SAHLGRENSKA
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Metabolic issues in nutrition: Implications for daily care

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Nutritional problems in cancer

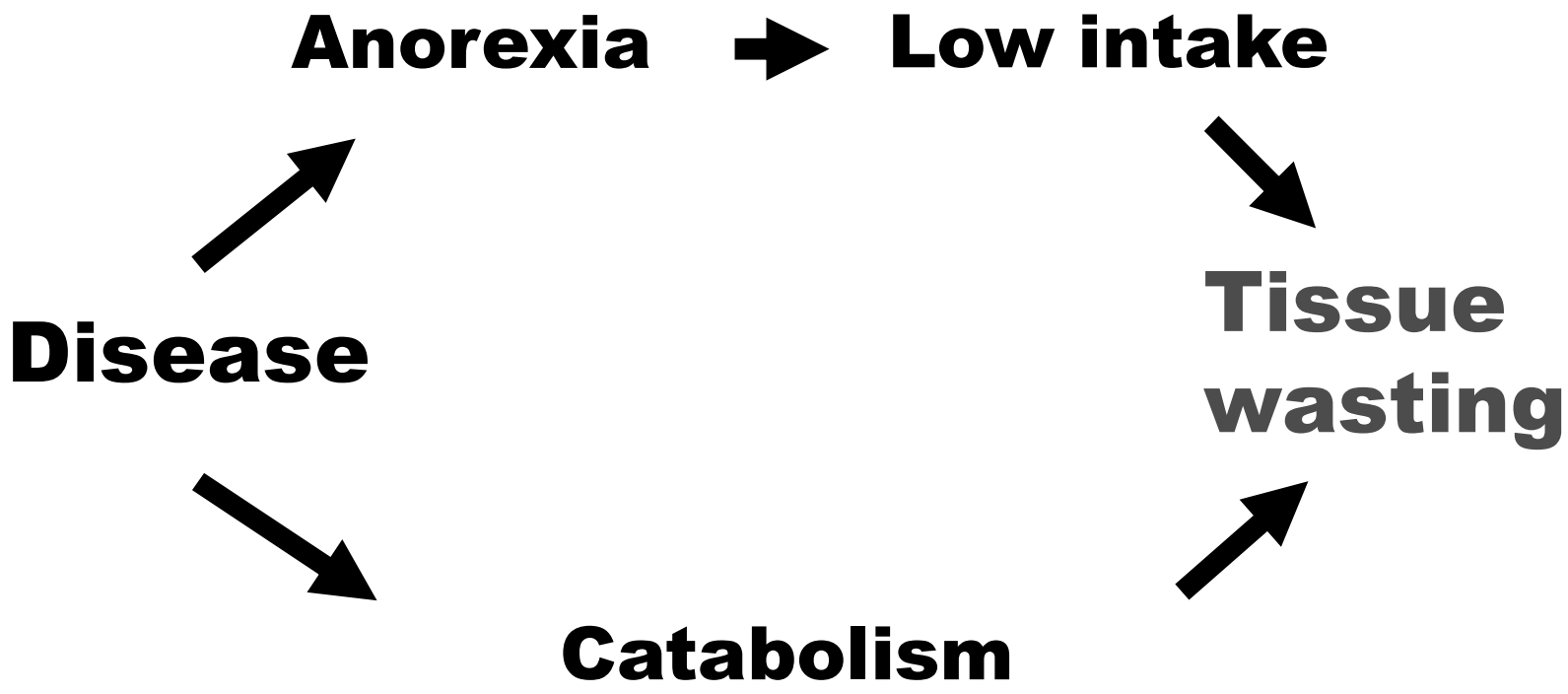
- In western countries, about half of cancer diagnoses end in cure, the other half in death
- Outcome cure: Nutritional problems largely treatment-related and reversible
- Outcome incurable: Frequent and severe progressive malnutrition and wasting

Baracos Annu Rev Nutr 2006

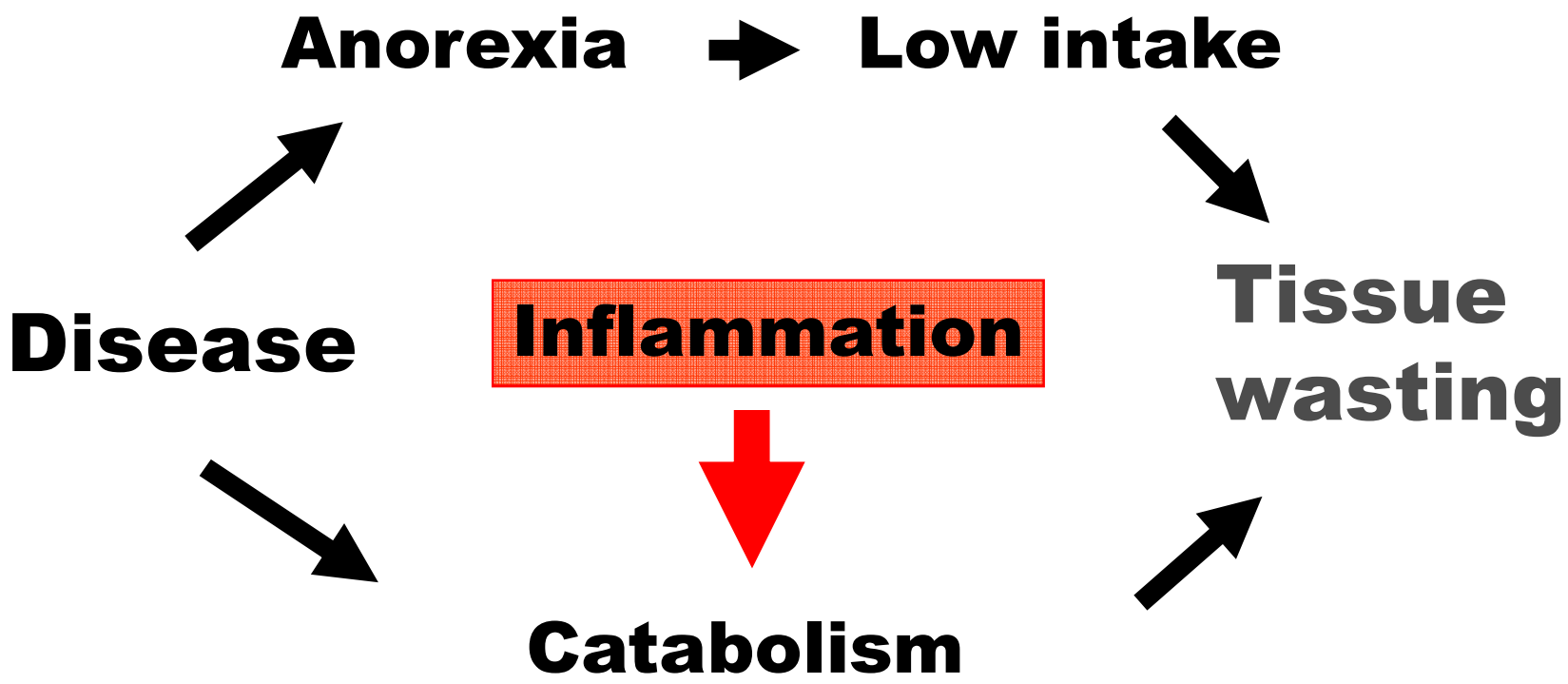
Malnutrition in cancer patients

- Associated with adverse outcomes
- Involves loss of muscle and fat
- Reflects a catabolic metabolism
  - Host response to tumour presence
  - Tumour factors

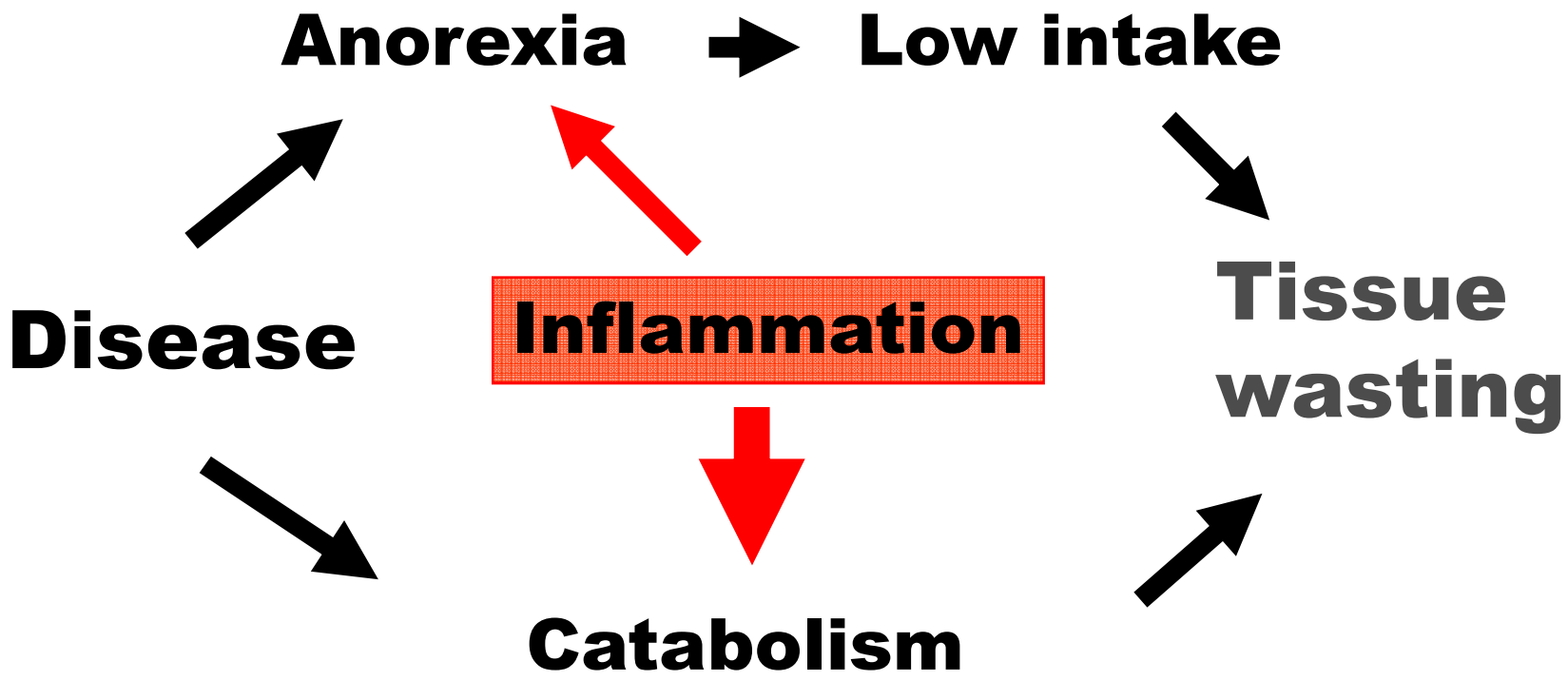
Development of malnutrition: The two pathways



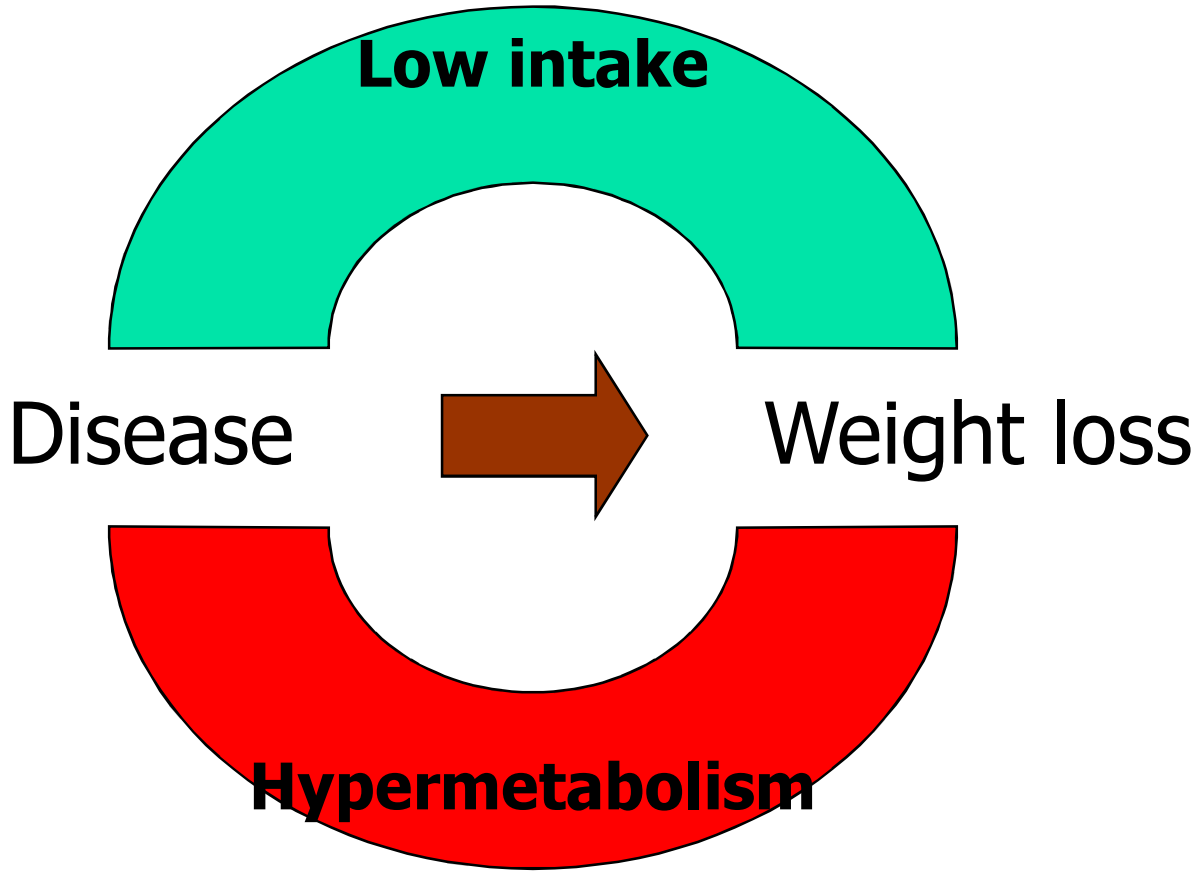
Development of malnutrition: The two pathways



Development of malnutrition: The two pathways



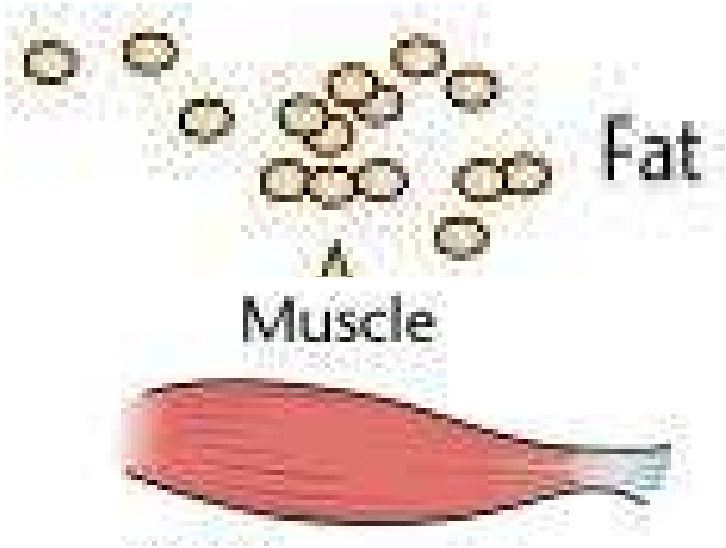
The pathways to weight loss



How do the pathways differ?

Low intake =
Negative energy balance

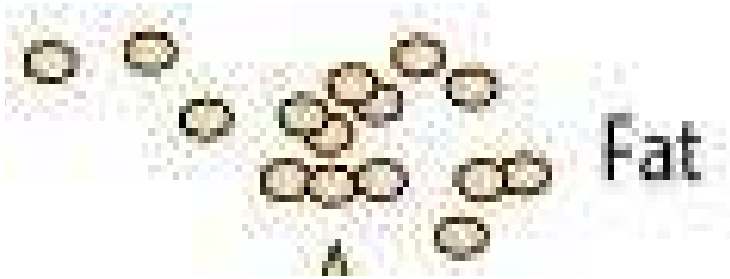
Fat stores depleted more than muscle



Cancer cachexia with systemic inflammation

Muscle breakdown and fat depletion

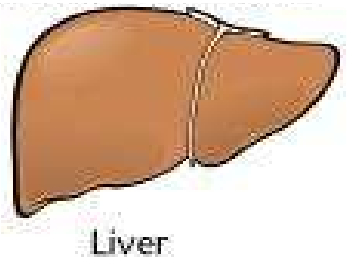
Cancer cachexia: Loss of muscle and fat



Fuel for energy deficit:
↑Lipolysis

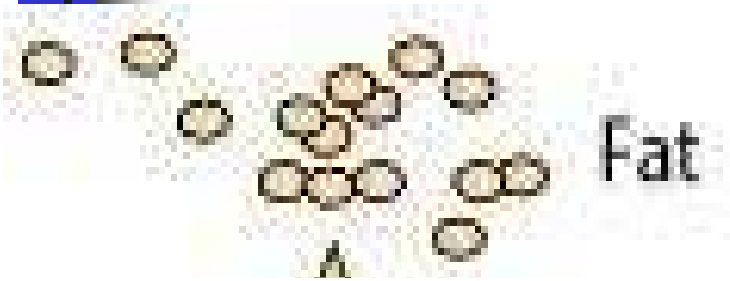
↓ Protein synthesis
↑ Protein breakdown

Fuel for hepatic protein & glucose synthesis



Preservation of viscera

Nutritional support in cachexia: Limited effect – one pathway

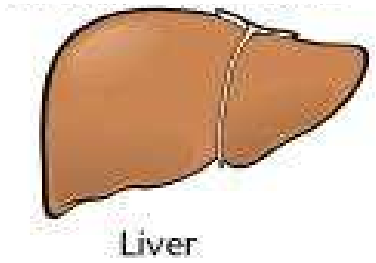


Fat stores repleted

but

Muscle breakdown continues
driven by systemic inflammation

Skeletal muscle loss

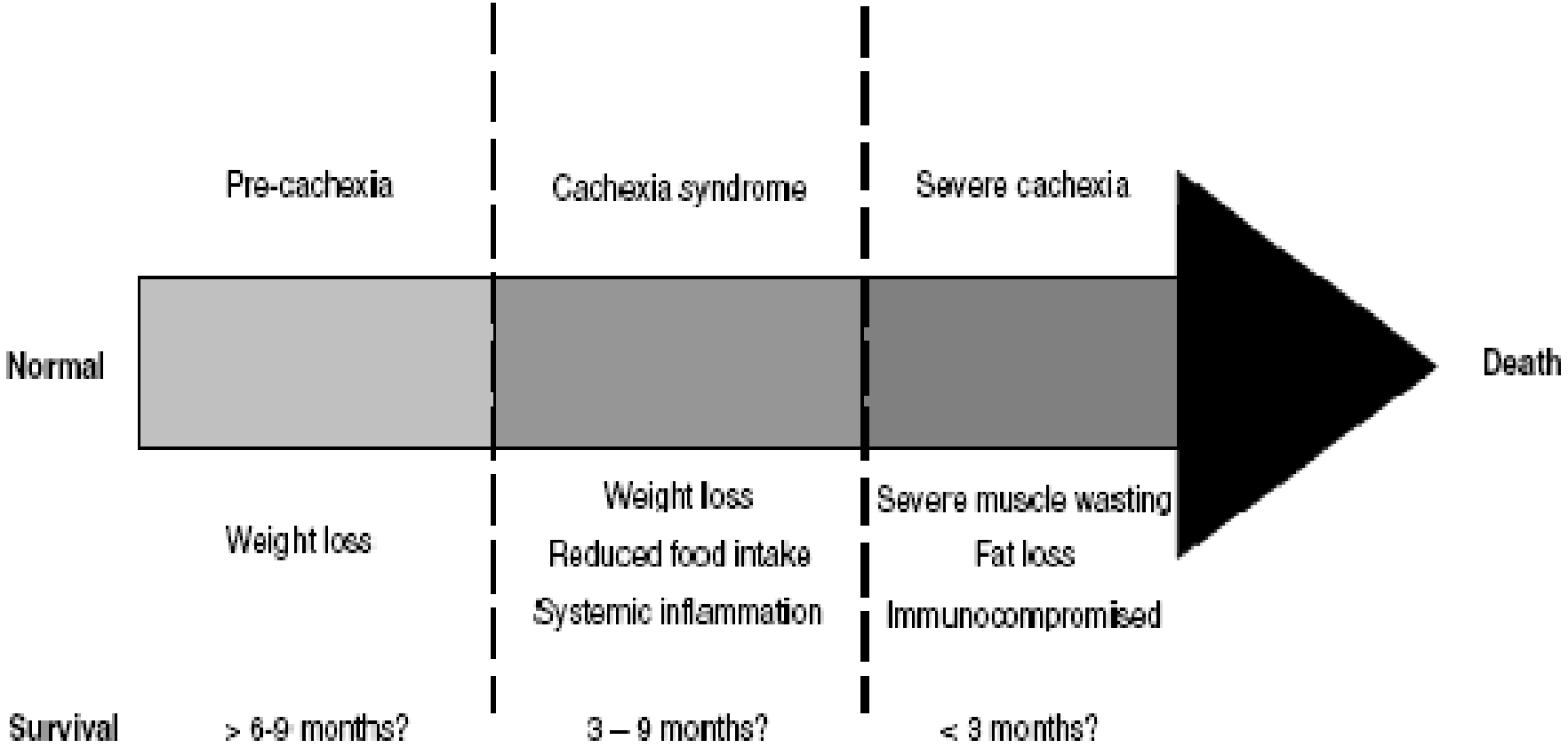


Preservation of viscera

Cancer cachexia – depletion perspective

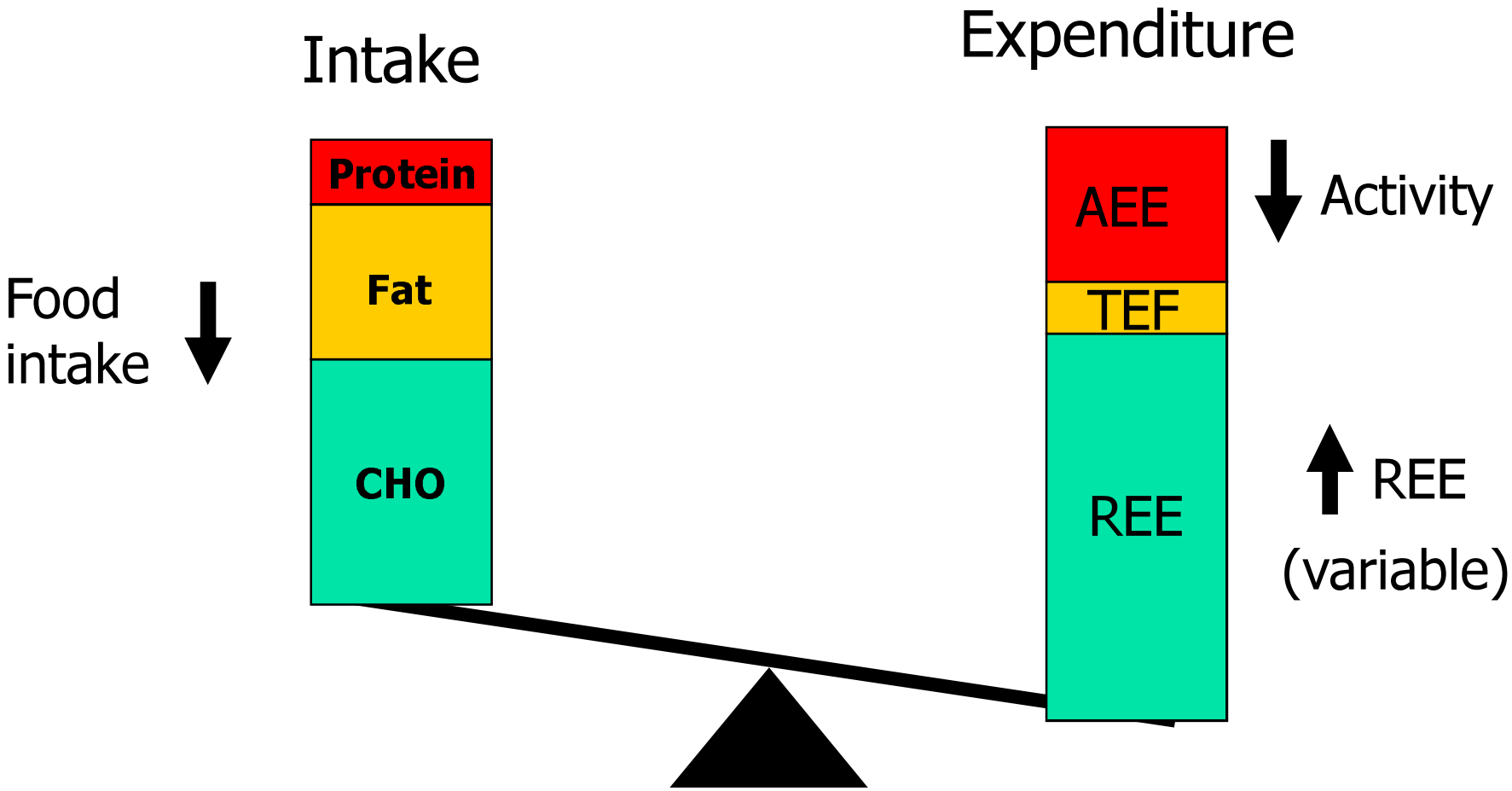
- Emaciation – ”skin and bones”
- A state of depletion: How quantify?
- Underweight:
  - Whole body level: BMI (kg/m^2)
  - Fat mass index (kg/m^2)
  - Fat-free mass index (kg/m^2)
  - Skeletal muscle mass index (kg/m^2)
- Requires defined cut-offs and standardized body composition measurements

The cachexia journey



Fearon 2008

Negative energy balance in cancer



Diet, REE and weight loss in cancer
Conclusions

- Weight loss, reflecting negative energy balance, decreases survival in advanced cancer
- Increased REE and low energy intake both contribute to negative balance
- Therapy based on intervention towards both mechanisms might improve survival

Bosaeus et al 2001

Diet, REE and weight loss in cancer
Follow-up at 4 months – energy intake

- Low energy intake was associated with decreased survival
- Increased energy intake during follow-up was associated with increased survival
- Mean survival w/increased intake: 480 d
- Mean survival w/decreased intake: 331 d

Bosaeus et al 2002

Catabolic response in cancer

- Many parallells with systemic inflammation
- Mechanisms of catabolism in acute and chronic illness are thought to be similar
- In cancer, both tumour-derived and host-derived mediators

Catabolic response - mediators

- Tumour-derived, e.g.
  - Proteolysis-inducing factor (PIF)
  - Lipid mobilizing factor (LMF)
- Host-derived:
  - Cytokines
  - Eicosanoids
  - Neuroendocrine

Anti-inflammatory agents

- N-3 fatty acids: EPA
- NSAIDs
- Macrolide antibiotics
- Cytokine inhibitors
- Thalidomide
- Pentoxyphylline

General: Few RCTs, trials needed to establish efficacy

Anabolic agents?

- Insulin
- Steroid hormones/analogues
- Growth hormone
- IGF-1
- Beta-adrenergic agonists

General: Trials needed to establish effect

Insulin effects in cancer cachexia

- RCT (n=138), all received best available palliative support (anti-inflammatory treatment (NSAID) + nutrition support + anemia prevention)
- Intervention: Insulin 0.11 ± 0.05 units/kg/d for 193 ± 139 days

Lundholm et al Clin Cancer Res 2007;13:2699

Insulin effects in cancer cachexia

- Carbohydrate intake, body fat and metabolic efficiency during exercise increased
- Physical activity, fat-free mass and quality of life scales were unchanged
- Survival was increased ($p<0.03$), mean 224 days (study), 175 days (control)

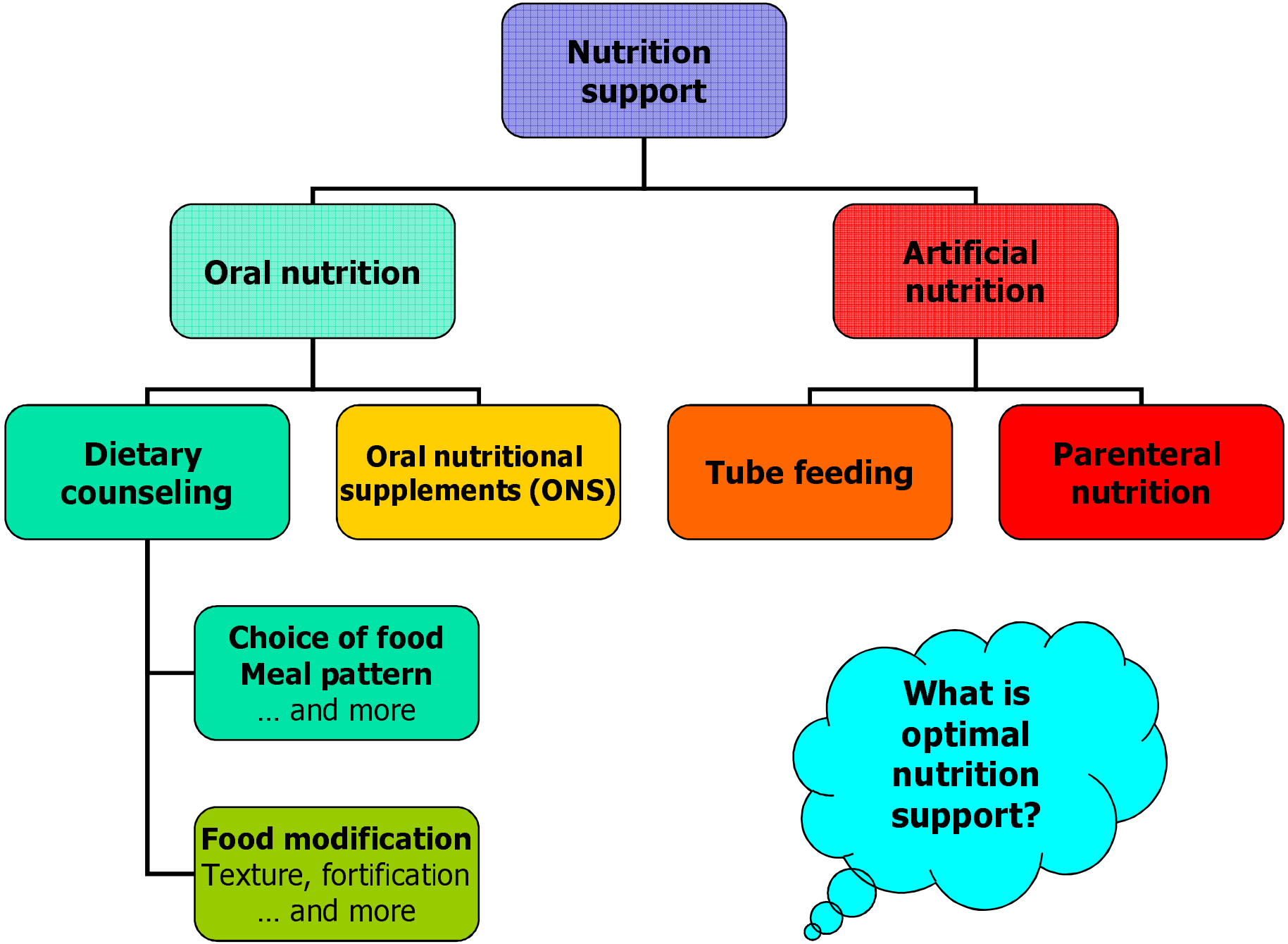
Lundholm et al Clin Cancer Res 2007;13:2699

How large is the energy deficit?

- Weight loss:

- 5 %/3m (BW 70 kg): 1.2 MJ/d (280 kcal)
- 1 kg/month: 1 MJ/d (240 kcal)
- 1 kg/week: 4 MJ/d (960 kcal)

(Assuming mixed tissue loss, 30 MJ/kg [Elia])

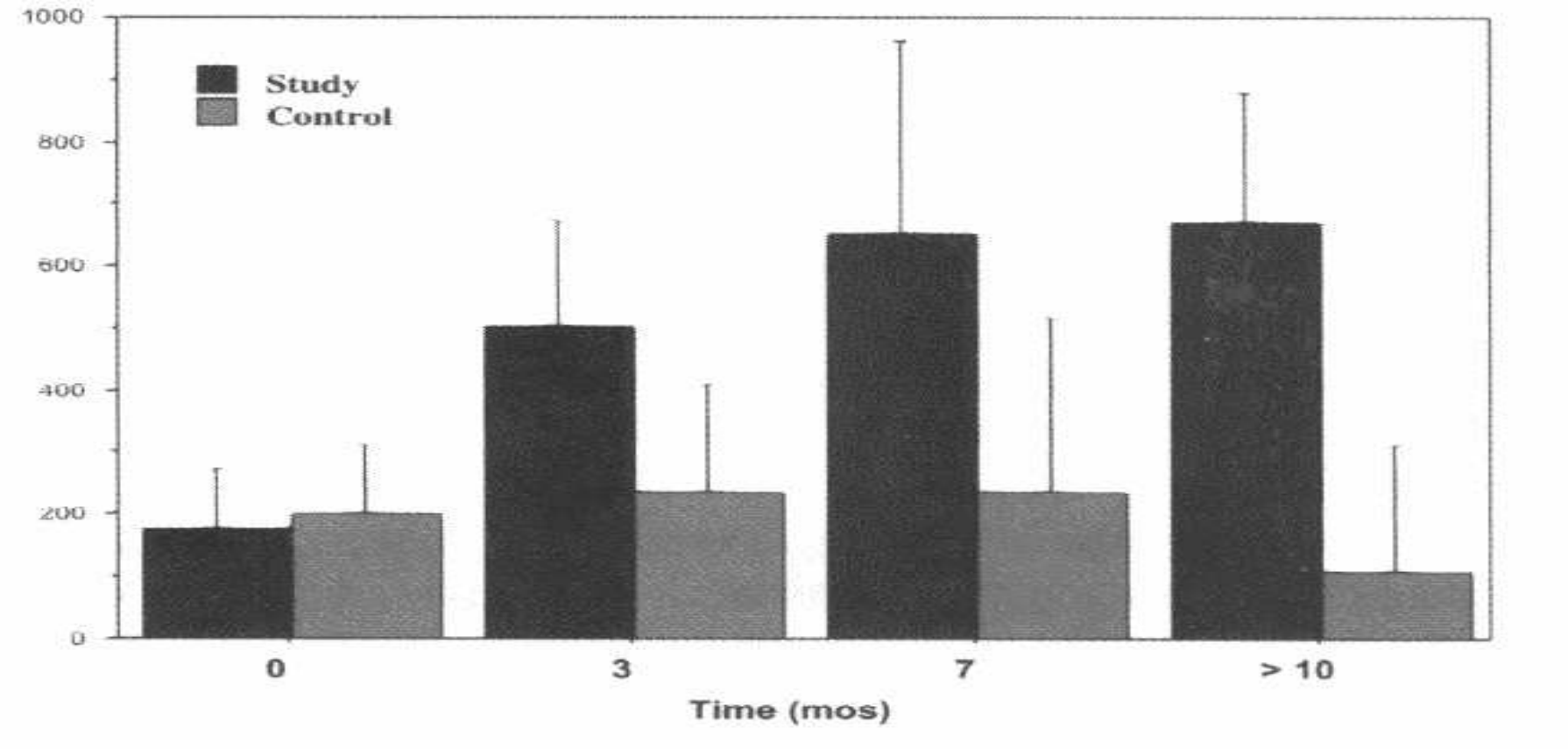

Nutrition support
Oral nutrition
Artificial nutrition
Dietary counseling
Oral nutritional supplements (ONS)
Tube feeding
Parenteral nutrition
Choice of food
Meal pattern
... and more
Food modification
Texture, fortification
... and more
What is optimal nutrition support?

Nutritional intervention

- All patients (n=309):
  - Anti-inflammatory treatment (NSAID)
  - Anemic patients: EPO
- Nutrition support group (n=139):
- 1/ Dietary counseling + oral nutritional supplements
- 2/ Home parenteral nutrition (about 50%, mean duration 46 days)

Lundholm et al 2004

Effects on energy metabolism (intake – REE)



Effects on survival

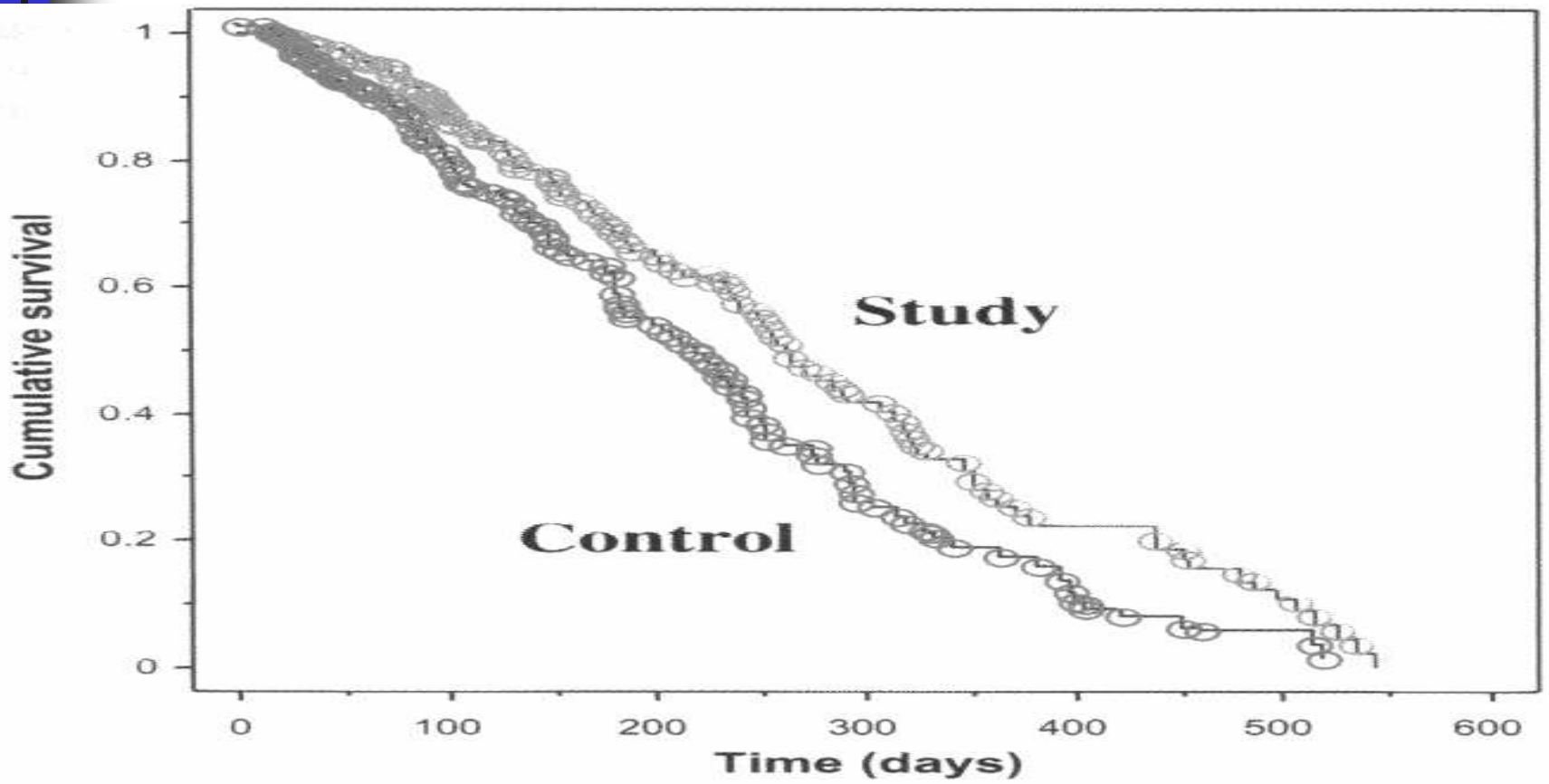


FIGURE 1. Survival data for the study (nutritional support) and control groups over the course of follow-up ('as-treated' analysis; $P < 0.001$).

Conclusions

Our results support that, in patients with wasting due to malignant disease:

1/ Nutrition is a limiting factor influencing survival

2/ Nutrition support can improve energy metabolism and function, when given together with anti-inflammatory treatment.

Perspectives

- What is optimal anti-inflammatory therapy?
- What is the possible role of anabolic therapies?
- What is optimal nutrition support?


Thanks for your attention!
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