



**BOND
UNIVERSITY**
BRINGING AMBITION TO LIFE

ANABOLIC RESPONSE IN CANCER: DOES IT REALLY EXIST?

Dr. Barbara van der Meij

CONTENTS

- Body composition
- Metabolic alterations in cancer
- Anabolic resistance
- Implications for clinical practice





The obesity epidemic in India

73%

of urban Indians
are overweight

Almost 3 out of 4 Indians are overweight



Almost

1/2

urban Indians
are obese!

Max Risk Age: 28 – 38 yrs

Highest risk of weight gain, for men & women

Average person goes from healthy at 26 to obese at 38 yrs.

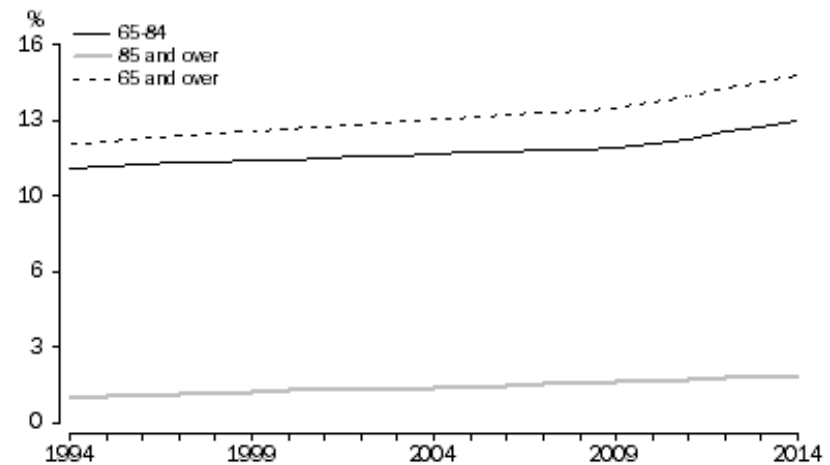
The obesity epidemic in Australia

Currently:

- 30% obesity
- 15% older than 65 y

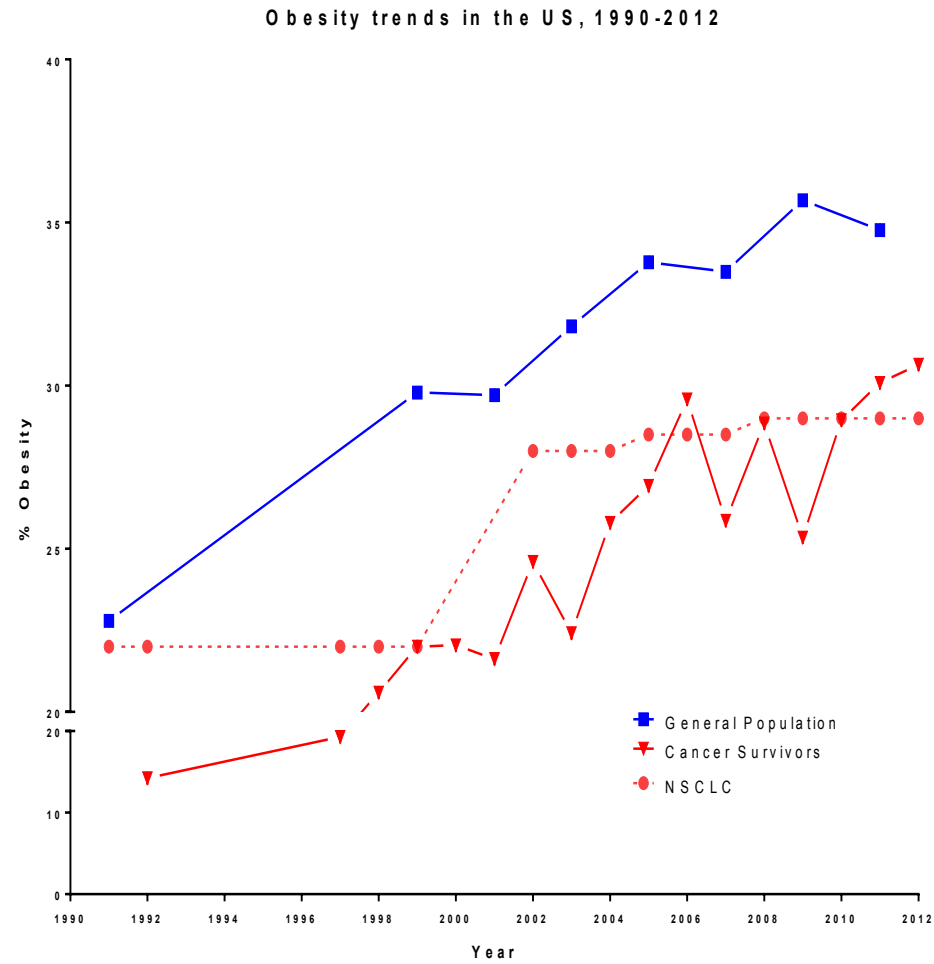
Within a few decades:

- 40% obesity
- 25% older than 65 y



→ More cancer patients with obesity and sarcopenia

The obesity epidemic in cancer

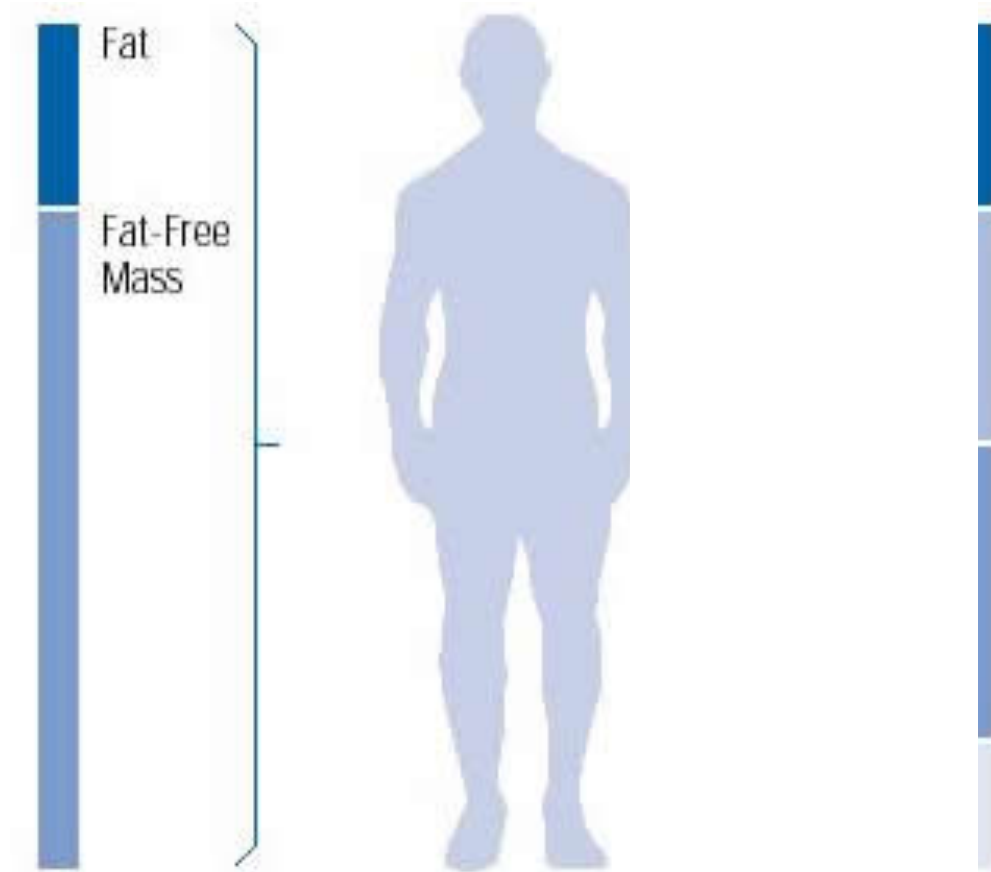




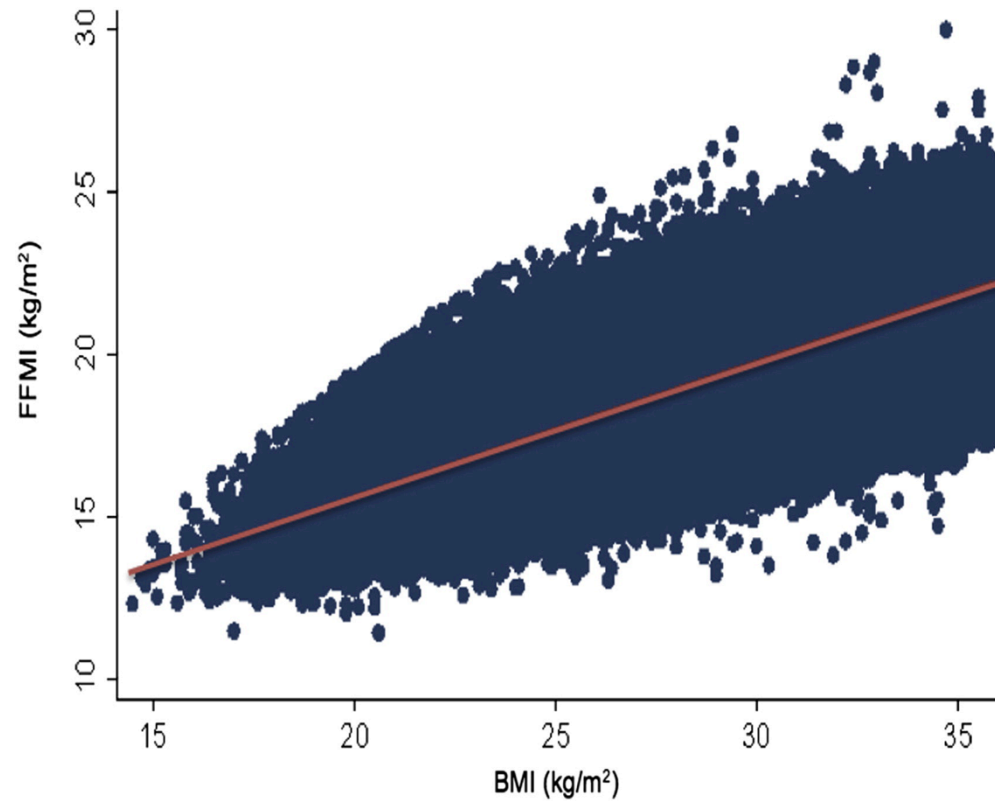
BODY COMPOSITION - INSIGHTS

Anatomic body composition model

- Subcutaneous
- Interorgan
- Skeletal muscle
- Organs
- Bone
- Blood / others



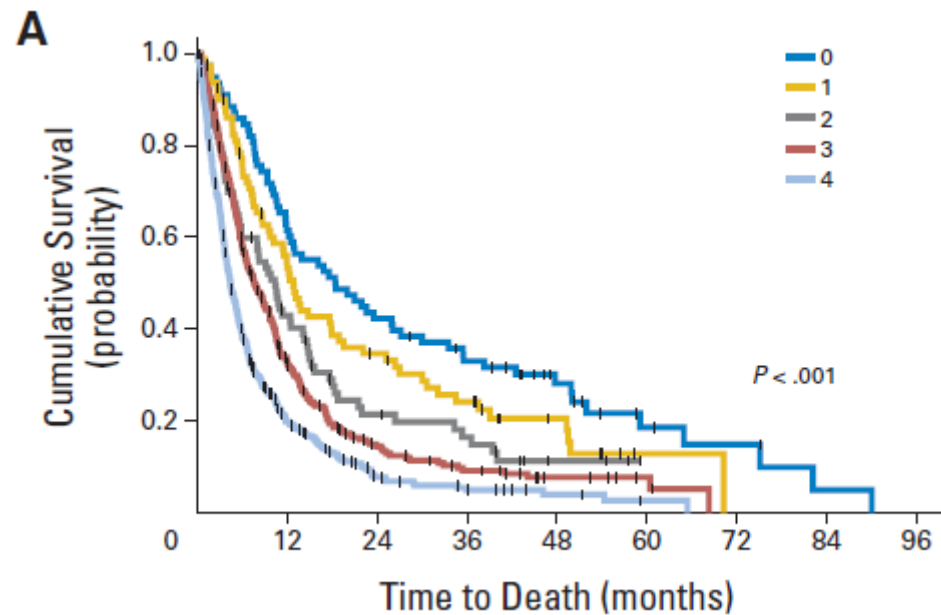
Correlation BMI and FFMi



Correlation between BMI and FFMi in 186,975 healthy white individuals.
R = 0.62, P < 0.001.

Weight loss and BMI – grading system

		BMI (kg/m ²)				
		28	25	22	20	
Weight Loss (%)	2.5	0	0	1	1	3
	6	1	2	2	2	3
	11	2	3	3	3	4
	15	3	3	3	4	4
	15	3	4	4	4	4



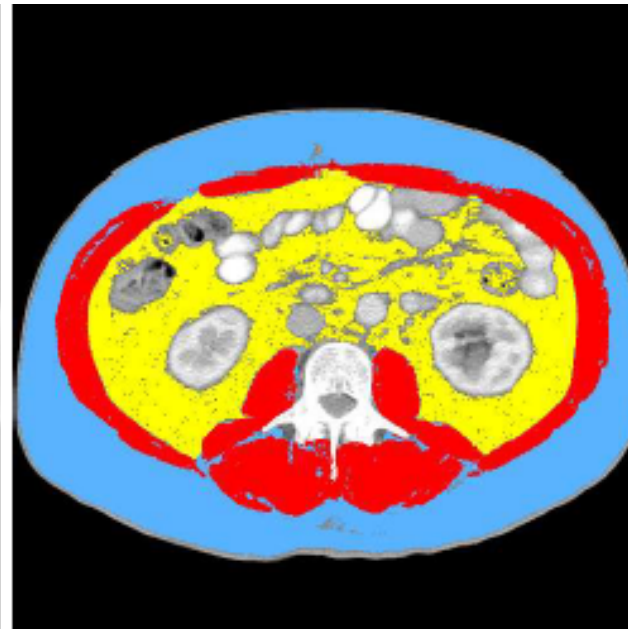
n=8160

Survival grading - independent of cancer, stage, age, performance status

Body composition analyses by CT-scans

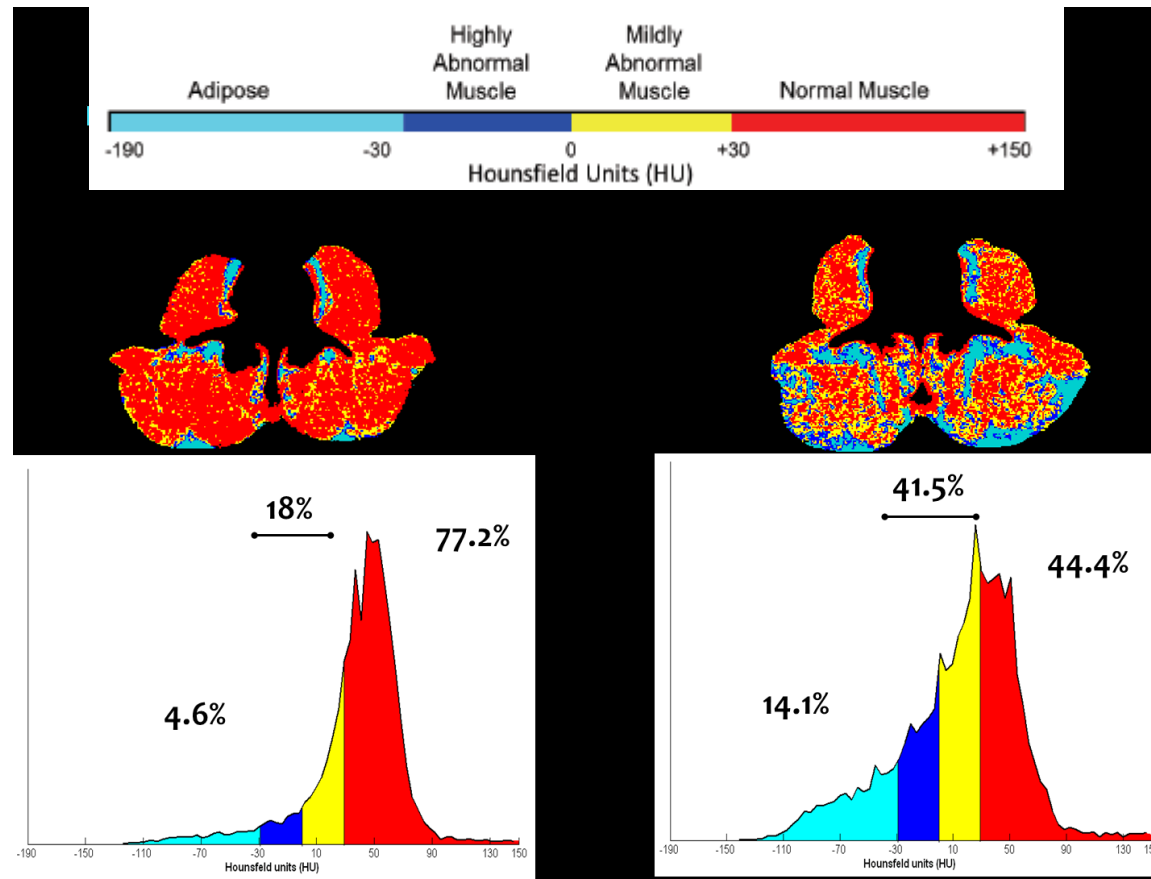


Initial CT-scan



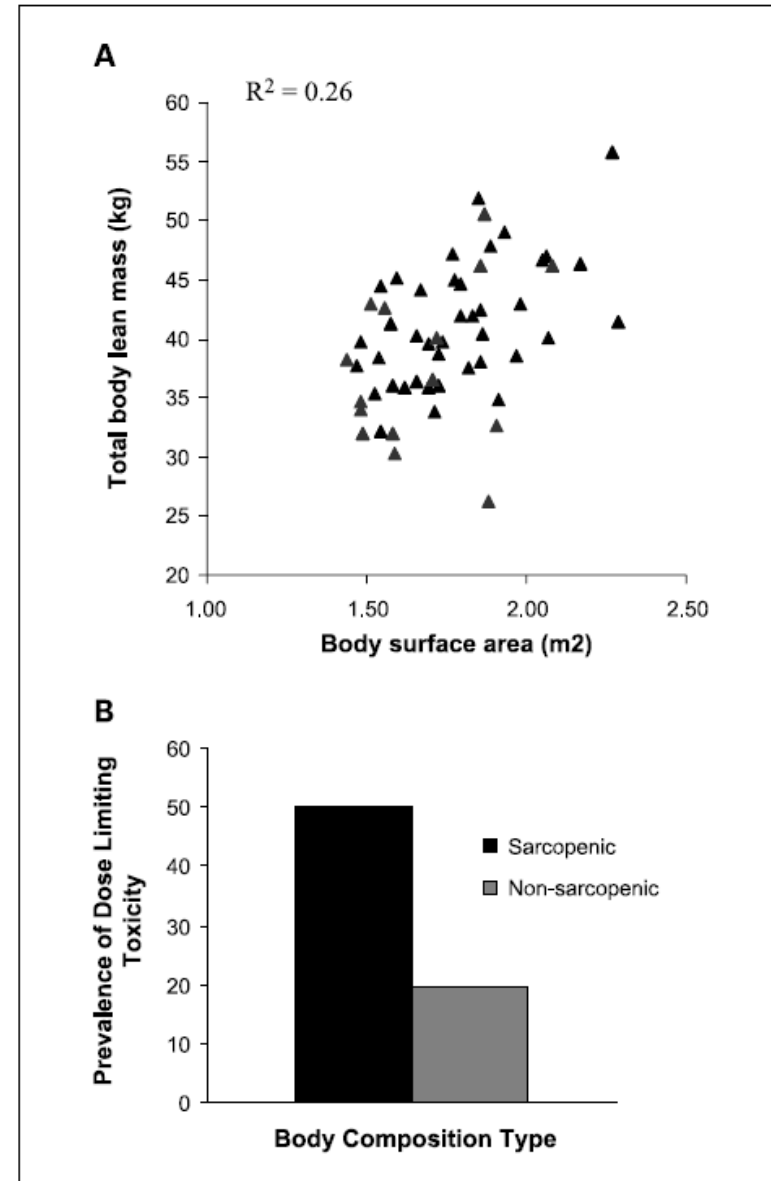
Red: muscle
Blue: subcutaneous fat
Yellow: visceral adipose fat

Muscle fat infiltration



Sarcopenia and toxicity

- Breast cancer, n=55
- Sarcopenia: n=14 (25.5%)
- Sarcopenic patients: more dose limiting toxicity



Weight loss / muscle wasting in cancer:

Associated with...

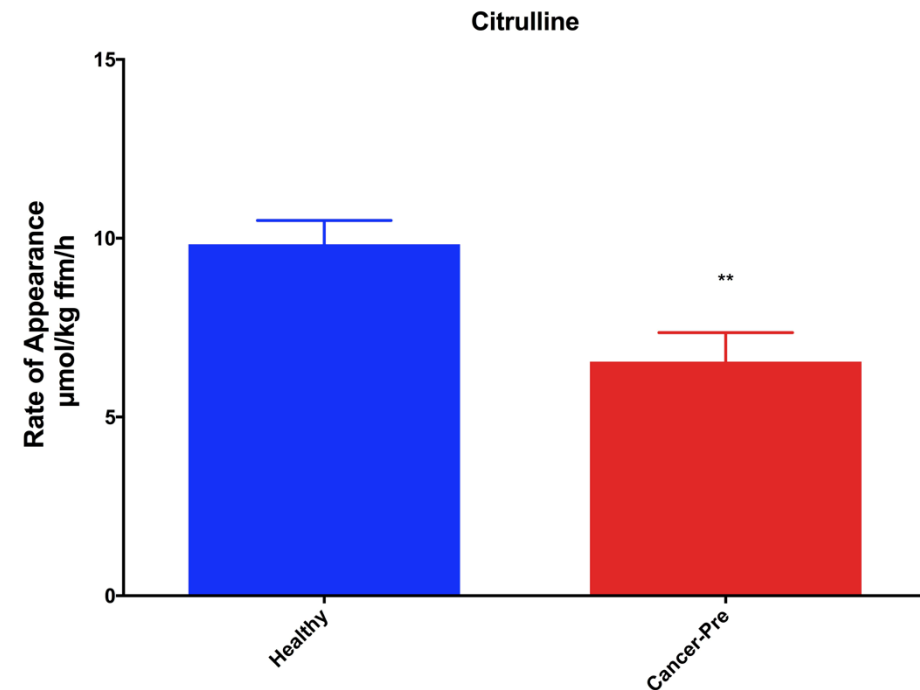
- Fatigue and apathy
- Hospital length of stay ↑
- Increased susceptibility to infection
- Postoperative complications and mortality ↑
- Delay in return to work
- Poor quality of life
- Response to chemo/radiotherapy ↓
- Treatment toxicity ↑

Komurcu, SO, 2000, Rosenbaum, JPEN, 2000,
Curt, Oncol, 2000; Grossmann, Surg, 2002;
Spelten, EJC, 2003, Argiles, Eur J Oncol Nurs, 2005, Gordon,
QJM, 2005, Prado, Appl Physiol Nutr Metab, 2014,
Barret, Nutr Cancer, 2014

Protein metabolism in cancer

Studies in different types of cancer:

- Increased protein turnover
- Increased muscle protein breakdown (and synthesis)
- Changes in amino acid metabolism (e.g. arginine, citrulline, tryptophane)



Characteristic changes in plasma amino acids

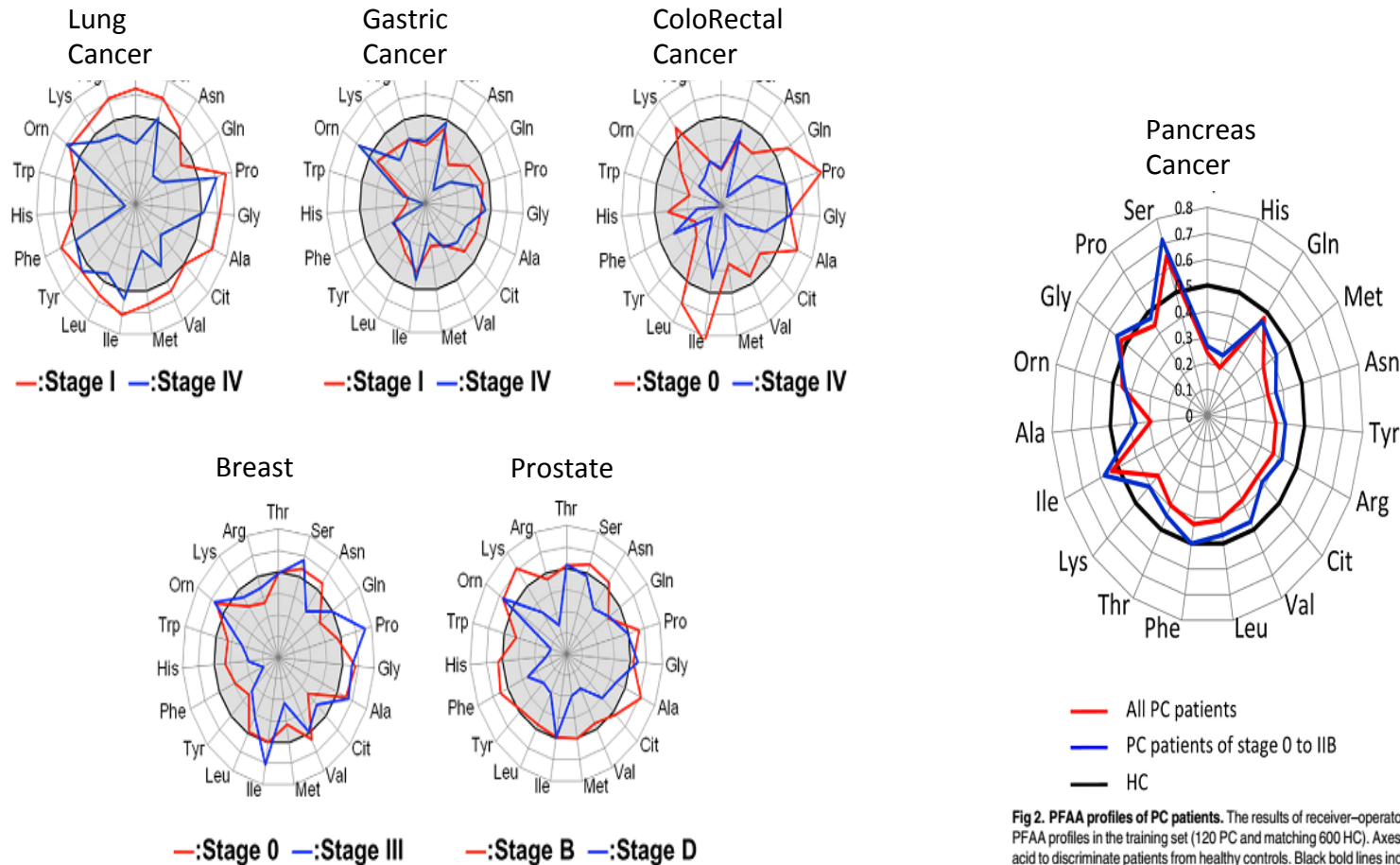
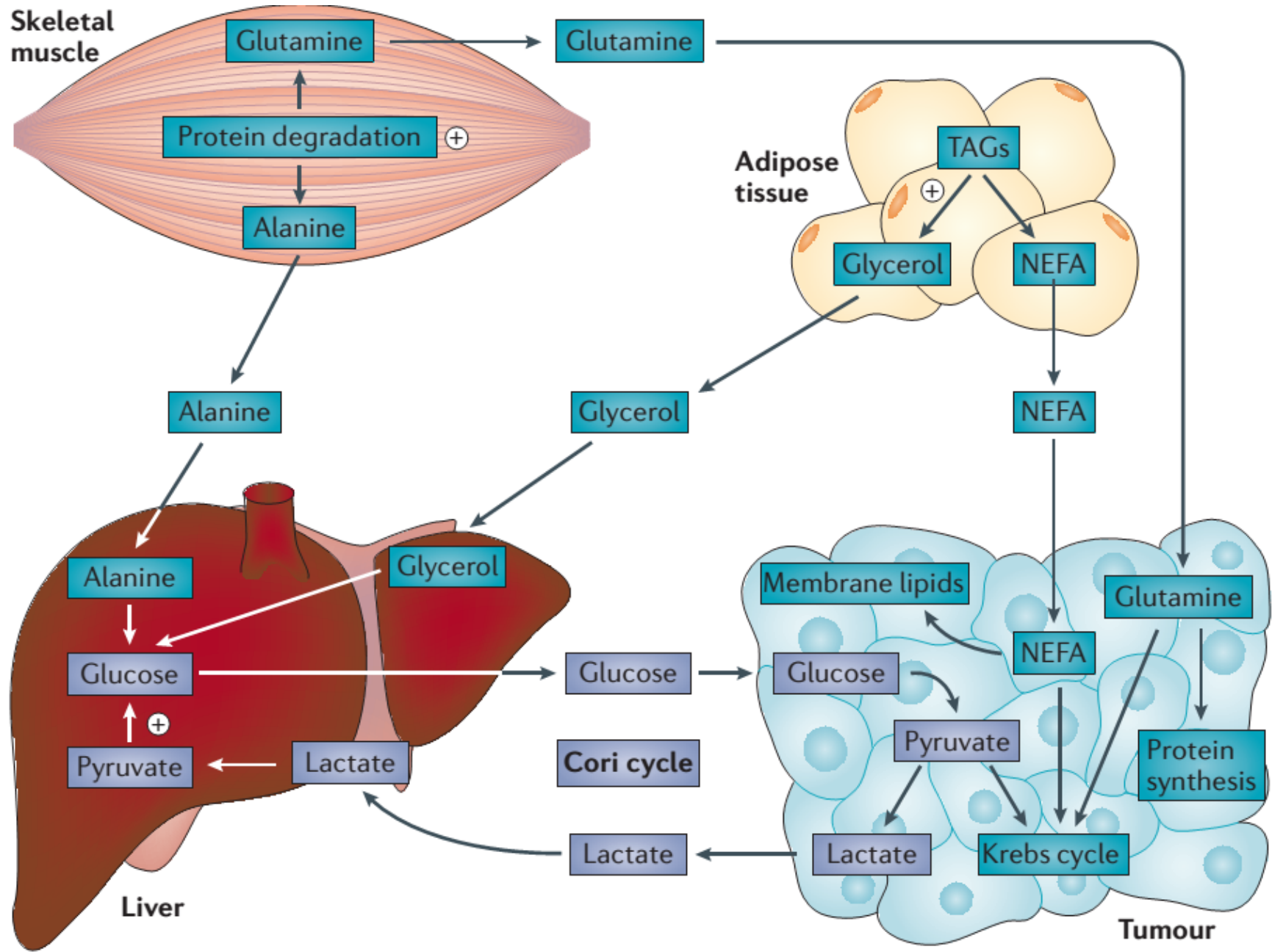
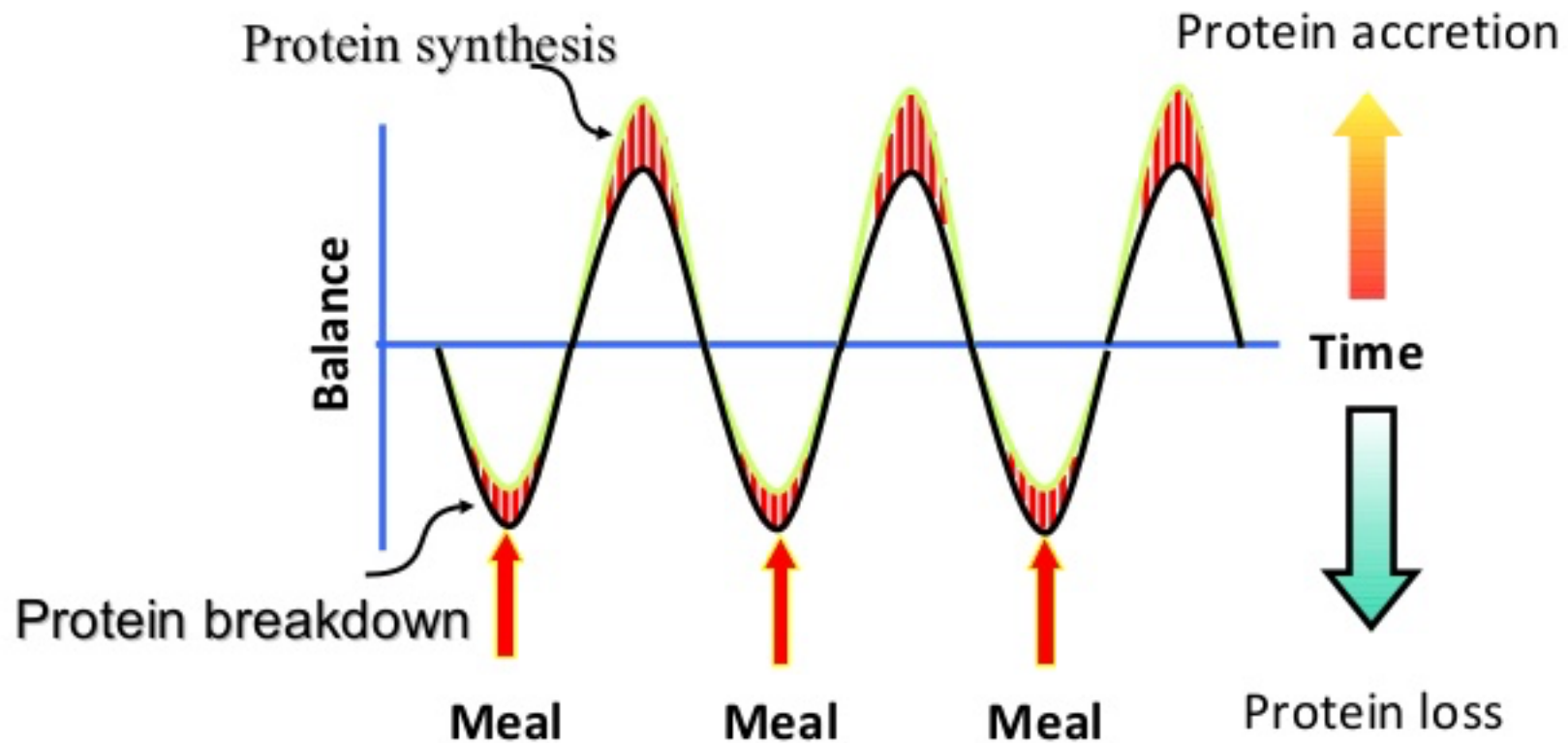


Fig 2. PFAA profiles of PC patients. The results of receiver-operator characteristic (ROC) curve analysis of PFAA profiles in the training set (120 PC and matching 600 HC). Axes show the AUC of ROC for each amino acid to discriminate patients from healthy controls. Black bold lines indicate the point where the AUC of ROC = 0.5.



Muscle Protein Balance



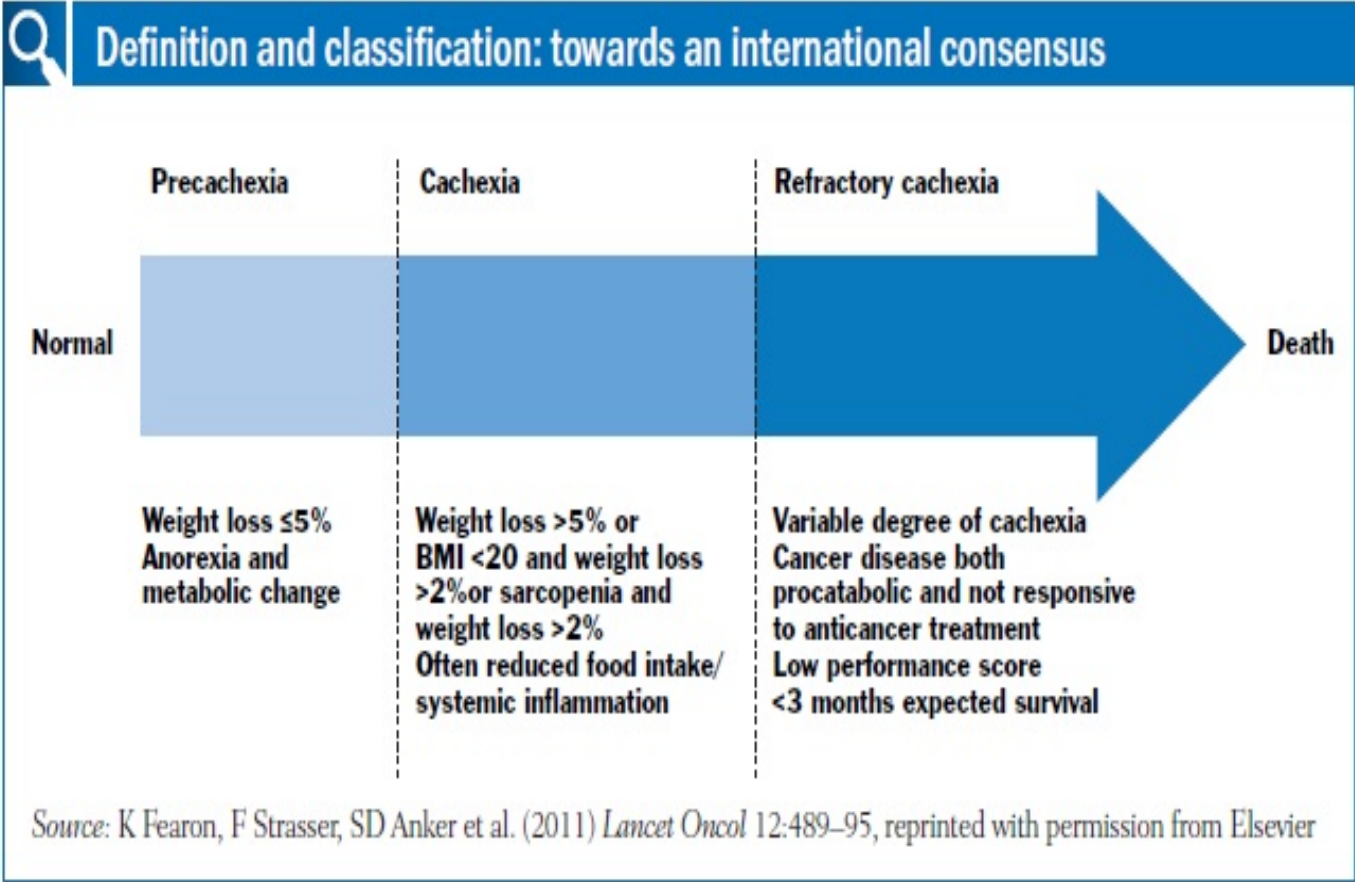
Net protein balance

Synthesis

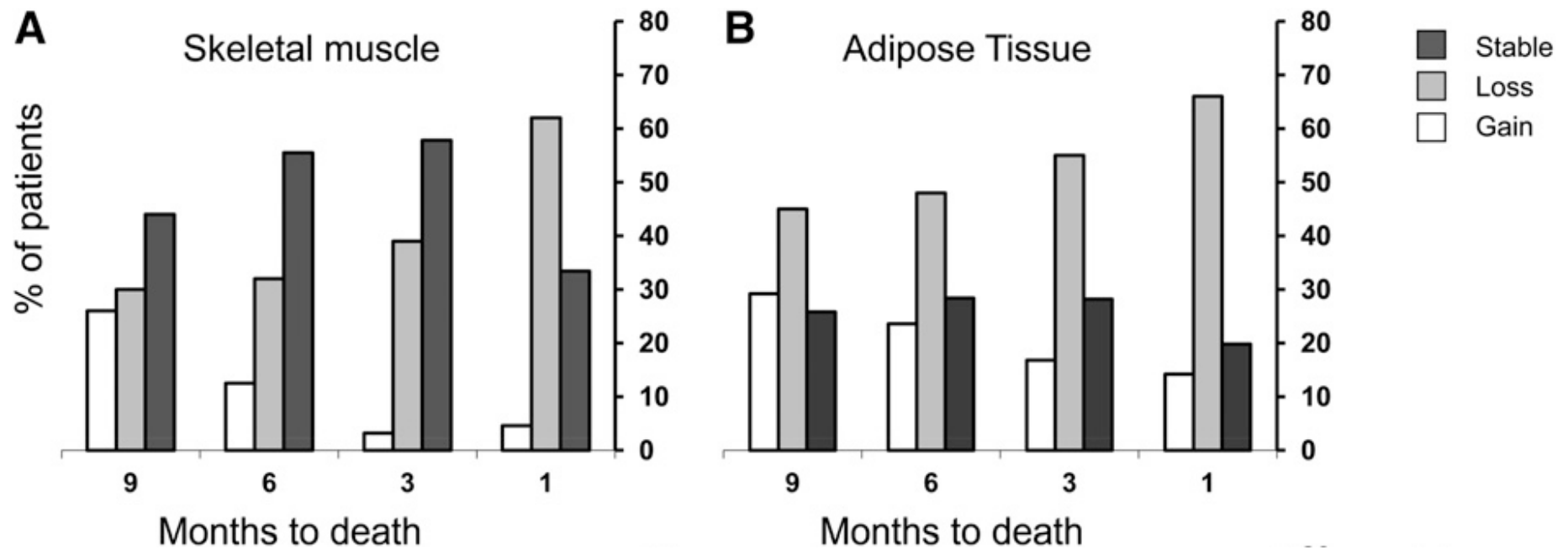


Breakdown

Reverse muscle mass loss in cancer



Muscle and fat loss in cancer



n=368 lung, colorectal, pancreatic and cholangiocarcinoma

Physical activity level

Pancreatic cancer (n=24)

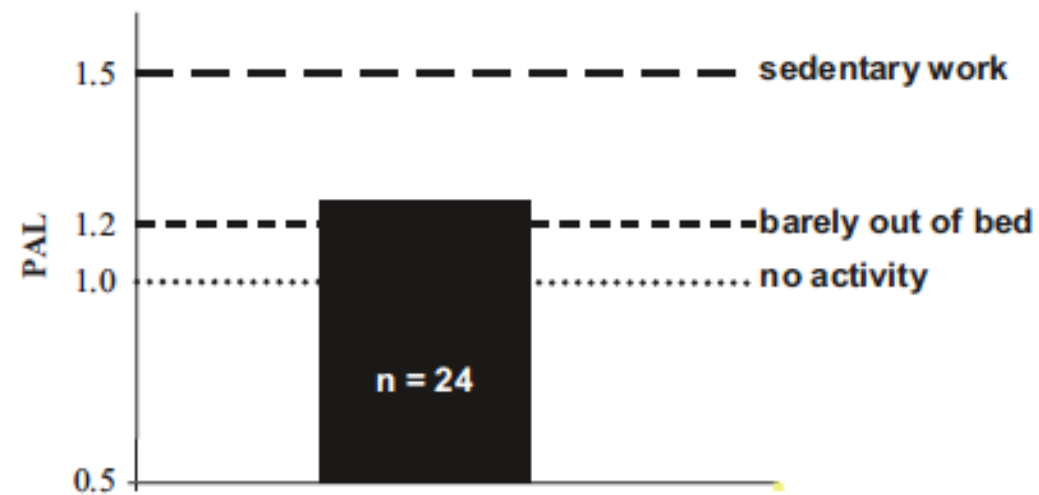
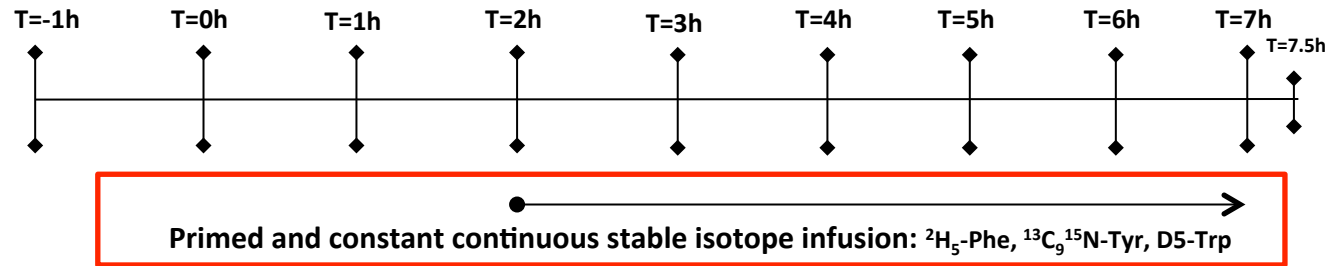


Figure 5 Physical activity (PAL) in cachectic cancer patients. Adapted from Moses et al.⁵⁵

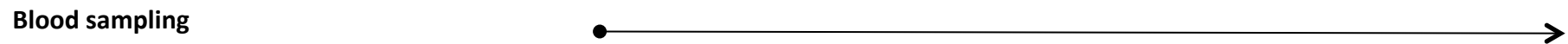
Can cancer patients have an anabolic response to food?



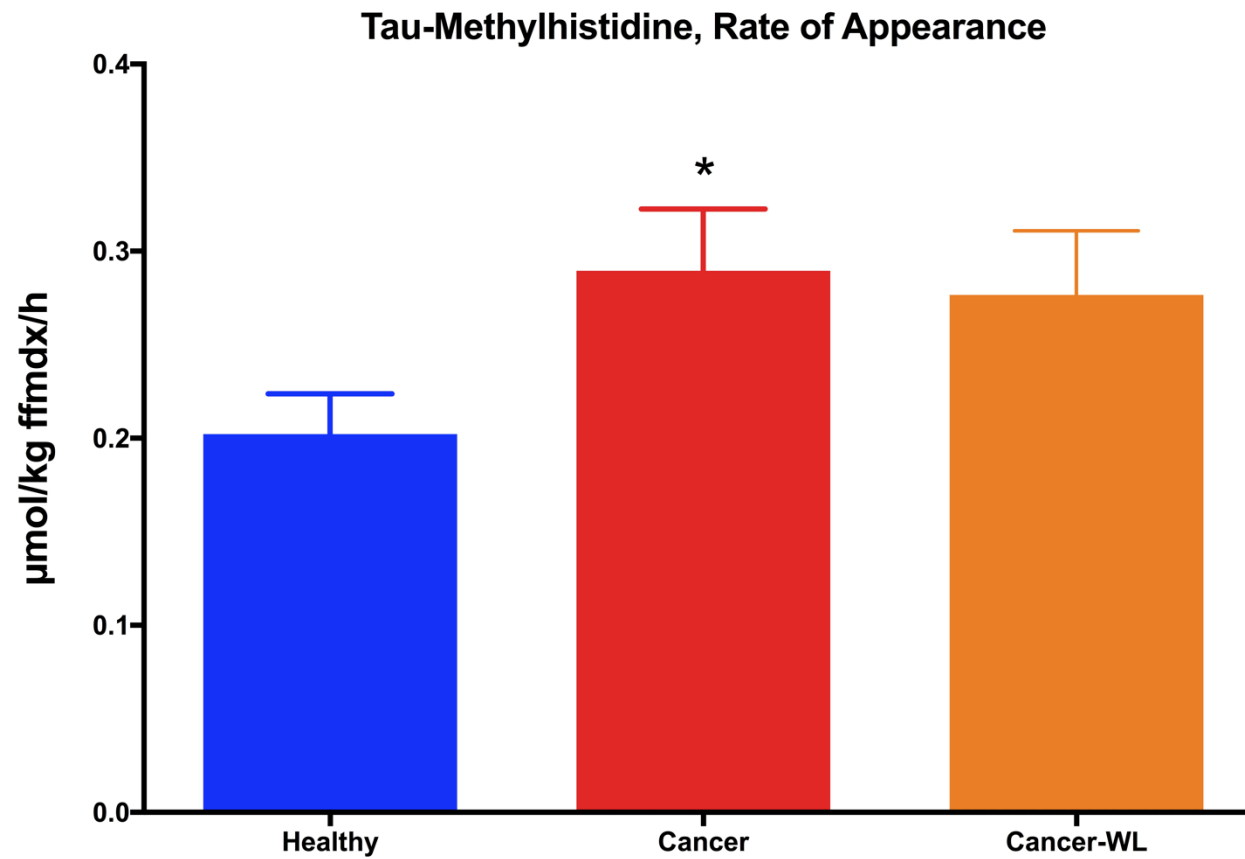


Stable isotope pulse:	X
$^2\text{H}_3\text{-Leu}$, [$^2\text{H}_3$]-3-MetHis, $^2\text{H}_2\text{-Gly}$, 2-D-OHPro,	X
1- $^{13}\text{C-KIC}$, $^{15}\text{N}_2\text{-ARG}$, $^2\text{H}_2\text{-CIT}$, $^{13}\text{C-Urea}$,	
1,2- $^{13}\text{C}_2$ Taurine	
Intake of complete high protein meal and $^{13}\text{C-Phe}$, $^{13}\text{C}_3\text{-Tripalmitin}$,	X
$^2\text{H}_2\text{-Palmitic acid}$, $^{15}\text{N-Spirulina}$	

DXA (wb, hip and spine) & BIA	X
Respiratory and handgrip muscle function	X
Kin Com one leg exercise	
Questionnaires (wellbeing, diet, and cognition)	

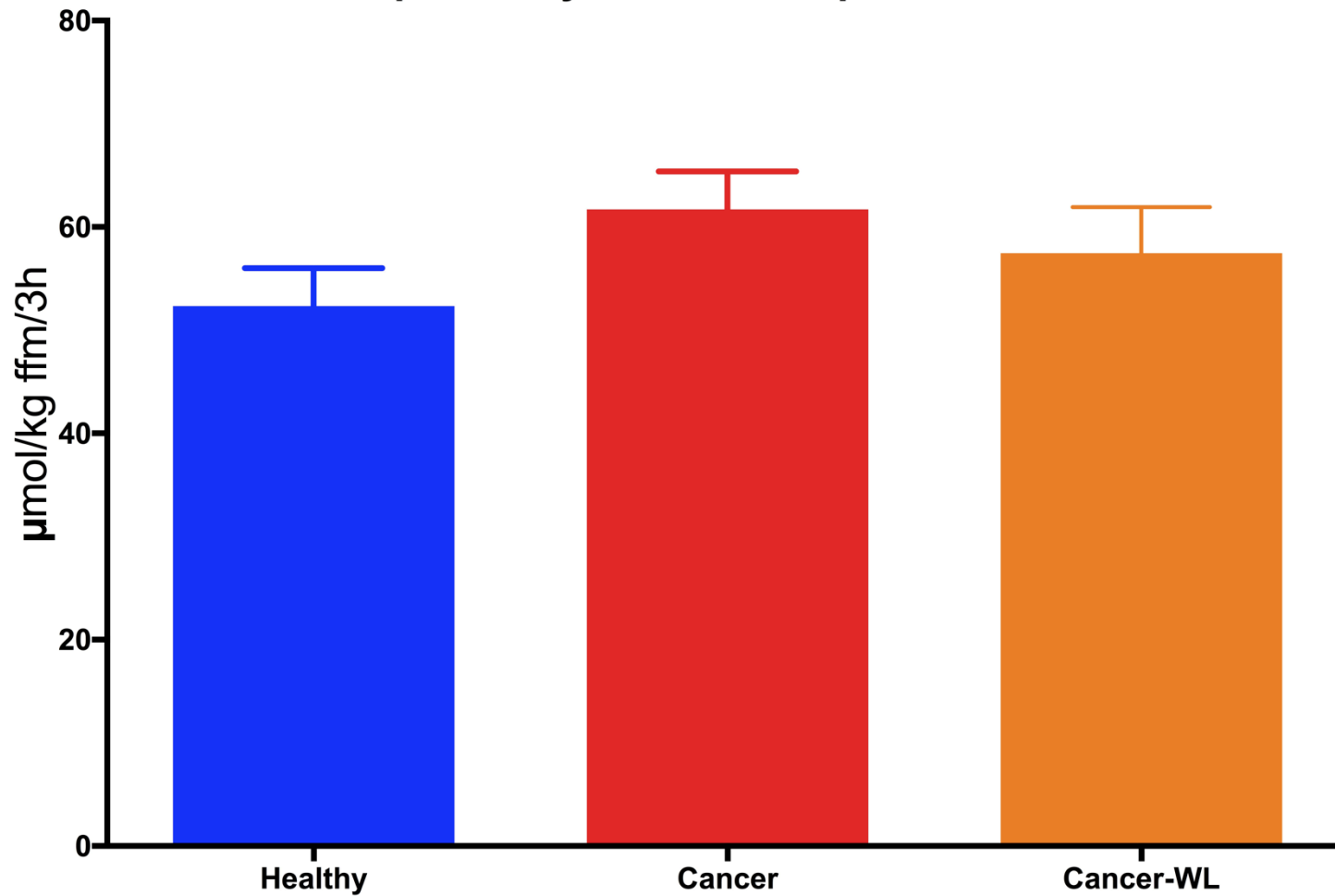


Myofibrillar protein breakdown – fasted



* p=0.03, cancer vs. healthy

Net protein synthesis in response to a meal



MEAL:

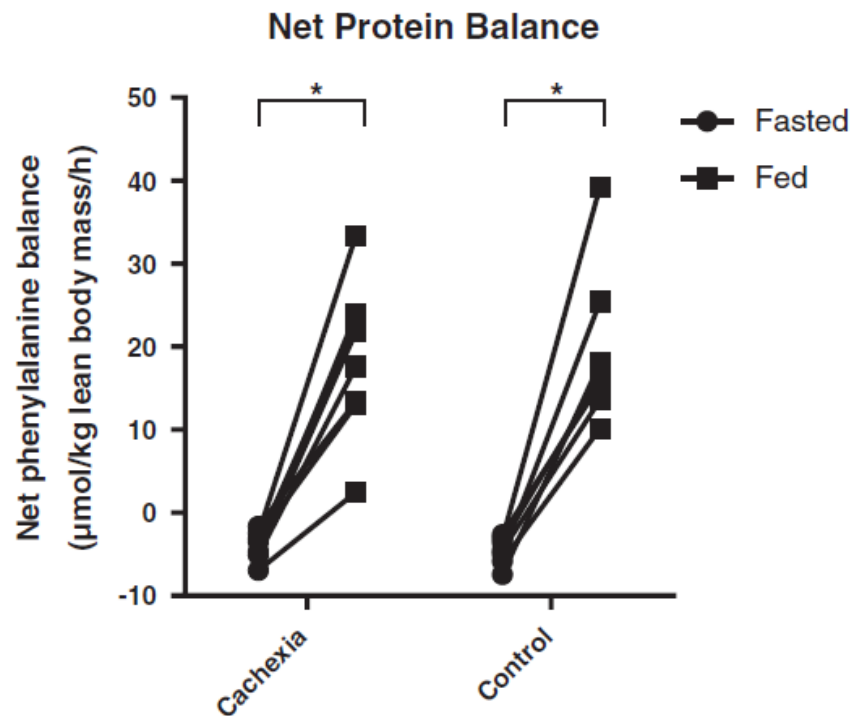
BOOST High Protein drink (237 mL)

15g protein, 6g fat, 33 g carbohydrates

van der Meij, unpublished data

High-protein supplement → anabolism

- n=8 pancreatic cancer and n=7 healthy controls
- Similar response to oral nutritional supplement

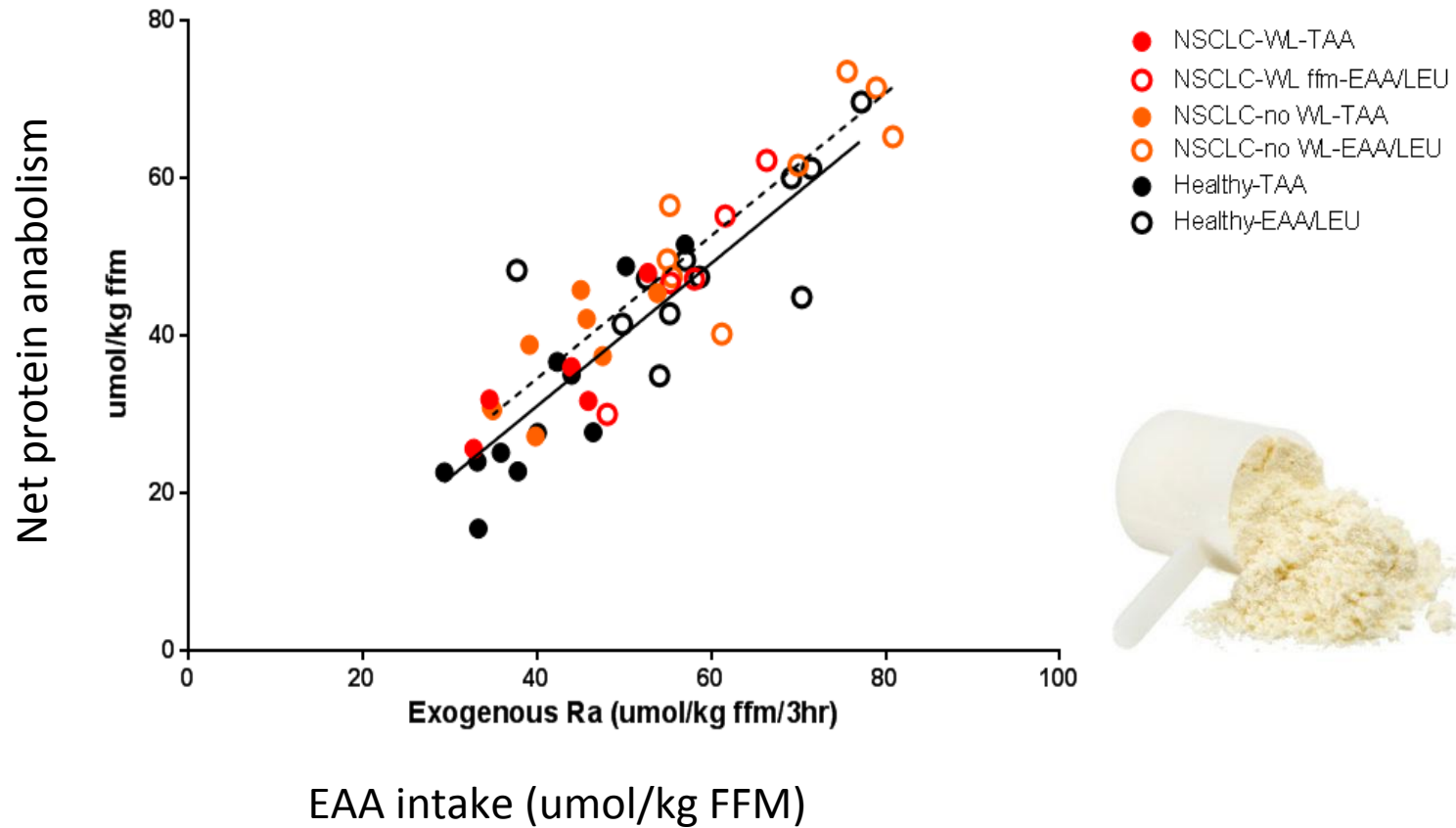


MEAL:

FORTISIP High Protein drink (200 mL)

12g protein, 6g fat, 37 g carbohydrates

Essential amino acid intake → anabolism



14 g EAA/leucine mixture



A systematic review on the role of vitamins, minerals, proteins, and other supplements for the treatment of cachexia in cancer: a European Palliative Care Research Centre cachexia project

Conclusion:

Not enough solid evidence for protein supplements in cancer

- HMB, arginine and glutamine:
 - Increase in lean body mass after 4 weeks in advanced solid tumour patients
 - No benefits in lung cancer after 8 weeks
- L-carnitine in pancreatic cancer: increase of BMI and survival

Summary

- Body composition in cancer is relevant:
 - Obesity and aging epidemic
 - High body fat and low muscle mass: associated with toxicity, muscle weakness, quality of life and mortality
- Cancer patients have a higher protein turnover
 - Higher muscle protein breakdown
 - Low physical activity level
 - Similar anabolic potential as healthy subjects
 - Protein supplementation works (short-term)
- How can we improve our daily care?



Implications for clinical practice

ESPEN guidelines on Nutrition in Cancer Patients:

- Aim: 1.2 – 1.5 g protein/kg body weight
- Higher quality protein is recommended
- Support physical activity throughout cancer treatment
- Future research:
 - Effects of LONG-TERM protein supplementation (>1.2 g/kg)
 - Effects on muscle mass, muscle function, quality of life
 - Additional effect of physical activity or pharmaceuticals (multimodal interventions)



ACKNOWLEDGEMENT



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THANK YOU VERY MUCH

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1



GRASS-FED BEEF

3 oz: 19 g

46% DV

2



WHEY PROTEIN

1/4 cup: 19-20 g

3



LENTILS

1 cup: 18 g

36% DV

4



WILD FISH

3 oz: 17 g

40% DV

5



ORGANIC CHICKEN

1 chicken breast: 16 g

38% DV

6



BLACK BEANS

1 cup: 15 g

7



NATTO

1/2 cup: 15 g

8



RAW MILK

1 cup: 8 g

16% DV

9



KEFIR OR YOGURT

6 oz: 6-9 g

16% DV

10



FREE-RANGE EGGS

1 large: 7 g

14% DV

11



RAW CHEESE

1 oz goat cheese: 7 g

14% DV

Dr. Axe
FOOD IS MEDICINE