Development of EirV3: A Computer-Based Tool for Patient-Reported Outcome Measures in Cancer

abstract

Purpose Immediate transfer of patient-reported outcome measures (PROMs) for use in medical consultations is facilitated by electronic assessments. We aimed to describe the rationale and development of Eir version 3 (EirV3), a computer-based symptom assessment tool for cancer, with emphasis on content and user-friendliness.

Methods EirV3's specifications and content were developed through multiprofessional, stepwise, and iterative processes (from 2013 to 2016), with literature reviews on traditional and electronic assessment and classification methods, formative iterative usability tests with end-users, and assessment of patient preferences for paper versus electronic assessments.

Results EirV3 has the following two modules: Eir-Patient for PROMs registration on tablets and Eir-Doctor for presentation of PROMs in a user-friendly interface on computers. Eir-Patient starts with 19 common cancer symptoms followed by specific, in-depth questions for endorsed symptoms. The pain section includes a body map for pain location and intensity, whereas physical functioning, nutritional intake, and well-being are standard questions for all. Data are wirelessly transferred to Eir-Doctor. Symptoms with intensity scores ≥ 3 (on a 0 to 10 scale) are marked in red, with brighter colors corresponding to higher intensity, and supplemented with graphs displaying symptom development over time. Usability results showed that patients and health care providers found EirV3 to be intuitive, easy to use, and relevant. When comparing PROM assessments on paper versus tablets (n = 114), 19% of patients preferred paper, 41% preferred tablets, and 40% had no preference. Median intraclass correlation coefficient between paper and tablets (0.815) was excellent.

Conclusion Iterative test rounds followed by continuous improvements led to a user-friendly, applicable symptom assessment tool, EirV3, developed for and by end-users. EirV3 is undergoing international testing of clinical and cross-cultural adaptability.

Clin Cancer Inform. © 2017 by American Society of Clinical Oncology

Hilde Krogstad

Cinzia Brunelli

Kari Sand

Eivind Andersen

Herish Garresori

Tarje Halvorsen

Ellinor C. Haukland

Frode Jordal

Stein Kaasa

Jon Håvard Loge

Erik Torbjørn Løhre

Sunil X. Raj

Marianne Jensen Hjermstad

Author affiliations appear at the end of this article.
H.K. and C.B. contributed equally to this work.
Corresponding author: Hilde Krogstad, MD, European Palliative Care Research Centre, Department of Clinical and Molecular Medicine, Faculty of Medicine and Health Sciences, NTNU, Norwegian University of Science and Technology and St.Olavs Hospital, Trondheim University Hospital, Trondheim 7491, Norway; e-mail: hilde.krogstad@ntnu.no.

INTRODUCTION

Systematic use of patient-reported outcome measures (PROMs) in clinical practice is essential for optimal patient care.[1-3] The recognition of PROMs as independent outcomes in cancer[4,5] is consolidated by the CONSORT Patient-Reported Outcomes Extension Statement developed to improve the reporting of PROMs on patients' evaluation of symptoms, functioning, and quality of life.[5]

Benefits of routine PROM registrations have been reported, such as improved patient-physician communication[6-8] and better patient well-being.[8,9] Regular PROM assessment during treatment with immediate feedback to clinicians has proven to be efficient in informing clinicians about symptoms and problems[7] and guiding treatment decisions.[2,10,11] A recent review reported improved symptom management and higher patient satisfaction when using PROMs in the clinical consultation, because this made physicians aware of symptoms that had not been discussed before.[12,13]

Despite these findings, systematic collection and use of PROMs in clinical oncology remain uncommon.[2,11,14,15] The most common barriers are logistical problems, cumbersome administration, and time constraints.[11,14-17] These barriers may be overcome by health information technology and Web-based communication now widely available. Indeed, electronic data collection permits dynamic symptom assessment (ie, tailored questions for individual patients based on the

patients' previous responses). This results in fewer repetitive questions and reduces patient burden by avoiding long and cumbersome questionnaires. In addition, Web-based technology permits immediate transfer of patients' responses to the attending physician's desktop. When used alongside clinical data, the follow-up of patients may be more comprehensive, especially for patients who are not hospitalized.

Our research group in the European Association of Palliative Care (EAPC) Research Network[18] and the European Palliative Care Research Centre (PRC)[19] has developed several electronic symptom assessment tools over the past decade[20-26] (Appendix). Our experiences led to the Eir Project in 2013. The long-term aim is to integrate PROMs and clinical data in a user-friendly software available on all platforms for use in treatment of adult patients with cancer across disease stages and settings.

This article describes the stepwise development process toward the current Eir version, version 3 (EirV3), which has the following two modules: Eir-Patient and Eir-Doctor. More specifically, qualitative and quantitative results from iterative test rounds are presented, focusing on the rationale behind the requirements, contents, adaptation of technical specifications, usability, patient preferences, and preference for using paper or electronic versions.

METHODS

Eir has been designed following expert-driven and user-driven approaches. The first step, selection of content, is based on literature searches, expert opinions, clinical experience, and evidence-based guidelines for symptom management,[27-33] guided by iterative formative tests of preferences, needs, and skills of the end-users—patients and health care providers (HCPs). Throughout development, regular meetings and discussions were carried out in the following two main working groups: an international palliative care (PC) expert panel, consisting of 26 PC experts from Italy, Norway, the United Kingdom, Denmark, Spain, and Germany experienced in clinical oncology/PC, symptom assessment/classification, questionnaire development, and PC research and recruited from the European Palliative Care Research Centre and EAPC Research Network, and a Norwegian core working group (n = 9 to 15) consisting of experienced oncologists, PC physicians, researchers, interaction designers, graphic designers, and software developers. Altogether, results from the international meetings and local

workshops (Appendix) led to the recommendations guiding the subsequent Eir development (Table 1) and to the final decisions on the content, based on reviews, guidelines, and evidence at the time (Table 2).[33-42]

Formative Usability Testing

The second step in Eir development was formative usability testing, an iterative design process conducted to detect weaknesses in the structure and content and software bugs and to problem solve issues based on end-users' input.[43] The aim of the usability tests was to obtain the opinion of patients and HCPs regarding ease of navigation, clarity of instructions, and content relevance in Eir-Patient and Eir-Doctor (Table 3; Appendix).

Equivalence Between Electronic and Paper PROM Assessments

In 2016, a comparative study was carried out among 114 patients with cancer at six Norwegian hospitals to examine agreement between PROM assessments on tablets and paper and to assess patients' preference for either method. Patients rated the intensity of 19 symptoms in EirV3. The order of assessment, either paper or tablet first, was randomly assigned, with 30 minutes between assessments. Intraclass correlation coefficients (ICCs) based on a two-way mixed effect analysis of variance, single measure and absolute agreement,[44] were used to examine agreement of tablet and paper scores. According to interpretation guidelines,[45] an ICC > 0.75 indicates excellent agreement.

Technical Specifications and Data Safety

EirV3 is a Web site using standard HTML5, CSS3, and Javascript and designed for ease of use and touch-based navigation. This allows the system to run on any hardware with a modern Web browser, including tablets, cell phones, laptops, workstations, and public terminals. It is designed for Windows Server using IIS, but also Windows Azure. The default database for storage is Microsoft SQL Server, but Azure Blob storage and document databases also work well.

Ethical Considerations

Confidentiality issues and adherence to all regulations regarding the registration, transfer, handling, and storage of data were major issues during the development process. Data communication between the device used for data entry and the storage server is secured using HTTPS over SSL. Verification of the patient's identity is ensured

Table 1. Requirements and Methods That Guided the Eir Development Process

Requirements*	Methods
Mimic a clinical consultation regarding content	Use a hierarchical, logical structure for questions Use photos of humans for body pain markings
Cover the most common cancer-related symptoms	Select symptoms based on literature reviews, clinical experience
Minimize ad hoc formulations and questions	Select items from well-validated tools If not available, reach consensus in international expert panel
Dynamic, flexible, and tailored to the individual patient	Define screening questions that guide subsequent questions if endorsed
Applicable in multiple settings (hospital, ambulatory, home care)	Ensure software compatibility with multiple platforms
User-friendly	Perform iterative usability testing in different patient samples (eg, diagnoses, settings, fit and frail)
Feasible	Ensure easy handling, self-explanatory layout, and immediate back-up
Immediate transfer of all PROMs from Eir-Patient to Eir-Doctor	Ensure a design in Eir-Doctor that immediately presents all PROMs on the same screen in Eir-Doctor, adapt for Wi-Fi use
Longitudinal presentation of patient data	Programmed with reader-friendly diagrams, charts, and output in Eir-Doctor
Safe transfer and storage of data	Collaborate with IT specialists and data protection supervisors to comply with all safety and confidentiality regulations
Applicable across cultures	Use scales and items from well-validated tools and questionnaires, available in multiple languages Perform international testing
Output reports on patient and group level	Enable data extraction as separate files, prints, and so on
Compatibility with existing databases	Incorporate Eir into electronic patient records

Abbreviation: IT, information technology; PROM, patient-related outcome measure.

*Consensus on these requirements was reached based on literature searches, expert opinions, clinical experience, and evidence-based guidelines for symptom management, as well as workshops, international expert meetings, and usability testing.

using token-based authentication, with support for authentication protocols (eg, OAuth, OpenId, and SAML2.0). Patient data are stored on secure servers hosted by each clinic. Data are encrypted using Advanced Encryption Standard requiring an encryption key to access the database. Access to patients' PROMs in Eir-Doctor is password protected.

The Regional Committee for Medical and Health Research Ethics Central Norway approved the comparative study, confirming that formal approval was not required for the usability tests (REK-2014/212, REK-2015/185).

RESULTS

Eir-PatientV3

Eir-Patient addresses all 12 symptoms in the EAPC Basic Dataset[31] (ie, pain, tiredness, drowsiness, nausea, reduced appetite, breathlessness, depression, anxiety, well-being, sleep, constipation, vomiting), supplemented by four items particularly related to chemotherapy (ie, numbness in hands or feet, diarrhea, mouth sores, dry mouth) and another four items adjusted from the Patient-Generated Subjective Global Assessment[42] for assessment of nutritional status (ie, altered sense of taste, altered sense of smell, problems swallowing, early satiety) and physical activity.

Dynamic Symptom Assessment

For Eir to be dynamic and patient tailored (Table 1), a symptom assessment hierarchy was developed as per requirements in the working groups. The opening question mimics a common start of a clinical consultation with a general question about the patient's well-being today (Fig 1). Then there is a symptom screening section (Level 0) followed by intensity ratings of all endorsed symptoms (Level 1) and specific questions on symptom characteristics (Level 2; Table 2).[33-41,46] To keep the number of questions to a minimum, it was decided to add follow-up questions only if the international expert panel considered this to be of clinical relevance. In the last section, questions on height, current weight, food intake, and current level of physical functioning are for all patients.

Eir-DoctorV3

PROMs reported on the tablet by the patient are immediately available in Eir-Doctor to focus the patient-physician communication on symptoms that need attention and treatment. The Eir-Doctor opening screen displays symptom scores in descending order of intensity from high to low, with scores $\geq$ 3 in red, indicating clinical

Table 2. The Dynamic Structure for Symptom Assessment in Eir

Symptom	Level 0 Screening	Level 1 Intensity	Level 2 Characterization	Source
Well-being	—	0-10 NRS	None	
Pain	Yes/no	0-10 NRS	Pain location: body map Neuropathic pain: verbal descriptors Breakthrough pain: intensity of pain flares, triggering factors	Kaasa et al[33]; Brunelli et al[34]; Zeppetella and Davies[35]; Portenoy and Hagen[36]; Hagen et al 2008[37]
Tiredness	Yes/no	0-10 NRS	None	
Drowsiness	Yes/no	0-10 NRS	None	
Nausea	Yes/no	0-10 NRS	None	
Reduced appetite	Yes/no	0-10 NRS	None	
Breathlessness	Yes/no	0-10 NRS	Shortness of breath at rest	
Depression	Yes/no	0-10 NRS	Patient Health Questionnaire-9	Kroenke et al[38]
Anxiety	Yes/no	0-10 NRS	General anxiety disorder-2	Kroenke et al[39]
Insomnia	Yes/no	0-10 NRS	Problems falling asleep Problems sleeping all night Whether insomnia interferes with daily activities	Based on Insomnia Severity Index[40]
Constipation	Yes/no	0-10 NRS	Last bowel movement	CTCAE[41]
Vomiting	Yes/no	0-10 NRS	Frequency	CTCAE
Numbness in fingers or toes	Yes/no	0-10 NRS	None	
Diarrhea	Yes/no	0-10 NRS	Frequency Blood in stools	CTCAE
Mouth sores	Yes/no	0-10 NRS	None	
Dry mouth	Yes/no	0-10 NRS	None	
Altered sense of taste	Yes/no	0-10 NRS	None	
Altered sense of smell	Yes/no	0-10 NRS	None	
Problems swallowing	Yes/no	0-10 NRS	None	
Early satiety	Yes/no	0-10 NRS	None	

Abbreviations: CTCAE, Common Terminology Criteria for Adverse Events; NRS, numerical rating scale.

significance (Fig 2). A graph on the right shows symptom intensity over time, if available. Well-being, physical activity, nutritional intake, and weight are shown on top, because these are considered key factors in patient-centered treatment.

Formative Usability Tests of Eir-Patient and Eir-Doctor

Patients were recruited from the cancer outpatient clinic (Table 3) and were heterogeneous with respect to age, sex, cancer diagnosis, and treatment intent (curative, adjuvant, or palliative). Overall, they had few problems using Eir-Patient and appreciated that the physician received updated information about their clinical condition.

The questions per se posed few difficulties for patients, although some patients with related symptoms (eg, tiredness, lack of appetite, and depression) found some of the follow-up questions

to be overlapping. Most of the outpatients had a limited number of symptoms and thus relatively few questions to which to respond. As expected, using EirV3 was perceived as more demanding for PC patients with a high symptom burden compared with patients who were in a better physical condition.

Observations of patients using Eir revealed that they did not notice all elements on the screen at a time; they focused mainly on the middle and inadvertently skipped items on the left and right sides. Even when they skipped the instructions on the screen, patients found it easy to navigate in Eir (eg, moving forward or backward, finding the right answer, and having the answer registered). However, the latter posed some difficulties for patients who either did not position the tablet in the right angle or who had fingers that were too dry or too cold to obtain sufficient pressure on their

Table 3. Iterative Usability Testing of Eir

Time	Type of Test	Participants	Procedures	Main Findings and Subsequent Changes
September-October 2013	Test of a computerized pain body map	Outpatients with cancer (n = 10)	Observations of patients using different way of marking pain on a tablet Subsequent debriefing interviews Field notes	Finding: Shading on the pain area of the body map did not seem intuitive to patients. They preferred to tap or press the relevant area Change: Tapping or pressing the area of the pain location was sufficient for the area to be marked in red.
November 2013	Test of Eir-PatientV1	Outpatients with cancer (n = 7)	Observations of patient completing Eir-PatientV1 Think-aloud strategy Subsequent debriefing interviews Field notes	Finding: When patients did not find a relevant response alternative, they tended to choose another. Change: The alternative "None of these" was added. Finding: Some patients did not manage to get their taps registered. Change: Short and long clicks or taps, as well as swipes, are registered. Finding: The zooming function of the body map and too many navigation buttons on the same screen image were confusing. Change: The layout was improved, and the number of navigation buttons was reduced. Finding: Most patients did not read the instructions regarding completion. Change: Instructions were available by clicking on a Help button.
January-May 2014	Changes made in content, functionality, and layout; development of EirV2			
May 2014	Pilot test of Eir-PatientV2	Outpatients with cancer (n = 7)	Observations of patient completing Eir-PatientV2 Think-aloud method Subsequent debriefing interviews Field notes	Finding: Patients had trouble understanding that they could not mark more than 1 painful area on the body map at the time. Change: An information page was added before the pain section. Finding: If patients had trembling hands, they accidentally double-clicked on the Next button and skipped a page. Change: Rapid double-clicks are registered as 1 tap (1 registration).
June-December 2014	Clinical test of Eir-PatientV2 and Eir-DoctorV2*	Outpatients with cancer (n = 42); physicians in cancer department (n = 8)	Observations of patient completing Eir-PatientV2 Think-aloud strategy Subsequent debriefing interviews Observations of physicians using Eir-DoctorV2 in consultation Regular group discussions with physicians during the test period Field notes	Findings for Eir-Patient Finding: Some elements on the screen went unnoticed; some elements were misunderstood; the elements in the middle of the screen were read first. Change: The number of elements on each screen was reduced. Question and response alternatives were placed in the middle. Finding: Taps were not registered as a result of cold/dry fingers or long nails. Change: Optional use of stylus. Finding: Patients accidentally quit Eir and had to start all over. Change: The tablets were locked to Eir.

(Continued on following page)

Table 3. Iterative Usability Testing of Eir (Continued)

Time	Type of Test	Participants	Procedures	Main Findings and Subsequent Changes
				Findings for Eir-Doctor Finding: Physicians misunderstood the summarized information of well-being, nutrition, and physical functioning on the opening screen and did not intuitively understand (or remember) what questions the patient had answered. Change: Extra information was added to clarify what information had been given by the patient. Finding: Detailed information on well-being, nutrition, and physical functioning was left out of Eir-Doctor. Change: All these variables were presented in 1 click. Finding: The list of symptoms could be difficult to follow if the patient has registered several symptoms. Change: More sorting functions for symptoms added (eg, high to low on intensity and development of intensity since last registration).
January-May 2015	Changes made in content, functionality, and layout; development of EirV3			
May-June 2015	Pilot test of Eir-PatientV3	Outpatients with cancer (n = 9)	Observations of patients using Eir-PatientV3 Think-aloud method Subsequent debriefing interviews Field notes	Findings: If the patient had more than 1 painful area, the second pain section was initiated with a confusing question. Change: New question added. Finding: Patients found the question about physical function confusing, because this item had too many response alternatives that were not mutually exclusive. Changes: Question was changed to a validated question on physical function with fewer response options

*Changes in Eir-Patient-versions led to immediate changes in the corresponding Eir-Doctor-versions, thus numbering of versions is identical.

touch for registration. The pain body map with zoom functions and related follow-up questions turned out to be the most challenging part of Eir-Patient. Difficulties were related to marking of the painful area, primarily because patients tried to mark multiple areas at a time, even if instructions told them not to. They also found some of the follow-up pain questions confusing, particularly those related to pain descriptors (eg, "burning" and "pins and needles"), whereas some patients missed an option for marking radiating pain. The technologic features and explanations were revised accordingly in EirV3. All follow-up questions applied to each pain site, and the number of elements on each screen was reduced (eg, by skipping some of the instructions for navigation or answers, dropping a progress bar, and consistently centering the relevant items on the screen). Increasing the user-friendliness was also pursued by adding a "Help" function; adding the response alternative "None of these," as appropriate; and accepting different types of taps, swipes, and drags for registration.

When testing Eir-Doctor, physicians defined the graphical presentation of symptom trajectories as a key factor to monitor effect of treatments. They also mentioned that the current display in EirV3, which resulted from iterative rounds of feedback from clinical testing, made them aware of symptoms they had not known troubled the patient. Physicians found it useful to start the consultations with the list of symptoms and intensity scores. Because the patient's symptoms are ordered by intensity, the list and order of
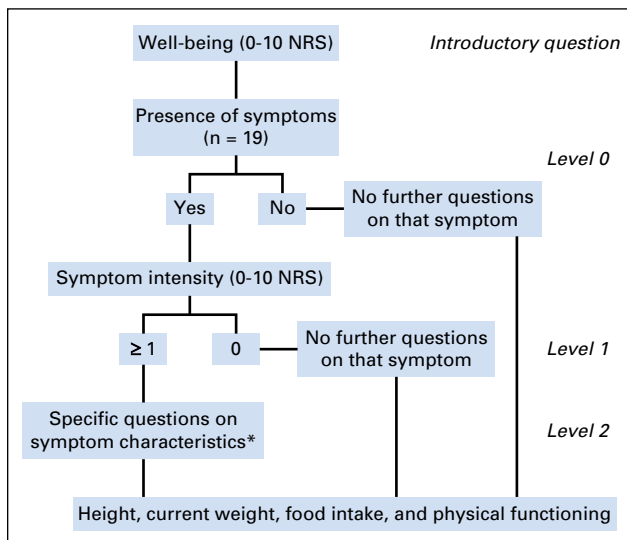
Fig 1. Symptom assessment algorithm. NRS, numerical rating scale. (*) Details in Table 2.

Fig 2. Eir-Doctor opening screen.

symptoms vary from one patient to the other. Some physicians preferred a fixed order, whereas others preferred high intensity as the default. All physicians regretted the fact that EirV3 is not yet integrated into the electronic patient records, because this would enhance the clinical decision making by combining individual patient data from different sources.[34]

Equivalence Between Electronic- and Paper-Based Assessment

Of the 114 patients included in the paper and pencil versus electronic assessments comparative study, 110 patients (97%) completed both

versions, 59 patients (54%) on tablets first and 51 patients (46%) on paper first. Mean age was 64.5 years (range, 27 to 86 years), and median Karnofsky performance score was 90 (range, 50 to 100). GI cancer was most common (47%), followed by prostate cancer (10%), breast cancer (9%), and malignant melanoma (9%). Eighty-nine percent of patients had metastatic disease. Overall, the median ICC was high (0.81; Table 4), with excellent values (> 0.75) for 15 of the 19 items (range, 0.64 [vomiting] to 0.92 [tiredness]). Overall, 41% of the patients preferred assessment on tablets, 19% preferred paper, and 40% had no preference. Preference for electronic assessment was more frequent among patients with higher education and patients with previous digital experience.

DISCUSSION

This study presents the requirements behind, the methods used, and the results achieved during the stepwise iterative development process of EirV3, an electronic symptom assessment system for cancer care. The main objective was to improve clinical consultations by focusing on the patient's perspective, through immediate transfer of PROMs to the HCP's computer. Thus, EirV3 represents something beyond a direct electronic version of paper PROMs, as is frequently done.[47-49] The real-time visual presentation of individually tailored PROMs supplemented with graphs for symptom development cannot be achieved by the paper-and-pencil format.
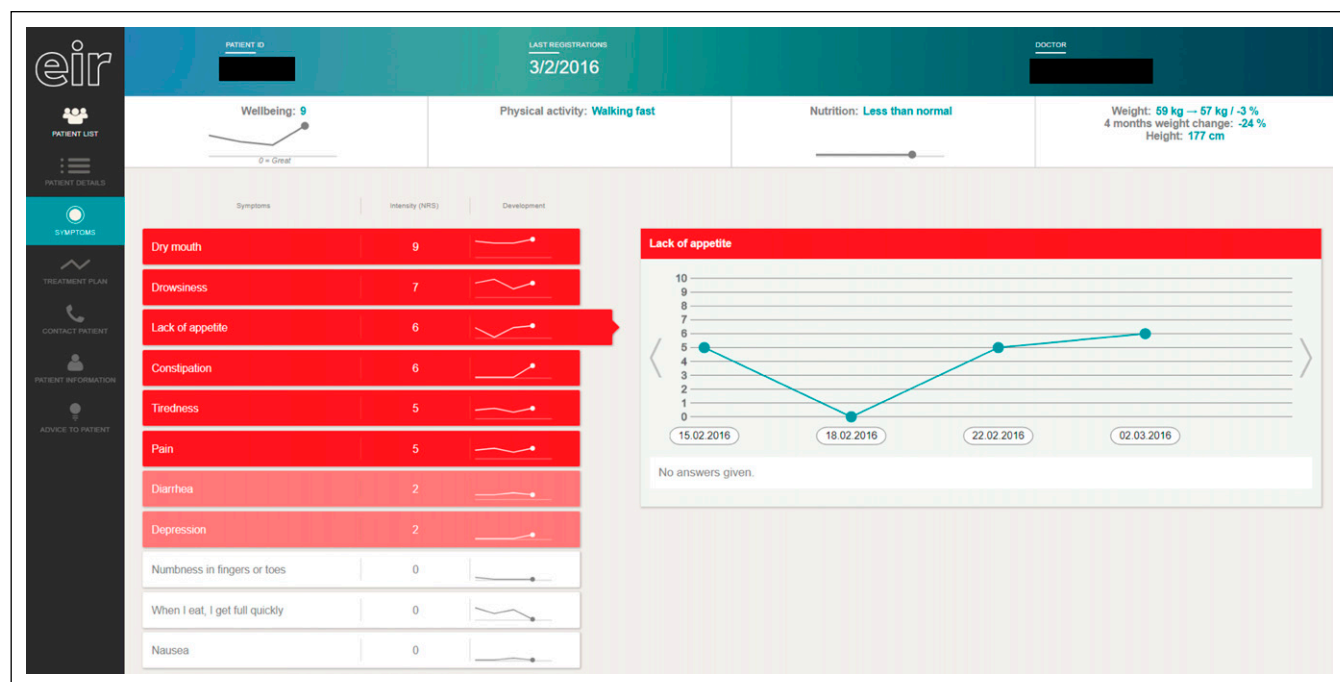
Table 4. Results From the Study Examining Equivalence Between Electronic and Paper Patient-Reported Outcome Measures

Symptoms	ICC	95% CI	Mean
Well-being	0.73	0.63 to 0.81	3.12
Pain	0.89	0.84 to 0.92	2.43
Numbness	0.87	0.82 to 0.91	2.06
Shortness of breath	0.83	0.76 to 0.88	2.40
Drowsiness	0.89	0.85 to 0.93	3.20
Tiredness	0.92	0.88 to 0.94	3.92
Insomnia	0.75	0.65 to 0.82	2.39
Anxiety	0.81	0.73 to 0.87	2.68
Depression	0.80	0.72 to 0.86	2.04
Nausea	0.76	0.67 to 0.83	1.06
Vomiting	0.65	0.53 to 0.75	0.37
Diarrhea	0.88	0.83 to 0.91	1.02
Constipation	0.90	0.86 to 0.93	1.81
Lack of appetite	0.91	0.87 to 0.93	2.05
Mouth sores	0.88	0.83 to 0.92	0.49
Dry mouth	0.82	0.75 to 0.88	2.50
Altered sense of taste	0.74	0.64 to 0.81	1.92
Altered sense of smell	0.77	0.69 to 0.84	1.29
Problems swallowing	0.72	0.61 to 0.80	0.69

NOTE. Median ICC for all items was 0.81 (25th-75th quartile, 0.75 to 0.89).
Abbreviation: ICC, intraclass correlation coefficient.

The content in EirV3 covers a wide range of common cancer-related symptoms. Some argue that electronic PROM tools should be diagnosis or treatment specific to capture relevant clinical information,[14,50] whereas Eir was developed for use in adult patients with cancer, independent of cancer diagnosis, treatment, age, and stage of disease. Thus, one may question the specificity of the included symptoms. However, relevance for an individual patient is documented by well-validated tools and guidelines and enhanced by the presentation in a dynamic, electronic format. This way, patients receive tailored questions based on their current symptom status. Because the primary aim is to improve symptom management, the cutoff levels that decide the subsequent in-depth questions deserve attention. The cutoff in EirV3 is > 1 and is purposefully low not to risk overlooking symptoms. Cutoffs for high values are important, and based on common clinical practice, systematic reviews,[51] and clinical studies,[52] values ≥ 3 were flagged to alert physicians.

We regard the continuous involvement of end-users—patients with cancer and HCPs—as

extremely valuable, leading to close collaboration and immediate improvements. Physicians' feedback on Eir-Doctor was paramount for improvement of several functional issues. The list of symptoms in Eir-DoctorV3 (Fig 2) was perceived as beneficial for a quick overview of the current situation, even if some preferred a fixed order. Physicians frequently commented that they liked the graphical presentation of symptom trajectories and that they occasionally became aware of symptoms they did not know troubled the patient. The integration of Eir into the hospitals' records is a priority that implies security issues related to patient confidentiality and data storage.

So far, results from this thorough, systematic, and iterative development process indicate that EirV3 is user-friendly and self-explanatory for most patients. Usability issues of the first versions (eg, shortcomings regarding layout and the pain body map) led to immediate system modifications. Many of these changes, such as reducing the number of elements on each screen and centering the text, were done to reduce the likelihood of errors, thereby optimizing reliability. In our opinion, this emphasizes the importance of including end-users to improve the usability of any tool, be it digital or on paper. This was also the benefit of developing and testing Eir-Patient and Eir-Doctor in parallel, as feedback from physicians could be used for amendments of Eir-Patient, and vice versa.

Most patients regarded Eir as intuitively easy to use and appreciated its relevance and that results reached the physicians immediately. However, this was true on the group level. It may be that the perceptions varied among subgroups of patients (eg, fit v frail patients, patients with few symptoms v those with many). As a result of a generally higher symptom burden, completion was more demanding for patients in the palliative outpatient unit than in the oncology unit, potentially supporting the issue about subgroup differences, corresponding with results from other studies using computerized assessment.[21,53-56] The most negative comments were that Eir is not yet automatically incorporated into the electronic medical records and that it should be opened in an Internet browser, not connected with the regular hospital network.

Patients judged to be cognitively impaired were not included in the studies. However, it could be that some patients with mild cognitive impairment may find it easier to use an electronic tool, but this

needs to be thoroughly examined using a cognitive screening tool and a simpler electronic tool, which was beyond the scope of this work.

The comparative study examining equivalence between electronic and paper-based PROMs showed excellent agreement between the two methods. However, it should be noticed that the mean symptom intensity scores were low (Table 4). This may indicate that more patients were fit than frail and calls for purposive, maybe even stratified, sampling in forthcoming Eir studies to examine use in frailer patients. The issue regarding subgroups relates to generalizability and validity and cannot be examined by formative testing. However, this is not related to electronic PROMs tools per se, but applies to most formative process developments. In Norway, 97% of all households (with at least one person age < 75 years) had access to the Internet in 2015.[57] Lack of access to the Internet is probably not a limiting factor. Electronic health records are implemented in most Norwegian hospitals. Considering this, preference for electronic assessment was not overwhelming. This was a short questionnaire, however, so the response method might be of less importance in this context.

Eir is still in development, which implies an evaluation of the pros and cons of the development methods. The obvious next steps on our agenda consist of summative methods to systematically assess and quantify validation and usability issues.[58] Topics to investigate are the feasibility of using EirV3 in different settings, including home care, the frequency of use, and how it is being used by patients and HCPs in inpatient and outpatient units. Moreover, we need to assess the perceived usefulness of electronic PROMs in improving patient outcomes such as better symptom management, satisfaction with care and communication with HCPs, time of completion for distinct and vulnerable patients, and the degree of errors and system flaws (eg, down time). Automatic alerts

when a patient has completed Eir will be developed. However, in the presented studies, study nurses were responsible for notifying the clinicians. The summative phase of Eir development has started with four small studies and one international validation study.

Some studies have documented an improvement in symptoms with systematic collections of PROMs, either electronically or on paper.[8,13,59,60] A recent randomized controlled trial concluded that this was attributed to the systematic monitoring that led to immediate symptom management in patients with a high symptom burden.[13] However, it is interesting that better satisfaction with patient-HCP communication is still the most prominent effect of systematic PROM registrations,[61] 15 years after the first publication by Velikova et al.[62]

Two take-home messages apply. First, even if newer studies do not show statistically significant effects of PROMs, the work toward patient-centered, electronic tools should continue to promote clinical uptake. Second, no tools are intended to replace the face-to-face interaction between patients and HCPs; instead, they should be regarded an asset for putting the patient's perspective in the center of the communication.

In conclusion, overall, technologic advances have led to an abundance of electronic PROM tools. In contrast to many others, EirV3 is not a direct electronic version of a paper-based questionnaire, but a dynamic tool adapted to the individual patient. EirV3 resembles a clinical consultation, and patients and HCPs endorsed the immediate transfer of PROMS to the physician's computer. Integration with electronic medical records is likely to improve symptom management and patient care by combining individual patient data from many sources simultaneously.

AUTHOR CONTRIBUTIONS
Conception and design: Hilde Krogstad, Kari Sand, Eivind Andersen, Tarje Halvorsen, Stein Kaasa, Jon Håvard Loge, Erik Torbjørn Løhre, Sunil X. Raj, Marianne Jensen Hjermstad
Administrative support: Kari Sand, Stein Kaasa, Marianne Jensen Hjermstad
Provision of study material or patients: Herish Garresori, Ellinor C. Haukland, Stein Kaasa, Marianne Jensen Hjermstad

Collection and assembly of data: Hilde Krogstad, Cinzia Brunelli, Kari Sand, Herish Garresori, Ellinor C. Haukland, Frode Jordal, Marianne Jensen Hjermstad
Data analysis and interpretation: Hilde Krogstad, Cinzia Brunelli, Kari Sand, Stein Kaasa, Erik Torbjørn Løhre, Marianne Jensen Hjermstad
Manuscript writing: All authors
Final approval of manuscript: All authors
Agree to be accountable for all aspects of the work: All authors

Affiliations

Hilde Krogstad, **Cinzia Brunelli**, **Kari Sand**, **Tarje Halvorsen**, **Stein Kaasa**, **Jon Håvard Loge**, **Erik Torbjørn Løhre**, **Sunil X. Raj**, and
Marianne Jensen Hjermstad, European Palliative Care Research Centre, Norwegian University of Science and Technology (NTNU)
and St Olavs Hospital, Trondheim University Hospital; **Hilde Krogstad**, **Tarje Halvorsen**, **Erik Torbjørn Løhre**, and **Sunil X. Raj**, Cancer
Clinic, St Olavs Hospital, Trondheim University Hospital; **Eivind Andersen**, NTNU Technology Transfer AS, Trondheim; **Stein
Kaasa**, **Jon Håvard Loge**, and **Marianne Jensen Hjermstad**, Oslo University Hospital, Oslo; **Herish Garresori**, Stavanger University
Hospital, Stavanger; **Ellinor C. Haukland**, Nordland Hospital Trust, Bodø; **Frode Jordal**, Østfold Hospital Trust, Grålum, Norway;
and **Cinzia Brunelli**, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale dei Tumori, Milano, Italy.

REFERENCES

1. Grol R, Grimshaw J: From best evidence to best practice: Effective implementation of change in patients' care. Lancet
   362:1225-1230, 2003

2. Basch E, Abernethy AP: Supporting clinical practice decisions with real-time patient-reported outcomes. J Clin Oncol
   29:954-956, 2011

3. Reeve BB, Mitchell SA, Dueck AC, et al: Recommended patient-reported core set of symptoms to measure in adult
   cancer treatment trials. J Natl Cancer Inst 106:dju129, 2014

4. NIH State-of-the-Science Statement on symptom management in cancer: pain, depression, and fatigue. NIH Consens
   State Sci Statements 19:1-29, 2002

5. Calvert M, Blazeby J, Altman DG, et al: Reporting of patient-reported outcomes in randomized trials: The CONSORT
   PRO extension. JAMA 309:814-822, 2013

6. Boyes A, Newell S, Girgis A, et al: Does routine assessment and real-time feedback improve cancer patients' psy-
   chosocial well-being? Eur J Cancer Care (Engl) 15:163-171, 2006

7. Detmar SB, Muller MJ, Schornagel JH, et al: Health-related quality-of-life assessments and patient-physician
   communication: A randomized controlled trial. JAMA 288:3027-3034, 2002

8. Velikova G, Booth L, Smith AB, et al: Measuring quality of life in routine oncology practice improves communication
   and patient well-being: A randomized controlled trial. J Clin Oncol 22:714-724, 2004

9. Basch E, Deal AM, Kris MG, et al: Symptom monitoring with patient-reported outcomes during routine cancer
   treatment: A randomized controlled trial. J Clin Oncol 34:557-565, 2016

10. Kaasa S, Loge JH, Fayers P, et al: Symptom assessment in palliative care: A need for international collaboration. J Clin Oncol 26:3867-3873, 2008

11. Greenhalgh J: The applications of PROs in clinical practice: What are they, do they work, and why? Qual Life Res 18: 115-123, 2009

12. Kotronoulas G, Kearney N, Maguire R, et al: What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. J Clin Oncol 32:1480-1501, 2014

13. Strasser F, Blum D, von Moos R, et al: The effect of real-time electronic monitoring of patient-reported symptoms and clinical syndromes in outpatient workflow of medical oncologists: E-MOSAIC, a multicenter cluster-randomized phase III study (SAKK 95/06). Ann Oncol 27:324-332, 2016

14. Velikova G, Awad N, Coles-Gale R, et al: The clinical value of quality of life assessment in oncology practice: A qualitative study of patient and physician views. Psychooncology 17:690-698, 2008

15. Snyder CF, Jensen RE, Geller G, et al: Relevant content for a patient-reported outcomes questionnaire for use in oncology clinical practice: Putting doctors and patients on the same page. Qual Life Res 19:1045-1055, 2010

16. Santana MJ, Feeny D, Weinkauf J, et al: The use of patient-reported outcomes becomes standard practice in the routine clinical care of lung-heart transplant patients. Patient Relat Outcome Meas 1:93-105, 2010

17. Rose M, Bezjak A: Logistics of collecting patient-reported outcomes (PROs) in clinical practice: An overview and practical examples. Qual Life Res 18:125-136, 2009

18. European Association for Palliative Care Research Network: Do you want to take part in palliative care research? http://www.eapcnet.eu/Themes/Research.aspx

19. Norwegian University of Science and Technology: European Palliative Care Research Centre. www.ntnu.edu/prc

20. Hølen JC, Hjermstad MJ, Loge JH, et al: Pain assessment tools: Is the content appropriate for use in palliative care? J Pain Symptom Manage 32:567-580, 2006

21. Fyllingen EH, Oldervoll LM, Loge JH, et al: Computer-based assessment of symptoms and mobility in palliative care: Feasibility and challenges. J Pain Symptom Manage 38:827-836, 2009

22. Hjermstad MJ, Lie HC, Caraceni A, et al: Computer-based symptom assessment is feasible in patients with advanced cancer: Results from an international multicenter study, the EPCRC-CSA. J Pain Symptom Manage 44:639-654, 2012

23. Di Maio M, Perrone F: Quality of Life in elderly patients with cancer. Health Qual Life Outcomes 1:44, 2003

24. Raj SX, Klepstad P, Brunelli C, et al: COMBAT study: Computer Based Assessment and Treatment—A computerized clinical decision support system for evaluation and treatment of pain and other cancer related symptoms. Palliat Med 28:549-550, 2014 (abstr)

25. Jaatun EA, Hjermstad MJ, Gundersen OE, et al: Development and testing of a computerized pain body map in patients with advanced cancer. J Pain Symptom Manage 47:45-56, 2014

26. Andreassen Jaatun EA, Haugen D, Dahl Y, et al: Designing a reliable pain drawing tool: Avoiding interaction flaws by better tailoring to patients' impairments. Pers Ubiquitous Comput 19:635-648, 2015

27. Knudsen AK, Brunelli C, Klepstad P, et al: Which domains should be included in a cancer pain classification system? Analyses of longitudinal data. Pain 153:696-703, 2012

28. Knudsen AK, Aass N, Fainsinger R, et al: Classification of pain in cancer patients: A systematic literature review. Palliat Med 23:295-308, 2009

29. Caraceni A, Hanks G, Kaasa S, et al: Use of opioid analgesics in the treatment of cancer pain: Evidence-based recommendations from the EAPC. Lancet Oncol 13:e58-e68, 2012

30. Rayner L, Price A, Hotopf M, et al: The development of evidence-based European guidelines on the management of depression in palliative cancer care. Eur J Cancer 47:702-712, 2011

31. Sigurdardottir KR, Kaasa S, Rosland JH, et al: The European Association for Palliative Care basic dataset to describe a palliative care cancer population: Results from an international Delphi process. Palliat Med 28:463-473, 2014

32. Fearon K, Strasser F, Anker SD, et al: Definition and classification of cancer cachexia: An international consensus. Lancet Oncol 12:489-495, 2011

33. Kaasa S, Apolone G, Klepstad P, et al: Expert conference on cancer pain assessment and classification: The need for international consensus—Working proposals on international standards. BMJ Support Palliat Care 1:281-287, 2011

34. Brunelli C, Bennett MI, Kaasa S, et al: Classification of neuropathic pain in cancer patients: A Delphi expert survey report and EAPC/IASP proposal of an algorithm for diagnostic criteria. Pain 155:2707-2713, 2014

35. Zeppetella G, Davies AN: Opioids for the management of breakthrough pain in cancer patients. Cochrane Database Syst Rev 10:CD004311, 2013

36. Portenoy RK, Hagen NA: Breakthrough pain: Definition and management. Oncology (Williston Park) 3:25-29, 1989 (suppl 8)

37. Hagen NA, Stiles C, Nekolaichuk C, et al: The Alberta Breakthrough Pain Assessment Tool for cancer patients: A validation study using a Delphi process and patient think-aloud interviews. J Pain Symptom Manage 35:136-152, 2008

38. Kroenke K, Spitzer RL, Williams JB: The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med 16: 606-613, 2001

39. Kroenke K, Spitzer RL, Williams JB, et al: Anxiety disorders in primary care: Prevalence, impairment, comorbidity, and detection. Ann Intern Med 146:317-325, 2007

40. Morin C: Insomnia: Psychological Assessment and Management. New York, NY, Guilford Press, 1993

41. National Cancer Institute: Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0. https://ctep.cancer. gov/protocoldevelopment/electronic_applications/ctc.htm

42. Bauer J, Capra S, Ferguson M: Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. Eur J Clin Nutr 56:779-785, 2002

43. Stinson J, McGrath P, Hodnett E, et al: Usability testing of an online self-management program for adolescents with juvenile idiopathic arthritis. J Med Internet Res 12:e30, 2010

44. McGraw K, Wong S: Forming inferences about some intraclass correlation coefficients. Psychol Methods 1:30-46, 1996

45. Cicchetti DV: Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. Psychol Assess 6:284-290, 1994

46. Løhre ET, Klepstad P, Bennett MI, et al: From "breakthrough" to "episodic" cancer pain? A European Association for Palliative Care Research Network expert Delphi survey toward a common terminology and classification of transient cancer pain exacerbations. J Pain Symptom Manage 51:1013-1019, 2016

47. Holzner B, Giesinger JM, Pinggera J, et al: The Computer-based Health Evaluation Software (CHES): A software for electronic patient-reported outcome monitoring. BMC Med Inform Decis Mak 12:126, 2012

48. Basch E, Iasonos A, Barz A, et al: Long-term toxicity monitoring via electronic patient-reported outcomes in patients receiving chemotherapy. J Clin Oncol 25:5374-5380, 2007

49. Jensen RE, Snyder CF, Abernethy AP, et al: Review of electronic patient-reported outcomes systems used in cancer clinical care. J Oncol Pract 10:e215-e222, 2014

50. Snyder CF, Wu AW, Miller RS, et al: The role of informatics in promoting patient-centered care. Cancer J 17:211-218, 2011

51. Oldenmenger WH, de Raaf PJ, de Klerk C, et al: Cut points on 0-10 numeric rating scales for symptoms included in the Edmonton Symptom Assessment Scale in cancer patients: A systematic review. J Pain Symptom Manage 45:1083-1093, 2013

52. Seow H, Sussman J, Martelli-Reid L, et al: Do high symptom scores trigger clinical actions? An audit after implementing electronic symptom screening. J Oncol Pract 8:e142-e148, 2012

53. Erharter A, Giesinger J, Kemmler G, et al: Implementation of computer-based quality-of-life monitoring in brain tumor outpatients in routine clinical practice. J Pain Symptom Manage 39:219-229, 2010

54. Abernethy AP, Herndon JE II, Wheeler JL, et al: Improving health care efficiency and quality using tablet personal computers to collect research-quality, patient-reported data. Health Serv Res 43:1975-1991, 2008

55. Velikova G, Wright EP, Smith AB, et al: Automated collection of quality-of-life data: A comparison of paper and computer touch-screen questionnaires. J Clin Oncol 17:998-1007, 1999

56. Kearney N, Kidd L, Miller M, et al: Utilising handheld computers to monitor and support patients receiving chemotherapy: Results of a UK-based feasibility study. Support Care Cancer 14:742-752, 2006

57. Statistics Norway: ICT usage in households, 2015, 2nd quarter. https://www.ssb.no/en/teknologi-og-innovasjon/ statistikker/ikthus/aar/2015-10-01

58. Theofanos MF, Quesenbery W: Towards the design of effective formative test reports. J Usability Stud 1:27-45, 2005

59. Johansen MA, Berntsen GK, Schuster T, et al: Electronic symptom reporting between patient and provider for improved health care service quality: A systematic review of randomized controlled trials. Part 2: Methodological quality and effects. J Med Internet Res 14:e126, 2012

60. Yount SE, Rothrock N, Bass M, et al: A randomized trial of weekly symptom telemonitoring in advanced lung cancer. J Pain Symptom Manage 47:973-989, 2014

61. Berry DL, Blumenstein BA, Halpenny B, et al: Enhancing patient-provider communication with the electronic self-report assessment for cancer: A randomized trial. J Clin Oncol 29:1029-1035, 2011

62. Velikova G, Brown JM, Smith AB, et al: Computer-based quality of life questionnaires may contribute to doctor-patient interactions in oncology. Br J Cancer 86:51-59, 2002

63. Helbostad JL, Holen JC, Jordhoy MS, et al: A first step in the development of an international self-report instrument for physical functioning in palliative cancer care: A systematic literature review and an expert opinion evaluation study. J Pain Symptom Manage 37:196–205, 2009

64. Rayner L, Price A, Hotopf M, et al: The development of evidence-based European guidelines on the management of depression in palliative cancer care. Eur J Cancer 47:702–712, 2011

65. Hjermstad MJ, Fayers PM, Haugen DF, et al: Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: A systematic literature review. J Pain Symptom Manage 41:1073–1093, 2011

66. Haugen DF, Hjermstad MJ, Hagen N, et al: Assessment and classification of cancer breakthrough pain: A systematic literature review. Pain 149:476–482, 2010

67. Martin-Moreno J, Albreht T, Krnl SR (eds): Boosting Innovation and Cooperation in European Cancer Control. Key Findings From the European Partnership for Action Against Cancer. Ljubljana, Slovenia, National Institute of Public Health of the Republic of Slovenia, 2013

APPENDIX

Former Development of Electronic Symptom Assessment Tools From Our Group

The Patient Assessment Tool-Computerized study (2007). In this descriptive study, patients with advanced cancer responded to 59 questions and a pain body map on touchscreen computers.[21] The selection of items was based on systematic reviews[20,63] and surveys among patients with cancer and expert groups. Most patients (93%) were able to report symptoms directly on the computer

The European Palliative Care Research Collaborative Computerized Symptom Assessment study (2008 to 2009). This international, multicenter study used a more sophisticated tablet version in 1,017 patients with advanced cancer. Patients were recruited from 17 centers and eight countries (Norway, the United Kingdom, Austria, Germany, Switzerland, Italy, Canada, and Australia). They responded to questions on symptoms, nutritional intake, and physical and emotional functions. The software was programmed in four languages (English, German, Italian, and Norwegian) and contained several skip sessions to reduce patient burden; if the patient had no pain, the rest of the pain section was omitted.[22] In agreement with results from other computerized assessment studies,[21,53-56] the completion rate was high (95%), with more missing information and need for assistance associated with higher age and lower performance status, similar to results when using paper-and-pencil assessments.[23]

Continuous software improvements and small-scale tests were performed based on feedback from patients and health care providers in the European Palliative Care Research Collaborative Computerized Symptom Assessment study. In 2012, a tablet version that included treatment recommendations for pain and depression was used in a Norwegian clinical trial of 143 outpatients with cancer.[24] Two studies comparing different versions of a computerized pain body map in randomized order and testing different ways of marking pain were also conducted and demonstrated the need to optimize the user-friendliness by simplifying the design for the frailest patients.[25,26]

Expert Meetings and Workshops to Decide the Content and Development of Eir

Between 2013 and 2015, regular meetings were held by the international expert panel and the core working group, in addition to two workshops.

International expert panel. The international expert group participated in workshops and roundtable discussions addressing symptom assessment, classification, and management in 2013 and 2014. Relevant symptom dimensions and validated symptom assessment tools for the choice of specific items were identified, aggregated, and presented to researchers and clinicians from different specialties to reach consensus regarding relevance and importance.[10,31,33,64-66]

The first international Eir expert group meeting in 2013 was organized as part of the European Partnership for Action Against Cancer.[67] Here, 26 participants discussed computerized symptom assessment and development of Eir. The meeting was organized with short introductions about the objectives of Eir and symptom assessment followed by plenary discussions and two workshops in which the participants worked in groups, addressing symptom assessment and treatment guidelines. The following decisions were made at the meeting:

- Eir's content should be based on evidence-based or consensus-based assessment methods.
- Eir should have a hierarchical structure, with an introductory question prior to a screening section on symptoms, followed by a section on symptom intensity and yet another for characterization for endorsed symptoms (Fig 1).
- Patients' registrations in Eir should be immediately transferred and visually presented.
- Eir should be user-friendly and relevant for heterogeneous cancer populations.
- Eir should be easy to adapt to cultural and clinical preferences.

The second international expert meeting (2013; n = 9) was arranged after the participants had tested the first tablet version of Eir-Patient (EirV1). Here, feedback regarding content and layout was collected and summarized for each of the screen images. Subsequent discussions resulted in consensus on which symptoms to include in Eir and the structure and presentation of the included items. The third international meeting (2014) consisted with experts in neuropathic and breakthrough pain (n = 5) and focused on achieving consensus on how to screen these pain types in Eir.

Norwegian core working group. The core working group (n = 15) consisted of oncologists, palliative care physicians, researchers, interaction designers, graphic designers, and software developers. Members of the core working group were the first to test each new feature of Eir, as part of the iterative development. Regular multiprofessional meetings were organized with group members, the software development team, and designers to discuss functionality and features and decide refinements.

Workshops. Prior to the development EirV1 in 2013 (Table 1), two national workshops were conducted to assess the needs and preferences of end-users. The first workshop (2013) presented the overall idea and intention of Eir to physicians, nurses, designers, and patients as participants (n = 20). Furthermore, the intended features of Eir-Patient, such as content, layout, and functionalities, were presented, and feedback suggestions from the participants were collected. The participants were positive about using an electronic tool and could foresee several advantages related to easy collection and more focus on symptom assessment, including immediate access to patients' patient-reported outcome measure scores and perhaps also improved communication.

The second workshop in 2013 was conducted with five physicians who suggested different ways of presenting patient-reported outcome measures in Eir-Doctor, either with as much information as possible on the opening screen in Eir-Doctor or to highlight only the most relevant information (eg, symptoms with the highest intensity, those with the most pronounced increase, or a combination of these).

Formative Usability Testing Methods

Formative usability tests[43] on separate sections (eg, general pain and breakthrough pain), as well as on more complete versions of Eir, were repeatedly performed by patients at the Cancer Clinic, St Olavs Hospital, Trondheim University Hospital, during the entire development process. Reports from these tests were presented to the core working group in weekly meetings, together with ideas for changes as drawn sketches or on a monitor. Consensus was reached regarding how to eliminate identified usability problems and to meet user preferences.

In November 2013, EirV1 was tested by outpatients with cancer for the first time (Table 3). On the basis of results from tests in end-users and feedback and discussion in all groups, major improvements from EirV1 to EirV2 were made in the first two quarters of 2014. The most important changes aimed to improve the user interface. For example, the display was radically changed to make the distinction between response options clearer, the buttons were slightly moved, and the layout on all questions in the symptom screening and follow-up sections were standardized. EirV2 included the Eir-Patient and Eir-Doctor modules, which were tested in 42 inpatients and outpatients and eight physicians at the Cancer Clinic in 2014 (Table 3). Patients completed Eir-Patient on tablets in the waiting room, and physicians used Eir-Doctor in the consultations. Usability data were collected through interviews and observations.