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Nutritional requirements in advanced cancer patients

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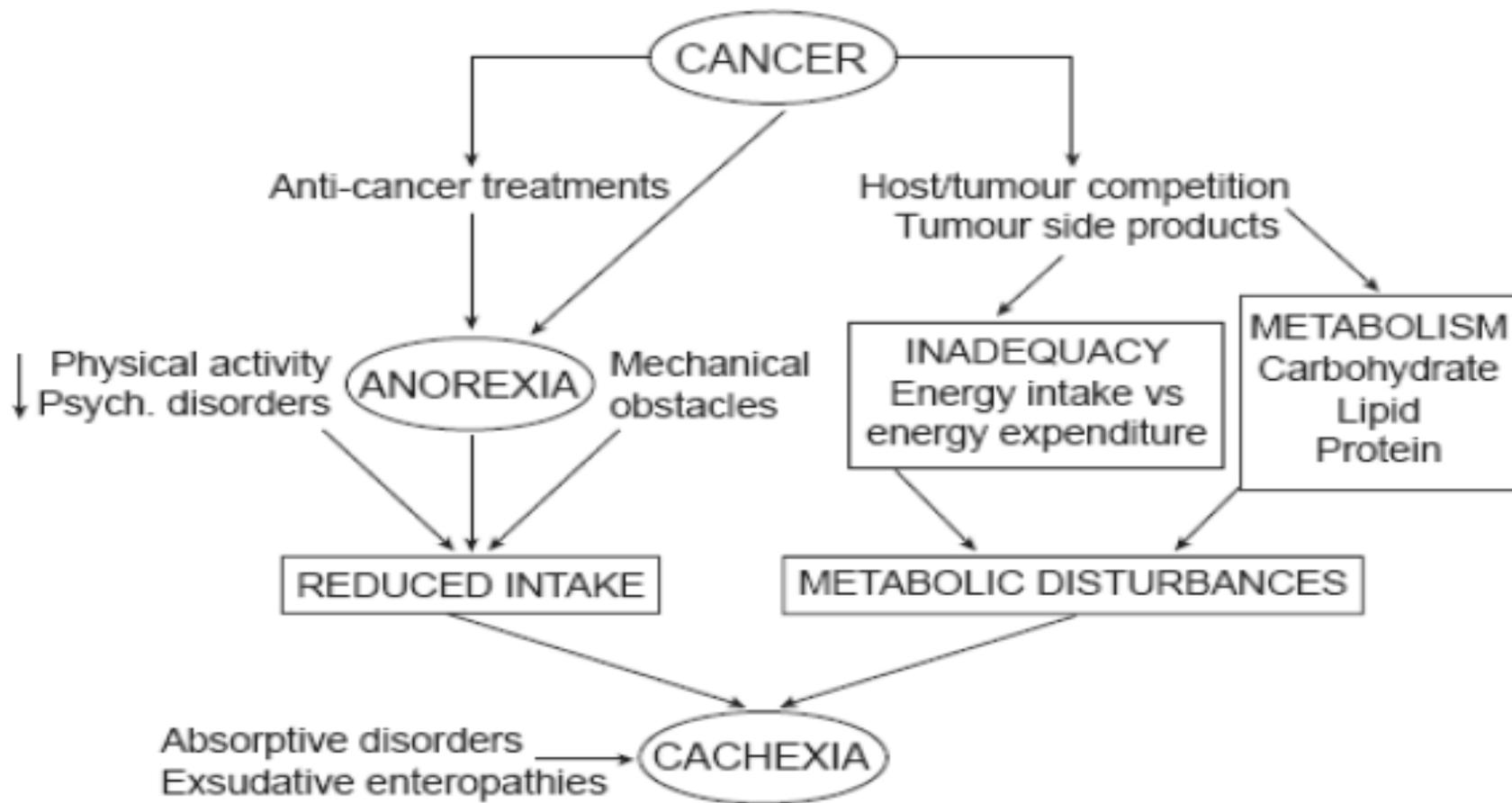
Cancer cachexia

“multifactorial syndrome with loss of skeletal muscle mass (with or without loss of fat mass), not fully reversed by conventional nutritional support. Leads to progressive functional impairment. Pathophysiology characterized by negative protein & energy balance driven by a variable combination of reduced food intake and abnormal metabolism”

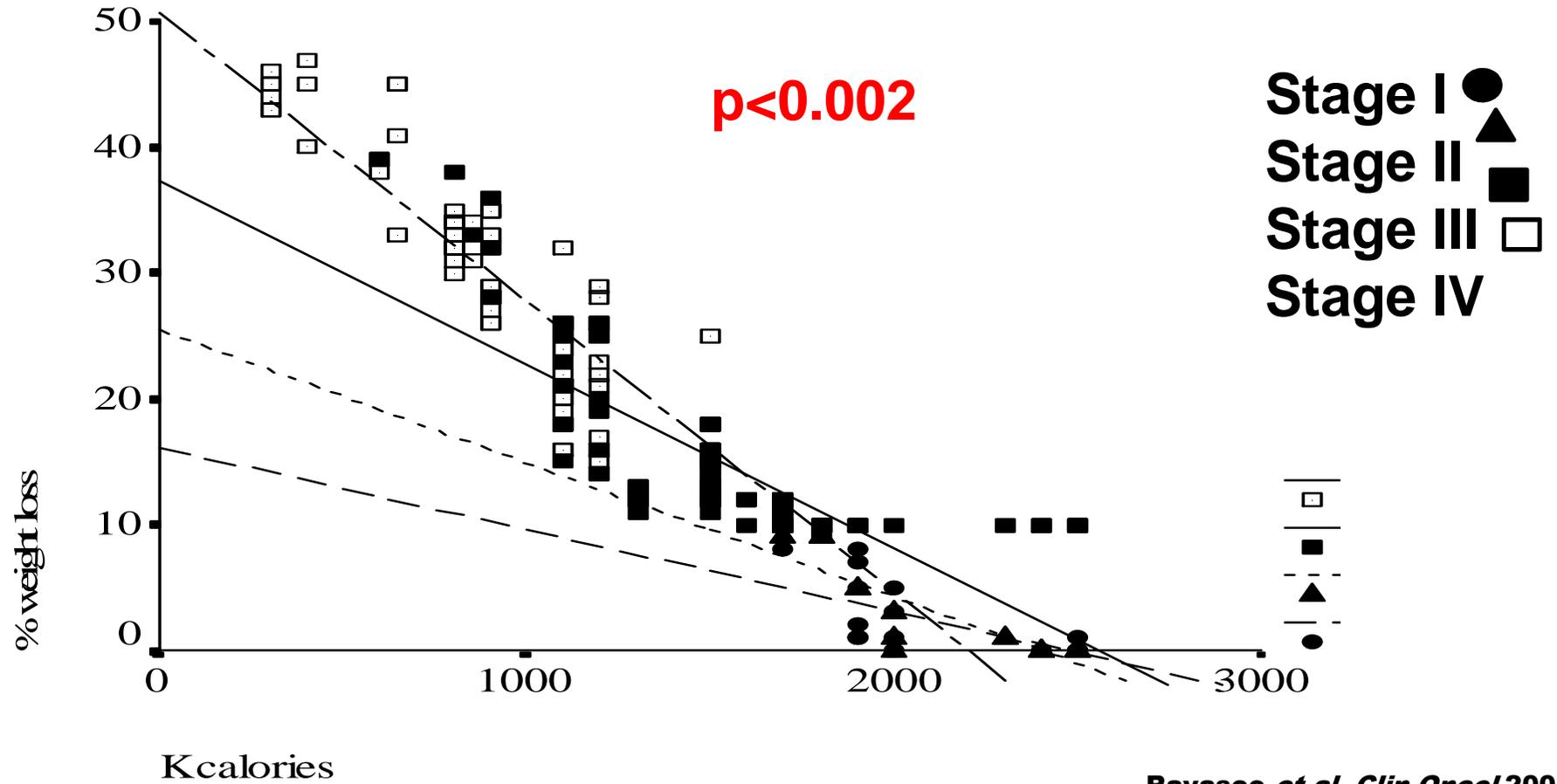


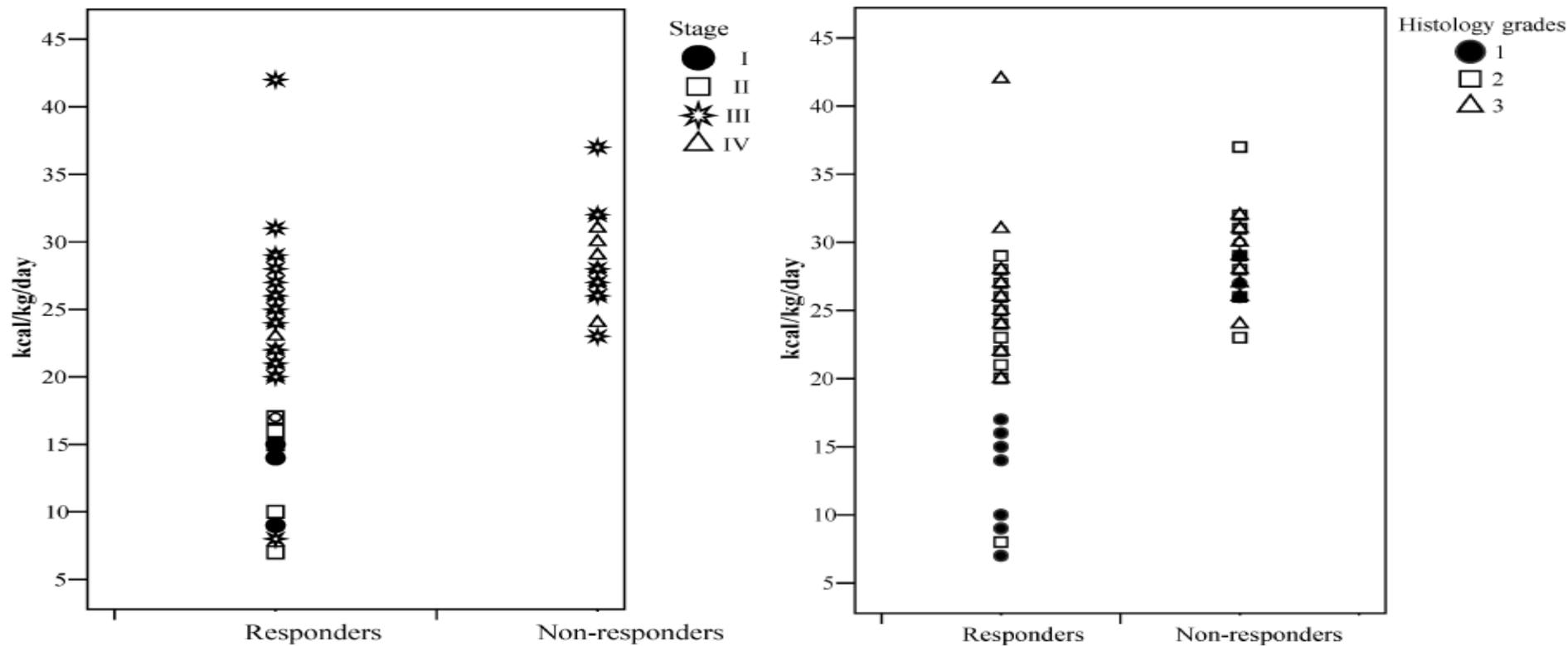
challenge

Fearon, Ravasco *et al.* Lancet Oncology 2011; 10: 1-7



weight loss, energy intake, advanced stage



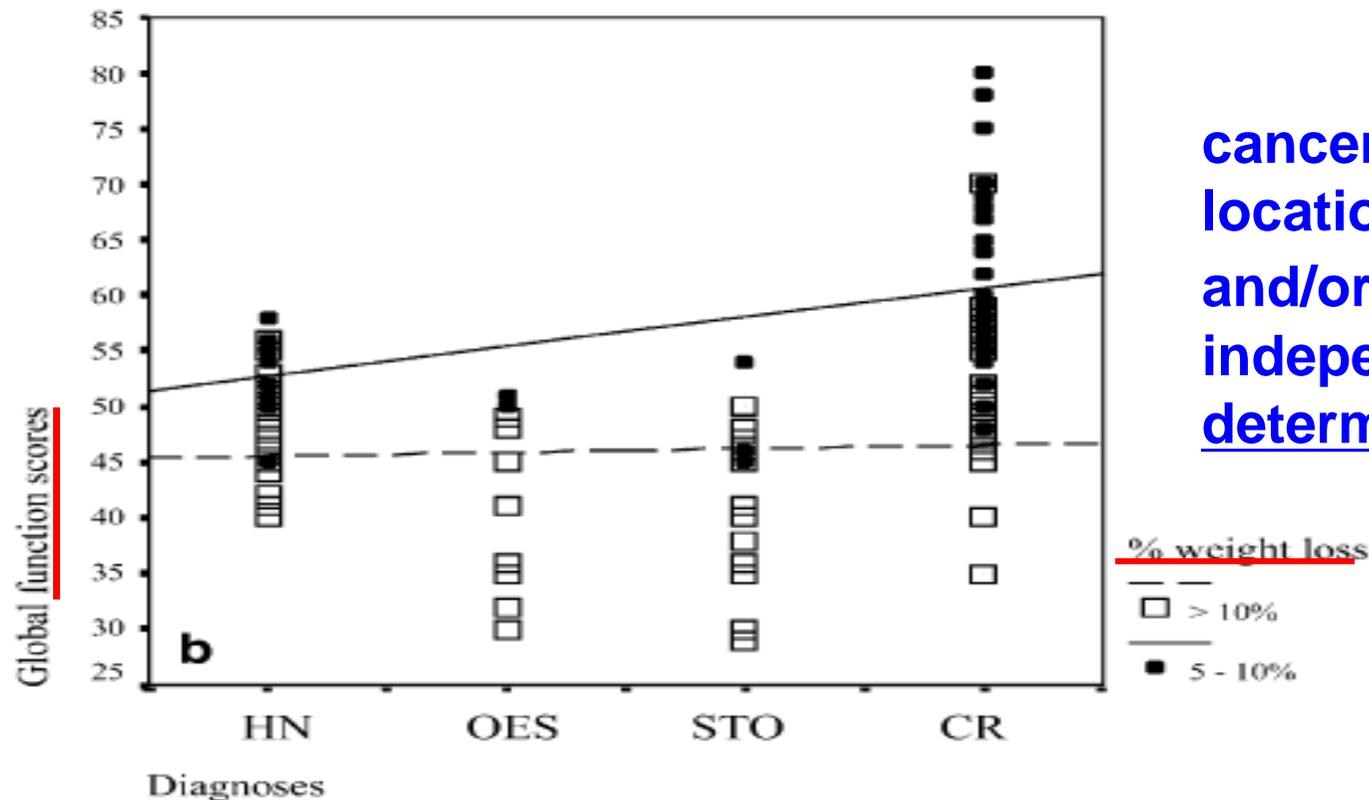


advanced disease & cancer histological aggressiveness

↔ ↑REE, wasting, marked intake deficits

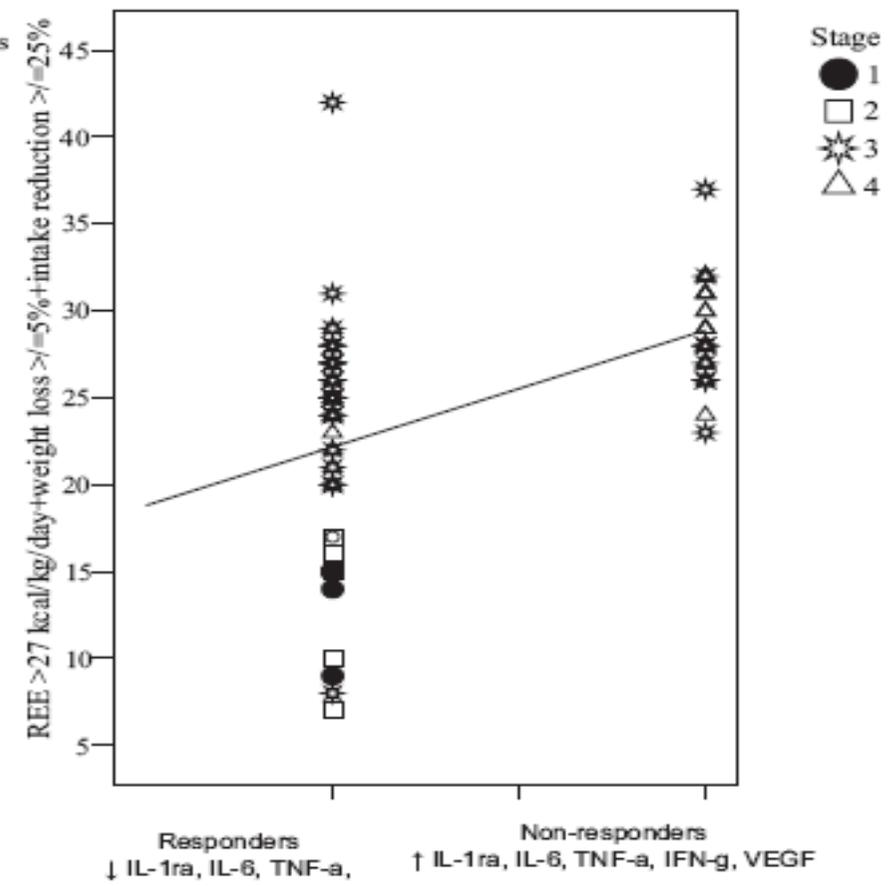
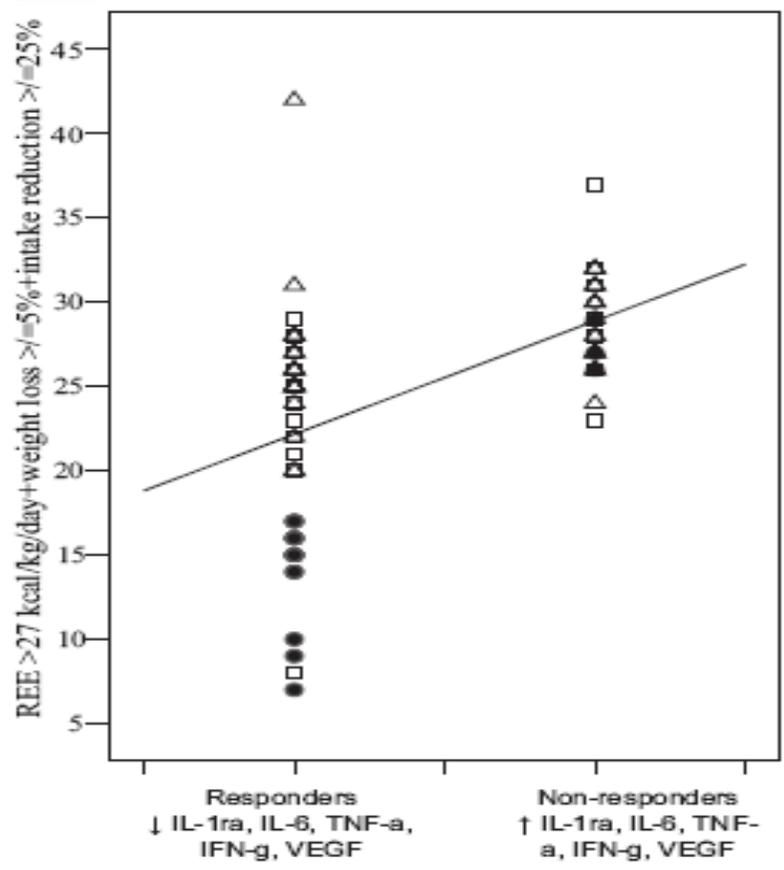
Ravasco *et al. Cancer Investigation* 2007

cachexia and QoL



cancer stage & location, weight loss and/or ↓ intake independent determinants of QoL

semi-starvation impairs functional & psychological abilities
progressive disease ↔ wasting

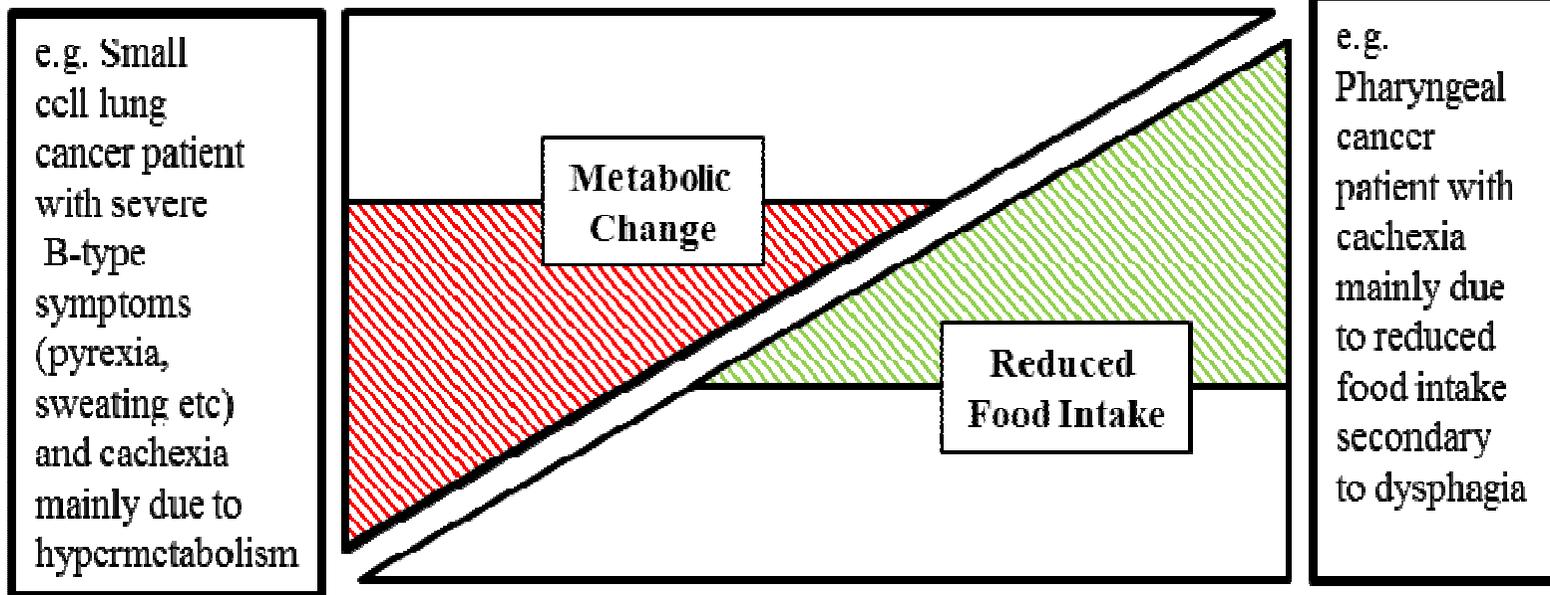


advanced disease & cancer histological aggressiveness

↔ ↑ TNF- α , IL1ra, IL-6, IFN- γ VEGF ↔ ↑ REE, wasting, intake deficits
Ravasco et al. Cancer 2012 (in press)

Variable	Starvation	Cancer
Energy intake	↓	↓(→*)
Energy expenditure (resting)	↓	↑
Body fat	↓	↓
Skeletal muscle	→	↓
Liver	↓†	↑‡

Clinical Heterogeneity



Variable proportion of metabolic change that can be reversed by treating catabolic factors



Variable proportion of reduced food intake that can be reversed by treating 'secondary anorexia'

Four Domains: framework

I. Depletion of Reserves



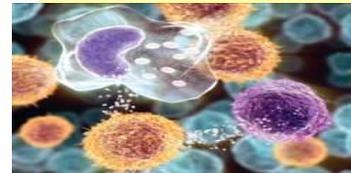
e.g.
Underweight
Weight loss
Lean tissue wasting
Sarcopenia
(severe muscle wasting)

II. Limitation of food intake



e.g.
Nutrition impact symptoms:
Anorexia
Dysphagia
Nausea
Social / psychological

III. Catabolic Drivers



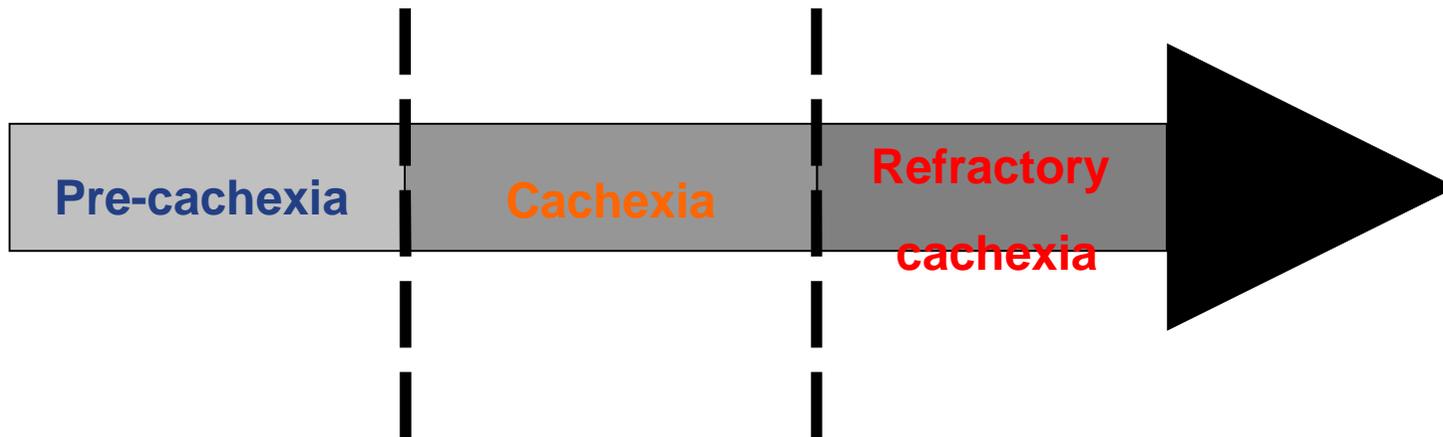
e.g.
Inflammation
Tumor burden
Insulin resistance
Hypogonadism
Corticosteroids
Comorbidities

IV. Impact and outcomes



e.g.
Physical function
Quality of life
Distress
Survival
Treatment outcomes
Costs

Early intervention: pre or early cachexia



	Incurable patients: screening and assessment
STRONG	<i>We recommend to routinely screen all advanced, incurable cancer patients - whether receiving or not receiving anti-cancer treatment - for inadequate nutritional intake, weight loss and low body mass index, and if found at risk, to assess these patients further for both treatable nutrition impact symptoms and metabolic derangements.</i>
Questions for research	Effects of malnutrition screening programs combined with multidisciplinary interventions on quality of life in incurable cancer patients

	Energy requirements
STRONG	<i>Total energy expenditure of cancer patients, if not measured individually, be assumed to range between 25 and 30 kcal/kg/day.</i>
Questions for research	improve prediction of energy requirements in individual patient

	Protein intake
STRONG	<i>Above 1 g/kg/day and if indicated go up to 1.5 g/kg/day</i>
Questions for research	effect on outcome of increased supply and composition of protein/amino acids

	Choice of energy substrates
STRONG	<i>In most patients general recommendations are applicable. In weight-losing patients with advanced cancer, in addition to an adequate protein intake, we recommend a fat intake of 35-50% of total energy requirement.</i>
Questions for research	effect of high fat on outcome in specific patient groups

	N-3 fatty acids to improve appetite and body weight
WEAK	<i>In incurable cancer patients undergoing chemotherapy and at risk of weight loss, we suggest to use the supplementation with long-chain n-3 fatty acids or fish oil to stabilize or improve appetite, food intake, lean body mass and body weight.</i>
Questions for research	Effect of long-chain N-3 fatty acids on body composition and clinical outcome in cancer patients undergoing antineoplastic treatment

Nutrition

- **Main goal is to promote energy balance and optimise protein intake**
- **Usual deficits are approx. 300-400 kcal/d and 0.5gProtein/kg/d**
- **Best approach is with normal food**
- **Can use conventional oral supplements but recent meta-analysis did not show benefit after correction for heterogeneity***
- **EPA enriched supplements result in increased energy and protein intake, increased LBM (1.6kg) and improved appetite and fatigue****

*Baldwin C et al J Natl,Can Inst 2012;104:371-85

**Sanchez-Lara K et al Clin Nutr 2014;e-pub

ORIGINAL ARTICLE

Oral nutritional supplements containing n-3 polyunsaturated fatty acids affects quality of life and functional status in lung cancer patients during multimodality treatment: an RCT

BS van der Meij¹, JAE Langius², MD Spreeuwenberg², SM Slietmaker³, MA Paul⁴, EF Smit⁵ and PAM van Leeuwen⁴

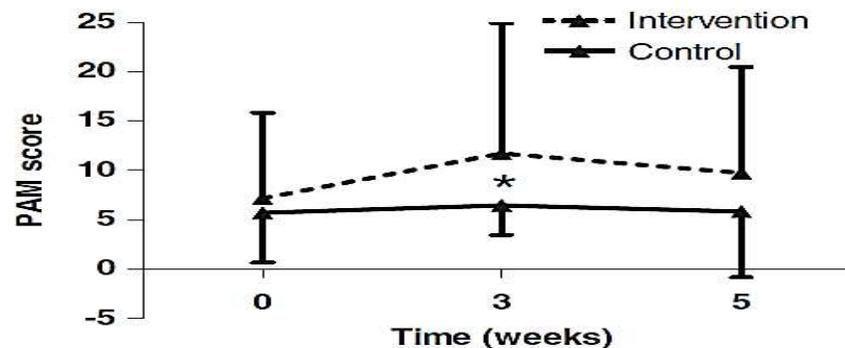
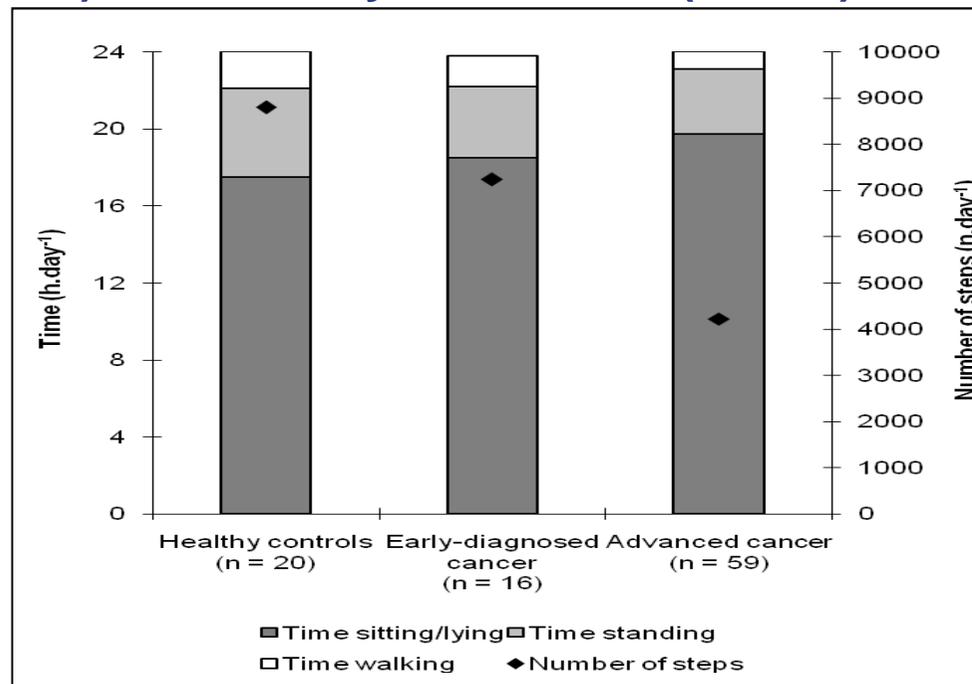


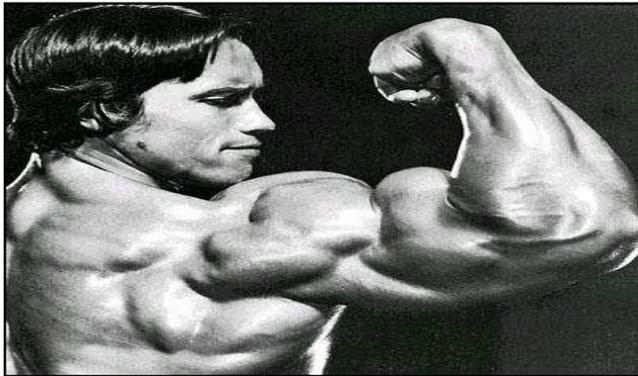
Figure 1. Physical activity (daily PAM score) over time for the I and C groups. Values are mean \pm s.d., baseline: $n = 12$ (I), $n = 16$ (C); week 3: $n = 13$ (I) and $n = 17$ (C); week 5: $n = 8$ (I), $n = 13$ (C). * $P < 0.05$, difference between the I and C group (analysed by generalised estimating equations, with baseline value and sex as covariate).

Spontaneous PA (time spent sitting / lying, time standing, time walking and number of steps/day) of cancer patients at different stages of disease (n = 75) and healthy volunteers (n = 20).



Ferrioli et al et al 2012

Exercise alongside nutrition



- Improved lower and upper limb strength (~20%)
- Increased lean body mass (~1kg)
- Improved HRQoL including physical functioning, role functioning, social functioning and fatigue

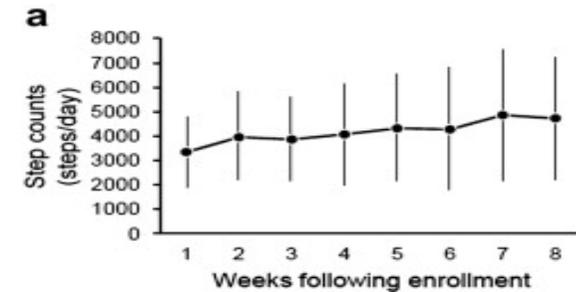
Mishra SI et al Cochrane 2012
StrasserB et al Med Sci Sports Exerc 2013
Stene GB et al Crit Rev Oncol Haematol 2013

At home

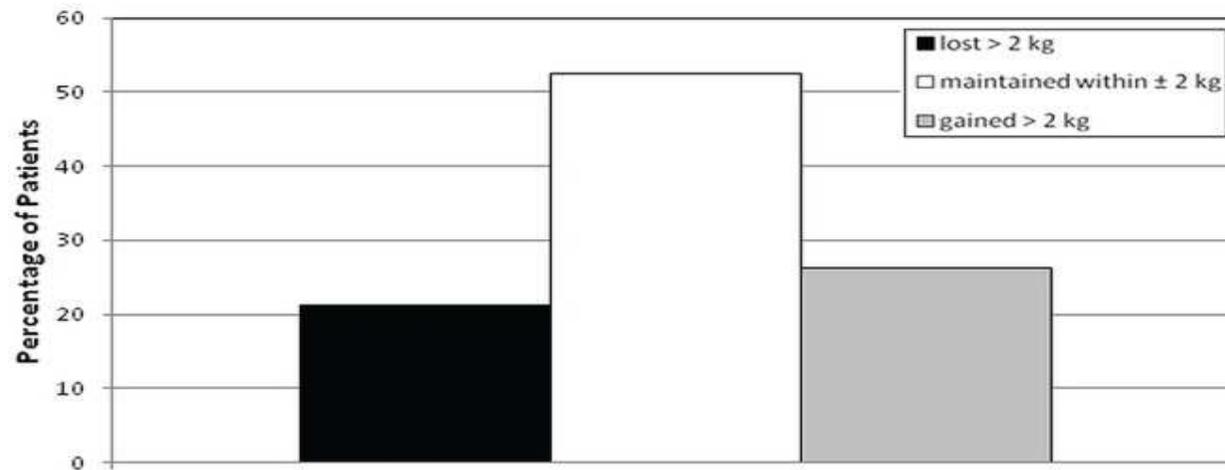
Original Article

A Home-Based Exercise Program to Improve Function, Fatigue, and Sleep Quality in Patients With Stage IV Lung and Colorectal Cancer: A Randomized Controlled Trial

- 66 patients (half on active treatment)
- resistance training + pedometer
- 90min, four times weekly, 8 weeks
- improved mobility, fatigue, sleep quality



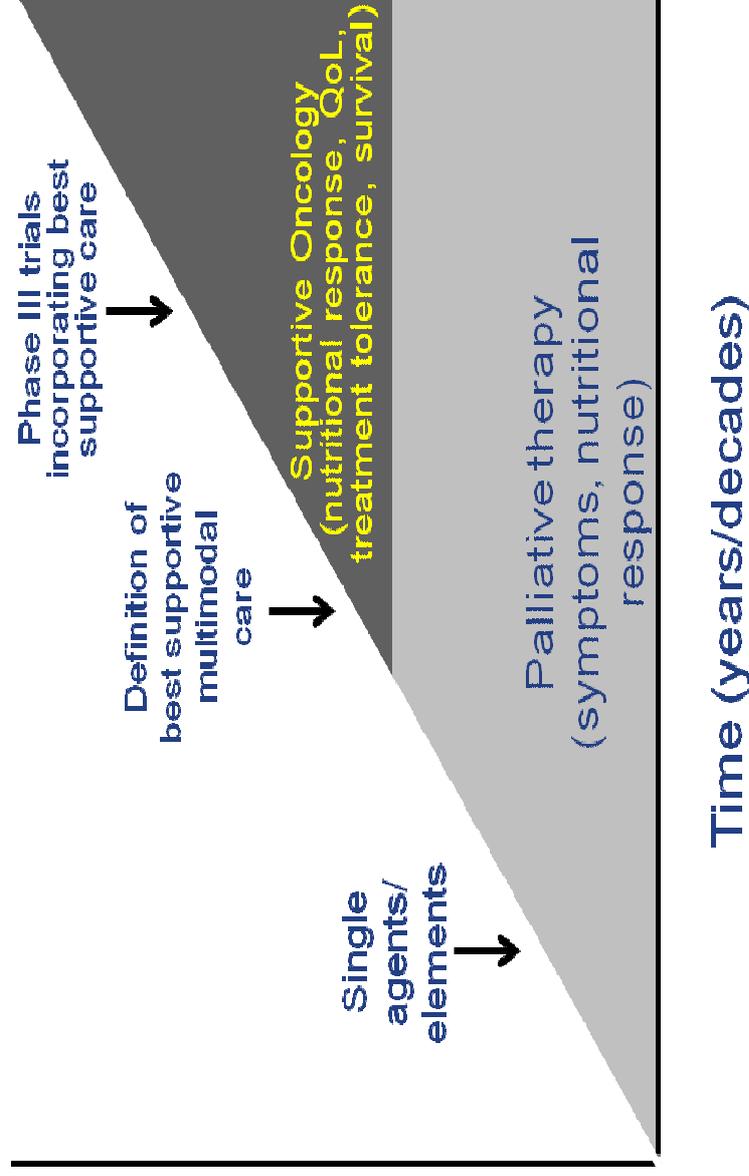
Interdisciplinary rehabilitation (10-12w) in advanced cancer (n=188)



- 30% did not complete all sessions
- Physician, nurse, dietician and regular visits and calls
- Improved QoL; activity and physical fatigue (E.S. 0.8-1.1)
- Six min walk increased by 41m (10%)
- Gait speed increased by 0.15m/s (10%)

Gagnon B et al Curr Oncol 2013;20:310-8

Evolution of Cachexia and Therapy



CONCLUSIONS...

- **No simple solution**
- **Cachexia therapy should be integrated in overall oncology management**
- **Early intervention**
- **Professionals and nurses need adequate knowledge on nutrition and exercise**
- **Assessment should be linked to treatment**
- **Goals should be realistic**
- **Multimodal care pathways are self-evident but still to be evidence-based**