

Measuring treatment-specific side effects from the patient perspective: Trial-specific item lists from PRO item libraries

Session 2: Novel approaches to the measurement of HRQoL and other PROs

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Conflicts of interest

- *None to declare*

PRO item libraries in oncology: An overview

Item Library Examples	
Derived from existing, validated questionnaires, e.g.:	Designed and developed with aim to create flexible item library, e.g.:
 EORTC Item Library	 PRO-CTCAE® <i>Designed as companion to CTCAE, covering 78 symptomatic toxicities in 124 items</i>
 FACIT Searchable Library	
 MDASI Symptom Library	

- **Item library:** collection of single items or multi-item scales that measure various PRO/HRQoL domains → allows for selection of specific items
- **Item list:** customised questionnaire created using select items from library

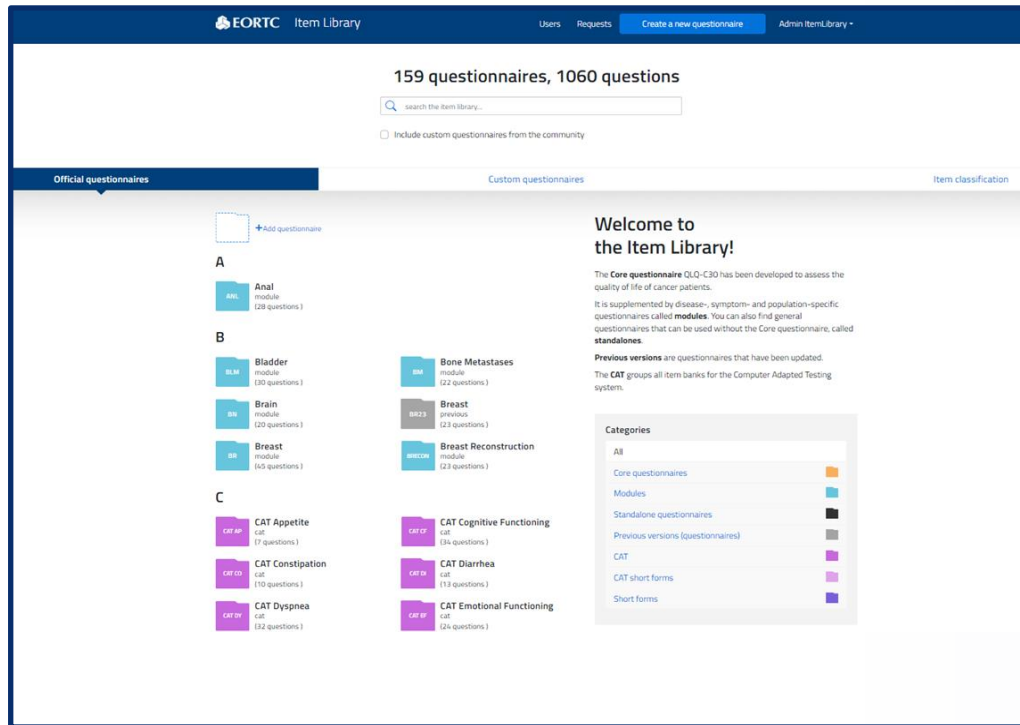
<https://itemlibrary.eortc.org/>

<https://www.facit.org/facit-searchable-library>

<https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/symptom-research/symptom-assessment-tools/md-anderson-symptom-inventory.html>

<https://healthcaredelivery.cancer.gov/pro-ctcae/>

How is the EORTC Item Library used?



To support the development and validation of new (static) questionnaires and questionnaire updates



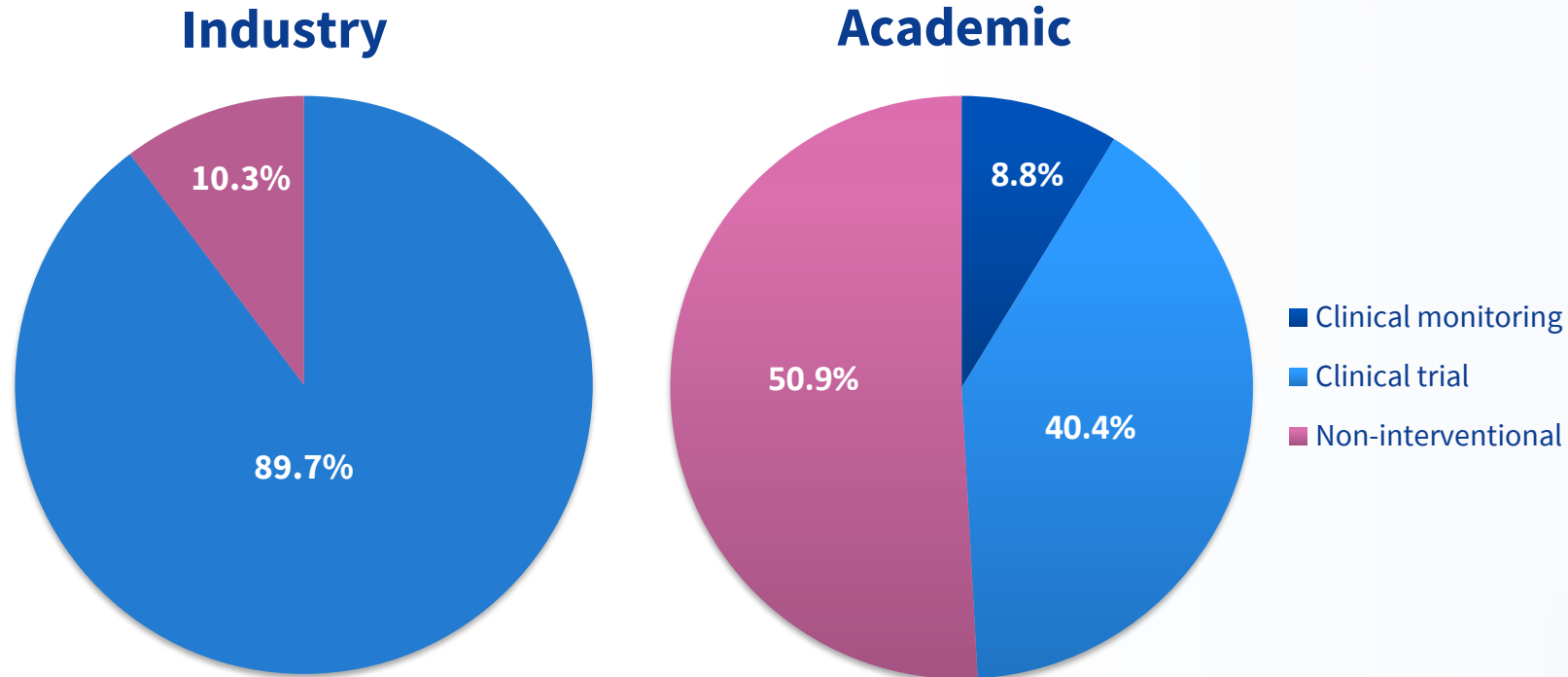
As a reference tool to search for items, translations, references, questionnaires, etc.



To create **new item lists** for use in different research and clinical settings

<https://itemlibrary.eortc.org/>

Trends in EORTC item list usage



- Patterns of use between industry and academic users emphasize different stakeholder needs and relevance of flexible approaches within observational studies and routine clinical care
- Recommendations should be **tailored based on context of use**

Piccinin C, Gilbert A, Groenvold M, Velikova G, Kuliš D, Bottomley A. Clinical characteristics of EORTC item list implementation: A summary based on four years of Item Library use. *Quality of Life Research*. 2022;31:S114-S115. <https://doi.org/10.1007/s11136-022-03257-1>

Example settings for item list use



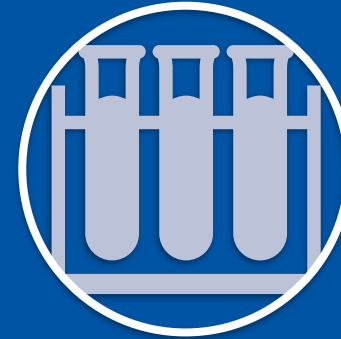
Novel treatments

To capture issues and symptomatic AEs not included in static questionnaire(s)



Rare disease groups

For whom static questionnaires may not be available



Early phase trials

When less is known about possible symptomatic AEs and more flexibility is required

Need to be pragmatic

What are frequently used EORTC item lists measuring?



Concept(s)	Core outcomes (functioning & symptoms)	Treatment-related side effects	Global impression of side effect burden
Approach(es)	<ul style="list-style-type: none"> Subset of QLQ-C30 domains 	<ul style="list-style-type: none"> Select treatment-specific items 	<ul style="list-style-type: none"> Single item measure of side effect burden <i>(Q168 To what extent have you been troubled with side-effects from your treatment?)</i>
PRO measurement strategy example(s)	<ul style="list-style-type: none"> QLQ-C30 + IL [alternating QLQ-C30 & IL at select timepoints] 	<ul style="list-style-type: none"> QLQ-C30 + module + IL QLQ-C30 + IL 	<ul style="list-style-type: none"> QLQ-C30 + module + IL QLQ-C30 + IL

Coverage of symptomatic AEs within the EORTC Item Library

- Previous work linking 950 EORTC items to CTCAE framework found considerable coverage of AEs
 - 208 different CTCAEs linked to EORTC items
 - 65.8% of EORTC items assigned at least one CTCAE classification
- Findings integrated into Item Library to facilitate identification of items based on symptomatic AE

SOCs	Total AEs covered by EORTC items N (%*)
Cardiac disorders	2 (1.0)
Ear and labyrinth disorders	3 (1.4)
Endocrine disorders	2 (0.1)
Eye disorders	14 (6.7)
Gastrointestinal disorders	37 (17.8)
General disorders and administration site conditions	15 (7.2)
Immune system disorders	1 (0.5)
Infections and infestations	5 (2.4)
Injury, poisoning and procedural complications	7 (3.4)
Investigations	3 (1.4)
Metabolism and nutrition disorders	1 (0.5)
Musculoskeletal and connective tissue disorders	17 (8.2)
Nervous system disorders	23 (11.1)
Psychiatric disorders	12 (5.8)
Renal and urinary disorders	9 (4.3)
Reproductive system and breast disorders	21 (10.1)
Respiratory, thoracic and mediastinal disorders	16 (7.7)
Skin and subcutaneous tissue disorders	16 (7.7)
Surgical and medical procedures	1 (0.5)
Vascular disorders	3 (1.4)
Total SOCs (N=20)	*Total AEs (N=208)

Gilbert A*, Piccinin C*, Velikova G, Groenvold M, Kuliš D, Blazeby JM, Bottomley A. Linking the European Organisation for Research and Treatment of Cancer Item Library to the Common Terminology Criteria for Adverse Events. Journal of Clinical Oncology. 2022;40(32):3770–80. <https://doi.org/10.1200/JCO.21.02017>

Developing a PRO measurement approach

Core outcomes: Integration with standard instruments

- Core questionnaires (e.g., QLQ-C30) & disease-specific modules

Tolerability: Identification of issues to include in an item list

- Investigator brochures, literature, clinicians, PPI

Special considerations

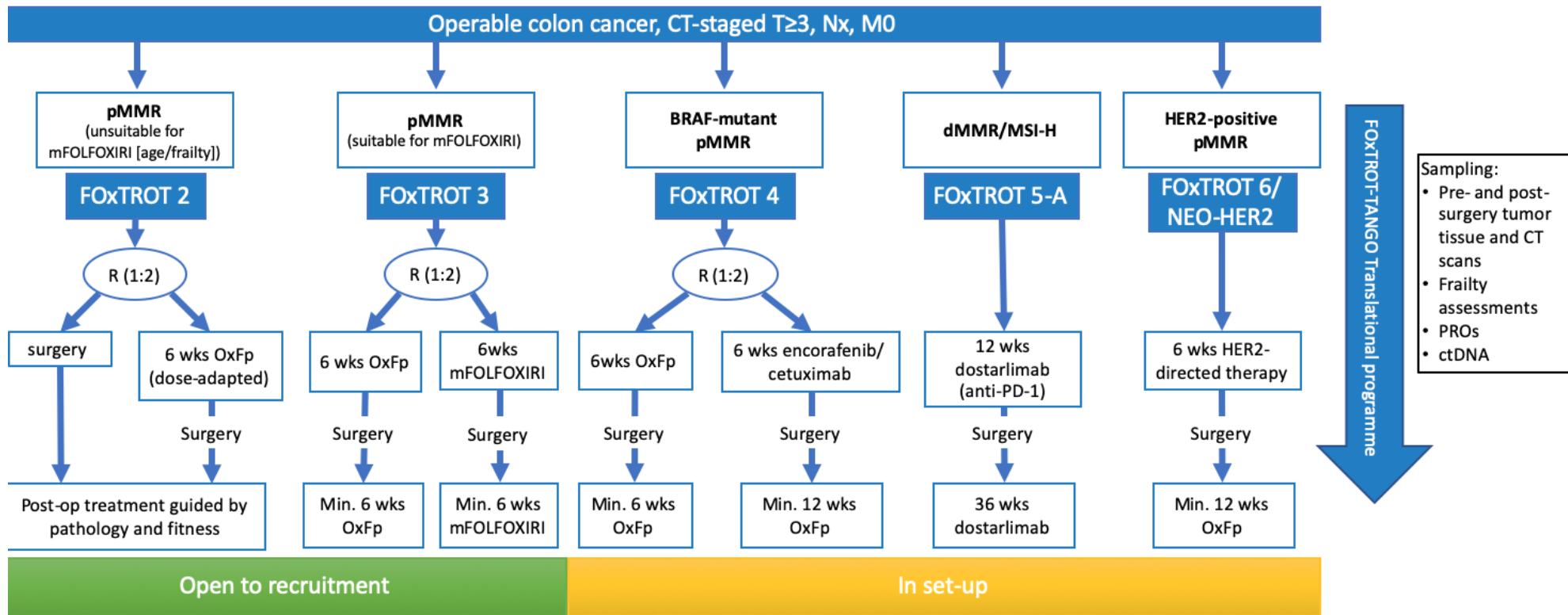
- Symptom burden item, Elderly module, decision regret

Guidelines

- Expert recommendations; ongoing funded consensus project

Piccinin C, Basch E, Bhatnagar V, Calvert M, Campbell A, Cella D, et al. Recommendations on the use of item libraries for patient-reported outcome measurement in oncology trials: findings from an international, multidisciplinary working group. *Lancet Oncol.* 2023;24(2):e86-e95. [https://doi.org/10.1016/S1470-2045\(22\)00654-4](https://doi.org/10.1016/S1470-2045(22)00654-4)

Neoadjuvant platform trial: FOxTROT



Bespoke timings designed to capture impact of novel regime on pre- and post-surgical outcomes; seamless shift between no stoma or stoma

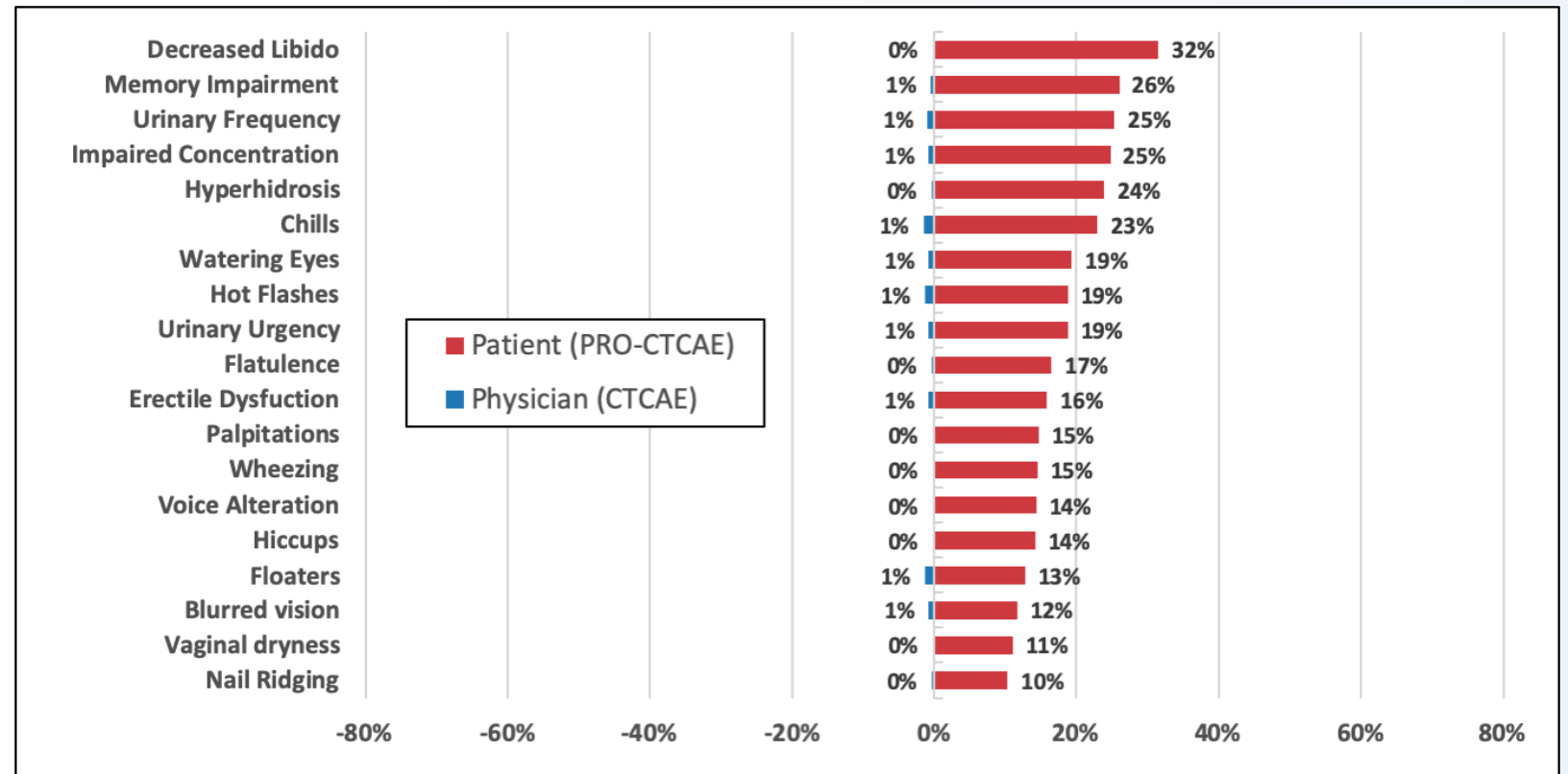
Early phase setting: Differences in tolerability reporting

Phase I trials in solid tumours at Princess Margaret Cancer Centre

Completed 80-item PRO-CTCAE[®] tablet-based survey

- 1) Baseline (n=243)
- 2) mid-cycle 1 (n=191)
- 3) mid-cycle 2 (n=118; 49%)

Multiple different systemic treatments



Courtesy of Veitch, ESMO 2019

AE reporting for items occurring with a patient frequency $\geq 10\%$ and physician frequency $\leq 1\%$

Measuring unexpected issues: The WISP

16. Have you had any additional, important symptoms or problems that have not been mentioned in the questions above?

No.

Yes. Please write the most important (up to three), and rate to what extent you have had the symptoms or problems during the past week:

During the past week, to what extent have you had:	Not at All	A Little	Quite a Bit	Very Much
Symptom/problem A: _____	1	2	3	4
Symptom/problem B: _____	1	2	3	4
Symptom/problem C: _____	1	2	3	4

Rojas-Concha L, Arrarras JI, Conroy T, Chalk T, Guberti M, Holzner B, et al. Acceptability and usefulness of the EORTC 'Write In three Symptoms/Problems' (WISP): A brief open-ended instrument for symptom assessment in cancer patients (under review). 2024.

Summary

Item Library

- Opportunity to establish tolerability

C30 and disease-specific module

- Core outcomes covered, including measurement of efficacy

Comparable toxicity

- Allows comparison across multiple modalities of treatments

Measuring what matters to patients

- Covers patient experience

THANK YOU

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