An integrated view on assuring quality for multimodal therapy in oncologic care

Schouwenburg, M.S.

7 A Standard Set of Value-Based Patient Centered Outcomes for Breast Cancer The International Consortium for Health Outcomes Measurement (ICHOM) Initiative

Schouwenburg MG[1], Ong WL[1], van Bommel ACM, Stowell C, Allison KH, Benn KE, Browne JP, Cooter RD, Delaney GP, Duhoux FP, Ganz PA, Hancock P, Jagsi R, Knaul FM, Knip AM, Koppert LB, Kuerer HM, McLaughin S, Mureau MAM, Partridge AH, Reid DP, Sheeran L, Smith TJ, Stoutjesdijk MJ, Vrancken Peeters MJTFD, Wengström Y, Yip CH, Saunders C

[1]The first two authors equally contributed to this manuscript

JAMA Oncol 2017 May 1;3(5):677-685

ABSTRACT

A major challenge in value-based health care is the lack of standardized health outcomes measurements, hindering optimal monitoring and comparison of the quality of health care across different settings globally. The International Consortium for Health Outcomes Measurement (ICHOM) assembled a multidisciplinary international working group, comprised of 26 health care providers and patient advocates, to develop a standard set of value-based patient-centered outcomes for breast cancer (BC). The working group convened via 8 teleconferences and completed a follow-up survey after each meeting. A modified 2-round Delphi method was used to achieve consensus on the outcomes and case-mix variables to be included. Patient focus group meetings (8 early or metastatic BC patients) and online anonymized surveys of 1225 multinational BC patients and survivors were also conducted to obtain patients' input. The standard set encompasses survival and cancer control, and disutility of care (eg, acute treatment complications) outcomes, to be collected through administrative data and/or clinical records. A combination of multiple patient-reported outcomes measurement (PROM) tools is recommended to capture long-term degree of health outcomes. Selected case-mix factors were recommended to be collected at baseline. The ICHOM will endeavor to achieve wide buy-in of this set and facilitate its implementation in routine clinical practice in various settings and institutions worldwide.

INTRODUCTION

Breast cancer (BC) is the most common cancer and the most common cause of cancer death in women worldwide [1]. BC management usually requires a multimodal approach, involving surgery, radiotherapy, chemotherapy, hormonal therapy and survivorship care [2, 3]. However, there is significant variation in BC treatment across institutions, geographical regions and countries [4-9]. Multiple randomized trials have shown equivalent survivals with different BC treatments [10], hence the treatment decision often comes down to the value each patient places on the potential gains/losses associated with each treatment option.

While achieving high *value* – defined as health outcomes per dollar spent – for patients is the overarching goal of healthcare delivery [11], often, defining and measuring health outcomes can be difficult. Outcome measurements need to encompass overall disease control, treatment complications, and quality of life (QOL) during and following treatment. Recognizing the lack of consistent outcome measurements, which hampers the monitoring of routine clinical practice, as well as quality of care and outcome comparison in a systematic and meaningful manner, the International Consortium for Health Outcomes Measures (ICHOM), a nonprofit organization has initiated efforts to develop standard sets of patient-centered outcome measurements for various medical conditions such as back pain [12], coronary artery diseases [13], cataract [14] and cancers (e.g. prostate cancer [15, 16] and lung cancer [17]). Building on previous ICHOM experience and successes, an international multidisciplinary working group (WG) for BC was assembled to develop a minimal standard set of outcomes that matter most to BC patients. The set can: 1) enhance clinician-patient shared decision-making; 2) provide quality outcome information to providers and institutions to drive transparency and improvement; and 3) increase the opportunity for comparative effectiveness research.

METHODS

ICHOM breast cancer working group

The development of the set was initiated by ICHOM (www.ichom.org), (eTable 1). The WG comprised 26 experts, including clinicians (breast/plastic surgeons, medical/radiation oncologists, pathologists, radiologists and palliative care physicians), nurses, epidemiologists, patient representatives and advocacy groups, from Europe, North America, Latin America, Australia and Asia. A smaller project team (PT) (W.L.O., M.S., A.V.B., C.S., and C.S.) guided the efforts of the larger WG.

Development of breast cancer standard set

The WG convened via eight videoconferences (August 2015–April 2016), and worked through a similar process as previous ICHOM WG [15-17]. Development of the set involved several phases (Figure 1).

Development of potential outcomes and case-mix list

The PT performed a structured PubMed literature review (January 1, 2005 to July 29, 2015) (eTable 2 and eFigure 1) to identify relevant clinical and patient-reported QOL outcomes, treatment-related complications, survival measures and case-mix factors. The literature review retrieved 1360 randomized controlled trials, and a total of 398 papers were included for review. Existing BC registries were also reviewed, and WG experts were asked to identify additional relevant sources. To ensure patients' input in the outcomes selection, a focus group meeting with eight early/metastatic BC patients was conducted (guided by W.L.O., M.S. and A.V.B.), to explore patients' perspective on the importance of different outcomes, and what affected them, or other patients, the most during their day-to-day lives.

Modified 2-Round Delphi Method

After each videoconference, a survey was circulated, requiring each working group member to vote on the proposed outcomes, case-mix variables and PROMs. A modified 2-round Delphi approach (eTables 3 and 4) was used to reach consensus. In brief, the proposed outcomes or variables needed to be voted as very important (ie, score of 7-9 on a 9-point Likert scale) in either voting rounds by more than 70% of the working group members for inclusion in the set.

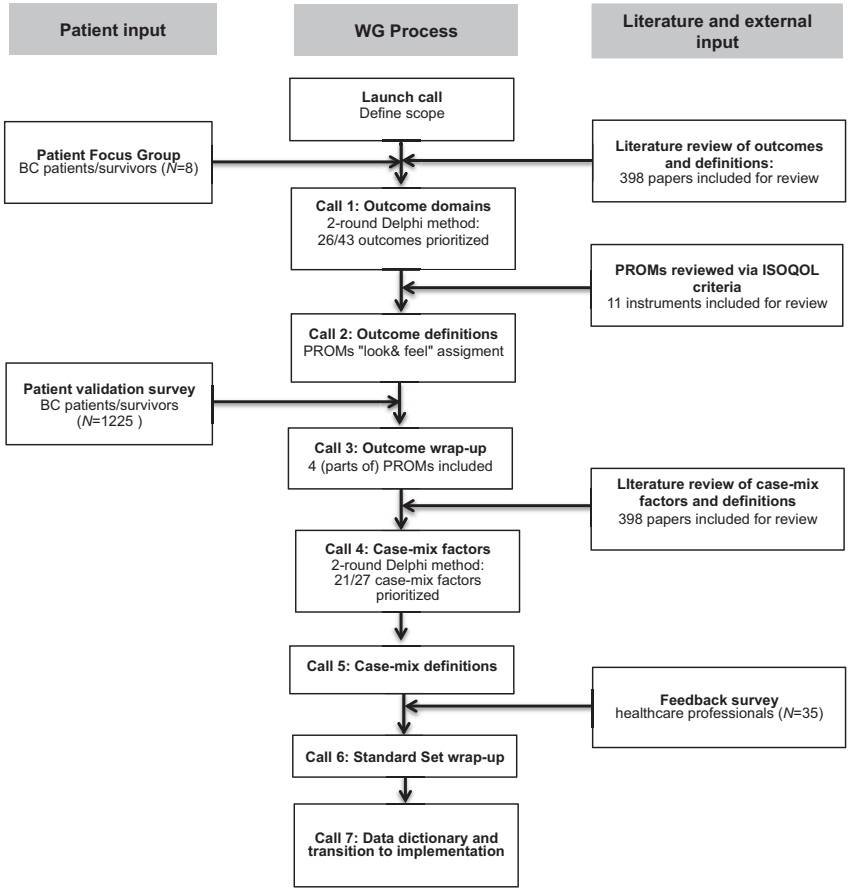


Figure 1. Summary of the development of the ICHOM Breast Cancer Standard Set
PROMs = patient-reported outcome measurements; ISOQOL = International Society for Quality of Life Research.

Outcomes Validation

The final list of outcomes was validated in 1225 multinational BC patients and survivors, recruited via several international patient organizations (eTable 5). Participants were asked to complete an anonymized survey, rating the importance of each outcome on a 9-point Likert scale, with an option of including additional outcomes in text form (eTables 6 and 7).

Selection of PROMs

After finalizing the list of outcomes, the corresponding PROMs were identified. The PROMs were evaluated by the project team, based on psychometric quality according to the International Society for Quality of Life Research (ISOQOL) criteria [18] (eTable 8) and the domain coverage (eTable 9). Prior to the voting, working group members were asked to complete the different PROMs, from a patient's perspective.

External Input

The final draft was presented to key stakeholders and others with an interest in outcome measurement for review and to provide feedback via online survey. They were asked to rate their confidence on several elements of the set (eg, completeness of the outcome list, implementation feasibility) on a 9-point Likert scale, with an open field for comments.

RESULTS

Condition and Treatment Scope

The set was designed for all pathologically confirmed American Joint Committee of Cancer (AJCC) patients with stages 0 to IV BC, including ductal carcinoma in situ (DCIS), in both men and women. Rare tumors such as Phyllodes tumors and lobular carcinoma in situ were excluded, given the difficulty in defining a standard of care for these tumor subtypes.

Outcomes

After consolidating the findings of the literature review and focus group meeting, a proposed list of 43 outcomes was identified for vote (eTable 9), the working group recommended the use of a combination of multiple PROMs (Table 1). The working group recognized that selection and recommendation of PROMs for inclusion in the set can be contentious given that there are multiple available PROMs of high psychometric quality (eg, European Organization for Research and Treatment of Cancer Quality of Life [EORTC-QLQ] and Functional Assessment of Cancer Therapy [FACT] questionnaires) that are already being used in different institutions. The PROMs were evaluated based on the outcomes cover-age, psychometric quality,

Table 1 – Summary of outcomes for the ICHOM Breast Cancer Standard Set

Patient Population	Measure		Data Sources[a]
Survival and Disease Control			
All patients	Overall survival		Administrative
	Death attributed to breast cancer		
Patients with curative intent	Recurrence free survival (local, regional or distant)		Clinical
Degree of Health			
All patients	Overall well-being	Tracked via EORTC QLQ-C30	Patient-reported
	Physical functioning		
	Emotional functioning		
	Cognitive functioning		
	Social functioning		
	Ability to work		
	Anxiety		
	Depression		
	Insomnia		
	Financial impact		
	Pain		
	Fatigue		
	Sexual functioning	Tracked via EORTC QLQ-BR23	
	Body image		
Patients with surgery/ radiotherapy	Satisfaction with breast(s)	Tracked via BREAST-Q- Satisfaction with Breasts domain	
	Arm symptoms	Tracked via EORTC QLQ-BR23	
	Breast symptoms		
Patients with systemic therapy	Vasomotor symptoms		
	Peripheral neuropathy	Tracked via EORTC QLQ-LMC21- one item	
	Vaginal symptoms	Tracked via ES of the FACT - six items	
	Arthralgia		

Table 1 – Summary of outcomes for the ICHOM Breast Cancer Standard Set (*continued*)

Patient Population	Measure	Data Sources[a]
Disutility of Care		
Patients with surgery	Reoperations due to involved margins	Clinical/patient-reported
All patients with treatment	Severity of acute complications based on the Clavien-Dindo and CTCAE	Clinical
	Name of acute complication	

EORTC QLQ= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, C= Core module BR= Breast Cancer module, LMC=Colorectal Liver Metastases, FACT =Functional Assessment of Cancer Therapy, ES= Endocrine Subscale, CTCAE= US National Cancer Institute Common Terminology Criteria for Adverse Events

[a] The data source reflects the way outcomes are collected and was determined as clinical (e.g. physician report), patient-reported (e.g. EORTC QLQ C-30) and administrative (e.g. Death registry), in some cases a combination.

clinical interpretability, and feasibility of PROMs implementation in daily practice (eTables 8 and 9). After extensive discussions and a "look-and-feel" assignment, the use of EORTC-QLQ-Core (C30) [24] and EORTC-QLQ-Breast Cancer (BR23) [25] was eventually recommended by the working group to capture the core cancer-specific and BC-specific outcomes. The working group also recommended additional questions from other PROMs to capture outcomes not encompassed by the EORTC questionnaires. These included the BREAST-Q [26] sub-scale for breast satisfaction, a single item from EORTC-QLQ-Liver Metastases (Colorectal) (LMC21) [27] for peripheral neuropathy, and 6 items from the FACT-Endocrine Subscale (ES) [28] for vaginal symptoms and arthralgia. The assessment of degree of health outcomes was recommended at baseline (ie, at diagnosis), 6 months after primary surgery, and annually thereafter (Figure 2). Follow-up was recommended up to 10 years in early BC patients to capture the period during which patients might still be on endocrine therapy.

Case-Mix Variables

The working group identified a minimal set of demographic, clinical, and tumor-related factors to be collected at baseline for meaningful outcome comparisons (Table 2). While socioeconomic status (SES) is an important demographic factor, accurate characterization of SES can be complex, involving multiple components

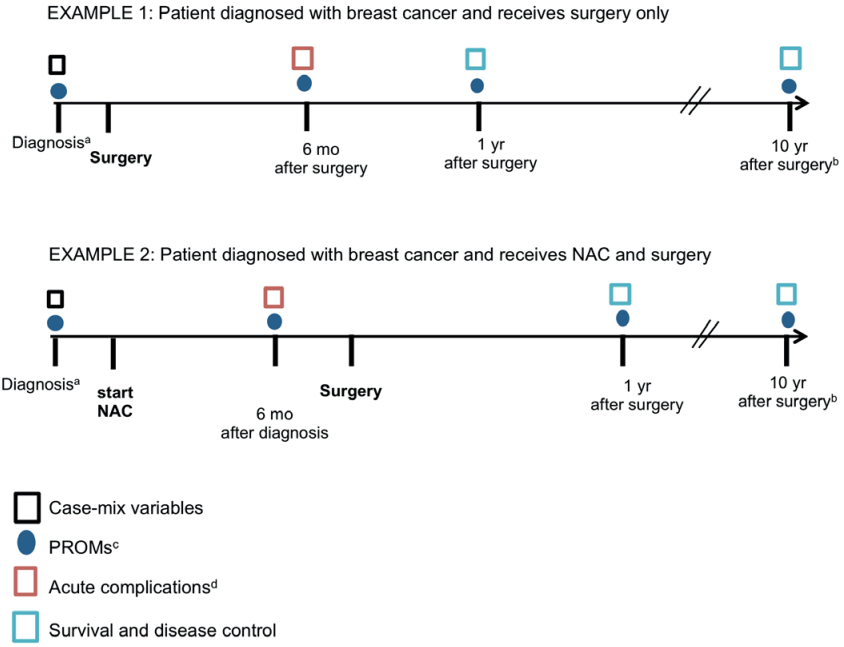


Figure 2. Sample timelines illustrating when particular outcomes and baseline factors should be collected for patients with breast cancer.

These timelines are intended to represent the outcome data collection points for possible treatment paths a patient could take, and do not advocate a particular treatment approach. Of note, a majority of baseline factors should be collected at the time of initiation of the Breast Cancer Standard Set, although several (eg, pathologic stage) are collected after treatment. NAC indicates neoadjuvant chemotherapy; PROMs, patient-reported outcome measurements.

[a]Collection of acute complications is recommended while the patient is undergoing treatment or within 90 days of treatment completion, except for complications of hormonal therapy which will be collected up to 1 year.

[b]All PROMs will be collected at baseline, 6 months after treatment, and then annually, except for the BREAST-Q-Satisfaction with Breasts domain, which will only be collected at baseline,1 year, and 2 years after treatment.

[c]Distinction for long-term follow-up: patients with local disease; follow-up up to 10 years, patients with advanced disease; follow-up annually for life

such as occupation and income. As with previous ICHOM working groups, the BC working group recommended the collection of education level based on the International Standard of Schooling Classification [29] because it is reported to be a good surrogate for SES, easy to obtain, and globally comparable [30]. Relationship

Table 2 – Summary of case-mix factors[a] and treatment approaches for the ICHOM Breast Cancer Standard Set

Patient Population	Measure	Data Sources[b]
Demographic Factors		
All patients	Gender	Patient-reported
	Date of birth	
	Body mass index	Clinical
	Ethnicity	Patient-reported
	Educational level[c]	
	Relationship status	
	Menopausal status	
Baseline Clinical Factors		
All patients	Comorbidities via the modified SCQ[d]	Patient-reported
	Laterality	Clinical
	Second primary tumor	
Baseline Tumor Factors		
All patients	Date of histological diagnosis	Clinical
	Histological type	
	Mutation status predisposing BC	
	Tumor grade (invasive)	
	Tumor grade (DCIS)	
Patients with NAC	Clinical TNM stage (AJCC 7th)	
Patients with surgery	Pathological TNM stage (AJCC 7th)	
	Size of invasive component of tumor (in mm)	
	Number of lymph nodes resected	
	Number of lymph nodes involved	
	Estrogen receptor status	
	Progesteron receptor status	
	Her-2 receptor status	
Treatment approaches		
All patients	(Reconstructive) surgery	Clinical/ patient-reported
	(Neo)adjuvant radiotherapy	
	(Neo)adjuvant chemotherapy	
	Targeted therapy	
	(Neo)adjuvant hormonal therapy	
	No therapy	

SCQ = Self-administered comorbidity questionnaire, DCIS = ductal carcinoma in situ, BC = breast cancer, NAC= neo-adjuvant therapy, AJCC = American Joint Committee on Cancer, DCIS = ductal carcinoma in situ

[a] All case-mix factors include measures with corresponding patient populations, definitions or supporting information, timing for collection and source of data.

[b] The data source reflects the way outcomes are collected and was determined as clinical (e.g. physician report), patient-reported (e.g. EORTC QLQ C-30) and administrative, in some cases a combination.

[c] Level of schooling defined in each country according to the International Standard Classification of Education.

[d] Have you ever been told by a doctor that you have any of the following? I have no other disease, heart disease (eg, angina, heart attack, or heart failure), high blood pressure, leg pain when walking due to poor circulation, lung disease (eg, asthma, chronic bronchitis, or emphysema), diabetes, kidney disease, liver disease, problems caused by stroke, disease of the nervous system (eg, Parkinson's disease or multiple sclerosis), other cancer (within the last 5 yr), depression, arthritis (select all that apply).

status is also included, because it is an indicator of available social support and is associated with survival and several functional outcomes [31]. Race and ethnicity did not meet the predefined voting criteria for inclusion in the set. However, because there is evidence suggesting its potential association with treatment decisions [32] and outcomes [33,34] for certain countries, it was decided to include this as optional.

Patients' baseline health status is another important factor influencing treatment decision-making and eventual treatment out-comes. However, the Eastern Cooperative Oncology Group (ECOG) performance status scoring is deemed to be an oversimplified representation of patients' health status, and is not commonly collected in patients with early stage BC. Likewise, collection of the Charlson Comorbidity Index (CCI) can be burdensome. Therefore, the working group recommended the use of the modified Self-administered Comorbidity Questionnaire (SCQ) to capture a list of relevant medical comorbidities [35], and baseline health status as measured by the EORTC-QLQ-C30/BR23 (Table 1). It has been shown that SCQ predicts functional outcomes as well as the CCI [36] Tumor factors to be collected are based on the AJCC TNM staging. Information on hormone and human epidermal growth factor receptor 2 status are recommended to be collected as a binary data ("yes" or "no"), recognizing variability in pathology reporting between institutions and countries.

Treatment Variables

To provide a standardized terminology of treatment options over heterogeneous, international health care settings, the most commonly used treatment modalities in daily practice were included (Table 2). Patients should also be asked to report on their ongoing treatments during follow-up because clinical data may be inaccurate, especially with endocrine therapy adherence [37].

External Input

A total of 35 health care professionals from different specialties completed the survey. The respondents were confident (mean score, 6.7 on 9-point Likert scale) of the comprehensiveness of the outcome list, case-mix variables, and feasibility of data collection in routine clinical practice (eTable 10). The main concerns raised were related to the lack of end-of-life (EOL) care outcomes, and the number of PROMs items, which could lead to noncompliance.

Data Collection and Implementation

The next crucial step after finalizing the BC set is the adoption and implementation of the set. To minimize variability and inconsistency in data collection, a reference guide including sample questionnaire s and a data dictionary has been created by ICHOM (http://www.ichom.org /medical-conditions/breast-cancer/). This will cover the potential source of the data, including clinical records and patient-reported sources, as well as frequency for each data collection.

DISCUSSION

With rising health care costs, and the options of multiple treatment modalities and prolonged survival among patients with BC, the importance of value-based health-care is increasingly being recognized [38]. However, a major challenge in value-based health care is the lack of standardization in outcome measurements meaningful to patients across different cultural and geographical settings [38]. The ICHOM has therefore convened an international multidisciplinary working group, from middle- to high-income countries, to develop a standard set of patient-centered outcomes that should be measured in all patients with BC.

The aim was to develop a set, which can, and should be collected in routine clinical practice, even in resource-limited health systems. We acknowledge that randomized controlled trials remain the gold standard for treatment outcomes comparison; however, the measurement of outcomes in routine clinical practice will better reflect outcomes in a real life setting. Furthermore, the set can function as a core outcomes measurement to be collected in trial set-tings, and can be expanded to include additional outcomes, based on individual trial requirements.

We are cognizant of the need to collect minimal data to limit bur-den to both health care providers and patients, but at the same time recognize the need to encompass important outcomes for meaningful comparisons. More than 80% of the multinational survey respondents agreed with the set, providing support that the set captures the key outcomes relevant to patients with BC. The working group is aware that the recommendation of collecting (part of) multiple PROMs, ranging from 59 to 82 questions, represents significant patient burden. However, patient representatives in the working group did not find the PROMs too cumbersome, because they are all salient questions. The EORTC is currently developing computerized adaptive testing (CAT) versions, which should reduce respondent burden [39]. In addition, there is evidence suggesting clinical benefits in symptom-monitoring with PROM during routine cancer treatment [40].

The primary PROMs recommended by the working group are based on the EORTC questionnaire. However, other PROMs, such as the FACT questionnaire, are also commonly used in many institutions. In fact there is no strong evidence to suggest that the psychometric properties of 1 PROMs are superior to the other [41]. However, the EORTC questionnaire was deemed to be less ambiguous by the working group (after having completed both EORTC and FACT questionnaires themselves), and has wider outcomes coverage, encompassing outcomes such as cognitive functioning and financial impact. The working group recognized that switching across to the EORTC questionnaire might cause disruption in longitudinal data collection in institutions not currently using it. Hence, future studies are definitely warranted in making commonly used PROMs comparable, to allow for transition into the implementation of the standardized measurement recommended by the working group.

To our knowledge, this is the first international set incorporating outcomes of almost a full cycle of BC care, from diagnosis to completion of treatment and long-term survivorship, with an emphasis on patient-reported outcomes. Other entities currently measuring BC care outcomes have largely been monodisciplinary, focusing largely on surgical treatments [42,43], are more related to measuring and de-fining quality by processes and short-term outcomes of BC care [44-46], or have been set up for a short research period [47]. It is also important to acknowledge that the BC set does not include outcomes measurement on EOL care. While EOL care was raised during several video-conferences, the working group felt that EOL care is often not BC-specific, and ICHOM will consider assembling a palliative care working group to develop a standard set encompassing EOL care across various cancers and medical conditions.

To facilitate the implementation and for practicality, the working group has developed a measurement timeline in such a way that the PROMs collection runs in conjunction with patients' follow-up visits, and so the data can be used as part of clinical consultation. Even so, ICHOM recognizes the challenges involved in implementation. Routine collection of this set in clinical settings will require investment in human resources and information technology, and will depend on the active involvement of clinicians, who must see the value of having such data at the point of care, as well as for retrospective and comparative analyses.

Initially, ICHOM aims to facilitate the implementation process in a number of pilot institutions. The experience and lessons learned from these institutions will be documented, and feedback to a steering committee comprising a subgroup of the current working group members, to refine the set and to prepare it for widespread adoption. This approach has been successfully adopted for the localized prostate cancer set, facilitated by the Movember Foundation [48]. The implementation process will involve 4 phases: (1) to engage clinical champions and establish proper governance process; (2) to identify current measurement audit practices and gaps, and suggest practical strategies for collecting structured clinical data and administrating PROM assessment at the indicated time points; (3) to use pilot sites to trial strategies including existing data sets collection; and (4) to establish how to feedback the data to the clinical teams (**eTable 12**).

CONCLUSIONS

Through the use of literature review and extensive patient input, an international multidisciplinary team of BC experts has developed a minimal standard set of value-based patient-centered outcome measures, deemed to be most important to patients with BC, and generally applicable worldwide. It is recommended that the set is collected in routine clinical practice. This will allow for monitoring and meaningful comparison of BC treatment outcomes within, and across, countries, and in the longer term facilitate improvement in BC care worldwide.

REFERENCES

1. IARC G. Breast Cancer Estimated Incidence, Mortality and Prevalence Worldwide in 2012. http: //globocan.iarc.fr/old/FactSheets/cancers/breast -new.asp. Accessed March 20, 2016.
2. Senkus E, Kyriakides S, Penault-Llorca F, et al; ESMO Guidelines Working Group. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24(suppl 6):vi7-vi23.
3. Cardoso F, Costa A, Norton L, et al; European School of Oncology; European Society of Medical Oncology. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). Breast. 2014;23(5):489-502.
4. Greenberg CC, Lipsitz SR, Hughes ME, et al. Institutional variation in the surgical treatment of breast cancer: a study of the NCCN. Ann Surg. 2011; 254(2):339-345.
5. Sariego J. Regional variation in breast cancer treatment throughout the United States. Am J Surg. 2008;196(4):572-574.
6. van Nes JG, Seynaeve C, Jones S, et al; Tamoxifen and Exemestane Adjuvant Multinational (TEAM) trialists. Variations in locoregional therapy in postmenopausal patients with early breast cancer treated in different countries. Br J Surg. 2010;97(5):671-679.
7. Dundas KL, Pogson EM, Batumalai V, et al. Australian survey on current practices for breast radiotherapy. J Med Imaging Radiat Oncol. 2015;59(6):736-742.
8. Fong A, Shafiq J, Saunders C, et al. A comparison of systemic breast cancer therapy utilization in Canada (British Columbia), Scotland (Dundee), and Australia (Western Australia) with models of "optimal" therapy. Breast. 2012;21(4):562-569.
9. Fong A, Shafiq J, Saunders C, et al. A comparison of surgical and radiotherapy breast cancer therapy utilization in Canada (British Columbia), Scotland (Dundee), and Australia (Western Australia) with models of "optimal" therapy. Breast. 2012;21(4):570-577.
10. Early Breast Cancer Triallists' Collaborative Group. Effects of radiotherapy and surgery in early breast cancer: an overview of the randomized trials. Early Breast Cancer Trialists' Collaborative Group. N Engl J Med. 1995;333(22):1444-1455.
11. Porter ME. What is value in health care? N Engl J Med. 2010;363(26):2477-2481
12. Clement RC, Welander A, Stowell C, et al. A proposed set of metrics for standardized outcome reporting in the management of low back pain. Acta Orthop. 2015;86(5):523-533.
13. McNamara RL, Spatz ES, Kelley TA, et al. Standardized outcome measurement for patients with coronary artery disease: consensus from the International Consortium for Health Outcomes Measurement (ICHOM). J Am Heart Assoc. 2015;4(5):e001767.
14. Mahmud I, Kelley T, Stowell C, et al. A proposed minimum standard set of outcome measures for cataract surgery. JAMA Ophthalmol. 2015;133(11): 1247-1252.
15. Martin NE, Massey L, Stowell C, et al. Defining a standard set of patient-centered outcomes for men with localized prostate cancer. Eur Urol. 2015;67(3):460-467.
16. Morgans AK, van Bommel AC, Stowell C, et al; Advanced Prostate Cancer Working Group of the International Consortium for Health Outcomes Measurement. Development of a stan-

dardized set of patient-centered outcomes for advanced prostate cancer: an international effort for a unified approach. Eur Urol. 2015;68(5):891-898.
17. Mak KS, van Bommel AC, Stowell C, et al; Lung Cancer Working Group of ICHOM. Defining a standard set of patient-centred outcomes for lung cancer. Eur Respir J. 2016;48(3):852-860.
18. Reeve BB, Wyrwich KW, Wu AW, et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. Qual Life Res. 2013;22(8): 1889-1905.
19. US Department of Health and Human Services. Common terminology criteria for adverse events (CTCAE) version 4.0. https://evs.nci.nih.gov/. Accessed February 18, 2016.
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240(2): 205-213.
21. Morrow M, Van Zee KJ, Solin LJ, et al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on margins for breast-conserving surgery with whole-breast irradiation in ductal carcinoma in situ. J Clin Oncol. doi:10.1200/JCO.2016.68.3573
22. Di Maio M, Gallo C, Leighl NB, et al. Symptomatic toxicities experienced during anticancer treatment: agreement between patient and physician reporting in three randomized trials. J Clin Oncol. 2015;33(8):910-915.
23. Trotti A, Colevas AD, Setser A, Basch E. Patient-reported outcomes and the evolution of adverse event reporting in oncology. J Clin Oncol. 2007;25(32):5121-5127.
24. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85(5):365-376.
25. Sprangers MA, Groenvold M, Arraras JI, et al. The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study. J Clin Oncol. 1996; 14(10):2756-2768.
26. Pusic AL, Klassen AF, Scott AM, Klok JA, Cordeiro PG, Cano SJ. Development of a new patient-reported outcome measure for breast surgery: the BREAST-Q. Plast Reconstr Surg. 2009; 124(2):345-353.
27. Kavadas V, Blazeby JM, Conroy T, et al; EORTC Quality of Life Group. Development of an EORTC disease-specific quality of life questionnaire for use in patients with liver metastases from colorectal cancer. Eur J Cancer. 2003;39(9):1259-1263.
28. Fallowfield LJ, Leaity SK, Howell A, Benson S, Cella D. Assessment of quality of life in women undergoing hormonal therapy for breast cancer: validation of an endocrine symptom subscale for the FACT-B. Breast Cancer Res Treat. 1999;55(2): 189-199.
29. United Nations Educational S; Cultural Organization (UNESCO). International Standard Classification of Education. ISCED; Montreal, Canada: 2011.
30. Shavers VL. Measurement of socioeconomic status in health disparities research. J Natl Med Assoc. 2007;99(9):1013-1023.

31. Aizer AA, Chen MH, McCarthy EP, et al. Marital status and survival in patients with cancer. J Clin Oncol. 2013;31(31):3869-3876.
32. Freedman RA, Kouri EM, West DW, Keating NL. Racial/ethnic differences in patients' selection of surgeons and hospitals for breast cancer surgery. JAMA Oncol. 2015;1(2):222-230.
33. Warner ET, Tamimi RM, Hughes ME, et al. Racial and ethnic differences in breast cancer survival: mediating effect of tumor characteristics and sociodemographic and treatment factors. J Clin Oncol. 2015;33(20):2254-2261.
34. Vaz-Luis I, Lin NU, Keating NL, et al. Racial differences in outcomes for patients with metastatic breast cancer by disease subtype. Breast Cancer Res Treat. 2015;151(3):697-707.
35. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum. 2003;49(2):156-163.
36. Olomu AB, Corser WD, Stommel M, Xie Y, Holmes-Rovner M. Do self-report and medical record comorbidity data predict longitudinal functional capacity and quality of life health outcomes similarly? BMC Health Serv Res. 2012;12: 398.
37. Partridge AH, LaFountain A, Mayer E, Taylor BS, Winer E, Asnis-Alibozek A. Adherence to initial adjuvant anastrozole therapy among women with early-stage breast cancer. J Clin Oncol. 2008;26(4): 556-562.
38. Berenson RA, Kaye DR. Grading a physician's value—the misapplication of performance measurement. N Engl J Med. 2013;369(22):2079-2081.
39. Petersen MA, Groenvold M, Aaronson NK, et al; EORTC Quality of Life Group. Development of computerised adaptive testing (CAT) for the EORTC QLQ-C30 dimensions - general approach and initial results for physical functioning. Eur J Cancer. 2010;46(8):1352-1358.
40. 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. 2016;34(6):557-565.
41. Luckett T, King MT, Butow PN, et al. Choosing between the EORTC QLQ-C30 and FACT-G for measuring health-related quality of life in cancer clinical research: issues, evidence and recommendations. Ann Oncol. 2011;22(10):2179-2190.
42. Itani KM. Fifteen years of the National Surgical Quality Improvement Program in review. Am J Surg.2009;198(5)(suppl):S9-S18.
43. Boult M, Cuncins-Hearn A, Tyson S, Kollias J,BabidgeW, Maddern G. National Breast Cancer Audit: establishing a web-based data system. ANZ JSurg. 2005;75(10):844-847.
44. Breast Cancer Audit NABON. Annual Reports 2011. https://www.dica.nl/. Accessed March 10, 2016.
45. Del Turco MR, Ponti A, Bick U, et al. Quality indicators in breast cancer care. Eur J Cancer. 2010; 46(13):2344-2356.
46. Brucker SY, Schumacher C, Sohn C, Rezai M, Bamberg M,Wallwiener D; Steering Committee. Benchmarking the quality of breast cancer care in a nationwide voluntary system: the first five-year results (2003-2007) from Germany as a proof of concept. BMC Cancer. 2008;8:358.

47. Jeevan R, Cromwell DA, Browne JP, et al. Findings of a national comparative audit of mastectomy and breast reconstruction surgery in England. J Plast Reconstr Aesthet Surg. 2014; 67(10):1333-1344.
48. Movember Foundation. Prostate Cancer Outcomes Info Sheet. https://cdn.movember.com/uploads/files/Funded%20Programs/Movember Foundation_Prostate_Cancer_Outcomes_Info_Sheet.pdf. Accessed April 7, 2016.
49. Fayanju OM, Mayo TL, Spinks TE, et al. Value-based breast cancer care: a multidisciplinary approach for defining patient-centered outcomes. Ann Surg Oncol. 2016;23(8):2385-2390.
50. Azad TD, Kalani M,Wolf T, et al. Building an electronic health record integrated quality of life outcomes registry for spine surgery. J Neurosurg Spine. 2016;24(1):176-185.
51. Carberry K, Landman Z, Xie M, Feeley T, Henderson J, Fraser C Jr. Incorporating longitudinal pediatric patient-centered outcome measurement into the clinical workflow using a commercial electronic health record: a step toward increasing value for the patient.

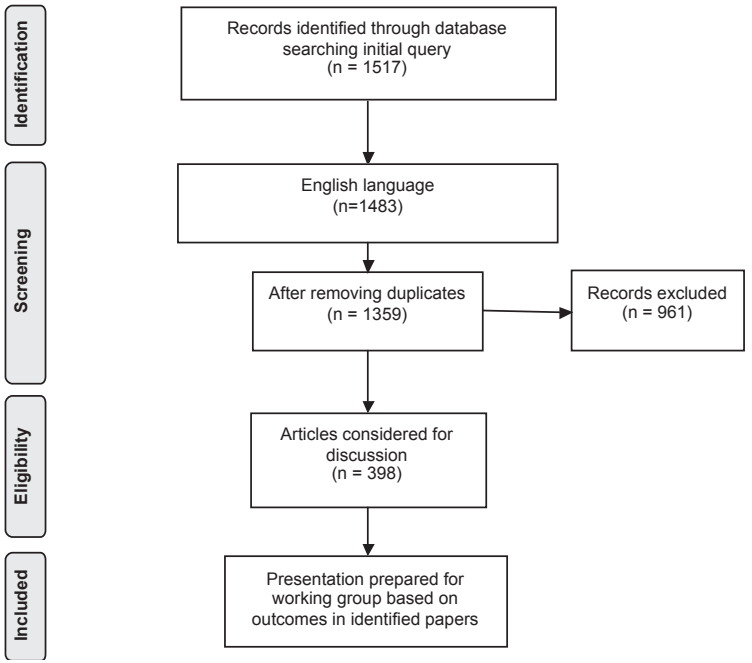
APPENDICES

eTable 1. List of contributors of the International Consortium for Health Outcomes Measurement

Hospitals and Health Systems	Patient advocacy and specialty organizations	Payors/ Governments	Founders
Alliance of Dedicated Cancer Centers	American Society for Clinical Pathology	Carl Benet AB	The Boston Consulting Group
Associacao Nacional de Hospitais Privados	American Heart Association/American Stroke Association	CZ	Institute for Strategy and Competitiveness
Boston Children's Hospital	British Heart Foundation	Harvard Pilgrim HealthCare Foundation	Karolinska Institutet
Canisius-Wilhelmina Ziekenhuis: Santeon	Bowel Cancer Australia	Government of South Australia	
Catharina Ziekenhuis: Santeon	International Urogynecological Association	NHS Camden Clinical Commissioning Group	
Connecticut Joint Replacement Institute	Macula Foundation	NHS Wales	
Erasmus University Medical Center	Macular Society	NHS England	
Generale de Sante	Movember Foundation	The Scottish Government	
Great Ormond Street Hospital	Ordem dos Enfermeiros	Dutch Institute for Clinical Auditing	
Hoag Orthopedic Institute	Oxford Academic Health Science Network		
Hoag	Retina Suisse		
Humanitas Research Hospital	NSW Agency for Clinical Innovation		
Jewish General Hospital Foundation	Wemind		
University Cancer Center Leiden The Hague	MD Anderson Physicians Network		
Martini Ziekenhuis: Santeon			
MD Anderson Cancer Center			

eTable 1. List of contributors of the International Consortium for Health Outcomes Measurement (*continued*)

Hospitals and Health Systems	Patient advocacy and specialty organizations	Payors/ Governments	Founders
Medisch Spectrum Twente: Santeon			
Onze Lieve Vrouwe Gasthuis: Santeon			
Partners Healthcare			
Providence Health&Services			
Ramsay Healthcare			
Sahlgrenska Universitetssjukhuset			
Saint Francis Care			
Save Sight Institute			
Sick Kids			
St. Antonius Ziekenhuis: Santeon			
St. Erik Eye Hospital			
Tenet Health			
Texas Children's Hospital			
The Chaim Sheba Medical Center at Tel Hashomer			
The Children's Hospital of Philadelphia			
UZ Leuven			
Uppsala University Hospital			
WillsEye Hospital			



eFigure 1. Modified PRISMA diagram

eTable 2. Search Strategy Overall

Search terms		Results
#1	"breast neoplasms"[MeSH Terms] AND ((("randomized controlled trials as topic"[MeSH Terms] OR (("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trial"[All Fields] OR "randomised controlled trial"[All Fields]) OR randomized controlled trial,[All Fields] OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomized controlled trials"[All Fields] OR "randomised controlled trials"[All Fields]))) OR (("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomised controlled trial"[All Fields] OR "randomized controlled trial"[All Fields]) OR ("randomized controlled trial"[Publication Type] OR "randomized controlled trials as topic"[MeSH Terms] OR "randomised controlled trials"[All Fields] OR "randomized controlled trials"[All Fields]))) OR randomized controlled trial[Publication Type]) AND ((("Quality of Life"[Mesh] OR "Outcome Assessment (Health Care)"[Mesh]) OR "Outcome and Process Assessment (Health Care)"[All Fields]) OR "Quality Indicators, Health Care"[Mesh]) AND ("2005/01/01"[PDAT] : "2015/07/31"[PDAT]) AND Clinical Trial[ptyp]	1517
#2	#1 AND English[lang]	1483
#3	Remove duplicates	1359
#4	Remove studies not meeting criteria (961 excluded in total) • 17 studies on screening or prevention of breast cancer • 13 studies on cancer imaging • 157 studies on histopathology reporting/ tumour biology/ genetic/ molecular/ biomarkers/ pharmacokinetics • 46 studies on prediction tools development • 61 studies on focusing on breast surgery/ radiotherapy techniques • 388 studies solely on lifestyle, dietary, behavioral, or other non-conventional interventions • 27 studies on cost-effectiveness study/ health services • 147 studies solely on intervention of specific treatment side effects • 105 studies outside the scope of this work (genetic counseling, study design evaluation, research methods, study protocol)	398

eTable 3. Voting percentages of modified Delphi method by working group members on outcomes

Outcomes	Patient subgroup	2-round Delphi % rating "very important" (7-9)		Final voting rounds % voted "yes""			Comments during final voting
		Round 1 19/24	Round 2 21/24	Round 3 21/24	Round 4 22/24	Inclusion in StSet?	
Survival and Disease Control							
Overall survival	All	100%				yes	
Recurrence free survival[a]	Curative intent	84%				yes	
Cause-specific survival	All	79%				yes	
Pathologic complete response	NAC	37%	24%			No	
Progression-free survival	Advanced disease	37%	29%			No	
Degree of Health - QoL and Functioning							
Physical functioning	All	95%				yes	
Emotional Functioning	All	95%				yes	
Ability to work	All	89%				yes	
Sexual functioning	All	89%				yes	
Body image	All	84%				yes	
Overall well-being	All	79%				yes	
Social functioning	All	79%				yes	
Depression	All	79%				yes	
Cognitive functioning	All	74%				yes	

eTable 3. Voting percentages of modified Delphi method by working group members on outcomes (*continued*)

Outcomes	Patient subgroup	2-round Delphi % rating "very important" (7-9)		Final voting rounds % voted "yes""			Comments during final voting
		Round 1 19/24	Round 2 21/24	Round 3 21/24	Round 4 22/24	Inclusion in StSet?	
Anxiety	All	68%	71%			yes	
Mobility	All	63%	33%			No	
Worry	All	63%	24%			No	
Confidence in decision making	All	63%	38%	67%	55%	No	Revote in final rounds brought up frequently by patients of WG/FG and survey respondents. However, it was considered too ambiguous, multifactorial and difficult to measure.
Stress	All	42%	24%			No	
Performance status	All	42%	24%			No	
New suggestions during or after 2 Delphi rounds							
Satisfaction with breast(s)	Surgery/RTx			90%		Yes	
Financial impact	All				77%	Yes	Brought up frequently in patient surveys.
Ability to fulfill household activities	All		38%			No	
Degree of Health - Long-term side-effects							
Breast symptoms	Surgery/RTx	100%				Yes	

eTable 3. Voting percentages of modified Delphi method by working group members on outcomes (*continued*)

Outcomes	Patient subgroup	2-round Delphi % rating "very important" (7-9)		Final voting rounds % voted "yes""			Comments during final voting
		Round 1 19/24	Round 2 21/24	Round 3 21/24	Round 4 22/24	Inclusion in StSet?	
Arm symptoms	Surgery/RTx	100%				Yes	
Pain/discomfort	All	89%				Yes	
Fatigue	All	84%				Yes	
Peripheral neuropathy	Systemic therapy	74%				Yes	
Arthralgia	Systemic therapy	74%				Yes	
Vasomotor symptoms	Systemic therapy	68%	52%	81%		Yes	Brought up frequently by patients of WG and FG.
Vaginal symptoms	Systemic therapy	68%	57%	81%		Yes	Brought up frequently by patients of WG and FG.
Skin fibrosis	Surgery/RTx	63%	43%			No	
Osteoporosis	Systemic therapy	63%	43%			No	
Donor site morbidity	Reconstruction	63%	57%	62%		No	Too specific for a minimum dataset.
Skeletal events	Advanced disease	63%	52%	62%		No	Too specific for a minimum dataset.
Cardiac dysfunction	Systemic therapy	58%	52%	33%		No	Too uncommon for a minimum dataset.

eTable 3. Voting percentages of modified Delphi method by working group members on outcomes (*continued*)

Outcomes	Patient subgroup	2-round Delphi % rating "very important" (7-9)		Final voting rounds % voted "yes""			Comments during final voting
		Round 1 19/24	Round 2 21/24	Round 3 21/24	Round 4 22/24	Inclusion in StSet?	
Infertility	Systemic therapy	58%	67%	67%		No	Only relevant for a relatively small subgroup.
Insomnia	All	53%	43%	70%		Yes	Brought up frequently by patients of WG and FG.
Menopausal state	Systemic therapy	53%	62%			No	
Shortness of breath	Advanced disease	53%	38%			No	
Weight disturbance	All	47%	48%			No	
Endometrial cancer	Systemic therapy	47%	24%			No	
Gastrointestinal symptoms	Systemic therapy	32%	19%			No	
Skin rash	Systemic therapy	32%	19%			No	
Hair loss	Systemic therapy	26%	24%			No	
Quality of death and dying							
Duration of time spent in hospital at end of life	Advanced disease	68%	62%			No	

eTable 3. Voting percentages of modified Delphi method by working group members on outcomes (*continued*)

Outcomes	Patient subgroup	2-round Delphi % rating "very important" (7-9)		Final voting rounds % voted "yes""			Comments during final voting
		Round 1 19/24	**Round 2** 21/24	**Round 3** 21/24	**Round 4** 22/24	**Inclusion in StSet?**	
Place of death	Advanced disease	53%	48%	43%		No	Too multifactorial, cultural and health system dependent.
New suggestion after two Delphi rounds							
Preference for place of death	Advanced disease			43%		No	Too variable between cultures, countries and patient health status.

During the 2-round delphi process, outcomes ranked as very important (score of 7-9 on 9-point Likert scale) by at least 70% in either round were included in, outcomes ranked as very important by at least 50-70% in the last voting round were voted again in the final vote and all outcomes ranked as very important by less than 50% in the last round were excluded. During the final vote, for a domain to be voted for inclusion, at least 70% had to be voted "yes".

Abbreviations: StSet = Standard Set, NAC = neoadjuvant chemotherapy, QoL = quality of life, RTx = radiotherapy, WG = Working Group, FG = Focus Group

eTable 4. Voting percentages of modified Delphi method by working group members on case-mix factors.

Case-mix domain	Patient subgroup	2-round Delphi % rating "very important"(7-9) Round 1 16/24	Round 2 19/24	Final voting rounds % voted "yes" Round 3 19/24	Inclusion in Standard Set?	Main comments during final voting
Demographic factors						
Date of birth	All	89%			Yes	
Educational level (surrogate for SES)	All	78%			Yes	
Ethnicity/race	All	67%	45%	67%	Yes	Included as optional as it has been shown to be associated with survival in several countries.
Relationship status (surrogate for social support)	All	56%	35%	81%	Yes	Included, because social support has been shown to be associated with survival.
Living status	All	56%	25%		No	
Residence (zip code)	All	50%	35%		No	
Clinical factors						
Comorbidity	All	83%			Yes	
BMI	All	83%			Yes	
Menopausal status	All	83%			Yes	
History of breast cancer	All	78%			Yes	
ECOG performance status	All	50%	40%		No	
ASA classification	All	28%	15%		No	

eTable 4. Voting percentages of modified Delphi method by working group members on case-mix factors. (*continued*)

Case-mix domain	Patient subgroup	2-round Delphi % rating "very important"(7-9) Round 1 16/24	Round 2 19/24	Final voting rounds % voted "yes" Round 3 19/24	Inclusion in Standard Set?	Main comments during final voting
New suggestion during Delphi:						
Past chest wall radiotherapy	All		40%		No	
Tumor factors						
Estrogen receptor	Surgery	94%			Yes	
Her-2 receptor	Surgery	94%			Yes	
Date of first histological diagnosis	All	89%			Yes	
Progesterone receptor	Surgery	89%			Yes	
Pathological TNM stage	Surgery	83%			Yes	
Size invasive component of tumor	Surgery	83%			Yes	
Number of positive lymph nodes	Surgery	83%			Yes	
Tumor grade	All	78%			Yes	
Second primary tumor	All	72%			Yes	
Histological type	All	72%			Yes	
mutation status	All	72%			Yes	
Multifocality	All	67%	45%		No	

eTable 4. Voting percentages of modified Delphi method by working group members on case-mix factors. (*continued*)

Case-mix domain		2-round Delphi % rating "very important"(7-9)		Final voting rounds % voted "yes"	Inclusion	Main comments during final voting
	Patient subgroup	Round 1 16/24	Round 2 19/24	Round 3 19/24	in Standard Set?	
Clinical TNM stage	All	67%	60%	76%	Yes	Included when it will only be collected for patients with NAC solely.
Number of resected lymph nodes	Surgery	61%	65%	95%	Yes	Included because it is associated with severity of lymphedema and could influence RT decisions.

During the 2-round delphi process, factors ranked as very important (score of 7-9 on 9-point Likert scale) by at least 70% in either round were included in, factors ranked as very important by at least 50-70% in the last voting round were voted again in the final vote and all outcomes ranked as very important by less than 50% in the last round were excluded. During the final vote, for a factor to be voted for inclusion, at least 70% had to be voted "yes".
Abbreviations: SES = socio-economic status, BMI = body mass index, ECOG = Eastern Cooperative Oncology Group, ASA = American Society of Anesthesiologists, NAC = neo-adjuvant chemotherapy

eTable 5. Description of breast cancer patients and survivors participating in the patient survey

	Survey respondents *N* = 1225
Baseline characteristics	N (%)
Age, years	
=/< 35 years	12 (1)
36 - 45 years	98 (8)
46 - 65 years	821 (67)
=/> 66 years	221 (18)
Continent	
North America	86 (7)
Australia	502 (41)
Europe	625 (51)
Diagnosis	
< 2 years ago	221 (18)
2-10 years ago	809 (66)
> 10 years ago	196 (16)
Disease stage	
Locoregional	1101 (90)
Metastatic	98 (8)
Treatment characteristics	
Currently on treatment	
Yes	515 (42)
No	698 (57)
Surgical treatment	
Mastectomy	662 (54)
Breast-conserving therapy	515 (42)
Breast reconstruction therapy	306 (25)
Sentinel node biopsy	698 (57)
Axillary/lymph node dissection	686 (56)
Non-surgical treatment	
Chemotherapy	784 (64)
Radiotherapy	784 (64)
Hormonal therapy	821 (67)
Targeted therapy	172 (14)
No treatment	12 (1)
Other	86 (7)

eTable 6. Results of item scores by breast cancer patients and survivors participating in the patient survey.

Outcomes	% rating "very important" (score 7-9)	Mean score
Survival and Cancer Control		
Recurrence free survival	97%	8.8
Overall survival	96%	8.8
Quality of Life and Functioning		
Emotional functioning	90%	8.0
Physical functioning	90%	8.0
Overall QoL	88%	8.1
Cognitive functioning	85%	7.8
Ability to work	83%	7.7
Social functioning	81%	7.6
Body image	64%	6.8
Sexual functioning	58%	6.6
Satisfaction with breast(s)	56%	6.4
Anxiety	45%	5.6
Depression	44%	5.4
Long-term side effects		
Fatigue	60%	6.6
Arthralgia	51%	5.9
Vasomotor symptoms	48%	5.8
Arm symptoms	47%	5.7
Peripheral neuropathy	45%	5.5
Pain	39%	5.4
Breast symptoms	36%	5.3
Vaginal symptoms	33%	4.7
Disutility of care		
Acute complications	50%	5.3

All outcomes were provided with supporting definitions and categorized into three types to make it more understandable for patients: 1) positive gains from treatment (e.g. reducing the risk of recurrence), corresponds with the tier survival and cancer control 2) negative impact from treatment (e.g. pain), corresponds with the tier degree of health - long-term side-effects and 3) impact on quality of life and other issues related to treatment (e.g. sexual functioning), corresponds with the tier degree of health - quality of life and functioning and the tier disutility of care

eTable 7. Additional outcomes reported by breast cancer patients and survivors participating in the patient survey.

Additional outcomes	**No of respondents[a]:**
No additional outcomes needed	992
Additional outcomes:	233
Decision-making process: Informing on QoL and side effects	42
Financial impact	15
Availability of peer groups/support teams	12
Fear of recurrence	10
Impact on (relationship with) family/friends	10
Acceptance of new life	10
Support/empathy from medical team	10
Hair loss	10
osteoporosis	5
Fertility	4
Support for family/children	4
Support from family/friends	4
Counseling partner/family	3
Information on alternative therapies	3
Worry about the future	3
Cardiomyopathy/cardiac toxicity	3
Weight gain	3
Genetic screening	3
Loss of confidence	2
Fear of lymphoedema	2
Spiritual well-being	2
Ability to eat	2
Insomnia/sleep disturbance	2
Able to do sport activities	2
Waiting times	1
Pulmonary embolism	1
Radiation pneumonitis	1
Balance problems	1
Sexual self-image	1
PTSD	1
Genetic screening	1
Information on nutrition	1
Nausea and vomiting	1

Abbreviations: QoL = quality of life, PTSD = post-traumatic stress disorder

[a] Survey respondents could provide more than one additional outcome in the open text box

eTable 8. Overview of patient reported outcome measurements (PROMs) and their specifications for the included outcome domains.

	Health-related quality-of- life (HRQOL) Instruments											
Specifications[a]	Cancer specific QoL			Breast cancer specific			Breast cancer treatment specific					
Abbreviated name	EORTC-C30	FACT-G	CARES-SF	EORTC-BR23	FACT-BCS	FACT-BCS+4	BCQ	Breast-Q	SWBCO	FACT-ES	BCPT	MenQOL
Conceptual framework	high	high	high	high	high	high	med	med	high	high	high	high
Target population	med	med	med	high	high	high	med	med	med	med	med	med
Test-retest reliability	high	high	med	unknown	high	high	unknown	high	unknown	high	unknown	high
Internal consistency	med	med	high	med	med	med	high	high	high	high	med	high
Content validity	high	high	high	high	high	high	high	high	med	high	high	high
Construct validity	high	high	med	med	high	high	med	unknown	unknown	high	high	unknown
Ability to detect change	high	high	high	high	high	high	high	unknown	unknown	high	unknown	high
Interpretability	med	med	med	med	med	med	med	med	med	med	med	med
Translation	high	high	low	high	high	high	low	med	low	high	unknown	med
Number of items	30	27	59	23	10	15	30	32-114*	6	19	18	32
Time to complete (min)	10	5-10	5-15	10*	10*	10*	10-15	10-20*	5	10	5-10	7
Administrative burden	high	high	high	high	high	high	med	high	high	high	high	high
Licensing	high	high	low	high	high	high	med	high	high	high	high	high
Locations in use	high	high	low	high	high	high	low	high	low	high	med	med
Number of citations	high	high	med	med	high	low	med	med	low	med	low	med
Year developed	med	med	med	med	med	high	med	high	high	med	med	med

Abbreviations: EORTC QLQ-C30= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core, FACT-G =Functional Assessment of Cancer Therapy-General, CARES-SF = Cancer Rehabilitation Evaluation System-Short Form, EORTC-BR23= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire- Breast Cancer, FACT-BCS= Functional Assessment of Cancer Therapy- Breast Cancer Subscale, BCQ= Breast Cancer Chemotherapy, SWBCO = Satisfaction with Breast Cosmetic Outcomes, FACT-ES= Functional Assessment of Cancer Therapy-Endocrine Subscale, BCPT = Breast Cancer Preventive Trial Symptom Scales, MenQOL = Menopausal Specific Quality of Life

[a] The psychometric quality of each PROM was evaluated, based on the International Society for Quality of Life Research (ISOQOL) criteria

eTable 9. Overview of domain coverage of patient reported outcome measurements (PROMs)

	Health-related quality-of- life (HRQOL) Instruments										
	Cancer specific QoL			Breast cancer specific		Breast cancer treatment specific					
Outcomes	EORTC-C30	FACT-G	CARES-SF	EORTC-BR23	FACT-BCS+4	BCQ	Breast-Q[a]	SWBCO	FACT-ES	BCPT	MenQOL
Nr of items covering outcomes	21/30	25/27	35/59	14/23	12/15	14/30	4-16	7/7	12/19	12/18	27/32
Overall well-being	2	1									
Physical functioning	4	7	10			1					2
Emotional functioning	2	3				5					
Cognitive functioning	2		1							3	1
Social functioning	2	6	17			2					7
Ability to work	1	2	1			1					
Anxiety	1	1	1		2	1					1
Depression	1	2				1					1
Financial impact	1										
Pain	2	1				1				1	3
Fatigue	3	1	1			1					1
Sexual functioning		1	3	3					2		2
Body image			1	4	5	1		3		1	3
Satisfaction with breasts							4-16	4			
Arm symptoms				3	5					2	
Breast symptoms				3					2		1

eTable 9. Overview of domain coverage of patient reported outcome measurements (PROMs) (*continued*)

	Health-related quality-of- life (HRQOL) Instruments										
	Cancer specific QoL			Breast cancer specific		Breast cancer treatment specific					
Outcomes	EORTC-C30	FACT-G	CARES-SF	EORTC-BR23	FACT-BCS+4	BCQ	Breast-Q[a]	SWBCO	FACT-ES	BCPT	MenQOL
Vasomotor symptoms				1					3	2	3
Peripheral neuropathy											
Vaginal symptoms									4	2	1
Arthralgia									1	1	1

Domain covered by instrument (number of questions)

Domain not covered by instrument

Abbreviations: EORTC QLQ-C30= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core, FACT-G =Functional Assessment of Cancer Therapy-General, CARES-SF = Cancer Rehabilitation Evaluation System-Short Form, EORTC-BR23= European Organization for Research and Treatment of Cancer Quality of Life Questionnaire- Breast Cancer, FACT-BCS= Functional Assessment of Cancer Therapy- Breast Cancer Subscale, BCQ= Breast Cancer Chemotherapy, SWBCO = Satisfaction with Breast Cosmetic Outcomes, FACT-ES= Functional Assessment of Cancer Therapy-Endocrine Subscale, BCPT = Breast Cancer Preventive Trial Symptom Scales, MenQOL = Menopausal Specific Quality of Life

eTable 10. Results of item scores by respondents of feedback survey

Statements on Breast Cancer Standard Set	% rating "very confident" (score 7-9)	Mean score	Comments[a]
Part I. High level overview of Standard Set			
The Breast Cancer Standard Set represents a comprehensive overview of the most essential outcomes for patients with BC.	63%	7.0	No outcomes specific to end of life care are included.
The in- and exclusion criteria cover the population sufficiently with treatment approaches that are considered standard of care.	74%	7.5	
The outcomes are sufficiently parsimonious to be collected routinely by patients and clinicians.	54%	6.5	Number of PROM items could lead to compliance issues in daily practice. Disutility of care could be shortened as complications are relatively uncommon in BC care and might not be useful for benchmarking.
Time points for measurement are feasible to follow up patients.	57%	6.2	Collecting long-term outcomes would require good IT support
The case-mix factors are appropriately comprehensive to enable risk-model development for provider performance comparison.	57%	6.3	
I agree with recommend tools, questions and methods.	71%[b]		
Part II. Complete overview of Standard Set			
Case-mix factors are defined properly, are comprehensive enough to enable risk-adjustment and can be collected in clinical practice.	62%	6.6	
Items of patient-reported form are comprehensive enough to cover PRO domains and can be collected by patients.	72%	6.7	It could be challenging to have patients complete all PROMs

eTable 10. Results of item scores by respondents of feedback survey (*continued*)

Statements on Breast Cancer Standard Set	% rating "very confident" (score 7-9)	Mean score	Comments[a]
Clinical outcomes and treatment approaches are defined properly and can be collected in routine clinical practice.	62%	6.5	Reoperation due to involved margins was considered a debatable measure for quality of care because it also relates to patient wishes and could create wrong incentives.

The online feedback survey consisted of two parts: 1) high-level overview of the Set for review of a summary of the recommended outcomes, treatment approaches, case-mix factors and in- and exclusion criteria. 2) complete overview of the Standard Set with access to the complete Reference Guide in order to review each variable with corresponding definitions and response options. Respondent had to rate their confidence on a 9-point Likert scale (e.g. 7-9 was very confident)

[a] Total of 35 healthcare professionals completed the survey, including 16 surgeons, 8 statisticians and researchers, 4 medical oncologists, 2 nurses, 1 radiation oncologist, 1 radiologist, 1 plastic surgeon and 1 consultant)

[b] Response option was binary ("yes/no") instead of the 9-point Likert scale

eTable 11. Types of treatment modalities and treatment-specific acute complications and long-term morbidity

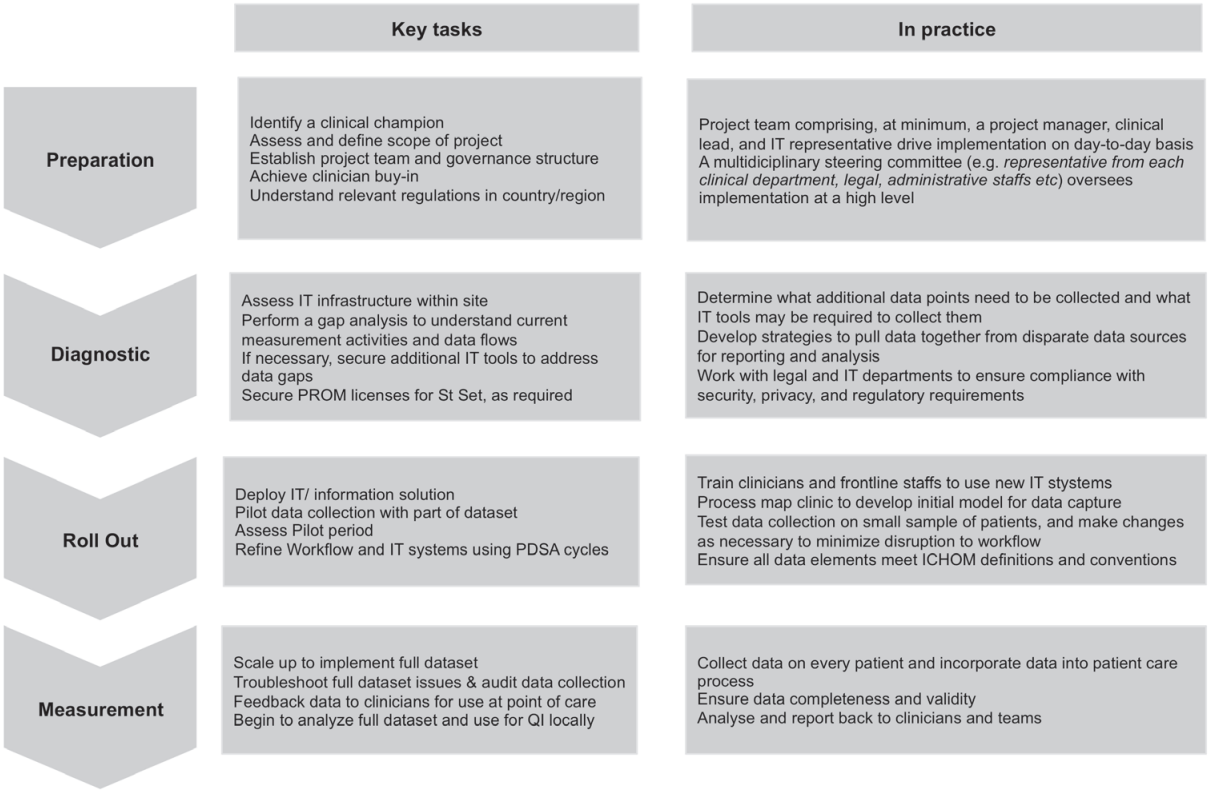
Baseline		Short-term follow-up- clinically reported[a]		Long-term follow-up - PROMs[b]
Category	**Treatment modality**	**Severity of acute complication**	**Name of acute complications**	**Long-term morbidity**
Local therapy	Surgery (with reconstruction) Surgery to axilla Delayed reconstruction	Any complication leading to: Requiring intervention[c] Prolonged hospitalization[d] Unplanned readmission MC/ICU management Discontinuation of treatment Reduce dosing Death	Wound infection	Breast symptoms Arm symptoms Breast satisfaction Fatigue Pain
			Seroma/hematoma	
			Mastectomy skin flap necrosis	
			Hemorrhage	
			Autologous flap loss/ necrosis (total/partial)	
			Implant loss	
			Thromboembolic	
			Nerve damage	
			Delayed wound healing/ dehiscence	
	Radiotherapy		Skin toxicity	
Systemic therapy	Chemotherapy Targeted therapy		Pneumonia Neutropenic sepsis Thromboembolic	Neuropathy Arthralgia Fatigue
	Hormonal therapy		Thromboembolic	Hot flashes Menopausal symptoms

[a] Collection of acute complications is recommended whilst the patient is undergoing treatment or within 90 days of treatment completion, except for complications of hormonal therapy which will be collected up to 1 year

[b] Tracked via patient-reported outcome measurements (PROMs) annually, up to 10 years

[c] Including surgical, radiological and endoscopic interventions

[d] Defined as a hospital stay of more than 14 days



eFigure 2. Phases involved in implementation of the Standard Set