

PRC

Dietary treatment of cachexia – challenges of nutritional research in cancer patients

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NTNU – Trondheim
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Science and Technology



ST. OLAVS HOSPITAL
TRONDHEIM UNIVERSITY HOSPITAL



NORWEGIAN CANCER SOCIETY

Outline

- **Cancer cachexia**
- Dietary treatment of cachexia
- Challenges of nutritional research
- How to move forward?
- Conclusion

Cancer cachexia

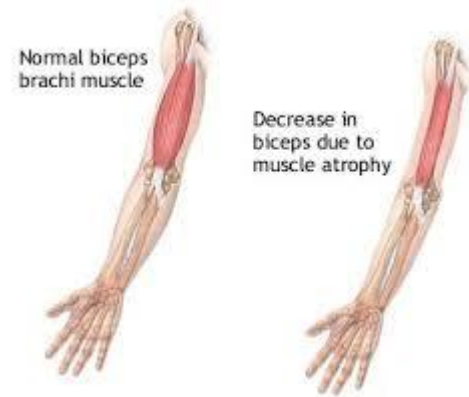
- Common in cancer patients
- Weight loss and reduced food intake
- Definition states that it «cannot be reversed by conventional nutritional support»

Fearon K, *et al.* **Definition and classification of cancer cachexia: An international consensus.** Lancet Oncology 2011

Cancer cachexia

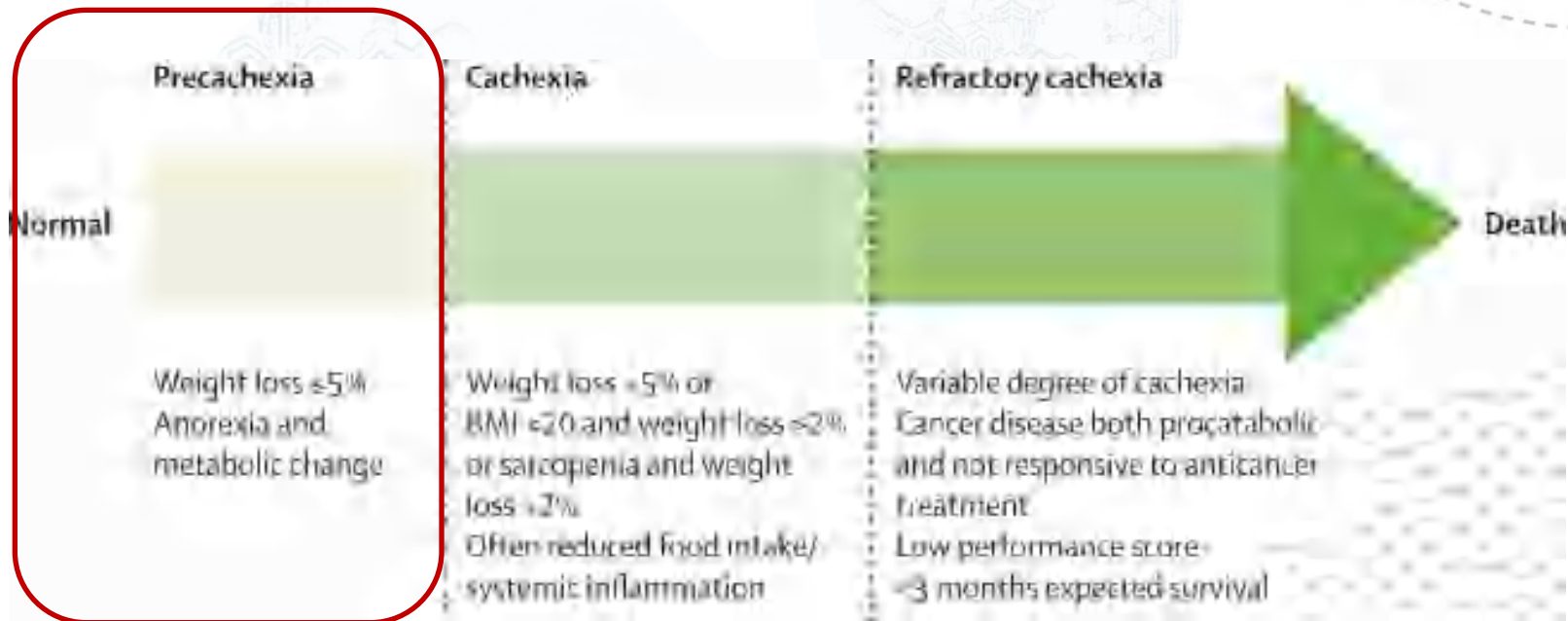
The pathophysiology of cancer cachexia:

- Anorexia
- Metabolic alterations
 - Inflammation
 - Increased muscle proteolysis
- Today no nutritional, pharmacological or metabolic intervention has proved to be effective

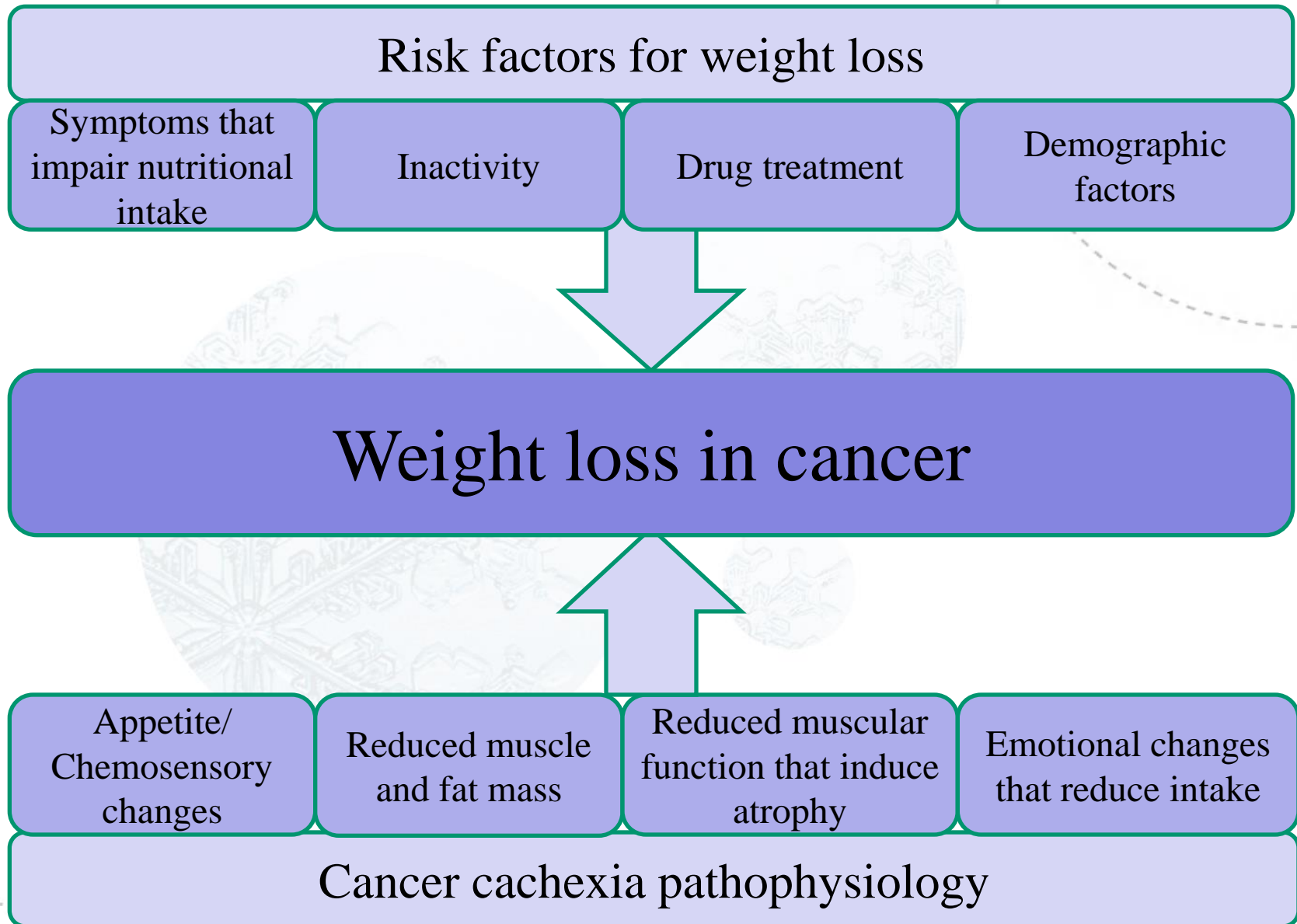


Classification of cachexia

Need to treat early in the trajectory of cachexia



Fearon K, *et al.* Definition and classification of cancer cachexia: An international consensus. Lancet Oncology 2011



Outline

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Dietary treatment of cancer cachexia

- Dietary counseling with or without oral supplements is often the first line method
 - Energy dense foods
 - Increase meal frequency
 - Nutritional supplements
- Treat nutritional impact symptoms
- What can be achieved with counseling?





Critical Reviews in Oncology/Hematology 91 (2014) 210–221

CRITICAL REVIEWS IN

*Oncology
Hematology*

Incorporating Geriatric Oncology

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Dietary treatment of weight loss in patients with advanced cancer and cachexia: A systematic literature review

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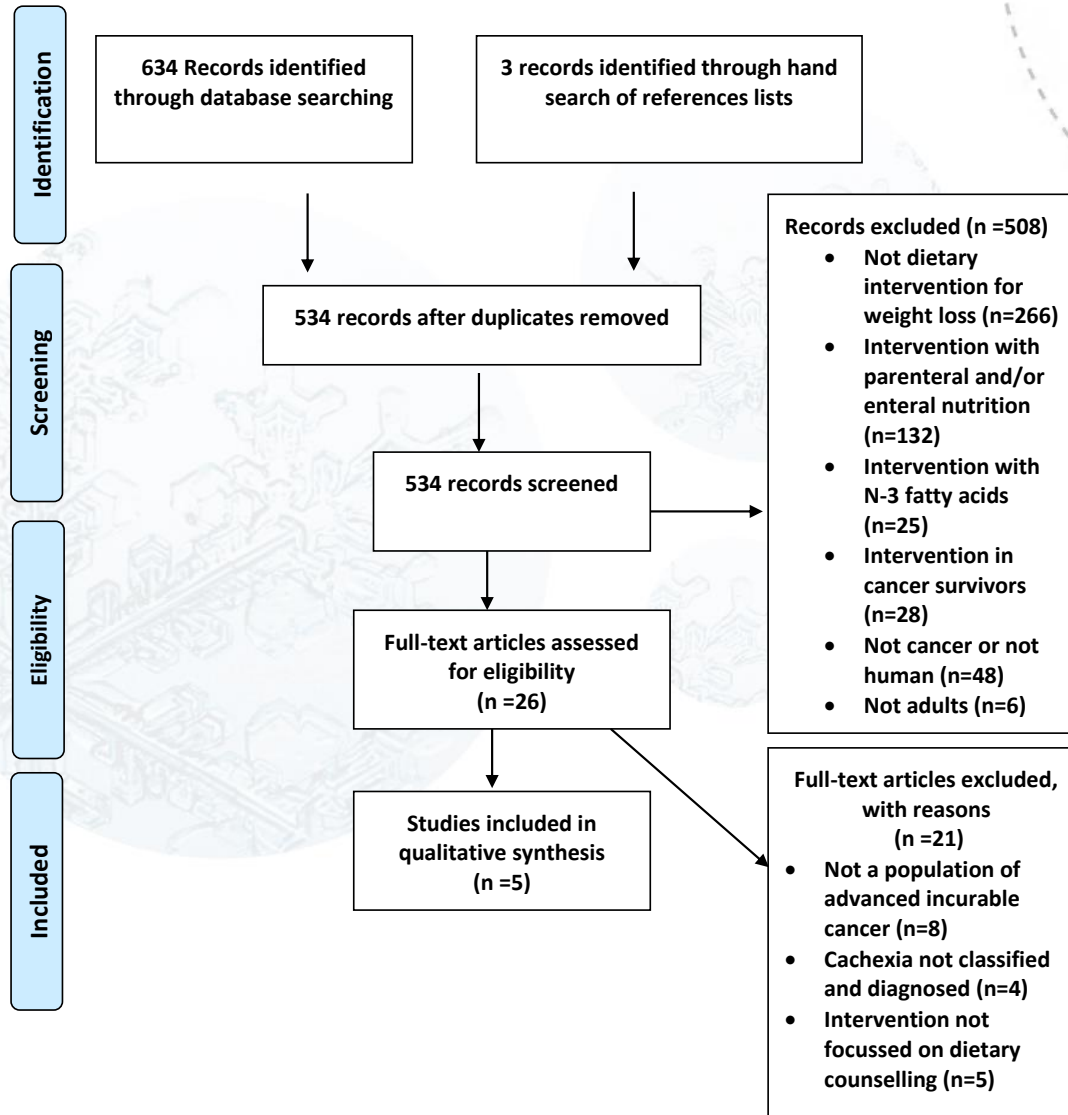
Aim of the systematic review

- What is the effect of dietary counseling in patients with advanced cancer and different stages of cachexia?
 - Primary outcomes: Body weight and energy intake
 - Secondary outcomes: Physical function and QoL

Inclusion and exclusion

Selection criterion	Inclusion Criterion	Exclusion Criterion
Population	<ul style="list-style-type: none">• Adults ≥ 18 years• Any advanced cancer• Possible to classify<ul style="list-style-type: none">- Pre-cachexia- Cachexia- Refractory cachexia	<ul style="list-style-type: none">• Curative intent• Data necessary to classify cachexia not presented
Intervention	<ul style="list-style-type: none">• Dietary counselling• Any duration of intervention	<ul style="list-style-type: none">• Parenteral- or enteral nutrition• Vitamins• Amino acids or proteins• Omega-3 fatty acids

Prisma flow chart



Results

	Full Search
No. studies	5 (n=842)
No. subjects per trial	23-358
Design	3 RCTs
Diagnosis	NSCLC; Colorectal; Head & Neck; GI cancer
Intervention period	1 – 5 months
- <i>Cachexia</i>	<i>3 studies (n=419), per study 23-358</i>
- <i>Mixed stages of cachexia</i>	<i>2 studies (n=423)</i>

Effect of dietary treatment on body weight

Cachexia

- Weight gain (n=23)
+ 1.4 kg vs. -2 kg, $p < 0.05$
- Weight gain (n=38)
+1% vs. -1.5%, $p = 0.03$
- No differences (n=358)
follow-up:
+4.8 kg vs. 1.4 kg, $p < 0.05$

Mixed stages of cachexia

- Less weight loss (n=180)
-0.6 kg vs. -2.1 kg, $p < 0.05$
- Weight gain or stable weight in
malnourished patients (n=243)

Breitkreuz et al, *Wiener Klinische Wochenschrift*, 2005
van den Berg et al, *Br J Nutr*, 2010
Baldwin et al, *J Hum Nutr Diet*, 2011

Evans et al, *J Clin Oncol*, 1987
Percival et al, *Respir Med*, 2013

Effect of dietary treatment on energy intake

Cachexia

- Assessed in one RCT (n=23)
1865±317 kcal vs. 1556±497 kcal, ns

Mixed stages of cachexia

- Assessed in one RCT (n=180)
92% vs. 73%, p<0.01

Breitkreuz et al, *Wiener Klinische Wochenschrift*, 2005

Evans et al, *J Clin Oncol*, 1987

Effect of dietary treatment on physical function and QoL

Cachexia

- Assessed in two RCTs
Improved ratings of leisure activities and psychological conditions (n=23)
- No differences (n=358)

Mixed stages of cachexia

- Not assessed

Breitkreuz et al, *Wiener Klinische Wochenschrift*, 2005
Baldwin et al, *J Hum Nutr Diet*, 2011

Summery of findings

- Three out of five studies included only patients with cachexia, one both pre-cachectic and cachectic patients and one with all stages
- All five studies evaluated the effect of dietary counselling on body weight. All studies reported improvements at some time points
- Results from two RCTs indicated that it is possible to increase energy intake by various combinations of high energy foods, fortifications and ONS

Outline

- Cancer cachexia
- Dietary treatment of cachexia
- **Challenges of nutritional research**
- How to move forward?
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Challenges of nutritional research — who are we treating?

- Patient population not properly described
 - Diagnosis, stage
 - Weight loss
 - Nutritional impact symptoms
 - Treatment and response
- “...as the most important predictor of weight gain was survival and not nutritional intervention”

Baldwin, C., et al., **Simple nutritional intervention in patients with advanced cancers of the gastrointestinal tract, non-small cell lung cancers or mesothelioma and weight loss receiving chemotherapy: a randomised controlled trial.** J Hum Nutr Diet, 2011.

Challenges of nutritional research – what is the treatment?

- Dietary counseling is often poorly described and difficult to replicate
- Often based on experience and clinical practice
- Adequate placebo to counseling is difficult to design

Challenges of nutritional research – does the counseling help?

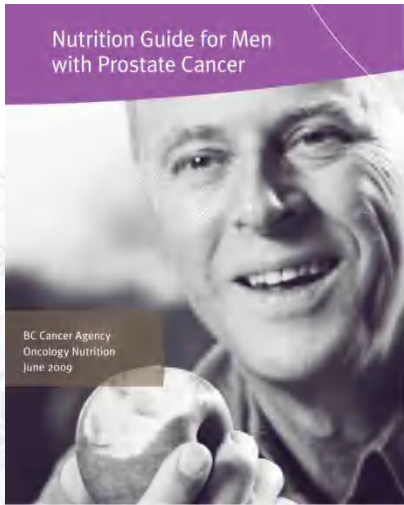
- Lack of compliance data
- Only one trial in our review reported on compliance:
 - 30% took their prescribed nutritional supplements after 3 weeks
 - 19% took their prescribed nutritional supplements after 6 weeks

Baldwin, C., et al., **Simple nutritional intervention in patients with advanced cancers of the gastrointestinal tract, non-small cell lung cancers or mesothelioma and weight loss receiving chemotherapy: a randomised controlled trial.** J Hum Nutr Diet, 2011.

Challenges of nutritional research – what is the comparator?

- «Standard care» or «usual care» is also an intervention
- Only one study in our review described nutritional treatment in the control arm
 - (15% received tube feeding)
- Contamination in the control group?
- Dilution of effects?





Nutrition Guide for Men with Prostate Cancer

BC Cancer Agency
Oncology Nutrition
June 2009

American Cancer Society

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families

Nutrition is an important part of cancer treatment. Getting the right kinds of food, eating enough, and after treatment can help you feel better and stay stronger. Chapters one of you and reading this booklet either you or someone you care about is going through cancer treatment. The American Cancer Society has prepared this guide to help you and your loved ones cope with treatment side effects that might affect how well you can eat.

Not everyone has nutrition-related side effects, but this guide will help you address them if and when they come up. You don't have to read straight through all of the information here. You can just read the sections you need and use the information that applies to you.

The information in this guide is not meant to replace the advice of a medical professional. If you have any questions or concerns, you should talk to a doctor, nurse, or dietitian about your nutritional needs. A registered dietitian (RD) can be one of your best sources of information about your diet. If you are going to meet with a dietitian, be sure to write down your questions before your meeting so you won't forget anything. And be sure to ask the dietitian to repeat or explain anything that's not clear. If you have questions about anything in this guide, a dietitian can give you a more detailed explanation.

You can find more detailed discussions of nutrition before, during, and after cancer treatment in our book called *The American Cancer Society Complete Guide to Nutrition for Cancer Survivors: Eating Well, Staying Well Through Life's Changes*. Call us at 1-800-227-2345 or visit our website online at www.cancer.org/foodandnutrition about costs or to place an order.

For more information or to find a registered dietitian, visit the Academy of Nutrition and Dietetics (or the "To Find More" section).

National Cancer Institute
Support for People With Cancer

Eating Hints
Before, During, and After Cancer Treatment

11 Chapters
160 Pages
www.nci.org
© 2008 National Cancer Institute

The ROYAL MARSDEN
NHS Foundation Trust

Eating well when you have cancer
A guide for cancer patients when eating may be difficult

1
Patient Information

NHS

Outline

- Cancer cachexia
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- Challenges of nutritional research
- **How to move forward?**
- Conclusion

How to move forward?

- Who are we treating?
- What is the treatment?
- Does the counseling help? Compliance?
- What is the comparator?

How to move forward?

- Classification of cancer cachexia has improved, but few clinically relevant diagnostic tools exist for its early identification and characterization
- TNM classification system in oncology
- What about nutrition? Do we have any tools for early identification of cancer cachexia that we can use?

Useful tools for early detection of cancer cachexia?



Fearon K, *et al.* Definition and classification of cancer cachexia: An international consensus. Lancet Oncology 2011

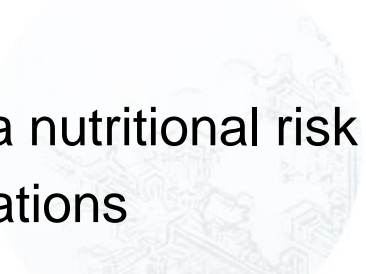
Nutritional screening and assessment

- Screening tools

Identification of persons with a nutritional risk
 Applied in large patient populations
 «quick and easy»

- Assessment tools

Allowing a definite diagnosis
 Staging of the condition
 Identify causal factors
 Resource consuming



Ref: ESPEN, ASPEN, ADA

Nutritional screening and assessment

- Screening tools
 - NRS2002
 - MST
 - MUST
- Assessment tools
 - MNA
 - SGA
 - PG-SGA

Scored Patient-Generated Subjective Global Assessment (PG-SGA)

History (Items 1-4 are designed to be completed by the patient.)

1. **Weight** (See Worksheet 1)

In summary of my lifetime and recent weight:

I currently weigh about _____ pounds.
I am about _____ feet _____ tall.

Five years ago I weighed about _____ pounds.
Six months ago I weighed about _____ pounds.

During the past six weeks my weight has:

increased remained the same decreased (Box 1)

2. **Food Intake**: As compared to my normal intake, I would rate my food intake during the past month as:

unchanged more than usual less than usual I am not eating.

normal food but less than normal amount like solid food only liquid only nutritional supplements very little or nothing only take sips of or only swallow by sips (Box 2)

3. **Symptoms** I have had the following problems that have kept me from eating enough during the past six weeks (check all that apply):

no problem eating vomiting diarrhea dry mouth trouble swallowing or have no taste smells bother me pain when I eat feel full quickly other (Box 3)

4. **Activities and Function**: Over the past month, I would generally rate my activity as:

normal with no limitations not feeling up to most things, but in bed or chair less than half the day able to do little activities and spend most of the day in bed or chair unable to do anything, barely out of bed (Box 4)

Adding Score of the Boxes 1-4 (Box 5)

The remainder of this form will be completed by your doctor, nurse, or therapist. Thank you.

5. **Illness and its relation to nutritional requirements** (See Worksheet 2)

All relevant diagnoses (specify): _____

Primary disease stage (circle all known or appropriate): I II III IV Other _____

Age: _____ Numerical score from Worksheet 2 (Box 6)

6. **Metabolic Demand** (See Worksheet 3)

Numerical score from Worksheet 3 (Box 7)

7. **Physical** (See Worksheet 5)

Numerical score from Worksheet 5 (Box 8)

Global Assessment (See Worksheet 5)

Well-nourished or anabolic (SGA-A)
 Moderate or suspected malnutrition (SGA-B)
 Severely malnourished (SGA-C)

Total PG-SGA score
(Total numerical score of A+B+C+D above)
(See Page Recommendations below)

Physician Signature _____ Date _____

Nutritional Triage Recommendations: A patient's score is used to define specific nutritional interventions including patient education, symptom management, metabolic pharmacologic intervention, and appropriate nutritional (oral/enteral) food/nutritional supplements, enteral, or parenteral (tube). Triage (nutritional intervention includes optimal symptom management.

0-1 No intervention required at this time. Re-assessment on routine and regular basis, during treatment.

2-3 Patient is likely malnourished by clinical course or other clinician with pharmacologic intervention (as indicated by symptom survey (Box 3) and laboratory values as appropriate).

4-5 Requires intervention by dietitian in conjunction with management of physician as indicated by symptom survey (Box 2).

≥ 6 Indicates a critical need for approved symptom management and/or nutritional intervention options.

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Useful tools for early detection of cancer cachexia?

- PG-SGA was developed from SGA for cancer patients
- PG-SGA includes more nutritional symptoms and short term weight loss and numerical scoring
- PG-SGA may reflect clinical changes over time

Bauer J et al. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr 2002, 56; 779–85

Useful tools for early detection of cancer cachexia?

- aPG-SGA contains the first self reported part:

weight and weight loss
food intake
nutritional impact symptoms
functional ability

The image shows a screenshot of the aPG-SGA (Advanced Practical Geriatric Subjective Global Assessment) form. The form is titled "Scored Patient-Generated Subjective Global Assessment (aPG-SGA)". It is divided into several sections. The first four boxes (1-4) are highlighted with a red border, indicating the self-reported part of the assessment. Box 1 is titled "Weight (Self-Report)" and includes questions about weight change and height. Box 2 is titled "Food Intake" and includes questions about eating habits and food intake. Box 3 is titled "Symptoms" and includes questions about various symptoms. Box 4 is titled "Activities and Function" and includes questions about daily activities and functional ability. Below these four boxes is a section for the "Additive Score of the Boxes 1-4". The form also includes a section for the "Global Assessment" and a "Total aPG-SGA score" section. The form is designed to be completed by the patient or a caregiver.

Useful tools for early detection of cancer cachexia?

- In a cohort study with advanced cancer patients a high score of aPG-SGA was found to be associated with:

CRP
 plasma proteins
 anorexia
 fatigue
 QoL
 grip strength
 performance status
 total fat mass
 dose reduction of chemo
 survival

The image shows a portion of the 'Scored Patient-Generated Subjective Global Assessment (PG-SGA)' form. The form is titled 'Scored Patient-Generated Subjective Global Assessment (PG-SGA)' and includes sections for 'Weight (Current and Ideal)', 'Desires', 'Activities and Activities', and a 'Total PG-SGA score' section. The form is divided into several sections, each with checkboxes and scales for various symptoms and functional status. The form is titled 'Scored Patient-Generated Subjective Global Assessment (PG-SGA)' and includes sections for 'Weight (Current and Ideal)', 'Desires', 'Activities and Activities', and a 'Total PG-SGA score' section. The form is divided into several sections, each with checkboxes and scales for various symptoms and functional status.

Vigano, A.L., et al., **The Abridged Patient-Generated Subjective Global Assessment Is a Useful Tool for Early Detection and Characterization of Cancer Cachexia.** J Acad Nutr Diet, 2014.

Useful tools for early detection of cancer cachexia?

- aPG-SGA may detect cancer cachexia features
- Along with increased markers of inflammation this could help to differentiate between cancer cachexia and simple starvation
- Give the right treatment to the right patient at the right time
- Ongoing studies are testing aPG-SGA in intervention trials

PREVIOUS

HELP

NEXT



Compared to your normal food intake, how would you rate your food intake during the past week?

Less than normal

Unchanged

More than normal

PREVIOUS

HELP

NEXT

What kind of nutrition are you taking?



Normal food but less than normal amount

Only liquids

Only nutritional supplements

Very little of anything

Only tube feeding or only nutrition by vein

PREVIOUS

HELP

NEXT



Indicate whether any of the following problems have kept you from eating enough during the past two weeks

Pain

Nausea

Diarrhea

Constipation

Lack of appetite

Altered sense of taste

Altered sense of smell

Outline

- Cancer cachexia
- Dietary treatment of cachexia
- Assessment of nutritional status
- How to move forward?
- **Conclusion**

Conclusion

- Cachexia is complex and challenging
- Identify cachexia early is important to achieve effects of intervention and treatment
- Adding assessment tools such as aPG-SGA can help differentiate cancer cachexia from simple starvation

Conclusion

- Dietary counseling can effect energy intake and body weight, however, apparent heterogeneity between studies is present
- There is not enough evidence to conclude whether patients with advanced cancer and different cachexia stages benefit from dietary counseling
- Future nutritional intervention studies in cachexia need to report better on patient population and specify the nutritional intervention