Health and Quality of Life Outcomes

REVIEW

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The current use and application of thresholds for clinical importance of the EORTC QLQ-C30, the EORTC CAT core and the EORTC QLQ-C15-PAL– a systematic scoping review

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Abstract

Background Thresholds for clinical importance (TCIs) were previously established for the cancer-specific patient reported outcome (PRO) measures EORTC QLQ-C30, EORTC QLQ CAT Core, and EORTC QLQ-C15-PAL. TCIs aim to aid the interpretation of scores for individual patients at a single point in time. They intend to indicate whether a symptom or functional health limitation is of clinical relevance, i.e., requires to be discussed with healthcare professionals. In this systematic scoping review, we aimed to describe the uptake of TCIs by the research community and discuss opportunities and threats in their application to PRO data.

Methods We systematically searched PubMed and Web of Science databases that contained search terms on the respective PRO measures and TCIs. Additionally, we performed a hand search on citations of the original TCI articles on Google Scholar. Articles were included if they applied TCIs in the analysis or the interpretation of PRO data or in clinical practice. Data concerning the study design, the use of TCIs, the terminology, and the application of TCIs were extracted.

Results A total of 512 articles were identified. After title, abstract and full-text screening, data extraction was performed on 117 of these articles. Most articles reported on longitudinal-observational ($n=55$) or cross-sectional observational ($n=49$) studies, whereby the most frequent cancer populations having mixed diagnoses ($n=25$), breast cancer ($n=23$), haematological malignancies ($n=18$), or colorectal cancer ($n=11$). Various terms were used to refer to the concept of TCIs, with "*thresholds for clinical importance*" being the most frequently used term (n = 63; 50.8%). Strikingly, 41 of the 117 articles (35.0%) reported that TCIs were applied to group-level data (e.g. mean scores), which is a clearly unintended application of the TCIs.

Conclusion TCIs are frequently used by the research community and thus enhanced the interpretability of PRO data in oncology. While most studies correctly applied TCIs in their analysis and interpretation, further guidance and clarification on their use are required. This article aims to contribute to this endeavour.

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Introduction

Assessments of health-related quality of life (HRQoL) through standardised patient-reported outcome (PRO) measures have emerged as crucial elements in clinical outcome evaluations [1–3]. These measures allow capturing the patients' perspectives in clinical cancer care [4, 5] and assessing key study endpoints in cancer clinical trials [6], thereby aiding in the determination of optimal treatment strategies. Although the validity and reliability of various PRO measures are established [7], standardised and meaningful analysis and interpretation of the assessed data still poses a relevant challenge [8]. Various efforts have been made to standardize the analysis [9] and the interpretation of PRO data [10, 11]. Approaches to aid the score interpretation of PRO data entail the publication of minimal important differences [12], general population normative values [13–15], reference values for specific cancer populations [16, 17], and thresholds for clinical importance [18–21]. While normative values allow, for example, to compare groups of patients to what would be an expected symptom state in the general population or patients with the same diagnosis [22], minimal important differences may serve to evaluate score differences/changes of individual patients or also of groups of patients. Most importantly for this manuscript, thresholds for clinical importance (TCIs), aim to enhance the interpretation of scores from individual patients at a single point in time [18, 19].

TCIs were established to improve the practicality and efficacy of PROs in daily clinical care by defining which PRO score is deemed clinically relevant (and therefore may require clinical attention). Further, they can be used for the graphical presentation (e.g. colour coding) [23, 24] of PRO scores and, therefore, may contribute to improved communication between patients and health professionals. Previously, TCIs were also used, for example, to refer patients with gynaecological cancer [25] or advanced cancers [26] to palliative care services.

In a previous project, such TCIs were developed for 14 of the 15 scales of the European Organisation of Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ-C30) [19], the computer-adaptive version of this questionnaire (EORTC CAT Core) [18], and the shortened version for use in palliative cancer patients (EORTC QLQ-C15-PAL) [20]. The EORTC QLQ-C30 [27] is one of the most widely used PRO measures in cancer clinical trials worldwide [28] and is also extensively used in daily clinical practice [5]. The definition of these TCIs relied on a binary anchor criterion summarizing whether patients or their significant others experienced "quite a bit" or "very much" limitations in daily life, worries, or need for help due to a certain symptom or functional health limitation. The selection of anchor items was based on a cross-cultural mixed-methods study, in which both qualitative interview data and quantitative importance ratings from patients and healthcare professionals were collected [29].

This systematic scoping review aimed to assess in which contexts the TCIs for the EORTC QLQ-C30 are currently utilised and whether the application in the analysis and interpretation of PRO data are consistent with their intended use (i.e., for individual patients at a single point in time).

Methods

A systematic search was conducted to identify published articles that utilised the TCIs for the EORTC QLQ-C30, the EORTC CAT Core, or the EORTC QLQ-C15-PAL. Therefore, we performed a search on the databases Medline (accessed via Pubmed.gov) and Web of Science that contained the following search terms: *"(qlq-c30 OR c30 OR qlq-c15-pal OR qlq-c15 OR c15 OR "CAT Core" OR "EORTC CAT" OR "EORTC CAT Core) and (threshold OR cut-off OR giesinger OR "clinical importance")"* the search was performed on the 15th of January 2024. Additionally, the study team performed a hand search of articles that were indexed on Google Scholar and cited the original publications of the TCIs for the EORTC QLQ-C30 [19], the EORTC CAT Core [18], or the EORTC QLQ-C15-PAL [20]. The last update of the hand search was performed on the 9th of February 2024.

Selection criteria

The inclusion criteria for the abstract screening were: any cancer entity and using the EORTC measurement system. Inclusion criteria for the full-text screening were as follows: TCIs were used (e.g. for the analysis or interpretation of the PRO results). Articles were excluded if they referred to other types of thresholds (such as minimal important differences) or if they only cited the original publications without further application of the TCIs in the analysis or interpretation of results. Two independent reviewers screened the titles/abstracts and full texts of the identified articles. In cases of conflicting inclusion/exclusion ratings, a third reviewer was consulted to help resolve the discrepancy.

Data extraction

The following information was extracted from the included articles: affiliation of the corresponding author,

patient population (diagnosis), disease stage, sample size, treatment status, treatment type, and study type. The use of TCIs was assessed by extracting whether TCIs were used for the main analysis (e.g. to dichotomize scores), in clinical routine, or merely for interpreting study results. Furthermore, additional details on the application, use, and reporting of results linked to TCIs were extracted. A detailed overview of the extraction form is provided in the Supplementary Figure S1.

Results

The initial search on the databases Web of Science and PubMed retrieved 141 and 383 publications, respectively. A hand search on Google Scholar of articles which cited the TCI publications yielded another 205 publications. After the removal of duplicates ($N = 217$) a total of 512 articles were retained in the review. In Level 1 (Title and Abstract Screening) a total of 255 articles were excluded as they did not meet the inclusion criteria (e.g. non-cancer population, no use of the EORTC measurement system, or use of other thresholds). From the 257 articles that underwent full-text screening, a total of 117 were retained for data extraction; reasons to eliminate articles from the review were the sole application of other thresholds in the analysis/interpretation of the PRO results or citation of the original TCI publications with no use in the analysis or interpretation of the PRO results. For details, see the Prisma flow chart (Fig. 1).

As of the affiliation of the corresponding authors, most publications ($n = 99$) appeared to be academic studies (Table 1). The sample size of the reviewed publications ranged from 17 to 27,857 study participants (median = 257; IQR = 871). Most identified studies were cross-sectional observational ($n = 49$) or longitudinal observational ($n = 55$) studies. Ten publications originated from randomised controlled trials, and two publications were trial protocols published in peer-reviewed academic journals (Fig. 2). Most study populations were

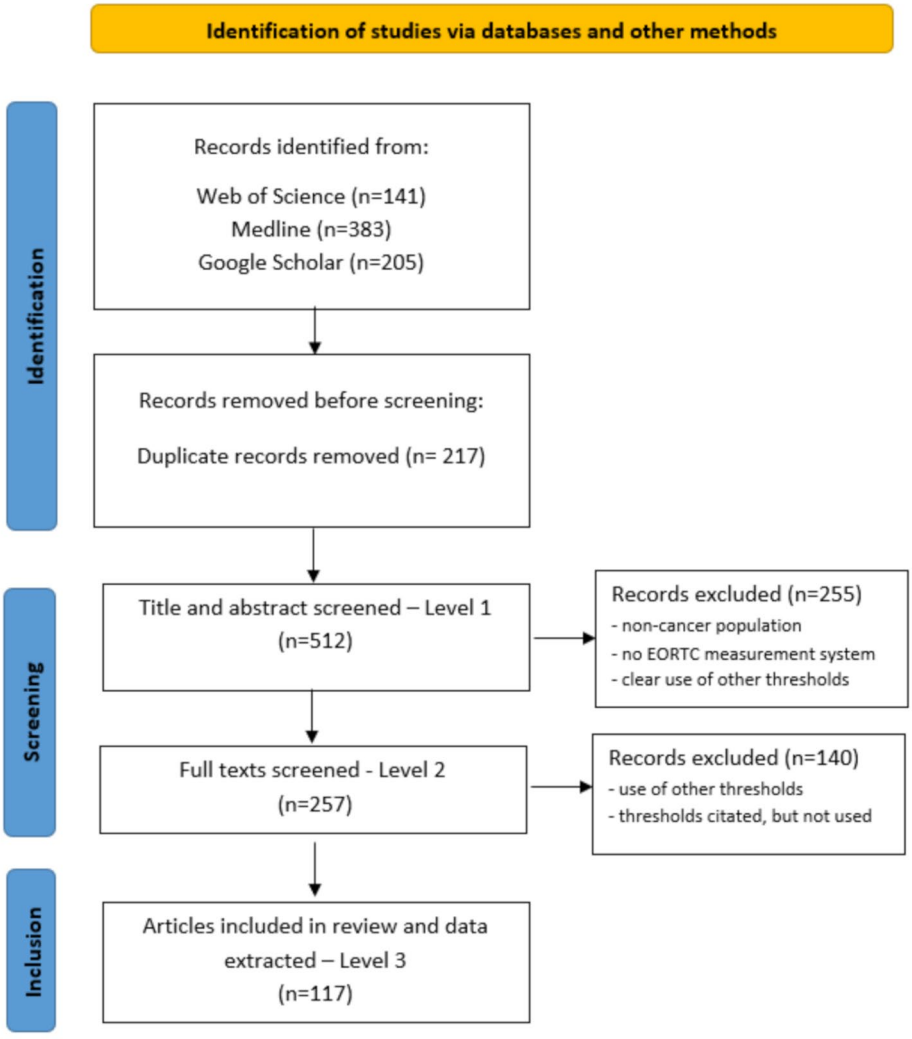

Fig. 1 Prisma Flow Chart on the identification, screening and data extraction of publications identified in this review

Table 1 Overview of study characteristics of publications included in the data extraction ($N = 117$)

	Median (IQR)	Min	Max
Sample size	257 (871)	17	27,857
		N	**%**
Affiliation (corresponding Author)*	Academia	99	84.6
	Research Organisation	21	17.2
	Industry	1	0.9
Article type*	Longitudinal observational	55	47.0
	Cross-sectional observational	49	41.9
	RCT	10	8.5
	Protocol	2	1.7
	Psychometric study	1	0.9
	Systematic review/ Meta- analysis	1	0.9
	Other	2	1.7
Population (diagnosis)	Mixed	25	21.4
	Breast	23	19.7
	Hematological	18	15.4
	Colorectal	11	9.4
	Gastrointestinal	6	5.1
	Gynecological	6	5.1
	Sarcoma	6	5.1
	Head and neck	4	3.4
	Lung	3	2.6
	Skin	3	2.6
	Cancer Survivors	2	1.7
	Prostate	2	1.7
	Thyroid	2	1.7
	Urological	2	1.7
	Brain	1	0.9
	Other	3	2.6
Disease Stage	Mixed	58	49.6
	Non-Metastatic	19	16.2
	Metastatic	16	13.7
	Unclear	24	20.5
Treatment status	Mixed	45	38.5
	On treatment	32	27.4
	Off treatment	29	24.8
	Unknown	11	9.4
Treatment type*	Mixed	58	49.6
	Chemotherapy	52	44.4
	Radiotherapy	36	30.8
	Surgery	35	29.9
	Targeted Therapy	22	18.8
	Endocrine Therapy	16	13.7
	Other	11	9.4
	Unknown	20	17.1

*= multiple categories per publication possible

cancer patients with mixed diagnoses ($n = 25$), followed by studies on breast cancer patients ($n = 23$) and studies in haematological cancer patients ($n = 18$). The majority of studies included patients with a mixed disease stages ($n = 58$), which also included purely non-metastatic samples ($n = 19$) and metastatic samples ($n = 16$). Of the 87 study populations that received active anti-cancer treatment at least partly ($n = 32$ on treatment; $n = 45$ mixed study population), 52 were reported to have received chemotherapy, with radiotherapy ($n = 36$) and surgery ($n = 35$) being the second and third most common types of treatment, respectively. Detailed results are reported in Table 1.

In most of the identified articles ($n = 98$, 83.8%) TCIs were applied to dichotomise PRO data for further analysis and report the results of PRO scores of the given studies (Table 2). Sixteen articles (13.7%) used TCIs to interpret the results, while four studies (3.4%) were identified that reported on the use of TCIs in clinical routine (e.g., e-health applications for outpatient monitoring). Furthermore, most studies ($n = 106$) reported using the TCIs as part of their main analysis, with 10.3% of the publications referring to the TCIs in their supplementary analysis. The most frequent term to refer to the TCIs was "*thresholds for clinical importance*" ($n = 66$; 56.4%), which reflects the original term defined by Giesinger et al. [29]; still, many variations in the terminology were observed. Other frequently used terms were *"thresholds of clinically important problem/limitation/impairment/etc"* ($n = 13$; 11.1%), "*Threshold of/by Giesinger, or Giesinger threshold*" ($n = 8$; 6.5%), "*Clinically relevant (score, level, problems,...)*" ($n = 8$; 6.5%), simply "*threshold*" ($n = 8$; 6.5%), "*Cut- off (value, score, points, for clinical relevance,...)*" ($n = 7$; 5.6%), or also "*Clinically important (threshold, problems, limitations, impaired,...)*" ($n = 7$; 5.6%) (Fig. 3). The description of the meaning of the anchor (e.g. the criteria on which the thresholds rely– limitations in daily life, need for help and care, worries) was provided in 10 out of the 117 articles (8.5%). For further details please see Table 2.

When investigating whether the TCIs were applied to individual patients' scores (i.e., the intended correct application) or to group-level scores (i.e., incorrect application) we observed that 41 studies (35%) applied the TCIs to group-level scores (e.g. mean scores) (Table 3).

The most frequent application of TCIs was for calculating prevalence rates of symptoms and functional health impairment ($n = 49$). Fifty-five studies applied the TCIs in a longitudinal study design ($N = 55$). In 32 of these studies the TCIs were applied separately to multiple time points to analyse how the proportion of patients with clinically important problems/symptoms evolves over time. In 23 studies, however, the TCIs have been incorrectly applied to interpret mean scores (i.e., group-level statistics) over

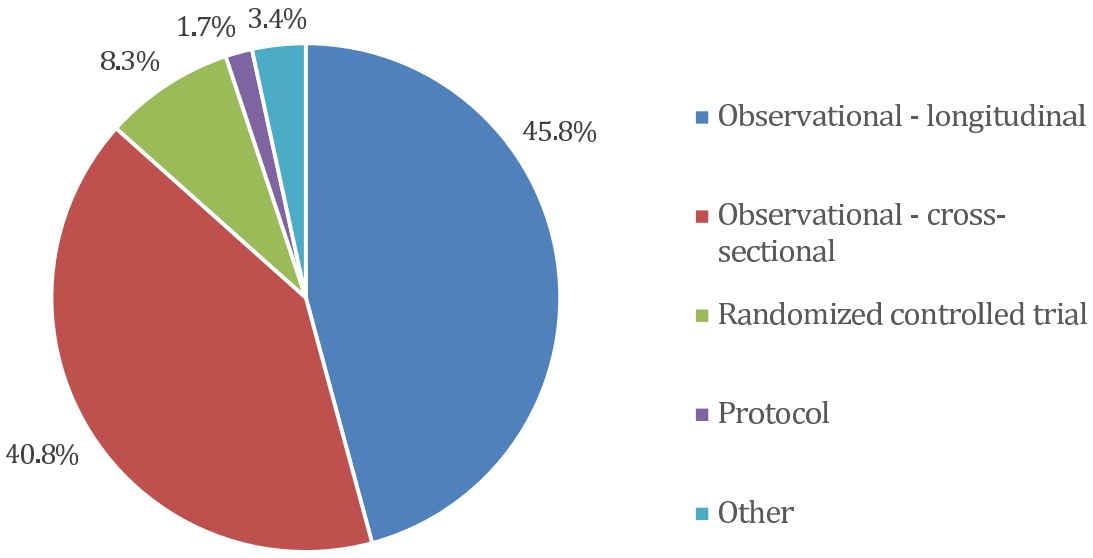

Fig. 2 Study type in articles included in the analysis

time. Another frequent application was the use of TCIs in the graphical presentation of results (e.g. bar charts with the proportion of patients above/below TCIs and dotted lines in graphs to illustrate the TCI). Lastly, TCIs were also used to make prognoses on clinical outcomes for individual patients or groups of patients in 19 publications (e.g. dichotomisation at baseline was informed by TCIs, and/or Odds Ratios were calculated based on TCIs). Full details are reported in Table 3.

Lastly, we investigated to which scales of the EORTC measurement system the TCIs were applied (Table 4). Forty-three studies applied the TCIs across all the scales of the EORTC QLQ-C30, the EORTC CAT Core, or the EORTC QLQ-C15-PAL. Beyond this, the Fatigue scale was the most frequently used if only specific scales were selected ($n = 28$), followed by Emotional Functioning and Cognitive Functioning ($n = 27$ each) and Physical Functioning ($n = 26$). The least frequently found scale TCIs were applied to was Dyspnoea ($n = 7$). Details are shown in Table 4.

Discussion

In our systematic scoping review, we identified 117 publications that utilised the TCIs for the EORTC QLQ-C30, the EORTC CAT Core, or the EORTC QLQ-C15-PAL to analyse or interpret study results or to support the interpretation in clinical practice. These results show the fast uptake and application of the TCIs by the research community, which reflects the long-standing call for enhanced interpretation of PRO results in the field of oncology [30].

Most identified studies applied the TCIs in methodologically sound ways; partly, this was done beyond the initially intended use of symptom detection in clinical practice; illustratively, a few examples are highlighted. One study used TCIs to cluster cancer survivors and investigate clinical characteristics associated with each group [31]. Further, one study in geriatric cancer patients calculated the prevalence of clinically important problems and compared it amongst groups based on the Karnofsky performance status [32], which reflects a similar approach to a study in colorectal patients [33] that used TCIs to dichotomise the patient groups and compare clinical characteristics of patients above/below the TCIs, or a study in breast cancer patients that investigated the association of peripheral neuropathy with impairments based on the TCIs [34]. Few studies have also calculated odds ratios for groups defined by TCIs. These studies investigated the association of groups based on TCIs with clinical characteristics [35], or for patients to receive or use social support services [36, 37]. Further, also hazard ratios (HR) for overall survival (OS), and event-free survival [38], whereby the TCIs were used to stratify Kaplan-Maier curves. These showed that at month 12, the HR for OS above vs. below TCIs was 2.04 (95% CI, 1.18–3.53) [38]. Lastly, one interesting use case was the application of TCIs in the sample size calculation as part of the power analysis in the published trial protocol [39]. Most of these examples extend beyond the initially intended purpose of the TCIs but are methodologically sound as the TCIs are applied to individual patient scores. The authors support such applications of TCIs in future studies.

Table 2 Use and terminology of thresholds for clinical importance (*N* = 117)

		N	%
Type of use*	Analysis	98	83.8
	Interpretations of results	16	13.7
	Clinical routine	4	3.4
TCIs reported in*	Main analysis	106	90.6
	Supplementary analysis	12	10.3
	Other	2	1.7
Terms used to refer to TCIs	Thresholds for/of clinical importance	66	56.4
	Thresholds of clinically important problem/ limitation/impairment/etc	13	11.1
	Threshold of/by Giesinger	8	6.5
	Clinically relevant score/level/problems/etc	8	6.5
	Threshold for impairment/ for clinical intervention/values/etc	8	6.5
	Clinically important threshold/problems/limitations/ impaired/etc	7	5.6
	Cut- off value/score/points/for clinical relevance/etc	7	5.6
	Clinically significant symptom/impairment/etc	6	4.8
	Clinical/Domain-specific/Evidence based/etc Threshold	3	2.4
	Other	4	3.2
Description of the anchors underlying the TCIs provided	Yes	10	8.5
	No	107	91.5

*= multiple selection of categories possible

Abbreviations: TCI = Threshold for clinical importance

Another finding of this review is the variation in terminology used to refer to one-and-the-same concept. While more than half of the publications relied on the original term "threshold for clinical importance" or its very close variations, such as "threshold of clinical importance", many publications used terminology more closely associated with other types of thresholds in the PRO research community. Terms such as "clinically significant" or "clinically meaningful" are often rather associated with the terminology around the concept of "minimal important differences" [40]. Here, the authors would like to emphasise the importance of clearly defined and precise terminology (e.g., we all speak of the same thing and know what we mean when we discuss it) and propose retaining the term "threshold for clinical importance" when these thresholds are applied.

One striking finding was the frequent incorrect application of TCIs for the interpretation of group-level scores. Applying TCIs on group-level scores merely allows a judgment if the mean score lies above/below the TCI; without further knowledge of distribution, it does not even allow to judge if the majority of patients experienced a clinically relevant symptom/functional impairment or if skewness of data and/or outliers impact on the interpretation. In the view of the authors, the application of TCIs to the interpretation of group-level data is misleading and not recommended. The TCIs were initially developed to be applied to individual patient scores, at a single time point, whereby clinical importance was defined as "*any aspect of a health problem that makes it relevant for the clinical encounter*" [29].

The confusion surrounding the application of thresholds to patient- or group-level data can also be observed in the application of thresholds for minimal important differences/changes and related concepts [9, 41]. The authors here would like to provide an example from a field different from PRO research– here systolic blood pressure - which aims to illustrate the different perspectives. A threshold of 140mmHg is applied to identify individual patients with hypertension [42]– analogous to the TCIs (i.e., for individual patients at single point in time). It would be misleading to claim that a *study group has a mean systolic blood pressure of 135mmHg and, therefore, no clinically relevant hypertension is observed*– this is done exactly when applying TCIs to group-level data.

This example shall illustrate the different perspectives and highlight the need for different evidence-based thresholds for each of these scenarios [9, 41]. One study identified in this review that makes a good differentiation of these concepts in the presentation of the results was done by Rogiers et al. [43], which shall be highlighted as a positive example.

Summarised, in our perspective, the methodologically sound ways to apply TCIs are primarily symptom screening in clinical practice, calculation of prevalence rates of symptoms and functional health impairments, application of TCIs as responder definition for individual patients in clinical studies, TCIs used to categorize individual patients into groups for further analysis. Any effort to apply TCIs to groups of patients should be avoided and viewed with caution.

The infrequent application of TCIs for the use in *"Screening monitoring in clinical practice" (*Table 3*)* identified in this review, may reflect a type of publication bias as healthcare providers may actually rely on the TCIs in clinical practice but do not publish this in the scientific literature.

This is a limitation of our review, which, with its focus on scientific articles, does not sufficiently cover the use of TCIs in clinical practice. Furthermore, our literature

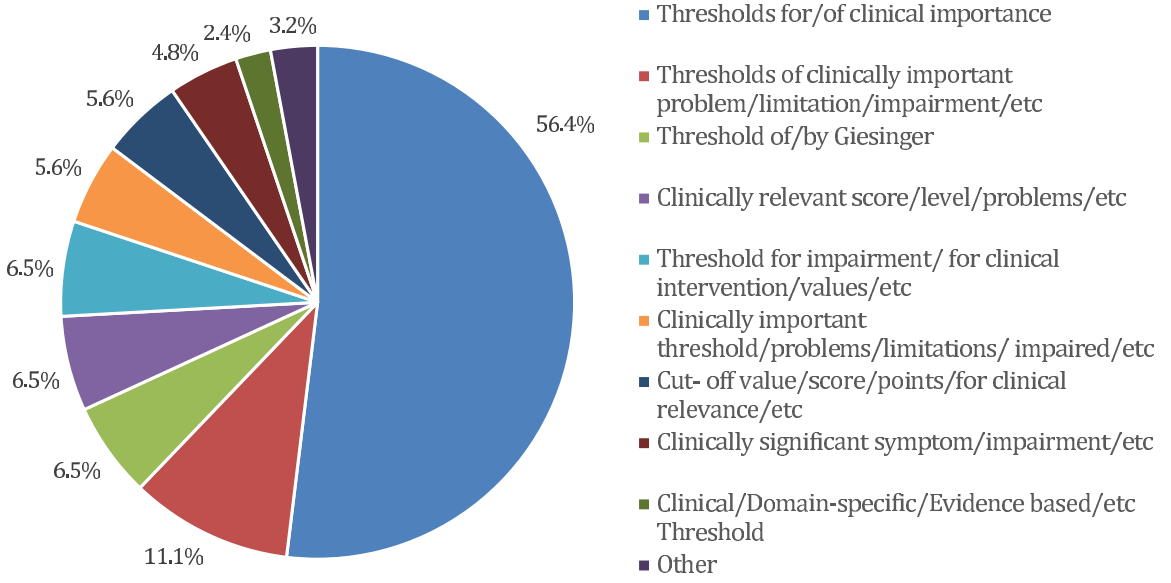

Fig. 3 Terminology used to refer to Thresholds for Clinical Importance

Table 3 Application of thresholds for clinical importance

Level of application	*N*	%
TCI used for patient-level data	76	65.0
TCI used for group-level data	41	35.0
Type of application		
Calculate prevalence rates	49	41.9
Responder definition in longitudinal settings	32	27.4
Graphical presentation of results	27	23.1
TCIs used for prognosis	19	16.3
Screening or monitoring in clinical practice	4	3.4
Compare prevalence rates to clinician ratings	2	1.7

*= multiple categories per publication possible

Abbreviations: TCI = Threshold for clinical importance

search was limited to the TCIs established by Giesinger et al. [18–20] and did not include other types of thresholds available for the EORTC measures.

Conclusion

The research community frequently uses the published TCIs for analysing and interpreting the core domains of the EORTC measurement system. However, a substantial number of studies apply these TCIs incorrectly to the interpretation of group-level data, such as mean scores. The authors advocate for clearly differentiating the various types of thresholds used to interpret PRO data and, for clarity, recommend the use of the term "thresholds for clinical importance" when such thresholds are referred to.

Table 4 EORTC QLQ-C30 scales for which TCIs have been applied to

	N	%
All Scales	43	36.8
Only if selected scales*:		
Physical functioning	26	22.2
Role functioning	20	17.1
Emotional functioning	27	23.1
Cognitive functioning	27	23.1
Social functioning	21	17.9
Fatigue	28	23.9
Nausea and vomiting	10	8.5
Pain	12	10.3
Dyspnoea	7	6.0
Insomnia	9	7.7
Appetite loss	10	8.5
Constipation	9	7.7
Diarrhoea	9	7.7
Financial difficulties	11	9.4

*= multiple categories per publication possible

Abbreviations: TCI = Threshold for clinical importance

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12955-025-02387-7.

Supplementary Material 1

Supplementary Material 2

Author contributions

MJP and JMG have contributed to the conception and design of the work; the acquisition, analysis, and interpretation of data; and have drafted and substantively revised the work.AMMT and DK have contributed to the

acquisition, analysis, and interpretation of data; and have drafted the work. LMS has contributed to the acquisition, analysis, and interpretation of data.All authors have approved the submitted version.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Competing interests
The authors declare no competing interests.

Ethics and Consent to Participate declarations
Not applicable.

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References

1. US Food and Drug Administration. Guidance for industry: Patient-Reported outcome measures: use in medical product development to support labeling claims. Silver Spring; 2009.
2. Bottomley A, Jones D, Claassens L. Patient-reported outcomes: assessment and current perspectives of the guidelines of the food and drug administration and the reflection paper of the European medicines agency. Eur J Cancer. 2009;45:347–53. https://doi.org/10.1016/j.ejca.2008.09.032.
3. Bellino S, La Salvia A. The importance of patient reported outcomes in oncology clinical trials and clinical practice to inform regulatory and healthcare Decision-Making. Drugs R D. 2024;24:123–7. https://doi.org/10.1007/s40268-024-00478-2.
4. Snyder C, Brundage M, Rivera YM, Wu AW. A PRO-cision medicine methods toolkit to address the challenges of personalizing Cancer care using Patient-Reported outcomes: introduction to the supplement. Med Care. 2019;57(5 Suppl 1):S1–7. https://doi.org/10.1097/MLR.0000000000001089.
5. Wintner LM, Sztankay M, Aaronson N, Bottomley A, Giesinger JM, Groenvold M, et al. The use of EORTC measures in daily clinical practice-A synopsis of a newly developed manual. Eur J Cancer. 2016;68:73–81. https://doi.org/10.1016/j.ejca.2016.08.024.
6. Calvert M, Blazeby J, Altman DG, Revicki DA, Moher D, Brundage MD. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. JAMA. 2013;309:814–22. https://doi.org/10.1001/jama.2013.879.
7. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Qual Life Res. 2010;19:539–49. https://doi.org/10.1007/s11136-010-9606-8.
8. Nguyen H, Butow P, Dhillon H, Sundaresan P. A review of the barriers to using Patient-Reported outcomes (PROs) and Patient-Reported outcome measures (PROMs) in routine cancer care. J Med Radiat Sci. 2021;68:186–95. https://doi.org/10.1002/jmrs.421.
9. Pe M, Alanya A, Falk RS, Amdal CD, Bjordal K, Chang J, et al. Setting international standards in analyzing Patient-Reported outcomes and quality of life endpoints in Cancer clinical Trials-Innovative medicines initiative (SISAQOL-IMI): stakeholder views, objectives, and procedures. Lancet Oncol. 2023;24:e270–83. https://doi.org/10.1016/S1470-2045(23)00157-2.
10. Cocks K, King MT, Velikova G, Martyn St-James M, Fayers PM, Brown JM. Evidence-based guidelines for determination of sample size and interpretation of the European organisation for the research and treatment of Cancer quality of life questionnaire core 30. J Clin Oncol. 2011;29:89–96. https://doi.org/10.1200/JCO.2010.28.0107.
11. Sztankay M, Wintner LM, Roggendorf S, Nordhausen T, Dirven L, Taphoorn MJB, et al. Developing an e-learning course on the use of PRO measures in oncological practice: health care professionals' preferences for learning content and methods. Support Care Cancer. 2022;30:2555–67. https://doi.org/10.1007/s00520-021-06676-x.
12. Musoro JZ, Coens C, Sprangers MAG, Brandberg Y, Groenvold M, Flechtner H-H, et al. Minimally important differences for interpreting EORTC QLQ-C30 change scores over time: A synthesis across 21 clinical trials involving nine different cancer types. Eur J Cancer. 2023;188:171–82. https://doi.org/10.1016/j.ejca.2023.04.027.
13. Pilz MJ, Gamper E-M, Efficace F, Arraras JI, Nolte S, Liegl G, et al. EORTC QLQ-C30 general population normative data for Italy by sex, age and health condition: an analysis of 1,036 individuals. BMC Public Health. 2022;22:1040. https://doi.org/10.1186/s12889-022-13211-y.
14. Pilz MJ, Loth FLC, Nolte S, Thurner AMM, Gamper E-M, Anota A, et al. General population normative values for the EORTC QLQ-C30 by age, sex, and health condition for the French general population. J Patient Rep Outcomes. 2024;8:48. https://doi.org/10.1186/s41687-024-00719-7.
15. Pilz MJ, Nolte S, Liegl G, King M, Norman R, McTaggart-Cowan H, et al. The European organisation for research and treatment of Cancer quality of life utility-Core 10 dimensions: development and investigation of general population utility norms for Canada, France, Germany, Italy, Poland, and the united Kingdom. Value Health. 2023;26:760–7. https://doi.org/10.1016/j.jval.2022.12.009.
16. Efficace F, Iurlo A, Patriarca A, Stagno F, Bee P-C, Ector G, et al. Validation and reference values of the EORTC QLQ-CML24 questionnaire to assess health-related quality of life in patients with chronic myeloid leukemia. Leuk Lymphoma. 2021;62:669–78. https://doi.org/10.1080/10428194.2020.1838509.
17. Mierzynska J, Taye M, Pe M, Coens C, Martinelli F, Pogoda K, et al. Reference values for the EORTC QLQ-C30 in early and metastatic breast cancer. Eur J Cancer. 2020;125:69–82. https://doi.org/10.1016/j.ejca.2019.10.031.
18. Giesinger JM, Loth FLC, Aaronson NK, Arraras JI, Caocci G, Efficace F, et al. Thresholds for clinical importance were defined for the European organisation for research and treatment of Cancer computer adaptive testing Core-an adaptive measure of core quality of life domains in oncology clinical practice and research. J Clin Epidemiol. 2020;117:117–25. https://doi.org/10.1016/j.jclinepi.2019.09.028.
19. Giesinger JM, Loth FLC, Aaronson NK, Arraras JI, Caocci G, Efficace F, et al. Thresholds for clinical importance were established to improve interpretation of the EORTC QLQ-C30 in clinical practice and research. J Clin Epidemiol. 2020;118:1–8. https://doi.org/10.1016/j.jclinepi.2019.10.003.
20. Pilz MJ, Aaronson NK, Arraras JI, Caocci G, Efficace F, Groenvold M, et al. Evaluating the thresholds for clinical importance of the EORTC QLQ-C15-PAL in patients receiving palliative treatment. J Palliat Med. 2021;24:397–404. https://doi.org/10.1089/jpm.2020.0159.
21. Rothrock NE, Cook KF, O'Connor M, Cella D, Smith AW, Yount SE. Establishing clinically-relevant terms and severity thresholds for Patient-Reported outcomes measurement information System(®) (PROMIS(®)) measures of physical function, cognitive function, and sleep disturbance in people with cancer using standard setting. Qual Life Res. 2019;28:3355–62. https://doi.org/10.1007/s11136-019-02261-2.
22. Nolte S, Liegl G, Petersen MA, Aaronson NK, Costantini A, Fayers PM, et al. General population normative data for the EORTC QLQ-C30 health-related quality of life questionnaire based on 15,386 persons across 13 European countries, Canada and the unites States. Eur J Cancer. 2019;107:153–63. https://doi.org/10.1016/j.ejca.2018.11.024.
23. Loth FL, Holzner B, Sztankay M, Bliem HR, Raoufi S, Rumpold G, Giesinger JM. Cancer patients' Understanding of longitudinal EORTC QLQ-C30 scores presented as bar charts. Patient Educ Couns. 2016;99:2012–7. https://doi.org/10.1016/j.pec.2016.08.004.
24. Snyder C, Smith K, Holzner B, Rivera YM, Bantug E, Brundage M. Making a picture worth a thousand numbers: recommendations for graphically displaying patient-reported outcomes data. Qual Life Res. 2019;28:345–56. https://doi.org/10.1007/s11136-018-2020-3.
25. Gressel GM, Dioun SM, Richley M, Lounsbury DW, Rapkin BD, Isani S, et al. Utilizing the patient reported outcomes measurement information system (PROMIS®) to increase referral to ancillary support services for severely symptomatic patients with gynecologic cancer. Gynecol Oncol. 2019;152:509–13. https://doi.org/10.1016/j.ygyno.2018.10.042.

26. Goldberg SL, Pecora AL, Contreras J, DeMarco KE, Paramanathan D, DeVincenzo V, et al. A Patient-Reported outcome instrument to facilitate timing of End-of-Life discussions among patients with advanced cancers. J Palliat Med. 2016;19:1092–7. https://doi.org/10.1089/jpm.2015.0459.
27. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European organization for research and treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85:365–76. https://doi.org/10.1093/jnci/85.5.365.
28. Giesinger JM, Efficace F, Aaronson N, Calvert M, Kyte D, Cottone F, et al. Past and current practice of Patient-Reported outcome measurement in randomized Cancer clinical trials: A systematic review. Value Health. 2021;24:585–91. https://doi.org/10.1016/j.jval.2020.11.004.
29. Giesinger JM, Aaronson NK, Arraras JI, Efficace F, Groenvold M, Kieffer JM, et al. A cross-cultural convergent parallel mixed methods study of what makes a cancer-related symptom or functional health problem clinically important. Psychooncology. 2018;27:548–55. https://doi.org/10.1002/pon.4548.
30. King MT. The interpretation of scores from the EORTC quality of life questionnaire QLQ-C30. Qual Life Res. 1996;5:555–67. https://doi.org/10.1007/BF00439229.
31. Keaver L, McLaughlin C. Applying the thresholds for clinical importance for fourteen key domains of the EORTC QLQ-C30: a latent class analysis of cancer survivors. Support Care Cancer. 2021;29:7815–23. https://doi.org/10.1007/s00520-021-06292-9.
32. Jensen CE, Vohra SN, Nyrop KA, Deal AM, Muss HB, Lichtman EI, et al. Geriatric-assessment-identified functional deficits among adults with multiple myeloma with normal performance status. J Geriatr Oncol. 2022;13:182–9. https://doi.org/10.1016/j.jgo.2021.08.004.
33. van Baar H, Bours MJL, Beijer S, van Zutphen M, van Duijnhoven FJB, Kok DE, et al. Body composition and its association with fatigue in the first 2 years after colorectal cancer diagnosis. J Cancer Surviv. 2021;15:597–606. https://doi.org/10.1007/s11764-020-00953-0.
34. Engvall K, Gréen H, Fredrikson M, Lagerlund M, Lewin F, Åvall-Lundqvist E. Impact of persistent peripheral neuropathy on health-related quality of life among early-stage breast cancer survivors: a population-based cross-sectional study. Breast Cancer Res Treat. 2022;195:379–91. https://doi.org/10.1007/s10549-022-06670-9.
35. Büttner M, Krogh D, Siggelkow H, Singer S. What are predictors of impaired quality of life in patients with hypoparathyroidism? Clin Endocrinol (Oxf). 2022;97:268–75. https://doi.org/10.1111/cen.14701.
36. Dayan D, Leinert E, Singer S, Janni W, Kühn T, Flock F, et al. Association of social service counseling in breast cancer patients with financial problems, role functioning and employment-results from the prospective multicenter BRENDA II study. Arch Gynecol Obstet. 2023;307:541–7. https://doi.org/10.1007/s00404-022-06604-2.
37. Singer S, Janni W, Kühn T, Flock F, Felberbaum R, Schwentner L, et al. Awareness, offer, and use of psychosocial services by breast cancer survivors in Germany: a prospective multi-centre study. Arch Gynecol Obstet. 2023;307:945–56. https://doi.org/10.1007/s00404-022-06665-3.
38. van Amelsfoort RM, Walraven I, Kieffer J, Jansen EPM, Cats A, van Grieken, Nicole CT, et al. Quality of life is associated with survival in patients with gastric cancer: results from the randomized CRITICS trial. J Natl Compr Canc Netw. 2022;20:261–7. https://doi.org/10.6004/jnccn.2021.7057.
39. Grimmett C, Bates A, West M, Leggett S, Varkonyi-Sepp J, Campbell A, et al. SafeFit trial: virtual clinics to deliver a multimodal intervention to improve psychological and physical well-being in people with cancer. Protocol of a COVID-19 targeted non-randomised phase III trial. BMJ Open. 2021;11:e048175. https://doi.org/10.1136/bmjopen-2020-048175.
40. King MT. A point of minimal important difference (MID): a critique of terminology and methods. Expert Rev Pharmacoecon Outcomes Res. 2011;11:171–84. https://doi.org/10.1586/erp.11.9.
41. Hays RD, Peipert JD. Between-group minimally important change versus individual treatment responders. Qual Life Res. 2021;30:2765–72. https://doi.org/10.1007/s11136-021-02897-z.
42. Flint AC, Conell C, Ren X, Banki NM, Chan SL, Rao VA, et al. Effect of systolic and diastolic blood pressure on cardiovascular outcomes. N Engl J Med. 2019;381:243–51. https://doi.org/10.1056/NEJMoa1803180.
43. Rogiers A, Willemot L, McDonald L, van Campenhout H, Berchem G, Jacobs C, et al. Real-World effectiveness, safety, and Health-Related quality of life in patients receiving adjuvant nivolumab for melanoma in Belgium and Luxembourg: results of PRESERV MEL. Cancers (Basel). 2023. https://doi.org/10.3390/cancers15194823.

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