Insight into the prevalence and severity of symptoms suffered by patients with a hematological malignancy, admitted to hospital;

a quantitative, explorative, descriptive study.

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Abstract

Background

Patients with hematological malignancies face various symptoms. Early recognition of symptoms facilitates optimal symptom management. This study is set up to gain insight into the prevalence and severity of symptoms experienced by patients admitted to hospital with a hematological malignancy. This study will also explore whether these experienced symptoms are associated with patient characteristics.

Method

This quantitative, explorative, descriptive study was conducted between January and June 2018. Data was collected prospectively by using a patient-scored instrument, the Utrecht Symptom Diary (USD). Data was collected on the day of admission, day 4, and day 8. Prevalence and severity are presented with descriptive statistics. Kruskal-Wallis tests are used for associations between patient characteristics and experienced symptoms at day 4; the timepoint with the most severe symptoms.

Results

A total of 55 patients were enrolled in the study. At all timepoints symptom prevalence ranged from 65.8% (dry mouth) to 29.3% (dysphagia). Symptoms that were most commonly reported as moderate or severe were sleeping problems, dry mouth, anorexia, disturbed stool and fatigue.

Patients admitted with lung complications had the driest mouths, highest reported dysphagia, disturbed stool, anorexia, and shortness of breath. Patients admitted for other complications had the most disturbed stool. Patients admitted for another aim had the most pain and dysphagia. Patients with a life-extending intent of treatment had more pain, more shortness of breath and were more anxious than patients with a curative intent of treatment.

Conclusion

Symptom burden appears to have impact at all timepoints, comprehensive symptom assessment is important. This study might help to improve proactive symptom management, including palliative care. A patient-scored instrument can contribute to this.

Implications of key findings

Further research is needed to develop a USD specific for hematological malignancies.

Keywords: Hematologic neoplasms (MeSH), Patient Reported Outcome (MeSH), symptom management.

Nederlandse samenvatting

Titel

Inzicht in prevalentie en ernst van symptomen bij patiënten met een hematologische maligniteit, tijdens ziekenhuisopname.

Aanleiding

Patiënten met een hematologische maligniteit lijden aan verschillende symptomen. Het vroeg signaleren van symptomen is nodig voor optimaal symptoommanagement.
Doel van dit onderzoek is het verkrijgen van inzicht in de prevalentie en ernst van symptomen bij patiënten met een hematologische maligniteit, tijdens ziekenhuisopname. Ook wordt gekeken of deze symptomen associëren met patiëntkarakteristieken.

Methode

Deze kwantitatieve, explorerende, beschrijvende studie is uitgevoerd tussen januari en juni 2018. Data zijn prospectief verzameld met een door patiënten ingevuld instrument; het Utrecht Symptoom Dagboek (USD), op de dag van opname, op dag vier en acht.
Analyse van symptoomprevalentie en ernst werd verricht met beschrijvende statistiek. Kruskal-Wallistoetsen zijn gedaan voor associatie tussen patiëntkarakteristieken en ervaren symptomen op dag vier; de dag waarop symptomen het meest intens ervaren werden.

Resultaten

In totaal werden 55 patiënten geïncludeerd. De prevalentie varieerde van 65,8% (droge mond) tot 29,3% (moeite met slikken). Patiënten hadden het meeste last van een droge mond, slaapproblemen, verminderde eetlust, verstoord ontlastingspatroon en vermoeidheid.
Patiënten met longcomplicaties hadden het ergst last van een droge mond, moeite met slikken, verstoord ontlastingspatroon, verminderde eetlust en benauwdheid. Patiënten met andere complicaties rapporteerden het ergst een verstoord ontlastingspatroon. Patiënten die met een andere reden werden opgenomen hadden de meeste pijn en moeite met slikken. Patiënten met een levensverlengende intentie van behandeling hadden meer pijn, voelden zich benauwder en waren angstiger dan patiënten met een curatieve opzet van behandeling.

Conclusie

Omdat symptoombelasting op alle momenten voor lijkt te komen, is het belangrijk om symptomen goed in kaart te brengen. Deze studie kan helpen bij het verbeteren van proactief symptoommanagement, inclusief palliatieve zorg. Een instrument dat wordt ingevuld door de patiënt zelf kan hieraan bijdragen. Vervolgonderzoek is nodig om een USD te ontwikkelen, specifiek voor patiënten met een hematologische maligniteit.

Sleutelwoorden: hematologische ziekten, symptoommanagement, patiënt gerapporteerde uitkomsten

Introduction

In 2016, 108,402 people in the Netherlands were diagnosed with cancer.[2] Eight percent of these were hematological malignancies, including leukemia, lymphoma and multiple myeloma.[3] These complex diseases often require intensive treatment, and have marked differences in presentation, treatment, progression and outcome.[4] The malignancy itself, the treatment and comorbid illnesses can cause symptoms.[5–7]
In this research, a symptom is defined as a problem expressed by a patient in the physical, psychological, social or spiritual area as the expression or consequence of an underlying illness or its treatment.[8–10]
The number and type of symptoms experienced by patients varied according to the type of cancer, but about 90% of patients reported one or more symptoms.[11,12] The patients suffer from physical burden, and are placed under a great deal of psychological pressure; they struggle with anxiety, uncertainty about prognosis of the disease and the effects of long-term hospital admissions.[13]

Research shows that hematological cancer patients experience a poorer quality of life or health-related quality of life than the general population[14], and that an allogenic stem cell transplantation (SCT) has a statistically significant adverse impact on patients' quality of life.[15] Therefore, treatment and illness can affect symptoms that are experienced by cancer patients. Different experienced symptoms are associated by different age-groups, and needs can differ by gender.[16,17]

Methods for symptom assessment have been developed; symptoms can be recognized easily and earlier, and their severity can be documented. Assessment can be linked to guidelines to perform optimal symptom management.[18] A common used method for symptom reporting is the patient reported outcome measure (PROM). There is growing evidence of using PROMs in settings with cancer patients.[19]

The Utrecht Symptom Diary (USD) was developed to improve patient assessment, monitoring and to evaluate treatment of symptoms. The USD is a PROM, a Dutch adapted translation of the Edmonton Symptom Assessment System (ESAS). [20] The ESAS is used around the world.[21–23] Since 2002, the USD has been used for patients suffering from incurable cancer in the University Medical Centre Utrecht (UMCU). On a daily basis, patients are asked questions relating to their symptoms and well-being and respond using a numerical rating scale. The Diary is a validated instrument for patients suffering from all phases of cancer.[20]

Because of the differences in symptom burden per type of cancer. Experience suggest that assessment and management of symptoms must be individually tailored or at least modified according to cancer type.[20] In the following years, several tumor- and treatment-specific USD modules were developed. In these modules are specific symptoms added to the basic set of the USD.[24]

Several studies have examined how various treatments and medications impact a particular symptom of patients receiving cancer treatment. However, studies reach divergent conclusions, indicating a lack of a 'core set' for the patient with a hematological malignancy. A PROM that is developed is the USD-graft versus host disease[25]; specific for a complication of allogenic stem cell transplantations. For a specific group of patients with a hematological disease, myeloproliferative neoplasms, a symptom burden scoring system is developed; the Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF).[26] Because of difference in type of disease and in treatment options, these instruments are not obviously suitable to use for all patients with a hematological malignancy.

Thus, in literature little is known about which symptoms patients with a hematological malignancy are suffering from, no studies are available to contribute in developing a specific USD for this patient population.

Research question and objectives

What is the symptom prevalence and symptom severity experienced by patients with hematological malignancies, measured by the patient by using the Utrecht Symptom Diary, during admission in hospital?

Primary objectives

The primary objective is to gain insight into the prevalence and severity of symptoms suffered by admitted patients with a hematological malignancy.

Secondary objectives

The secondary objective of this study is to explore whether symptoms experienced by these patients are associated with gender, age, hematological diagnosis, aim of admission and intent of treatment.

Methods

Design

Since little is known about symptoms of patients with a hematological malignancy admitted to hospital, an explorative, descriptive study is performed. Quantitative data is collected prospectively at three timepoints. Since data was collected prospectively in the daily care, all items that were considered as important could be accurately collected.

Patients

This single center study used a convenience sample. Patients with a hematological malignancy admitted to the hematology ward of the University Medical Centre Utrecht (UMCU) were included. Several exclusion criteria were used; patients who were younger than 18 years old, unable to speak or write in Dutch, or unwilling or mentally incompetent to self-assess their symptoms. Patients with graft versus host disease were excluded because there is an instrument to chart symptoms at this subgroup (USD- graft versus host disease).[25]

Preparing data collection

Data collection started in February 2018, at the start of the implementation of the Utrecht Symptom Diary (USD) at the hematology ward of the UMCU. To make sure that the multidisciplinary team was competent in working with the USD, nurses and doctors were trained during an educational meeting by an oncologist (AG) and a project leader quality and safety (BV), both experienced in implementing and using the USD. During a staff meeting of hematologists, a presentation is given about using the USD by an oncologist (AG) and a hematology nurse (CK). At the start of the use of the USD, educational outreach visits[27] took place. Nurses and doctors were coached for two weeks in using the instrument in daily practice. Coaching is done by an expert (BV). Since then, using the USD became standard daily care on the hematology ward.

Instrument

The USD (appendix 1) is used to assess symptoms. The USD is an instrument that is developed in the Netherlands, in the UMCU. It is an adapted and translated version of the Edmonton Symptom Assessment System (ESAS)[20], a validated self-assessment questionnaire for patients with cancer in all phases of disease. Eleven symptoms were measured; pain, sleeping problems, dry mouth, dysphagia, anorexia, disturbed stool, nausea, shortness of breath, fatigue, anxiety, depressed mood and a quality of life question; wellbeing. Each item was scored on a 0–10 scale; no symptom to the worst possible symptom, experienced at the moment of completion. There was also an opportunity for

patients to add items and give prioritization to symptoms.[20] It took the patient a few minutes to complete the USD.

Data collection

Data is collected between February and May 2018. The USD scores at the day of admission (T=0), at day 4 (T=1) and at day 8 (T=2) were used for this study. These timepoints were selected because of the scatter of duration of admissions of the year before the start of this study, in 2016; baseline, interquartile range 1 and interquartile range 2 (median).
The completed USDs were entered by a nurse in the electronic patient file; a standardized fill-in schedule. The scores of the three timepoints were obtained by the researcher (CK) from the electronic patient files. If the patient was admitted more than once in the period of data collection, the USDs of the first admission is included in the study. All collected data is checked by an oncology nurse (ST).

Patient characteristics

Patient characteristics, that were collected of the electronic patient files, are gender, age (categorized in quartiles; <48, 49-62, 63-66, >66 years of age), hospital admission duration (in days), hematological diagnosis (lymphoma, acute leukemia, multiple myeloma, chronic leukemia, others), aim of admission (chemotherapy, autologous SCT, allogenic SCT, manage lung complications, manage gastrointestinal complications, manage other complications, other aims of admission), and intent of treatment (curative, life-extending, palliative, end-of-life, unknown).

Ethical approval

This study was performed according to the declaration of Helsinki[28], principles of good clinical practice[29], the Dutch law in general and the Medical Research Involving Human Subjects Acts (WMO)[30] as approved by the ethics committee of the UMCU (11-113/C,16/713, 16/509).
The backside of the USD (appendix 2) contains written information for patients explaining that the data can be used anonymously for research. An ‘opt-out procedure’ was used; the data of the completed USDs may be used for research, unless the patient indicates differently.[31,32] The collected data is anonymized and coded, so not identifiable to individual patients. The data will be secured saved by the organization for at least 15 years.

Data analysis

Data analysis is done cross-sectional because the research question does not focus on a longitudinal answer (whether the symptoms change over time). Descriptive statistics were

summarized using the mean, median, frequencies and percentages to analyze symptom prevalence (score >0), symptom severity and patient characteristics. Symptom severity data were categorized to mild (≤3), moderate (4≤6), or severe (≥7) symptoms.[20,33] The scores of wellbeing were given in percentages with a mean per timepoint. The eventually added symptoms by the patient and the given prioritization were described and categorized.

To explore the secondary objective, associations between symptoms and patient characteristics, the timepoint with the most severe symptoms will be used for further exploration.

The normality of the data was confirmed by using the Shapiro-Wilk test. A p-value smaller than 0.05 was considered significant. Because of the significant result (p=0,00), non-parametric statistics were used.[34] Three non-parametric tests were appropriate; Chi-square for independence, Mann-Whitney U test, and Kruskal-Wallis test. These are used with a significance level of 0,05.[34] The data did not met the assumptions for a Chi-square test for independence[34–36] (at least 80% of cells should have expected frequencies of 5 or more[34]). The variables were grouped where it was possible to meet the assumptions (symptoms-scores recoded to 0-3 and 4-10, age under and above the median; ≤62 and ≥63). There were no significant results. The Mann-Whitney U test [34–36] is used to test symptoms for differences between gender. There were no significant results.

Kruskal-Wallis tests[34–36] are used to detect differences in mean percentages between groups with the same patient characteristic. For the tests with a significant outcome, a post hoc test was done (pairwise comparisons) with another Kruskal-Wallis test, to detect between which subgroups there was a difference.[37]

Since data were collected in daily care, missing items were expected. A total of 39 USDs (24%) were not completed. There were missing items in the USDs itself as well, 17 times. Which symptom was not entered, differed. Because of the explorative character of the study, available case analysis is applied.[38,39]

Statistical analysis was performed by using IBM SPSS Statistics for Windows, version 23 (Armonk, New York, USA).

Results

Demographics

A total of 58 patients with a hematological malignancy were admitted to the hematology ward and met the inclusion criteria in the period of data collection. Three patients were excluded because they did not want to use the USD, so a total of 55 patients was included.

Table 1 provides patient characteristics and disease related data. Most of the patients were male (63.6%) and the median age was 62. Most patients had acute leukemia (30.9%) or lymphoma (36,4%). The main aims for admission were stem cell transplantations (SCTs) (36.4%) and chemotherapy (29.1%).

Prevalence

During admission in hospital, patients experienced on average 5.2 symptoms concurrently. Per timepoint differences were minimal (T=0 4,9; T=1 5,38; T=2 5,24). For the prevalence of all symptoms, see table 2. The top 5 of patient reported symptoms were having a dry mouth, sleeping problems, anorexia, disturbed stool and pain. For the prevalence of all symptoms per timepoint, see figure 1.

Severity

Symptoms were over all timepoints mainly reported with a mild severity (table 3). The most reported symptoms with a moderate or severe score were fatigue, dry mouth, sleeping problems, anorexia and disturbed stool. For details, see figure 2.

Wellbeing

Quality of life is scored in 111 completed USDs, with a mean of 2,79. Over the different timepoints, differences are minimal, scoring respectively 2,76; 2,82; 2,80; which means that the quality of life was in the first eight days of admission mild influenced. A good quality of life is reported 25 times (22.5%), mild influenced 44 times (39.6%), moderate influenced 33 times (29.7%) and a severe influenced quality of life 9 times (8.2%).

Added items

Patients added in total 28 items to the USD, that occurred 36 times. The most added item (5 times, 17.8%) was having a bad taste in mouth. Almost all items were physical symptoms. Details are presented in table 4.

Prioritization of symptoms

There were 34 patients who gave a prioritization in their symptoms, that occurred in 56 USD's. In total there were 65 unique prioritizations, some patients gave more than one. The most frequently named symptoms with priority were shortness of breath (7 times, 10.8%),

fatigue (6 times, 9.2%), dry mouth (5 times, 7.7%), limited mobility (4 times, 6.1%), edema (4 times, 6.1%) and uncertainty about the future (4 times, 6.1%).

Association between symptoms and patient characteristics

Patients had the most severe symptoms at day 4 of admission (T=1) (see table 3). This timepoint is used for further exploration of the associations between symptoms and patient characteristics (gender, age, hematological diagnosis, aim of admission and intent of treatment). For all results, see table 5.

Aim of admission

A clinically significant difference was found in experienced pain and the six aims of admission (p=0.007). Patients admitted for another other aim experienced significantly more pain than autologous SCT patients (p=0.024) and patients receiving chemotherapy (p=0.042). The allogenic SCT-group experienced less pain than autologous SCT patients (p=0.006), patients who were admitted with a lung-complication (p=0.007), other complications (p=0.002), chemotherapy (p=0.025) and other aims of admission (p=0.001).

In having a dry mouth, a clinically significant difference was found (p=0.001). Patients with an autologous SCT experienced a less dry mouth than patient who were admitted with chemotherapy (p=0.042), other aims of admission (p=0.016), other complications (p=0.007) and lung complications (p=0.002). Patients with an allogenic SCT had a less dry mouth than patients with lung complications (p=0.001), other complications (p=0.002), other aims of admission (p=0.011) and patients who received chemotherapy (p=0.005).

A clinically significant difference was found in experienced dysphagia (p=0.005). The lung-complication-group had more experienced dysphagia than autologous SCT patients (p=0.022), allogenic SCT patients (p=0.006), and chemotherapy patients (p=0.003). Other aims of admission do have more experienced dysphagia than chemotherapy patients (p=0.03).

In experienced anorexia, a clinically significant difference was found (p=0.013). Allogenic SCT patients do have a less reported anorexia than chemotherapy patients (p=0.046), patients with lung complications (p=0.003) and other complications (p=0.001)

A clinically significant difference was found for disturbed stool (p=0.043). Autologous SCT patients do have a less experienced disturbed stool than other complications (p=0.006). Allogenic SCT patients do have a less experienced disturbed stool than patients who were admitted for another complication (p=0.013).

Intent of treatment

A clinically significant difference was found for experienced pain and the intent of treatment (p=0.048). Patients with a life-extending intent of treatment had more pain than patients with a curative intent of treatment (p=0.025).

In shortness of breath, a clinically significant difference was found (p=0.001). Patients who had a life-extending intent of treatment experienced more shortness of breath than patients with a curative intent (p=0.000).

A clinically significant difference was found for experienced anxiety (p=0.044). The life-extending had a higher score for anxiety than the curative intended group (p=0.025).

Discussion

This study used a PROM to assess the prevalence and severity of symptoms suffered by hematological patients, admitted to hospital. A total of 55 patients participated in the study. At all timepoints symptom prevalence ranged from 65.8% (dry mouth) to 29.3% (dysphagia). The symptoms that were most commonly reported as moderate or severe were sleeping problems, dry mouth, anorexia, disturbed stool and fatigue. The secondary objective was to explore whether symptoms suffered by hematological patients were associated with patient characteristics. Age, gender and hematological diagnosis seems not associated. Of all aims of admission, patients who were admitted for complications had the most experienced symptoms. Patients with a life-extending intent of treatment experienced more symptoms than patients with a curative intent of treatment.

To the best of my knowledge this is the first prospective study that assess experienced symptoms at three timepoints, in patients with a hematological malignancy admitted to hospital. In 2011, Manitta et al.[40] measured symptoms in this population at one moment. After this, no studies about experienced symptoms in this population were published. The most prevalent symptom found in this study was having a dry mouth, which was reported by 66% of the patients in the sample. In the study of Manitta[40], 58% of the patients reported having a dry mouth. Different frequencies can be explained by the fact that this sample also included patients who undergone a SCT, in contrast to the study of Manitta. In a study of Johnsen[41], the questionnaire did not even enquire as to whether participants had a dry mouth.

Good (end-of-life) care is important for all patients with a life-limiting disease. Hematology patients require appropriate symptom management when dealing with complex diseases and associated symptoms. Palliative care is a precarious topic in the hematology specialism.[47–49] None of the patients in this study were identified as a palliative intent of treatment. In the three months of data collection for this study, five participants (9%) died. Palliative care teams, that focus on the management of symptoms, can play an important role in this regard. Several studies note that patients with a hematological malignancy are not referred to palliative care as frequently as those with solid cancers.[4,50–53]

To appreciate the findings of this study, some aspects require further consideration. A strength of this study is that the data were gathered in a real-life setting, using prospectively collected data. The sample was small, but included a wide range of ages and different treatments. what increases the generalizability. The skewed distribution of gender in the sample (35 men, 20 women) corresponds with the literature; men more often suffer from hematological malignancies than women.[42,43] A considerable number of patients did not

participate, either because they did not want to, were too ill, were in intensive care, were cognitively impaired or did not speak Dutch. Therefore, the presumption can be made that the results of this study are an underestimation of the actual overall symptom prevalence, severity and quality of life.
The researcher worked at the same department as this study is executed, which could have influenced the motivation of nurses to encourage the patients to complete the USDs. This may have a positive effect on the number of collected data; the response rate of patients who were physically at the department was good (91%). Reasons for not completing were admission at another ward, and for the rest the reason is unknown.
A limitation was the statistics that were used for the association between experienced symptoms and patient characteristics. Because of the small sample size, the groups who experienced a symptom were relatively small, so non-parametric test had to be used.

A study by Lobb[54] described the hematological patients' need to feel like they are managing their health together with the medical team. A PROM can contribute to this feeling. Since the USD is implemented on the hematology ward in the UMCU, the concern of symptoms and their management frequently subjects of discussion. The experience and the added value of the USD for the patients and the medical team, can be further explored with a qualitative design.
One of the aims of this study for daily practice was to gain insight into the most prevalent added symptoms by patients, so a specific hematological-malignancy USD could be developed. Only having a bad taste in mouth was frequently added by patients, a finding that is supported by literature.[44,45] A wide range of other symptoms were added, these seems mostly side effects of treatments, in concordance with an immunotherapy USD[46] and the MPN-SAF[26]. Because of difference in type of disease and in treatment options, a hematological malignancy USD will probably look different. So future research needs to be done to make a hematological malignancy USD, including an investigation of the nature of symptoms, can be valuable.
As mentioned, this study focused on symptom burden in the first eight days of admission. A recommendation for further research is a study that examine for a longer period, during the entire illness trajectory. How symptoms varies over time and between different groups can be studied with a longitudinal design.

In summary, the current study gives insight into the considerable symptom burden in patients with a hematological malignancy. Symptom burden appears to have an impact at all timepoints, comprehensive symptom assessment is important. This study might help to improve proactive symptom management, including palliative care. Development of a

hematological malignancy specific USD can be helpful in this.

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Table 1. Patient characteristics

Demographics	**Patients (N=55)**	**%**
Completed USD forms	126	
Hospital admission duration, in days. Median (min-max)	15 (4 – 82)	
Age, in years. Median (IQR)	62 (47 – 66)	
Gender		
Male	35	63.6
Hematological diagnosis		
Lymphoma	20	36.4
Acute leukemia	17	30.9
Multiple Myeloma	8	14.5
Chronic leukemia	6	10.9
Others	4	7.3
Aim of admission		
Chemotherapy	16	29.1
Autologous stem cell transplantation	11	20
Allogenic stem cell transplantation	9	16.4
Manage complications – lung problems	9	16.4
Manage complications – gastrointestinal	0	0
Manage complications – others[1]	6	6
Others[2]	4	4
Intent of treatment		
Curative	43	78.2
Life-extending	11	11
Palliative	0	0
End-of life	0	0
Unknown	1	1.8

[1] Pain, renal dysfunction, sepsis, shingles, and urinary tract infections.

[2] Ascertain diagnoses, experimental study.

Table 2. Prevalence of symptoms (score >1), all timepoints.

Item	N (%)
Pain	65 (52.4)
Sleeping problems	82 (65.6)
Dry mouth	83 (65.8)
Dysphagia	37 (29.3)
Anorexia	81 (64.8)
Disturbed stool	78 (63.4)
Nausea	41 (32.5)
Shortness of breath	41 (32.5)
Fatigue	47 (37.6)
Anxiety	61 (48.4)
Depressed mood	60 (47.6)

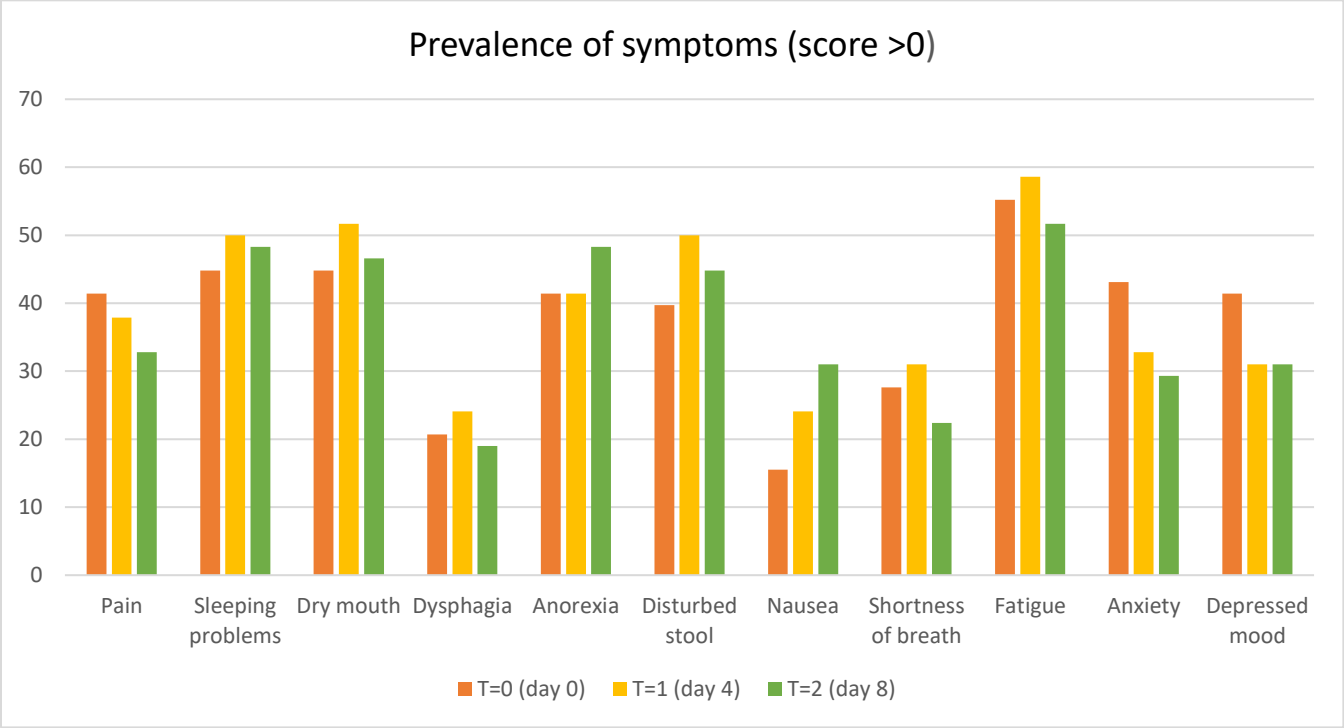

Figure 1: Symptom prevalence in percentages, per timepoint.

Table 3. Severity of symptoms

	T=0 (day of admission)	T=1 (admission day 4)	T=2 (admission day 8)	Total
Pain				
N	42 (76.4%)	43 (78.2%)	39 (70.9%)	
0	18 (32.7%)	21 (38.2%)	20 (36.4%)	59
Mild (1-3)	15 (27.3)	14 (25.5%)	15 (27.3%)	44
Moderate (4-6)	7 (12.7%)	6 (10.9%)	4 (7.3%)	17
Severe (≥7)	2 (3.6%)	2 (3.6%)	-	4
Missings	13 (23.6%)	12 (21.8%)	16 (29.1%)	41
Sleeping problems				
N	43 (78.2%)	43 (78.2%)	39 (70.9%)	
0	17 (30.9%)	14 (25.5%)	11 (20%)	42
Mild (1-3)	11 (20%)	12 (21.8%)	17 (30.9%)	40
Moderate (4-6)	10 (18.2%)	11 (20%)	9 (16.4%)	30
Severe (≥7)	5 (9.1%)	6 (10.9%)	2 (3.6%)	13
Missings	12 (21.8%)	12 (21.8%)	16 (29.1%)	40
Dry mouth				
N	44 (80%)	43 (78.2%)	39 (70.9%)	
0	18 (32.7%)	13 (23.6%)	12 (21.8%)	43
Mild (1-3)	6 (10.9%)	12 (21.8%)	14 (35.5)	32
Moderate (4-6)	14 (25.5%)	12 (21.8%)	7 (12.7%)	33
Severe (≥7)	6 (10.9)	7 (12.7%)	6 (10.9%)	19
Missings	11 (20%)	12 (21.8%)	16 (29.1%)	39
Dysphagia				
N	44 (80%)	43 (78.2%)	39 (70.9%)	
0	32 (58.2%)	29 (52.7%)	28 (50.9%)	89
Mild (1-3)	10 (18.2%)	10 (18.2%)	8 (14.5%)	28
Moderate (4-6)	1 (1.8%)	2 (3.6%)	2 (3.6%)	5
Severe (≥7)	1 (1.8%)	2 (3.6%)	1 (1.8%)	4
Missings	11 (20%)	12 (21.8%)	16 (29.1%)	39
Anorexia				
N	44 (80%)	43 (78.2)	38 (69.1%)	
0	20 (36.4%)	14 (25.5)	10 (18.2%)	44
Mild (1-3)	9 (16.4%)	12 (21.8%)	9 (16.4%)	30
Moderate (4-6)	4 (7.3%)	12 (21.8%)	14 (25.5%)	30
Severe (≥7)	4 (7.3%)	5 (9.1%)	5 (9.1%)	14
Missings	11 (20%)	12 (21.8%)	17 (30.9%)	40
Disturbed stool				
N	42 (76.4%)	43 (78.2%)	38 (69.1%)	
0	19 (34.5%)	14 (25.5%)	12 (21.8%)	45
Mild (1-3)	10 (18.2%)	16 (29.1%)	10 (18.2%)	36
Moderate (4-6)	9 (16.4%)	9 (16.4%)	10 (18.2%)	28
Severe (≥7)	4 (7.3%)	4 (7.3%)	6 (10.9%)	14
Missings	13 (23.6%)	12 (21.8%)	17 (30.9%)	42

Table 3. Severity of symptoms (continued)

	T=0 (day of admission)	T=1 (admission day 4)	T=2 (admission day 8)	Total
Nausea				
N	44 (80%)	43 (78.2%)	39 (70.9%)	
0	35 (63.6%)	29 (52.7%)	21 (38.2%)	85
Mild (1-3)	7 (12.7%)	9 (16.4%)	14 (25.5%)	30
Moderate (4-6)	2 (3.6%)	5 (9.1%)	3 (5.5%)	10
Severe (≥7)	-	-	1 (1.8%)	1
Missings	11 (20%)	12 (21.8%)	16 (29.1%)	39
Shortness of breath				
N	44 (80%)	43 (78.2%)	39 (70,9%)	
0	28 (50.9%)	25 (45.5%)	26 (47,3%)	79
Mild (1-3)	7 (12.7%)	8 (14.5%)	11 (20%)	26
Moderate (4-6)	5 (9.1%)	5 (9.1%)	1 (1,8%)	11
Severe (≥7)	4 (7.3%)	5 (9.1%)	1 (1,8%)	10
Missings	11 (20%)	12 (21,8)	16 (29,1%)	39
Fatigue				
N	44 (80%)	42 (76.4%)	39 (70.9%)	
0	12 (21.8%)	8 (14.5%)	9 (16.4%)	29
Mild (1-3)	12 (21.8%)	16 (29.1)	13 (23.6%)	41
Moderate (4-6)	12 (21.8%)	10 (18.2%)	11 (20%)	33
Severe (≥7)	8 (14.5%)	8 (13.5%)	6 (10.9%)	22
Missings	11 (20%)	13 (23.6%)	16 (29.1%)	40
Anxiety				
N	44 (80%)	43 (78.2%)	39 (70.9%)	
0	19 (34.5%)	24 (43.6%)	22 (40%)	65
Mild (1-3)	15 (27.3%)	13 (23.6%)	12 (21.8%)	40
Moderate (4-6)	6 (10.9)	4 (7.3%)	5 (9.1%)	15
Severe (≥7)	4 (7.3)	2 (3.6%		6
Missings	11 (20%)	12 (21.8%)	16 (29.1%)	39
Depressed mood				
N	44 (80%)	43 (78.2%)	39 (60%)	
0	20 (36.4%)	25 (45.5%)	21 (38.2%)	66
Mild (1-3)	13 (23.6%)	11 (20%)	12 (21.8%)	36
Moderate (4-6)	8 (14.5%)	5 (9.1%)	6 (10.9%)	19
Severe (≥7)	3 (5.5%)	2 (3.6%)	1 (1.8%)	6
Missings	11 (20%)	12 (21.8%)	16 (29.1%)	39
Total mild	115	133	135	
Total moderate	78	81	79	
Total severe	41	42	29	
Total missings	126	133	178	

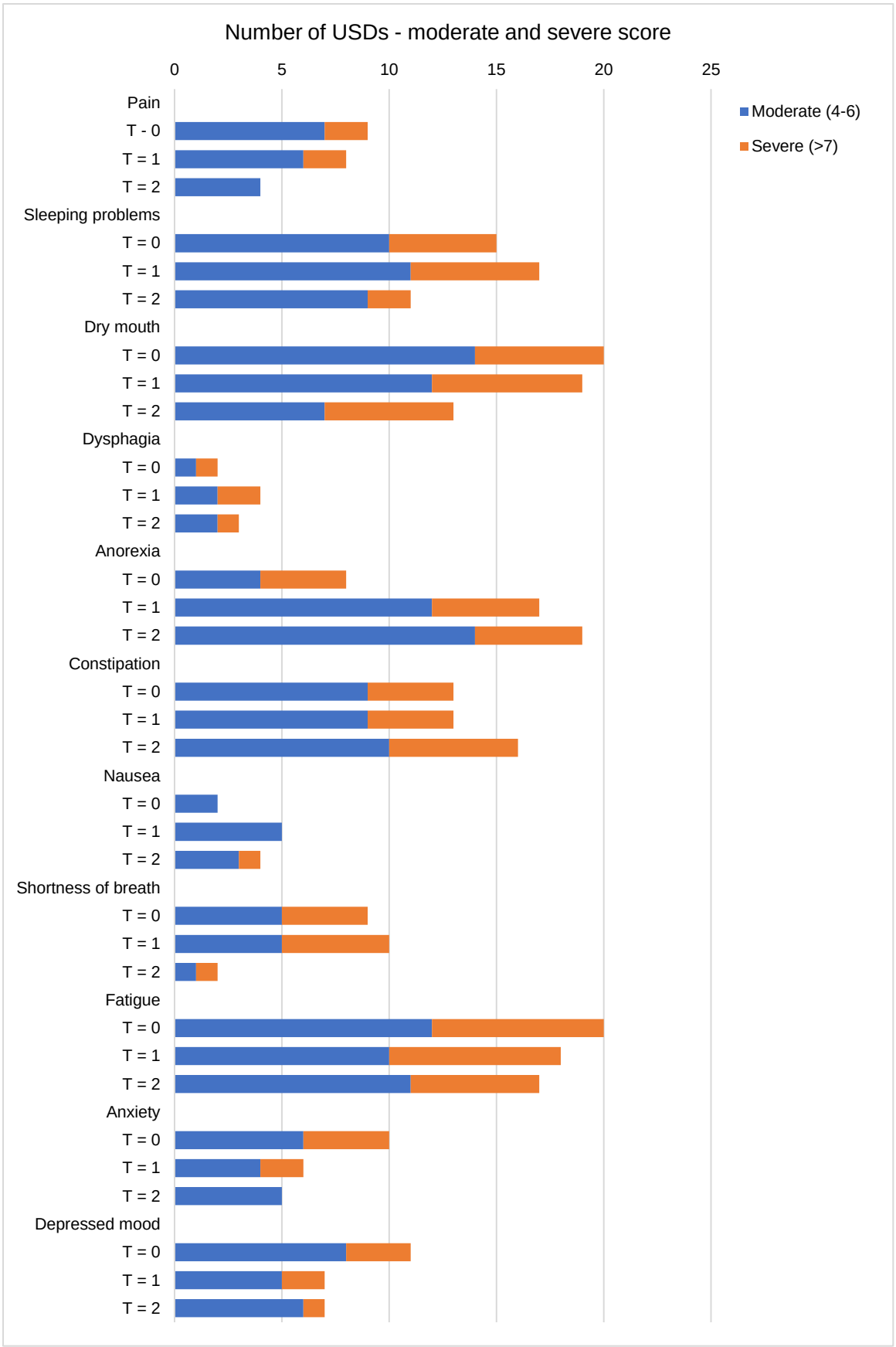

Figure 2: Severity of symptoms.
Day of admission (T=0), day 4 (T=1), day 8 (T=2).

Table 4. Added items

Item	Times added
Bad taste	5
Blood pressure	2
Dizziness	2
Edema	2
Headache	2
Itching	2
Limited mobility	2
Stuffy nose	2
Abscess	1
Back problems	1
Burning eyes	1
Confusion	1
Drowsiness	1
Dry lips	1
Frog in throat[1]	1
Hallucinations	1
Heartburn	1
Palpations	1
Poor condition	1
Rash	1
Dyspnea, during exertion[2]	1
Dyspnea, during rest[2]	1
Sore mouth	1
Thirst	1
Tingling in fibula	1
Tinnitus	1
Visual complaints	1

[1] Explanation of dysphagia

[2] Explanation of shortness of breath

Table 5. Kruskal-Wallis tests (T=1)

	Sex Df 1	**Age** [1] Df 3	**Age**[2] Df 1	**Hematological diagnosis**[3] Df 4	**Aim of admission**[4] Df 5	**Intent of treatment**[5] Df 2
Pain	H=1.209 p=0.271	H= 2.669 p=0.446	H= 0.284. Df 1. p=0.594	H= 7.483 p=0.112	H= 16.055 p=0.007	H= 6.054 p=0.048
Sleeping problems	H= 0.078 p=0.780	H= 5.791. p=0.122.	H= 0.149 p=0.700	H= 4.624 p=0.328	H= 7.351 p=0.196	H= 1.507 p=0.471
Dry mouth	H= 0.052 p=0.820	H= 2.113. p=0.549.	H= 1.246 p=0.264	H= 3.132 p=0.536	H= 21.109 p=0.001	H= 0.358 p=0.836
Dysphagia	H= 0.395 p=0.530)	H= 0.378. p=0.945.	H= 0.0 p=0.988	H= 6.507 p=0.164	H= 16.849 p=0.005	H= 4.417 p=0.110
Anorexia	H= 1.482 p=0.224)	H= 2.397. p=0.494.	H= 1.576 p=0.209	H= 4.451 p=0.348	H= 14.409 p=0.013	H= 2.267 p=0.322
Constipation	H= 2.208 p=0.137)	H= 3.288. p=0.349.	H= 2.579 p=0.108	H= 5.583 p=0.232	H= 11. 481 p=0.043	H= 1.060 p=0.589
Nausea	H= 0.108 p=0.742)	H= 1.405. p=0.704.	H= 0.474 p=0.491	H= 4.541 p=0.338	H= 10.961 p=0.052	H= 1.324 p=0.516
Shortness of breath	H= 0.562 p=0.454)	H= 1.506. p=0.681	H= 0.002 p=0.967	H= 9.212 p=0.056	H= 16.979 p=0.005	H= 14.479 p=0.001
Fatigue	H= 0.033 p=0.856)	H= 3.384. p=0.336.	H= 2.206 p=0.137	H= 8.282 p=0.082	H= 7.559 p=0.182	H= 1.348 p=0.510
Anxiety	H= 0,697 p=0,404)	H= 4,6. p=0,204	H= 2,061 p=0,151	H= 4,862 p=0,302	H= 9,875 p=0,079	H= 6,261 p=0,044
Depressed mood	H= 0,49 p=0,824)	H= 5,052. p=0,168.	H= 3,077 p=0,079	H= 6,900 p=0,141	H= 8,840 p=0,116	H= 5,961 p=0,051

[1] Age <48, 49-62, 63-66, <66 years of age

[2] Age ≤62 and ≥63

[3] Lymphoma, acute leukemia, multiple myeloma, chronic leukemia, others

[4] Chemotherapy, autologous stem cell transplantation, allogenic stem cell transplantation, manage lung complications, manage gastrointestinal complications manage complication-others, other aims of admission

[5] Curative, life-extending, palliative, end-of-life, unknown.

Appendix 1

Utrecht Symptoom Dagboek (USD)

USD basis

UMC Utrecht
Cancer Center

Instructie
Door het dagelijks invullen van klachten en/of problemen die u ervaart kunnen we samen de passende zorg vaststellen, evalueren en waar nodig bijstellen.

Wilt u omcirkelen welk cijfer past bij hoe u de klachten en/of problemen ervaart op het moment van invullen?

We vragen ook naar uw kwaliteit van leven door de vraag over 'wellbevinden'.

patiëntsticker

Datum _____

Ik heb op dit moment:												
geen pijn	0	1	2	3	4	5	6	7	8	9	10	erg veel pijn
geen slaapprobleem	0	1	2	3	4	5	6	7	8	9	10	erg groot slaapprobleem
geen drogemond	0	1	2	3	4	5	6	7	8	9	10	erg droge mond
geen slikklachten	0	1	2	3	4	5	6	7	8	9	10	erg veel slikklachten
goede eetlust	0	1	2	3	4	5	6	7	8	9	10	geen eetlust
normaal ontlastingspatroon	0	1	2	3	4	5	6	7	8	9	10	erg verstoord ontlastingspatroon
Anders												
_____	0	1	2	3	4	5	6	7	8	9	10	_____
_____	0	1	2	3	4	5	6	7	8	9	10	_____
Ik voel me op dit moment:												
niet misselijk	0	1	2	3	4	5	6	7	8	9	10	erg misselijk
niet benauwd	0	1	2	3	4	5	6	7	8	9	10	erg benauwd
niet moe	0	1	2	3	4	5	6	7	8	9	10	erg moe
niet angstig	0	1	2	3	4	5	6	7	8	9	10	erg angstig
niet somber	0	1	2	3	4	5	6	7	8	9	10	erg somber
Anders												
_____	0	1	2	3	4	5	6	7	8	9	10	_____
_____	0	1	2	3	4	5	6	7	8	9	10	_____
Ik voel me op dit moment:												
goed	0	1	2	3	4	5	6	7	8	9	10	erg slecht

Welke klachten en/of problemen moeten wat u betreft als eerste aandacht krijgen?

_____

Appendix 2

PATIENTENINFORMATIE UTRECHT SYMPTOOM DAGBOEK

Geachte mevrouw, meneer,

Graag informeren wij u over het gebruik van het Utrecht Symptoom Dagboek (USD) tijdens uw opname.

Waarom deze werkwijze?

Door uw ziekte en/of behandeling kunt u last hebben van meerdere klachten of problemen. Wij noemen dat symptomen. Voorbeelden zijn pijn, vermoeidheid, verminderde eetlust of obstipatie. We willen deze klachten zo goed mogelijk behandelen. Om een goed beeld te krijgen van de klachten waar u last van heeft vragen we u dit symptoomdagboek in te vullen. Uit onderzoek is gebleken dat door op deze wijze te vragen naar uw klachten, deze beter besproken en gevolgd kunnen worden.

Wat houdt de werkwijze voor u in?

- Eén keer per dag zal u gevraagd worden het Utrecht Symptoom Dagboek in te vullen. Dit is een vragenlijst waarop 12 symptomen/ klachten staan.
- Met een cijfer kunt u aangeven hoeveel last u van iedere klacht ervaart op dit moment. Het cijfer '0' betekent geen last en het cijfer '10' betekent heel veel last. Het cijfer wat het eerste bij u opkomt, is vaak het juiste.
- Wanneer u een klacht ervaart die niet in het symptoomdagboek beschreven staat, kunt u deze er zelf bijschrijven.
- Er wordt ook aan u gevraagd om aan te geven welk symptoom, volgens u, als eerste moet worden aangepakt.
- Het invullen van het symptoomdagboek zal per keer ongeveer 1 tot 5 minuten in beslag nemen.
- Indien u niet in staat bent om zelf het symptoomdagboek in te vullen zal de verpleegkundige u daarbij ondersteunen.
- De verpleegkundige bespreekt uw scores dagelijks met uzelf en met de arts.

Wetenschappelijk onderzoek

De uitkomsten van het USD worden daarnaast **anoniem** gebruikt voor wetenschappelijk onderzoek. Bijvoorbeeld om te inventariseren welke symptomen veel voorkomen en welke behandelingen effectief zijn. Uw USD samen met uw geslacht, leeftijd en gegevens over uw ziekte en behandeling worden uit uw dossier gehaald. Deze gegevens worden gecodeerd gebruikt en zijn niet herleidbaar tot u persoonlijk. Mocht u hier bezwaar tegen hebben of wilt u geen toestemming verlenen voor inzage in uw dossier, dan vragen wij u uw naam, geboortedatum en patiëntennummer te mailen naar usdonderzoek@umcutrecht.nl