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Original research

The development of an archive of patient-reported outcome measures (PROMs) in oncology: The Italian PRO4All project

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ABSTRACT

Background: Choosing the most adequate measure of patient-reported outcomes (PROs) for a specific medical condition is not straightforward. This study aimed to develop a comprehensive archive of patient-reported outcome measures (PROMs), observer-reported outcome measures (ObsROMs) and caregiver-reported outcome measures (CROMs) in oncology and identify their main characteristics and target outcome domains.
Materials and methods: As part of the Italian PRO4All Project, we retrieved questionnaires through an extensive search of online databases. We developed a data extraction form to collect information on cancer type, questionnaire variant(s), recall period, and scoring system. We performed a content analysis of the questionnaires to assign each item a specific outcome domain according to a predefined 38-item taxonomy.
Results: A total of 386 PROMs (n = 356), ObsROMs (n = 13) and CROMs (n = 17) were identified and described; of these, 358 were also analyzed in their content. 47.3 % of the instruments were cancer type-specific, 45.1 % were generic for cancer and 7.9 % were developed for the general population but also recommended in oncology. The great majority (92.2 %) were patient-reported. In 50.3 % the recall period was "last week". The mean number of items per questionnaire was 22.0 (range: 1–130). 7794 items were assigned an outcome domain, the most frequent being emotional functioning/wellbeing (22 %), physical functioning (15.7 %), general outcomes (10.1 %) and delivery of care (8.9 %).
Conclusions: There are a variety of patient and caregiver-reported measures in oncology. This archive can guide researchers and practitioners in selecting the most suitable measures and fostering a patient-centered approach in clinical trials, clinical practice, and regulatory activities.

1. Introduction

Beyond objective data provided by healthcare professionals and organizations (e.g., laboratory results, medical images), high-quality clinical care is also rooted in processing direct feedback from patients regarding their feelings, symptoms, and any side effects of prescribed treatments. In this regard, patient-reported outcomes (PROs) are a type of Clinical Outcome Assessment (COA) that allows to describe, monitor, and reflect, in a standardized way, how a patient feels, functions, or generally lives. The FDA defined a PRO as "a measure of a patient's health status as reported directly from the patient without added interpretation by a healthcare worker or anyone else". PRO is an

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"umbrella" term that can refer to the patient's overall health status, symptomatology, multidimensional health-related quality-of-life (HRQoL), functional status (physical, emotional, social, etc.) and side effects, in relation to a disease or treatment, or to the patient's experience with healthcare (e.g., adherence, acceptability, satisfaction). They can be measured either in absolute terms, like a "pain severity rating", or in relative terms, like "pain improvement after receiving a treatment" [1]. The observer-reported outcome (ObsRO) is another type of COA defined as "a report of observable signs, events or behaviors related to a patient's health condition, without any medical judgement or interpretation, by someone other than the patient (i.e., parent, spouse, caregiver) who observes the patient in daily life", and particularly useful for patients who cannot report for themselves, such as infants or cognitively impaired [2]. PROs (and ObsROs) are measured through instruments called patient-reported outcome measures, PROMs (and observer-reported outcome measures, ObsROMs), usually in the form of self-administered questionnaires. PROMs can be either specific, i.e., tailored to symptoms and health issues of a given disease, health condition, or treatment, or generic, i.e., applicable to heterogeneous conditions and covering broader aspects like pain, HRQoL, physical abilities, emotional and mental well-being, and social interactions [3].

In oncology, both disease and treatment have often a severe negative impact on patients and family's wellbeing. In 2019, the percentage of disability-adjusted life years (DALYs) - a time-based measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health - due to cancer disease within the EU was estimated at almost 20 % [4]. In clinical trials, PROs typically supplement (as secondary or exploratory endpoints) primary outcomes such as survival rates or treatment response, offering a more comprehensive and holistic understanding of treatment benefits and harms [5]. For instance, despite trial evidence of few additional months of progression-free survival, measuring PROs might reveal that patients do not adhere to the drug regimen due to reported side effects, complex dosing, or reduced HRQoL. Informal caregivers are key family members or friends who provide daily life support throughout the disease trajectory, including managing patients' symptoms and adverse effects, helping patients cope with emotional distress, and coordinating with healthcare professionals. As new treatments extend survival and cancer often becomes a chronic condition, the so called 'caregiver burden' including physical, emotional, social, and financial distress tends to increase [6,7]. Caregiver-reported outcome measures (CROMs) are ad hoc instruments allowing for a caregiver's assessment of the impact of caring tasks on their health or personal life, and of their experience in interacting with healthcare providers because of caring for a loved one with cancer.

Although many verified instruments have recently emerged in the literature, selecting the most suitable PROM (and, when appropriate, ObsROM and CROM) for use in clinical practice, clinical research and patient-centered evaluations in oncology may be an intricate task. This choice involves addressing methodological aspects like validity, sensitivity, reliability, generalizability, translation, interpretability and feasibility [8].

This study aimed to create a comprehensive archive of PROMs, ObsROMs, and CROMs developed and used in oncology and outline their main characteristics, content, modes of administration and interpretation in relation to different cancer types, to serve as a useful reference point for various stakeholders (physicians, researchers, regulators, patients) interested in the use of such instruments for clinical research and practice.

2. Materials and methods

This study is part of the PRO4All project, a multistakeholder initiative intended to generate awareness and knowledge around the potential and use of PROs in healthcare. We aimed to retrieve PROMs, ObsROMs and CROMs in oncology by searching various sources, starting from the European Organisation for Research and Treatment of Cancer (EORTC) [9], and the Functional Assessment of Chronic Illness Therapy (FACIT) group [10]. Additionally, we manually searched the ePROVIDE database [11] using as keywords 'tumor,' 'cancer,' and 'neoplasm.' For each measure identified, we analyzed the 'Basic Description' scheme and selected those reporting 'Neoplasms' among the 'Population of development/Disease(s)' section and 'PRO' or 'Composite COA' including PRO in the 'Type of Clinical Outcome Assessment (COA)' section. Additionally, we searched PubMed by using as keywords "patient--reported outcome", "patient-reported outcome measures", "caregiver-reported outcome measures", "cancer", "oncology", "review" to retrieve any undetected instruments in the published literature [Appendix A]. The instruments identified were categorized as PROMs when used (or recommended) for cancer patients in either research or clinical practice, as ObsROMs when intended to assess the patient's health status but reported by someone other than the patient (e.g., a parent) and as CROMs when assessing self-reported caregiver's health status or caregiving situation. The questionnaire selection and classification were done by one reviewer (FM) and double-checked by other two (MM and OC), with any disagreement solved by consensus.

To perform a content analysis [12], we extracted individual items from either the questionnaire full-text (when freely available) or related publications or websites. We developed a data extraction form to collect information on each instrument including the cancer type based on the International Classification of Diseases, ICD-10 [13]. Moreover, we conducted searches via Google Scholar, PubMed, and Scopus to identify published articles reporting a validation process, psychometric evaluation or Minimal Clinically Important Difference (MCID) determination for individual instruments in cancer populations, which are essential to facilitate use of PROMs and findings interpretation for decision-making. Finally, questionnaire items were extracted and assigned with a specific domain according to a predefined 38-item taxonomy [14] developed for the classification of outcomes included in clinical trials, Core Outcome Sets (COS), systematic reviews, and trial registries to identify the most targeted dimensions by specific cancer indications. The domain assignation was performed by one reviewer (MM) and double-checked by the other two (FM and OC), leveraging on the experience gained in a previous work on outcome classification in COS [15] and solving any disagreement by consensus.

3. Results

3.1. Instrument identification

The initial searches retrieved 128 and 34 questionnaires from FACIT and EORTC websites, respectively. Of these, four FACIT instruments were excluded because intended for other medical conditions.[6] From the EORTC website only questionnaires considered as validated, instead of in development, were included. To these 162 instruments, 164 additional measures were added from ePROVIDE database and 60 from the published literature [Appendix A], reaching a total of 386 instruments (Figure 1). Of these, 356, 13 and 17 were classified as patient-reported (PROMs), observer-reported (ObsROMs), and caregiver-reported (CROMs), respectively.

3.2. Instrument description

As shown in Table 1, according to the ICD10 classification, 161 (45.2 %) of the 356 PROMs were generic for cancer and 167 (46.9 %) were cancer type specific; of these last, 8 were classified as intended for

[6] (FACIT-TB: Functional Assessment of Chronic Illness Therapy – Tuberculosis; FAHI: Functional Assessment of HIV Infection; FAMS: Functional Assessment of Multiple Sclerosis; FACIT-Sp-NI: Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being - Non-Illness).

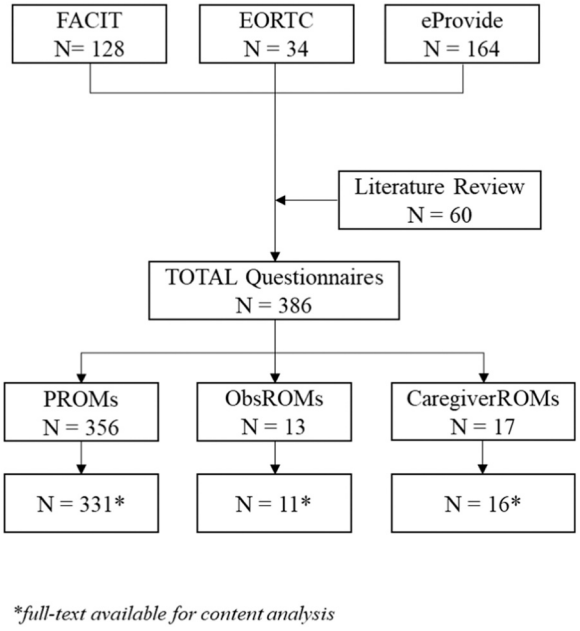

Fig. 1. Flow chart of the instruments' selection process.

pediatric cancer in the absence of a specific ICD10 code. The remaining 28 (7.9 %) were intended for the general population but also recommended or used for cancer patients based on the literature or expert opinion. Breast neoplasms (code 50) and digestive system neoplasms (codes 15–26) were the two most represented cancer types, with 31 (8.7 %) and 23 (6.5 %) questionnaires, respectively. As expected, 9 out of the 13 (69.2 %) ObsROMs were intended for pediatric cancer, whilst CROMs were more frequently intended for general cancer (52.9 %), pediatric cancer (23.5 %), or general population (17.6 %).

Out of the total 386 questionnaires, evidence on psychometrics and/or validation was found for 355 (92 %), and on MCID determination for 64 (16.6 %) only. Besides 311 original questionnaires, we identified 68 variants (e.g., short, updated, parental versions) and 7 duplicates (i.e., same items). The recall period was 'last week' in half of the cases, 'last month' in 10.1 %, 'today' in 8.5 %, and treatment-related (e.g., 'during your hospital stay', 'since your last chemotherapy cycle', 'since your last appointment') in 7.3 %. It was more often unspecified for CROMs (35.3 %), for which referring to past symptomatology is less relevant. As for the scoring system, 169 (43.8 %) questionnaires had both total and sub scores, while 139 (36.0 %) had only the total score. In addition, 4 macro-families of questionnaires were identified: FACIT (30.1 %), EORTC (9.1 %), MD Anderson (3.9 %) and PROMIS (3.1 %) (Table 2).

3.3. Content analysis

The content analysis was conducted on 7838 items extracted from 358 instruments out of the total 386 included (93 %). For FACIT questionnaires also including the general FACT-G module (45.6 %), only the specific module was considered in the content analysis. The most frequent outcome domain assigned to individual items was 'emotional functioning/wellbeing' (21.9 %), followed by 'physical functioning' (15.6 %), 'general outcomes' (e.g., fatigue, malaise, anorexia, pain) (10.0 %), and 'delivery of care' (9.4 %). The mean number of items per questionnaire was 22.0 ± 17.4 (range: 1- 130). In CROMs, 'delivery of care' was the most frequent domain (37.0 %), as caregivers play a crucial role in interacting with health service providers, followed by 'societal/carer burden' (12.4 %), representing time or financial losses due to caring for the patient (Table 3).

The bubble chart (Figure 2) illustrates the outcome domain frequency by cancer type for PROMs items only (6976). For example, items related to 'emotional functioning/wellbeing' (16.2 %) were more frequent in PROMs for breast neoplasms, while the 'respiratory outcomes' (8.1 %) domain was more represented in instruments for neoplasms of bronchus and lung.

Table 1
Total questionnaires (N = 386) by type and cancer type (ICD10 codes).

ICD10	PROM (%)	ObsROM (%)	CROM (%)	TOTAL (%)
Malignant neoplasms (C00-C97)	161 (45.2)	4 (30.8)	9 (52.9)	174 (45.1)
General population	28 (7.9)	0 (0.0)	3 (17.6)	31 (8.0)
Malignant neoplasm of breast (C50-C50)	31 (8.7)	0 (0.0)	0 (0.0)	31 (8.0)
Malignant neoplasms of digestive organs (C15-C26)	23 (6.5)	0 (0.0)	0 (0.0)	23 (6.0)
Malignant neoplasms of male genital organs (C60-C63)	20 (5.6)	0 (0.0)	1 (5.9)	21 (5.4)
Paediatric cancer	8 (2.2)	9 (69.2)	4 (23.5)	21 (5.4)
Malignant neoplasm of bronchus and lung (C34)	17 (4.8)	0 (0.0)	0 (0.0)	17 (4.4)
Malignant neoplasms of lip oral cavity and pharynx (C00-C14)	14 (3.9)	0 (0.0)	0 (0.0)	14 (3.6)
Malignant neoplasms of urinary tract (C64-C68)	12 (3.4)	0 (0.0)	0 (0.0)	12 (3.1)
Malignant neoplasms of female genital organs (C51-C58)	11 (3.1)	0 (0.0)	0 (0.0)	11 (2.8)
Malignant neoplasms of lymphoid haematopoietic and related tissue (C81-C96)	11 (3.1)	0 (0.0)	0 (0.0)	11 (2.8)
Malignant neoplasms of eye brain and other parts of central nervous system (C69-C72)	8 (2.2)	0 (0.0)	0 (0.0)	8 (2.1)
Malignant neoplasms of bone and articular cartilage (C40-C41)	5 (1.4)	0 (0.0)	0 (0.0)	5 (1.3)
Malignant neoplasm of nasal cavity and middle ear (C30)	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.5)
Malignant neoplasms of thyroid and other endocrine glands (C73-C75)	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.5)
Melanoma and other malignant neoplasms of skin (C43-C44)	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.5)
Malignant neoplasm of larynx (C32)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
Total	**356 (100.0)**	**13 (100.0)**	**17 (100.0)**	**386 (100.0)**

4. Discussion

A multidomain approach in patient benefit evaluation, covering functional status, treatment satisfaction, and HRQoL, is crucial to provide high-quality cancer care [16]. The collection of PROs can significantly improve the management of cancer patients in routine care, by informing the choice between alternative treatment options or decisions about ending treatments [17]. PROs make health care professionals more aware of symptoms, clinical presentation and disease course, thus facilitating recurrence or metastases detection and make patients more

Table 2
Questionnaires (N = 386) characteristics by type.

Validation	PROM (%)	ObsROM (%)	CROM (%)	Total (%)
Yes	326 (91.6)	13 (100.0)	16 (94.1)	355 (92.0)
No	30 (8.4)	0 (0.0)	1 (5.9)	31 (8.0)
Scoring				
Total and sub score	156 (43.8)	10 (76.9)	3 (17.6)	169 (43.8)
Only total score	129 (36.2)	2 (15.4)	8 (47.1)	139 (36.0)
Only sub score	26 (7.3)	0 (0.0)	5 (29.4)	31 (8.0)
Other	30 (8.4)	0 (0.0)	0 (0.0)	30 (7.8)
Not found	15 (4.2)	1 (7.7)	1 (5.9)	17 (4.4)
Recall period				
Last Week	186 (52.2)	7 (53.8)	1 (5.9)	194 (50.3)
Last Month	34 (9.6)	3 (23.1)	2 (11.8)	39 (10.1)
Not specified	32 (9.0)	1 (7.7)	6 (35.3)	39 (10.1)
Today	33 (9.3)	0 (0.0)	0 (0.0)	33 (8.5)
Treatment-related	25 (7.0)	0 (0.0)	3 (17.6)	28 (7.3)
Not found	23 (6.5)	2 (15.4)	2 (11.8)	27 (7.0)
Other	23 (6.5)	0 (0.0)	3 (17.6)	26 (6.7)
Type of questionnaires				
Variant	57 (16.0)	8 (61.5)	3 (17.6)	68 (17.6)
Original	292 (82.0)	5 (38.5)	14 (82.4)	311 (80.6)
Duplicate	7 (2.0)	0 (0.0)	0 (0.0)	7 (1.8)
MCID				
Yes	62 (17.4)	0 (0.0)	2 (11.8)	64 (16.6)
No	294 (82.6)	13 (100.0)	15 (88.2)	322 (83.4)
Family				
FACIT	112 (31.4)	4 (30.8)	3 (17.6)	119 (30.1)
EORTC	35 (9.8)	0 (0.0)	0 (0.0)	35 (9.1)
MD Anderson	15 (4.2)	0 (0.0)	0 (0.0)	15 (3.9)
PROMIS	12 (3.4)	0 (0.0)	0 (0.0)	12 (3.1)
No family	182 (51.2)	9 (69.2)	14 (82.4)	205 (53.1)
Total	**356 (100.0)**	**13 (100.0)**	**17 (100.0)**	**386 (100.0)**

comfortable in their communication with their care team and more apt to disease self-management, thus potentially improving survival, HRQoL and cancer treatment tolerability [18].

This study aimed at developing and making available a repository collecting measures (PROMs, ObsROMs and CROMs) developed in oncology to facilitate the choice of suitable instruments to be used in research and clinical practice. In addition, the repository may serve as a tool to assist regulatory evaluations of data collected through such instruments [19]. The PRO4All archive developed and described in this study is available online [20]. A comparable online database is the ERICA repository that compiles measures (PROMs, ObsROMs, Performance-Reported outcomes) for rare diseases [21].

By consulting a variety of sources, we could identify and characterize 386 instruments and analyze the full content of 358 (93 %) either retrieving free full-texts or extracting individual items from related publications. We might have still missed measures not included in the databases or literature covered through our searches. In addition, the assignment of outcomes across the 38 domains taxonomy could suffer from subjective judgements. The mean number of items per questionnaire (22.0, range: 1–130) was high, which could place an excessive burden on respondents that, in turn, may reduce their willingness to complete the questionnaire or hamper the completeness and quality of the collected data. Recently, a set of 19 recommendations to mitigate the PRO respondent burden in healthcare research and clinical practice have been published [22].

Previous reviews attempted to comprehensively map PROMs developed or used in oncology. Among them, one study collected all generic and specific PROMs validated in diseases with a high burden, including cancer, and highlighted the difficulties in choosing an appropriate, reliable, valid, and fit-for-purpose instrument from the variety of questionnaires developed [23]. Another study used a survey to investigate which PROMs were known by health professionals in cancer clinical practice, coming up with a list of 17. [24] In 2023, another study identified 48 PROMs in oncology considered by health care organizations in 14 countries [25].

A different stream of research has focused on specific tumors and especially on breast cancer, the most common cancer among women worldwide with 2.3 diagnoses every year [26]. Tevis et al. identified and compared ten PROMs in breast surgical oncology [27]. Turner-Bowker et al. reviewed 11 PROMs suitable in stage IV breast cancer with distant metastases (e.g., bone, lung, liver, brain), revealing that EORTC QLQ-C30 and FACT-B were the most frequently used [28]. Both studies [27,28] intended to offer a repository to facilitate the selection of suitable instruments in breast cancer. Bouazza et al. compared four PROMs (i.e., EORTC QLQ-LC13, FACT-L, LCSS, MDASI-LC) in lung cancer, concluding that the EORTC QLQ-C30 with its add-on QLQ-LC13 remains the most frequently used in research [29].

In our study we found evidence on MCID determination for only 64 (16.7 %) of the 386 instruments retrieved. The MCID of a PROM represents a threshold value of change in PROM score deemed to represent a clinically relevant improvement [30]. The availability of MCID estimates is essential to inform the interpretation of treatment effect size in terms of significant HRQoL and other PRO changes for clinical research and guideline development, contributing to the overall reliability of the collected data [31–33]. The MCID has been identified more often for the instruments commonly used in pivotal clinical trials, such those from the EORTC and FACIT library, allowing for the evaluation of the clinical

Table 3
Content analysis: items (N = 7838) categorization based on the outcome taxonomy (Dodd et al., 2018) by questionnaire type.

Domain	PROM (%)	ObsROM (%)	CROM (%)	Total (%)
28. Emotional functioning/wellbeing	1519 (21.8)	109 (24.2)	87 (21.2)	1715 (21.9)
25. Physical functioning	1098 (15.7)	103 (22.8)	25 (6.1)	1226 (15.6)
9. General outcomes	733 (10.5)	38 (8.4)	15 (3.6)	786 (10.0)
32. Delivery of care	587 (8.4)	1 (0.2)	152 (37.0)	740 (9.4)
26. Social functioning	533 (7.6)	51 (11.3)	34 (8.3)	618 (7.9)
8. Gastrointestinal outcomes	565 (8.1)	33 (7.3)	0 (0.0)	598 (7.6)
29. Cognitive functioning	339 (4.9)	26 (5.8)	9 (2.2)	374 (4.8)
17. Nervous system outcomes	203 (2.9)	12 (2.7)	0 (0.0)	215 (2.7)
15. Musculoskeletal and connective tissue outcomes	178 (2.6)	12 (2.7)	0 (0.0)	190 (2.4)
23. Skin and subcutaneous tissue outcomes	167 (2.4)	10 (2.2)	0 (0.0)	177 (2.3)
22. Respiratory, thoracic and mediastinal outcomes	143 (2.0)	8 (1.8)	0 (0.0)	151 (1.9)
19. Renal and urinary outcomes	123 (1.8)	6 (1.3)	0 (0.0)	129 (1.6)
27. Role functioning	99 (1.4)	11 (2.4)	19 (4.6)	129 (1.6)
37. Societal/carer burden	59 (0.8)	4 (0.9)	51 (12.4)	114 (1.5)
33. Personal circumstances	87 (1.2)	0 (0.0)	9 (2.2)	96 (1.2)
20. Reproductive system and breast outcomes	87 (1.2)	0 (0.0)	0 (0.0)	87 (1.1)
6. Ear and labyrinth outcomes	65 (0.9)	11 (2.4)	0 (0.0)	76 (1.0)
36. Need for intervention	70 (1.0)	1 (0.2)	5 (1.2)	76 (1.0)
Other	321 (4.6)	15 (3.3)	5 (1.2)	341 (4.4)
Total	**6976 (100.0)**	**451 (100.0)**	**411 (100.0)**	**7838 (100.0)**

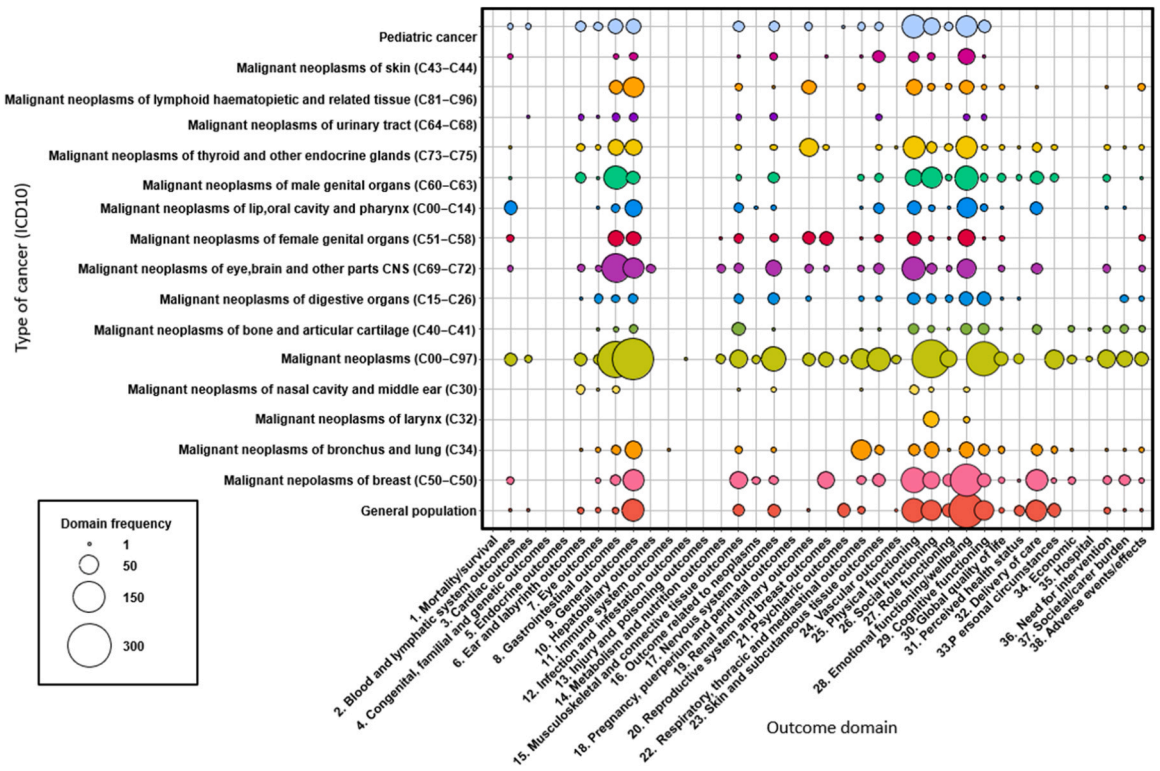

Fig. 2. Content analysis: categorization of the PROM items (N = 6976) by cancer type (ICD10) and outcome domains (Dodd et al., 2018).

relevance of the differences in PROs by regulatory agencies for drug registration purposes. The use of cancer-specific thresholds would enhance the reliability of outcomes measurement and address the variability in different cancer populations [34].

The most common recall period was "last week," adopted in 194 (50.3 %) of the instruments analyzed, in line with a previous study recommending a recall period over two weeks [35] and with a review that found more than one-third of the studies make comparisons between daily and weekly recall periods [36]. The temporal aspect further complicates the instrument selection process, as aligning the timelines of instrument administration with those of treatment schedules is crucial to ensure accurate data collection and interpretation. This issue is clearly illustrated in randomized trials that compare treatments with different schedules [37,38] or when the HRQoL assessments are conducted on day 1 of treatment cycles, after one or more weeks of recovery after each dosing period [39]. Most instruments had sub scores that allow a modular approach, defined as administering a subset of subscales out of a multi-scaled PROM when not all subscales are equally relevant for all target patient populations [40].

Besides a wide variety of disease-specific measures, we identified also measures developed for specific treatments [41], such as the Chemotherapy Convenience and Satisfaction Questionnaire (CCSQ). From a routine care perspective, using a treatment-specific rather than a more general questionnaire can provide more precise data on treatment (side) effects but requires aligning the administration to each treatment schedule. In addition, the availability of questionnaires in different languages is a key to enhance their accessibility and diffusion [42].

The in-depth investigation conducted in this study has unveiled the sheer multitude of instruments available in oncology, the existence of variants, different scoring systems and the length of questionnaires. In addition, this study shows that most measures have overlapping domains, especially for physical functioning and emotional functioning/wellbeing, as illustrated also in previous research [15].

The high number of questionnaires identified highlight the challenge of picking up the most appropriate measure and interpreting different scoring systems and measurements. In this regard, an archive such as the one generated can support the prioritization of validated instruments and those for which a MCID has been determined, with the final goal of promoting standardization in the use of high-quality measures.

5. Conclusion

The escalating complexity of the PROMs landscape in oncology calls for a systematic and comprehensive consideration of the available instruments to guide researchers and healthcare practitioners in making informed choices regarding the most suitable option for capturing the diverse needs of cancer patients. The archive described in this study can guide the selection of the most suitable instruments for patient-centered evaluations in cancer clinical research, clinical practice, and regulatory activities.

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CRediT authorship contribution statement

ORIANA CIANI: Writing – review & editing, Validation, Supervision, Methodology, Funding acquisition, Conceptualization. **Francesco De Lorenzo:** Writing – review & editing. **Carmine Pinto:** Writing – review & editing, Supervision, Methodology. **Massimo Di Maio:** Writing – review & editing, Supervision, Methodology. **Michela Meregaglia:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Data curation. **Francesco Malandrini:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation.

Declaration of Competing Interest

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ejca.2024.114161.

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