

# Differential diagnosis, assessment and management of **fatigue**: depression, cognitive impairment, malnutrition and anorexia/cachexia

**Florian Strasser, MD**

Supportive & Palliative Oncology  
Clinic Oncology/Hematology  
Dept. Internal Medicine & Palliative Center  
Cantonal Hospital St.Gallen, Switzerland

Cancer-therapy related fatigue vs  
Fatigue in cancer patients

Screening for & Assessing Fatigue

Symptomatic treatment of Fatigue

Principles of cancer cachexia related  
fatigue management

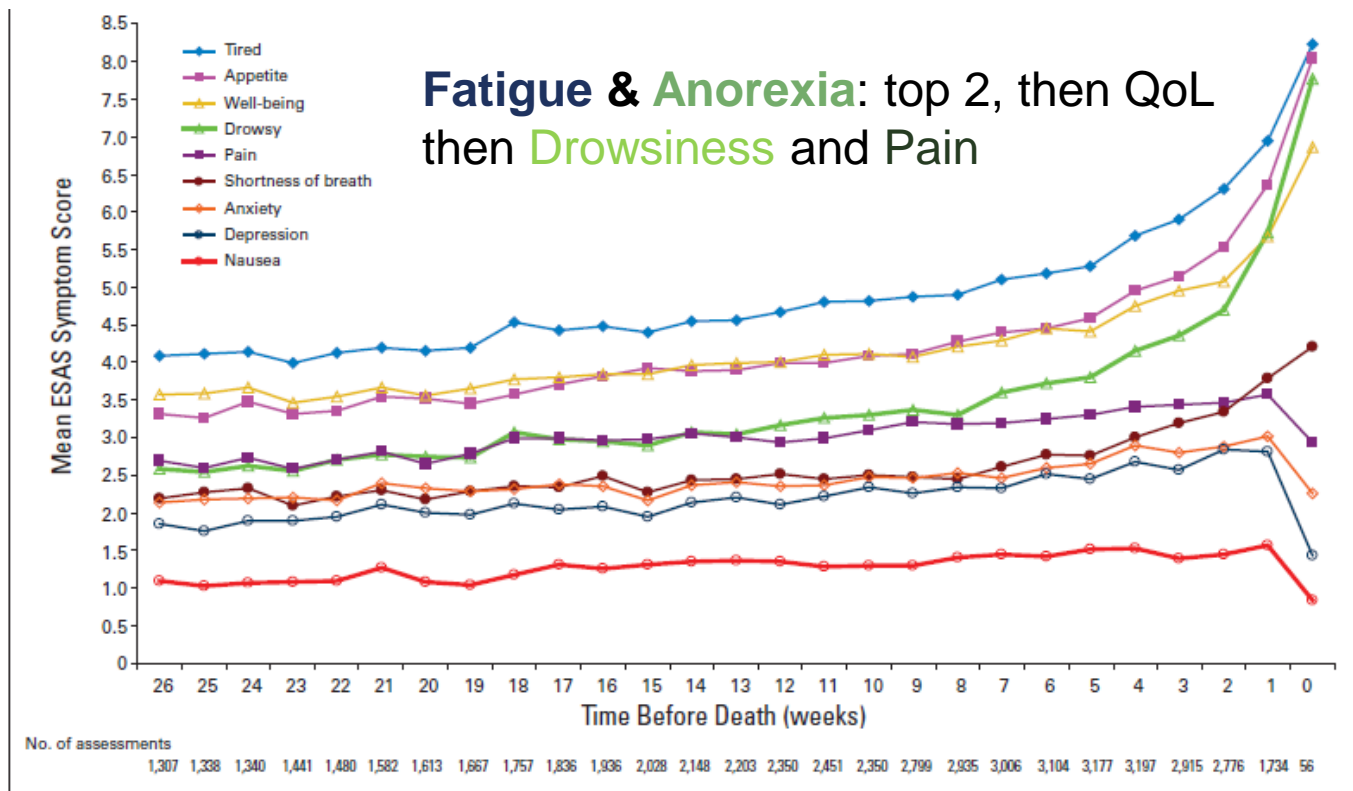
# Mr K, 72-j, Pancreas-adenocarcinoma liver-mets progression during second cycle of Folfox

**How to approach and manage this patient and his wife?**

*„It is difficult seeing him getting thinner he does not eat enough*

*„How are you“: swollen legs, people do nothing about it. Am tired and weak, poor appetite, I want living at my home.*

# Symptom distress (ESAS) last 6 months of >10'000 cancer patients



**Fig 2.** Mean Edmonton Symptom Assessment System (ESAS) symptom scores over time. Number of assessments is maximum number available among all nine symptoms. Missing ESAS values for a given symptom were not included when calculating the mean.

## **Cancer (treatment-) related Fatigue Syndrome (CRF)**

- 2-week period significant fatigue
- feel weak all over or heavy all over?
- trouble concentrating or paying attention
- losing your interest or desire to do things
- trouble falling asleep, staying asleep
- don't feel rested or refreshed
- ....

- Syndrome occurs as side-effect of anticancer treatments in curative and non-curative situations
- Causes are not fully understood: inflammatory, «neuro-hormonal»

## **Fatigue in cancer patients**

- Malnutrition
- Cancer cachexia
- Toxicity cancer therapy
- Depression
- Uncertainty
- Pharmacological psychoactive
- Delirium
- Dehydration
- Electrolytes (Ca, Phosp, Na)
- Organ-Dysfunction
- Infection
- Endocrine (Thyroid, Testosterone)
- Anemia
- Sleep-disturbances

***In clinical practice:  
identify main causes of  
fatigue by phenotypes***

**Physical**

*Malnutrition, Sarcopenia,  
Cachexia, Toxicity*

**Emotional**

*Depression, Uncertainty*

**Cognitive**

*Delirium, Psychotropic  
Medication, CNS-Metastases*

**Mixed**

*Hypercalcemia, Dehydration,  
Organdysfunction, etc.*

*«How much are you tired because:»*

. **C**ognitive:

Problems thinking, concentrate, dizzy

. **E**motiona

No meaning, no energy, depressed

. **P**hysical:

No strength in the body, muscle weak

## Fatigue Phenotypic Approach – Assessments

- |             |                                      |
|-------------|--------------------------------------|
| ● cognitive | SQIDS, m-MMSQ, DOS, mini-COG         |
| ● emotional | HGWS (J.Holland), HADS               |
| ● physical  | Muscles – Weight loss, physical Fct. |

SQIDS: single question in Delirium<sup>1</sup>

s-MMSW : short mini-mental state exam<sup>2</sup>

DOS: Delirium observation scale<sup>3</sup>

HGWS: Hope, Guilt, Worthlessness, passive suicidal<sup>4</sup>

HADS: Hospital Anxiety Depression Scale<sup>5</sup>

Muscles: weight loss (% in mts) corrected for edema<sup>6</sup>

1: Sands M et al., Pall Med 2011; 24:561-5;

2: Fayers PM et al., JPSM 2005;30:41-50;

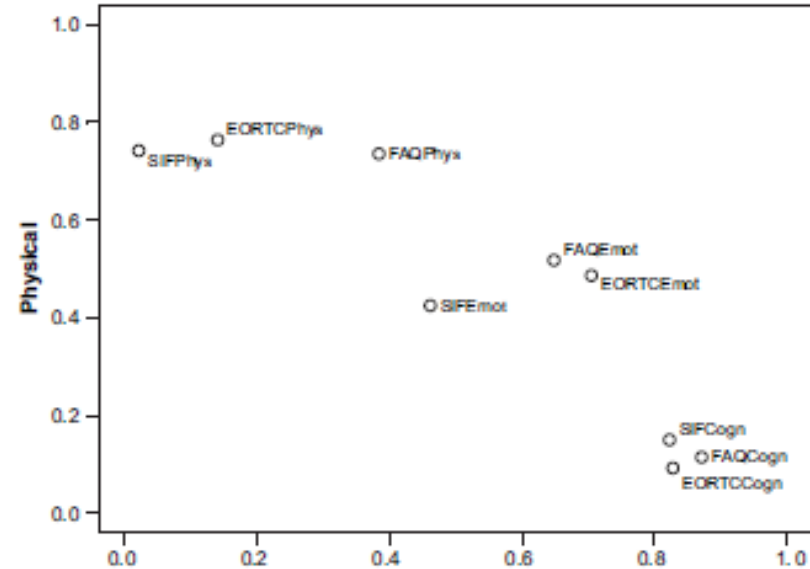
3: Wong CL et al., JAMA 2010; 304:779-86;

4: several textbooks; 5: Wateson E et al, Pall Med 2009;23:739-53;

6: Fearon K & Strasser F et al., Lancet Oncol 2011;12:489-95

# Phenotypic Approach to Fatigue

## Single-Item-Fatigue: 3 questions



SIF: Single-Item Fatigue: emotional (SIFEmot), cognitive (SIFCogn), and physical (SIFPhys)

FAQ: Fatigue Assessment Questionnaire domains: physical (FAQPhys), cognitive (FAQCogn), and affective (FAQEmot)

EORTC: EORTC-QLQ-C30 functional subscales: physical (EORTCPhys), emotional (EORTCEmot), and cognitive (EORTCCogn)

<sup>2</sup> Ich fühle mich **müde**, weil ich „**im Kopf**“ müde bin, weil ich Mühe habe mich zu konzentrieren, weil meine Auffassungsgabe verlangsamt ist:

Brain

0	1	2	3	4	5	6	7	8	9	10
Nicht müde wegen „dem Kopf“										Sehr stark müde wegen „dem Kopf“

<sup>3</sup> Ich fühle mich **müde**, weil ich „**keine Freude**“ verspüre, weil ich keine Lust habe, keinen Antrieb habe, weil „es“ keinen Sinn (mehr) macht:

Mood

0	1	2	3	4	5	6	7	8	9	10
Nicht müde wegen „keine Freude mehr“										Sehr stark müde wegen „keine Freude“

<sup>4</sup> Ich fühle mich **müde**, weil ich „**keine Kraft**“ mehr habe, weil mein Körper schwach meine Muskeln schwach sind:

Muscle

0	1	2	3	4	5	6	7	8	9	10
Nicht müde wegen „keine Kraft“										Sehr stark müde wegen „keine Kraft“

Useful in clinical practice to roughly classify patients

## Mechanistic approach: search causes

- Malnutrition: nutritional intake measurement & impact causes, weight loss
- cancer cachexia: weight loss, anorexia, CRP, tumor activity
- Side effect cancer-directed therapy: history
- Depression: ESAS, Hospital Anxiety Depression Scale (scores <10, 10-12, >12)
- Uncertainty: illness- and prognosis-understanding
- Pharmacological: history & reality check, opiates, benzod., antidepress., etc.
- Delirium: DOS, other tools, fluctuation during the day
- Dehydration: history (urin, oral intake), skin, neck veins
- Electrolyte: Phosphate, Calcium, Na & ev Osmolality, Glucose, ev Mg
- Organ-Function: kidney, liver, heart, lung (RR, O2-Sat)
- Infection: history, dynamics of CRP (double in 2-3 days), ev. ProCalcitonin
- Endocrine: TSH, free Testosterone (male)
- Anemia (Hb < 10g/dl)
- Sleep-disturbances (e.g. symptoms)



# How do I manage in clinical practice a fatigued patient?

## ● «symptomatic» Intervention

- *Patients without «clear» cause*
- *often mixed Phenotypes*
- *«Cancer-related Fatigue»*

## ● Tailored, mechanism-based Intervention

- **Malnutrition:** *nutrition intervention*  
*nutrition impact symptoms*
- **Cachexia:** *Multimodal therapy*
- **Delirium:** *symptomatic & tailored treatment*
- **Depression:** *Psychotherapy, counsel, SSRIs*
- **Anemia:** *Blood transfusions, consider EPO*
- **Electrolytes, Organs, Endocrine, Infection**

*see also later this preceptorship:*

*J Arends, P Ravasco*

*A Caraceni, F Scotte, K Jordan*

*T Skeidvoll, M Maddocks*

*A Caraceni*

*L Travado*

*Internal Medicine*

## Methylphenidate - Ritalin

10mg Pills, breakable (require special triplicates)

Start: 5 mg Testdose (Anxiety, Tachykardia, [may cause Epilepsia])

If after 1 hour Fatigue VAS better (2/10) → >80% likely, that after 1 week better

Then: 5-10mg morning, midday, ev. evening

After weeks: personality disorders may (rarely) develop

Long-acting Methylphenidate: controversial, maybe use in advanced pts

Effective: Fatigue in far advanced Patients, when no other severe Fatigue-cause present

## Some randomized trials for methylphenidate

Study	N	Setting	Dose	Result
Lower EE (2009)	168	various tumor entities after chemotherapy	10-50 mg/d	Significant improvement in FACIT-F at week 8 ( $p=0.02$ ) Reduction in fatigue also reflected in a decrease in other scales
Bruera E (2006)	112	palliative patients with various malignancies	5-20 mg/d	No significant difference in FACIT-F
Moraska AR (2010)	148	various types of solid tumors 64% current chemotherapy	18-54 mg/d	No significant difference in BFI
Roth AJ (2010)	39	prostate cancer	5-30 mg/d	BFI total scores significantly decreased for both groups Significant benefit for BFI severity subscale ( $p=0.03$ )
Mar Fan HG (2008)	59	resected breast cancer, standard adjuvant chemotherapy	10-20 mg/d	No significant difference in FACIT-F

# Methylphenidate and/or a Nursing Telephone Intervention for Fatigue in Patients With Advanced Cancer: A Randomized, Placebo-Controlled, Phase II Trial

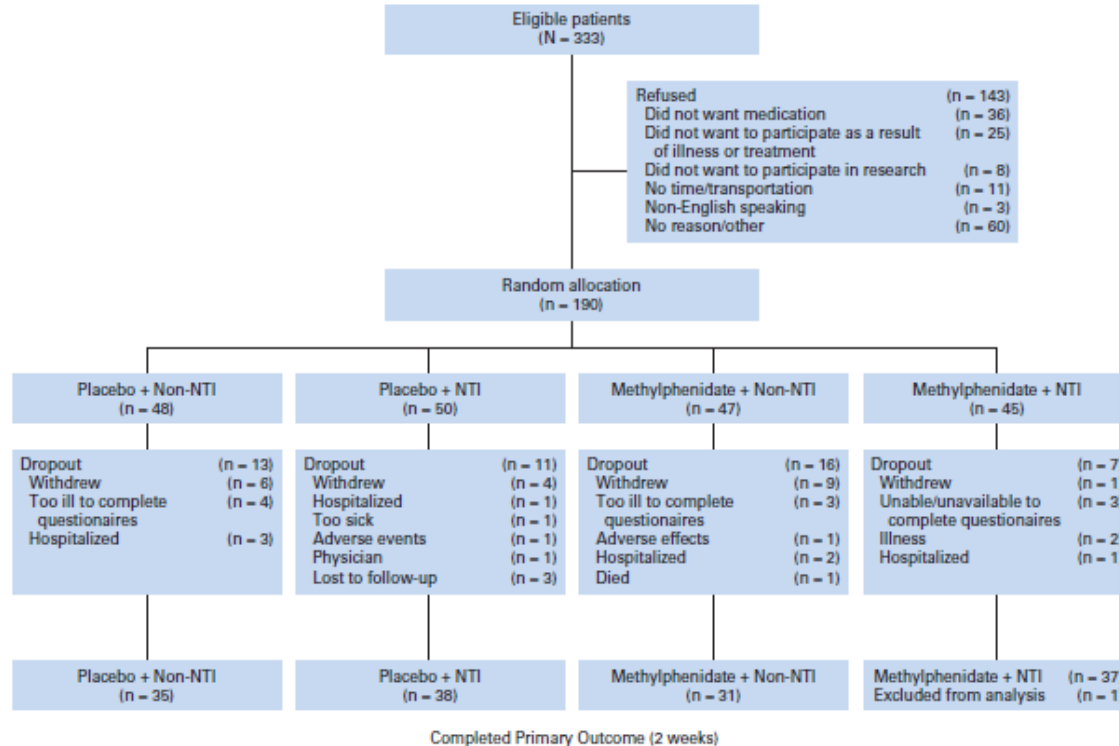
## Patient population

Advanced cancer

fatigue  $\geq 4$  ESAS

Mini-Mental State normal ( $>24/30$ )

Hb  $> 8$  g/dL



5 mg Ritalin every 2 hours max 20 mg per day for 14 d

Nurse practitioner phone 4-6 x in 14 days

→ Both same effect, together not better

# Reduction of Cancer-Related Fatigue With Dexamethasone: A Double-Blind, Randomized, Placebo-Controlled Trial in Patients With Advanced Cancer

Patients with  $\geq 3$  Symptoms ESAS  $\geq 4/10$   
Dexamethasone 4 mg 2 x day / 14 d

Instrument	Day 15 From Baseline					Day 8 From Baseline				
	Dexamethasone (n = 43)		Placebo (n = 41)		P	Dexamethasone (n = 43)		Placebo (n = 41)		P
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
FACIT-F subscale	9.0	10.30	3.1	9.59	.008	8.01	7.81	3.06	7.28	.005
FACIT physical	5.25	6.01	1.32	5.52	.002	4.37	5.14	1.34	4.50	.007
FACIT social/family	-0.05	5.50	0.2	4.77	.820	-0.22	4.06	0.52	3.58	.40
FACIT emotional	1.85	4.93	1.18	4.49	.490	0.59	3.57	1.44	4.07	.33
FACIT functional	1.3	6.21	1.51	5.17	.820	0.55	5.20	1.11	4.80	.56
FACIT-F total score	18.16	22.88	7.87	19.93	.030	13.37	13.22	7.5	14.04	.06
ESAS pain	-1.35	3.11	-0.17	2.66	.09	-1.77	2.89	-0.13	2.80	.014
ESAS fatigue	-2.70	2.85	-1.61	2.69	.158	-1.97	2.78	-0.82	2.85	.056
ESAS nausea	-1.08	2.95	-0.36	3.17	.32	-1.18	2.91	-0.45	2.81	.09
ESAS depression	-0.89	2.58	-0.80	2.67	.54	-0.90	2.67	-1.03	2.90	.89
ESAS anxiety	-0.72	2.81	-1.17	2.45	.77	-1.20	2.44	-0.84	2.79	.49
ESAS drowsiness	-1.59	3.46	-0.89	2.94	.35	-1.00	2.77	-0.45	2.54	.37
ESAS shortness of breath	-2.16	2.92	-0.89	2.40	.06	-1.56	2.44	-0.58	2.37	.07
ESAS appetite	-2.19	3.78	-0.63	3.11	.06	-1.74	3.42	-0.83	3.71	.27
ESAS sleep	-0.22	3.22	-0.14	2.93	.91	-0.13	2.87	-0.11	2.45	.97
ESAS feeling of well-being	-0.32	3.03	-1.22	3.38	.24	-1.31	3.43	-0.73	2.86	.43
ESAS physical	-10.86	9.55	-4.78	10.86	.013	-9.10	7.50	-3.42	10.79	.009
ESAS psychological	-1.48	4.67	-2.08	4.73	.65	-1.26	4.68	-1.81	5.01	.65
ESAS symptom distress	-12.2	13.49	-8.86	15.91	.15	-10	12.28	-6.95	16.38	.15
HADS anxiety	-0.66	3.45	-1.00	3.54	.75	-0.85	3.16	-1.09	2.32	.59
HADS depression	-1.39	3.59	-0.31	3.90	.29	-1.23	4.02	-0.43	3.12	.65
FAACT	6.82	8.95	1.95	8.54	.013	4.78	8.44	1.49	8.23	.08

FACIT-F but  
not ESAS-Fat  
better

FAACT but  
not ESAS-App  
better

Yennu S et al.  
J Clin Oncol  
2013;31:3076-82

Abbreviations: ESAS, Edmonton Symptom Assessment Scale; FAACT, Functional Assessment of Cancer Therapy-Anorexia-Cachexia; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HADS, Hospital Anxiety Depression Scale; SD, standard deviation.

# Reduction of Cancer-Related Fatigue With Dexamethasone: A Double-Blind, Randomized, Placebo-Controlled Trial in Patients With Advanced Cancer

## Side effects

Adverse Event	Total No. of Patients	Grade $\geq 3^*$		Total No. of Patients	Grade $< 3$	
		Dexamethasone (n = 17)	Placebo (n = 11)		Dexamethasone (n = 24)	Placebo (n = 33)
Pain	7	5	2	22	13	9
Insomnia	6	2	4	3	1	2
Fatigue	5	5	0	9	3	6
Infection	2	2	0	3	2	1
Cough	1	0	1	1	0	1
Death NOS	1	1	0	0	0	0
Dysphagia	1	1	0	0	0	0
Dizziness	1	0	1	1	1	0
Dyspnea	1	0	1	5	0	5
Edema	1	0	1	4	1	3
Neuropathy	1	1	0	0	0	0
Somnolence	1	0	1	3	0	3
Nausea/vomiting	0	0	4	4	1	3
Blurred vision	0	0	1	1	1	0
Depression	0	0	1	1	1	0

→ Dexamethasone not more side-effects than Placebo.

→ Effect on Fatigue, Appetite maximum 14 days

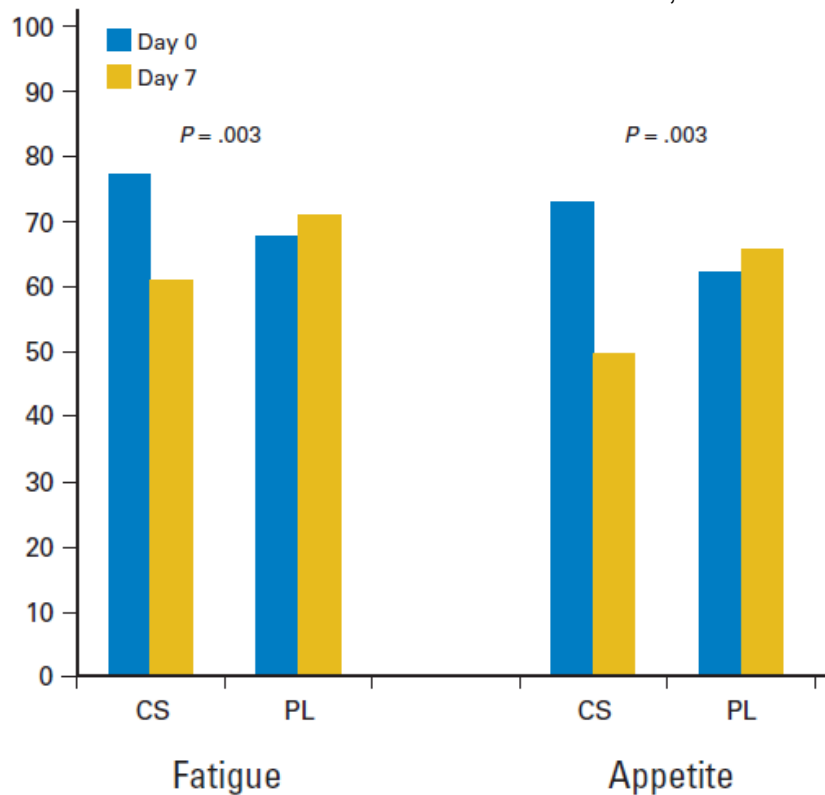
Yennu S et al. J Clin Oncol 2013;31:3076-3082

# Efficacy of Methylprednisolone on Pain, Fatigue, and Appetite Loss in Patients With Advanced Cancer Using Opioids: A Randomized, Placebo-Controlled, Double-Blind Trial

Ørnulf Paulsen, Pål Klepstad, Jan Henrik Rosland, Nina Aass, Eva Albert, Peter Fayers, and Stein Kaasa

Patients Pain 4/10 in 24 h,  
opioid-Analgesia, survival >4wks

Paulsen O et al. J Clin Oncol 2014;32:3221-8



Methylprednisolone 16 mg 2 x day for 7 days

Fatigue and Appetit become better after 7  
days, few side-effects

Predefined AE Category	Methylprednisolone (n = 25)		Placebo (n = 22)	
	No.	%	No.	%
Oral symptoms	6	24	7	32
Restlessness	6	24	3	14
Psychic change	2	8	3	14
Anxiety	2	8	3	14
Edema	1	4	5	23
Muscle weakness	1	4	3	14
Sleeplessness	4	16	3	14
Dyspepsia	3	12	4	18
Other	2	8	3	14
Total	27		34	
Mean No. of AEs	1.08		1.55	
P		.28		

# Fatigue and Appetit but not pain become better after 7 days, few side-effects

**Table 3.** Primary and Secondary Outcomes

Outcome	Methylprednisolone (n = 25)		Placebo (n = 22)		P*
	Mean	95% CI	Mean	95% CI	
Average pain intensity†‡					
Day 0	4.76	4.33 to 5.19	4.36	3.88 to 4.85	.21
Day 7	3.60	2.79 to 4.41	3.68	2.99 to 4.37	.88
Mean difference	-1.16	-1.96 to -0.35	-0.68	-1.28 to -0.08	.50
Morphine consumption (OMEs), mg§					
Day 0	273.8	167.8 to 379.8	165.8	93.1 to 238.5	.09
Day 7	318.6	192.3 to 444.8	188.2	103.2 to 273.2	.08
Mean difference	44.8	-16.0 to 105.6	22.4	-5.6 to 50.4	.51
Relative difference (day 7/day 0)	1.19	1.00 to 1.38	1.20	0.90 to 1.51	.95
Pain intensity at rest (day 1 to 7)‡§					
AUC	19.9	14.4 to 25.4	17.9	12.2 to 23.6	.60
Fatigue§  ¶					
Day 0	77.1	68.3 to 85.9	67.2	56.3 to 78.1	.15
Day 7	60.4	49.7 to 71.2	70.5	61.4 to 79.6	.16
Mean difference	-16.7	-27.0 to -6.3	3.3	-4.5 to 11.1	.003
Appetite loss§  ¶					
Day 0	73.3	60.2 to 86.5	63.6	50.8 to 76.5	.28
Day 7	49.3	34.9 to 63.7	65.2	51.9 to 78.4	.10
Mean difference	-24.0	-37.5 to -10.5	1.5	-8.1 to 11.2	.003
Patient satisfaction with treatment‡§	5.4	4.05 to 6.70	2.0	0.71 to 3.29	.001



# Testosterone replacement for fatigue in hypogonadal ambulatory males with advanced cancer: a preliminary double-blind placebo-controlled trial

Del Fabbro E et al. Supp Care Cancer 2013;21:2599–2607

i.m. (gluteal) Testosteron enanthate every 14 days, monitoring free testost. (70-270ng/dl)

Testosteron free <70ng/dl  
cancer out-pts, Fatigue >3/10 (ESAS), Hb >9g/dl

ESAS Fatigue after 29 days not better, ECOG clearly better (1 vs 0, p=0.02)

	Day 29 vs. baseline			Day 72 vs. baseline		
	Placebo N=16 Mean(SD)	Testosterone N=13	One sided p value	Placebo N=6	Testosterone N=6	One sided p value
PWB_Score	0 (6)	1 (4)	0.21	3 (6)	3 (3)	0.44
SWB_Score	2 (3)	-1 (4)	0.03	1 (3)	1 (4)	0.34
EWB_Score	-2 (3)	2 (3)	0.007	0 (2)	2 (3)	0.21
FWB_Score	-1 (3)	-1 (4)	0.40	0 (5)	-2 (5)	0.26
Fatigue Subscale	-2 (12)	4 (8)	0.11	1 (10)	11 (4)	0.03
FACIT_F Score	-4 (20)	4 (14)	0.14	5 (20)	16 (12)	0.32
FAACT Score	-2 (13)	2 (9)	0.18	4 (15)	13 (5)	0.16

FACIT-F Functional Assessment of Chronic Illness Therapy-Fatigue, FAACT Functional Assessment of Anorexia/Cachexia Therapy, PWB physical well-being, SWB social well-being, EWB emotional well-being, FWB functional well-being

# Testosterone replacement for fatigue in hypogonadal ambulatory males with advanced cancer: a preliminary double-blind placebo-controlled trial

Del Fabbro E et al. Supp Care Cancer 2013;21:2599–2607

Day 29 vs. baseline

	Placebo N=16 (%)*	Testosterone N=13 (%)*	p value
SDI, average (SD)	−2 (12)	11 (17)	0.054
ESAS, average (SD)			
Pain	0 (2)	0 (2)	0.98
Fatigue	0 (2)	0 (2)	0.76
Nausea	0 (2)	0 (1)	0.35
Depression	0 (2)	1 (2)	0.64
Anxiety	0 (2)	1 (1)	0.80
Drowsiness	0 (2)	0 (3)	0.77
Dyspnea	0 (1)	1 (2)	0.22
Appetite	−1 (3)	−2 (3)	0.43
Sleep	−1 (2)	−1 (3)	0.97
Well being	−1 (3)	−2 (4)	0.55
ECOG, average (SD)	1 (1)	0 (1)	0.02
HADS, average (SD)			
Anxiety	1 (3)	0 (2)	0.38
Depression	2 (3)	0 (4)	0.20

ESAS Fatigue after 29 days not better,  
ECOG clearly better (1 vs 0, p=0.02)

# Symptomatic Fatigue treatment

- Methylphenidate (Ritalin) yes, start slow, watch anxiety  
Antidepressants not for CRF but for Depression  
Modafinil maybe, one trial<sup>1</sup>, Phytotherapeutics may be promising<sup>2</sup>
- Behavioural interventions (cancer advocacy education)
  - Regular physical Activity
  - Energy planning (Expectations – Reality)
  - Sleep-Hygiene (but not too much)
  - Restorative Activities
- Corticosteroids: yes (most often), but ONLY <2 weeks!  
Tox: myopathy (proximal), infections (candidiasis), insulin resistance, bones
- Testosterone if hypogonadism (Men, not Prostate-Ca)
- Physical activity and strength training: define expectations & goals
- «Psychosocial» Interventions<sup>3</sup>: controversial, many methods (Yoga, Acupuncture<sup>4</sup>), v.a. in postcurative „survivors“

1: Hovey E Support Care Cancer 2014;22:1233-42

2: Bar-Sela G Support Care Cancer 2015;23:1979-8

3: Larkin D Int J Nurs Pract 2014;20:549-60

4: Zeng Y Integr Cancer Ther 2014;13:193-200

# How do I manage in clinical practice a fatigued patient?

- «symptomatic» Intervention

- *Patients without «clear» cause*
- *often mixed Phenotypes*
- «Cancer-related Fatigue»

- Tailored, mechanism-based Intervention

- **Malnutrition:** *nutrition intervention*  
*nutrition impact symptoms*
- **Cachexia:** *Principles of multimodal therapy*
- **Delirium:** *symptomatic & tailored treatment*
- **Depression:** *Psychotherapy, counsel, SSRIs*
- **Anemia:** *Blood transfusions, consider EPO*
- **Electrolytes, Organs, Endocrine, Infection**

*see also later this preceptorship:*

*J Arends, P Ravasco*

*A Caraceni, F Scotte, K Jordan*

*T Skeidvoll, M Maddocks*

*A Caraceni*

*L Travado*

*Internal Medicine*

# Cancer Anorexia Cachexia Framework

Cancer cachexia is a multifactorial syndrome defined by a ongoing loss of **skeletal muscle mass** (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive **functional impairment**.

Its pathophysiology is characterized by negative protein and negative energy balance driven by a variable combination of **reduced food intake** and **abnormal metabolism**

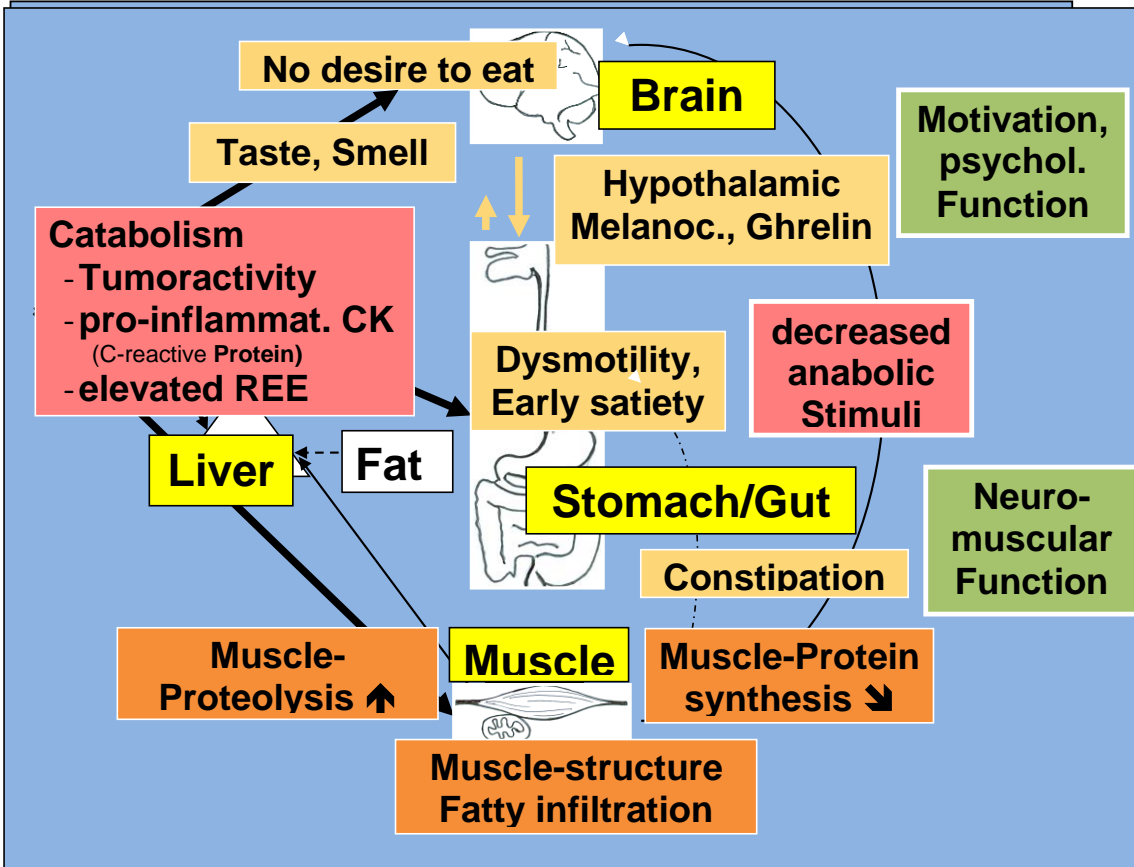
**Muscle**

no **S**tarvation alone  
Dual **P**athophysiology

1: Fearon K & Strasser F, et al. Lancet Oncol 2011 ;12:489-95

2: Argilés JM et al. J Am Med Dir Assoc 2010;11:229-30

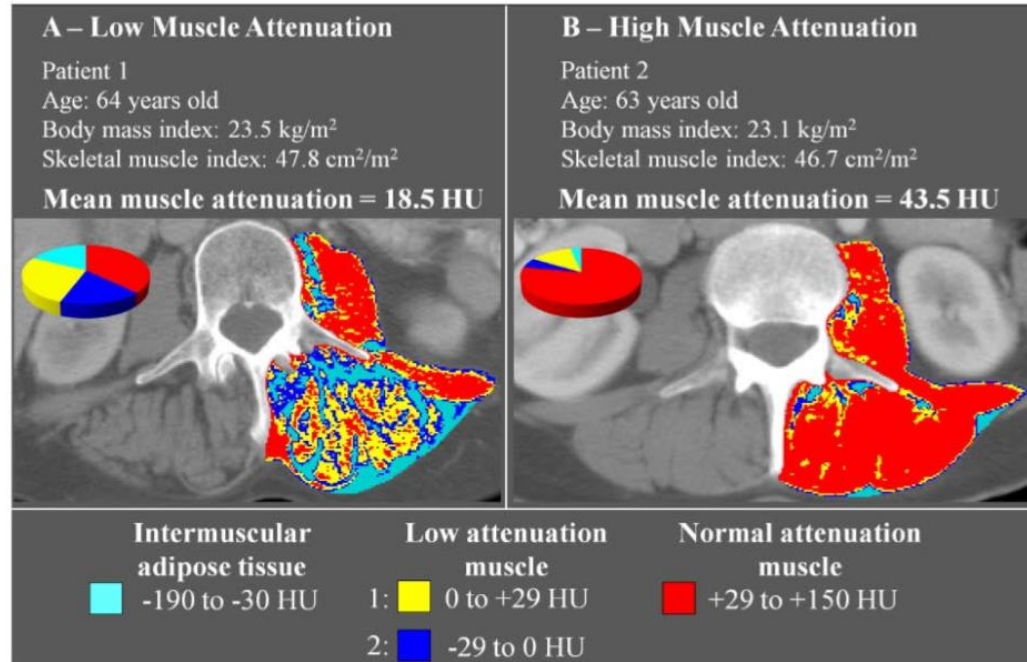
# Need to understand the mechanism of cancer cachexia



Patients with same grade (1) of weight loss and BMI, survival if **CRP < or ≥ 10mg/dl** is 30.6 mts or 7.7 mts

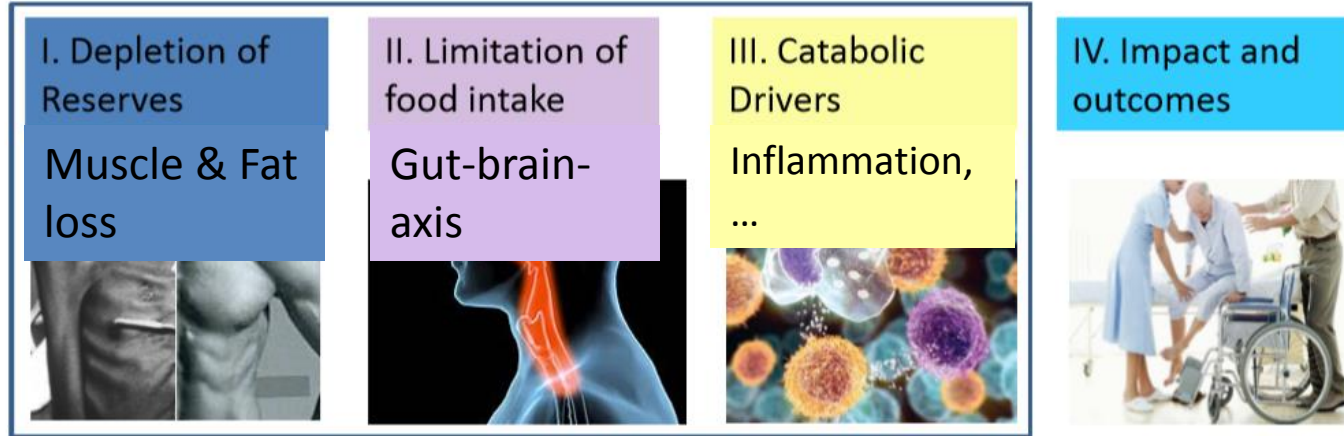
Martin L et al. JCO 2015;90

## Fatty infiltration of the muscle as manifestation of a **hypo-anabolic, pro-catabolic, inflammatory status**



picture courtesy of Vickie Baracos 9.2014, adapted by FS

In clinical practice, several mechanism and cofactors happen at the same time → *structured thinking helpful*



Slide courtesy of Vickie Baracos 9.2014

***Sarcopenia***



***Malnutrition***



***Cachexia***

- 1: Fearon K & Strasser F, et al.  
Lancet Oncol 2011;12:489-95  
2: Argilés JM et al. J Am Med Dir  
Assoc 2010;11:229-30



### ***Sarcopenia caused by:***

Hypogonadism

Physical inactivity

Corticosteroids

Thyroid dysfunction

Age-related\*

- *Less muscle stem cell response to acute resistance exercise*
- *Same Type I, less Type II fibres*
- *myogenic program reduced*
- *impaired induction of MyoD in Pax7 cells*

### **Cachexia**

\* McKay B et al. FASEB J 2012;(26):2509–2521  
Joseph AM et al. Aging Cell 2012; 11: 801–809

## Malnutrition (Starvation) caused by:

## II. Limitation of food intake

- **Diet mistakes / misconceptions: too healthy, ..**
- **neglect for maintenance of nutritional intake**
  - “no eating” due to procedures, hospitalization<sup>1</sup>
  - helping patients to eat (edentulousness<sup>1</sup>)
- **Secondary Nutrition-Impact symptoms<sup>2</sup>**
  - Pain, breathlessness, constipation, dysgeusia, ...
  - Periods of nausea/vomiting, stomatitis, dysphagia, gastric acid
  - (partial) bowel obstruction, diarrhea, malabsorption, prolonged constipation, ..
- **Cachexia**

1: van der Pols-Vijlbrief R et al. Ageing Res Rev 2014;18:112-31

2: Omlin A et al. J Cach Sarcop Muscle 2013;55-61

### ***Inflammation caused by:***

#### Infections

- If steep increase of C-Reactive Protein (x 2-5 /3-5 days)
- may consider empirical antibiotic therapy (after cultures)
- *may*<sup>1</sup> measure Pro-CalciTonin (neg & pos predictive value)<sup>2</sup>
- *may* use PCT/CRP ratio<sup>3</sup>

#### Corticosteroids

#### Chronic inflammatory diseases

#### Pro-inflammatory drugs & herbal therapies

### **Cachexia**

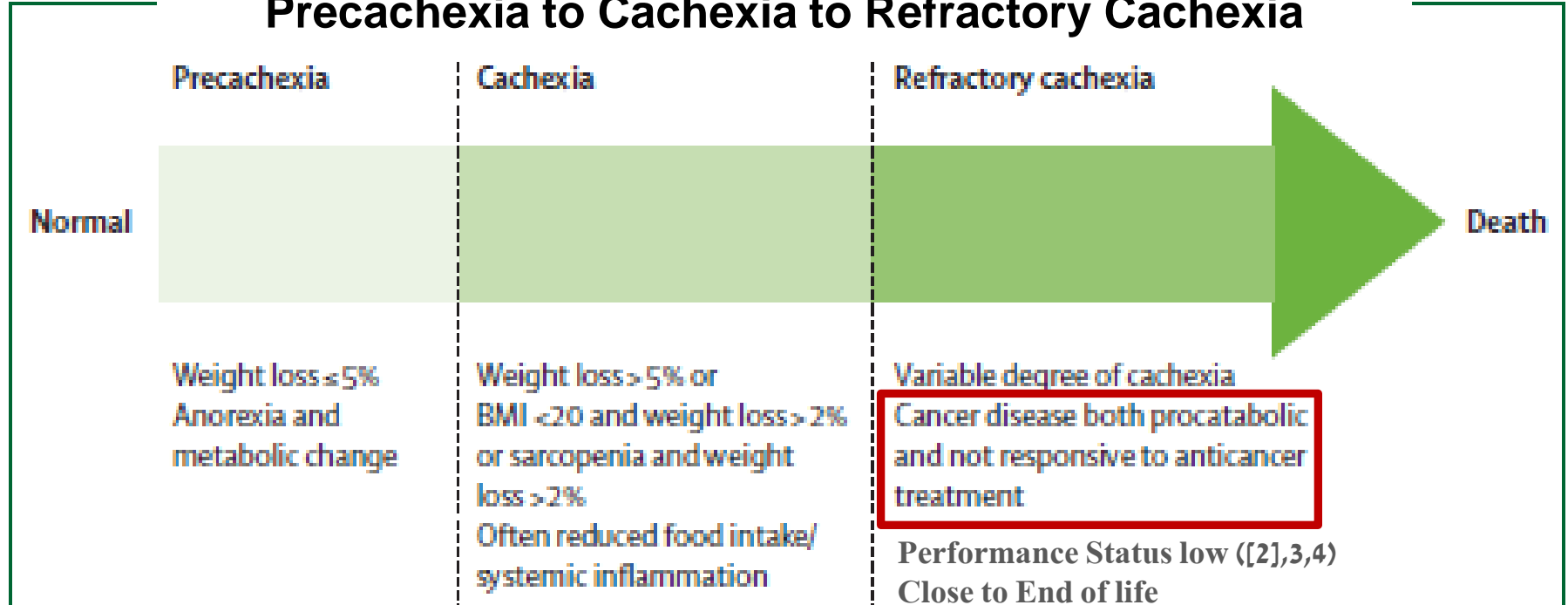
1: Naito T et al. Intern Med 2015;54:1989-94; Chaftari AM et al. PLoS ONE 2015;10:e0130999

2: Sbrana A et al. New Microbiol 2016;39(3); Wu CW et al. Support Care Cancer 2015;23:2863-72

3: Hangai S et al. Leuk Lymphoma 2015;56:910-4; Markova M et al. Support Care Cancer 2014;21:2733-42



## Cancer Anorexia Cachexia Syndrome can develop from Precachexia to Cachexia to Refractory Cachexia



**Conceptual Framework:** Fearon K & Strasser F, et al. Definition and classification of cancer cachexia, an international consensus. Lancet Oncol 2011;12(5):489-95

## **Patient-centred care** requires adequate assessment of patients cachexia domains

<b>Reserves</b> (muscles)	<b>Weight loss history</b> (%; 1, 2, 6 mts), <b>BMI</b> check for edema (thigh), ( <i>if fluid retention</i> consider <b>CT L3/4</b> or DEXA)
<b>Intake</b> (gut-brain)	<b>2 day diet diary</b> , % kcal/protein / needs (Harris Benedikt) <b>Appetite, hunger, satiety, taste/smell</b> Search nutrition impact symptoms (S-NIS checklist, PG-SGA), <b>treat</b>
<b>Catabolism</b>	Estimate cancer <b>disease dynamics &amp; responsiveness to Tx</b> <b>CRP &gt;10mg/l</b> (no clinical infection, consider PCT/CRP) <b>Albumin</b>
<b>Function</b>	<b>Physical function (KPS)</b> , muscle strength (stairs – floors) Estimate Patients Motivation/Participation

→ **Decide on cachexia phase\*** and goals of intervention

**Goals of cachexia interventions depend on cachexia phase**

Normal

Precachexia

Cachexia

Refractory

Death

<u>Goals</u>	Pre-emptive	Stabilize	Alleviate
Reserves	prevent loss	stabilize - improve	unavoidable loss
Nutritional Intake	prevent decrease	stabilize - improve	alleviate distress
Inflam / Cancer Act.	control cancer	control cancer	not controllable
Function	maintain	maintain - improve	unavoidable loss

## Influencing factors & interventions

Cancer Supportive & Palliative Care	Cancer Therapy Toxicities	Important effects	Short-term alleviation, EOL
Anticancer therapy	early lines	≥ 2nd lines	no standards

# Multidimensional Cachexia interventions delivered by multiprofessional teams

- **Nutritional intake** (educate, oral nutrition supplement; alleviate distress)<sup>1,2</sup>
- **Physical activity & strenght** increase & maintenance<sup>3</sup>
- **Disease coping, life goals**, support of and by **family**<sup>4</sup>
- **Tumor control** - slowing progression / activity<sup>5</sup>
- Various **anti-cachexia drugs** (some soon available)<sup>6</sup>

«**Best Supportive Care**<sup>1</sup>»

«**Early Integrated Palliative Care**<sup>2</sup>»

1: Cherny JCO 2009; Zafar Lancet Oncol 2012

2: Smith T JCO 2012; Temel NEJM 2011; Jacobsen J J Pall Med 2011 Zimmermann C Lancet 2014, Bakitas M JAMA 2011 & JCO 2015

1: Baldwin C J Natl Cancer Inst 2012 // 2: Oberholzer R JPSM 2013., Reid J J Adv Nurs. 2013, Amano K, JSCM 2016 // 3: Stene GB Crit Rev Oncol Hematol. 2013 // 4: Quill TE & Abernethy A. NEJM 2013. Smith TJ et al. JCO 2012 // 5: Köberle D JCO 2008; Au H-J JCO 2009 // 6: Fearon K Nat Rev Clin Oncol 2013; Bruggemann AR JOP 2016;12:1163-71.

A photograph of two young women standing together in a room with a light-colored wall and a grey floor. The woman on the left is wearing a white short-sleeved top and a black skirt, and is holding a yellow rose. The woman on the right is wearing a patterned dress and is also holding a yellow rose. To their left, there are two tall, rustic wooden pillars. The taller pillar on the left has a lit candle on top, a small bouquet of flowers, and a string of green ivy hanging down its side. The shorter pillar next to it also has a lit candle on top. The overall atmosphere is warm and intimate.

**Thank you**  
**[florian.strasser@kssg.ch](mailto:florian.strasser@kssg.ch)**