
Incorporating the patient voice in sarcoma research:

How can we assess health-related quality of life in this heterogeneous patient group?

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The future of cancer therapy



Radboudumc

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- Evaluation (new) treatments and care protocols traditionally focused on **objective outcomes** (e.g. disease-free and overall survival, response rate, adverse events) or centered around **provider's perspective** (e.g. number of complications)

 - Assessment of **patient perspective** can provide important additional information to assess the benefits and risks of cancer treatments



Health care professionals and researchers increasingly be aware of how patient perspective may differ from theirs

Patient-reported outcomes (PROs)

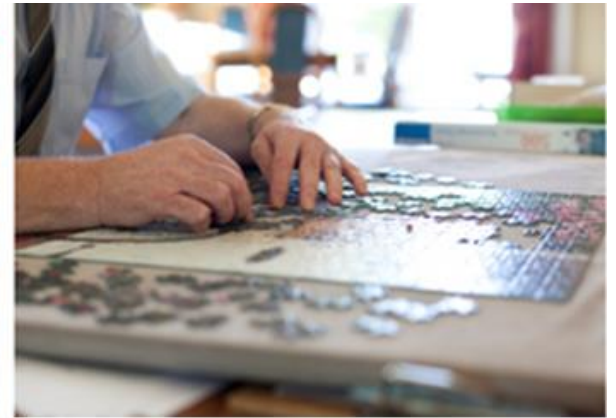
“Refer to a host of outcomes coming directly from patients about how they feel or function in relation to a health condition and its therapy without interpretation by healthcare professionals or anyone else”¹

- Symptoms (e.g. pain, fatigue)
- Perception of daily functioning (e.g. physically, socially)
- Satisfaction with care
- Health-related quality of life

¹ U.S. Department of Health and Human Services, Food and Drug Administration. Guidance for industry: Patient-reported outcomes measures: Use in medical product development to support labeling claims.

Why is it important to measure PROs in daily clinical practice?

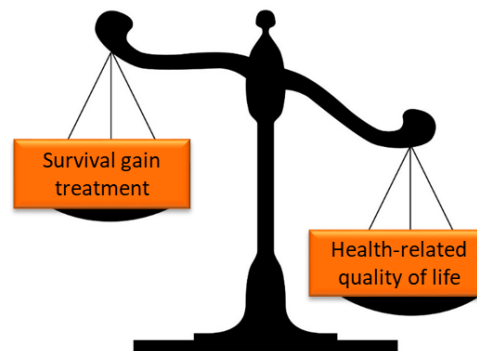
- The use of PROs in clinical practice improves patient-provider communication and can also improve problem detection, management, and outcomes^{1,2}



- Several recent studies have even demonstrated improved survival with PRO monitoring²

Why is it important to measure PROs in clinical studies

- Many sarcoma patients experience a substantial treatment burden of physical and psychosocial symptoms, with an adverse impact on HRQoL.



- Integration of HRQoL with traditional measures of therapeutic response will provide a more comprehensive assessment of efficacy and toxicity of (novel) therapies for sarcoma patients: **net clinical benefit**

Health-related quality of life (HRQoL)

The impact of disease and treatment on domains of physical, psychological, and social functioning

Reviewing HRQOL in sarcoma patients is 'hot' in psychosocial research



[The Patient - Patient-Centered Outcomes Research](#)

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REVIEW

Health-related unmet health review

Hindawi
Sarcoma
Volume 2019, Article ID 9730867, 18 pages
<https://doi.org/10.1155/2019/9730867>

Review Article

Joshua McDonoug
Phyllis Butow^{3,4}

A Critical Review of the Impact of Sarcoma on Psychosocial Wellbeing

Lesley Storey,¹ Lorna A. Fern,² Ana Martins,² Mary Wells,³ Lindsey Bennister,² Craig Gerrand,⁴ Maria Onasanya,² Jeremy S. Whelan,² Rachael Windsor,² Julie Woodford,⁴ and Rachel M. Taylor

WILEY



.....But in clinical research HRQoL is NOT “HOT” ENOUGH YET



Novel Therapeutic and Diagnostic Advances in Bone and Soft Tissue Sarcomas

Published online December 8, 2017

[Sarcoma: The Merging of Science and Clinical Care](#) *Schwartz et al*

Sarcomas are cancers of connective tissues. There will be approximately 15,000 new cases of sarcoma diagnosed in the United States this year, collectively making them a rare form of cancer. The situation is made more complex in that sarcoma is not one diagnosis, any more than lung cancer is. Rather, sarcomas comprise at least 50 different histologic subtypes, each characterized by a unique biology, pathology, and genetics, with the extra complexity of anatomic locations from head to toes. As a result, sarcomas represent a complex family of cancers.

[Read more »](#)

In this issue

- [Contemporary Sarcoma Diagnosis, Genetics, and Genomics](#) *Schaefer et al*
 - [Local Control of Soft Tissue and Bone Sarcomas](#) *Crompton et al*
 - [Perioperative Management of Extremity Soft Tissue Sarcomas](#) *Haas et al*
 - [Emerging Targeted and Immune-Based Therapies in Sarcoma](#) *Pollack et al*
 - [Gastrointestinal Stromal Tumors](#) *von Mehren et al*
 - [Soft Tissue and Uterine Leiomyosarcoma](#) *George et al*
 - [Clinical and Molecular Spectrum of Liposarcoma](#) *Lee et al*
 - [Biology and Management of Undifferentiated Pleomorphic Sarcoma, Myxofibrosarcoma, and Malignant Peripheral Nerve Sheath Tumors: State of the Art and Perspectives](#) *Widemann et al*
 - [Rhabdomyosarcoma, Ewing Sarcoma, and Other Round Cell Sarcomas](#) *Pappo et al*
 - [Synovial Sarcoma: Current Concepts and Future Perspectives](#) *Stacchiotti et al*
 - [Osteosarcoma, Chondrosarcoma, and Chordoma](#) *Whelan et al*
 - [Pathologic Angiogenesis of Malignant Vascular Sarcomas: Implications for Treatment](#) *Khan et al*
 - [Locally Aggressive Connective Tissue Tumors](#) *Gounder et al*
 - [Carcinosarcomas and Related Cancers: Tumors Caught in the Act of Epithelial-Mesenchymal Transition](#) *Pang et al*
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THIS NEEDS TO CHANGE

Health-Related Quality of Life in Patients With Sarcoma: Enhancing Personalized Medicine

TO THE EDITOR: We read with great interest the Special Series entitled "Novel Therapeutic and Diagnostic Advances in Bone and Soft Tissue Sarcomas." These articles provide comprehensive insight into current knowledge and evolving research in this heterogeneous group of tumors. Although relevant diagnostic and therapeutic aspects of patient care are considered, there is almost no reference to the patient perspective on these advances. Most authors acknowledge the need for individualized care, with respect to clinical, genetic, and molecular factors; however, only Gounder et al¹ refer to health-related quality of life (HRQOL) measures as potentially meaningful clinical end points in locally advanced connective tissue tumors.

Historically, evaluation of oncologic treatments has focused on objective outcomes such as radiologic response, progression-free and overall survival, and health care provider perspectives on treatment-related toxicities. More recently, increasing attention has been given to patient-reported outcomes (PROs), defined as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else,"²(p2) to evaluate treatment efficacy. PROs include a range of outcomes such as symptoms, functioning, and HRQOL. HRQOL is the most widely used PRO and is a multidimensional concept that includes the patient's perception of the impact of the disease and its treatment on physical, psychological, and social functioning.³ Incorporating PROs into clinical practice can facilitate communication, improve symptom control and patient satisfaction, and reduce hospital admissions.⁴ A recent study in patients with metastatic solid tumors showed that routine PRO monitoring and immediate response to adverse events led to a 5-month survival benefit compared with standard care,⁵ longer than that associated with most new drugs for metastatic cancers approved by the US Food and Drug Administration in 2016.⁶

Data on HRQOL in patients with sarcoma are limited; however, many patients experience a substantial burden of physical and psychological symptoms, with an adverse impact on HRQOL.⁷ Integration of HRQOL with traditional measures of therapeutic response will provide a more comprehensive assessment of the efficacy and toxicity of novel therapies for patients with sarcoma.⁸ Symptomatic toxicities are frequently underreported by clinicians; therefore, PROs are a vital component of symptom detection, monitoring, and early intervention.⁹ Precise assessments of how patients feel and function offer important additional information in evaluating the risks and benefits of treatments.³ Patient experience is a key aspect of drug development, and survival alone is inadequate to determine net clinical benefit.¹⁰ Although some novel treatments have been approved for sarcomas over the last few decades, detailed

data on short- and long-term adverse effects and HRQOL are scarce.⁷ The PALETTE (Pazopanib for Metastatic Soft Tissue Sarcoma) study of pazopanib versus placebo as second-line or greater treatment of advanced soft tissue sarcomas is one of the few sarcoma trials to report HRQOL as an exploratory end point.¹¹ Pazopanib improved progression-free survival without relevant deterioration in HRQOL compared with placebo. This demonstrates that combining HRQOL with clinical data can show overall clinical treatment benefit.

One of the biggest challenges in sarcoma is how to assess HRQOL in this heterogeneous patient group. Previous studies have predominately used generic HRQOL instruments (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, Short Form 36, Functional Assessment of Cancer Therapy-General); however, these tools do not efficiently capture the unique experiences of patients with sarcoma (eg, disease localization, treatment-specific symptoms) and thus lack content validity. Traditionally, inadequate content coverage has been addressed using a tumor-specific questionnaire that captures all disease-specific HRQOL issues, in conjunction with generic HRQOL measures. Given the heterogeneity of sarcomas, including patient age, histologic subtype, physiologic locations, disease stage, and rapidly changing treatment landscape, associated with variable mechanisms of action and toxicity profiles, it may be challenging to develop one sarcoma-specific questionnaire that meets the needs of clinical practice, academia, and industry. Standardized, so-called static, questionnaires consisting of a fixed set of items may not be relevant for every patient with sarcoma and may miss important patient-reported adverse events. Consequently, a more flexible approach is needed to assess the impact of treatments, provide optimal supportive care, and ultimately translate into meaningful outcomes for patients with sarcoma.¹² One option is to combine standardized PRO questionnaires with validated items from item libraries (eg, Patient-Reported Outcomes Measurement Information System, European Organisation for Research and Treatment of Cancer) to ensure adequate assessment of specific treatments and their effects on common health problems.¹²

In this era of personalized medicine, the principal focus has been on clinical and tumor characteristics, without addressing individual patient perspectives. If we really want to make a difference, truly provide personalized care, and conduct trials that are attractive to patients, we should routinely involve patients in trial design and integrate HRQOL assessments into clinical practice and research.¹³ This will enable provision of a more holistic approach in the overall management of patients.

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How to assess HRQoL?

- One of the biggest challenges in sarcoma is how to assess HRQoL in this heterogeneous patient group.
- Previous studies all used generic HRQoL instruments (e.g. EORTC QLQ-C30; SF36, FACT-G).



EORTC QLQ-C30 (versie 3)

Wij zijn geïnteresseerd in bepaalde dingen over u en uw gezondheid. Wilt u alle vragen zelf beantwoorden door het getal te omcirkelen dat het meest op u van toepassing is? Er zijn geen "juiste" of "onjuiste" antwoorden. De informatie die u geeft zal strikt vertrouwelijk worden behandeld.

Wilt u uw initialen invullen:

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Uw geboortedatum (Dag, Maand, Jaar):

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De datum van vandaag (Dag, Maand, Jaar):

31

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	Helemaal niet	Een beetje	Nogal	Heel erg
1. Heeft u moeite met het doen van inspannende activiteiten zoals het dragen van een zware boodschappentas of een koffer?	1	2	3	4
2. Heeft u moeite met het maken van een lange wandeling?	1	2	3	4
3. Heeft u moeite met het maken van een <u> korte </u> wandeling buitenshuis?	1	2	3	4
4. Moet u overdag in bed of op een stoel blijven?	1	2	3	4
5. Heeft u hulp nodig met eten, aankleden, uzelf wassen of naar het toilet gaan?	1	2	3	4

Gedurende de afgelopen week:

	Helemaal niet	Een beetje	Nogal	Heel erg
6. Was u beperkt bij het doen van uw werk of andere dagelijkse bezigheden?	1	2	3	4
7. Was u beperkt bij het uitoefenen van uw hobby's of bij andere bezigheden die u in uw vrije tijd doet?	1	2	3	4
8. Was u kortademig?	1	2	3	4
9. Heeft u pijn gehad?	1	2	3	4
10. Had u behoefte om te rusten?	1	2	3	4
11. Heeft u moeite met slapen gehad?	1	2	3	4
12. Heeft u zich slap gevoeld?	1	2	3	4
13. Heeft u gebrek aan eetlust gehad?	1	2	3	4
14. Heeft u zich misselijk gevoeld?	1	2	3	4
15. Heeft u overgegeven?	1	2	3	4
16. Had u last van obstipatie? (was u verstopt?)	1	2	3	4

DUTCH

DUTCH

Gedurende de afgelopen week:

	Helemaal niet	Een beetje	Nogal	Heel erg
17. Had u diarree?	1	2	3	4
18. Was u moe?	1	2	3	4
19. Heeft pijn u gehinderd bij uw dagelijkse bezigheden?	1	2	3	4
20. Heeft u moeite gehad met het concentreren op dingen, zoals een krant lezen of televisie kijken?	1	2	3	4
21. Voelde u zich gespannen?	1	2	3	4
22. Maakte u zich zorgen?	1	2	3	4
23. Voelde u zich prikkelbaar?	1	2	3	4
24. Voelde u zich neerslachtig?	1	2	3	4
25. Heeft u moeite gehad met het zich herinneren van dingen?	1	2	3	4
26. Heeft uw lichamelijke toestand of medische behandeling uw <u> familielevens </u> in de weg gestaan?	1	2	3	4
27. Heeft uw lichamelijke toestand of medische behandeling u <u> belemmerd </u> bij uw <u> sociale </u> bezigheden?	1	2	3	4
28. Heeft uw lichamelijke toestand of medische behandeling financiële moeilijkheden met zich meegebracht?	1	2	3	4

Wilt u voor de volgende vragen het getal tussen 1 en 7 omcirkelen dat het meest op u van toepassing is?

29. Hoe zou u uw algehele gezondheid gedurende de afgelopen week beoordelen?

1	2	3	4	5	6	7
Erg slecht						Uitstekend

30. Hoe zou u uw algehele "kwaliteit van het leven" gedurende de afgelopen week beoordelen?

1	2	3	4	5	6	7
Erg slecht						Uitstekend



Modular system

C30

Module

Validated Modules

QLQ-BIL21	CHOLANGIOCARCINOMA AND GALLBLADDER CANCER
QLQ-BM22	BONE METASTASES
QLQ-BN20	BRAIN
QLQ-BR23	BREAST
QLQ-CR29	COLORECTAL
QLQ-CX24	CERVICAL
QLQ-ELD14	ELDERLY CANCER PATIENTS
QLQ-EN24	ENDOMETRIAL
QLQ-FA12	CANCER-RELATED FATIGUE
QLQ-GI.NET21	NEUROENDOCRINE CARCINOID
QLQ-HCC18	HEPATOCELLULAR CARCINOMA
QLQ-H&N35	HEAD & NECK
QLQ-INFO25	INFORMATION
QLQ-LC13	LUNG
QLQ-LMC21	COLORECTAL LIVER METASTASES
QLQ-MY20	MULTIPLE MYELOMA
QLQ-OES18	OESOPHAGEAL
QLQ-OG25	OESOPHAGO-GASTRIC
QLQ-OH15	ORAL HEALTH
QLQ-OV28	OVARIAN
QLQ-PR25	PROSTATE
QLQ-STO22	GASTRIC

Modules in Phase IV

QLQ-BrR24	BREAST RECONSTRUCTION
QLQ-CAX24	CANCER CACHEXIA AND NUTRITIONAL STATUS
QLQ-CIPN20	PERIPHERAL NEUROPATHY
QLQ-CML24	CHRONIC MYELOID LEUKAEMIA
QLQ-H&N43	UPDATE OF H&N35
QLQ-LC29	UPDATE OF LC13
QLQ-PRT23	RADIATION PROCTITIS
QLQ-SHQ22	SEXUAL HEALTH
QLQ-SWB32	SPIRITUAL WELLBEING
QLQ-TC26	TESTICULAR CANCER

Modules Phase III Completed

QLQ-ANL27	ANAL CANCER
QLQ-BLM30	MUSCLE INVASIVE BLADDER CANCER
QLQ-CLL17	CHRONIC LYMPHOCYTIC LEUKAEMIA - REPLACING QLQ-CLL16
QLQ-CLL16	CHRONIC LYMPHOCYTIC LEUKAEMIA - BEING REPLACED BY QLQ-CLL17
QLQ-COMU26	COMMUNICATION
QLQ-HDC29	HIGH-DOSE CHEMOTHERAPY
QLQ-HL27	HODGKIN LYMPHOMA
QLQ-MEL38	MELANOMA
QLQ-NHL-HG29	HIGH-GRADE NON-HODGKIN LYMPHOMA
QLQ-NHL-LG20	LOW-GRADE NON-HODGKIN LYMPHOMA
QLQ-NMIBC24	NON-MUSCLE INVASIVE BLADDER CANCER
QLQ-OPT30	OPHTHALMIC CANCER
QLQ-PAN26	PANCREATIC CANCER

Modules in Phase III

Nasopharyngeal Carcinoma
Outpatient Satisfaction
Satisfaction with Cancer Care Core
Symptom-Based Questionnaires
Thyroid Cancer
Vulva Cancer

Modules in Phase I-II

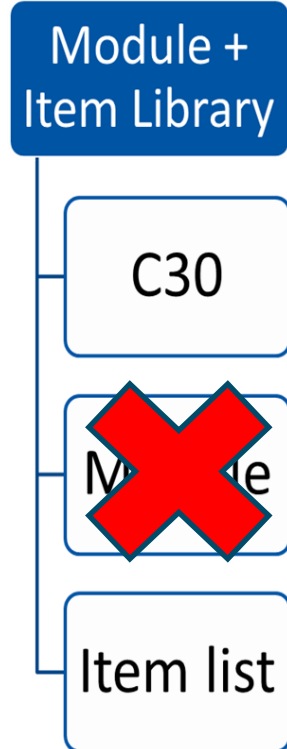
Adolescents and Young Adults
Breast Cancer (update of BR23)
Hereditary Cancer Predisposition Syndrome
IADL in Brain Tumor Patients
Pancreatic Neuroendocrine Tumor
Spinal Cord Compression
Survivorship



 EORTC Item Library

64 questionnaires, 902 questions

 search the item library...



Module development process – co-creation with patients

- **Phase 1: Generation of HRQoL issues**

Compiling an exhaustive list of relevant HRQoL issues based on three sources: literature, patients and health care professionals

- **Phase 2: Construction of the item list**

Issues is converted into questions with the format and time frame compatible with the EORTC QLQ-C30

- **Phase 3: Pre-testing**

Identify and solve potential problems in its administration (e.g., the phrasing of questions, the sequence of questions) and identify missing or redundant issues.

- **Phase 4: Field-testing**

Determine its acceptability, reliability, validity, responsiveness and cross-cultural applicability

Sarcoma-specific HRQoL?

 **EORTC** Item Library

64 questionnaires, 902 questions

 sarcoma

0 Results

Sarcoma - Heterogeneity

Subtypes:

Angiosarcoma

Malignant neoplasm in the vessel walls

Osteosarcoma

Tumor in a bone

Ewing's sarcoma

Bone

Chondrosarcoma

Cartilage

Hemangioendothelioma

Vascular neoplasms

Ages:

Localizations:

-Head and neck

-Thorax

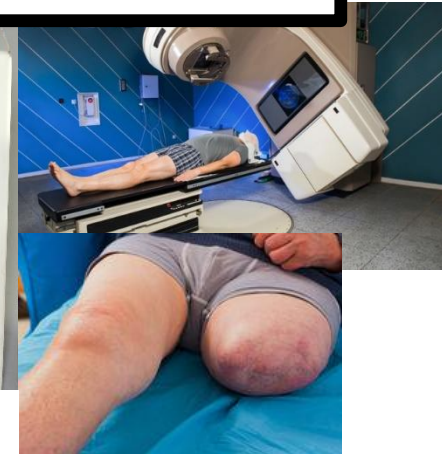
-Retroperitoneal /

intra-abdominal

logical

lower

What is the optimal measurement strategy for HRQoL among sarcoma patients?



1 cm

2 cm

4 cm

5 cm

Stages:

Treatments:

Ongoing EORTC QLQ-STBSG project

- Phase 1: Generation of HRQoL issues
- Phase 2: Construction of the item list
- Phase 3: Pre-testing
- Phase 4: Field-testing

Workplan(1)

Compile an exhaustive list of QoL issues relevant to sarcoma patients:

Phase 1 - Part A:



+



+



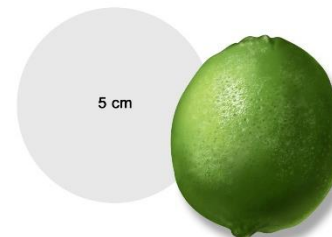
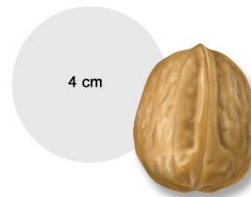
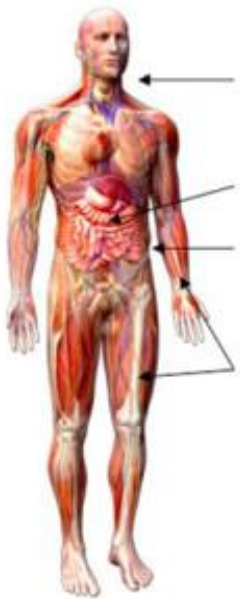
- Issues
- Used questionnaires

- Experiences
- Review questionnaire

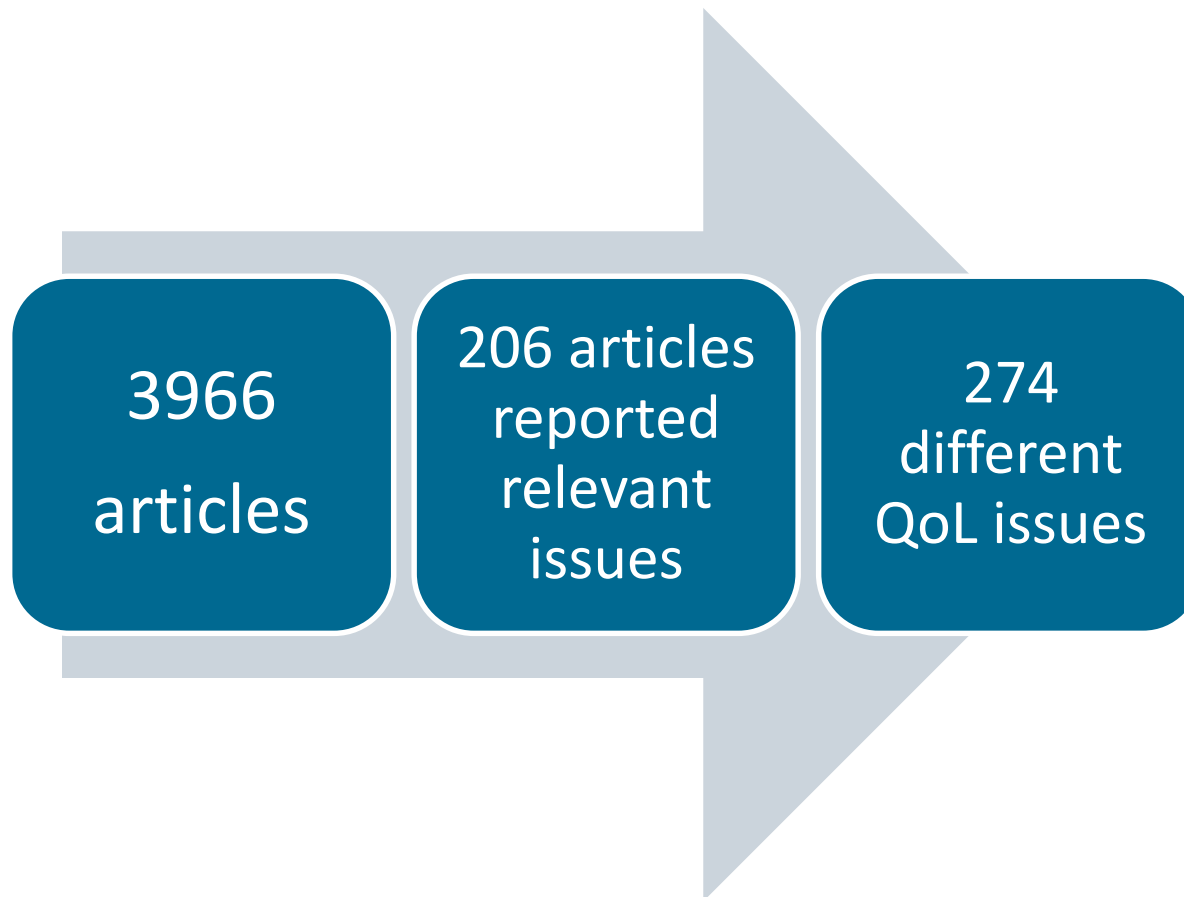
- Experiences
- Review questionnaires

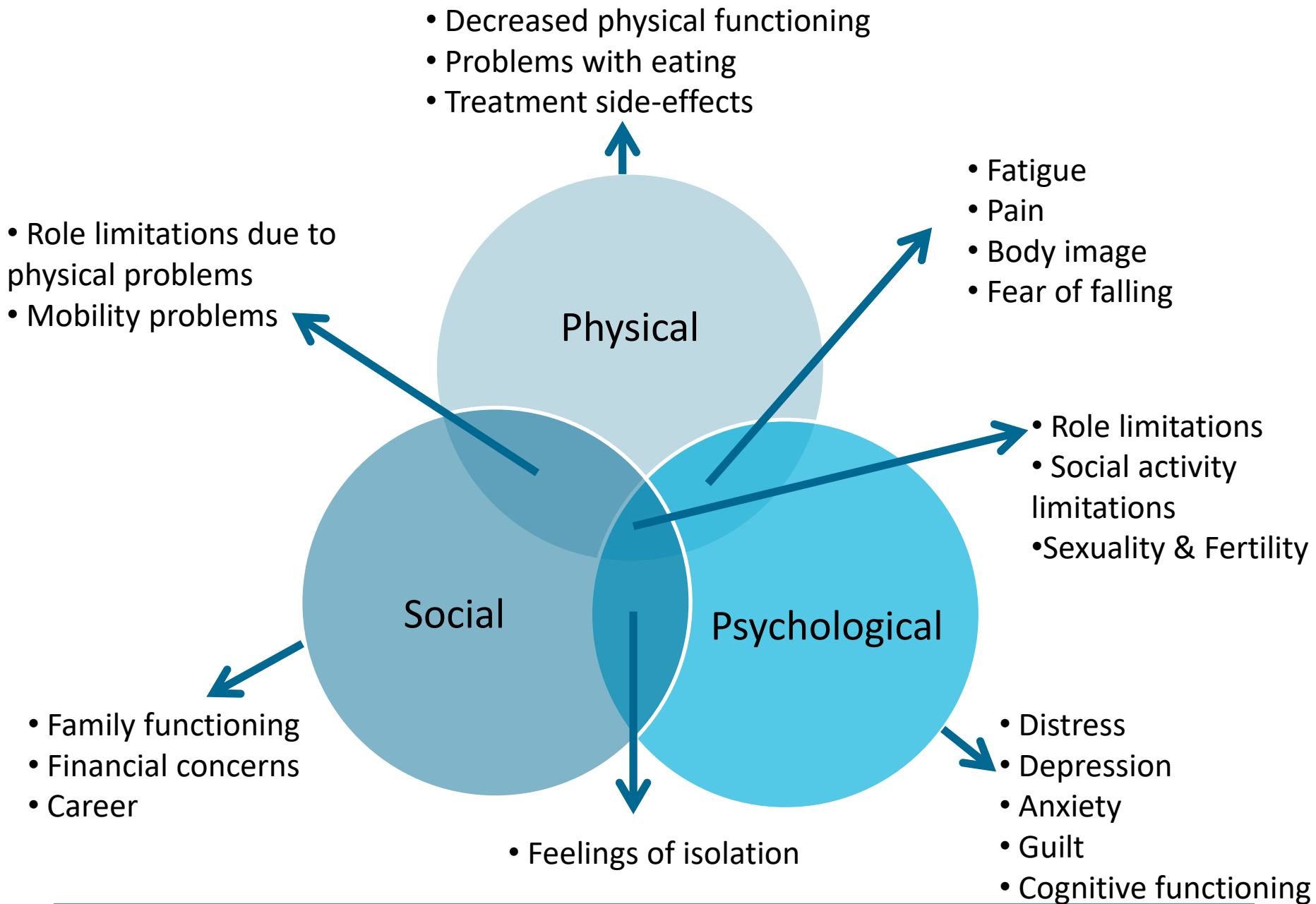
Workplan(2)

Phase 1 - Part B: 475 patients rate issue list on relevance and importance; indicate relevant issues missing from this list.



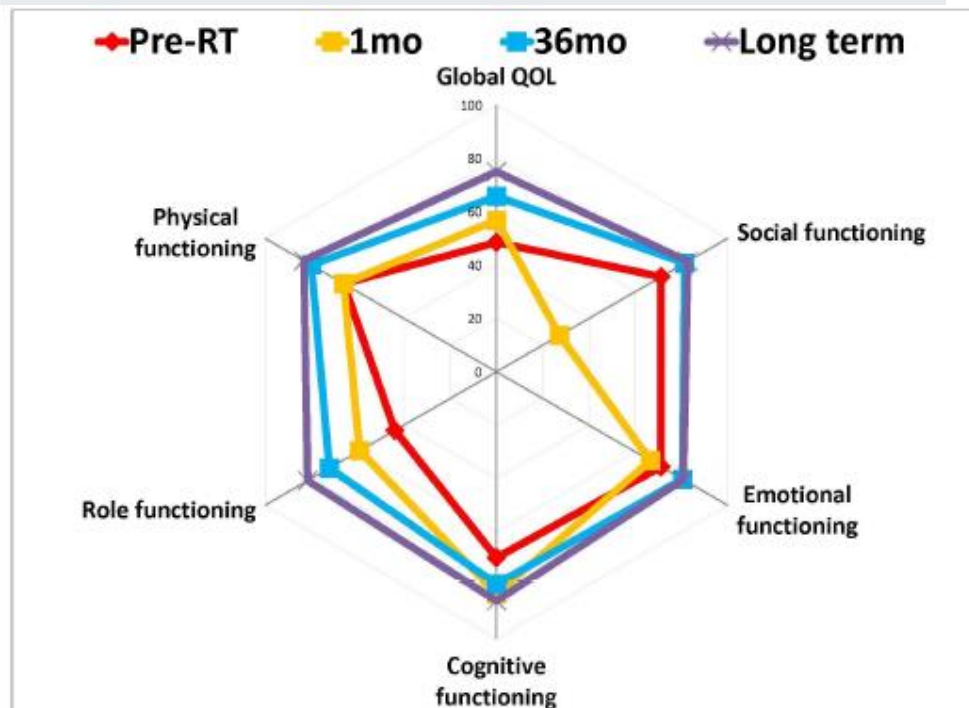
Results literature review





Retroperitoneal sarcoma: 2 articles

Surgery	Preoperative radiation + surgery
Sensory disorders of thigh, groin	Diarrhea during radiation therapy
Impaired motor function	Decreased social functioning during radiation
Need for crutches, falling	
Change in bowel habits	
Change in urinary habits	
Change in sexual function	



Callegaro et al. 2015, Wong et al. 2017

Extremity sarcoma: > 50% of articles

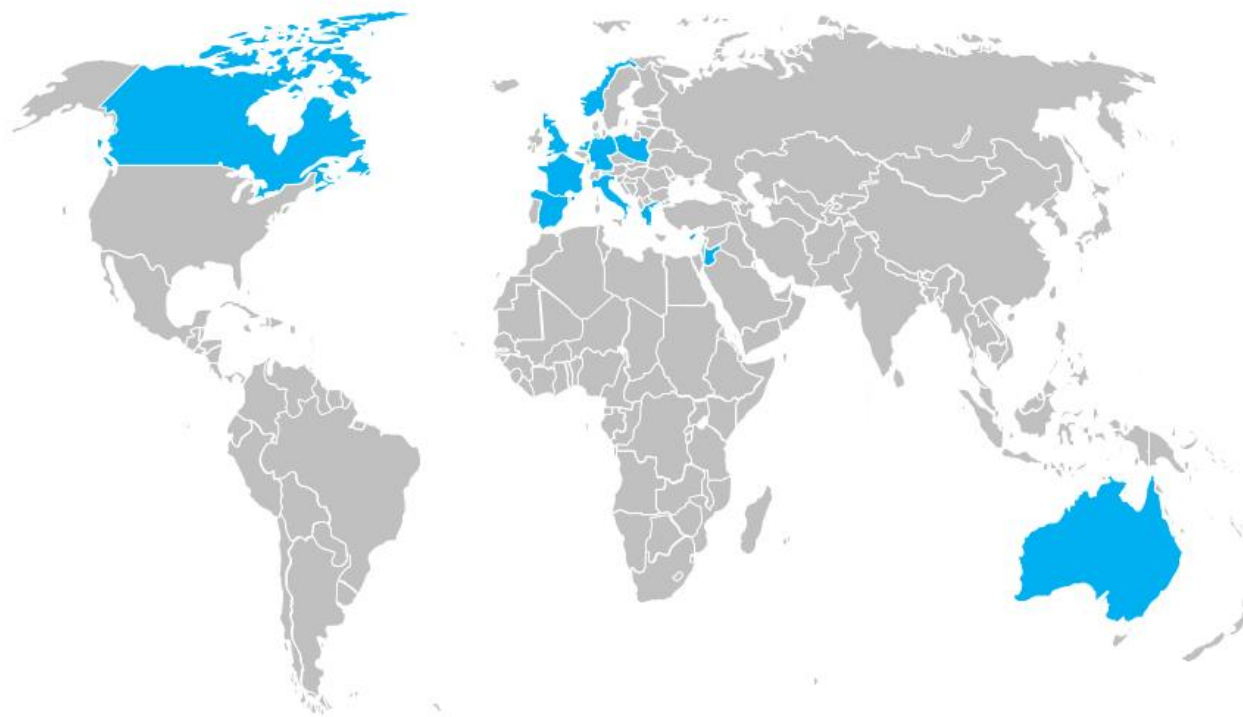


Athlete

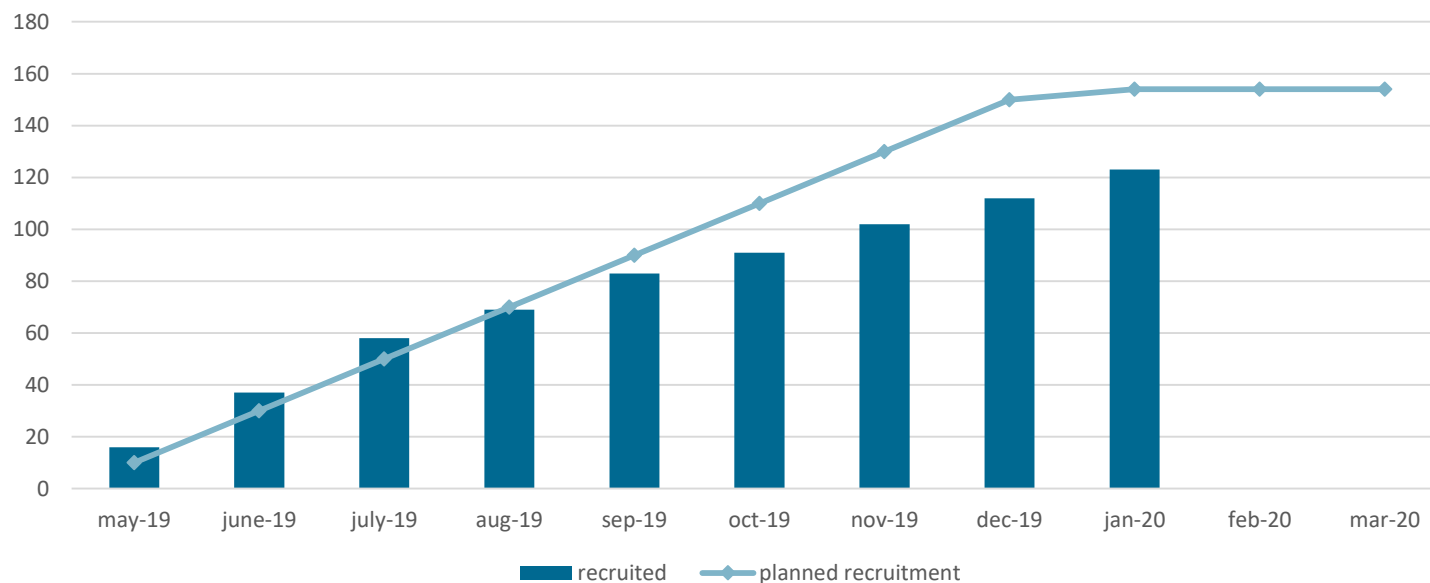


Needs ongoing assistance

Interviews: 26 sites in 12 countries

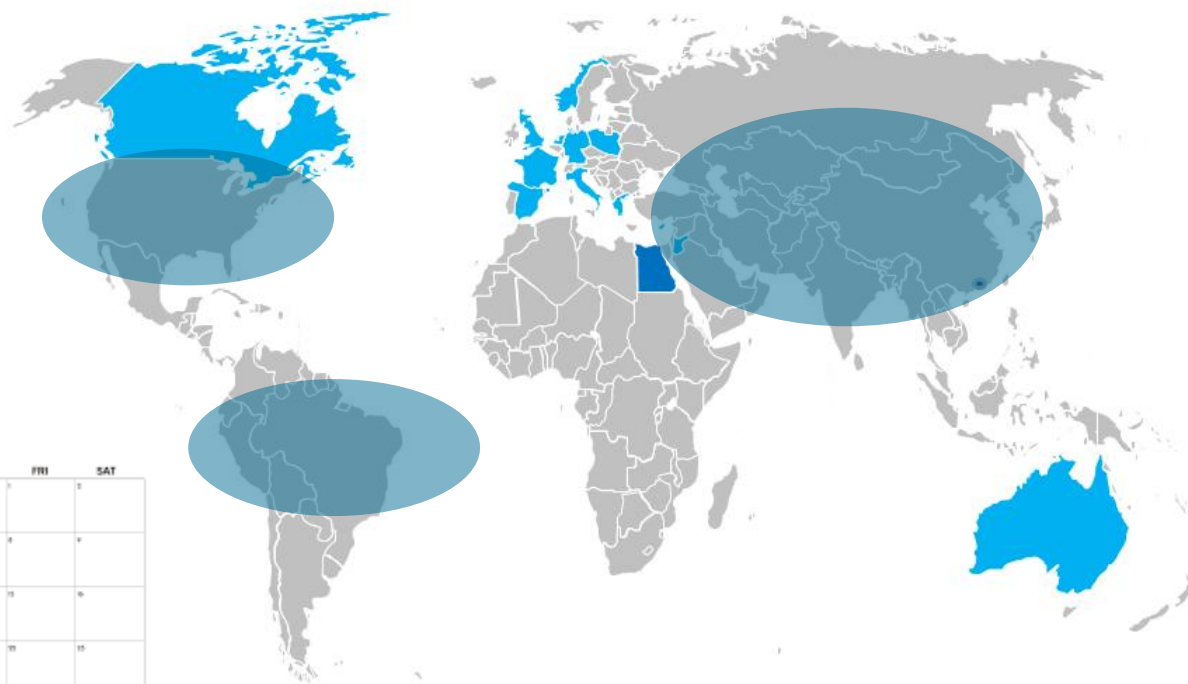


Recruitment phase 1a



+ 39 health care professionals from 9 countries

Phase 1b: 29 sites in 14 countries

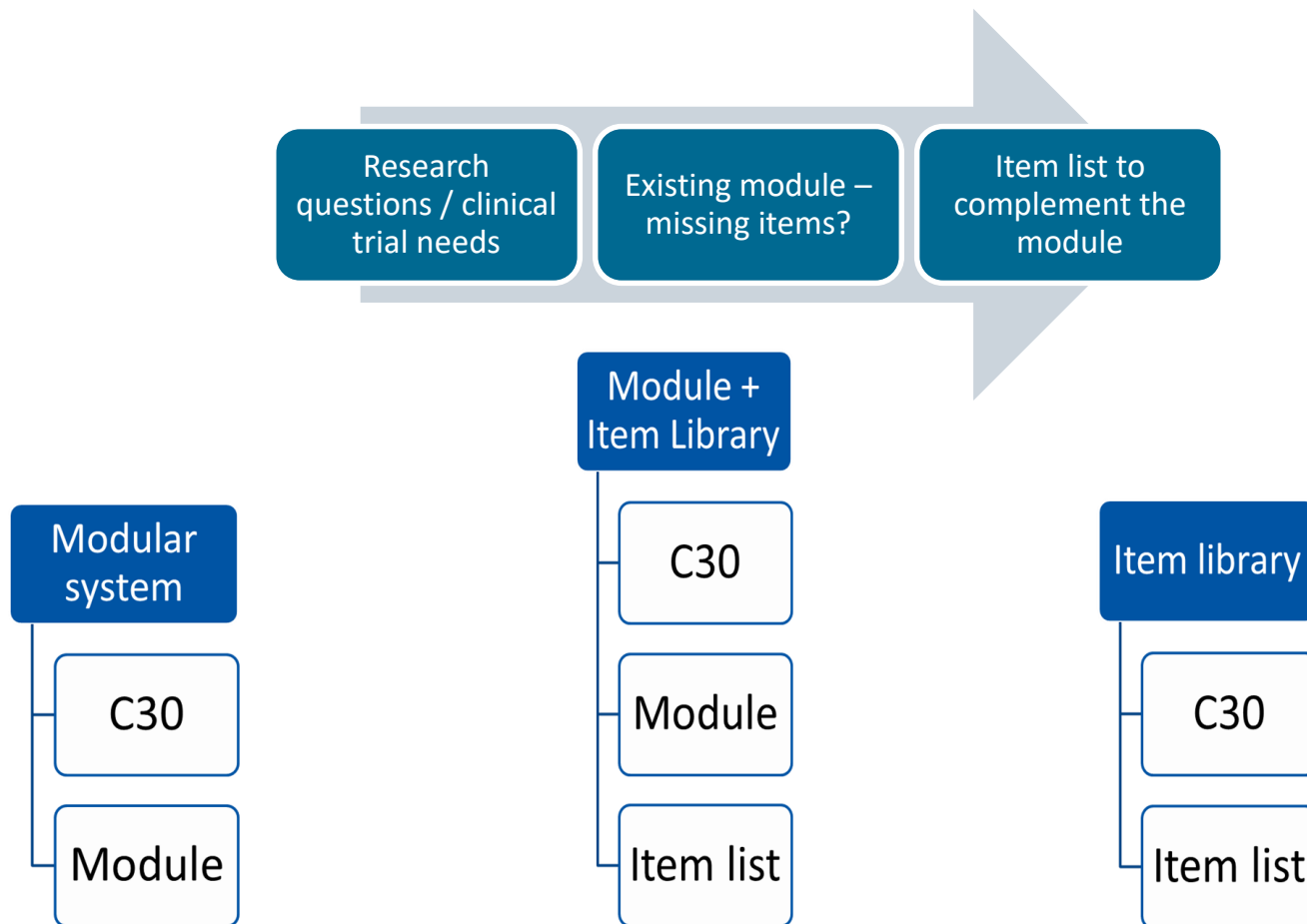


MAY 2020

SUN	MON	TUE	WED	THU	FRI	SAT
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

CC

Expected results



Questions or ideas?

Please contact us!

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