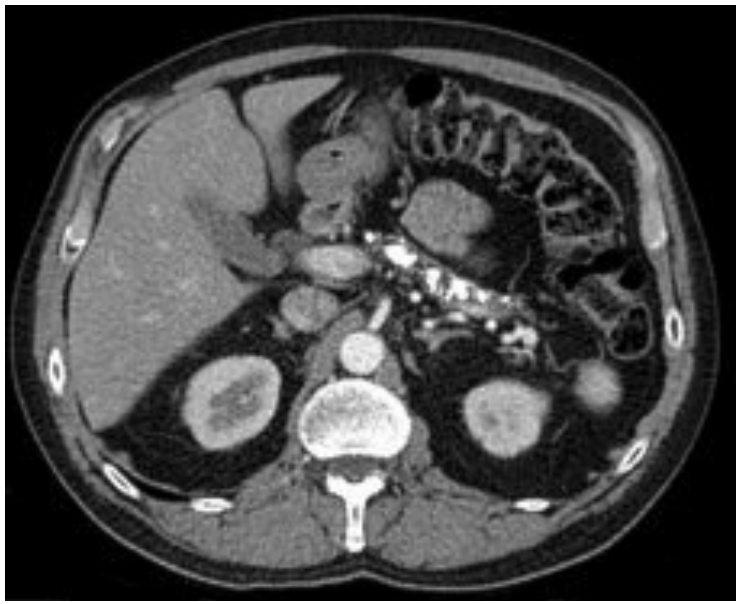
Multidisciplinary approach to the patient with chronic pancreatitis

Søren Schou Olesen
MD, PhD
Department of Gastroenterology and Hepatology
Aalborg University Hospital
Denmark

Chronic pancreatitis – a complex disease



Pain

EPI

Diabetes

Common bile duct stenosis

Malnutrition

Pseudocysts

Osteopathy

Duodenal obstruction

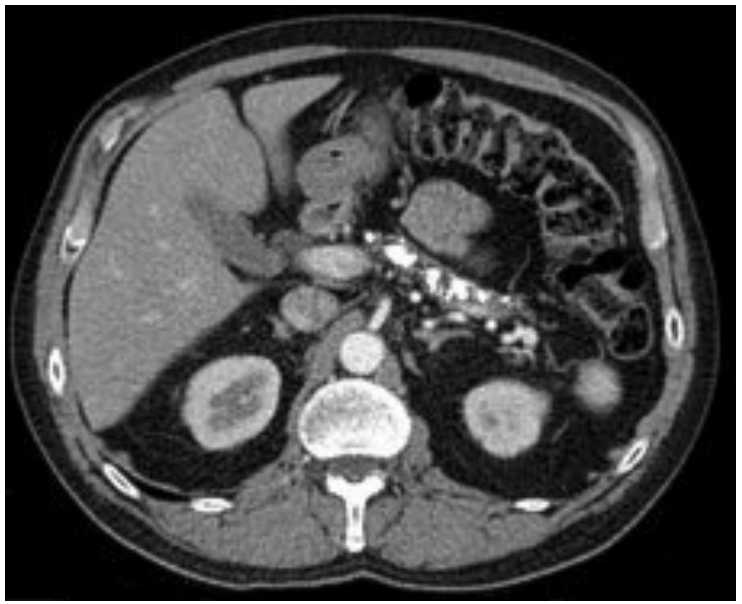
Metabolism

Co-morbidity

Cancer

…

Chronic pancreatitis – a complex disease



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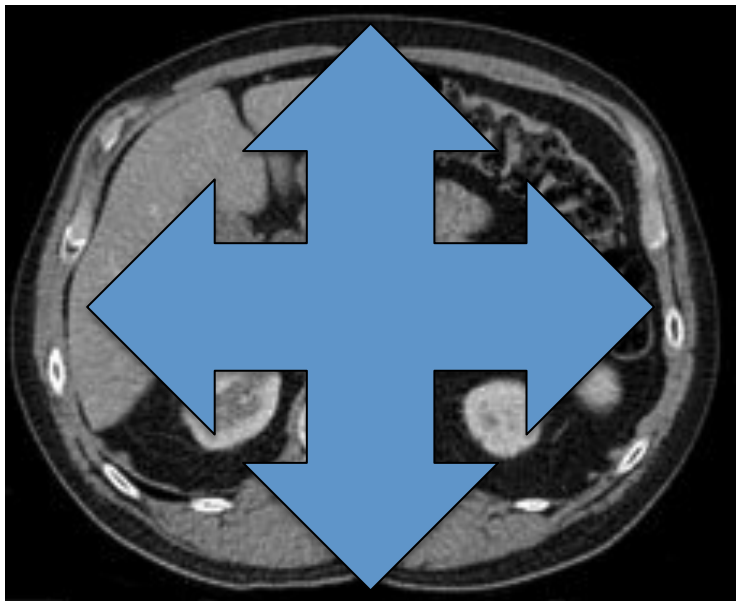
Chronic pancreatitis – a complex disease



Pain

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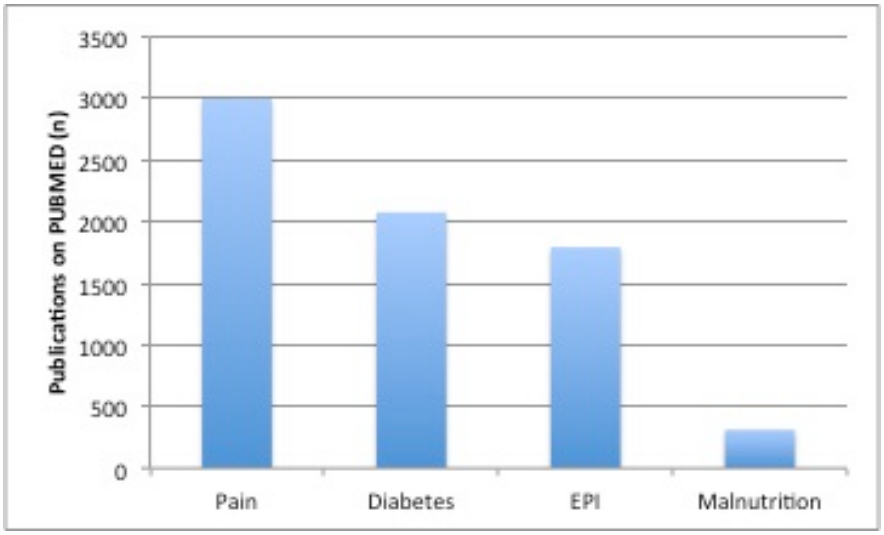
…

Malnutrition and CP: evidence gap?

- PUBMED November 2015



- MESH ”chronic pancreatitis and malnutrition”: 313 papers
- 85 reviews = 3.7 original paper per review
- Very few prospective studies
- GOBSAT evidence?

Pathogenesis of pancreatic malnutrition

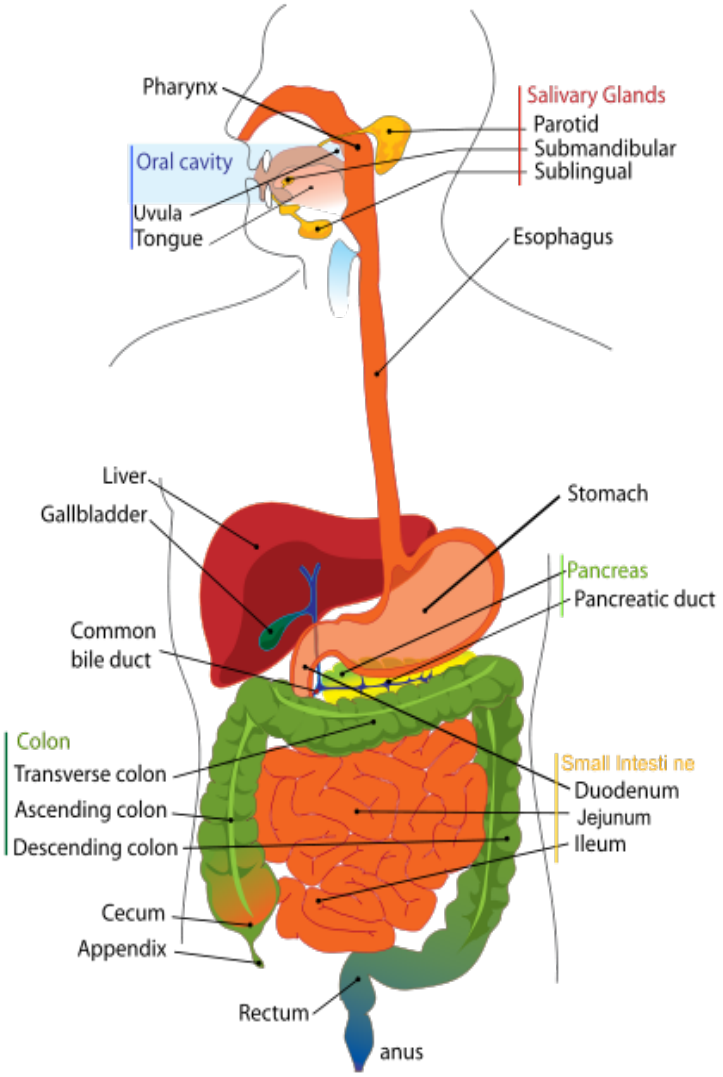
Decreased oral intake:
Pain, vomiting, anorexia, opioid treatment, alcoholism

Maldigestion and malabsorption:
EPI (enzymes + bicarbonate), dysmotility, bacterial overgrowth

Endocrine dysfunction:
Diabetes, changes in ”gut hormones” (CCK, PP, incretins, etc.)

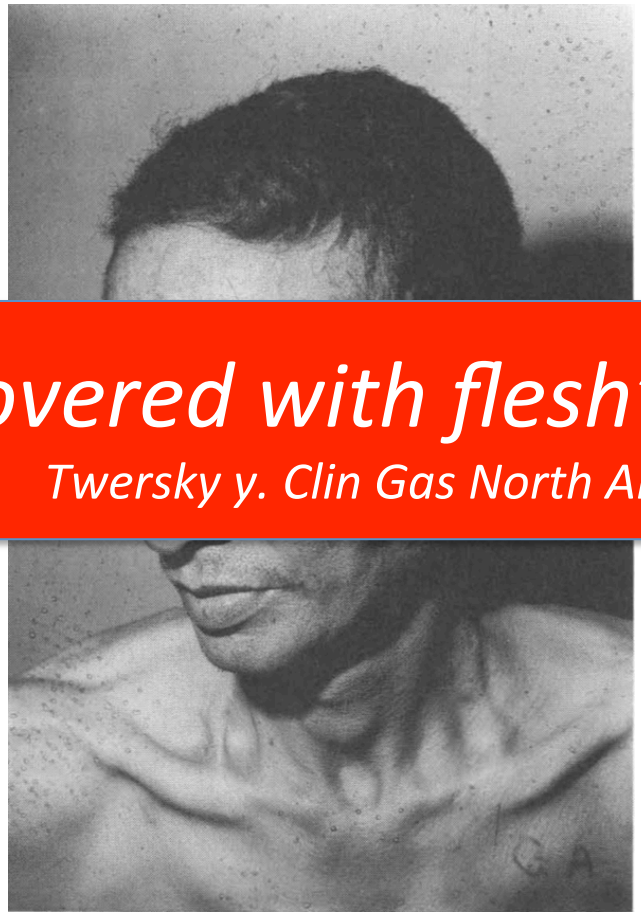
Changes in metabolism:
Inflammation, infections, metabolic adaption, endocrine dysfuntcion

…



Rasmussen et al. WJG 2013

Clinical presentation



”A bag of bones covered with flesh”

Twersky y. Clin Gas North Am 1989

Prevalence of malnutrition in chronic pancreatitis?

- **In hospital prevalence:**
  - ✓ *Filipovic B. et al. Hepato-Gastroenterology 2011*
  - ✓ *Vaudin R. Clin Nutr, suppl 2012*
    - ✓ Patients admitted with Chronic pancreatitits (214 patients),
    - ✓ Prevalence of malnutrition 41% (BMI< 20 kg/m^2)

Definition?

- **Outpatient clinic prevalence?**

Contents lists available at ScienceDirect

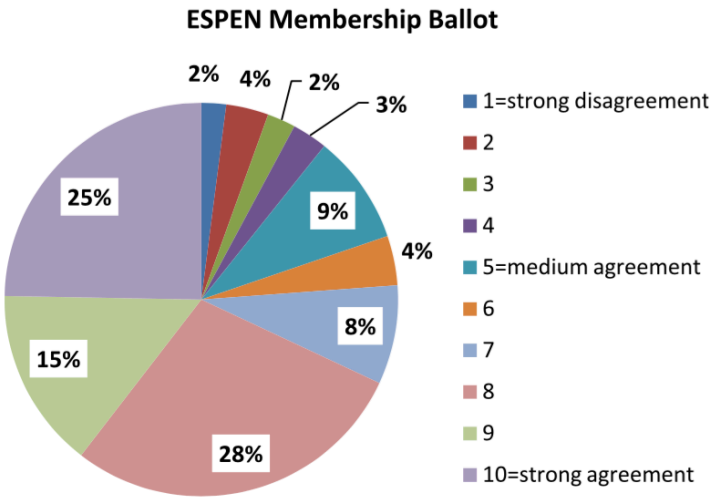
Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

ESPEN endorsed recommendation

Diagnostic criteria for malnutrition – An ESPEN Consensus Statement

T. Cederholm [a, *], I. Bosaeus [b], R. Barazzoni [c], J. Bauer [d], A. Van Gossum [e], S. Klek [f], M. Muscaritoli [g], I. Nyulasi [h], J. Ockenga [i], S.M. Schneider [j], M.A.E. de van der Schueren [k, l], P. Singer [m]



Fact box: Two alternative ways to diagnose malnutrition. Before diagnosis of malnutrition is considered it is mandatory to fulfil criteria for being "at risk" of malnutrition by any validated risk screening tool.

Alternative 1:

- BMI <18.5 kg/m^2

Alternative 2:

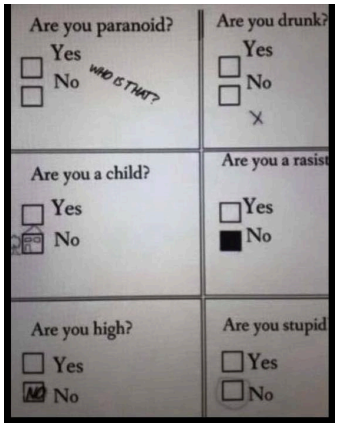
- Weight loss (unintentional) > 10% indefinite of time, or >5% over the last 3 months combined with either
- BMI <20 kg/m^2 if <70 years of age, or <22 kg/m^2 if ≥70 years of age or
- FFMI <15 and 17 kg/m^2 in women and men, respectively.

Malnutrition in CP outpatients and associated risk-factors (Aalborg)

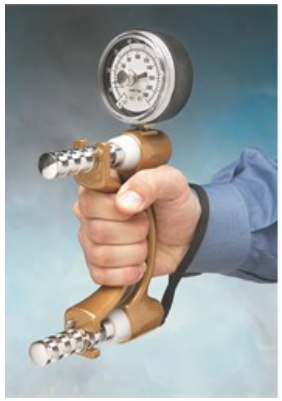
- November 1st 2015: 195 chronic pancreatitis patients
- Malnutrition at index visit (BMI<18.5kg/m^2): 11% (95%CI 6%-17%)

	Malnutrition	Normal nutritional state	OR (95% CI)	P-value
Age, years (IQR)	57.4 (51.6-61.7)	58.8 (49.8-66.3)	0.99 (0.95-1.03)	0.55
Male sex, n (%)	8 (44)	109 (74)	0.29 (0.11-0.78)	0.015
Duration of CP, years (IQR)	6.5 (2.0-13.0)	5.0 (2.0-10.0)	1.01 (0.95-1.08)	0.68
Alcoholic aetiology, n (%)	14 (78)	86 (60)	2.36 (0.74-7.53)	0.15
Excessive alcohol consumption, n (%)	4 (25)	9 (7)	4.52 (1.21-16.89)	0.025
Smoking, n (%)	14 (88)	88 (67)	3.50 (0.76-16.1)	0.11
Pain severity (VAS)	4.5 (3.0-5.9)	3.8 (1.3-5.3)	1.25 (0.96-1.63)	0.094
Pain pattern, n (%)				
-No pain	2 (14)	23 (20)	1.00	
-Intermittent pain	1 (7)	7 (6)	1.64 (0.13-20.93)	0.70
- Constant pain	11 (79)	86 (74)	1.47 (0.30-7.11)	0.63
Opioid use, n (%)	10 (71)	51 (40)	3.77 (1.12-12.69)	0.032
Exocrine pancreatic insufficiency, n (%)	17 (100)	111 (76)	N/A	0.025
Diabetes, n (%)	4 (24)	56 (38)	0.51 (0.16-1.63)	0.25

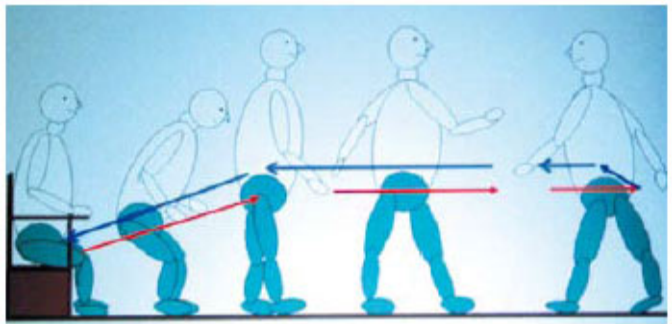
Nutritional assessment in Aalborg



Questionnaires



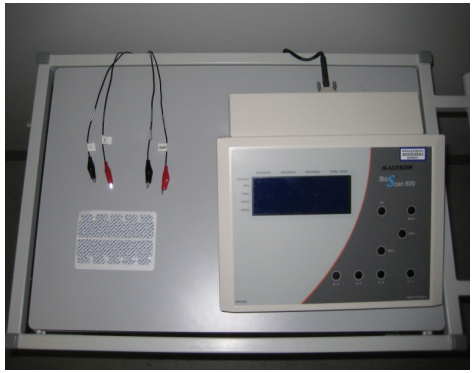
HGS



Time up and go-test (TUG)

Anthropometrics

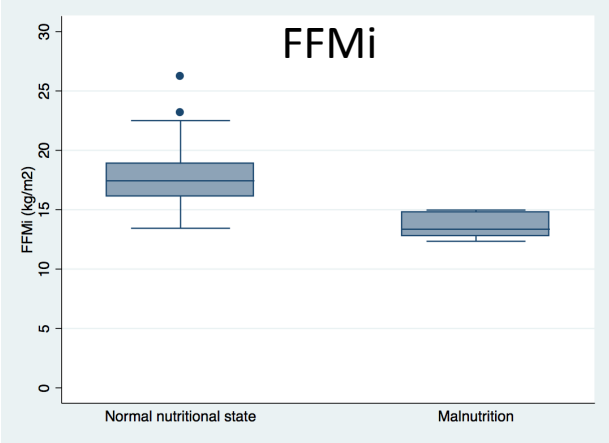
REE

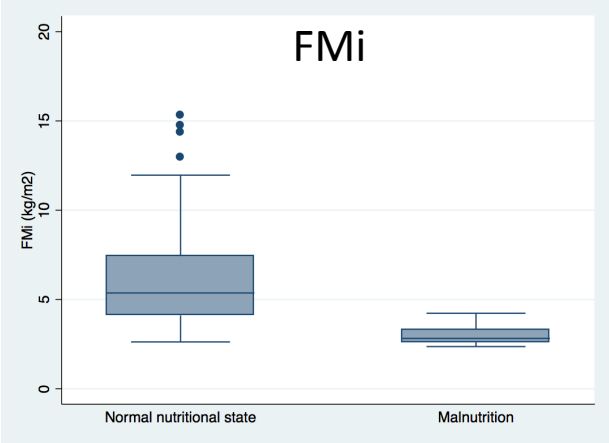


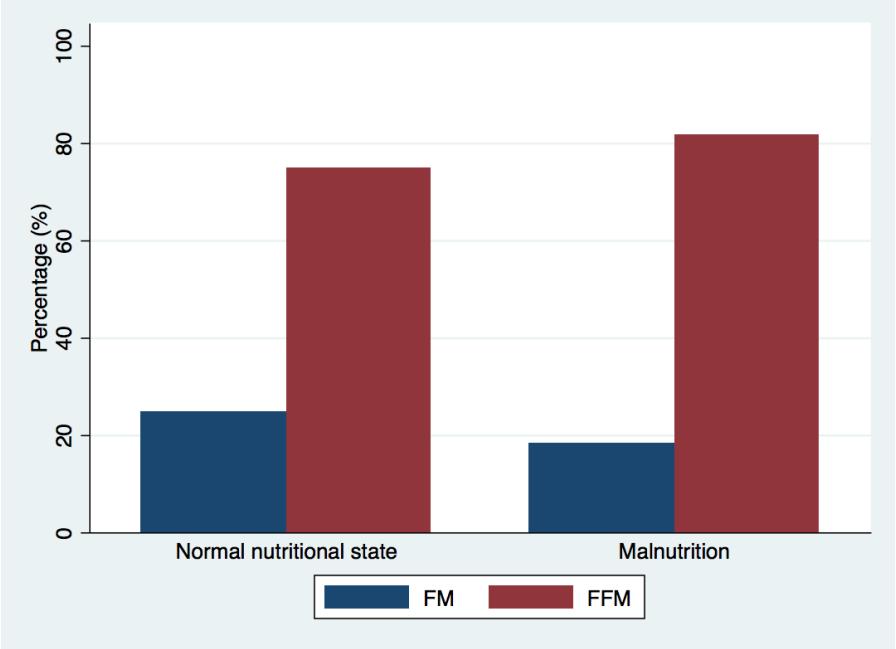
BIA

C-13 MTG breatht test

Consequences of malnutrition I
Body composition

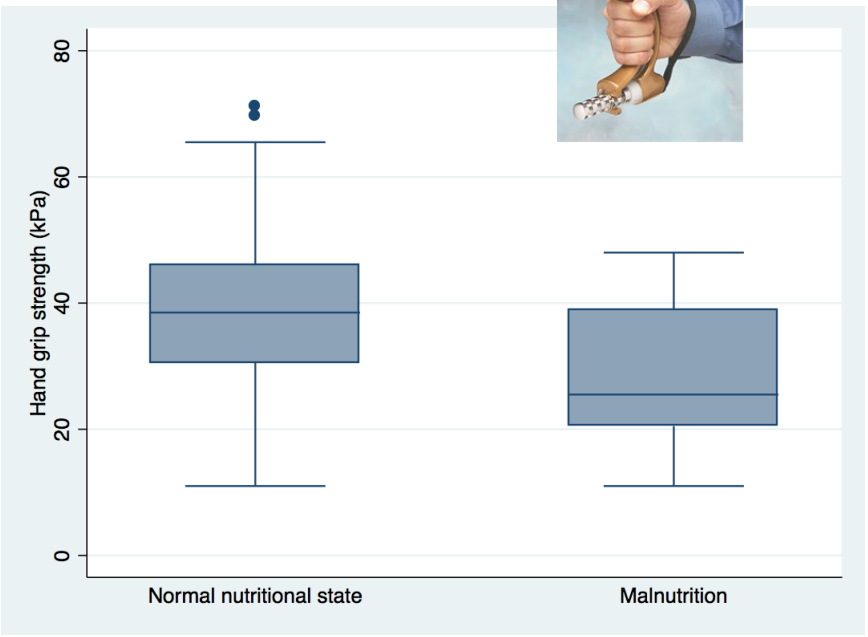


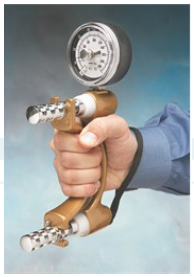


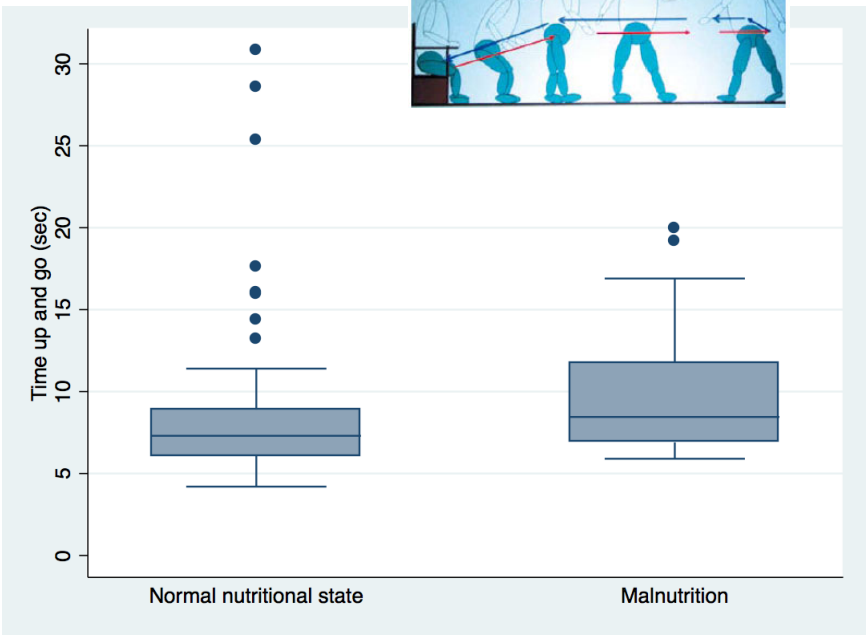


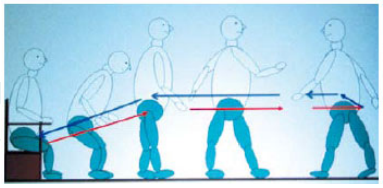
Consequences of malnutrition II

Impaired muscle function

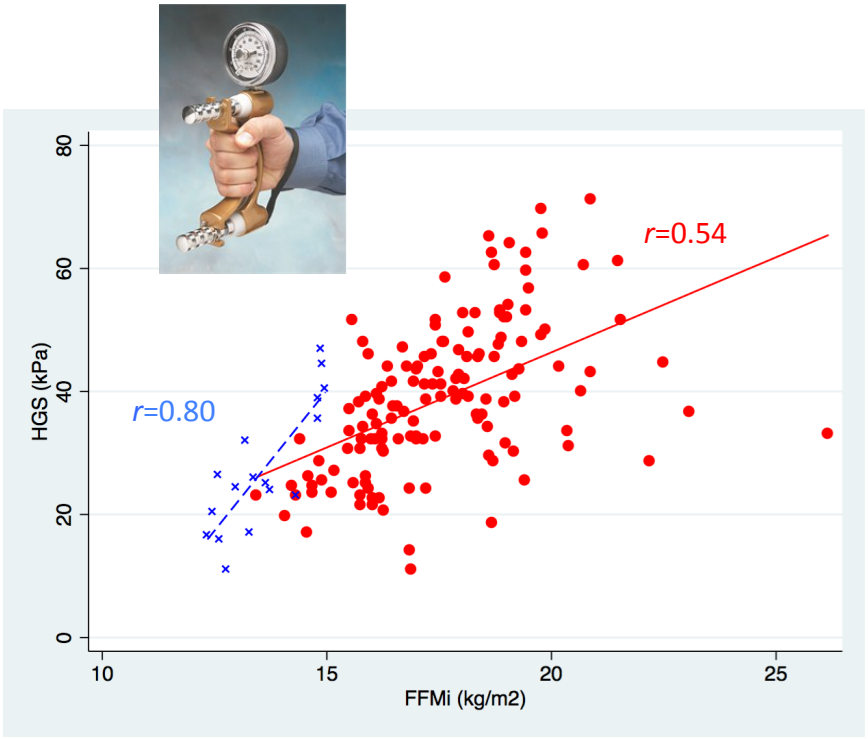


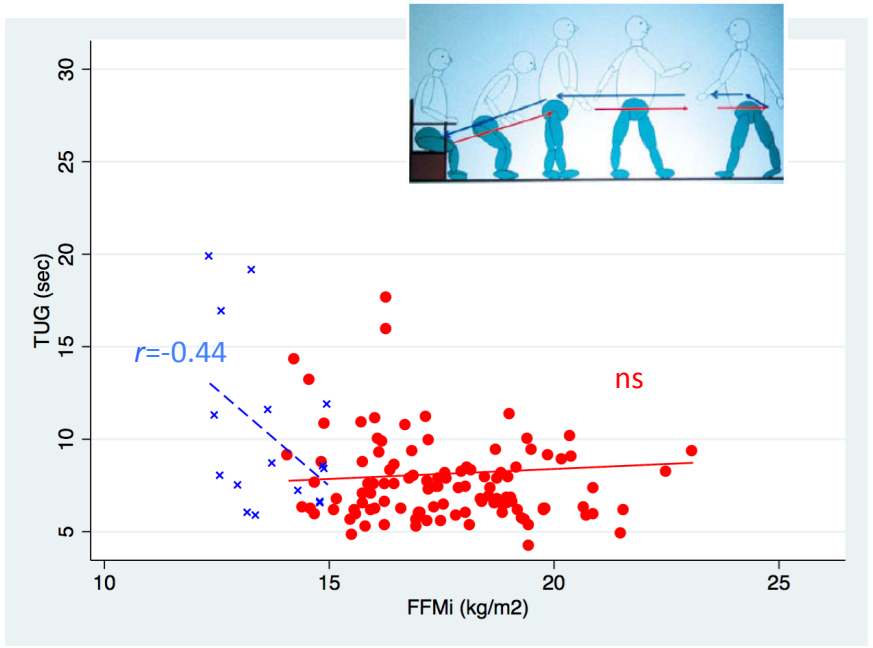






Consequences of malnutrition II
Impaired muscle function





X=BMI<18.5 kg/m² **●=BMI≥18.5 kg/m²**

Consequences of malnutrition III

Quality of life (EORTC QLQ C-30)

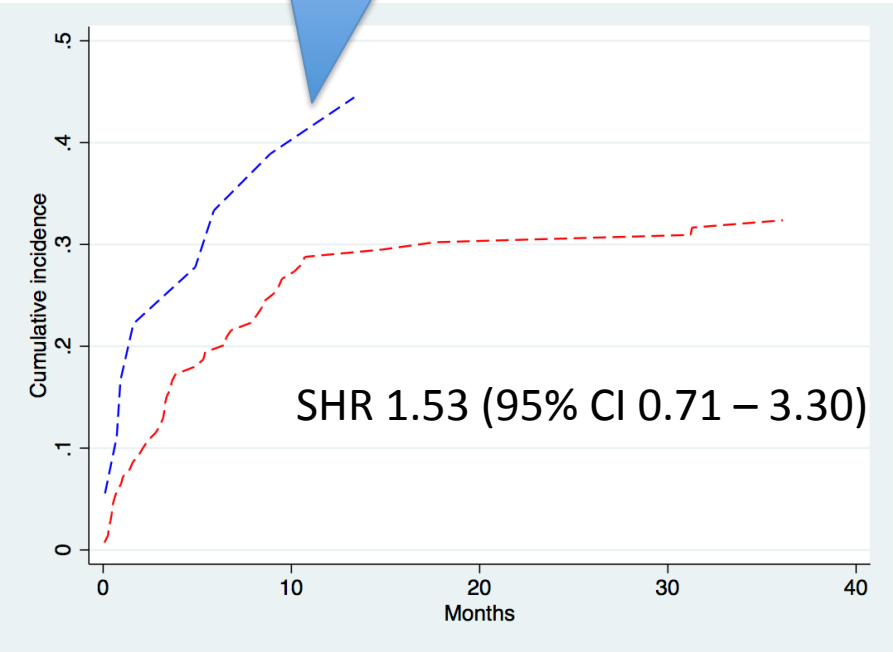
	Malnutrition	Normal nutritional state	P-value
Global health	45.8 (41.7-50.0)	50 (29.2-66.7)	0.76
Functional scales			
Physical functioning	46.7 (40.0-66.7)	60 (40.0-86.7)	0.20
Role functioning	50.0 (33.3-66.7)	50.0 (33.3-83.3)	0.73
Emotional functioning	43.8 (16.7-66.7)	66.7 (50.0-91.7)	0.036
Cognitive functioning	66.7 (33.3-66.7)	66.7 (50.0-100.0)	0.10
Social functioning	66.7 (50.0-83.3)	66.7 (33.3-100.0)	0.70
Symptom scales / items			
Fatigue	66.7 (55.6-77.8)	55.6 (33.3-77.8)	0.093
Nausea and vomiting	16.7 (0-33.3)	0 (0-33.3)	0.26
Pain	66.7 (66.7-83.3)	66.7 (33.3-83.3)	0.15
Dyspnoea	33.3 (0-33.3)	33.3 (0-33.3)	0.94
Insomnia	50.0 (33.3-66.7)	33.3 (0-66.7)	0.56
Appetite loss	66.7 (33.3-100)	33.3 (0-66.7)	0.0093

Malnutrition: a ”silent” complication?

Consequences of malnutrition IV

Increased hospitalisation rates

BMI<18.5kg/m^2



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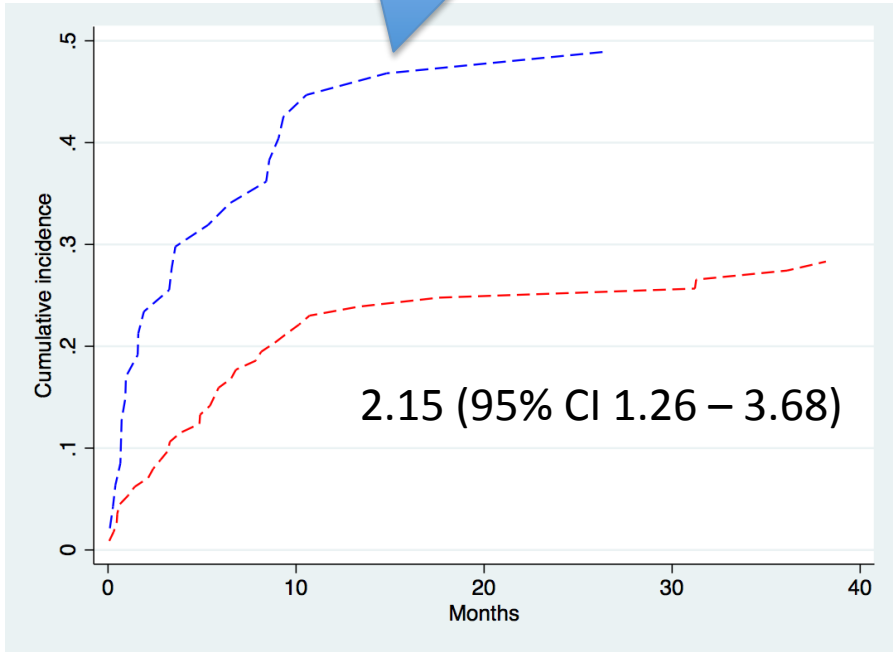
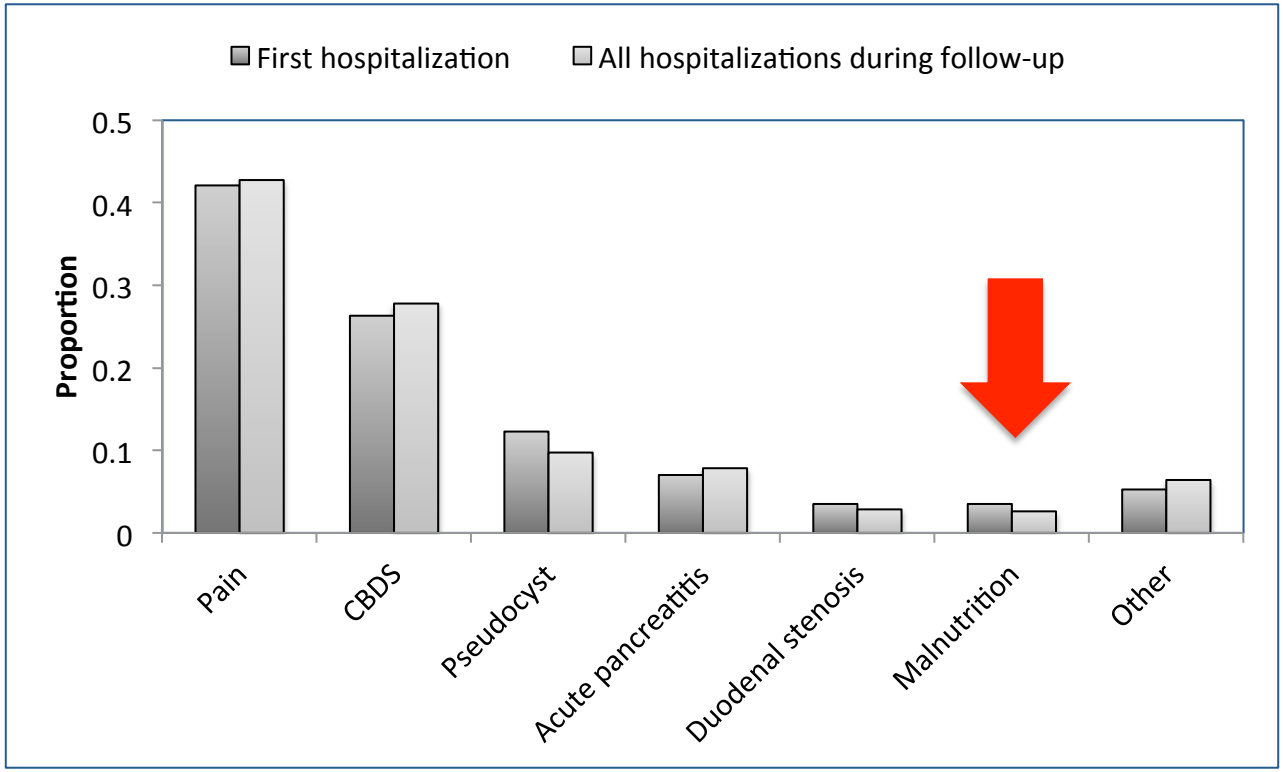


Causes of pancreatitis related hospitalizations



Malnutrition: a ”silent” complication?

Consequences of malnutrition V

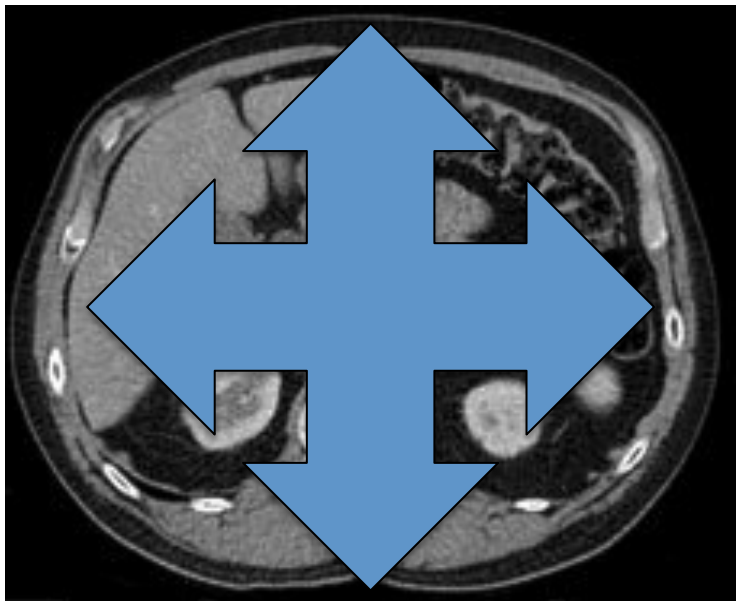
Mortality?

- Follow-up period insufficient for mortality analysis
- 6 patients died during follow-up – one patient was malnourished (BMI<18.5 kg/m^2)

- Association between mortality and malnutrition well-established in various patient groups

Stratton RJ et al. Disease-related malnutrition: an evidence-based approach. CABI Publishing 2003

Chronic pancreatitis – a complex disease



Pain

EPI

Diabetes

Common bile duct stenosis

Malnutrition

Pseudocysts

Osteopathy

Duodenal obstruction

Metabolism

Co-morbidity

Cancer

…

Osteopathy

Nutritional disorder

Malnutrition

Micronutrient abnormalities

Overnutrition

Starvation-related under-weight

Cachexia/ disease-related malnutrition

Sarcopenia

Frail

Overweight

Obesity

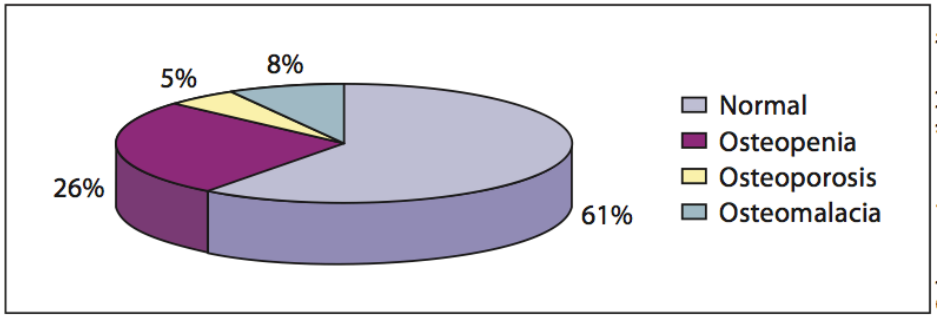
Osteopathy
- osteopenia
- osteoporosis
- osteomalacia

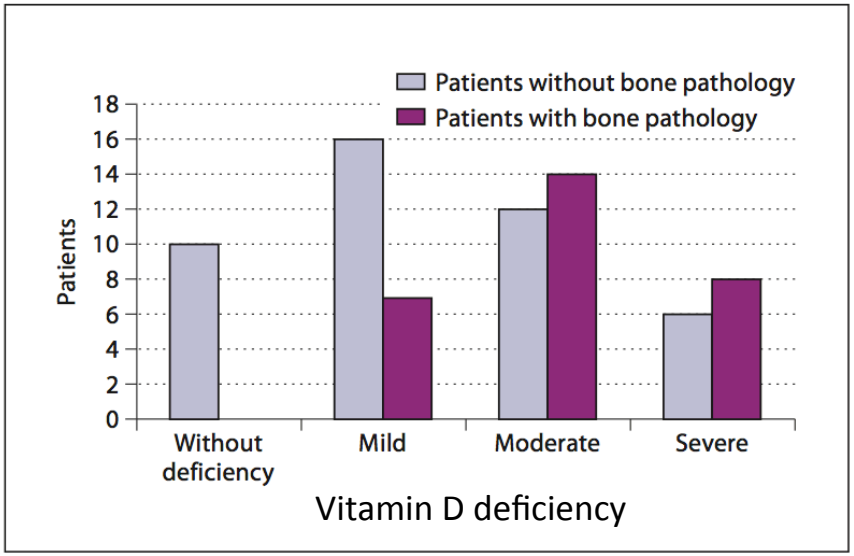
↑PTH

Vitamins A,D,E,K
Mg, Ca, Zn
...

Prevalence of osteopathy and associations to D-vitamin deficiency and EPI

N=73





Dujsikova et al. Pancreatology 2007

Bone mass denstity

- normal 45%
- osteopenia 45%
- osteoporosis 10%

N=40

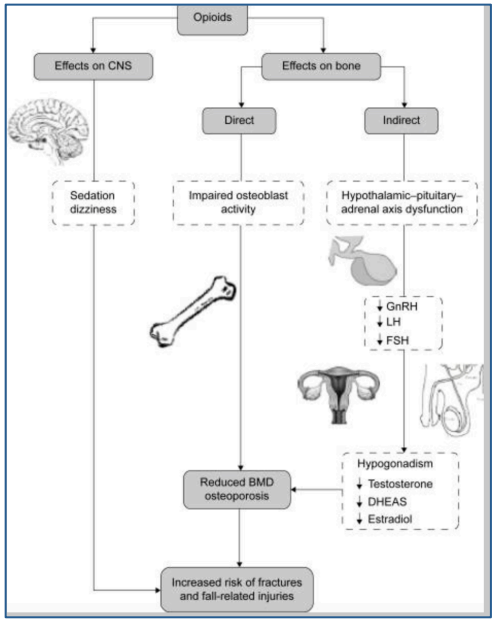
Association to EPI and enzyme treatment

	Dutch reference population	All patients $N = 40$ (100%)	Exocrine sufficient $N = 12$ (30%)	Exocrine insufficient Using enzymes $N = 19$ (48%)	Exocrine insufficient Without enzymes $N = 9$ (23%)	p Value[b]
Left femur						
T score		−0.9 (−1.68 to −0.2)	−0.4 (−1.13 to 0.15)	−0.75 (−1.63 to −0.15)	−1.65 (−1.8 to −1.0)	
Z score		−0.2 (−1.0 to 0.58)	0.3 (−0.93 to 0.85)	0.0 (−0.8 to 0.73)	−0.5 (−1.12 to −0.05)	
Lumbar spine						
T score		−0.65 (−1.25 to 0.58)	−0.5 (−1.2 to 1.1)	−0.4 (−1.1 to 0.8)	−1.05 (−1.75 to −0.18)	
Z score		−0.15 (−0.9 to 0.98)	0.05 (−1.05 to 1.93)	0.15 (−0.83 to 1.07)	−0.55 (−1.0 to 0.83)	
Decreased BMD — no. (%)	(10–15%) [22–24]	22 (55)	5 (42)	9 (47)	8 (89)	0.039
Osteopenia — no. (%)	(10%)	18 (45)	4 (33)	7 (37)	7 (78)	0.053
Osteoporosis — no. (%)	(1–5%)	4 (10)	1 (8)	2 (11)	1 (11)	1.0
Common bone fractures — no. (%)		16 (40%)	6 (50)	5 (26)	5 (56)	0.361

Sikkens et al. Pancreatology 2013

Additional risk factors for osteopathy in patients with CP

- Smoking
- Excessive alcohol consumption
- Opioid treatment
- Inflammation

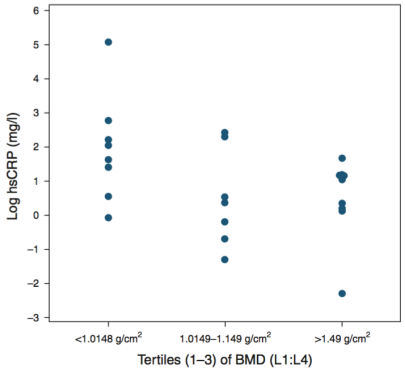



ORIGINAL CONTRIBUTIONS

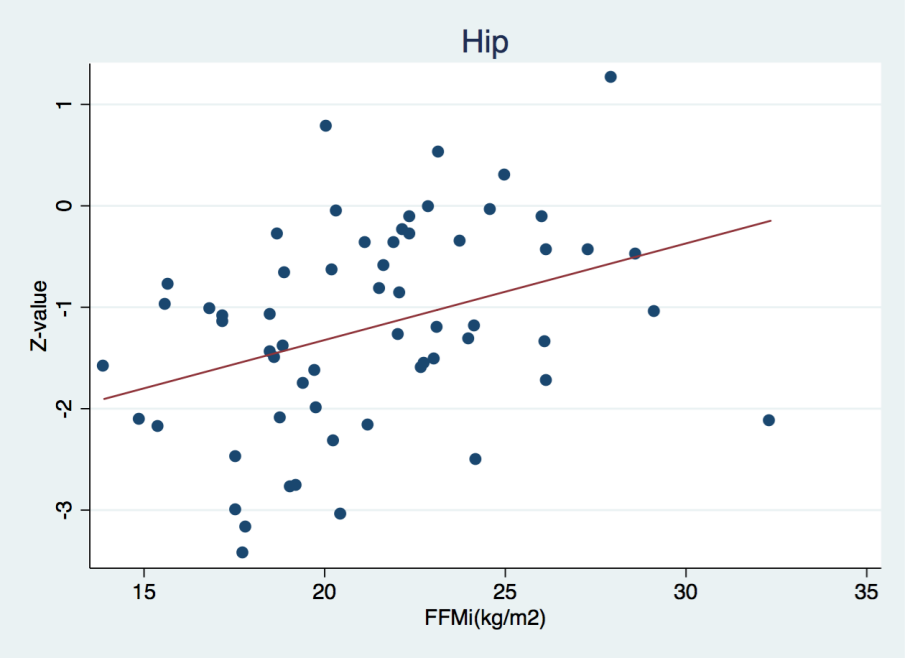
nature publishing group

An Association Between Abnormal Bone Turnover, Systemic Inflammation, and Osteoporosis in Patients With Chronic Pancreatitis: A Case-Matched Study

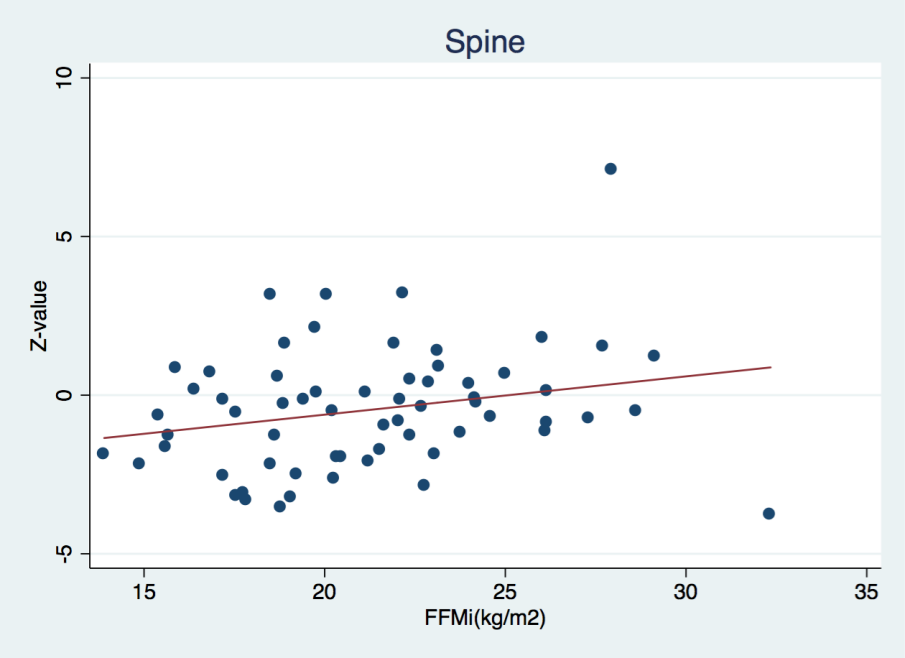
Sinead N. Duggan, PhD[1], Christina Purcell, BSc[1], Mark Kilbane, PhD[2], Myra O'Keane, MSc[2], Malachi McKenna, MD[2], Peter Gaffney, MSc[3], Paul F. Ridgway, MD[1], Gerard Boran, MD[3] and Kevin C. Conlon, MD[4]



BMD and fat free mass (FFMi)

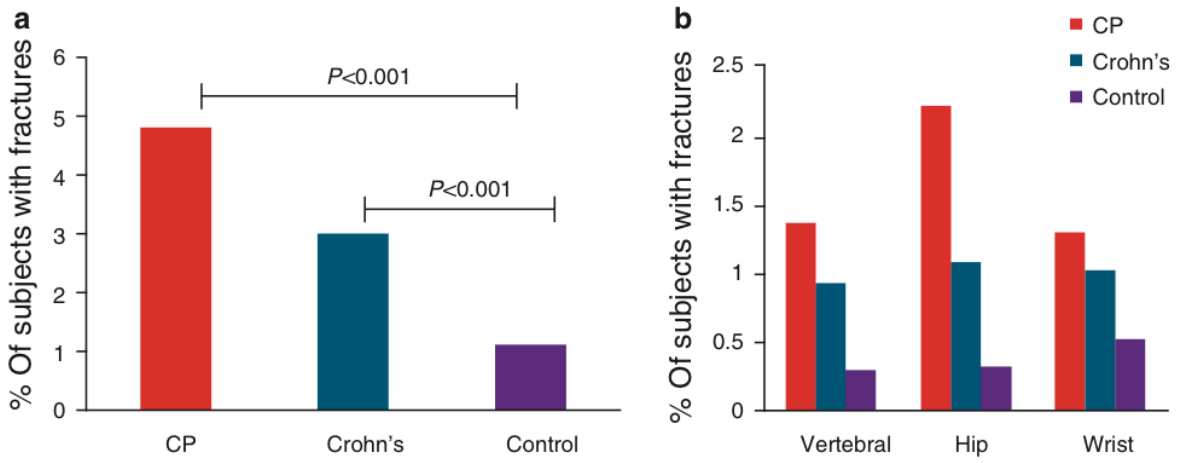


r=0.36; p=0.005

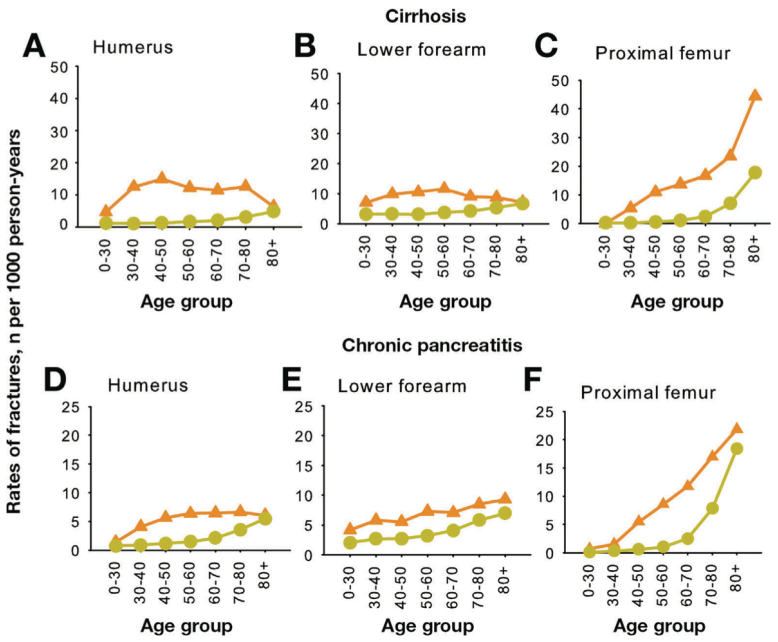


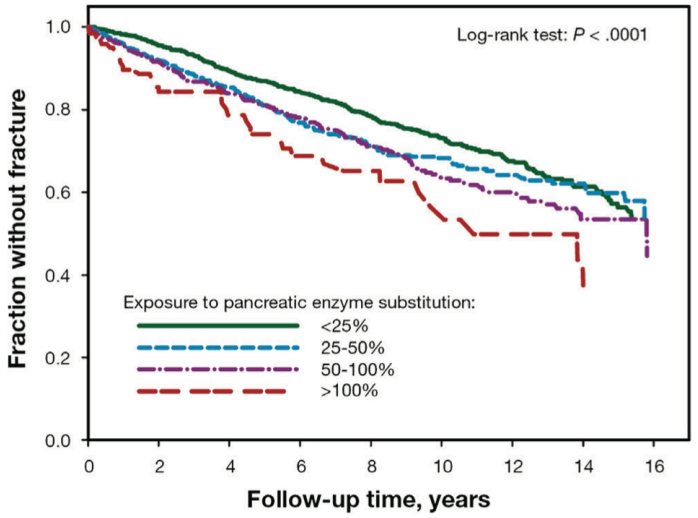
r=0.11; p=0.41

Low energy fractures and CP



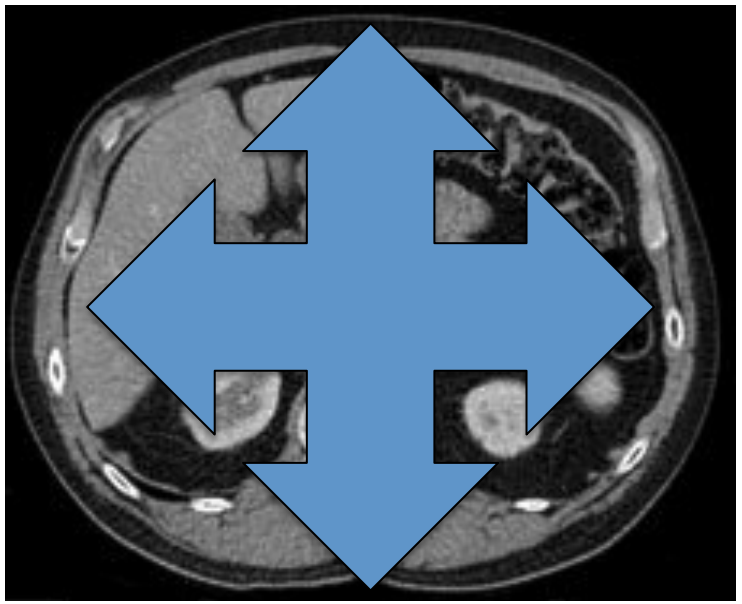
Tignor et al. AJG 2010





Bang et al. CGH 2014

Chronic pancreatitis – a complex disease



Pain

EPI

Diabetes

Common bile duct stenosis

Malnutrition

Pseudocysts

Osteopathy

Duodenal obstruction

Metabolism

Co-morbidity

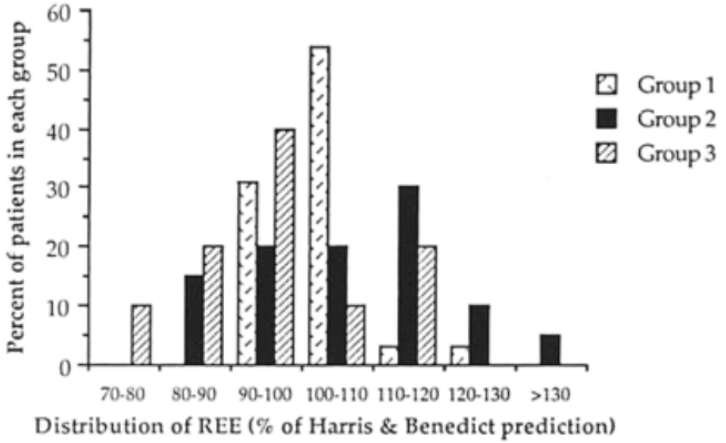
Cancer

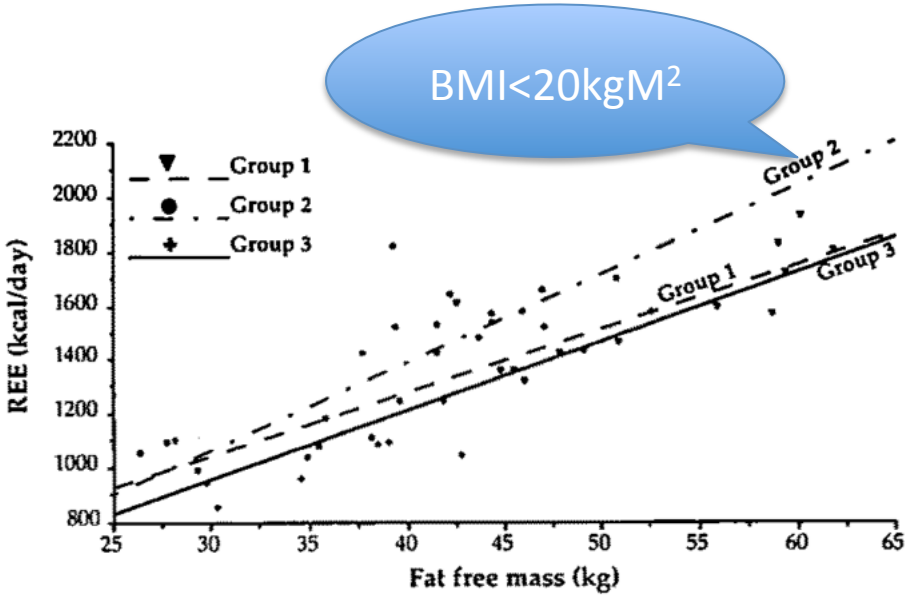
…

Resting Energy Expenditure in Patients with Alcoholic Chronic Pancreatitis

XAVIER HÉBUTERNE, MD, PATRICK HASTIER, MD, JEAN-LUC PÉROUX, MD,
NABIL ZEBOUDJ, MD, JEAN-PIERRE DELMONT, MD, and PATRICK RAMPAL, MD

Digestive Diseases and Sciences, Vol. 41, No. 3 (March 1996), pp. 533–539





Group I: CP normal nutritional state (n=13)
Group II: CP malnutrition (BMI < 20kgM^2) (n=20)
Group III: Control group (n=11)

Conclusion: Underweight is accompanied by hypermetabolism in CP

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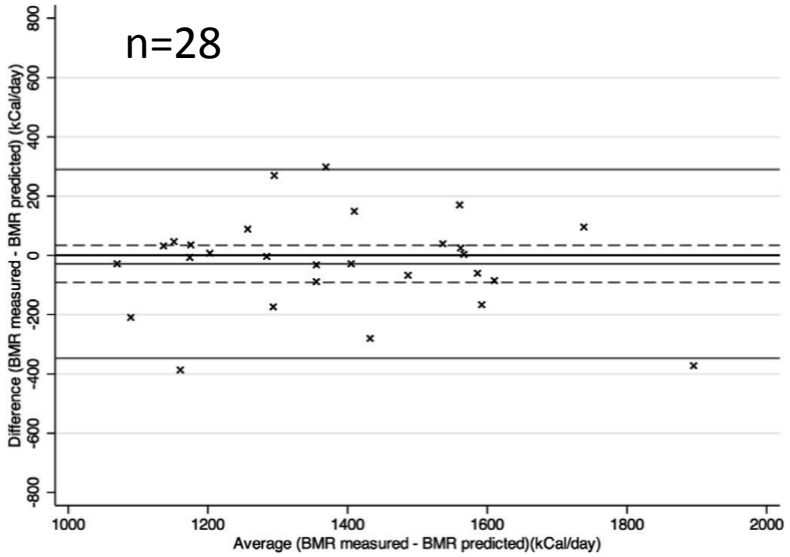
journal homepage: http://www.clinicalnutritionespen.com

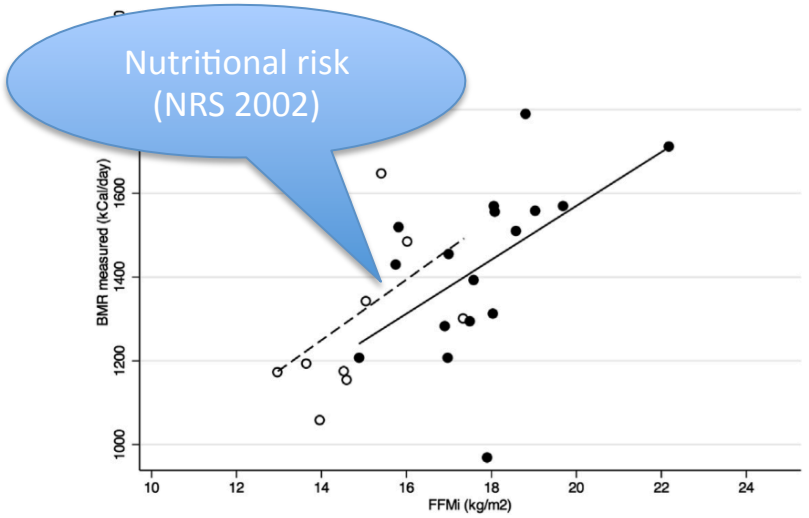
Original article

Can we rely on predicted basal metabolic rate in chronic pancreatitis outpatients?☆

Søren Schou Olesen [a, b, *], Mette Holst [b], Marianne Køhler [b], Asbjørn Mohr Drewes [a], Henrik Højgaard Rasmussen [b]

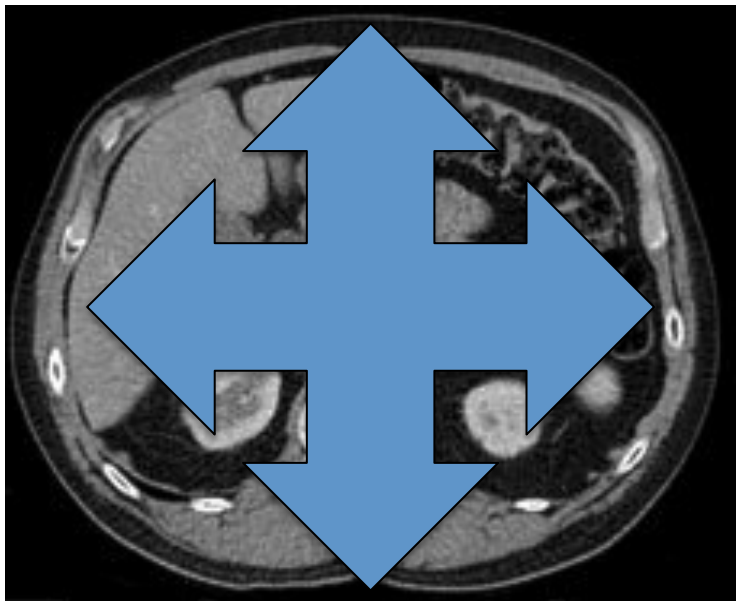
[a] Mech-Sense, Department of Gastroenterology & Hepatology, Aalborg University Hospital, Denmark
[b] Centre for Nutrition and Bowel Disease, Department of Gastroenterology & Hepatology, Aalborg University Hospital, Denmark





The Harris-Benedict equation reliable predicted the measured BMR in 4 out of 5 clinical stable chronic pancreatitis outpatients. BMR independent of nutritional risk.

Chronic pancreatitis – a complex disease



Pain

EPI

Diabetes

Common bile duct stenosis

Malnutrition

Pseudocysts

Osteopathy

Duodenal obstruction

Metabolism

Co-morbidity

Cancer

…

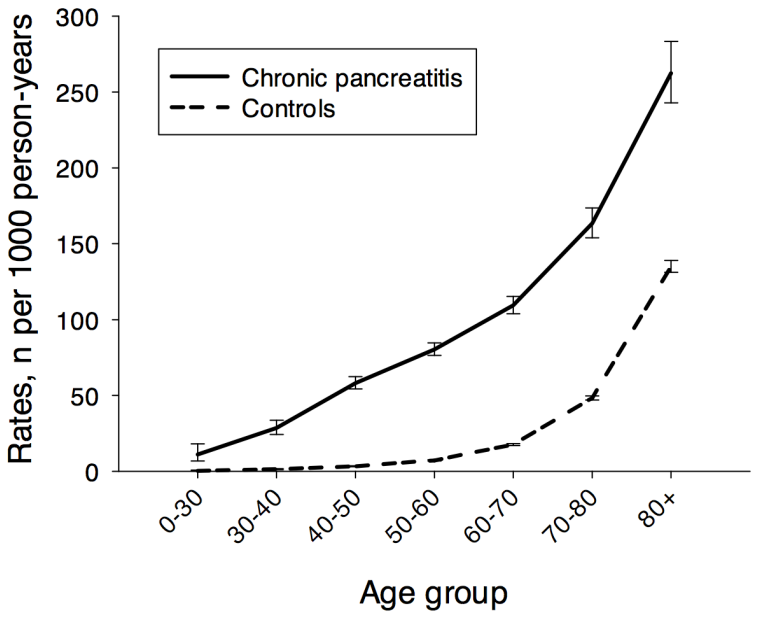
Comorbidity, cancer and mortality

Comorbidity (Charlson index):

•Diabetes	HR 6.7 (6.3 – 7.1)
•Peptic ulcer	HR 5.7 (5.3 – 6.2)
•Chronic renal disease	HR 3.7 (3.4 - 4.1)
•COPD	HR 2.9 (2.7 – 3.1)
•Cerebrovascular disease	HR 2.2 (2.0 – 2.3)

Cancer:

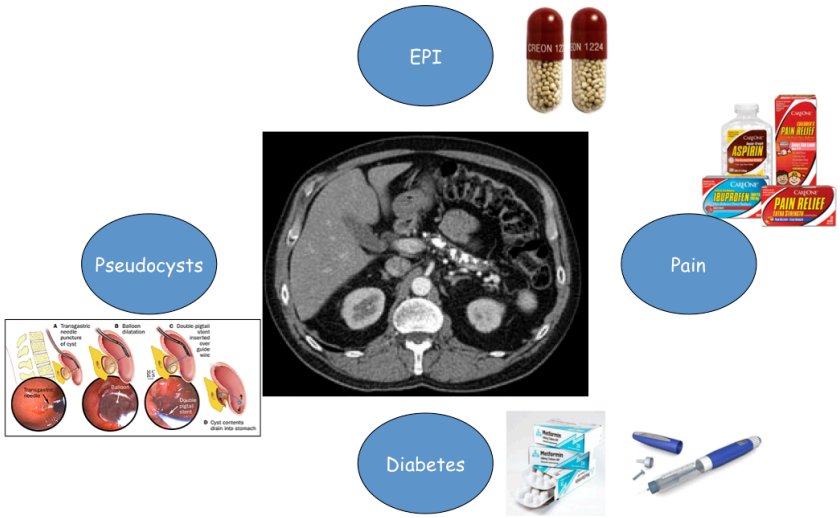
•Pancreas	HR 6.9 (5.6 - 8.6)
•Small bowel	HR 2.9 (1.4 – 6.1)
•Liver	HR 2.0 (1.3 – 3.1)
•Lung	HR 1.5 (1.2 – 1.8)
•Oesophagus	HR 1.4 (1.0 - 1.9)
•Melanoma	HR 0.6 (0.4 – 0.9)



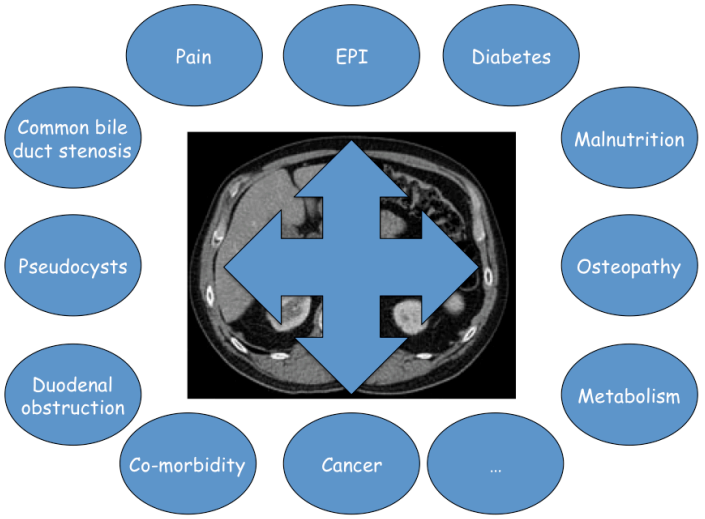
Bang et al. Gastroenterology 2014

Time for a paradigm shift?

Chronic pancreatitis – conventional wisdom



Chronic pancreatitis – a complex disease



multidiciplinary approach