EORTC
European Organisation for Research and Treatment of Cancer
The future of cancer therapy

EORTC QUALITY OF LIFE GROUP

MANUAL FOR THE USE OF EORTC MEASURES IN DAILY CLINICAL PRACTICE

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- Thresholds for clinical importance are currently being developed for the EORTC QLQ-C30. They can guide health care professionals to correctly identify and interpret changes in QoL scores that are meaningful to patients. Clinicians explicitly state that they need threshold scores to enable them to correctly interpret the results for individual patients.

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- Successful integration of routine PRO assessments into the clinical routine is a complex health care intervention.
- Although standardizing design and delivery is challenging, there are commonalities and best practices that can be adapted and applied to improve the process of implementation.
- To guide integration, considerations need to be extended beyond technical and psychometric issues to additional factors related to diffusion of innovation and organizational changes that affect the uptake of routine assessments with EORTC measures.

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- Electronic assessment of EORTC measures requires both technical and educational infrastructure.
- Electronic versions have demonstrated generally to yield equivalent results to those generated by paper-and-pencil versions of EORTC measures. Electronic data capture prevents a double burden in administration, calculation and storage.
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- Even if PROs are assessed routinely at the hospital, there may be insufficient information about the patients' self-reported health experience after discharge and during follow-up.
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- Computerized adaptive testing will decrease patient burden and may enable very ill patients to participate as well.
- Privacy, confidentiality and disclosure are major issues in PRO assessments that always need to be addressed. This includes technical, regulatory and organizational issues.
- Efforts to include as many patients as possible need to be made, e.g. by systematically improving access to PRO and electronic PRO assessments for underprivileged persons.

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00. INTRODUCTION

Key messages:

- Patient-reported outcomes (PRO) are of crucial importance for monitoring quality of life and symptoms, and for assessing patients' needs adequately over the course of their cancer journey.
- The EORTC Quality of Life Group is engaged in the whole spectrum of quality of life research (instrument development, basic methodological research, advice on study design and data analysis, implementation of PROs and training of people engaged in PRO research, and application in clinical practice).
- This manual provides guidance on how to use EORTC quality of life and other PRO measures in daily clinical practice. It covers the methodological, technical and clinical issues driving the choice and implementation of EORTC-based PRO measurements in clinical practice.

The growing importance of patient-reported outcomes

Due to advances in treatment, cancer survival rates are improving and the nature of cancer care is changing. Some cancers are now being treated over the course of several years, even for patients with advanced-stage cancer, with the focus of care on long-term disease palliation [1]. However, treatment can be associated with various acute and chronic side effects. As such, there is now a growing demand to monitor the adverse effects of cancer and treatments on patients and to include these issues in clinical decision-making [2]. Dealing with cancer as a chronic condition, the patients' perspective on their quality of life (QoL, e.g. mobility, pain, fatigue, depression and familial/social issues) adds important information to high-quality cancer care, improving communication between health care professionals and patients [3-5], as well as continuity of care [6] and symptom management [7], and possibly enabling patient-tailored intervention [8, 9]. Chapter 1 provides detailed information on the benefit of such patient-reported outcomes (PRO) if used with the European Organisation for Research and Treatment of Cancer (EORTC) measures in daily clinical practice.

The EORTC Quality of Life Group

Since its establishment in 1980, the EORTC Quality of Life Group (QLG) has dedicated its intellectual and financial resources to the steadily growing need for comprehensive QoL research. The aims of the group encompass the whole spectrum of this area [10]:

- To develop reliable instruments for measuring QoL of cancer patients participating in international clinical trials
- To conduct basic research in the methodology of QoL assessment
- To advise the EORTC about the assessment of the multidimensional aspects of patients' QoL as a measurable outcome of cancer treatment
- To advise on the design, implementation and analysis of QoL studies within EORTC trials, in collaboration with the Quality of Life Department at the EORTC Headquarters

- To contribute to teaching/training initiatives to promote the EORTC approach to QoL assessment e.g. through preparation of teaching material, oral presentations, etc. in collaboration with the EORTC Quality of Life Department

Accordingly, the EORTC QLG provides high-quality information on important issues of QoL assessment and research by publishing several manuals [11].

The purpose of this manual

This manual aims to provide guidance for both health care professionals and researchers on how to use these EORTC measures in daily clinical practice. It describes methodological, technical and clinical aspects of the implementation, choice and use of EORTC measures. To date, the work of the EORTC QLG has resulted in a large number of instruments, including stand-alone questionnaires, validated modules and work-in-progress modules, an item library, and an "experimental" computerized adaptive measure for the EORTC QLQ-C30 (please refer to Chapter 2 for more details).

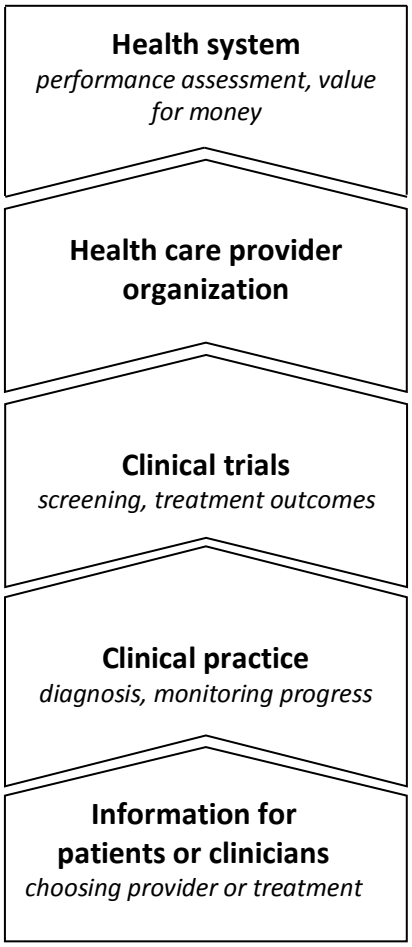

Figure 1 Uses of patient-reported outcome measures, slightly modified [20]

EORTC measures have a broad range of applications, as patients' QoL has become a significant outcome measure in clinical trials over the last three decades. PRO data are routinely collected alongside biomedical outcomes such as progression-free and overall survival to assess the value of a given therapeutic intervention. QoL has also been found to predict response to treatment and to be associated with survival [12-18]. Depending on the specific purpose of PRO data collection, which changes over the course of the cancer journey, assessment time points (Chapter 3), score calculation (Chapter 4) and presentation of results (Chapter 5) play an important role. For successful implementation of an innovation like routine PRO assessments, an adequate strategy is needed that includes all types of future users (e.g. patients, health care personnel, organizational) and gives guidance for the whole spectrum of the implementation process (Chapter 6). Electronic assessment of PRO instruments offers many advantages over traditional paper–pencil assessments, but needs special IT requirements and financing up front (Chapter 7). It will, however, quickly yield good results, especially if patients are given the opportunity to provide data from their homes as well (so called "telemonitoring"; see Chapter 8). The use of EORTC measures is not restricted to the most prominent contexts of clinical trials and routine clinical practice. Their profile is complex, including individual and group-level as well as societal issues. Discussions have begun about starting to use PRO as a quality indicator when assessing service delivery and outcomes [19]. Figure 1 depicts possible levels for implementation of PRO instruments such as the EORTC measures [20]. Although this manual particularly promotes the use of PRO assessments in clinical practice, it also deals with fields of application of the EORTC measures beyond clinical trials and routine care (Chapter 9) and ethical considerations (Chapter 10).

01. RATIONALE FOR USING EORTC MEASURES IN DAILY CLINICAL PRACTICE

Key messages:

- EORTC measures are cancer-specific, multidimensional, and cover a broad range of physical and psychological symptoms, as well as the impact on daily functioning.
- EORTC measures are available in many different languages and show high levels of cross-cultural validity.
- EORTC measures have shown to be beneficial for routine care, as they cover both symptoms and the impact on functioning, are well accepted by patients, can improve communication between health care personnel and patients, and enable facilitated shared medical decision-making and personalized care.
- Most common barriers to the routine use of EORTC measures can be overcome by following an appropriate implementation strategy.

The regular assessment of patients' symptoms, functioning and QoL in daily oncology practice can be useful for obtaining information on how patients experience their illness and evaluate their QoL, supporting shared decision-making when it comes to treatment choices or adjustments because of toxicities, continuity of cancer care, and referral to supportive care. Hence, assessment of patients' QoL is recommended in evidence-based national guidelines for cancer care (e.g. in the Netherlands, Germany or in the USA [21-23]).

EORTC measures are especially suitable for use in daily clinical practice

The available EORTC QoL measures have been carefully developed following detailed guidelines, including an extensive validation process [24]. The basic core questionnaire is suitable for all cancer diagnoses [25] and can be supplemented by a variety of disease-specific modules (e.g. lung or breast cancer), single items taken from the EORTC item library or additional questionnaires that cover further important issues (e.g. information on patients' satisfaction). Consequently, the multidimensionality, broad coverage of various physical, psychosocial symptoms and functions, and variability are major strengths of the EORTC measures for routine use. In addition, the EORTC measures can be useful tools for early detection of adverse events and therefore used for symptom screening and monitoring. EORTC measures are not only one of the most popular and often-used PRO instruments for cancer patients, but the EORTC QLQ-C30 is also preferred by patients [26, 27] and has attested a high acceptability [28]. As the development of EORTC measures already attaches importance to cross-cultural appropriateness [24], and high-quality translations [29] are available, the PRO instruments have been shown to be applicable across multiple nations and nationalities [30-32]. To enhance accessibility of routinely collected PRO data and to improve their acceptance by health care professionals, PRO should be assessed electronically and their results integrated into the existing electronic medical record [33-35]. There are already many different software solutions available [36, 37], many of which are equipped with a special interface for connection with electronic health records (EHR; for further details refer to Chapter 7).

Patient–physician communication

Several studies have provided evidence that the regular use of PROs, including the EORTC measures, facilitate and improve communication between patients and health care professionals [4, 6, 38, 39]. Physicians who have access to patients' self-reports are more likely to discuss intimate and less commonly addressed issues [3, 7, 40], to develop an increased awareness of patients' functioning and well-being [3, 7], and to discuss chronic non-specific symptoms [5], without prolonging consultation time [3, 5, 41-43].

Shared medical decision-making

The use of PROs in clinical routine has the potential to enable shared medical decision-making as patient participation is enhanced [44]. As patients' perceptions of "acceptable" adverse events may differ from those of clinicians, truly informed decision-making needs to incorporate the patient perspective by collecting comprehensive self-report data, for example from the EORTC measures. PRO data could enhance shared decision-making in different ways: one might use the individual patient scores for identifying QoL issues needing further intervention (medical, psychological, psychiatric or social); or group-level data from clinical trials could guide treatment choices, taking a patient's preferences into account. Successful shared decision-making can positively affect patients by enhancing confidence in the treatment decision, satisfaction with treatment, mental health and self-efficacy as well as a greater trust in health care professionals [45].

Referral to supportive and palliative care

By assessing PRO on a regular basis and applying cut-off scores, patients can also benefit from an appropriate referral to specialists such as psychologists, social workers, or physical therapists. In older patients with advanced cancer, the additional collection of patient-reported data via telephone enabled a more timely referral to psychosocial interventions and consequently better anxiety and depression management than educational material alone [46]. PRO completion revealed in one third of female cancer patients the need for psychosocial referral (e.g. regarding stress management, coping with diagnosis and financial difficulties) [47] and identified in 29% of head and neck cancer outpatients emotional distress, of which only 18% already received psychological or psychiatric treatment [48]. More than half of the patients using an electronic system for PRO data collection, score calculation and presentation and provision of personalized supportive care options were interested in being given advice for supportive care, and nearly one third of those patients actively engaged in one of the provided care options [49]. Compared to the medical records, PRO assessments, using amongst others the QLQ-C30, additionally capture symptoms like fatigue and sleep disturbances [50], thus enabling appropriate intervention. Electronic PRO data capture can improve distress management via involvement of a multidisciplinary team (e.g. automated notifications to specialized health care professionals) [51].

Continuity of care and personalized/patient-centred health care

Patients who completed the EORTC QLQ-C30 and whose PRO results were available to clinicians rated their continuity of care as being better than those patients who did not complete any PRO measures [6]. Additionally, when compared to patients who only completed PRO questionnaires without feedback, patients who received clinician feedback felt to a greater extent that their treatment considered their daily activities, emotions and QoL [6]. Another study did not find any effect of feeding back EORTC QLQ-

C30 data to nurses on patients' perception of their continuity of care, but patient satisfaction was very high in both groups [7]. Continuity of care plays an important role as cancer becomes a more chronic disease and people with advanced-stage cancers live longer. Consequently, care pathways for various patient groups according to the phase of their cancer journey are needed, such as developing policies for the use of PRO instruments for cancer survivors receiving survivorship care and for advanced cancer patients receiving palliative care. Especially for those patients with long intervals between follow-up appointments, assessment with EORTC measures via the internet can be useful for screening for physical symptoms or emotional distress (e.g. fatigue, anxiety, and depression), evaluation of rehabilitation interventions, and psychosocial, supportive or palliative care [52]. Linking results of PRO assessments to tailored, specific health care interventions can provide advice to patients on how they can self-manage symptoms and guide them if they need further medical assistance and should consult their health care team [49]. Since this is a relatively new area of application of PRO instruments, further development of existing tools and their scientific evaluation is warranted.

Linking routine assessments to research purposes

As already mentioned, specific software solutions for EORTC measures offer the possibility of linking self-reported data to EHR or other medical registries, which support clinicians in both therapy-associated data interpretation and scientific data processing. The successful implementation of routine PRO assessments with EORTC measures facilitates the conduct of QoL studies within both highly selected and real-world patient samples, as data sets can be tailored according to research questions that arise, or all available data can be analyzed together. Furthermore, scientific data analysis of repeated patient self-reports can increase knowledge of the development of the disease with respect to applied treatments and related quality of life.

Contribution to quality assurance

EORTC measures allow the incorporation of patient perspective into clinical practice, as there is strong evidence that clinicians' ratings alone do not present a complete picture of cancer patients' symptom burden, but systemically underestimate how patients perceive the severity of their symptoms and disease [53-56]. Consequently, routine assessments with EORTC measures can contribute to high-quality and adequate treatment in various ways (e.g. in terms of an improvement in the accuracy of symptom reporting [36], early detection of changes in QoL and monitoring of treatment). For more details on the potential benefit of EORTC measures for quality assurance issues please refer to Chapter 9.

Major barriers to the routine use of EORTC measures

Even though there are many reasons why EORTC measures should be an integral part of routine clinical care, there is still a long way to go to reach this goal. Barriers can include individual, structural and organizational factors. One of the most frequently reported reasons for clinicians not engaging in routine PRO assessment is a low familiarity with the concept of PROs and available validated questionnaires like the EORTC measures. Additionally, health care professionals might be concerned that incorporating PRO instruments disturbs their workflow, decreases efficiency and adds to their already existing workload, creating new responsibilities for issues important to patients and for which they do not feel sufficiently prepared. To many clinicians, the benefits of PRO data may seem theoretical and their assessment to be more laborious than useful. Others think that their rating of patients' health

status and QoL is a sufficient source of information, and some are simply reluctant to change [57, 58].

On the patients' side, the biggest reason for denial of PRO instrument completion is apprehension of the additional burden. Some patients fear they will lose personal contact with their health care professionals if they provide information via a questionnaire [57, 59].

However, integrating EORTC measures into routine clinical care is a process dependent upon more than just the clinicians' and patients' motivation. Factors in the local context, such as organizational culture and leadership, feedback on performance, and facilitation can be equally influential. Structural problems may furthermore include difficult or complex team structures or insufficient preparation of technical requirements, such as availability of enough and appropriate electronic assessment devices, stable internet connection, and necessary software support.

Most of these barriers can be overcome by following a tailored implementation strategy (please refer to Chapter 6 for further details) right from the start, if PRO measures are supposed to be introduced to an existing working routine. The published literature also offers strategies to improve the acceptance and implementation of routine PRO assessments, e.g.[57].

Areas for further research

Linking PRO data to electronic health records (EHR) can increase their retrieval by health care personnel [33] and seems to be an effective method for their integration into existing care pathways [60]. Although it seems reasonable to link electronic data assessment of PRO with EHR, and existing software solutions already have interfaces available (please refer to Chapter 7) or their connection to EHR has been tested in clinical trials [61], further research is needed to develop standards of, for instance, instrument choice and templates, choice of presented data, and presentation design. As there can be tension between the interests of different stakeholders engaging in PRO data (patients, health care personnel, clinical management, insurance companies, etc), science also needs to address issues like customizability of electronic PRO systems, perception of PRO data and their usefulness by health care personnel, and recommendations or standards for timing of assessments and best practices of utilizing PRO data in routine care and research alike [62].

02. SELECTION OF EORTC MEASURES

Key messages:

- The choice between the EORTC QLQ-C30, EORTC modules, the EORTC item library and the EORTC CAT measures or a combination of these measures facilitates the use of appropriate PRO instruments in a variety of PRO assessment settings.
- The psychometric properties of EORTC QoL measures are stable across modes of administration (paper–pencil or computer-based), cultures and translations. These measures carry with them only modest patient burden.

Choosing appropriate PRO measures for a study requires prior clarification of several questions (e.g. the content of the questionnaire, its psychometric properties, cultural issues and available languages). Because of rigorous development guidelines [63], using EORTC measures ensures the appropriateness of the instruments' psychometric properties, as these are extensively tested and evaluated. Nonetheless, users need to choose which of the available EORTC measures they want to use and whether computerized adaptive testing (CAT, EORTC CAT measures) could be an option to be used along with the conventional EORTC QLQ-C30.

EORTC QLQ-C30 and EORTC modules

From the outset, the EORTC QLQ-C30 is a generic QoL questionnaire designed to cover issues important to all cancer patients, although it can be tailored to have disease specificity. It can be complemented by modules focussing on particular diagnoses, treatment modalities or additional QoL domains. There are a large number of modules, some of them already validated and available for use, some awaiting psychometric evaluation, and others still under development [64]. For detailed information on the development procedure of EORTC measures, please refer to the development guidelines [63].

The EORTC QLQ-C30 and its modules are static EORTC measures; in other words, the content and length of the questionnaires can only be adapted to a limited degree. They may be complemented with selected items taken from the EORTC item library to increase specificity of PRO assessments. Shortening of the EORTC QLQ-C30 can only be done if complete single scales are used (e.g. all questions of the social functioning scale need to be used to assess social functioning), as doing otherwise compromises their psychometric properties.

EORTC item library

The EORTC item library (http://www.eortc.be/ItemLibrary/) encompasses all items developed for EORTC measures and their translations, and stores information on their wording. The purpose of this database is to classify available data (around 1,100 items representing 635 unique questions in English), to speed up the item construction procedure in phase II of module development, and to allow rapid creation of new item lists to be used in conjunction with already existing EORTC measures. The item library can be accessed online and a search function provides information on whether a specific issue is already covered by any of the available EORTC measures or indicates which of the existing items can be used to assess the issue, for example, new symptoms or treatment-related side effects. The item library can also be used to create an ad hoc trial checklist when a specific module or tool is not available for an

individual trial or for patient monitoring in clinical practice.

EORTC CAT measures

Computerized adaptive testing (CAT) offers several advantages over the use of conventional PRO measures by reducing patient burden, focussing on questions relevant for patients and increasing measurement precision (in particular for the individual patient). Items presented to patients are chosen based on preceding answers, constructing a patient-tailored instrument with each assessment. A previously defined level of measurement precision or maximum number of questions regulates how many items are presented. The increased measurement precision at patient level is important for the use of the EORTC measures in daily clinical practice, where individual patient scores are more relevant than group-level statistics.

The EORTC CAT is a newly developed CAT instrument measuring the same functions and symptoms as the EORTC QLQ-C30. For each domain, an item bank has been created with the items and their psychometric properties. The measurement characteristics have been determined based on an item response theory model. In this way, patient scores obtained by EORTC CAT measures are directly comparable to scores derived from the QLQ-C30 [65-73].

Thus, EORTC CAT measures are characterized by high measurement precision, high flexibility, reduced floor and ceiling effects and less non-informative questions. Another advantage is their backward compatibility with conventional EORTC QLQ-C30 data. The EORTC CAT measures are undergoing full psychometric validation in an international EORTC field study, which will be completed by 2017. Currently the CAT measures can be used as an extension of the conventional EORTC QLQ-C30, for example, for validation purposes [74]. It has to be considered that the EORTC CAT measures can only be administered on electronic devices (e.g. tablet PCs). The software used for electronic questionnaire administration needs to be capable of linking to the official EORTC CAT engine, a program that provides the CAT algorithm for item selection from the EORTC item library. As an alternative, for example, if electronic administration is not possible, so-called short forms, that is, classical static (paper) questionnaires, can be constructed based on the EORTC item library and the CAT item bank. Short forms can be tailored to fit the target population.

Other practical considerations

Mode of administration: All EORTC measures are available for paper–pencil assessment. In the context of a collaborative project, the CHES software (**C**omputer-based **H**ealth **E**valuation **S**ystem) [75] is provided as a special CHES.EORTC version, which enables online assessment with EORTC measures, including the EORTC CAT. There are a large number of other specialized software solutions for ePRO assessment, which mirrors the growing interest in an electronic mode of administration, data calculation and storage [36, 37]. As their availability is variable and often limited, the EORTC QLG decided to engage in the development of CHES as a widely accessible tool offering a variety of features associated with ePRO (please refer to Chapter 7 for more details on the infrastructure for routine electronic assessment with EORTC measures). Next to paper–pencil or classic electronic assessment of PRO data, an interactive voice response system (IVRS) can be a mode of administration to include patients who would otherwise not be able to complete such instruments, for example due to vision impairment, computer illiteracy or higher age. Up till now, equivalence of IVRS and paper–pencil version, and psychometrics of IVRS data, have only been tested for the EORTC QLQ-C30, but have been widely confirmed [76, 77].

Cultural aspects and translations: The development of EORTC measures includes various languages and cultures at all stages of the process to ensure cross-cultural consistency [63]. The translation of EORTC measures and documents needs to follow comprehensive guidelines specially developed for this purpose [29]. The EORTC QLQ-C30 is available in more than 95 languages and the number of translations of other EORTC measures is steadily increasing. For academic use, all available EORTC questionnaires and modules can be downloaded from the QLG website [64], with the opportunity to choose translations, scoring manuals, reference values and the current QLG newsletter.

Amount of information and patient burden: The use of EORTC measures must not overstrain patients' time, effort, and physical or emotional resources; consequently, as few instruments as possible should be chosen to gather the information needed (please refer to Chapter 3 for more details on patient burden and effort for health care personnel).

03. ASSESSMENT TIME POINTS

Key messages:

- Inappropriate timing of assessments can result in a failure to capture, or a misinterpretation of, important information about patients' symptom burden and functional health.
- Frequency of assessments depends on their purpose and the stage of cancer treatment or follow-up. For example, evaluation of QoL during chemotherapy may require a different schedule of assessments than long-term routine QoL monitoring.
- When determining the time and frequency of assessments with EORTC measures, different factors need to be balanced, such as workload for health care personnel, patient burden, and aspects like disease stage and current treatment of patients.

Alongside adequate psychometric properties of EORTC measures, the timing of their use plays a crucial role in gaining reliable information on patients' QoL and its development over the disease course. Although the issue of the correct timing of PRO assessments has already been identified as a potential biasing factor [78-81], until now, only minimal research effort has been spent on developing evidence-based guidelines for the timing of QoL capture in various settings. Available recommendations are primarily based on expert opinion [82, 83].

Adequate time points of assessments with EORTC measures

As the timing of EORTC measures can meaningfully change data, the time points should be chosen carefully. The literature regarding adequate time points for the use of EORTC measures is not comprehensive and lacks evidence-based results and, thus, recommendations. Overall, the timing of the use of EORTC measures should consider the timing of possible clinical changes, which requires comprehensive knowledge of the disease and specific cancer types, treatment effects and their interaction [82], or at least elaborate hypotheses concerning this matter. Premature or delayed assessments might miss important information. It has been shown that QoL measurement conducted only on the day of ambulant chemotherapy administration results in a systemic underestimation of patients' QoL [84]. This finding illustrates the importance of an elaborate assessment schedule which takes into account the time frame required by the chosen PRO instrument (e.g. EORTC measures in general refer to the week before the actual assessment).

Frequency

It is necessary to predefine the frequency of assessments with EORTC measures. Similar to the issue of adequate time points of assessments, their frequency depends on what one wants to know: Are EORTC measures used for routine monitoring of inpatients or outpatients undergoing actual treatment? Is their purpose to evaluate applied interventions for QoL stabilization or improvement? Are they supposed to capture patients' QoL over time, even when they are not at the hospital? Those single aspects may overlap, which is why multiple considerations should ultimately determine the frequency of assessments with EORTC measures.

Klee et al. [85] developed a clinical model for determining assessment time points and frequency that differentiates between types of symptoms (acute, chronic, disease-related or not), which was tested on

a relatively small sample of newly-diagnosed ovarian cancer patients. Using a disease-specific PRO instrument, Hollen et al. [86] report a three-times-a-week assessment interval as being as useful as twice a week. In this study, only a one-item overall QoL scale was used for analysis, which is why the reported results need to be analyzed critically, as such overall scales might not reflect changes occurring in QoL subdomains. For instance, it has been shown that the EORTC QLQ-C30 overall QoL scale remained stable, despite declining scores on individual scales [87]. Although less frequent assessments might be helpful to minimize patient burden and efforts of health care personnel, the gathered data could miss important information about patients' health status.

Rationales for the choice of assessment time points

Consequently, there are different rationales for the timing of assessments with EORTC measures. They might be conducted when specific events occur (e.g. scheduled outpatient visits or hospital admission) or follow a fixed time schedule (1, 3 and 6 months after discharge). In any case, the schedule of assessments with EORTC measures should refer to the purpose of their use; for example, the detection of the need for supportive care requires a sufficiently long period of repeated assessments [87]. Often, timing is related to more pragmatic rationales, like assessment at clinical follow-up appointments. In this way, additional trips to the hospital are reduced and compliance might be enhanced. However, such assessment time points do not necessarily relate to rationales, which are taking the disease, effects of treatments, or worsening/improvement trajectories into account and may consequently gather data with reduced informational value. Remote monitoring using the internet may overcome this issue and allow adequate assessments to be planned.

Patient burden and effort for health care personnel

Considering all the above-mentioned issues, it is important to strike a balance between the number of EORTC measures used and their expected benefit. The associated effort needs to be reasonable and useful for both patients and health care personnel. Patients undergoing active treatment might benefit from closer monitoring to detect recent changes in their QoL, which possibly require interventions (such as dose reduction or changes to supportive medications). This might not be the case for relatively healthy patients who attend follow-up appointments and may become annoyed by frequent assessments. Furthermore, health care professionals' skills regarding the interpretation of PRO data gathered with EORTC measures and integrating them into their practical work are of special importance and should be specifically addressed with educational programs [88-90].

04. SCORING OF EORTC MEASURES FOR USE IN DAILY CLINICAL PRACTICE

Key messages:

- Calculation of scores for EORTC measures should follow standard procedures as described in the scoring manual.
- High scores on the functioning scales indicate better functioning, whereas high symptom scores represent higher levels of symptom burden.
- Score interpretation can be aided by the availability of reference values for different cancer patient populations, the general population, and specific age and gender groups.
- Thresholds for clinical importance are currently being developed for the EORTC QLQ-C30. They can guide health care professionals to correctly identify and interpret changes in QoL scores that are meaningful to patients. Clinicians explicitly state that they need threshold scores to enable them to correctly interpret the results for individual patients.

Psychometrics

EORTC measures comprise a substantial number of scales with scores being calculated from a single item or multiple items. All scales are scored on a metric from 0 to 100 by adding the individual items and transforming them linearly [91]. Within the EORTC framework, there is a distinction between functioning scales (for which a score of 100 indicates a good health status and a score of 0 indicates severe impairments) and symptom scales (for which 0 indicates low or no symptom burden and 100 indicates severe symptoms). The valence (direction) of a scale is usually evident from the name (e.g. for "Pain" a score of 100 indicates high levels of pain, whereas a score of 100 for "Emotional Functioning" indicates good mental health)[92].

Reference values and thresholds

To facilitate the interpretation of EORTC scores, the scores on the standard 0 to 100 metric can be related either to reference populations or to thresholds for clinical importance.

Reference populations such as the general population or specific groups of cancer patients allow health care professionals to appraise patients' health status through comparison, using either percentiles or score transformations such as T-scores (a standardized distribution with a mean of 50 points and a standard deviation of 10 points) [93].

Score interpretation

The use of T-scores or percentiles highlights a common problem with interpretation of scores. Frequently, health care professionals and researchers alike falsely assume that a score such as 33 points on the nausea/vomiting scale and 33 points on the sleep disturbances scale indicate the same symptom level. It is important to note that first, scores from different scales are not directly comparable as the questions themselves may refer to different symptom levels. Second, using general population norms, it

becomes obvious that 33 points for sleep disturbances deviate less from the general population mean than 33 points for nausea/vomiting (general population [94]: sleep disturbances mean 14 (SD 23), nausea mean 3 (SD 23)). In addition, comparability of scales is further limited as the various scales comprise different numbers of items resulting in varying differences between possible scale scores.

Reference populations

Reference populations can be used to calculate T-scores or percentiles to facilitate interpretation of EORTC scores. For such a normative scoring, the population has to be selected carefully to obtain meaningful results. For example, the general population may be a good comparator for disease-free cancer survivors that are supposed to have a good quality of life, low symptom burden and high level of functioning. In contrast, for patients in the palliative care setting, the more suitable reference population may be patients with the same stage of disease receiving comparable treatment regimens. In addition, decisions have to be made with regard to whether or not to adjust for age and gender of the patient. Adjusting may be reasonable for functioning domains and symptoms for which the literature suggests an impact of gender and age (e.g. physical functioning). However, the differences with regard to certain factors, such as sleep disturbances, found in the general population [94] may not justify the use of different thresholds for men and women.

Thresholds for clinical importance

Recently, there has been an increase in studies aimed at establishing thresholds for clinically important levels of symptoms and problems for the EORTC QLQ-C30 to improve interpretability of scores in daily clinical practice [95-97]. Such thresholds allow health care professionals to discriminate between patients with and without clinically important problems, help them to screen patients, and can guide the discussion about PRO results between the patient and the health care professional.

There are already a small number of studies available from the literature that developed thresholds for the EORTC QLQ-C30 using anchors such as patients' care needs [95, 97] or patients' prioritisation of specific symptoms and impairments [96].

Within an ongoing cross-cultural project funded by the EORTC Quality of Life Group, thresholds for clinical importance are being developed for all scales of the EORTC QLQ-C30. The project comprises interviews with patients and health care professionals to investigate what makes a symptom or impairment clinically important, enabling the creation of adequate anchor questions. In a next step, these anchor questions can be used to determine thresholds for clinical importance for the QoL domains covered by the EORTC QLQ-C30. The thresholds will improve identification of problems and symptoms which should be discussed in a clinical setting.

05. PRESENTATION OF RESULTS OF EORTC MEASURES

Key messages:

- To make scores of EORTC measures easily accessible and interpretable to health care professionals and patients, the choice of presentation format can be important.
- Presentation of results needs to fit its purpose: presenting group-level data from clinical trials to facilitate patients and their caregivers in making clinical decisions about choice of treatment may be different from presentation of results from individual patients for use in routine care.
- Health care professionals need adequate training and patients need adequate information to ensure correct interpretation of the results of EORTC measures.

Incorporation of EORTC measures into daily clinical practice requires a presentation of results, which is easily accessible and understood by the recipient (e.g. health care professionals and/or patients).

Graphical presentation formats

In studies investigating the use of EORTC measures in daily clinical practice, results are usually presented as graphical charts displaying cross-sectional or longitudinal patient data. Whereas other formats such as tables or text descriptions are possible, graphical presentation is advantageous because of the possibility of displaying comprehensive data from multiple domains and time points at a glance.

Available literature on graphical presentation formats for the QLQ-C30 mostly focus on group-level data [98] from clinical trials. Such data can be used to inform the patient about the impact of a certain treatment and can support shared medical decision-making. Two recent studies [99, 100] investigated presentation styles for PRO results from individual patients, which is of relevance to the use of PRO data in daily clinical practice. These studies, comparing different types of line and bar charts and heat maps, demonstrated a need to help patients and health care professionals to understand the scale direction (valence). While the current state of research is not conclusive enough to make a definite recommendation on the optimal chart type, it is likely that patients and health care professionals may have different preferences with regard to chart type and amount of information contained in the charts. The use of training and information materials for patients and health care professionals is likely to improve the correct interpretation of the results of the EORTC measures.

Electronic results presentation

Below we give an example of the graphical presentation of QLQ-C30 results displayed in the CHES.EORTC software. Figure 2 shows results for selected QLQ-C30 scales from an individual patient assessed at six time points. For comparison, the same results are displayed as line and bar charts. The colour coding in the charts reflects general population norms [93].

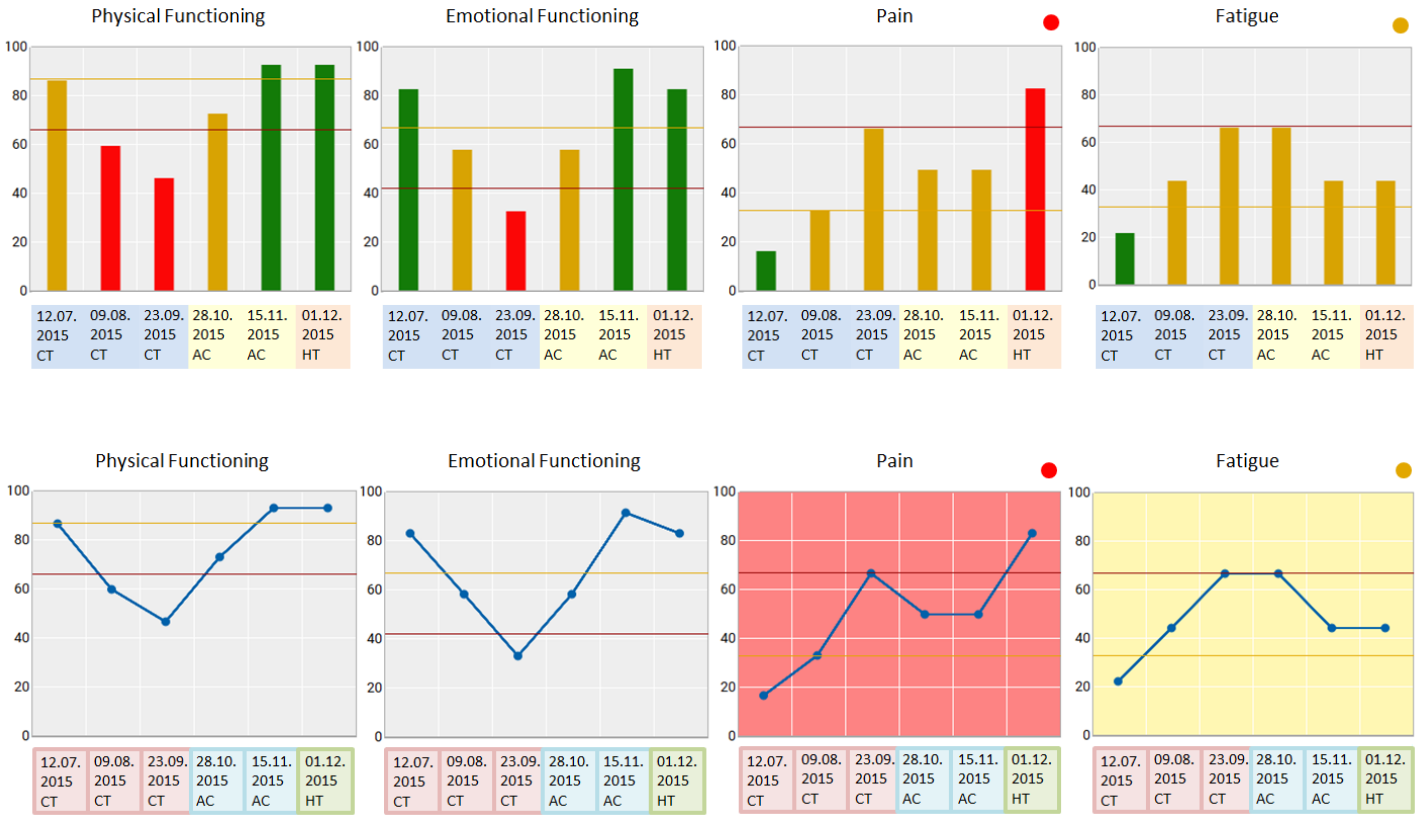

Figure 2 Display of EORTC QLQ-C30 data as bar charts (top row) and line graphs (bottom row).
The yellow and red horizontal lines in the charts indicate reference values from the general population [93]. The red line shows the 10th percentile for functioning scales and the 90th percentile for symptom scales. The yellow line shows the 25th percentile for functioning scales and the 75th percentile for symptom scales. In the bar charts (top row), the bars are coloured in reference to these percentiles. In addition, red and yellow flags next to the scale name indicate that a patient's score exceeds these percentiles. In the line charts (bottom row), the chart background is coloured accordingly. Information on the treatment phase is given below the x-axis using abbreviations and a colour code (CT = chemotherapy/blue (top row) or red (bottom row), AC = aftercare/yellow (top row) or blue (bottom row), HT = hormone therapy/red (top row) or green (bottom row)).

Further research

Whereas more research is needed to improve and evaluate graphical presentation styles and teaching materials for patients and health care professionals, another important focus of research activities should be the psychological processes triggered by confrontation of patients with their own results (i.e. in patients with a poor and/or deteriorating health status).

06. INTEGRATING ROUTINE ASSESSMENTS WITH EORTC MEASURES INTO THE CLINICAL WORKFLOW AND TREATMENT

Key messages:

- Successful integration of routine PRO assessments into the clinical routine is a complex health care intervention.
- Although standardizing design and delivery is challenging, there are commonalities and best practices that can be adapted and applied to improve the process of implementation.
- To guide integration, considerations need to be extended beyond technical and psychometric issues to additional factors related to diffusion of innovation and organizational changes that affect the uptake of routine assessments with EORTC measures.

To realise the evidence-based benefits of routine PRO screening and monitoring (Chapter 1), optimal integration into the clinical routine is essential [38, 101-103]. Integration of assessments with EORTC measures into the clinical routine is a complex health care intervention with multiple interacting components on different levels of the clinical system, all of which are sensitive to multiple influences and barriers [104, 105]. Successful implementation depends on changing the behaviour of many stakeholders. This requires a thorough understanding of the behaviours that need to change, the factors maintaining current behaviours, barriers as well as facilitators to change, and the expertise to develop strategies to achieve change based on this understanding [106, 107]. To guide integration, considerations need to be extended beyond technical and psychometric issues to additional factors affecting the uptake of routine assessments with EORTC measures. Though standardizing design and delivery is challenging, there are commonalities and best practices that can be adapted and applied to improve the process of implementation. Based on available recommendations on PRO implementation into clinical practice (e.g. [57, 83, 108-111]) and its own experience, the EORTC QLG proposes some practical approaches to supporting successful integration (see Figure 3).

Understand current practice before applying strategies for integration

Successful implementation of EORTC measures should be tailored by identifying and addressing potential barriers according to the setting. There are factors in the local context, such as culture and leadership, evaluation, feedback on performance, and facilitation, which are likely to be equally influential. To design a targeted action plan for the integration of assessments with EORTC measures, it is important to understand current practices and existing patient care pathways, assess knowledge and attitudes toward EORTC measures as well as the skills of potential adopters, and analyze resources and barriers [112]. Identifying possible gaps is the starting point of integrating new practices and analysis should involve all relevant stakeholders [113]. Consider running a baseline assessment to identify elements relevant for the adaptation of practice change, such as benefits, harms and costs [60].

Engage all relevant stakeholders

Engaging all relevant stakeholders (i.e. health care professionals, policy makers and patients) in the process of initial consultation and development, as well as during delivery and evaluation, is the key to

success [114] and facilitates the tailoring of assessments with EORTC measures to local needs. This should include:

- Introducing existing national guidelines (e.g. in the Netherlands, Germany or the USA [21-23])
- Providing an opportunity for clinicians to discuss current practice [115] and to develop a shared understanding of PROs in general
- Integrating EORTC measures in clinical care and components in need of adaptation into requirements of the local setting [116]
- Trying to engage senior clinicians, nurse champions and opinion leaders and assigning a coordinator throughout the implementation process [90]
- Finding a local "champion" and building ownership over the integration and application of routine with EORTC measures in the clinical team whenever possible.

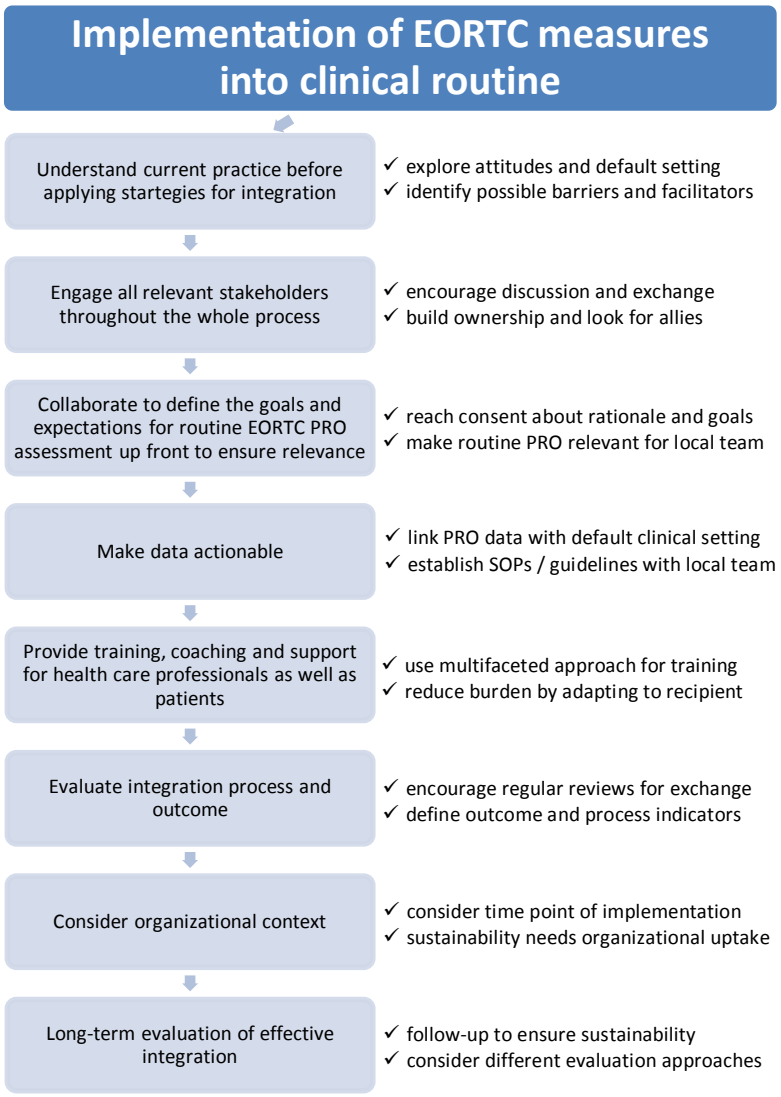

Figure 3 Flow chart of implementation of EORTC measures in clinical routine

Collaborate to define the goals and expectations for routine assessments with EORTC measures up front to ensure relevance

Health care professionals considering the use of EORTC measures in clinical practice need to clarify, as well as reach consensus about, their goals and expectations concerning routine assessments with EORTC measures and assess the resources available for integration [52]. Is routine assessment intended for incorporating electronically pre-assessed results from EORTC measures into patient–physician communication, symptom screening, or stepped care and improved referral pathways? As mentioned before, health care professionals' active participation in the ongoing integration process ensures that they regard assessments with EORTC measures to be relevant for their clinical practice, thereby facilitating uptake of the new intervention into the clinical routine.

Make data actionable

Patient adherence depends on health care professionals using the information [117]. Enablers to health care professionals' use may include automatic 'flagging' of clinically important scores, incorporating the service-user perspective into development, providing longitudinal interpretation of what signifies a clinically important difference in EORTC measures data, and linking EORTC measures data with clinical practice guidelines and interventions [39, 109, 115]. Multidisciplinary team members need to consult with each other about establishing standard operating procedures that are adapted to the default clinical setting (e.g. current clinical practice, networks, pathways and assessment/feedback tools in use). In the long term, the development of clinical practice guidelines and algorithms to support clinicians in the management of identified areas of intervention [112, 118] should be considered to connect EORTC measures data with interventions and referral patterns as well as to integrate discussion of EORTC measures data into patient–clinician communication.

Provide training, coaching and support for health care professionals as well as patients and their informal caregivers

Although health care professionals use outcome scores more readily, they need more support in the use and interpretation of PROs [119]. Large-scale, passive education materials can increase initial awareness as part of the promotional plan but are not effective for practice change [120]. Hence, it will be necessary to use a multifaceted, interactive approach including educational meetings, audits, feedback, reminders, and local consensus processes [121-123]. Programs for training clinicians to effectively use PRO data in routine practice are presented in detail elsewhere [124, 125]. At the patient level, minimal response burden can be ensured by considering disease and cultural aspects (right module, translations and computerized adaptive testing). Also, it should be ensured that PROs address issues relevant to patients including cancer type, stage, phase of the cancer journey and patient comfort level with technology [115].

Evaluate integration process and outcome

Collaboration with health care professionals in defining outcome as well as process indicators (e.g. patient adherence with EORTC measures completion) will help health care professionals reflect on the progress of integration, to identify obstacles and to adapt implementation strategies where necessary

[30]. Considering doing regular (e.g. monthly) reviews will determine progress, elicit problems and engage health care professionals in identifying efficient strategies to overcome barriers [112].

Consider organizational context

Regarding context, we suggest avoiding implementation concurrent with other major organizational changes [124]. In the long term, however, organizational adoption is necessary to support sustainability of routine assessment of EORTC measures and wider adaptation into integrated cancer care pathways.

Long-term evaluation of effective integration

Long-term follow-up is necessary to determine whether short-term changes persist and whether surrogate outcomes point toward benefits [105]. Given the complex nature of routine assessments with EORTC measures, traditional methods for evaluating the effectiveness of individual components such as RCTs might miss organizational or contextual aspects effective in the process of implementation. To account for all components, other study designs such as quasi-experimental, observational or service development and evaluation models based on quality-improvement and implementation science methods might be more informative [52].

07. SETTING UP THE DATA COLLECTION INFRASTRUCTURE FOR ROUTINE ASSESSMENTS WITH EORTC MEASURES

Key messages:

- Electronic assessment of EORTC measures requires both technical and educational infrastructure.
- Electronic versions have demonstrated generally to yield equivalent results to those generated by paper-and-pencil versions of EORTC measures. Electronic data capture prevents a double burden in administration, calculation and storage.
- Before choosing a software system for ePRO assessment, decisions need to be made regarding the desired software features (e.g. registry, educational content, assessment outside of the hospital, etc.). The feasibility/compatibility for potential integration with existing clinical systems and Electronic Health Records should be checked.

At the time of implementation, most innovations require some initial effort and expenditure. Careful preparation of the requirements for routine assessments with EORTC measures can reduce costs, which is worthwhile, as time, labour (for data entry and calculation), and continuous resources (e.g. for printing) are saved and high data quality and improved care may be achieved.

Infrastructural requirements

Infrastructural requirements comprise both technical and educational aspects. From a technical point of view, using EORTC measures with electronic devices requires a comprehensive IT infrastructure (technical devices for data collection and output, appropriate software solutions and network facilities for data transmission, storage and backup, technical support and updates). Next to those structural conditions, special user skills (e.g. understanding the concept of EORTC measures, correct data interpretation, and knowledge of possible interventions or referrals) are key for any positive effect of electronic EORTC measures on the clinical routine. This chapter deals predominantly with the technical requirements.

Choosing between paper–pencil and electronic assessment

EORTC measures were originally developed as paper–pencil instruments and some authors argue against exclusively offering computerized versions of PRO measures because these might be more difficult to access for some patient populations and create a disadvantage for older people [126, 127]. For the purpose of daily clinical practice, to have a paper–pencil version as an emergency backup seems reasonable but should not be a common assessment method. The main reason is that additional data entry and scoring will take extra time and the real-time presentation of results, which is essential for clinical practice, will not be achieved. Additionally, using EORTC measures on paper could become a double burden in terms of material and workload for personnel, because the preparation and data entry required could cause the measures to lose most of their inherent benefits.

Current knowledge concludes a general equivalence between paper–pencil and computer-based versions of PRO measures [128]. Determination of equivalence of the two administration modes, for

example for EORTC measures, does not necessarily require full psychometric testing but careful evaluation of applied changes. If no substantial adaptation has been made to item presentation or wording/meaning, cognitive debriefing and usability testing provide sufficient levels of evidence [129]. At present, Mapi (www.mapi-trust.org) is developing, jointly with the EORTC QLG, guidelines for migrating EORTC measures to electronic versions.

Software solutions

There are a variety of ePRO systems available which allow electronic PRO data capture and focus on enhancing symptom screening and management, improving communication between patients and health care professionals, and providing patient-centred interventions in the clinical routine [37]. Nonetheless, there is considerable variation between software features, which should incorporate both patients' and clinicians' needs and offer appropriate content. Some software solutions may serve as data registries only, although systems combining features for daily clinical practice and registry purposes are most beneficial for both areas of interest [36, 37]. Depending on the specific use and the features of the software, it may need to undergo a certification or validation procedure (e.g. CE-marking is necessary for software systems that are intended for use in patient care).

Since 2009, the EORTC QLG has been supporting the development of the CHES.EORTC software [75], which allows electronic data capture in daily clinical practice and clinical studies and provides an elaborated graphical results presentation of patient-level data. CHES provides feasible and secure solutions for using EORTC measures both in the hospital setting for monitoring in the daily clinical routine and for telemonitoring via web access [130]. CHES.EORTC provides data exchange interfaces for clinical information systems based on the Health Level Seven (HL7) standard.

CHES.EORTC – a practical example of required IT infrastructure

The technical infrastructure requires a server on which the CHES.EORTC server component is hosted. Preferably, servers already used for holding health care information and records are to be used, whenever possible, to ensure patient data security and confidentiality. The CHES.EORTC server component is implemented as a modular Java application, which allows it to be run on all modern operating systems supporting Java. For instance, the current implementations run on several Linux (CentOS, Ubuntu) and Windows versions (Windows Server 2012, Windows 10). To provide adequate response and processing times, at least 4GB of memory and reasonable processing speed and modern multicore processors are required (at least two cores are recommended). The CHES.EORTC platform has been developed to support multiple databases – currently, versions for MySQL and Microsoft SQL Server are provided and actively maintained. To prevent loss of data, daily backup as well as storing the backup at a safe third-party location is highly recommended. Also, we strongly recommend regular updates of the server to guard against security issues of outdated systems.

To make the CHES.EORTC platform available to clinicians and patients, a modern web interface is provided, making a network connection to the server necessary. This connection may be established through the hospital's wired network (LAN) or wireless network (WiFi). As WiFi is nowadays a common and inexpensive technology that is also practical in a hospital setting, it eases work for both data collectors and clinicians. Collected data is immediately encrypted and safely transmitted to the central CHES.EORTC server component, which allows immediate access to patients' data.

For telemonitoring via web, a feasible and user-friendly website with special security features is needed. Especially online data transfer, privacy of health information, data security and patients' safety need

special attention [131]. In the case of CHES.EORTC, it is ensured that all data that lead to the identification of patients stay within the hospital's network behind the firewall and all data exchange outside the hospital's network is performed securely via an SSL-encrypted connection. Patient online access is secured by unique login with a username and password.

Compatibility issues

Integration of PRO reports into electronic health records not only facilitates retrieval of results by medical personnel [33], but also allows health care professionals to communicate and coordinate assessments, treatments and referrals. Stand-alone ePRO systems not integrated into a higher clinic information system should use compatible programming. Common standards for exchange, integration and sharing of electronic documents (e.g. Health Level Seven, HL7 v3) [132] allow information exchange within and between institutions and as such are timely, adequate and facilitate continuous care.

Assessment devices

The choice of devices is associated with space requirements for assessment with EORTC measures. Personal computers or laptops (preferably with touch screens) could be placed in a separate room or the waiting area as a self-service kiosk. Hand-held devices (e.g. tablet PCs and smart phones) are spatially independent and can be used for both inpatients and outpatients. Inpatients can complete assessments without leaving their bed or room and outpatients could spend queuing time in the waiting area completing EORTC measures. Multiple hand-held devices can be used simultaneously without increasing space requirements, which might be a further advantage. Given the increasing economic viability of using touch screen tools, routine PRO assessments are likely to be increasingly conducted electronically in the near future. Using tools and systems that are well known and understood by patients will facilitate the electronic assessment process.

Beyond technical requirements

Even an ideal setup of technical requirements for electronic data collection of EORTC measures does not automatically result in successful implementation of such a new procedure in the common clinical routine. Some efforts have already been made to identify key aspects that need to be addressed to integrate telemedicine in a broader sense in the routine clinical workflow, such as provision of explanatory models, related conceptual tools and step-by-step implementation recommendations based on practical experience [133, 134]. Chapter 6 provides more details on implementation issues.

08. PRO TELEMONITORING – USING EORTC MEASURES FOR QUALITY OF LIFE MONITORING BETWEEN HOSPITAL VISITS

Key messages:

- Even if PROs are assessed routinely at the hospital, there may be insufficient information about the patients' self-reported health experience after discharge and during follow-up.
- Telemonitoring can complement knowledge of a patient's health status between hospital visits.
- Incorporating telemonitoring into patient portals can facilitate the linking of patients' scores with individually composed educational material and appropriate self-management advice, and referral to care.

Even if EORTC measures are regularly assessed within the clinical routine in the hospital setting (in inpatients and outpatients), information about patients' health status and QoL is still incomplete, as their monitoring ends when they leave the hospital. To bridge this gap, telemonitoring allows the monitoring of patients during phases when no hospital visits or appointments are scheduled. Primarily developed for distant assessment of medical data like heart rate, blood pressure, oxygen levels or blood sugar, telemonitoring can also be used for assessing PRO data. This can be of special interest for patients undergoing active outpatient treatment, as side effects and treatment-related symptom burden might occur after discharge [135]. This approach may enhance follow-up after completion of active treatment as well. Consequently, telemonitoring with EORTC measures helps to more comprehensively incorporate cancer patients' perspectives into symptom estimation, screening, monitoring, and treatment.

Advantages of telemonitoring with EORTC measures for patients and health care professionals

Telemonitoring with EORTC measures may increase a patient's feeling of security when they spend time at home because occurring symptoms can be recognized by health care professionals in real time despite the geographic distance between the patient and medical services. Patients are no longer left alone with the management of adverse events, and alert systems allow health care professionals to contact patients and intervene appropriately, even when they are not hospitalized [136].

Researchers and clinicians might also benefit from telemonitoring with EORTC measures as such data can be merged with routine assessments at the hospital. In addition to tailored and timely care for arising complications, knowledge of the disease itself and treatment-related symptoms might be deepened.

Modes of administration of telemonitoring with EORTC measures

Although studies have shown that traditional paper–pencil questionnaires may have a better rate of return [137, 138], they are more expensive because of printing and postage costs, and the workforce needed for inputting data. However, electronic data assessment has the potential to improve data quality (e.g. better completeness of data) [137] and is especially cost effective if a larger number of patients are included [139]. Horevoorts et al. [140] report a mixed mode of administration combining electronic assessments as a standard and paper–pencil assessments on patients' demand as a feasible method for PRO data collection in older colorectal cancer patients, though willingness to complete an

online questionnaire decreased with age. The internet provides an inexpensive platform using widespread technology that makes easy, user-friendly and reliable data collection possible, but favours patients with access to such technology. Therefore, auxiliary tools to overcome access barriers (e.g. related to a patient's age or health status) need to be offered. This can include adjustable font sizes, voice output or interactive voice response (e.g. for visually impaired people), or additional input devices (e.g. for patients with impaired motor skills). Next to internet-based assessments, telephone interviews might be a substitute for patients who do not have access to the internet or do not want to use electronic administration of EORTC measures.

Requirements for telemonitoring with EORTC measures

The use of telemonitoring with EORTC measures via the internet imposes requirements on patients and on health care professionals. Patients need to be at least somewhat familiar with the use of internet-ready devices (PCs, laptops, tablet PCs, smart phones) and keen to use them for transmission of health-related data. The rising availability of internet access, the growing percentage of patients who use the internet for health-related information searches [141], and study reports indicating that patients are open to electronic and remote assessments [142] suggest that telemonitoring with EORTC measures may be feasible for a considerable percentage of cancer patients. However, health care professionals need to be familiar with the assessment possibilities on offer, should be able to provide assistance if needed and should incorporate the gathered PRO data within their routine clinical work (for example having allocated time for "virtual clinics" to review PROs).

Telemonitoring with EORTC measures as a component of patient portals

Electronic patient portals can enable patients to access their own personal health records, provide additional information on their health status via EORTC measures and supply them with educational/illustrating material. The use of such portals can result in a shift of the traditional relationship between health care professionals and patients, as patients have the possibility to engage themselves actively in their own care [143, 144]. Though only a little is known about the effect of patients' use of portals on their clinical outcomes, there is some evidence suggesting that they feel better prepared for their clinical appointments, develop better coping strategies, are more satisfied with treatment choices and are more adherent to medical advice [145]. As patients show more and more interest in the use of electronic portals [146] it is of special importance to provide trustworthy information and reliable self-assessment instruments like the EORTC measures.

Technical issues and difficulties

Regarding electronic assessment with EORTC measures, the most common concerns reported by patients relate to their privacy and data security. Many patients worry about who can access their answers and what possibly negative influence this might have on their care. Next to medical issues, these concerns need to be addressed by the clinic personnel to enhance patients' trust in the systems provided. If systems for electronic assessment with EORTC measures are incorporated into the hospital IT structure and secure hospital servers are used, data privacy and security generally can be guaranteed. The European directive on the protection of personal data is currently undergoing an extensive reform to set a new standard across Europe. Individuals' rights will be reinforced and those who assess, collect and process personal data will have increased responsibility and accountability [147].

Though telemonitoring has the potential to positively affect patients' health care management and quality of life even outside the clinical setting, its implementation poses additional demands on all parties involved. Besides, aspects of software compatibility, data and transmission security, and issues of interpretability and responsibility need to be considered under the specific conditions of the setting. If patients complete EORTC measures outside of the hospital, it is of major importance that the health care professionals responsible are well trained in data interpretation and that they understand presented data and their clinical meaningfulness correctly. In the absence of personal contact with the patient, this might be a difficult task for health care professionals and require specific training and an internal agreement on how to proceed if patient data indicates problems needing acute medical attention. Additionally, patients need to be educated that completing EORTC measures via telemonitoring must not replace or delay their visit to the hospital or doctor if they are feeling unwell. Although telemonitoring can support patients with educational material and self-help advice, they need to be aware of their personal responsibility to seek professional help sufficiently early instead of sticking to self-treatment. These very sensitive issues should already be considered in patient portals and need to be addressed in educational programs for health care professionals, who in turn need to inform their patients.

09. FURTHER USE OF EORTC MEASURES (E.G. QUALITY ASSURANCE AND HEALTH ECONOMICS)

Key messages:

- Although originally developed for PRO assessment in clinical trials, EORTC measures are versatile and suitable for clinical practice, comparative effectiveness research and health economics analysis.
- Other fields of application of EORTC measures include the evaluation of practices, care pathways, policies, and quality assurance which could disclose systematic differences in distribution of health care between patient populations and care settings. These fields, however, need further research.

The use of EORTC measures is not necessarily restricted to clinical trials and daily clinical practice, but offers advantages for quality assurance and health economic analysis as well.

Using EORTC measures for quality assurance, benchmarking and comparative effectiveness research

Usually quality assurance programs define a set of minimal requirements for good care, collect data to compare indicators with the predefined quality standards, and develop strategies for improvement (e.g. treatment guidelines), starting the cycle all over again [148]. Measures for the performance of health care professionals are often restricted to conventional outcomes such as survival, recurrence, readmissions and mortality. If patients' opinions are included in performance measures, they are generally limited to structural aspects of medical care delivery (e.g. waiting times) or satisfaction with care [26].

How patients themselves perceive the effects of the treatment they receive is widely ignored, but efforts to systematically include the patient perspective by using PRO instruments have increased in recent years. The US National Quality Forum published a white paper providing advice and best practices on how to develop new PRO performance measures or evaluate if existing PRO measures are suitable for quality assurance and performance assessment [149]. The Health and Social Care Information Centre in the UK suggests that using PRO measures for quality assurance may even facilitate the setting of new benchmarks complementing common quality standards, for example by assessing the patient's relative health status before surgery [150]. Talcott et al. [151] report a clear example of comparative effectiveness research using PRO measures: two patient groups treated with brachytherapy for prostate cancer differed in PRO scores for urinary symptoms. Worse scores were associated with differences in treatment procedures and therefore provided practice-changing evidence that would not have been available without patients' self-reports.

By using EORTC measures as routine screening and monitoring tools in daily clinical practice, collected PRO data not only contributes to more patient-centred cancer care, but is also a valuable data source for comparing outcomes with predefined benchmarks. They provide information on areas of medical treatment that would still benefit from improvements, for example by implementing treatment guidelines or revising existing standards of care. EORTC measures would also allow the comparison of the performance of individual health care professionals or institutions.

Dealing with cancer as an illness, which, thanks to improved screening and treatment possibilities, has increasingly become a more chronic condition, PROs are gaining importance regarding holistic and long-term medical care. Therefore, EORTC measures could in the future be integrated into certification requirements, as they stand for both the incorporation of patients' perceptions and patient empowerment. International groups, such as the International Consortium for Health Outcomes Measurement (ICHOM), are developing international recommendations of common data sets, which include several EORTC tools as well (e.g. in lung cancer to use the EORTC QLQ-30 and the QLQ-LC13 lung cancer module [152]; in advanced prostate cancer to use the EORTC QLQ-C30 and the QLQ-PR25 prostate cancer module [153, 154]). These recommendations give advice on PRO measurements, assessment time points/frequency and further clinical variables, and want to set global standards for both improved cancer care and quality assurance [155].

Even though quality assurance can be a promising area for the use of PRO measures, there is still a strong need for further research before any advice on their use can be given, as the interests of different stakeholders (health care providers, patients, insurance companies, etc) vary widely. So far, there are no standards on how PRO data has to be collected to consider the needs of all stakeholders without privileging or disadvantaging any of the parties involved, although some efforts have been undertaken to develop recommendations concerning this matter [156].

Using EORTC measures for analysis in health economics

An ongoing QLG project aims at developing value sets for the EORTC QLQ-C30 that will enable the estimation of quality adjusted life years (QALYs) and economic evaluations [157]. Such analyses may focus on new treatment modalities or compare existing options which patients need to weigh against each other.

For example, since April 2009, a project of the National Health Service in England has funded PRO assessments prior to and after four types of surgery (hip and knee replacement, varicose vein surgery and groin hernia surgery) collecting both generic and condition-specific PRO data [158]. Cost-effectiveness analysis showed that participating centres rarely differed in achieved QALYs, but did differ in costs for each QALY. Those results indicate that it is reasonable to investigate why providers' performance is considerably different with regard to costs but not to the achieved effect of treatment. [159]. Similarly, EORTC measures can provide data for cost-utility/cost-effectiveness analysis, which could also be used for comparative benchmarking [160]. This developmental work on converting EORTC QLQ-C30 responses into health utility measures has recently been completed, resulting in the EORTC QLU-C10D measure. The utility values were generated in English-speaking countries and further research is continuing to generate utility values in European countries.

Further possibilities of application of PRO instruments, e.g. EORTC measures

Possible applications of PRO data, such as that assessed with EORTC measures, includes the evaluation of practices, care pathways and policies [161].

Data analysis from the previously mentioned NHS PROMs programme gives insights regarding the cooperation of the NHS with private institutions for selected types of surgery and sociodemographic differences between patients. Patients' reports allow the conclusion that there are only minor differences in patient characteristics between private health care professionals and NHS providers. Though patients who chose a private institution for surgery were slightly healthier and had less severe conditions, those differences were much smaller than previously suspected (there was a previous

assumption that private providers could be selectively picking only relatively healthy and uncomplicated patients) [162]. However, analysis regarding sociodemographic characteristics has shown systematic differences in health states at the time of access to surgery. Non-white and deprived patients reported overall more, and a higher extent of, longstanding problems. One might assume that those patients had surgery at a later stage in the course of their disease [163].

Consequently, PRO measures can contribute to the evaluation of newly implemented care pathways, care strategies and treatment technologies and disclose systematic differences in distribution of health care amongst patients [164, 165].

10. ETHICAL CONSIDERATIONS

Key messages:

- Choice of EORTC measures always needs to consider the patient burden. If whole instruments are too burdensome, alternatives are available (e.g. the EORTC QLQ-C15-PAL for palliative care settings).
- Computerized adaptive testing will decrease patient burden and may enable very ill patients to participate as well.
- Privacy, confidentiality and disclosure are major issues in PRO assessments that always need to be addressed. This includes technical, regulatory and organizational issues.
- Efforts to include as many patients as possible need to be made, e.g. by systematically improving access to PRO and electronic PRO assessments for underprivileged persons.

When completing EORTC measures, patients provide valuable data to their health care professionals, who in return are bound to handle this information with special care. Ethical considerations include a variety of issues that need to be addressed (e.g. patient burden, privacy, informed consent, confidentiality, data security and storage, disclosure, and practical use of data).

Patient burden

Completing any PRO instrument imposes a certain amount of effort on patients. Depending on their health state and current treatment, answering the questions of the EORTC QLQ-30 can be burdensome, even without any additional items or modules. In general, patients need around 10 to 15 minutes per assessment to complete the EORTC QLQ-C30 and an additional module. For patients in a palliative setting, the EORTC QLQ-C15-PAL, with an average completion time of 5 to 10 minutes, could be an acceptable alternative instead of abandoning PRO assessment completely [166].

Consequently, the choice of appropriate EORTC measures may reduce patient burden to an acceptable minimum. For example, it needs to be considered that the targeted patient group could have special needs, though patients' ability and willingness to complete EORTC measures should not be underestimated just because they seem to be "too ill". Unintentionally excluding these patients biases data for any further analysis at the group level (e.g. for epidemiological or health economy analysis) and may deprive exactly those patients who are in special need of particular interventions (e.g. referral to psychosocial services). Some studies and ongoing clinical trials in the EORTC are currently exploring the value of proxy assessment, which may be useful in patients with major cognitive problems, such as patients with brain cancers. If these confirm some scales offer similar scores, maybe assessment in some scales could be shortened [167, 168].

The ongoing development of CAT (please refer to Chapter 2 for further details on EORTC CAT measures) will decrease the patient burden of completing EORTC measures, as CAT achieves a higher measurement precision than static questionnaires, simultaneously choosing questions relevant to the individual patient and reducing the number of items.

Privacy and confidentiality (data protection issues)

Ideally, patients should have the opportunity to complete EORTC measures unobserved on their own, with the possibility of receiving help if necessary. Inadequate privacy or time constraints during questionnaire completion might pressure patients, possibly reducing their willingness and openness to use the PRO instrument, resulting in altered self-reports.

Electronic assessment of EORTC measures, either directly entered by patients or entered from completed paper–pencil forms by dedicated personnel, requires IT structures ensuring the maximum protection of patients' data when collected, transmitted and stored. Even within a secure IT environment, data access needs to be restricted using different user groups with different access rights. As EORTC measures assess sensitive data, some patients might not want all members of their clinical team to see their data; for example, regarding satisfaction, as they might fear negative consequences because of critical answers, or sensitive topics such as sexual function. Snyder et al. [169] suggest presenting such data on an aggregated basis and emphasize the need for the development of standard procedures for integration of PRO data in electronic medical record systems, considering confidentiality and clinical utility of patients' self-reports. Additionally, though protection of patients' data privacy, confidentiality and ownership is paramount, solutions need to be found to make those data still useable for the ongoing development of sophisticated electronic health technologies and solutions [170] (please refer to Chapter 7 for more details on IT issues).

Regulatory requirements regarding data security, data protection and confidentiality may vary between different institutions and health care organizations, even if working within the framework of Data Protection rules in the EU. Therefore, it is recommended that the Information Governance offices are contacted early in the planning of PRO projects for daily practice, in order to discuss and meet the necessary requirements and receive their approval.

Disclosure

Administration of EORTC measures should be accompanied by essential information about their general nature and purpose. Patients should be informed about the duration of data storage, who can access their data, their right to withdraw from studies, and their right to request destruction of their PRO and personal data. Furthermore, they should be informed that data collection respects national and EU data protection and privacy standards. Additionally, patients need to be informed about any other way their data could be used, such as possible statistical analysis for quality assurance or scientific reasons. This information has to be given before patients start providing their data in order to correspond to the requirements of proper informed consent. If agreed with the Information Governance office or other relevant local ethics committee, informed consent may be given online before the first administration of the PROs.

Reasons for refusal of PRO assessments, especially at patients' homes via telemonitoring, include unfamiliarity with computer technology or a fear of unfamiliarity, and concerns of losing contact with known health care personnel or replacement of personal services by PRO assessments should be collected. Moreover, some patients assign negative stereotypes to eHealth interventions, for example, they see their use as a sign that their health is very bad, that they are highly dependent, and that the coping skills they have developed in the course of their illness are not sufficient [171].

Implementation of such electronic monitoring systems should include appropriate information material and the possibility of discussing such issues with patients, preventing them from developing wrong expectations and dispelling existing doubts. For instance, cancer survivors were more likely to provide

PRO data by means of telemonitoring when personally asked, if compared to recruitment by phone or postal letter [172].

Equitable distribution of services (issues of eligibility and access to services)

Though one promise of the electronic assessment of EORTC measures is to reach as many patients as possible and ease access to services, the use of electronic devices may put certain patients who are unfamiliar with computer technology at a disadvantage. Especially non-white, older and male patients with lower education and income are in danger of being additionally deprived because they are less likely to engage in electronic health activities [173]. Consequently, while implementing EORTC measures, a special focus needs to be put on the encouragement of potentially underprivileged patients to transmit their health status and QoL information to providers [174].

Implications for clinical practice and research

Collecting PRO data with EORTC measures entails some responsibilities, which should be carefully addressed in clinical practice. Implementing routine assessments with EORTC measures and telemonitoring poses several questions: Who can access the data? To what extent are patients' profiles available for health care personnel and patients themselves? Which is the most useful output format? How will it guide health care professionals in their work? Are educational materials necessary and available? Could any disadvantages arise for patients who provide PRO data? Who is the contact person if patients report severe problems needing medical attention? Unfortunately, as of now, there is no obvious remedy available for any of these questions, which consequently need to be addressed according to the context and purpose of the use of EORTC measures.

Regarding the presentation of PRO results, data needs to be processed in a comprehensible way without losing important information. Simple output formats like single line graphs or written text are preferred by patients [98]. Choosing between graphical formats, patients again rated single line graphs as easiest to understand and most useful. Clinicians too prefer line graphs, though they would add markers for scores needing clinical attention and reference values [99]. To tap the full potential of PRO data, including that assessed with EORTC measures, still more knowledge is needed on how the results can be prepared accordingly, for both patients and health care personnel, to become a valuable data source for routine clinical decision-making. Chapter 5 provides more detail on ongoing research regarding graphical presentation formats especially for EORTC measures.

In clinical trials, the use of alert systems may have some influence on study results. As no consensus is available on how clinicians should deal with notifications about patients' extreme PRO scores representing severe burden, they might prompt ad hoc interventions. If such an intervention changes routine care, trial results may be unwittingly biased. Possible solutions for this issue range from blinding research personnel to PRO data (thus risking trial patients not getting the optimal care they need) to active PRO monitoring (requiring clear strategies for staff training, provision of intervention and capture of additional interventions) [175]. Similarly, guidelines for relevant cut-off scores and interventions are needed for equitable and effective patient care. Contact people for immediate support for patients who get upset while or after completing ePRO at home are needed but cannot be provided like in the clinical setting. Therefore, patients ideally need to be explicitly informed at the hospital about where to turn should they experience any bothersome symptoms or feel agitated after ePRO assessment.

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