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## Opportunities to improve palliative care: towards a more patient-centred and proactive approach

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## **CHAPTER 5**

### **Surprise Question and performance status indicate urgency of palliative care needs in patients with advanced cancer at the Emergency Department: an observational cohort study**

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## **ABSTRACT**

### **Background**

The surprise question (SQ), 'Would I be surprised if this patient died within 1 year?', is a simple instrument to identify patients with palliative care needs. The SQ-performance has not been evaluated in patients with advanced cancer visiting the emergency department (ED).

### **Objective**

To evaluate SQ's test characteristics and predictive value in patients with advanced cancer visiting the ED.

### **Design**

Observational cohort study.

### **Setting**

Patients >18y with advanced cancer in the palliative phase visiting the ED of an academic medical centre.

### **Methods**

Attending physicians answered the SQ (not surprised (NS) or surprised (S)) and estimated ECOG-performance status. Disease, visit, and follow-up characteristics were retrospectively collected from charts. SQ's sensitivity, specificity, positive (PPV) and negative predictive values (NPV) and Harrell's c-index were calculated. Prognostic values of SQ and other variables were assessed using Cox proportional hazards models.

### **Results**

Two-hundred-and-forty-five patients were included (203 NS (83%) and 42 S (17%)), median age 62 years, 48% male. Follow-up on overall survival was updated until February 2019. At ED-entry, NS-patients had worse ECOG-performance and more symptoms. At study closure, 233 patients had died (95%). Median survival was 3.0 months for NS-patients (IQ-range 1-8); 9.0 months for S-patients (IQ-range 3-28) ( $p < 0.0001$ ). SQ-performance for 1-year mortality: sensitivity 89%, specificity 40%, PPV 85%, NPV 50%, c-index 0.56, HR 2.1 for approaching death. ECOG 3-4 predicted death in NS-patients; addition to the SQ improved c-index (0.65); sensitivity (40%), specificity (92%), PPV (95%), NPV (29%).

### **Conclusions**

At the ED, the SQ plus ECOG 3-4 helps identifying patients with advanced cancer and a limited life-expectancy. Its use supports initiating appropriate care related to urgency of palliative care needs.

## INTRODUCTION

Palliative care can improve the quality of life and satisfy care needs of patients with advanced disease and family.<sup>1-3</sup> Initiating palliative care early in the disease trajectory of advanced cancer is accepted to timely prepare them for deterioration and death.<sup>4,5</sup> However, identification of patients with limited life-expectancy and palliative care needs is difficult. Previous studies indicate that initiation of palliative care in patients with advanced cancer can follow ‘trigger-moments’, such as visits to the emergency department (ED).<sup>6,7</sup> Patients with advanced cancer visit the ED more often in the last year of life.<sup>8,9</sup> Since ED-triggered palliative care effectively improves their quality of life, identifying these patients at the ED can be useful.<sup>10</sup> Familiar screening tools identifying patients with advanced cancer having palliative care needs are the Supportive and Palliative Care Indicators Tool (SPICT), Necesidades Paliativas (NECPAL) identification tool, Golden Standards Framework – Proactive Identification Guidance (GSF-PIG), Radboud indicators for Palliative Care Needs (RADPAC) and a Centre to Advance Palliative Care’s checklist.<sup>11-15</sup> However, these screening tools may be too elaborate for use at the ED. Moreover, prediction scores for approaching death focus on prediction of death within a few days or weeks, missing out the opportunity to initiate palliative care early.<sup>16-18</sup>

An example of a simple tool to timely identify patients with palliative care needs is the ‘Surprise Question’ (SQ): ‘Would I be surprised if this patient died within one year?’. The SQ was developed for identification of palliative care needs by estimating the probability that the patient would die from current or future physical problems in the next year.<sup>19,20</sup> A ‘not surprised’ (NS)-answer should trigger further screening for palliative care needs.<sup>21,22</sup> In a qualitative study, attending ED-physicians indicated that the SQ was easy to use and could influence discussions about care delivery and goals of care.<sup>23</sup> In addition, answering the SQ is more related to ‘gut feeling’, than on stern estimation of remaining life-expectancy of a patient.<sup>24</sup> Although the aim of the SQ is to mark patients with palliative care needs, focus in research lies on the performance of the SQ to screen for patients dying within one year.<sup>21,25</sup> Studies have shown that the SQ is accurate in screening dialysis and heart failure patients.<sup>20,26</sup> Cancer patients with NS-answers in oncology outpatient wards<sup>27</sup> and general practices<sup>28</sup> had hazard ratios (HR) of death <1yr of 7.8 and 7.0, respectively. The SQ also identifies hospitalized patients with hematologic and solid tumours with unmet palliative care needs.<sup>29</sup>

A recent meta-analysis of Downar et al.<sup>20</sup> demonstrated that, in the overall population of patients with advanced cancer, the SQ might not be sufficient as a screening tool for death within one year. It lacked sensitivity and therefore under-estimated the number of patients with palliative care needs (sensitivity 67.0%, specificity 80.2%, positive



predictive value 37.1%, negative predictive value 93.1%).<sup>21</sup> The SQ may be more accurate combined with other indicators of palliative care needs, such as symptoms prevalent in the palliative phase, performance status and indicators of increased utilization of formal and informal care.<sup>11,13,30-34</sup> NECPAL and GSF-PIG combine the SQ with these indicators for screening of patients with palliative care needs; however, it is not yet published whether the combination of these indicators with the SQ improves the performance of these screening instruments.<sup>13,30</sup> At the ED, the SQ has been tested in patients with heart failure and in elderly.<sup>35,36</sup> In elderly, SQ's c-statistic increased after adding the physician's working experience and the PREDICT-criteria for identification of elderly with a limited life-expectancy.<sup>36</sup> To our knowledge, the performance of the SQ with and without other indicators of palliative care needs has not been studied yet in adult patients with advanced cancer visiting the ED.

Objectives of this study were to evaluate the prognostic value of the SQ in patients with advanced cancer visiting the ED; and to study the yield of adding other predictors for approaching death.

## **PATIENTS AND METHODS**

### **Setting and patients**

This cohort study took place at the ED of a Dutch academic medical centre, where acute care is offered 24/7. On average, eighty patients are seen per day for both oncological and non-oncological problems. All ED-visits from May 2013 to July 2014 were prospectively screened. Inclusion criteria for patients were: diagnosis of cancer in the palliative phase<sup>2</sup>, i.e. metastasized or incurable cancer; who were at least 18 years of age. Patients with a haematological malignancy or who were not admitted to the ED for the Medical Oncology Department were excluded. Only the first ED-visits of patients were included; subsequent ED-visits by the same patients were excluded. Follow-up on overall survival was updated until February 2019. Survival data were obtained from the EPRs, which is monthly updated via the Dutch population register.

### **Data collection**

After the ED-visit, a list of patients who visited the ED were screened if they met the inclusion criteria by two trained research assistants; if they did, attending physicians were sent an e-questionnaire with the SQ. E-questionnaires were sent within 1 working day to limit recall bias. Patients were divided into two groups according to the SQ: 'Would I be surprised if this patient died within one year?'; 'NS-patients' of whom the physician would not be surprised, and 'S-patients' of whom the physician would be surprised. For NS-patients, the e-questionnaire proceeded with the Eastern Cooperative Oncology Group

(ECOG) scale.<sup>37</sup> Data abstraction was performed using a code book about which consensus was reached among members of the scientific team of the hospital's PCCT. The code book contained definitions of all variables for data collection and data were imported into a digital database accordingly. Four chart abstractors were trained on how to use the code book. One expert of the PCCT monitored the work of the chart abstractors, was available in cases of doubt and performed random checks to assess interrater agreement. Electronic patient records (EPRs) were assessed to collect additional patient-, referral-, ED-visit- and follow-up characteristics and ECOG performance score of S-patients. The disease phase was evaluated and classified according to Lynn and Adamson: disease-modifying phase (anti-cancer treatment to prolong life and/or symptom management); symptom-management phase (treatment directed to symptom-relief); or terminal phase.<sup>38</sup> The EPRs were searched for reports about PCCT-consultations 3 months before the current ED-visit. 'Limitations on life-sustaining treatments (LSTs)' included the codes: 'do-not-resuscitate'; 'do-not-ventilate'; and 'no admission to the intensive care unit' (ICU). Time of arrival at the ED was within office hours if the visit occurred Monday-Friday between 8am-6pm. The 'main symptom' was the referring symptom for the ED-visit according to the attending physician's notes in the EPR. A 'new symptom' was a main symptom not described in the EPR <3 months before the ED-visit. Main symptoms were considered 'acute symptoms' if the onset was within one working day before the ED-visit. Using the Dutch Edmonton Symptom Assessment Scale (ESAS), symptoms were scored as present or absent based on documentation in the EPRs.<sup>39</sup> The clinical diagnosis was defined as the conclusion of the attending physician at the ED.

## Statistical analysis

Characteristics of NS- and S-patients were compared using the Chi-square test and Fisher's exact test (nominal variables) and Mann-Whitney U test (ordinal variables and not-normally distributed continuous variables). Survival was estimated using Kaplan-Meier's methodology. A log-rank test was used to compare overall survival between NS- and S-groups.

## Prognostic value of the SQ

Two-by-two tables were used to calculate test characteristics (sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV)) of the SQ as screening tool for death <1 year. Harrell's c-index was calculated to estimate the discriminative power of the SQ for death <1 year.<sup>40,41</sup>

## Addition of other predictors of approaching death to the SQ

To identify predictors of palliative care needs, univariable regression analyses using Cox proportional hazards models were performed to estimate the association between death

(from ED-visit) and the following predefined candidate predictors: SQ, poor performance status (ECOG 3-4), acute symptoms, palliative disease phase, symptom-management treatment, home care, ED-visits in the previous six months, limitations on life-sustaining treatments. Next, the SQ and predictors with a p-value of <0.10 in univariable analyses were entered in a multivariable analysis. Discriminative ability of the final multivariable model (including the SQ and any independent predictors) was estimated using Harrell's c-statistic. Akaike's information criterion was calculated to compare the ability of the predictive models with and without SQ to explain the variance in our dataset.<sup>42</sup>

## **Ethical approval and informed consent**

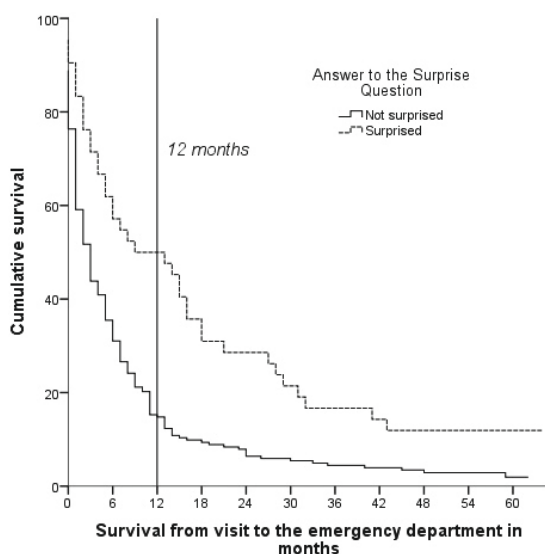
The Committee of Medical Ethics of the LUMC approved this study on May 27, 2013. According to Dutch Law (WGBO, article 458) and European Law (General Data Protection Regulation), written consent from included patients was not required. Data from this study were analysed after de-identification.

## **RESULTS**

### **Patient and ED-visit characteristics**

ED-visits of 245 patients with advanced cancer were included. The attending physician at the ED answered the SQ with 'No' (NS) in 203 patients (83%), and 'Yes' (S) in 42 patients (17%) (Table 1). Overall median age was 62 years (interquartile (IQ)-range: 45-79 years) and 48.2% was male. Compared to S-patients, NS-patients more often received symptom-management therapy (29.6% versus 16.7%,  $p=0.049$ ), reported more main symptoms at the ED and had a worse clinical condition (ECOG 3-4 in 40% vs. 21%,  $p=0.034$ ). Most frequently reported ESAS-symptoms were pain (overall 60.8%; NS 64.0% versus S 45.2%,  $p=0.023$ ), nausea (29.8%; 31.0% versus 23.8%,  $p=0.46$ ) and shortness of breath (29.8%; 31.0% versus 23.8%,  $p=0.46$ ). During or after the ED-visit, changes emerged in limitations on LSTs: before the ED-visit, 64 patients (26.1%) had documented limitations on LSTs; after the ED-visit, this had risen to 104 patients (42.4%) (Table 2). Within 1 year, 193 patients (78.8 %) had died: 172 NS-patients (85%), and 21 S-patients (50%). At the end of follow-up, 233 patients had died (95%). Overall median survival was 3.0 months (IQ-range 1-11); 3.0 months for NS-patients (IQ-range 1-8) and 9 months for S-patients (IQ-range 3-28; log-rank  $p<0.0001$ , Figure 1).





**Figure 1.** Observed survival of patients with advanced cancer from their first visit to the emergency department.

**Table 1.** Patient and disease characteristics of patients with advanced cancer visiting the emergency department

	Total (n=245)	NS-patients (n=203)	S-patients (n=42)	P-value
<b>Age, median (IQ-range)</b>	62 (45-79)	62 (53-69)	59 (49.50-69.25)	0.23
<b>Sex, male, n (%)</b>	118 (48.2)	91 (44.8)	27 (64.3)	0.021
<b>Location primary tumour, n (%)</b>				0.001
Breast	29 (11.8)	24 (11.8)	5 (11.9)	
Gynaecologic	27 (11.0)	27 (13.3)	0 (0.0)	
Bowel (gastro-intestinal-colorectal)	75 (30.6)	66 (32.5)	9 (21.4)	
Head/neck	10 (4.1)	7 (3.4)	3 (7.1)	
Lung	14 (5.7)	14 (6.9)	0 (0.0)	
Urologic	31 (12.7)	21 (10.3)	10 (23.8)	
Hematologic	11 (4.5)	6 (3.0)	5 (11.9)	
Unknown	3 (1.2)	3 (1.5)	0 (0.0)	
Other <sup>a</sup>	45 (18.4)	35 (17.2)	10 (23.8)	
<b>Disease phase, n (%)</b>				0.049
Disease-modifying	174 (71.0)	139 (68.5)	35 (83.3)	
Symptom-management	67 (27.3)	60 (29.6)	7 (16.7)	
Terminal	2 (0.8)	2 (1.0)	0 (0.0)	
Unknown	2 (0.8)	2 (1.0)	0 (0.0)	

**Table 1.** Patient and disease characteristics of patients with advanced cancer visiting the emergency department (continued)

	Total (n=245)	NS-patients (n=203)	S-patients (n=42)	P-value
<b>Anti-cancer treatment in preceding 3 months<sup>b</sup>, n (%)</b>				
Local treatment <sup>c</sup> , n (%)	69 (28.2)	59 (29.1)	10 (23.8)	0.49
Systemic treatment <sup>d</sup> , n (%)	174 (71.0)	146 (71.9)	28 (66.7)	0.50
None	41 (16.7)	33 (16.3)	8 (19.0)	0.66
<b>Informal caregiver available, n (%)</b>	205 (83.7)	168 (82.8)	37 (88.1)	0.59
<b>Homecare, n (%)</b>	36 (14.7)	36 (17.7)	0 (0.0)	0.039
<b>PCCT consulted in preceding 3 months, n (%)</b>	12 (4.9)	11 (5.4)	1 (2.4)	0.70
<b>Number of ED-visits in the preceding 6 months, n (%)</b>				0.88
0 ED-visits	155 (68.3)	128 (63.1)	27 (64.3)	
≥1 ED-visit	90 (36.7)	75 (36.9)	15 (35.7)	
<b>Limitations on LSTs discussed and documented, n (%)</b>	64 (26.1)	62 (30.5)	2 (4.8)	<0.0001
<b>Main symptom, n (%)</b>				
Pain	53 (21.6)	43 (21.2)	10 (23.8)	0.71
Nausea or vomiting	27 (11.0)	25 (12.3)	2 (4.8)	0.19
Constipation	4 (1.6)	4 (2.0)	0	>0.999
Neurologic deterioration or delirium	1 (0.4)	1 (0.5)	0	>0.999
Weakness, loss of strength	7 (2.9)	5 (2.5)	2 (4.8)	0.34
Dyspnoea	34 (13.9)	31 (15.3)	3 (7.1)	0.14
Bleeding or blood loss	19 (7.8)	16 (7.9)	3 (7.1)	>0.999
Fever	48 (19.6)	38 (18.7)	10 (23.8)	0.46
Fatigue	1 (0.4)	1 (0.5)	0	>0.999
Diarrhoea	6 (2.4)	6 (3.0)	0	0.59
Oedema	6 (2.4)	5 (2.5)	1 (2.4)	>0.999
Feeling unwell	18 (7.3)	13 (6.4)	5 (11.9)	0.21
Other	14 (5.7)	10 (4.9)	4 (9.5)	0.27
<b>Referral for new<sup>e</sup> symptom, n (%)</b>	99 (40.4)	68 (33.5)	31 (73.8)	0.001
<b>Referral for acute<sup>f</sup> symptom, n (%)</b>	88 (35.9)	66 (32.5)	22 (52.4)	0.29
<b>Number of symptoms, median (range)</b>	2 (0-7)	2 (1-4)	2 (1-3)	0.030
<b>ECOG performance status, n (%)</b>				0.034
ECOG 0-2	151 (61.6)	119 (58.6)	32 (76.2)	
ECOG 3-4	90 (36.7)	81 (39.9)	9 (21.4)	
Unknown	4 (1.6)	3 (1.5)	1 (2.4)	
<b>ED-visit outside office hours, n (%)</b>	107 (43.7)	93 (45.8)	14 (33.3)	0.13

<sup>a</sup> other tumours (n=45): skin (19, 42.2%); sarcoma (12, 26.7); (retro-)peritoneum (5, 11.1%); eye (3, 6.7%); thymus (2, 4.4%); unknown primary (2, 4.4%); brain (1, 2.2%); ear, nose, throat (1, 2.2%). <sup>b</sup> total number can exceed 100%, as patients can have undergone more than 1 treatment. <sup>c</sup> local treatment: surgery, nuclear therapy, radiotherapy. <sup>d</sup> systemic treatment: chemotherapy, hormonal therapy, stem cell transplantation, targeted-/immunotherapy. <sup>e</sup> "new": not mentioned in electronic patient record in previous 6 months. <sup>f</sup> "acute": onset <24 hours. List of abbreviations: NS: not surprised; S: surprised; PCCT: palliative care consultation team; ED: emergency department; LSTs: life-sustaining treatments

**Table 2.** Visit and follow-up characteristics of 245 patients with advanced cancer visiting the emergency department

	Total n=245	SQ = no n=203	SQ = yes n=42	P-value
Diagnostic imaging, n (%)	148 (60.4)	119 (58.6)	29 (69.0)	0.65
Laboratory testing, n (%)	201 (82.0)	168 (82.8)	33 (78.6)	0.027
Limitations on LSTs discussed and documented, n (%)	104 (42.4)	102 (50.2)	2 (4.8)	<0.0001
Time spent at the ED in hours (IQ-range)	3:31 (2:37-4:29)	3:30 (2:37-4:29)	3:34 (2:32-4:49)	0.51
Hospitalization after ED-visit, n (%)	186 (75.9)	157 (77.3)	29 (69.0)	0.37
Observed survival after ED-visit in months, median (IQ-range)	3 (1-11)	3 (1-8)	9 (3-28)	<0.0001
Place of death, n (%)				0.50
Home	89 (36.3)	77 (37.9)	12 (28.6)	
Hospice	26 (10.6)	25 (12.3)	1 (2.4)	
Hospital ward	44 (18.0)	37 (18.2)	7 (16.7)	
Intensive Care Unit or ED	4 (1.6)	2 (1.0)	2 (4.8)	

List of abbreviations: LSTs: life-sustaining treatments; ED: emergency department

### Prognostic value of the SQ

Table 3 lists the test characteristics of the SQ for death <1 year: sensitivity 89.1% (95%CI 83.9%-93.1%), specificity 40.4% (95%CI 27.0%-54.9%), PPV 84.7% (95%CI 81.5%-87.5%) and NPV 50.0% (95%CI 37.3%-62.8%). Harrell's c-index for the SQ to discriminate patients who died <1 year was 0.56 (95%CI 0.53-0.60).

### Addition of other predictors to the SQ

Significant univariable predictors of approaching death are presented in Table 4. The following predictors were significant in multivariable analyses: NS-answer to the SQ (HR 3.16);  $\geq 1$  ED-visit in the preceding 6 months (HR 1.70); ECOG performance status 3-4 (HR 2.10); neurologic deterioration or delirium at the ED (HR 11.33). Harrell's c-index for this model including an NS-answer to the SQ was 0.66, and 0.63 without an NS-answer to the SQ. Akaike's information criterion was better in the model with NS-answer to the SQ than in the model without NS-answer to the SQ (2136.317 versus 2154.737,  $p < 0.0001$ ).

In a sub-analysis among the 203 NS-patients, only ECOG performance status 3-4 was predictive of approaching death (HR 2.50; 95%CI 1.88-3.33;  $p < 0.0001$ ). NS-patients with ECOG 3-4 had a HR of 2.45 (95%CI 1.85-3.25;  $p < 0.0001$ ) of approaching death compared to S-patients or NS-patients with ECOG 0-2. Median survival for NS plus ECOG 0-2 was 6.0 months (95%CI 4.7-7.3) and 1.0 month (95%CI 0.6-1.4) for NS-ECOG 3-4 patients.

Test characteristics of the SQ plus ECOG 3-4 for death >1 year were: sensitivity 40.1% (95%CI 33.1%-47.4%), specificity 92.3% (95%CI 81.5%-97.9%), PPV 95.1% (95%CI 88.1%-98.0%) and NPV 29.4% (95%CI 26.6%-32.4%; Table 5). Harrell's c-index for the combination of SQ and ECOG 3-4 to discriminate patients who died <1 year was 0.65 (95%CI 0.62-0.69).



**Table 3.** Test characteristics of the Surprise Question and Surprise Question plus Poor Performance for screening for palliative care needs in advanced cancer patients visiting the emergency department

	<b>Median survival (95% CI)</b>	<b>Death &lt;1 year</b>	<b>Death &gt;1 year</b>	<b>Total</b>	<b>Test characteristics</b>	<b>% (95% CI)</b>
Aim: identifying palliative care needs						
SQ					Sensitivity	89.1 (83.9-93.1)
NS	3 months (2.1-3.9)	172	31	203 (82.9%)	Specificity	40.4 (27.0-54.9)
S	9 months (0.8-17.2)	21	21	42 (17.1%)	Positive predictive value	84.7 (81.5-87.5)
Total	3 months (1.8-4.2)	193 (78.8%)	52 (21.2%)	245	Negative predictive value	50.0 (37.3-62.8)
p<0.0001						
	<b>Median survival (95% CI)</b>	<b>Death &lt;1 year</b>	<b>Death &gt;1 year</b>	<b>Total</b>	<b>Test characteristics</b>	<b>% (95% CI)</b>
Aim: identifying end-of-life phase						
SQ + ECOG					Sensitivity	40.1 (33.1-47.4)
NS + ECOG 3-4	1 month (0.6-1.4)	77	4	81 (33.2%)	Specificity	92.3 (81.5-97.9)
NS + ECOG 0-2; S	6 months (4.7-7.3)	115	48	163 (66.8%)	Positive predictive value	95.1 (88.1-98.0)
Total	3 months (1.8-4.2)	192 (78.7%)	52 (21.3%)	244	Negative predictive value	29.4 (26.6-32.4)
p<0.0001						

In the upper part of the table the test performance of the Surprise Question in all 245 patients is displayed. The lower part of the table presents the test performance of the SQ plus the ECOG performance status. For this, patient population is split in two groups: 1) NS-patients (n=203) with an ECOG performance status of 3 or 4, and 2) NS-patients with an ECOG 0-2 or S-patients with any ECOG status. 1 patient had an unknown ECOG performance status and was excluded for this sub-analysis. List of abbreviations: SQ: surprise question; CI: confidence interval; NS: not surprised; S: surprised; ECOG: Eastern Cooperative Oncology Group

**Table 4.** Predictors of approaching death in 245 patients with advanced cancer visiting the emergency department

Predictors	Univariable analysis			Multivariable analysis		
	HR	95% CI	P-value	HR	95% CI	P-value
Surprise Question	2.06	1.44-2.94	<0.0001	3.16	1.75-5.70	<0.0001
Local anti-cancer treatment in preceding 3 months	1.07	0.80-1.42	0.65			NS
Systemic anti-cancer treatment in preceding 3 months	0.69	0.52-0.92	0.010			NS
≥1 ED-visit in the preceding 6 months	1.31	1.00-1.71	0.048	1.70	1.17-2.47	0.006
Home care	1.48	1.02-2.15	0.041			NS
LST discussed and documented	1.66	1.24-2.23	0.001			NS
ECOG 3-4	1.99	1.53-2.61	<0.0001	2.09	1.44-3.05	<0.0001
Neurologic deterioration or delirium	12.39	1.66-92.55	0.014	11.33	1.42-90.68	0.022
Dyspnoea	1.51	1.04-2.19	0.029			NS
Referral for new symptom	0.66	0.49-0.88	0.005			NS
Referral for acute symptom	0.75	0.56-1.01	0.054			NS

Abbreviations: HR: hazard ratio; CI: confidence interval; NS: not significant; ED: emergency department; LST: life-sustaining treatment; ECOG: Eastern Cooperative Oncology Group

## DISCUSSION

In our study, the Surprise Question (SQ) identified patients with advanced cancer at the ED with a poor performance status and multiple symptoms. The SQ had a high sensitivity (89.1%) for death within one year for patients in whom attending physicians would not be surprised (NS-patients). NS-patients had a HR of 2.1 for approaching death compared to patients in whom attending physicians would be surprised (S-patients). However, with a Harrell's c-index of 0.56, the SQ discriminates poorly between patients who died within one year or not. Besides the SQ, other predictors for approaching death in patients with advanced cancer visiting the ED were: recent multiple ED-visits, a poor performance status and neurologic deterioration or delirium. In NS-patients, only ECOG performance status 3-4 was predictive of approaching death (HR 2.5). Addition of ECOG 3-4 to the SQ improved specificity (92.3%) at cost of sensitivity (40.1%) in screening for death within one year.

Our study shows that all patients with advanced cancer visiting the ED in the palliative phase of disease have a limited life-expectancy: median survival was three months. This explains our findings of the high sensitivity (89.1%) but poor discriminative ability (c-index 0.56) of the SQ for death within one year after the ED-visit. Our results are in

contrast with the meta-analysis by Downar et al.<sup>21</sup> where sensitivity of the SQ was lower than specificity (67% versus 80%, area under the curve 0.83 (95%CI 0.79-0.87)). This is similar to two earlier studies in cancer patients on the performance of the SQ in a general practice stage IV cancer population by Moroni et al.<sup>28</sup> and in an outpatient oncology clinic by Moss et al.<sup>27</sup> Our finding that sensitivity of the SQ was higher at the ED (89.1%) than in the studies by Moroni (70%) and Moss (75%) confirms that patients included in this study had higher a priori risk of death within one year compared to Moroni's and Moss' studies. In addition, it is likely that physicians working in different healthcare settings estimate the SQ differently.<sup>21, 27, 28</sup> In screening for palliative care needs at the ED, identifying as many truly deteriorating patients as possible (hence high sensitivity), is preferred over selecting very accurately who might not benefit from palliative care (high specificity). Specificity may be low in our study, because the ED-visit can also be accompanied with temporary deterioration, in which patients' condition can improve after interventions at the ED. These interventions may encompass improvement of pain medication, start of antibiotics and blood transfusions. A study in the ED-setting in patients with heart failure showed comparable performance of the SQ (sensitivity 79%, specificity 57%), but with a higher c-index (0.68).<sup>35</sup> The poor discriminative ability of the SQ for death within one year indicates that the SQ should not be used as a predictor of one-year-survival; however, with a HR of 2.1 for approaching death in NS-patients (with a median survival of three months) compared to S-patients (with a median survival of nine months), the SQ can identify those who have more urgent palliative care needs.

Downar et al. suggested that the SQ would perform better with addition of other indicators of palliative care needs.<sup>21, 43</sup> We therefore added poor physical performance status (ECOG 3-4), which resulted in increased specificity (from 40% to 92%) at cost of sensitivity (from 89% to 40%). This is probably because most patients visit the ED with problems causing a decreased physical performance (which might improve after the ED-visit), regardless of their prognosis. The high positive predictive value (95.1%) demonstrates that SQ plus ECOG 3-4 is correct in 95% (PPV) in identifying patients who die within the year, with a hazard ratio for approaching death of 2.5. The c-index of SQ plus ECOG 3-4 increased to a moderate 0.65. It may feel obvious that performance status is part of the assessment associated with answering the SQ; however, both the SQ and ECOG 3-4 were independent predictors of approaching death in multivariable analysis. Since addition of ECOG 3-4 improved the SQ's discriminative ability, an NS-answer should be followed by an assessment of the performance status to differentiate between urgency of palliative care needs.

Our study shows that the SQ plus ECOG 3-4 can discern three groups of patients with different levels of urgency for initiating palliative care. Firstly, although S-patients had the



longest survival in our study, their median survival was only nine months, indicating that they were likely to already have had palliative care needs before the ED-visit. Therefore, for all patients with advanced cancer, we recommend a two-track approach in which disease-modifying treatment is complemented with palliative care and conversations about patient's wishes to prepare for the last phase of life.<sup>44</sup> Secondly, NS-patients were characterized by a poor performance status with multiple symptoms and a median survival of three months. In these patients, palliative care directed to symptom-management and quality of life should be discussed as soon as possible. Thirdly, NS-patients with ECOG 3-4 had the shortest median survival of only 1 month, indicating that they are in the end-of-life phase. Therefore, in NS plus ECOG 3-4 patients, end-of-life care according to patient's wishes should be initiated immediately.

In our study, it seems that physicians at the ED were able to mark deterioration and futility of treatment in the most vulnerable patients. In 16% of the patients without documented limitations on life-sustaining treatments (LSTs) before the ED-visit, limitations on life-sustaining treatments were documented afterwards. This phenomenon is known as ED-initiated palliative care, in which ED-visits function as 'trigger' to evaluate a patient's health status and situation.<sup>6</sup> Interestingly, all patients in whom LSTs were discussed after the ED-visit were NS-patients, demonstrating that LST-documentation in our hospital was focused on those with the shortest life-expectancy. However, S-patients had a limited survival as well, which means that all patients with advanced cancer can benefit from ED-initiated palliative care.

### *Strengths and limitations*

This prospective study with a long follow-up until February 2019 evaluates the prognostic value of the one-year SQ in patients with advanced cancer visiting the ED. Recall bias of attending physicians answering the SQ and assessing ECOG performance status is possible because e-questionnaires were sent within one working day. After this time period, physicians might regard their patients differently, with possible bias that sicker patients were remembered more likely than those not as sick. As patient and disease characteristics were abstracted from EPRs, under- or over-registration of symptoms is possible; also, physicians might have individual preferences for documenting the main symptom. Since symptoms of the four domains of palliative care are not systematically registered at the ED, this is especially true for psychological, social, and spiritual symptoms. We chose to study the association between indicators of palliative care needs with approaching death rather than with death <1 year, because predictors for approaching death indicate which patients need palliative care most urgently.

Our study shows that the SQ is useful for identifying patients with advanced cancer having palliative care needs at the ED. Since ED-initiated palliative care effectively improves the quality of life of patients, all actions at the ED in NS-patients who, in our study, had a median survival of only three months, should be performed in coherence with appropriate end-of-life care.<sup>10</sup> In practice, this includes goals-of-care conversations and palliative care needs assessments at the ED (e.g., Screen for Palliative and End-of-life care needs in the ED (SPEED)<sup>45</sup> or the shorter 5-SPEED<sup>46</sup>), consultation of a palliative care consultation team and referral to appropriate care at the place preferred by the patient and family.

More knowledge should be obtained about the use of the 'double surprise question' at the ED, adding 'Would I be surprised if this patient is still alive after one year?' after an S-answer. The double surprise question could improve the SQ's specificity by identifying a third group more associated with frailty and gradual deterioration.<sup>47</sup> The effect of the SQ on the quality of care and whether NS-patients have more palliative care needs than S-patients should be studied.

## **CONCLUSION**

The SQ is useful to screen for patients with advanced cancer having palliative care needs at the ED with a sensitivity of 89% and positive predictive value of 85%. Addition of ECOG performance status 3-4 in NS-patients further differentiates prognosis and urgency of palliative care needs. We recommend using SQ plus ECOG 3-4 at the ED as trigger to start ED-initiated palliative care and goals-of-care conversations to arrange appropriate care according to patient's wishes.

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