


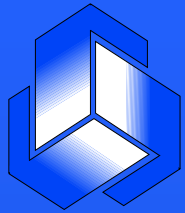
Advanced metastatic cancer

A yellow oval containing the text "Advanced metastatic cancer" is connected to a list of cancer types by a yellow bracket-like line.



The prognostic value of baseline QOL parameters in EORTC Studies





MULTIVARIATE ANALYSES

Locally advanced Breast

(Efficace et al. J Clin Oncol, 2004)

No. Patients

359

Independent QOL prognostic factor

None

Metastatic Breast

(Efficace et al. Eur J Cancer, 2004)

219

Appetite Loss

Metastatic Colorectal

(Efficace et al. ASCO, 2005)

299

Social Functioning

Metastatic Lung

(Bottomley et al. ISOQOL, 2005)

391

Pain, Dysphagia,
Diarrhea, Cognitive Functioning

Glioblastoma

(Bottomley et al. ASCO, 2005)

490

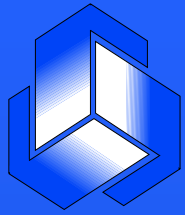
Cognitive Functioning,
Social Functioning
Physical Functioning
Dyspnea

Hormone-refractory Prostate

(Collette et al. J Clin Oncol, 2004)

391

Appetite Loss, Insomnia



METASTATIC BREAST CANCER PATIENTS

Eur J Cancer, 40:1021-30, 2004

PATIENTS AND METHODS

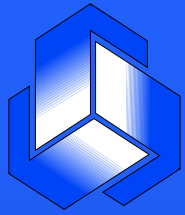
- 219 patients have valid baseline QOL data
- 14 QOL parameters evaluated by EORTC QLQ-C30 and QLQ-BR23

CLINICAL VARIABLES INCLUDED

Age, Performance status, Bone metastases, Dominant site of disease, Number of sites involved, Disease free-interval, Estrogen and Progesterone receptor status

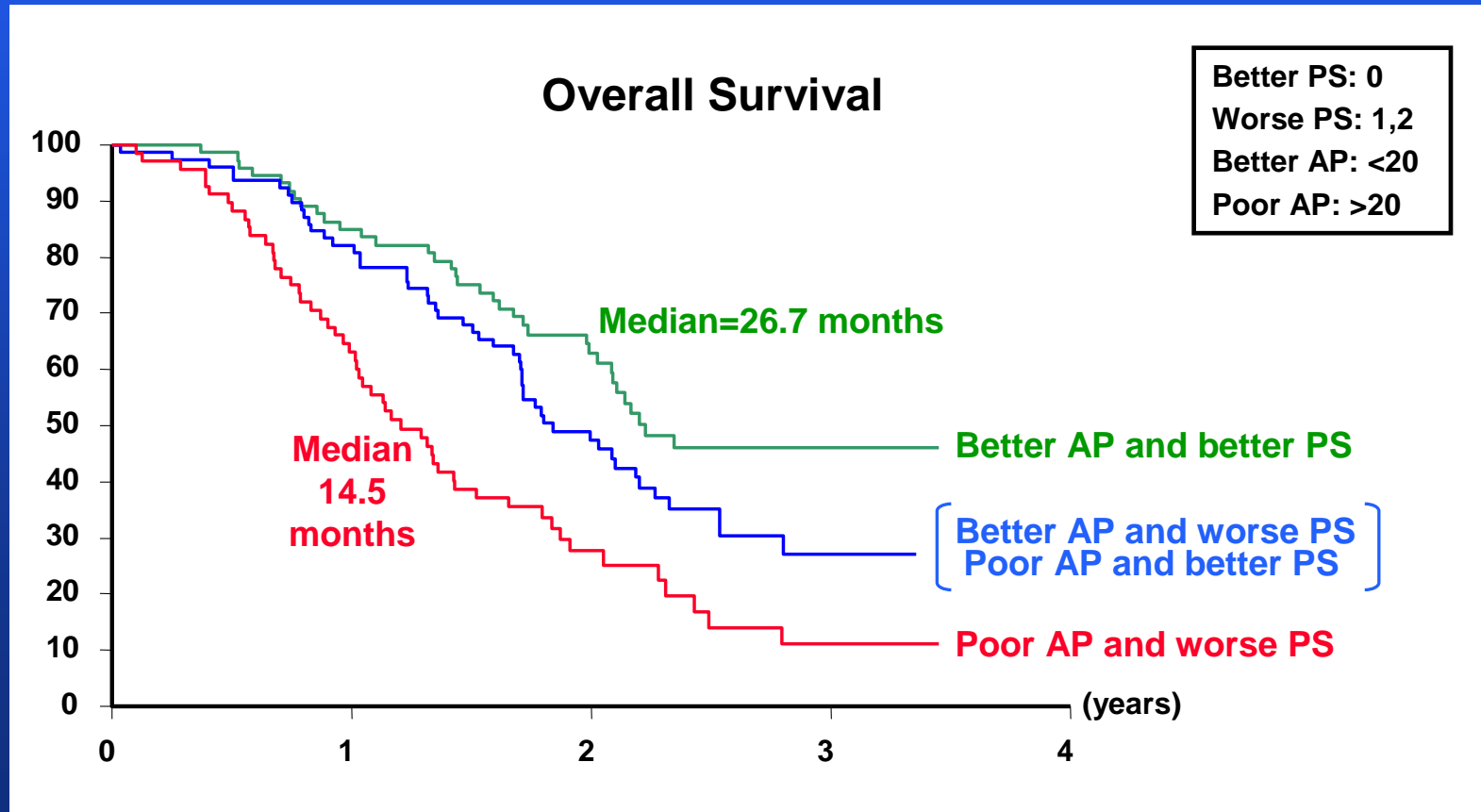
STATISTICS

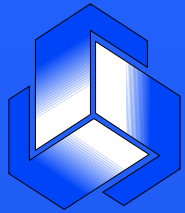
Cox proportional hazards regression model for Overall survival



Multivariate model predicting survival

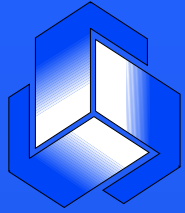
Variables	Hazard Ratio	95% CI	P value
Appetite loss (AP) 10 points	1.08	1.020 – 1.138	0.005
Performance status (PS)	1.77	1.340 – 2.359	<0.001





Prognostic Factor Analyses including QOL in BREAST CANCER

	STAGE	QOL SCALE	QOL MEASURE
Coates et al, 1992 <i>J Clin Oncol</i>	METASTATIC	Physical well-being	LASA
Seidman et al, 1995 <i>J Natl Cancer Inst</i>	METASTATIC	Global QOL	FLIC
Coates et al, 2000 <i>J Clin Oncol</i>	METASTATIC	Appetite, Mood Physical wellbeing, coping	LASA
	EARLY STAGE	None	LASA
Kramer et al, 2000 <i>Eur J Cancer</i>	METASTATIC	Pain	EORTC QLQ-C30
Luoma et al, 2003 <i>Eur J Cancer</i>	METASTATIC	Pain	EORTC QLQ-C30
Efficace et al, 2004 <i>Eur J Cancer</i>	METASTATIC	Appetite loss	EORTC QLQ-C30 EORTC QLQ-BR23
Efficace et al, 2004 <i>J Clin Oncol</i>	LOCALLY ADVANCED	None	EORTC QLQ-C30
Goodwin et al, 2004 <i>J Clin Oncol</i>	EARLY STAGE	None	EORTC QLQ-C30



GLIOBLASTOMA CANCER PATIENTS

To be presented at ASCO 2005

PATIENTS AND METHODS

- 490 Patients have valid baseline QOL data
- 12 QOL parameters evaluated by the EORTC QLQ-C30 and QLQ-BN20

CLINICAL VARIABLES INCLUDED

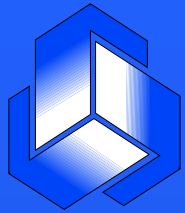
Performance status, Age (**cut-off 50 years**), Extent of surgery (**biopsy only, partial resection, total resection**)

STATISTICS

Cox proportional hazards regression model for Overall survival

Bootstrap Validation*

* (In collaboration with Dr. K. Van Steen, Harvard School of Public Health, Boston, USA)



BOOTSTRAP VALIDATION PROCEDURE



ORIGINAL
DATASET
N patients



IDEA:

Original dataset is a 'random' sample of patients from the general population.

Generate a number (B) of datasets each of which have the same sample size as the original one:

- Copy the full data from N randomly chosen patients with replacement (ie. an already selected patient may be selected again)
- Repeat B times



(B sets of N patients)

Simulation
dataset

1



Model 1

Simulation
dataset

2



Model 2

Simulation
dataset

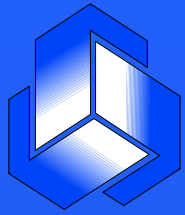
B



Model B

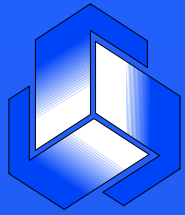
Prognostic factor analysis on each simulation dataset

(B = bootstrap size)



Cox analysis and Bootstrap Validation (1000 Bootstrap samples)

	Cox Univariate Analysis HR (P-value)	Final Cox Multivariate Model HR (P-value)	Inclusion Variable (%)
CLINICAL PARAMETERS			
→ Perf status 0 vs 1	1.306 (0.027)	1.342 (0.011)	100
→ Perf status 0 vs 2	1.206 (0.036)	1.231 (0.014)	100
→ Age	1.280 (0.037)	1.290 (0.029)	100
→ Extent of Neurosurgery	0.646 (0.002)	0.624 (<.001)	100
EORTC QLQ-C30			
→ Physical Functioning	0.998 (0.097)	0.998 (0.039)	44 *
→ Cognitive Functioning	0.989 (<.001)	0.990 (<.001)	97 *
→ Social Functioning	1.008 (<.001)	1.007 (<.001)	93 *
Fatigue	1.002 (0.569)	-	12
Nausea / Vomiting	1.003 (0.534)	-	9
Pain	0.997 (0.271)	-	18
→ Dyspnoea	0.993 (0.017)	0.993 (0.011)	65 *
EORTC QLQ-BN20			
Visual disorder	0.995 (0.140)	-	17
Motor dysfunction	1.003 (0.215)	-	30
Comm. deficit	0.999 (0.648)	-	9
Headaches	1.001 (0.537)	-	8
Seizures	1.002 (0.499)	-	10



METASTATIC COLORECTAL CANCER PATIENTS

To be presented at ASCO 2005

PATIENTS AND METHODS

- 299 Patients have valid baseline QOL data
- 10 QOL parameters evaluated by the EORTC QLQ-C30

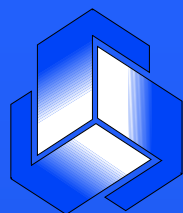
CLINICAL VARIABLES INCLUDED

Performance status, WBC count, alkaline phosphatase, number of metastatic sites involved, presence of liver metastases, previous adjuvant chemotherapy and primary site of disease

STATISTICS

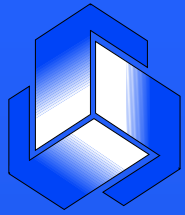
Cox proportional hazards regression model for Overall survival

Bootstrap Validation



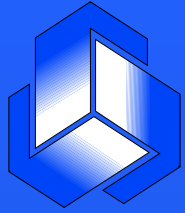
Cox analysis and Bootstrap Validation (1000 Bootstrap samples)

	Cox Univariate Analysis HR (P-value)	Final Cox Multivariate Model HR (P-value)	Inclusion variable (%)
CLINICAL PARAMETERS			
Performance status	1.528 (<.001)	-	43
Number of sites involved	1.119 (.003)	1.108 (.010)	74 *
WBC count	2.064 (<.001)	1.961 (<.001)	94 *
Alkaline phosphatase	1.762 (<.001)	1.509 (.005)	63 *
Liver metastases	1.282 (.143)	-	Not included
Adjuvant chemotherapy	0.909 (.609)	-	Not included
Site of primary tumour	0.862 (.243)	-	Not included
EORTC QLQ-C30			
Global health status / QoL	0.990 (.001)	-	21
Physical Functioning	0.991 (.001)	-	15
Emotional Functioning	0.995 (.064)	-	7
Social Functioning	0.993 (.001)	0.991 (<.001)	73 *
Fatigue	1.008 (<.001)	-	Not included
Nausea / Vomiting	1.010 (.009)	-	23
Pain	1.003 (.117)	-	Not included
Appetite loss	1.006 (.006)	-	11
Constipation	1.004 (.101)	-	Not included
Diarrhoea	1.005 (.054)	-	31



Concluding remarks

- ➔ **Baseline QOL parameters independently predict survival beyond key clinical data, in several metastatic cancer disease sites.**
- ➔ **In addition to being a well established endpoint for treatment comparisons, this evidence provides further arguments for measuring QOL both in cancer research and clinical practice.**
- ➔ **It is reasonable to speculate that patients' self assessment of their own health status provides a better and stronger indicator of their prognosis than a number of traditional clinical factors.**
- ➔ **Further research is needed to identify specific baseline QOL parameters that are relevant to each specific disease site.**



Thanks to:

- **EORTC Breast Cancer Group**
- **EORTC Gastrointestinal Cancer Group**
- **EORTC Genito-Urinary Group**
- **EORTC Brain Tumor Group**
- **EORTC Radiotherapy Group**
- **EORTC Lung Cancer Group**
- **NCI-C CTG**
- **EORTC *Lady Grierson* Research Fellowship**