

Exploring internal relationships among EORTC QLQ-C30 indicators from EORTC clinical trials

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- **Health-Related Quality of Life (HRQoL) data are, by their very nature, complex**
 - because they aim to measure abstract parameters like ‘pain’;
 - because they are reported by the patients themselves, involving a subjective component.
- **One of the aims of the PROBE project is to attempt to understand what lies *behind* patient-reported outcomes.**

- **Cluster analysis in cancer patients**
- **Cluster analysis in metastatic prostate cancer patients**
- **A symptom index for cancer patients**

Cluster Analysis in cancer patients

- **28 closed randomized EORTC clinical trials**
- **6709 cancer patients**
- **11 cancer sites**
- **34 countries**
- **EORTC QLQ-C30 questionnaire**
- **Baseline QoL data available for all patients**

- **Socio-demographic and clinical data available:**
 - **Age**
 - **Gender**
 - **Cancer site**
 - **Pre-treatment status**
 - **Metastatic status**
 - **World Health Organization performance status**

- **HRQoL data available:**

- **Physical functioning (pf)**
- **Role functioning (rf)**
- **Emotional functioning (ef)**
- **Cognitive functioning (cf)**
- **Social functioning (sf)**
- **Global Health status / QoL (ql)**

- **Fatigue (fa)**
- **Nausea and vomiting (nv)**
- **Pain (pa)**
- **Dyspnoea (dy)**
- **Insomnia (sl)**
- **Appetite loss (ap)**
- **Constipation (co)**
- **Diarrhoea (di)**
- **Financial difficulties (fi)**

Socio-demographic and clinical data (N = 6709)

Age	≤ 60	4458 (66%)
	> 60	2251 (34%)
Gender	Male	4236 (63%)
	Female	2471 (37%)
Systemic pre-treatment	No	5077 (76%)
	Yes	1302 (19%)
Presence of metastases	No	3391 (51%)
	Yes	2037 (30%)
Performance status	0-1	5893 (88%)
	2-3	458 (7%)

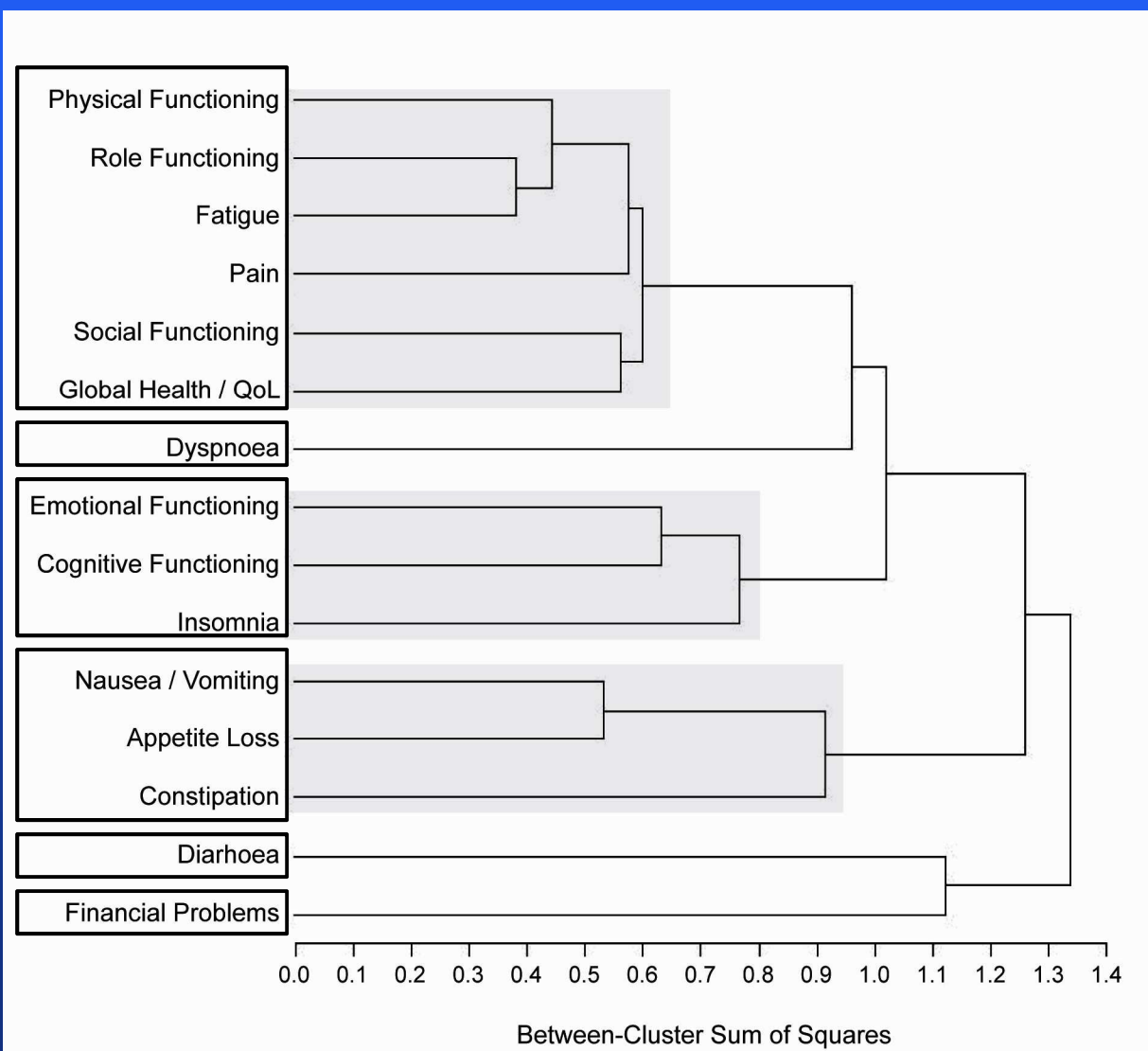
Cancer site	Melanoma	2345 (35%)
	Colorectum	1056 (16%)
	Lung	976 (15%)
	Brain	741 (11%)
	Head and neck	416 (6%)
	Prostate	382 (6%)
	Testis	242 (4%)
	Breast	225 (3%)
	Ovary	186 (3%)
	Pancreas	81 (1%)
	Oesophagus	59 (1%)

HRQoL data (N = 6709)

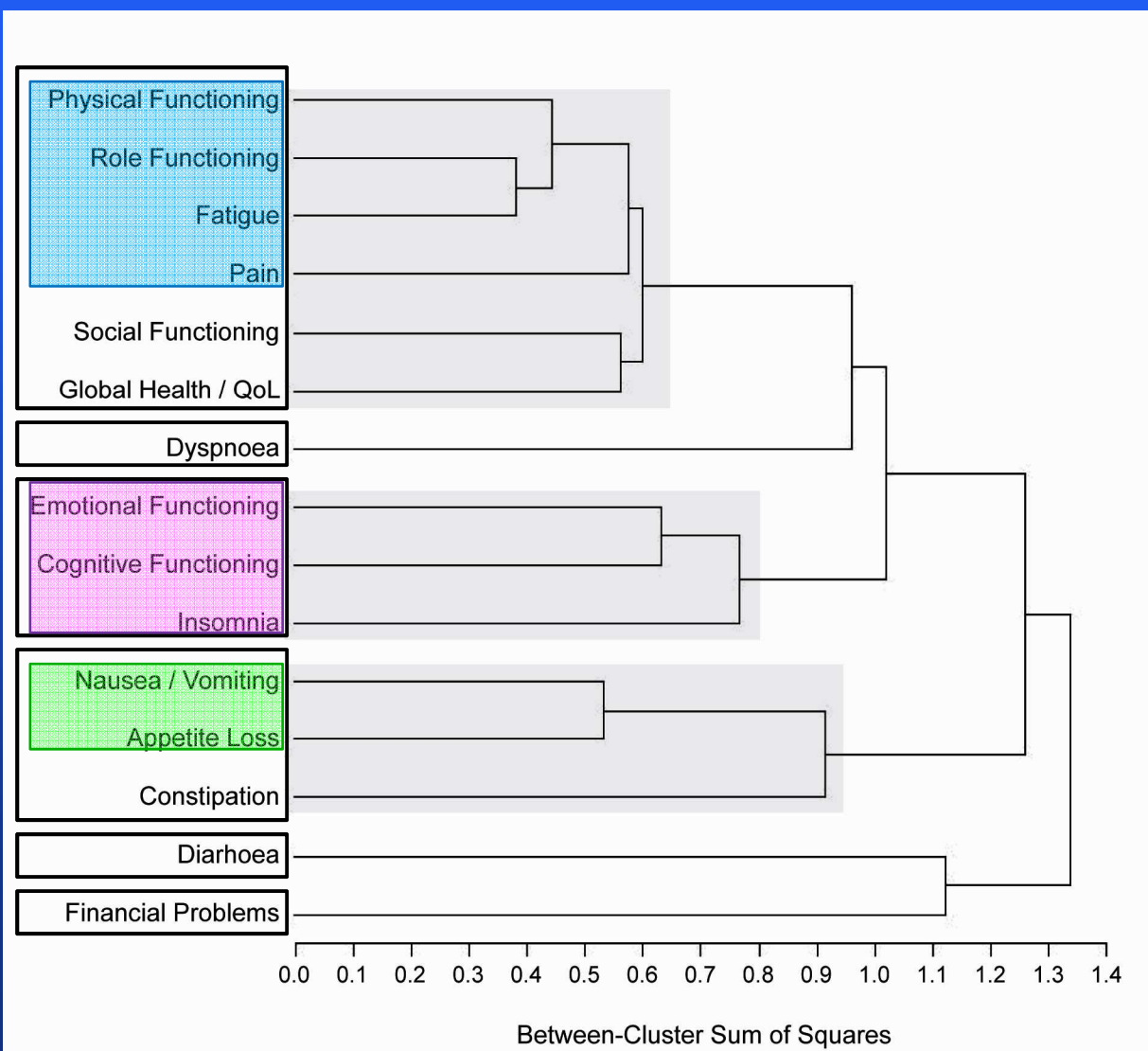
HRQoL indicator	Mean (sd)
pf	81 (24)
rf	69 (33)
ef	71 (23)
cf	86 (20)
sf	77 (28)
ql	63 (23)

fa	31 (26)
nv	6 (15)
pa	24 (28)
dy	15 (24)
sl	27 (30)
ap	16 (28)
co	13 (25)
di	6 (17)
fi	15 (27)

Dendrogram: all cancer patients



Dendrogram: all cancer patients



Cluster Analysis in metastatic prostate cancer patients

- **3 closed randomized EORTC clinical trials**
- **382 cancer patients**
- **EORTC QLQ-C30 questionnaire**
- **Baseline QoL data available for all patients**

- **Socio-demographic and clinical data available:**
 - **Age**
 - **Pre-treatment status**
 - **World Health Organization performance status**

- **HRQoL data available:**

- **Physical functioning (pf)**
- **Role functioning (rf)**
- **Emotional functioning (ef)**
- **Cognitive functioning (cf)**
- **Social functioning (sf)**
- **Global Health status / QoL (ql)**

- **Fatigue (fa)**
- **Nausea and vomiting (nv)**
- **Pain (pa)**
- **Dyspnoea (dy)**
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- **Diarrhoea (di)**
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Socio-demographic and clinical data (N = 382)

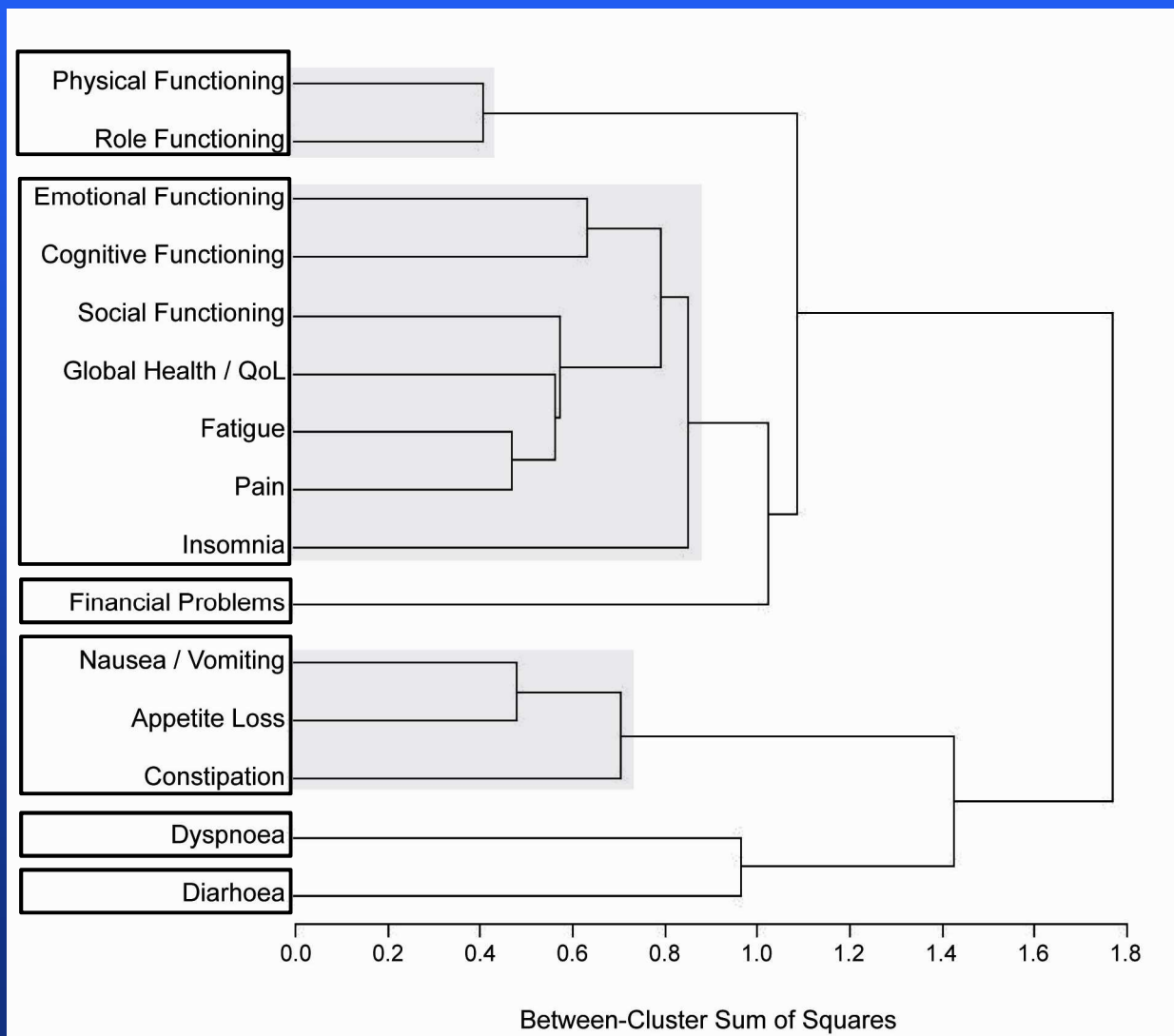
Age	≤ 60	41 (11%)
	> 60	341 (89%)
Pre-treatment	Orchiectomy	130 (34%)
	Hormonal	193 (51%)
	Both	56 (15%)
Performance status	0-1	265 (69%)
	2-3	117 (31%)

HRQoL data (N = 382)

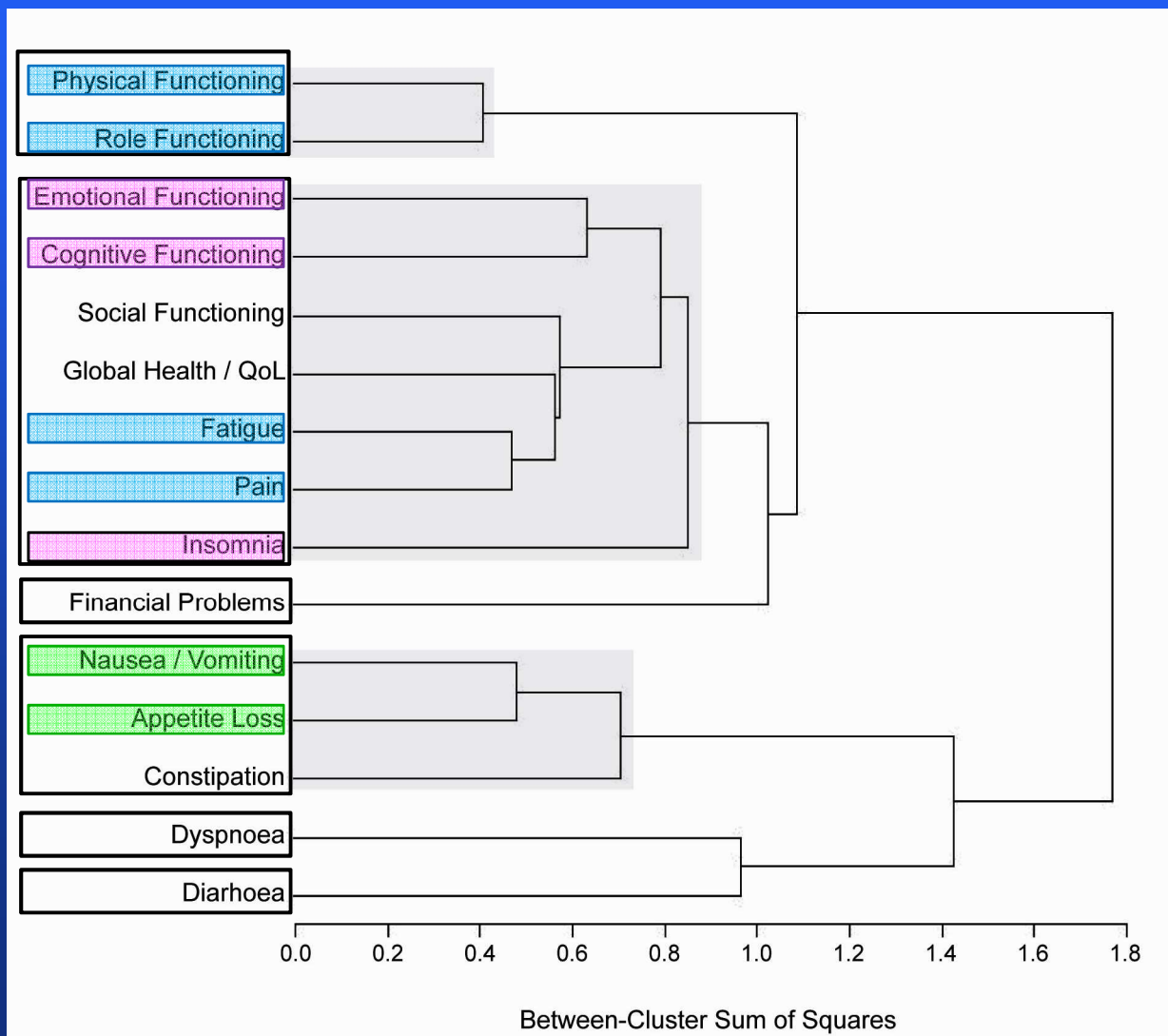
HRQoL indicator	Mean (sd)
pf	59 (27)
rf	59 (38)
ef	68 (24)
cf	80 (22)
sf	69 (30)
ql	50 (21)

fa	46 (26)
nv	13 (22)
pa	55 (27)
dy	21 (24)
sl	37 (33)
ap	27 (33)
co	33 (36)
di	9 (18)
fi	11 (24)

Dendrogram: metastatic prostate patients



Dendrogram: metastatic prostate patients



A symptom index for cancer patients

- **Objectives of this study:**
 - to construct a clinically-relevant symptom index for cancer patients from the EORTC QLQ-C30, using 2 datasets from 2 MD Anderson studies in which all patients had completed both the EORTC Quality of Life Core Questionnaire (QLQ-C30) and the MD Anderson Symptom Inventory (MDASI);
 - to validate the obtained symptom index, using a pooled dataset of 22 closed randomized EORTC clinical trials.

- For this study, 17 questions that relate to symptoms were selected from the QLQ-C30.
- Questions relating to the same symptoms are also present in the MDASI and were used to test the concurrent validity of the index.

- **Dyspnoea**
- **Pain**
- **Need to rest**
- **Insomnia**
- **Weakness**
- **Appetite loss**
- **Nausea**
- **Vomiting**
- **Constipation**
- **Diarrhoea**
- **Tiredness**
- **Difficulty concentrating**
- **Tension**
- **Worry**
- **Irritability**
- **Depression**
- **Difficulty remembering**

1st analysis

Construction of the symptom index

- 2 datasets from validation studies of the Japanese and Korean versions of the MDASI were used to build the symptom index.
- 252 Japanese cancer patients with a variety of cancer sites
- 177 Korean cancer patients with a variety of cancer sites
- All the patients had filled in both the EORTC QLQ-C30 and the MDASI.

A symptom index for cancer patients

		Japanese cancer patients (N = 252)	Korean cancer patients (N = 177)
Age	mean (range)	62 (19 - 86)	51 (22 - 76)
Gender	male	146 (58%)	107 (60%)
	female	106 (42%)	70 (40%)
Metastases	yes	108 (43%)	100 (56%)
	no	144 (57%)	77 (44%)
ECOG performance status	0-1	207 (82%)	143 (81%)
	2-3-4	45 (18%)	34 (19%)

- The factor structure of the 17 selected questions was retrospectively explored in each of the 2 datasets.
- A certain number of new variables, called factors, was constructed using the 17 original questions.
- Each question contributed a certain weight to each factor.
- Questions with weights above 0.5 in both datasets were retained.
- **11 questions met selection criteria and were summed to construct the index.**

- **Dyspnoea**
- **Pain**
- **Need to rest**
- **Insomnia**
- **Weakness**
- **Appetite loss**
- **Nausea**
- **Vomiting**
- **Constipation**
- **Diarrhoea**
- **Tiredness**
- **Difficulty concentrating**
- **Tension**
- **Worry**
- **Irritability**
- **Depression**
- **Difficulty remembering**

- **Nausea**
- **Vomiting**
- **Worry**
- **Need to rest**
- **Depression**
- **Weakness**
- **Appetite loss**
- **Irritability**
- **Tiredness**
- **Difficulty concentrating**
- **Pain**

- The reliability of the index was measured with Cronbach's alpha (α).
High reliability was seen:
 - $\alpha = 0.86$ for the Japanese dataset
 - $\alpha = 0.91$ for the Korean dataset
- Concurrent validity was assessed by computing Pearson's correlation coefficient (ρ) between the index and the MDASI symptom summary score.
Significant correlations were found:
 - $\rho = 0.71$, $p < 0.0001$ for the Japanese dataset
 - $\rho = 0.72$, $p < 0.0001$ for the Korean dataset

- Student's t-test was used to compare index scores between subgroups of patients that were defined according to metastatic status (no vs. yes) and ECOG performance status (0-1 vs. 2-3-4).

The index could discriminate patients by metastatic status in the Japanese dataset only, by ECOG performance status in both datasets:

- metastatic status:

- $p = 0.0005$ for the Japanese dataset

- $p = 0.3159$ for the Korean dataset

- ECOG performance status:

- $p < 0.0001$ for the Japanese dataset

- $p < 0.0001$ for the Korean dataset

2nd analysis

Validation of the symptom index

- A pooled external dataset was used to assess the ability to reproduce and generalize the findings.
- 22 closed randomized EORTC clinical trials.
- 5,302 patients from 32 countries, 8 different cancer sites.
- The 5 most frequent cancers were melanoma, colorectal, lung, head & neck and prostate.
- All the patients had filled in the EORTC QLQ-C30 at baseline.

A symptom index for cancer patients

		Pooled dataset (N = 5,302)	Japanese dataset	Korean dataset
Age	mean (range)	54 (16 - 89)	62 (19 - 86)	51 (22 - 76)
Gender	male	3338 (63%)	58%	60%
	female	1964 (37%)	42%	40%
Metastases	yes	2088 (39%)	43%	56%
	no	3214 (61%)	57%	44%
WHO performance status	0-1	4989 (94%)	82%*	81%*
	2-3	313 (6%)	18%*	19%*

- Reliability was measured with Cronbach's alpha. In the pooled dataset, the index showed high reliability:
 - $\alpha = 0.86$
- To compare index scores between subgroups of patients, Student's t-test was used. The index was able to discriminate patients by metastatic status (no vs. yes) and WHO performance status (0-1 vs. 2-3):
 - metastatic status:
 $p < 0.0001$
 - WHO performance status:
 $p < 0.0001$

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Thank you for your attention.

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