

Are Four Simple Questions Able to Predict Weight Loss in Outpatients With Metastatic Cancer? A Prospective Cohort Study Assessing the Simplified Nutritional Appetite Questionnaire

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ABSTRACT

Background: Severe weight loss is directly responsible for up to one-fifth of all cancer deaths and has a major impact on quality of life. The simplified nutritional appetite questionnaire (SNAQ) was validated to predict weight loss within 6 mo in community-dwelling adults and nursing home residents. **Methods:** We prospectively assessed the SNAQ in 133 palliative cancer outpatients. The SNAQ predictions were validated after 3 and 6 mo with the observed weight change. In addition, the treating oncologists gave their predictions concerning future weight loss according to their clinical judgment. **Results:** A significant weight loss of 5% of the original body weight within 6 mo occurred in 20 (24%) of the 133 patients. The SNAQ predicted weight loss with a sensitivity of 0.38 and a specificity of 0.66 (P -value 0.81). The treating oncologists predicted weight loss with a sensitivity of 0.67 and a specificity of 0.7 (P -value 0.002). **Conclusion:** The SNAQ does not represent a useful tool to predict impending weight loss in palliative cancer outpatients. The predictions of the treating oncologists were more reliable than those from the SNAQ, but remain poor. Better methods to predict weight loss in this patient group are therefore required.

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Introduction

Involuntary weight loss is a major symptom of advanced cancer (1) and is directly responsible for up to one-fifth of all cancer deaths (2). Weight loss is caused by the complex multifactorial cancer cachexia syndrome characterized by persistent skeletal muscle wasting, which cannot be reversed by conventional nutritional treatment (3). The resulting frailty is a major contributor to discomfort and diminishes quality of life (4,5). Over 50% of outpatients with cancer who lose more than 10% of their original body weight are anorexic (6). Cancer cachexia is characterized by three stages: precachexia, cachexia, and refractory cachexia. In refractory cachexia, the burden and risks of an extended nutritional treatment are likely to outweigh the benefits (3). So far, there is no useful method to detect patients at risk.

The European Society for Clinical Nutrition and Metabolism (ESPEN) proposes the nutrition risk score

(NRS) in a hospital setting and the mini nutritional assessment (MNA) for elderly patients as nutritional screening tools (7). However, these tools evaluate the current nutritional status. They are not designed to predict impending weight loss and are therefore of limited value for cancer patients in ambulatory care. An accurate prediction of weight loss would allow earlier interventions and thus perhaps increase quality and efficacy of nutritional care and even quality of life, which is closely related to the nutritional state in cancer patients (8).

The simplified nutritional appetite questionnaire (SNAQ) has been shown to predict weight loss in community-dwelling adults and nursing home residents (9). The test assesses anorexia with questions on appetite and eating behavior. Thus, it should be possible to detect impending weight loss, in contrast to other tests, which

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rely on apparent weight changes. We prospectively assessed the SNAQ in palliative cancer outpatients.

Methods

Study sample

All outpatients with cancer, receiving palliative care at the Department of Medical Oncology at the Kantonsspital Winterthur, were eligible. Inclusion criteria were pathologically confirmed metastatic cancer, an estimated life expectancy of at least 6 mo, and an understanding of the written German language. Excluded were patients under the age of 18 and patients unable to give informed consent. Enrolment started in January 2013 and lasted until April 2013. We identified 266 eligible patients, of whom 153 agreed to participate and returned the questionnaire.

Study measurements

Questionnaire

Eligible patients were presented with the study questionnaire, consisting of the German translation of the SNAQ and two additional questions in order to evaluate a baseline NRS.

The SNAQ contains four statements; patients are asked to weigh them from 1 to 5. The statements evaluate appetite, regular meal size, taste, and the number of meals per day. A score ≤ 14 predicts a weight loss of at least 5% of the original body weight within the next 6 mo (Appendix 1).

The additional questions were used to detect a weight loss within the last 3 mo and to evaluate the eating behavior of the previous week. An NRS > 2 indicates a patient with a nutritional risk (7).

Clinical assessment

All treating oncologists participating in the trial were asked to give their predictions concerning the patients' weight in 3 and 6 mo. They were not aware of the SNAQ score or the questionnaire.

Clinical data collection

The weight loss at 3 and 6 mo as well as the additional baseline clinical data were collected from the patients' medical files. Baseline clinical data included sex, age, height, Eastern Cooperative Oncology Group Performance Status (ECOG PS) (10), cancer type, and disease status (tumor under control vs. progressive disease). For weight measurements at 3 and 6 mo, a time window of ± 14 days for the measurement points was accepted. For the few patients for whom weight could not be obtained in the given time frame, weight changes were interpreted

using common sense. That is, if there was no weight loss in a later measurement, we interpreted the missing value as a stable weight; if a significant weight loss was found in an earlier measurement, we assumed the missing value was a significant loss.

The baseline body mass index (BMI) was calculated using the baseline height and weight. Any baseline BMI < 18.5 kg/m² was considered underweight according to the current WHO guidelines (11). In line with the original SNAQ validation, we formed two age groups: < 60 and > 60 yr.

Statistical measurements

The primary endpoint of the study was the sensitivity of the SNAQ to predict a significant weight loss of 5% within the next 6 mo compared to baseline weight.

We estimated that a minimal sample of 121 patients was necessary to obtain an 80% power for all and 90% power for most possible outcomes, based on the assumptions of a minimal prevalence of 40% for weight loss in the whole population and a minimal index of Youden ($J = \text{Sensitivity} + \text{Specificity} - 1$) of 0.4 for the SNAQ to detect such a loss.

Secondary endpoints were SNAQ weight prediction at 3 mo and the oncologists' weight predictions at 3 and 6 mo. Patients' characteristics were expressed as median values \pm interquartile ranges. Exploratory subgroup analyses were performed, investigating the role of tumor progression, NRS > 2 , sex, PS > 2 , underweight, age $<$ or > 60 yr, and the type of cancer.

Data analyses were done with the JMP 11.00 statistical software. The sensitivity and specificity of the SNAQ score and the treating physician's weight predictions were established at each endpoint. The P -value was calculated with Fisher's exact test. P -values < 0.05 were considered significant. In addition, positive predictive value (PPV) and negative predictive value (NPV) and the index of Youden were calculated and receiver-operating characteristics (ROC) curves were plotted to determine the optimal thresholds of the SNAQ and the oncologists' predictions. McNemar's test was used to investigate homogeneity between the oncologists' 3- and 6-mo predictions. In the exploratory subgroup analysis, likelihood ratios were used to evaluate differences between subgroups.

Study protocol

The protocol was written under the guidance of the World Medical Association (WMA) Declaration of Helsinki, the International Conference on Harmonization (ICH) Guideline for Good Clinical Practice, and the

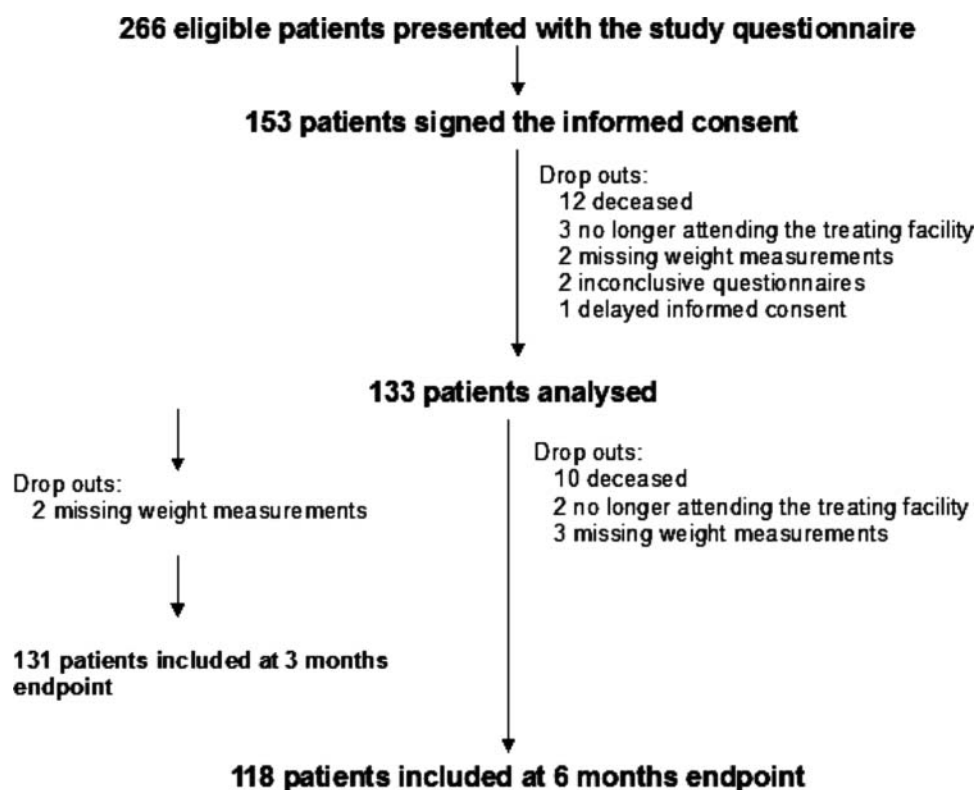


Figure 1. Diagram of Patient Flow.

requirements of the Swiss authorities (12,13). It was approved by the local ethical committee, and all patients gave written informed consent.

Results

Enrolment

From the 266 identified eligible patients (Fig. 1), 153 agreed to participate and returned the questionnaire. We were able to prospectively analyze 133 patients. A total of 118 patients were included in the primary endpoint analysis at 6 mo after study inclusion and 131 patients were analyzed at the 3-mo endpoint.

Patients' characteristics

In the 118 patients included in the primary endpoint analysis, the median age was 69 yr, the median weight was 69.25 kg, and the median BMI was 25 kg/m². Of these, 58% were female. Thirty-six patients (31%) were classified as being at nutritional risk with an NRS >2, and cancer progression was seen in 46 patients (39%). According to the SNAQ, a significant weight loss within the next 6 mo (SNAQ ≤14) was predicted in 41 patients (35%). The treating oncologists predicted a significant weight loss within the next 6 mo in 44 patients (37%). Detailed characteristics are shown in Table 1.

A total of 131 patients were analyzed at the 3-mo endpoint. The treating oncologists predicted a significant weight loss within the next 3 mo in 14 patients (11%) and the SNAQ in 48 patients (37%).

Table 1. Patients' characteristics at the primary endpoint.

Patients	118 (100%)
Female	68 (58%)
Male	50 (42%)
Age (years)	69 (31–91)
Height (cm)	165 (144–199)
Weight (kg)	69.25 (45–129)
BMI (kg/m ²)	25 (18–52)
ECOG-PS	1 (0–3)
NRS	2 (1–5)
SNAQ	15 (9–19)
BMI <18.5	3 (3%)
ECOG-PS >2	3 (3%)
NRS >2	36 (31%)
Cancer progression	46 (39%)
Oncologist predicts weight loss	44 (37%)
SNAQ ≤14	41 (35%)
Malignancies	
Breast cancer	29 (25%)
Prostate cancer	15 (13%)
Non small cell lung cancer	15 (13%)
Small cell lung cancer	5 (4%)
Cancer of the upper gastrointestinal tract	8 (7%)
Cancer of the lower gastrointestinal tract	13 (11%)
Gynecological cancers	8 (7%)
Low grade non Hodgkin lymphoma	7 (6%)
High grade non Hodgkin lymphoma	4 (3%)
Multiple myeloma	8 (7%)
Others	6 (5%)

Table 2. Results after 6 mo.

		Sens.	Spec.	<i>P</i> -value	PPV	NPV	Index of Youden
Prevalence of weight loss	24 (20%)						
SNAQ		0.38	0.66	0.8119	0.22	0.81	0.04
Oncologists' predictions		0.67	0.7	0.0017	0.36	0.89	0.37

Primary endpoint: The accuracy of the SNAQ to predict weight loss

After 6 mo, a significant weight loss was seen in 24 patients (20%). The SNAQ was able to predict this weight loss with a sensitivity of 0.38 and a specificity of 0.66 ($P = 0.8$, Table 2). The corresponding ROC curve is shown in Fig. 2.

Secondary endpoints

The treating oncologists were able to predict a weight loss within 6 mo with a sensitivity of 0.67 and a specificity of 0.7 ($P = 0.0017$). The PPV was 0.36, the NPV was 0.89, and the index of Youden was 0.37. The ROC curve of the oncologists' prediction showed an area under the curve of 0.653 (Table 2, Fig. 3). The results of the SNAQ and oncologists' predictions after 3 mo are depicted in Table 3. The sensitivity of the treating oncologists' 3-mo predictions (sensitivity = 0.29) was significantly worse than their 6-mo estimates (sensitivity = 0.67) as confirmed by McNemar's test (P -value = 0.003).

Exploratory subgroup analyses

None of the baseline parameters was predictive of imminent weight loss (data not shown). More specifically, at

the 6-mo endpoint we found no statistically significant differences in the SNAQ predictions with respect to the type of malignancy (Table 4).

The only subgroup analysis with a significant result was the finding that the oncologists were able to predict weight loss in patients without cancer progression at baseline, but not in patients whose tumor was progressing ($P = 0.0005$, data not shown).

Discussion

In this study, the SNAQ was not able to predict impending weight loss in cancer outpatients. The oncologists' predictions were better, although the PPV of their assessment was also low.

Assessment of the SNAQ

The SNAQ was originally tested on 868 community-dwelling adults and nursing home residents aged 20–102 yr, 53 subjects (10%) had a weight loss of at least 5% of the original body weight within the following 6 mo (9). In that trial, a sensitivity of 0.81, a specificity of 0.76, and a P -value < 0.0001 after the Pearson correlation test were found.

Our aim was to test the SNAQ in an oncology outpatient ward and a real-life situation. The four SNAQ

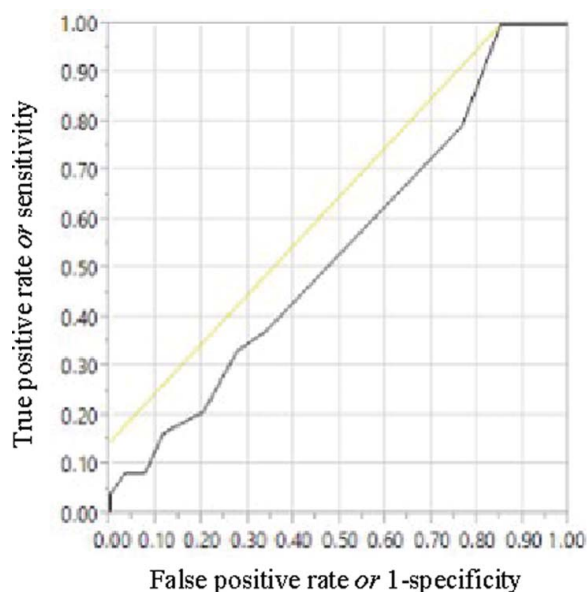
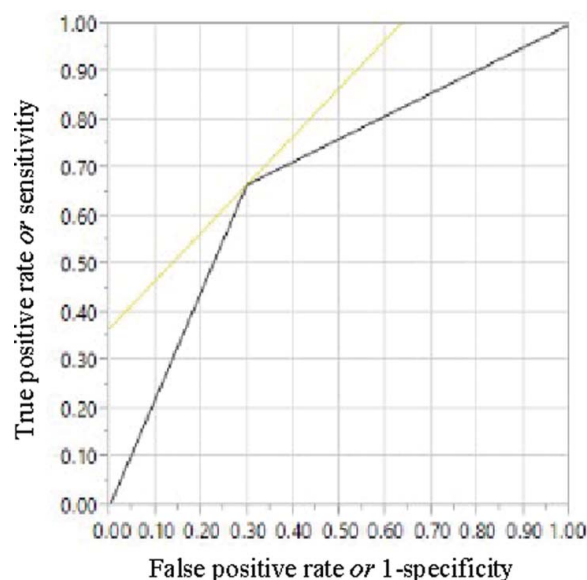
**Figure 2.** ROC of SNAQ after 6 months.**Figure 3.** ROC of Oncologists' predictions after 6 months.

Table 3. Results after 3 mo.

		Sens.	Spec.	P-value	PPV	NPV	Index of Youden
Prevalence of weight loss	14 (11%)						
SNAQ		0.29	0.62	0.5723	0.08	0.88	-0.09
Oncologists' predictions		0.29	0.91	0.0441	0.29	0.91	0.2

questions were unable to represent the complex factors influencing imminent weight loss in cancer patients. The questions are based on the patient's appetite and eating behavior, whereas other factors such as cancer diagnosis, tumor extension, and the ongoing treatment are not considered. A successful cancer treatment is ultimately required to stop weight loss. This was described in a retrospective study in patients with head and neck cancers, where the tumor stage was shown to be the strongest predictor of weight loss (14). In their study, all the other investigated parameters for imminent weight loss were insignificant.

We included patients with a wide variety of different malignancies, both solid and hematological. Prognosis and weight loss are different in each cancer type; thus, the performance of the SNAQ could vary significantly. However, our subgroup analysis could not detect any tumor entity for which the SNAQ was predictive. The SNAQ high NPV in patients with breast cancer most likely reflects the low rate of weight loss in this subgroup. These subgroup analyses have to be interpreted with caution; they were not planned and the numbers are very low. Even when pooling solid cancer together (breast, prostate, lung, and colorectal cancer, data not shown), representing two-thirds of the patients analyzed, there was no significant change in the overall results.

The current palliative cancer treatments usually come with various side effects. Many chemotherapies cause nausea, fatigue, and loss of appetite. These side effects interfere with the SNAQ, resulting in false-positive scores even if the treatment is successful in controlling the underlying cancer; thus, they are able to avert significant weight loss. In contrast, the added toxicity of an unsuccessful treatment might even further advance and accelerate weight loss. In addition, other therapeutic agents, like steroids, have anabolic effects and might likewise alter the results. A separate analysis eliminating patients in groups treated with steroids would therefore have been of special interest. This was, however, impossible, as steroids are regularly given to all patients as part of the antiemetic treatment.

In spite of these concerns, we believe that our trial reflects everyday reality on an oncology outpatient ward.

Assessment of the oncologists' predictions

The treating oncologists were aware of the patients' cancer diagnoses, the tumor status, and the ongoing treatment. Thus, their assessment achieved better results, although the PPV was low.

Interestingly, the oncologists tended to overestimate the prevalence of weight loss, suggesting that they either underestimated the effect of the applied cancer treatment

Table 4. The SNAQ according to different subgroups.

	Sens.	Spec.	PPV	NPV	Fisher's exact Test
Breast cancer (3%*)	0	0.57	0	0.94	1
Prostate cancer (20%)	0.33	0.67	0.2	0.8	1
Non small cell lung cancer (40%)	0.33	0.56	0.33	0.56	1
Small cell lung cancer (20%)	1	0.75	0.5	1	0.4
Cancer of the upper gastrointestinal tract (50%)	0.25	0.5	0.33	0.4	1
Cancer of the lower gastrointestinal tract (23%)	0.67	0.8	0.5	0.89	0.2028
Other cancers of the female fertility tract (25%)	0	0.5	0	0.6	0.4643
Low grade non Hodgkin lymphoma (0%)	—	0.86	—	1	—
High grade non Hodgkin lymphoma (0%)	—	0.75	—	1	—
Multiple myeloma (25%)	0.5	0.83	0.5	0.83	0.4643
Others (33%)	0.5	0.75	0.5	0.75	1
BMI underweight (0%)	—	0.67	—	1	—
ECOG-PS >2 (33%)	1	—	0.67	—	—
NRS >2 (10%)	0.6	0.35	0.26	0.69	1
Cancer progression (24%)	0.27	0.51	0.15	0.69	0.3024
Cancer no progression (18%)	0.46	0.75	0.29	0.86	0.1798
Age <60 years (18%)	0.38	0.71	0.33	0.75	0.6456
Age ≥60 years (28%)	0.38	0.64	0.19	0.82	1
Female (16%)	0.45	0.6	0.18	0.85	0.751
Male (26%)	0.31	0.76	0.31	0.76	0.7193

*Prevalence of weight loss shown in brackets.

or overestimated the seriousness of the disease. This is remarkable since oncologists were known to overestimate their treatment impact and the prognosis of their patients (15). Yet recent research in patients with brain metastases not only show medical oncologist to be significantly more pessimistic in their survival prediction than their neurosurgical and radiation oncologist colleagues, but also show medical oncology to be the only subspecialty to underestimate the actual median survival (16). All these results suggest a paradigm change in the medical oncologists' view of their patients' prognosis.

In addition, the oncologists' predictions in the subgroup without progression were more accurate than in the group with cancer progression. Their predictions clearly lose power once the disease is no longer under control. The 3-mo predictions were significantly inferior to the ones at 6 mo. A sudden weight loss in a short period occurs more often due to an unpredictable cause, like pneumonia, treatment toxicities, or rapid metastatic spreading.

In summary, while it is far from satisfactory, the oncologist's judgment is currently the most effective method to predict impending weight loss.

Exploratory subgroup analysis

Our exploratory analysis suggests that the NRS is not useful to detect impending weight loss in ambulatory cancer patients. This indicates that short-time weight changes and temporarily reduced dietary intake are not decisive for future significant weight loss.

Study strengths and limitations

To our knowledge, this is the first study assessing the SNAQ in palliative cancer outpatients. The study is unique in its attempt to test known nutritional screening tools in a real-life clinical setting. The patients included in the study reflect the average cancer patient population in Switzerland.

However, our prestudy sample size calculation overestimated the prevalence of weight loss and the power of the tests, assuming a minimal prevalence of 40% and a minimal index of Youden of 0.4. Therefore, significance for all results could not have been expected. Of the 266 subjects presented with the study questionnaire, 113 patients did not consent to participate in the study. No data were collected concerning these patients. This could have led to a selection bias; it is possible that those patients refused to participate because they were doing poorly and were in fact at risk of weight loss. A German translation of the original SNAQ was used; a certain loss of information can therefore not be excluded.

Conclusion

This study shows how difficult weight predictions are in this patient group. Cancer remains today a disease of a highly unpredictable nature. All known tests, apart from the treating oncologists' predictions, fail to show a significant correlation with impending weight loss. However, the oncologists' predictions are neither sensitive nor specific enough; thus, there is a clear unmet need for better tools to detect impending weight loss.

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Appendix 1

Simplified nutritional appetite questionnaire (SNAQ)

Name: _____ Sex (circle): Male Female
 Age: _____ Weight: _____ Height: _____
 Date: _____

Administration Instructions: Ask the subject to complete the questionnaire by circling the correct answers and then tally the results based upon the following numerical scale: a = 1, b = 2, c = 3, d = 4, e = 5. The sum of the scores for the individual items constitutes the SNAQ score.

SNAQ score ≤ 14 indicates significant risk of at least 5% weight loss within six months.

1. **My appetite is**
 - a. very poor
 - b. poor
 - c. average
 - d. good
 - e. very good
2. **When I eat**
 - a. I feel full after eating only a few mouthfuls
 - b. I feel full after eating about a third of a meal
 - c. I feel full after eating over half a meal
 - d. I feel full after eating most of the meal
 - e. I hardly ever feel full
3. **Food tastes**
 - a. very bad
 - b. bad
 - c. average
 - d. good
 - e. very good
4. **Normally I eat**
 - a. less than one meal a day
 - b. one meal a day
 - c. two meals a day
 - d. three meals a day
 - e. more than three meals a day

Source: Wilson MM, Thomas DR, Rubenstein LZ, Chibnall JT, Anderson St, Baxi MR, Morley JE. Appetite assessment: Simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. *Am J Clin Nutr* 2005;82:1074–81.