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Symptom Patterns in Young Adults with Cancer: An App-Based Study

Giulia Locatelli[a,*], Alessandro Pasta[b], Line Bentsen[c], Signe Hanghøj[c], Karin Piil[d], Helle Pappot[e]

[a] School of Nursing, Midwifery and Paramedicine - Faculty of Health Sciences, Department of Biomedicine and Prevention, University of Rome Tor Vergata, Rome, Italy; Faculty of Health Sciences, Australian Catholic University, Fitzroy Victoria, Melbourne, Australia
[b] Department of Applied Mathematics and Computer Science, Technical University of Denmark, Kongens Lyngby, Denmark
[c] Researcher at Department of Hematology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
[d] Researcher at Department of Oncology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, and Department of Public Health, Aarhus University, Aarhus, Denmark; Department of People and Technology, Roskilde University, Roskilde, Denmark
[e] MD at Department of Oncology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, and Copenhagen University, Department of Clinical Medicine, Copenhagen, Denmark

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ABSTRACT

Objectives: To investigate symptom patterns in young adults with cancer using a smartphone-based app. The authors sought to explore symptom frequency and severity, cluster patients based on their symptom severity, investigate the co-occurrence of severe symptoms, and explore the relationship between symptoms and activities.
Data Sources: Data were collected, using a mobile app, from 161 young adults with cancer (mean age 25.5 years, 75% female, 59% with solid cancer). Symptom frequency/severity was investigated with descriptive statistics. K-means clustering technique was used to cluster patients based on the average symptom severity. Co-occurrence of severe symptoms was investigated with the association rule technique. The relationship between symptom severity and likelihood of performing a physical/social activity was explored with mixed-effects logistic regression.
Conclusion: The most frequently reported symptom was mood disturbance, followed by fatigue, which was also the most severe one. Two clusters of patients were identified, experiencing higher and lower severity for all symptoms. Severe appetite disturbances were frequently reported together with severe lack of energy and nausea. Severe lack of energy, either alone or together with mood disturbance, was often reported together with severe fatigue. Higher mood disturbance was associated with lower probability of performing physical and social activities. This study provides new insights into the symptom experience of young adults with cancer.
Implications for Nursing Practice: Using a symptoms-tracking app may be a valid strategy for healthcare professionals, nurses, and researchers to support patients in symptom monitoring and, consequently, to identify and implement tailored symptom-management strategies.

INTRODUCTION

The World Health Organization estimated that in 2020 nearly 862,000 of young adults between 20 and 39 years of age were affected by cancer globally, causing approximately 360,000 deaths.[1] The spectrum of cancer types in young adults is very broad, comprising both childhood cancers (eg, leukemia), cancers that are more common in general adults (eg, breast cancer), as well as cancers that are more prevalent in this specific age group than in younger or older individuals (eg, testicular cancers).[2-4] Moreover, most research focuses on cancer in either children or older adults, leaving the cancer burden in this specific age group less explored.[5] For these reasons, young adults with cancer might experience difficulties in receiving optimal care for their cancer type and their age-related needs.[5] Since young adults have a large proportion of their life expectancy remaining, it is crucial to explore the specific issues of this age group of cancer patients and to eventually contribute to improve their cancer-related outcomes.[6]

Young adults with cancer experience a multitude of symptoms, such as nausea, fatigue, pain, sleep problems, and difficulties concentrating.[7] In addition, existing research showed that young adults with cancer have significantly higher physical and psychological distress compared to older patients with cancer[8] and to the general population.[9] Young adults with cancer who perceive a lack of control over their symptoms also report higher insecurity and psychological

* Address correspondence to: Giulia Locatelli, Via Montpellier, 1, 00133 Rome, Italy.
E-mail address: giulia.locatelli@outlook.it (G. Locatelli).

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distress and lower independence and quality of life, especially when symptoms become chronic.[10-12] Therefore, addressing the symptom experience in young adults with cancer is essential to increase symptom awareness, to facilitate symptom recognition and communication, and, ultimately, to improve symptom management. However, studies comprehensively exploring symptom patterns in young adults with cancer are scarce.

Many symptom theories highlight how crucial it is to monitor and manage symptoms so that illness exacerbations are prevented and/or addressed in a timely fashion. As highlighted by the theory of self-care in chronic illness integrated with symptoms,[13] a symptom needs to be first perceived and monitored in order to be subsequently managed. Symptoms in cancer patients have usually been assessed through traditional survey instruments,[14] but several authors highlighted the need to explore the symptom experience by taking advantage of more informative approaches, such as through the use of mobile technologies.[5,14-16] In a previous study,[14] authors implemented an iPad-based application that they used to show, at one specific timepoint, images of symptoms to cancer patients. Patients were asked to verbally report and elaborate on some symptoms experienced in the previous 24 hours.

The overall aim of this study was to investigate symptom patterns in young adults with cancer through the implementation of a smartphone-based symptom-tracking application (app) that patients could autonomously use any time they wanted to. Specifically, we aimed to explore symptom frequency and severity, cluster patients based on their symptom severity; investigate the co-occurrence of the most severe symptoms, and explore the relationship between symptoms and activity.

METHODS

Study Design and Participants

This is an observational study in which we collected data on the symptom experience of young adults with cancer by using a smartphone-based app called Kræftværket. This study has been primarily led by a research team at Copenhagen University Hospital in Denmark but further involved all Danish hospitals treating adolescents and young adults with cancer. The Kræftværket app has been developed through a co-creation process between adolescents and young adults with cancer and the research team at Copenhagen University Hospital. It included three main features: an interactive diary to track symptoms and daily activities, an online network between the users, and a database of educational material for users.[17-19] The protocol for this study has been previously published,[17] and the app has already been pilot tested.[19]

Inclusion criteria for the present study were being a young adult between 18 and 39 years (this age range is in accordance with previous studies on young adults with cancer[20-22]), having a diagnosis of any type of cancer, receiving or having received cancer treatment at a hospital in Denmark, and having access to a smartphone and an internet connection. Exclusion criteria were being unable to read and write in Danish and having participated in the app co-creation process.[17] Participants were recruited from five Danish hospitals by nurses who were either youth coordinators or specialized oncology nurses. The recruiting nurses approached and screened all potential participants meeting the inclusion criteria, explained how to use the app, the study aims, risks and benefits to the potential participants, and collected informed content forms. If patients were eligible and willing to participate and sign the consent form, they were instructed on how to download and use the app. Participants in this study used the app from June 2020 to April 2022. Frequency and intensity of use of the app are subjective based on the wishes of each patient.

Procedures and Outcome Measurements

Symptoms were measured through an interface in the app where users could select a symptom among seven predefined categories (ie, nausea, fatigue, pain, lack of energy, sleep, appetite, mood) or type a new one. Once a symptom was selected or typed in, the user was asked to report its perceived severity on a 5-point visual scale (1 = very mild, 5 = very severe). Please note that the Danish word for "fatigue" does not fully match the meaning of the Danish term for "lack of energy." Indeed, the Danish term for "fatigue" also includes "tiredness," whereas the Danish term for "lack of energy" does not necessarily imply tiredness. For this reason, during the co-creation process of the app, the users suggested to have both fatigue and lack of energy were tracked. The app also allowed to plan and track daily activities. As for activities, users could select among predefined categories (ie, cycling, running, yoga, strength training, other physical activity, social activity) or type a new one, whenever they wanted. Demographic data (ie, age, gender, diagnosis) were provided by the users themselves when logging into the app. All collected data were automatically sent to and stored by the platform Daman Digital.

Statistical Analysis

The collected data were preprocessed by excluding patients who used the app very seldom (ie, submitted in total <10 entries, either symptoms or activities). Moreover, we categorized the nonpredefined newly typed symptoms and activities among the predefined categories. To investigate the symptom frequency, the total number of entries submitted by each patient was computed for each symptom. To explore the severity of each symptom, the average severity reported by each patient was computed.

Additionally, inspired by previous research on healthcare app users,[23] patients were clustered based on the average severity reported for each symptom. We applied the k-means clustering technique,[24] which aims to partition the observations in k clusters by minimizing the within-cluster variance (ie, square Euclidean distances). The optimal number of clusters (k) was determined by using the elbow method[25] and computing the average silhouette coefficient,[26] which aims to evaluate the cluster separation and cohesion. Subsequently, the differences between the symptom severity reported by the patients belonging to the resulting clusters was tested. To determine which test to perform, Levene test for homogeneity of variances and Shapiro-Wilk test for normality were performed. As the assumption of normality was violated, the Mann-Whitney U test,[27] a nonparametric version of the t-test for independent samples, was performed. Similarly, the age difference between the clusters was tested. The differences in terms of gender and diagnosis were tested by performing the χ^2 test.

Furthermore, we investigated whether some symptoms frequently occur together by determining association rules,[28] a technique native of other fields but already adopted in healthcare research.[29] Starting from a set of the seven symptoms $S = \{s_1, s_2, \ldots, s_7\}$, we analyzed the symptoms reported with the highest severity (ie, 5) by each patient in each day. In a specific day, each patient reported (with severity = 5) a subset of symptoms from the set S. An association rule is defined as an implication of the form $X \Rightarrow Y$, stating that if a symptom X is reported, another symptom Y is also reported (X is the antecedent symptom, Y is the consequent symptom, $X, Y \subseteq S$, and $X \cap Y = \emptyset$).[30] The rules were evaluated based on several metrics (ie, support, coverage, confidence, lift). The support of a rule defines how often a rule appears in the data set (ie, all patient/day combinations). The coverage refers to how often the antecedent of a rule appears in the data set and measures how often the rule can be applied. The confidence measures how often a rule is correct out of the applicable cases. The lift measures the deviation of the support of the whole rule

from the support expected if the antecedent and the consequent were independent.[30]

Finally, we explored the relationship between the symptom severity and the likelihood of performing an activity in the same day. Specifically, we fitted two separate mixed-effects logistic regression models, one for physical and one for social activities. The dependent variable was a binary variable describing, respectively for the two models, whether a physical or social activity was performed (in a specific day, by a specific user). Equally for both models, the fixed-effect independent variables were the average severities reported for each symptom in the same day by the same user. Additionally, we included the patient ID variable as random effect to control for the subject-specific propensity to performing an activity. This allowed us to obtain effects that hold for all patients and are not driven by peculiar tendencies of some patients (eg, patients reporting higher average symptom severity and having lower activity propensity).

The data manipulation and most of the data analysis (ie, data visualization, clustering, association rule mining) were performed in Python. The mixed-effects logistic regression analysis was performed in R.

RESULTS

Sample Description

A total of 161 young adults with cancer were included in the analysis. Patients were, on average, 25.49 (±4.68) years old and mainly female (75%). Clinically, 59% of the patients reported a solid cancer, whereas 41% had a hematologic cancer. The patients used the App from June 2, 2020, to 3rd April 3, 2022.

Symptom Frequency and Severity

Each patient reported, on average, 92 symptom entries (min: 7; max: 1,136), and 109 patients reported ≥20 symptom entries. Fig 1 shows, for each of the predefined symptoms, the number of entries reported by the 161 patients. Mood disturbance was the most frequently reported symptom (red line in Fig 1), followed by fatigue (green line in Fig 1).

Fig 2 shows the frequency for each average severity level of the different symptoms. For instance, mood was the most frequently reported symptom (reported, on average, 16.20 times), and most patients reported it with an average severity of 2 to 3 of 5 (severity; M = 2.47, SD = 0.63). Fatigue was the second most frequent (reported, on average, 14.21 times) and the most severe symptom (severity; M = 3.01, SD = 0.82), followed by lack of energy (severity; M = 2.79, SD = 0.88). Patients reported nausea as the least severe symptom (severity; M = 2.29, SD = 0.81), followed by appetite disturbances (severity; M = 2.34, SD = 0.77) and pain (severity; M = 2.41, SD = 0.85).

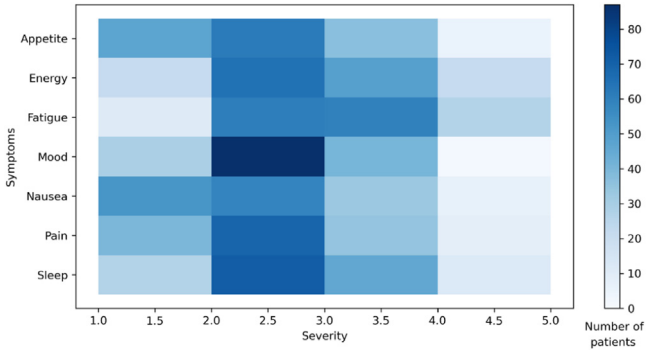

FIG 2. Average severity of symptoms. To create this figure, for each patient, the average severity of each symptom was computed. Note. Severity of symptoms ranges from 1 (very low) to 5 (very high).

Clustering Patients Based on their Symptom Severity

The 161 patients were clustered based on the severity of their symptoms. A two-cluster solution, explaining 31.50% of the variance, was selected based on the elbow plot and the silhouette score (0.277). Fig 3 shows the average symptom severity for the patients belonging to the two clusters. Patients in cluster 1 (n = 86) reported all symptoms with lower severity, whereas patients in cluster 2 (n = 75) reported all symptoms with higher severity (Mann-Whitney U test, $P < .01$). Age (Mann-Whitney U test, $P = .132$), gender (χ^2 test, $P = .266$), and diagnosis (χ^2 test, $P = .734$) were not significantly differently distributed between the two clusters.

Co-Occurrence of Symptoms

Association rule mining was performed to investigate whether some symptoms frequently occurred together with high severity (Fig 4). The detailed metrics of the selected rules are presented in the Appendix (Table A). Two rules indicated that patients who reported severe appetite disturbances also frequently reported severe lack of energy (rule 1) and nausea (rule 2). Moreover, patients who reported

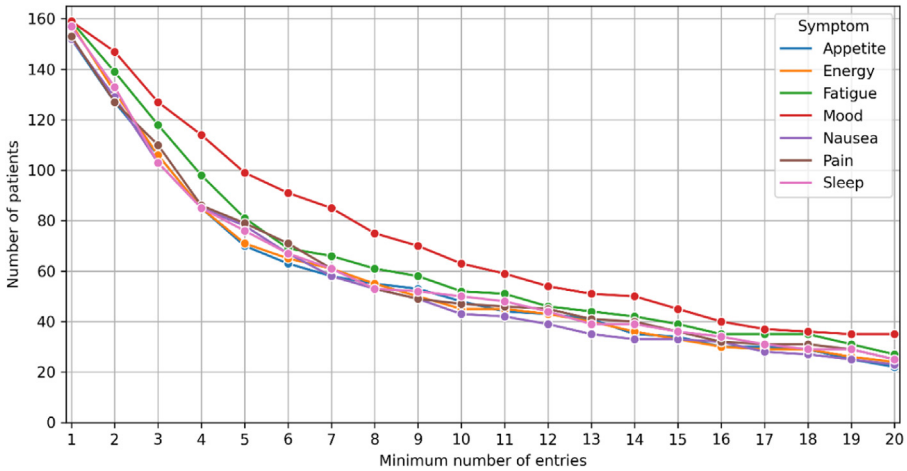

FIG 1. Number of patients (total sample = 161) vs minimum number of symptom-entries in the app. For instance, 99 patients reported mood disturbances at least 5 times, while 81 patients reported fatigue at least 5 times. Note. The figure shows up to 20 entries for each symptom. A higher number of entries were reported by maximum 33 patients only (for mood, the most frequent symptom). Thus, they are not showed in this figure for visualization and clarity reasons.

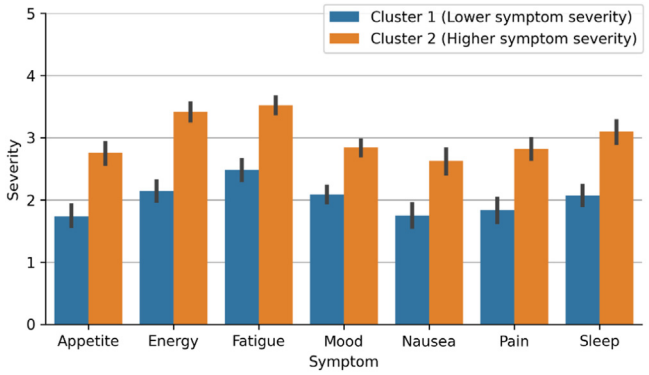

FIG 3. Average symptom severity for the patients belonging to the two clusters. Note. Error bars represent the 95% confidence interval. The two clusters reported significantly different severity for all symptoms (Mann-Whitney U test, $P < .01$).

lack of energy, either alone (rule 3) or together with mood disturbance (rule 4), also reported severe fatigue.

Relationship between Symptoms and Activity

Two different mixed-effects logistic regression models were fitted to investigate the relationship between symptom severity and, respectively, physical and social activity (Table 1). Both models fitted the data significantly better ($P < .001$) than a null model (ie, a model including only the patient-specific random effect). The coefficients indicated that the severity of mood disturbances was negatively associated with physical activity ($P < .001$). Specifically, for a 1-unit increase in the severity of mood disturbances, the log odds of performing a physical activity decreases by 0.436. In other terms, higher mood disturbance was associated with lower probability of performing a physical activity. Similarly, the severity of mood disturbances was negatively associated with social activity ($P < .001$). That is, higher mood disturbance was associated with lower probability of engaging in a social activity.

DISCUSSION AND CONCLUSION

The aim of this paper was to explore symptom patterns among young adults with cancer through the implementation of a symptoms-tracking app. Other authors[15] already stressed the importance of exploring the symptom experience and symptom clusters in young adults with cancer by taking advantage of mobile technologies. Thus, this study represents one of the very first contribution in that direction. Understanding symptom patterns as reported by patients themselves through an interactive and always-available technology (ie, a symptom-tracking app) allows clinicians, researchers, and patients themselves to obtain an appropriate and realistic understanding of the symptom burden and, therefore, to manage symptoms in the most efficient way.

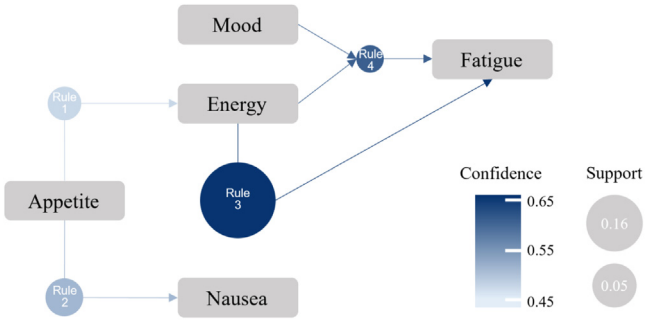

FIG 4. Association rules among the symptoms most frequently reported together with high severity (severity = 5). Note. The support of a rule refers to how often the rule appears in the dataset. The confidence of a rule refers to how often a rule is correct out of the applicable cases. For example, in this figure, energy and fatigue (rule 3) are reported together 16% out of the total number of symptom entries (support). When the antecedent symptom is reported (eg, energy in rule 3), the rule holds for 66% of entries (confidence), meaning that, in 66% of the entries where energy was reported, the consequent symptom (eg, fatigue in rule 3) was also reported.

We found that each patient reported, on average, 92 symptom entries. The most frequently reported symptom was mood disturbance, followed by fatigue; the most severe symptom was fatigue, while the least severe was nausea. These results are coherent with previous studies reporting fatigue among the most frequent[10,14,31,32] and distressing[32] symptoms, and a systematic review highlighting depression as reaching 77% prevalence among cancer patients.[31] In our results, contrarily to most of previous studies, mood disturbances clearly stood out, and this may highlight the necessity to further address this symptom in the clinics and in future research.

We also found that patients could be clustered in two groups based on the severity of their symptoms. Indeed, patients reported either consistently high or consistently low symptom severity. To the best of our knowledge, this is the first study clustering young adults with cancer based on their symptom severity. Indeed, a few previous studies clustered symptoms based on their co-occurrence (eg, gastrointestinal cluster of symptoms including nausea, eating, and appetite problems).[7,14] However, our approach (ie, clustering patients based on their symptoms) enabled understanding how the same symptoms burden patients differently. Thus, this could support clinicians and researcher to identify and implement tailor symptom management strategies. In our sample, we did not observe significant differences regarding patients' age, gender, or diagnosis between the two clusters. A few previous studies reported higher physical and psychological symptoms in females compared to males.[33,34] However, such studies included older patients, and research exploring gender differences in symptom clusters among young adults is still scarce. Thus, further research would be beneficial to better understand which characteristics predict the levels of symptom burden in young cancer patients.

We also identified association rules explaining the co-occurrence of severe symptoms. We observed that severe appetite disturbances were often reported together with severe lack of energy and nausea, coherently with much scientific evidence.[35,36] We also found that severe lack of energy, both when experienced alone and in combination with severe mood disturbance, was often reported together with severe fatigue. This further support existing evidence showing that fatigue is a comprehensive phenomenon, often resulting from a combination of physical and emotional distress.[37,38] This result could also suggest that fatigue may not always be related to sleep,[38,39] meaning that one can sleep very well but still experience fatigue as noted by previous studies,[37] and this may be the reason why we did not observe a co-occurrence of severe fatigue and severe sleep disturbances. From the analysis of the relationships between symptoms and activities, we found that higher mood disturbance was significantly associated with lower probability of engaging in physical and social activities. Consistent with previous evidence,[40] this suggests that mood plays a crucial role in decision-making process; therefore, it should be given particular attention to prevent further complications. However, such a finding could also suggest that both physical and social activities have a positive effect on the patient's mood. In this case, considering that our results showed that mood was the most frequent symptom, this result may indicate that prompting patients to engage in physical and social activities may be particularly beneficial to reduce the high prevalence of this symptom. Furthermore, the positive effect of physical activity on mood was already reported by some previous studies.[41,42] However, the association between social activity and mood has been underinvestigated. Thus, this study provides new insight on the potential relevance of social, not only physical, activities on patients' mood.

TABLE 1
Mixed Effects Logistic Regression Model Predicting Physical and Social Activity Based on Symptom Severity.

	Physical Activity					Social Activity				
Independent variable (fixed effects)	B	SE	Z value	*P*	Odds Ratio	B	SE	Z value	*P*	Odds Ratio
Appetite	.010	.096	0.103	.918	1.010	.002	.092	0.023	.982	1.002
Energy	.149	.094	−1.584	.113	0.861	.064	.096	0.668	.504	1.066
Fatigue	.053	.088	0.601	.548	1.055	−.019	.091	−0.207	.836	0.981
Mood	−.436	.090	−4.835	<**.001*****	0.647	−.398	.087	−4.599	<**.001*****	0.672
Nausea	−.046	.083	−0.551	.582	0.955	−.012	.082	−0.151	.880	0.988
Pain	.059	.077	0.774	.439	1.061	−.016	.074	−0.216	.829	0.984
Sleep	.019	.079	0.243	.808	1.019	.062	.077	0.800	.424	1.064
			AIC = 1661.1					AIC = 1693.4		
			BIC = 1710.4					BIC = 1742.7		
			logLik = −821.6					logLik = −837.7		
			Deviance = 1643.1					Deviance = 1675.4		
			Df resid = 1760					Df resid = 1760		

Note. N = 1,769 (patient/day combinations). Patient ID was included as random effect. Significant *P*-values are reported in bold. *** *P* = .001, ** *P* = .01, * *P* = .05.

The results from the pilot testing of the Kræftværket app showed that patients who used the app for 6 weeks reported an increased quality of life.[19] The present study adds meaning to those results by suggesting that tracking symptoms may have allowed patients to increase their symptom awareness, which, in turn, may have led to a more accurate estimation of the burden the symptoms were causing (instead of underestimating or overestimating them). Ultimately, as emerged in our previous qualitative study,[43] this may have facilitated the adoption of symptom communication and symptom management strategies. All this may be seen as contributing to improved quality of life in the app users. Therefore, this study further highlights the necessity to implement symptoms monitoring strategies, such as a symptom-tracking app, also considering the impact of both physical and psychological symptoms on quality of life.[44,45]

Strengths and Limitations

To the best of our knowledge, this is the first study implementing a mobile app to comprehensively track symptoms in young adults with cancer. Indeed, despite a few other studies that implemented an app to collect symptoms information, the one we implemented in this study allowed to keep track and monitor a broad range of physical and psychological symptoms, while a previous study tracked only one specific symptom.[46] Moreover, the app we implemented in this study allowed patients to autonomously report symptoms anytime they wanted over a long period of time, while a previous study only measured symptoms experienced in the previous 24 hours, at one timepoint, and under the guidance of a researcher.[14] Finally, this study provided a comprehensive description of a broad range of symptoms patterns in young adults with cancer, allowing a thorough understanding of the symptom experience in this population. Prospectively, this symptoms-tracking app can be further adopted on bigger samples to keep track of symptom patterns in this population and obtain even more solid evidence.

This study also has limitations. First, the app could have allowed us to report symptoms together with the activities they were interfering with. This would have facilitated a deeper understanding of the impact of specific symptoms on daily life. Future studies may consider linking these two features. Second, allowing patients to register how many symptoms and activities they wanted at any time point facilitates richness of data but also makes results more complex to analyze. Third, it was difficult for us to explore tendencies over time because only few patients consistently used the app for a period longer than 14 days. In future studies, it would be important to inform the patients on the relevance of tracking symptoms and nudge them to use the app regularly, as this would allow a deeper understanding of symptoms patterns over time.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Helle Pappot reports financial support was provided by TrygFonden.

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Supplementary materials

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