Symptom clusters in cancer patients: An Italian survey to validate and describe unwarranted clinical variation, inequality in access to healthcare, knowledge, and risk of malpractice

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Abstract. *Background and aims:* The perceptions of professionals involved in cancer care regarding the importance of their symptoms-specific knowledge, unwarranted clinical variation (UCV), and inequalities in access to healthcare are still underdescribed. This study aims to confirm the construct validity of a previously initially developed questionnaire and describe nurses' perceptions about the relevance of their knowledge referred to cancer symptoms management, the UCV, the inequalities in access to healthcare, and malpractice risk. *Method:* A cross-sectional pan-national study was conducted using a convenience sample, collecting data through a previously initially validated questionnaire. Construct validity was corroborated through confirmatory factor analysis, and descriptive statistics were employed for summarizing the questionnaire's scores. The scores between the nurses working in accredited cancer centers and nurses employed in general hospitals were inferentially compared. *Results:* The sample comprised 810 nurses, 480 were nurses working in accredited cancer centers, and 330 were nurses working in general hospitals. The questionnaire showed adequate construct validity and reliability. Nurses perceived the cluster of psychosocial symptoms with a greater risk of UCV and inequalities in access to cancer services than the cluster of physical symptoms. *Discussion and conclusions:* A paradigm shift aimed at integrating psychosocial cancer symptoms in the care paths emerged as pivotal for improving cancer care in Italy.

Key words: care, cancer symptoms, inequities, oncology nursing, survey, symptoms science management

Introduction

Symptom science is a preeminent focus in research, considering the field of cancer symptoms management (1). The extremely high genetic diversity in cancer profiles, which results in different symptoms' presentation and treatment response, strengthens the need for multidimensional and targeted approaches (2). Consequently, multiple symptoms are highly prevalent in patients with cancer, and great emphasis has been placed on enhancing research related to symptom science (1). In addition, the incidence of cancer is increasing globally, with 18.1 million new cases in 2018, and the 5-year relative survival rate is about 67% (3). As the survival rate is increased, side effects and cancer symptoms are more commonly seen in cancer survivors. Worse clinical outcomes are highly prevalent among patients with underrecognized and undertreated symptoms (4).

As some of the cancer symptoms co-occur, increasing evidence suggests a cluster approach in the management of the symptoms performed by several professionals involved in cancer care (1). Recognizing a relationship among symptoms within a cluster could have significant consequences in management strategies (5,6). Recently, although the pain, fatigue, and sleep disturbances have been identified as the most prevalent symptoms among cancer patients (5,7–9), physical and psychosocial clusterings of these symptoms were recently described (10). Identifying symptom clusters is an important step to creating population clusters for developing evidence-based interventions to manage the symptoms (1,11).

In practice, symptoms management could be associated with the unwarranted clinical variation (UCV) and/or inequalities in accessing care services (12). UCV is recently defined as the "variation that cannot be explained by the condition or the preference of the patient; it is the variation that can only be explained by differences in health system performance" (12). UCV is often associated with the higher inequality in access to healthcare (13), as UCV could lead to amplify social inequalities, which are not only related to diverse income levels, but also geography, age, and employment status (13). Overall, UCV has become evident in survival rate differences between countries (14). Even where resources are limited, identifying priorities for action and research and implementing evidence-based strategies represent the most reasonable approaches to overcome such complexity and guarantee high-quality care standards (14–16).

However, whereas clinical practice guidelines represent one potential solution to UCV, the implementation of evidence-based practice still faces resistance, considering both unintentional and intentional non-adherence to the best practices (12). In symptom management, it is fundamental to define research priorities for closing the gaps between the daily clinical activity and best practice, tackling the challenges of UCV and/or inequalities in delivering care. In this regard, the Italian Association of Cancer Nurses (AIIAO) has recently developed a questionnaire, which showed initial evidence of validity and reliability, to investigate the nurses' perception about their symptoms-specific knowledge, the UCV, and the inequalities in access

to healthcare (10). The preliminary results derived from the pan-national investigation of AIIAO in Italy during the first months of 2019 showed that fatigue, impairments of social function, and psychological disorders were the areas in which nurses perceived greater UCV and inequalities in access to healthcare (10).

Thus far, the final testing of psychometric properties of the developed questionnaire, as well as the final descriptive results derived from the pan-national investigation of AIIAO, could be strategic for better describing how nurses perceive their knowledge in the field of symptoms management, UCV, and the inequalities in access to healthcare (10). Having these descriptions could also enhance cross-national research, allowing comparisons between different national contexts and driving specific policy actions at a national level.

Aims

This study had two aims: to corroborate the construct validity and reliability of the questionnaire previously initially validated (10): to describe nurses' perception about the relevance of their symptoms-specific knowledge, the perceived UCV, the perceived inequalities in access to healthcare, and the risk of malpractice arising from the specific risks of UCV and inequalities in access to cancer services.

Methods

Study Design, participants, and procedure

We conducted a cross-sectional Internet-based survey in Italy between September 2019 and March 2020. This survey was the second round of data collection, performed following the first pilot testing of the adopted questionnaire, which was published elsewhere (10). Participant inclusion criteria included nurses coming from different geographical areas of Italy, with at least six months of working experience. Nurses were enrolled using the mailing list of the AIIAO (972 contacts). A total of 810 nurses agreed to participate in the survey (response rate = 83.3%). The invitation

to the study was sent via email, outlining the aim and inclusion criteria of the study and the estimated time for completing the survey (roughly 20 minutes). The study's procedure was approved by the Institutional Review Board of the AIIAO (protocol n° 03/2019).

Measurements

Demographic and professional data

Demographics included sex, age, and geographical provenience. In addition, nurses self-reported information about their professional background, educational level, cancer-specific education, clinical setting, and years of working experience. Considering that the responders to this study worked in both accredited cancer centers and general hospitals, we also collected this variable to allow specific sub-samples comparisons. In Italy, accredited cancer centers act nationally as focal points for cancer control and treatment, and general hospitals are involved as well in delivering cancer care services for the general population (17). Accordingly, comparing answers between nurses working in accredited cancer centers and nurses employed general hospitals could help identify different perceptions derived from the context, as the standards of care in the accredited cancer centers have to be strictly monitored over time, while there is heterogeneity in evaluating standards of care in general hospitals (17).

Questionnaire

A self-report online questionnaire was adopted based on a previous initial validation study (10). The adopted questionnaire aimed to investigate nurses' perception of their symptoms-specific knowledge, the perceived UCV, and the perceived inequalities in access to healthcare. More precisely, the first part of the questionnaire collected socio-demographic and professional characteristics of the responders. The second part consisted of 14 groups of symptoms, which were fatigue, pain, sleep disorders, immune system disorders, cardiovascular alterations, gastrointestinal and oral cavity alterations, central and peripheral nervous

system alterations, metabolic and endocrine alterations, tegumentary system alterations, hematopoietic alterations, coagulation disorders, electrolyte alterations, social functioning alterations, and psychosocial disorders.

For each group of symptoms, nurses had to answer five questions for exploring (1) how they perceive relevant for practice their symptoms-specific knowledge (5-point Likert scale), (2) the perceived risk of UCV (3-point Likert scale), (3) the perceived UCV (5-point Likert scale), (4) the perceived risk of inequalities in access to healthcare (3-point Likert scale), (5) the perceived inequalities in access to healthcare (5-point Likert scale). The previous initial validation suggested that the questionnaire could be scored by (1) the total risk of UCV & inequalities in access to healthcare (with two specific sub-scores for UCV and inequalities), (2) the total UCV, (3) the total inequalities in access to healthcare, and (4) the perception of their knowledge as pivotal for daily practice (10). Furthermore, each score encompassed sub-dimensions for two main symptom clusters, which were psychosocial and physical symptoms.

The cluster of physical symptoms included the interactions of pain, immune system disorders, cardiovascular alterations, gastrointestinal and oral cavity alterations, central and peripheral nervous system alterations, metabolic and endocrine alterations, hematopoietic alterations, coagulation disorders, and electrolytes alterations on the individual's physical functioning. Likely, the cluster of psychosocial symptoms included the interactions of fatigue, sleep disorders, tegumentary system alterations, social functioning, and psychosocial disorders on the individual's social and psychological functioning. Overall, the proposed scoring from the previous research has not yet been supported by a confirmation of the psychometric structure of the questionnaire (10).

Statistical analysis

Descriptive statistics were employed to summarize the enrolled nurses' demographics and their answers to the questionnaire (frequency, percentage, mean, standard deviation [SD]). The normality

of quantitative data was assessed through the visual inspection of quantile-quantile plots (Q-Q plots), followed by the Shapiro-Wilk test. Missing data were assessed at the variable and item level and were deleted pairwise. We used a higher-order confirmatory factor analysis (CFA) approach within the structural equation modeling framework to test the structural validity, hypothesizing the factor structure derived from the initial validation of the questionnaire, as described in the paragraph about measurements (questionnaire). Factor loadings >|.30| were considered as adequate. Given that items were not always normally distributed, we adopted the robust generalized least squares approach for estimating the model parameters. Model fit was assessed using χ^2 statistics, comparative fit index (CFI), Tucker and Lewis index (TLI), root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR). Overall, the criteria for considering adequate goodness of fit were: CFI and TLI values of .90–.95 indicate good fit; RMSEA values ≤ .08 indicate adequate fit; values of SRMR ≤ .08 indicate good fit as well. The reliability was estimated with Cronbach's α coefficient for each domain. The scores for each domain were standardized to 0-100 for allowing a more straightforward interpretation of the scores with different metrics (e.g., 5-point Likert measures and 3-point Likert measures). The questionnaire scores were also compared between nurses employed in accredited cancer centers and nurses employed in general hospitals. The level of significance was set at $p < 0.05$. All statistical analyses were perform using IBM Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) version 22 and Mplus version 8.1 (Muthen & Muthen, 1998–2017).

Results

Socio-demographic and professional characteristics

The sample comprised 810 nurses, 480 were nurses working in accredited cancer centers (within the cancer network), and 330 were nurses working in general hospitals (outside the cancer network). They were mainly females (n = 564; 69.6%) with a mean age

of 40.9 (SD = 9.8). Overall, the enrolled nurses had no cancer-specific training (n = 738; 91.1%), and most of them had a post-graduate education. The majority of the nurses were working in a medical ward (n = 252; 31.1%), reporting to have 16.39 years (SD=10.68) as the mean of working experience. **Table 1** shows the socio-demographic characteristics of the sample and the comparisons of socio-demographic and professional characteristics between nurses working in accredited cancer centers and nurses working in general hospitals. Overall, nurses employed in general hospitals showed higher rates of post-graduate education (p <0.001), higher rates of nurses involved in research and education (p<0.001), and slightly higher mean age (p <0.001).

Construct validity and reliability

The questionnaire, previously initially validated in the Italian context, was tested for confirming its dimensionality, with the hypothesis of four higher-order dimensions (factors) for the two symptoms clusters (physical and psychosocial symptoms): The UCV, the importance of specific knowledge for symptoms management, the inequalities in access to healthcare, and the general risk of malpractice (given by both risks for inequalities and UCV). The CFA model showed a good fit to data: $\chi^2_{(2329)}$ = 10509.25, p < 0.001; χ^2/df=4.5; RMSEA = 0.066, 90% CI (0.065–0.067); CFI = 0.909; TLI = 0.906; SRMR = 0.043. **Figure 1** depicts the model structure and factor loadings. Overall, all the items were well retained by their latent factors.

As **Table 2** shows, the internal consistency (reliability) was adequate for each domain (all Cronbach's α were higher than 0.800).

Descriptive results and comparisons between scores of nurses working in accredited cancer centers and nurses employed in general hospitals

The standardized scores related to the perceived importance of symptoms-specific knowledge of symptoms management reported a mean of 83.03/100 (SD=11.60) for the cluster of psychosocial symptoms
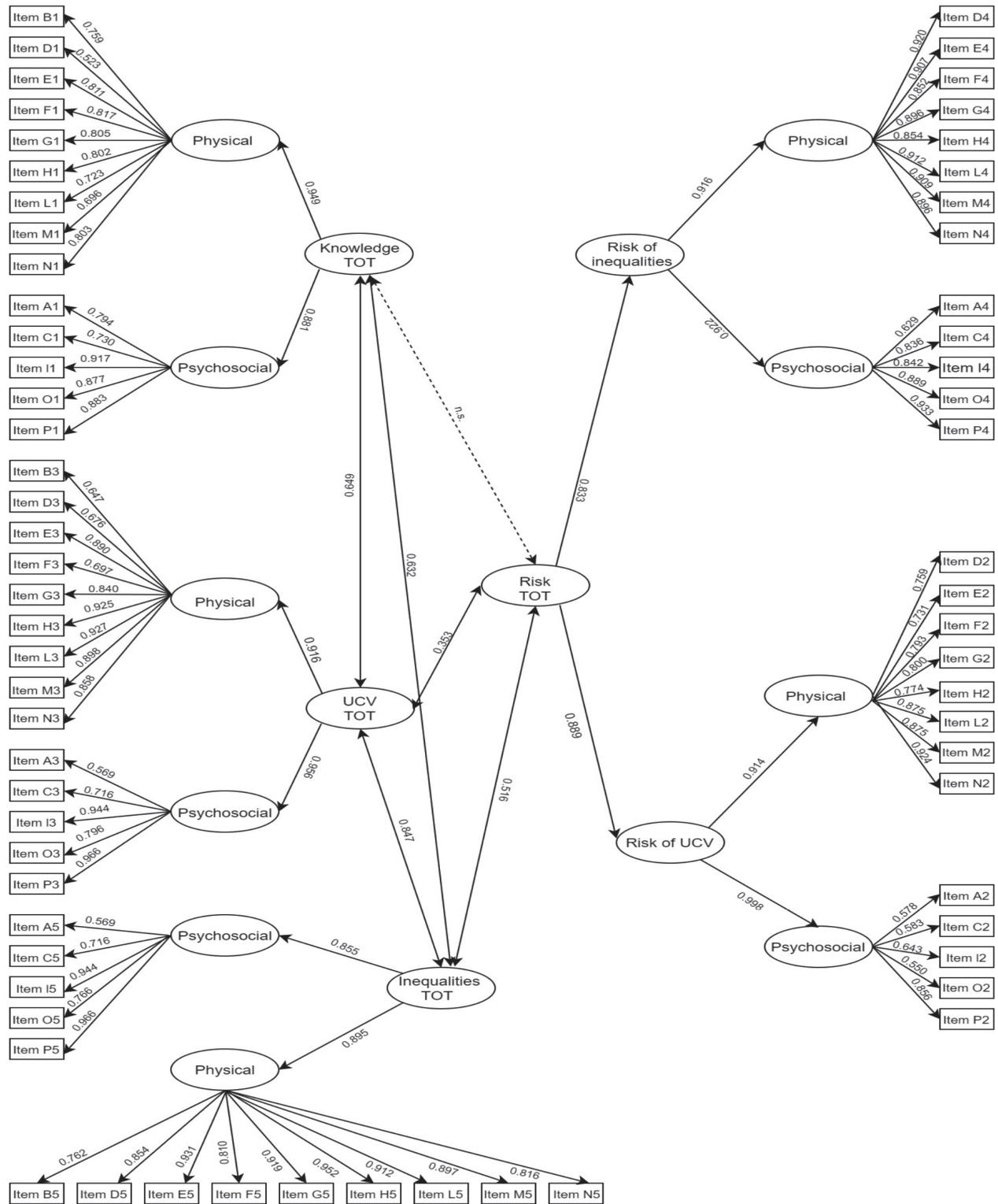
Model fit:
$(\chi^2_{(2329)}=10509.251, P<0.001; \chi^2/df=4.5; RMSEA=0.066, 90\%CI[0.065-0.067]; CFI=0.909; TLI=0.906)$.

Figure 1. Dimensionality of the questionnaire.

Table 1. Socio-demographic characteristics of the sample

	Overall (*n*=810)		Nurses working in accredited cancer centers (*n*=480)		Nurses working in general hospitals (*n*=330)		*p*
	n	%	*n*	%	*n*	%	
Sex							
Male	246	30.4	144	30	102	30.9	0.780
Female	564	69.6	336	70	228	69.1	
Educational level							
Bachelor degree	156	19.3	96	20	60	18.2	
Post-graduate course	396	48.9	264	55	132	40	0.001
Master's degree	156	19.3	84	17.5	72	21.8	
PhD	42	5.2			42	12.7	
Second Bachelor degree	60	7.4	36	7.5	24	7.3	
Specific education							
Cancer education (yes)	72	8.9	48	10	24	7.3	0.181
Clinical context							
Medicine	252	31.1	156	32.5	96	29.1	
Surgery	174	21.5	108	22.5	66	20	
ICU	120	14.8	96	20	24	7.3	<0.001
Home care	48	5.9	36	7.5	12	3.6	
Outpatient	78	9.6	36	7.5	42	12.7	
Research-Education-Management	138	170.	48	10	90	27.3	
Geographical area							
North	270	33.3	162	33.8	108	32.7	
Central	261	32.2	156	32.5	105	31.8	0.880
South	279	34.4	162	33.8	117	35.5	
Age							
Years (mean; SD)	40.9	9.82	38.98	10.47	41.71	8.56	<0.001
Job experience							
Years (mean; SD)	16.39	10.68	16.18	10.86	16.69	10.43	0.500

and a mean of 79.20/100 (SD=16.21) for the cluster of physical symptoms. The higher mean scores were obtained among nurses working in general hospitals (all *p* < 0.001).

The standardized scores of the perceived risk of malpractice (UCV and inequalities in access to healthcare) reported a moderately high mean score (mean = 68/100; SD = 26.93). More precisely, the perceived risk of UCV was higher for psychosocial symptoms (mean = 79.85/100; SD = 25.74) than the physical symptoms (mean = 66.39/100; SD = 35.43) without significant

differences between nurses working in general hospitals and nurses working in accredited cancer centers. Likely, the perceived risk of inequalities in access to healthcare reported a higher mean score for psychosocial symptoms (mean = 73.40/100; SD = 31.32) compared to the mean score for physical symptoms (mean = 55.74/100; SD = 31.32) without significant differences between nurses working in general hospitals and nurses working in accredited cancer centers.

The mean of the UCV total standardized score was equal to 67.04/100 (SD=14.12), and it was

Table 2. Nurses' perception of cancer symptoms cluster management in practice

	Cronbach's α	Overall (*n*=810)		Nurses working in accredited cancer centers (*n*=480)		Nurses working in general hospitals (*n*=330)		*p*
		Mean	SD	Mean	SD	Mean	SD	
Importance of specific knowledge of symptoms management								
Cluster of physical symptoms	0.916	79.20	16.21	77.40	15.62	82.01	16.60	<0.001
Cluster of psychosocial symptoms	0.881	83.03	11.60	81.80	10.60	84.56	12.85	0.010
Total Score	0.891	81.65	12.45	80.20	11.41	83.90	13.38	<0.001
Risk of UCV & inequalities in access to healthcare								
Risk of UCV (Cluster of physical symptoms)	0.823	66.39	35.43	66.88	35.34	65.68	35.59	0.638
Risk of UCV (Cluster of psychosocial symptoms)	0.851	79.85	25.74	80.50	27.77	78.91	22.41	0.387
Risk of UCV (Total)	0.882	73.12	27.42	73.69	27.65	72.30	26.95	0.710
Risk of inequalities in access to healthcare (Cluster of physical symptoms)	0.867	55.74	31.71	55.0	32.12	56.82	31.11	0.423
Risk of inequalities in access to healthcare (Cluster of psychosocial symptoms)	0.916	73.40	31.32	73.50	31.46	72.36	31.15	0.612
Risk of inequalities in access to healthcare (Total)	0.828	64.39	28.74	64.25	28.57	64.59	29.40	0.868
Total Risk Score of malpractice	0.861	68.75	26.93	68.97	27.17	68.44	26.61	0.785
Unwarranted clinical variation (UCV)								
Cluster of physical symptoms	0.911	71.60	14.10	72.40	14.80	70.65	12.65	0.890
Cluster of psychosocial symptoms	0.915	69.40	15.61	68.20	17.45	71.50	12.20	0.088
Total Score	0.902	67.04	14.12	65.17	15.24	68.31	12.22	0.039
Inequalities in access to healthcare								
Cluster of physical symptoms	0.844	64.58	16.53	63.09	18.23	66.75	13.41	0.003
Cluster of psychosocial symptoms	0.888	69.35	15.15	69.20	16.52	69.56	13.01	0.756
Total Score	0.897	66.65	14.02	65.64	15.15	68.12	12.06	0.016

significantly higher (*p* = 0.039) among nurses working in general hospitals (mean = 68.44/100; SD = 26.61) than nurses working in accredited cancer centres (mean = 65.17/100; SD = 15.24). The UCV sub-score for the cluster of physical symptoms was equal to 71.60/100 (SD = 14.10), and the one for psychosocial symptoms was equal to 69.40/100 (SD = 15.61). Both UCV sub-scores did not differ between nurses working in general hospitals and nurses working in accredited cancer centers.

The mean score of inequalities in access to healthcare was equal to 66.65/100 (SD=14.02), and it was significantly higher (*p* = 0.016) among nurses working in general hospitals (mean = 68.12/100; SD = 12.06) than nurses working in accredited cancer centers (mean = 65.64/100; SD = 16.53). The mean related to the sub-score of inequalities in access to healthcare for the cluster of physical symptoms was equal to 64.58/100 (SD = 16.53), with a higher mean score among nurses working in general hospitals (*p* = 0.003). The mean related to the sub-score of inequalities in

access to healthcare for psychosocial symptoms was equal to 69.35/100 (SD = 15.15), without significant differences between nurses working in general hospitals and nurses working in accredited cancer centers (p = 0.756).

Discussion

This study provided the first Italian pan-national description of UCV, inequality in access to healthcare, perceived importance of symptom-specific knowledge, and risk of malpractice by considering the perspective of nurses working in accredited cancer centers and general hospitals. It also provided evidence of validity and reliability for the adopted questionnaire for the investigation. Each investigated domain was designed to be specific for the clusters of physical and psychosocial symptoms. The involved nurses reported a higher perception of the importance of symptoms-specific knowledge for the cluster of psychosocial symptoms. Overall, they also perceived the cluster of psychosocial symptoms with a greater risk of UCV and inequalities in access to healthcare than the cluster of physical symptoms. Conversely, the cluster of physical symptoms was reported to have higher UCV in practice.

Given the standardized scores of the descriptive results, responders generally perceived the importance of symptoms-specific knowledge as a highly impactful and relevant factor for cancer symptoms management. This trend is highly evident among nurses working in general hospitals who appear to have a higher need for symptoms-specific knowledge in managing cancer patients, particularly for the psychosocial cluster. Conversely, nurses working in accredited cancer centers seem to underrate the importance of symptoms-specific knowledge. This result could reflect the fact that nurses in accredited cancer centers are often involved in continuing medical education courses about symptoms-specific knowledge (18,19) and, accordingly, their need for further knowledge could be mitigated by the specific education that they often already have (20).

The risk of malpractice, given by both risks of UCV and inequalities in access to healthcare, could be considered an essential element for boosting reflections among decision-makers and orienting policies (21).

We found a moderately high risk of overall malpractice with higher perceived risks for UCV and inequalities in access to healthcare in managing psychosocial symptoms. In contrast, the perceived risks for UCV and inequalities in access to healthcare in managing physical symptoms were generally reported with lower scores. These results highlighted the need for investing more energy in integrating the assessment and management of the psychosocial needs of patients with cancer (22–24).

UCV standardized mean total score was reported to be higher among nurses working in general hospitals. This result can reflect the endeavors towards best practices of the accredited cancer centers (25,26). Accordingly, cancer care involves a growing number of disciplines and healthcare professionals, as intervention areas expand to embody psychosocial needs, genetics, and clinical characteristics (22). For these reasons, accredited cancer centers are committed to providing a comprehensive strategy for delivering care, combining translational cancer research with an adequate portfolio of cancer care services (26). The lower UCV standardized mean total score reported by nurses working in accredited cancer centers contributes to corroborating the accreditation paths' adequacy followed by each accredited cancer center. Overall, the literature describes that UCV could be referred to three key elements: the variation across geographical areas or providers; the criteria for assessing absolute variation against a standard of care, or relative variation within a comparator group; and proxy measures or indirect measurement to gauge UCV including adopted resources in practice and achieved outcomes (12).

The domain that investigated the inequalities in access to healthcare reported the lower standardized mean total score of the survey. This result can reflect the characteristics of the Italian national healthcare service (INHS), as the INHS is based on the principles of universalism and comprehensiveness (27). However, nurses working in general hospitals reported a significantly higher total mean score of perceived inequalities in access to healthcare than the one reported by nurses working in accredited cancer centers. This result can be explained by some critical issues related to the healthcare management of general hospitals, such as the waiting times for having access to

healthcare services (27). Overall, it seems that waiting times are the result of the imbalance between the health demands and supply of healthcare services (28). This issue in Italy seems to be more prevalent in public and general hospitals (27). Furthermore, the increasing healthcare needs, the aging of the Italian population, and the technological developments are acting as contributing factors to the increased demand for healthcare services, increasing the public and professionals' perception of inequalities in access to healthcare (29). The increasing Italian population healthcare demands could trigger the imbalance between demands and supply, especially for the general hospitals (27); for these reasons, these aspects have to be considered in planning future actions aimed at balancing demands and supply in cancer care with a particular focus in supporting the quality of general hospitals.

Overall, self-report data are a critical component of all sciences (30). For this reason, the validity of self-report data is an important characteristic of every research collecting data through questionnaires (31). The described dimensionality of the questionnaire adopted in this study, which showed good evidence of validity and reliability, could guide similar studies in other national settings and decrease measurement bias.

This study has some limitations. The first limit is given by the cross-sectional approach to collect data, as we have not information on the trajectory of the described domains over time. Second, the convenience sampling might limit the generalizability of results, as we reported slight heterogeneity considering the demographic and professional characteristics between nurses enrolled in accredited cancer centers and nurses working in general hospitals (e.g., age and post-graduate education). Third, the study included only nurses; future research with broader inclusion of healthcare providers (e.g., oncologists, surgeons, psychologists) is needed to deeply investigate the unwarranted clinical variation, inequality in healthcare access, perceived importance of symptoms-specific knowledge, and risk of malpractice. However, the current limitations are consistent with the nature of the study, and they are balanced by adequate strengths, such as the large sample size and the homogeneity of the responders' geographical distribution for achieving a pan-national coverage of responses.

Conclusions

The adopted questionnaire for the investigation showed a four-higher-factor solution that supports its scoring. The Italian nurses' perception of managing physical and psychosocial symptoms about UCV, inequality in access to healthcare, perceived importance of symptom-specific knowledge, and risk of malpractice could be used as a guide for policy actions aimed at improving cancer care standards. Accordingly, general hospitals appear to be more susceptible to UCV and inequalities in access to care than accredited cancer centers. Given that the perceived risk of malpractice (in terms of specific risks of UCV and inequalities in access to cancer services) was higher for psychosocial needs, especially in general hospitals, an accurate paradigm shift aimed at integrating cancer's psychosocial symptoms in the care paths is required.

Nurses perceived their symptoms-specific knowledge as the most impactful factor for delivering high-quality cancer symptoms management. This characteristic is highly evident among nurses employed in general hospitals who appear to have a higher need for specific knowledge in the management of cancer patients. For this reason, we recommend higher support from scientific societies and institutions to facilitate continuing medical education courses about symptom-specific knowledge among nurses delivering cancer care in general hospitals. Future research, including the perspective of the other healthcare providers involved in caring for patients with cancer, is required to deepen the description of unwarranted clinical variation, inequality in access to healthcare, perceived importance of symptoms-specific knowledge, and risk of malpractice.

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