J Rehabil Med 2004; Suppl. 44: 43–48

Taylor & Francis
healthsciences

IDENTIFYING THE CONCEPTS CONTAINED IN OUTCOME MEASURES OF CLINICAL TRIALS ON BREAST CANCER USING THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH AS A REFERENCE

Thomas Brockow,[1] Katharina Duddeck,[1] Szilvia Geyh,[2] Susanne R. Schwarzkopf,[3] Martin Weigl,[2,3] Thomas Franke[1] and Mirjam Brach[2]

From the [1]Spa Medicine Research Institute, Bad Elster, [2]ICF Research Branch of the WHO FIC CC (DIMDI), IMBK – Department of Physical Medicine and Rehabilitation, Ludwig-Maximilians-University and [3]Department of Physical Medicine and Rehabilitation, University of Munich, Munich, Germany

Objectives: **To systematically identify and quantify the concepts contained in outcome measures of clinical breast cancer trials using the International Classification of Functioning, Disability and Health (ICF) as a reference.**

Methods: **Randomized controlled trials between 1991 and 2000 were located in MEDLINE and selected according predefined criteria. The outcome measures were extracted and the concepts contained in the outcome measures were linked to the ICF.**

Results: **A total of 640 trials were included. Ninety-four different health status questionnaires were extracted. Three questionnaires were breast cancer-specific and 12 cancer-specific. Of 19 692 extracted concepts, 88% could be linked to the ICF. The most used ICF categories within the components *body structures, body functions,* and *activities and participation* were *structure of the reproductive system* (s630), *sensations associated with the digestive system* (b535), and *looking after one's health* (d570) with frequencies of 64%, 46% and 14%, respectively. No category of the *environmental factors* component reached a frequency of 10%.**

Conclusion: **The ICF provides a useful reference to identify and quantify the concepts contained in outcome assessment used in clinical breast cancer trials. There seems to be a lack of health concepts evaluating specific aspects of disability and participation in breast cancer. Similarly, *environmental factors* with an impact on individual life of breast cancer survivors seem to be poorly represented.**

Key words: breast cancer, outcome assessment, systematic review, ICF.

J Rehabil Med 2004; suppl. 44: 43–48

Correspondence address: Mirjam Brach, Department of Physical Medicine and Rehabilitation, University of Munich, Marchioninistr. 15, 81377 Munich, Germany. Tel: +49 89 7095 4055. Fax: +49 89 7095 8836. E-mail: Mirjam.Brach@med.uni-muenchen.de

INTRODUCTION

Breast cancer (BC) is the most common cancer among women worldwide and is the second leading cause of cancer death today after lung cancer (1). Lifetime risk is estimated at 1 in 10 (2). Of all women diagnosed with breast cancer, approximately 50% will survive for 5 years with the appropriate treatment (3). BC accounts for about one-fifth of all deaths in women aged 40–50 years (4).

Physical, psychological, and social functioning are important aspects in female BC. Functional health status in BC is determined by psychosocial reactions to the cancer experience, disease-related issues, and the consequences of treatment (5). Common psychological sequelae of cancer experience include depression, anxiety, stress, decreased self-esteem, or loss of sense of control (6–8). Primary treatment often results in impairments of emotional functioning, body image, sexual functioning, social and work role functioning (9) besides potential late physical effects of treatment. In metastatic disease, bone involvement is most common (10) leading to disability due to pain, pathological fracture, hypercalcaemia, and spinal cord compression (11).

Despite the obviously important role of functioning in BC survivors, this aspect seems to be less considered in clinical research. Similarly, in follow-up care the detection of recurrences is often the only objective without providing any physical and psychosocial rehabilitation (12).

Based on the new International Classification of Functioning, Disability and Health (ICF) (13) which was endorsed by the World Health Assembly in May 2001 and provides a common language of functioning and health, it is now possible to identify and compare the concepts contained in different outcome measures (14).

The objective of this systematic review therefore was to identify and quantify the concepts contained in the outcome measures of randomized controlled trials (RCTs) for interventions in BC using the ICF as a reference tool.

METHODS

Study design

A systematic review was performed in 3 steps: step 1, selection of studies; step 2, outcome measures extraction; and step 3, linkage

 ISSN 1650–1977
DOI 10.1080/16501960410015434

of the concepts contained within the outcomes measures to the corresponding categories of the ICF. All steps were carried out by 2 independent reviewers.

In step 1, selection of studies, RCTs between the years 1991 and 2000 were located in MEDLINE®, Silver Platter, 2000 Edition, using Dickersin et al.'s (15) highly precise search strategy (sets 1–8). Thereafter, the Dickersin search was combined with a condition-specific search strategy using the "and" operator.

To locate BC trials, the explode-function for "Breast-Neoplasms" with all subheadings and the composite term ("(cancer* or, tumo?r* or carcinoma* or neoplas* or malign*) and (breast or breasts)") restricted to the title and abstract section were combined using the "or" operator.

All searches were limited to articles in English. The abstracts were checked applying general and condition-specific eligibility criteria. For the selected trials the original study reports were ordered and reviewed applying again the same eligibility criteria. The studies finally included entered step 2 of the review.

A study met general eligibility, if the study design was a RCT, the experimental intervention had a therapeutic aim, the outcome measures had to be evaluated on patients and, if none of the following exclusion criteria were fulfilled: reviews, secondary analyses, psychometric studies, primary prevention studies (healthy population at risk), mode of action studies, and studies with heterogeneous population (e.g. BC and multiple myeloma). In the case of multiple publications, the paper with the highest impact factor was included.

To identify the appropriate study population condition-specific eligibility criteria were applied. The diagnosis of BC or related terms (e.g. breast neoplasm, mammary cancer, breast carcinoma, etc.) has to be reported to describe the study population.

Populations with male BC, carcinoma *in situ* of the breast, benign neoplasms of the breast, inflammatory disorders of the breast, breast hypertrophy or risk patients (e.g. family history of BC, etc.) were excluded.

In step 2, outcome measures extraction was performed. All types of outcome measures including recurrence and survival rates, clinical tests (e.g. examination of arm and shoulder mobility, arm swelling, muscle strength), single item measures on different domains (e.g. body image, sexual function, nausea, vomiting, dizziness, appetite, tiredness, pain, hot flushes, coping with illness (16), physical well-being, performance status (17)), biochemical, immunological, imaging tests, biopsy, common toxicity lists, as well as questionnaires were extracted. If the number of items used in a determined study was not specified in a publication, the corresponding questionnaire was obtained by reference checking, searches in databases or books on health status measures (14, 15), e-mail consultation with the developers of the questionnaire in demand, or internet searches. After this procedure the items were extracted. Only questionnaires available in English were included. Additional information, such as study population characteristics (e.g. stage of disease, age, etc.), country of performance and type of experimental intervention (response options: "drug therapy", "surgery", "radiotherapy", "non-pharmacological therapy", "different therapeutic modalities") was extracted. Non-pharmacological therapy included physical, complementary, nutritional, educational, and psychological therapy. The response option "different therapeutic modalities" was chosen in studies with more than 1 experimental group and different intervention types, such as comparisons of primary surgery vs primary tamoxifen (20) or adjuvant surgical oophorectomy vs adjuvant CMF-chemotherapy (21). In many trials the experimental intervention was administered as an adjunct (adjuvant intervention). In those trials, the type of adjuvant intervention was classified. For example, in a trial comparing adjuvant tamoxifen with surgery alone (22), drug therapy was considered the experimental intervention just as in a trial comparing postoperative radiotherapy with surgery alone, radiotherapy was considered the experimental intervention (23).

In step 3, we performed the linkage of the concepts contained within the outcomes measures to the corresponding categories of the ICF. According to content analysis, concepts were defined as single content categories (24). The concepts contained within the outcome measures were extracted and linked to the most specific ICF category by 2 independent health professionals according to a recently developed set of 10 linking rules (14). If the outcome measure was a test (magnetic resonance imaging), the goal (brain metastases) rather than the concept was linked to the ICF. Concepts of outcome measures that could not be linked to the ICF were documented and classified in 2 ways. (i) If a concept of an outcome measure was not sufficiently specified to make a decision which ICF category the concept should be linked to, the "not definable" option was chosen (linking rule 9). To give an example, unspecified concepts such as "loco-regional recurrence" (loco-regional recurrence can be linked to various structures such as involvement of lymph nodes, subcutaneous tissue, muscles, skin of the chest wall, or ipsilateral breast tumour recurrence (25)), "distant recurrence", "visceral metastases", "quality of life", or "physical well-being" were considered not to be definable for linking. (ii) If a concept of an outcome measure was not represented by the ICF, the option "not covered" was chosen (linking rule 10). To give an example, concepts such as "leaving it all to the doctors", "putting oneself in the hands of God", extracted from the Mental Adjustment to Cancer Scale (MAC scale) (26), or "accepting one's illness" extracted from the Functional Assessment of Cancer Therapy Scale; General (FACT-G) (27) were considered not to be covered by the ICF.

Consensus between the 2 health professionals was used to decide which ICF category should be linked to each item/concept of the questionnaires. To resolve disagreements between the 2 health professionals concerning the selected categories, a third person trained in the linking rules was consulted. In a discussion led by the third person, the 2 health professionals that linked the item stated their pros and cons for the linking of the concept under consideration to a specific ICF category. Based on these statements, the third person made an informed decision.

To control the plausibility of the linkage procedure the concepts of the outcome measures assigned to the same single ICF category were analysed (e.g. the concepts "feeling less feminine" (28), "finding it difficult to look at yourself naked" (28), "feeling unattractive" (29), "being uncomfortable with changes in my body" (30) which were linked to the ICF category "experience of self and time functions" (b180)).

Analyses

Descriptive statistics were used to examine the frequency of ICF categories linked to the concepts contained in the outcome measures. Large-scale cross tables generated from a SQL-database (SQL-Server 2000) were thereby analysed. If the same ICF category was assigned repeatedly in a study, the category was counted only once.

ICF categories are presented on the second level. If a concept of an outcome measure was linked to a third or fourth level ICF category, the overlying second level category was considered. Within the ICF the lower-level category shares the attributes of the higher-level category (13). Only ICF categories with a frequency equal or greater than 10% are shown (pre-set frequency).

RESULTS

In step 1, 2443 studies were located by the search strategy, 994 studies were preliminarily selected by abstract checking and 640 were included into the review by screening the respective original papers.

In step 2, 94 different questionnaires (different versions of a questionnaire were considered as 1 questionnaire) were chosen as outcome measures. Among them we identified 3 BC-specific questionnaires, the European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module (QLQ-BR23) (28), the Functional Assessment of Cancer Therapy-Breast quality of life instrument (FACT-B) (31), and the Breast Cancer Chemotherapy Questionnaire (BCQ) (29)), 12 cancer-specific questionnaires (e.g. the Cancer Rehabilitation Evaluation System-Short form (CARES-SF) (30), the European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire (QLQ-C30) (32),

the Functional Living Index-Cancer (FLIC) (33), etc.), 72 dimension-specific questionnaires without an intended specificity to cancer (on dimensions such as depression (34), anxiety (35), self-esteem (36), social support (37), etc.), and 7 generic questionnaires (e.g. the general health questionnaire (GHP-60) (38) or the Nottingham Health Profile (NHP) (39)). At least 1 health status questionnaire per trial was selected in 103 or 16% of the studies. The 4 most used questionnaires were the QLQ-C30 (32), the Rotterdam Symptom Checklist (RSCL) (40), the Profile of Mood States (POMS) (41), and the Hospital Anxiety and Depression Scale (HADS) (42) with a prevalence of 3% (15 studies), 2% (14 studies), 2% (12 studies) or 2% (11 studies), respectively. Frequent outcome measures were recurrence rates, survival/death rates, tumour response, haematological tests for the evaluation of toxicity, and clinical side-effects of chemotherapy (e.g. nausea, vomiting, heart dysfunction, pain, fatigue) (data not shown).

In all, 537 trials provided details on tumour staging. In 160 or 30% of these trials early BC (stage I and II) was the most used disease-subset, followed by metastatic cancer (stage IV), which was present in 98 or 18% of the trials. The remaining trials included study populations with different stages (31%) and locally advanced cancer (stage III) (18%). Most trials were conducted in the USA (24%), followed by the UK (13%). Drug therapy was the most frequently used intervention type with a prevalence of 74% ($n = 472$ studies), followed by non-pharmacological therapy in 59 studies (9%). Non-pharmacological therapy consisted mainly of psychoeducational interventions ($n = 30$ studies), followed by physical therapy ($n = 14$ studies). Most studies on psychoeducational interventions applied cognitive behavioural therapy, while most studies on physical therapy applied decongestive lymphatic therapy.

A total of 19,692 concepts were extracted from the outcome measures. 17,395 or 88% of concepts could be linked to the ICF, 1316 or 7% of concepts were considered not to be sufficiently specified for an assignment to the ICF ("not definable option"), and 981 or 5% of concepts were considered to be not covered by the ICF. Of the assignable concepts, 62% ($n = 10\,831$) were linked to the component *body functions*, 27% ($n = 4667$) to the component *body structures*, 8% ($n = 1372$) to the component *activities and participation*, and 3% ($n = 525$) to the component *environmental factors*.

The concepts contained in the outcome measures were linked to 401 different ICF categories. Of these there were 200 categories which were linked to component *body functions*, 50 to the component *body structures*, 128 to component *activities and participation*, and 23 to the component *environmental factors*.

Table I shows the relative frequency in percentage of ICF categories linked to the concepts contained in the outcome

Table I. *Relative frequency in percentage of ICF categories linked to the concepts contained in the outcome assessment*

ICF code	ICF category title	All trials ($n = 640$)	Drug ($n = 472$)	Surgery ($n = 35$)	Non pharmacological ($n = 59$)	Radiotherapy ($n = 36$)	Different modalities ($n = 38$)
b126	Temperament and personality functions	14	12	8	42	2	7
b130	Energy and drive functions	20	18	17	49	2	10
b134	Sleep functions	13	12	2	23	2	13
b152	Emotional functions	18	15	14	55	2	10
b198	Mental functions, other specified	16	22		3	2	7
b265	Touch function	24	30	2	6	8	13
b280	Sensation of pain	16	16	8	22	8	13
b289	Sensation of pain, other specified and unspecified	31	37	5	22	2	10
b410	Heart functions	31	40	2	3	5	13
b430	Haematological system functions	43	55	8	5	5	13
b435	Immunological system functions	24	29	5	3	2	13
b440	Respiration functions	23	29		3	2	10
b455	Exercise tolerance functions	14	13	2	30	5	2
b510	Ingestion functions	41	52	5	10	2	13
b525	Defecation functions	37	45	8	16	5	10
b535	Sensations associated with the digestive system	46	57	8	20	5	18
b539	Functions related to the digestive system, other specified and unspecified	22	28			2	13
b730	Muscle power functions	22	28	2		2	10
b840	Sensation related to the skin	23	29		1	2	10
b850	Functions of hair	30	38	5	5	5	13
s110	Structure of brain	42	45	34	3	52	57
s320	Structure of mouth	18	23	2	1	2	7
s420	Structure of immune system	53	58	34	6	58	68
s430	Structure of respiratory system	58	64	37	5	61	71
s560	Structure of liver	54	59	37	5	55	68
s630	Structure of reproductive system	64	70	48	5	80	73
s770	Additional musculoskeletal structures related to movement	58	65	37	5	55	68
d570	Looking after one's health	14	15		20	5	7

measures for all trials as well as stratified by "type of experimental intervention".

In the *body functions* component the 5 most used categories over 10% were *sensation associated with the digestive system* (b535), *hematological system functions* (b430), *ingestion functions* (b510), *defecation functions* (b525) and *heart functions* (b410), all reaching a frequency of over 30%. The concept "nausea" was linked to the category b535, the concepts "anemia", "neutropenia", "granulocytopenia", "leukopenia", "myelosuppression", "lymphocytopenia", "thrombocytopenia", and "prolonged blood clotting" were linked to the category b430. "Dry mouth", "swallowing", "vomiting/emesis" and "heartburn" were linked to b510, "diarrhea", "constipation", "fecal incontinence", and "flatulence/wind/gas production" to b525 and "cardiac dysfunction/cardiac failure", "arrhythmia/dysrhythmia", "tachycardia" to b410.

In the *body structures* component the 5 most used categories exceeding the pre-set frequency of 10% were *structure of reproductive system* (s630), *additional musculoskeletal structures related to movement* (s770), *structure of the respiratory system* (s430), *structure of the liver* (s560) and *structure of immune system* (s420), all reaching a frequency over 50%. "Response in BC", "BC recurrence", "endometrial cancer", and "breast deformity" were the concepts linked to the category s630. "Bone metastases", "pathologic fracture", and "bone mineral density" were the concepts linked to the category s770. "Lung metastases", "pulmonary fibrosis", and "chest wall metastases" were the concepts linked to s430, "liver metastases" were linked to s560, and "lymph node metastases", "lymphedema" and "bone marrow recovery" were linked to s420.

In the *activities and participation* component *looking after one's health* (d570) was the only category reaching the pre-set level of 10%. The concepts "doing breast self-evaluation", "following medical advice", and "following doctor's instruction" were linked to this category.

In the *environmental factors* component no category reached a frequency of 10%. All domains were represented by at least 1 ICF category except for *attitudes* (e4), a domain describing the impact of opinions and beliefs of groups, cultures, societies and norms on individual health (13).

DISCUSSION

Using the ICF as a reference it was possible to identify and quantify the concepts within the outcome measures used in RCTs for interventions in BC. Most concepts within the outcome measures could be linked to the ICF and those that could not be linked were mostly not specified in enough detail for an assignment. Loco-regional recurrence and distant recurrence/disease without further structural specifications were the most frequent concepts not assignable to the ICF. Only a very small portion of concepts was considered not to be covered by the ICF. In these cases the content of the concepts did not lie in the defined universe of the ICF. This was most often the case for mortality/death. Furthermore, health status measures on dimensions such as "locus of control" (43), "adjustment to illness" (26), "personality" (44), "openness to discuss cancer in the family" (45), "impact of event" (46), "self-esteem" (36), or "uncertainty in disease" (47) contained personal concepts that are not covered by the current ICF and could therefore not be linked. Similarly, aetiological concepts (e.g. stomatitis after chemotherapy), and concepts on patient satisfaction could not be linked.

As expected, structural concepts were the most used concepts in the outcome assessment of clinical BC trials. Surgery, radiation and anti-neoplastic drug therapy are all treatments primarily directed to cure or reduce cancer. Because some of the structural concepts such as "loco-regional recurrence" or "distant recurrence" could not be linked to the ICF, the frequencies of the structural concepts are somewhat higher than presented in Table I.

Physiological and psychological concepts were the second leading concepts. Physiological concepts referred to a great extent to the assessment of side-effects, toxicity, tolerability, or safety in studies on drug interventions. The high frequency of ICF categories such as *heart functions* (b410), *haematological systems functions* (b430), or *ingestion functions* (b510) reflects this fact. Surprisingly, genital or reproductive functions such as *sexual-* (b640), *menstruation-* (b650) or *procreation functions* (b660), which can be affected by chemo- and hormonal therapy, did not reached the pre-set frequency of at least 10%. In studies on non-pharmacological therapies mainly psychological concepts were used in the outcome measures. The reason was that almost 50% of these studies dealt with psychoeducational interventions. *Temperament and personality functions* (b126), *energy and drive functions* (b130), or *emotional functions* (b152) were prevailing ICF categories in this subgroup.

Functional concepts relating to activities or the involvement of a BC survivor in life situations were less frequent assessed concepts. *Looking after one's health* (d570) was the only category within the "activities and participation" component reaching the pre-set level of 10%. Potentially important ICF categories for BC survivors like *handling stress or other psychological demands* (d240), creating and maintaining *family relationships* (d760) and *intimate relationships* (d770) or engaging in *remunerative employment* (d850) were only represented by a frequency of 3, 4, 2 or 6% respectively.

Similarly, concepts describing external conditions with an impact on individual life of BC survivors were poorly addressed. In the environmental-factors component no category reached a frequency of 10%. Potentially important ICF categories on support by *immediate family* (e310), *friends* (e320), *health professionals* (e355) only reached frequencies of 3%, 3% or 2%, respectively. Furthermore, other relevant ICF categories, for example on individual attitudes of family members, friends or health professionals or support by health services, were not considered at all.

The data presented reflect that functional and environmental aspects related to the disease or consequences of treatment were poorly addressed in the outcome measurement of clinical BC

trials. This was not only true for typical cancer therapy trials, but also for trials on quality of life interventions (in our review categorized as "non-pharmacologic trials") aimed to mitigate the sequelae or side-effects of cancer treatment or to cope with the cancer experience.

The review shows type and frequency of concepts assessed in the outcome measurement of clinical BC trials over the last 10 years reaching a prevalence of at least 10%. From a conceptual point of view, outcome assessment in BC should include a broader range of quality of life issues including activities, participation, and environmental aspects related to the disease. A standardized measure that encompasses these areas would benefit any research on BC.

In this study we have looked at concepts within outcome measures without considering the relationship among them. Relational analysis (48, 49) will be the objective of secondary papers and seems to be particularly important for the analysis of single items within questionnaires to put individual concepts into a more specific context (e.g. "feeling worried or upset" as a result of "thinning or loss of hair", Item 1 from the Breast Cancer Chemotherapy Questionnaire (29)).

In conclusion, the ICF provides a useful reference to identify and quantify the concepts within the outcome measures used in RCTs for interventions in BC. There seems to be a lack of health concepts evaluating specific aspects of disability and participation in BC. Similarly, some environmental factors with an impact on individual life of BC survivors seem to be poorly represented. Our findings indicate a need to define "what should be measured" in clinical BC trials.

REFERENCES

1. Lacey JV, Jr, Devesa SS, Brinton LA. Recent trends in breast cancer incidence and mortality. Environ Mol Mutagen 2002; 39: 82–88.
2. Fraser GE, Shavlik D. Risk factors, lifetime risk, and age at onset of breast cancer. Ann Epidemiol 1997; 7: 375–382.
3. Quinn MJ, Martinez-Garcia C, Berrino F. Variations in survival from breast cancer in Europe by age and country, 1978–1989. Eur J Cancer 1998; 34: 2204–2211.
4. McPherson K, Steel CM, Dixon JM. ABC of breast diseases. Breast cancer-epidemiology, risk factors, and genetics. BMJ 2000; 321: 624–628.
5. Courneya KS, Friedenreich CM. Physical exercise and quality of life following cancer diagnosis: a literature review. Ann Behav Med 1999; 21: 171–179.
6. Cain EN, Kohorn EI, Quinlan DM, Schwartz PE, Latimer K, Rogers L. Psychosocial reactions to the diagnosis of gynecologic cancer. Obstet Gynecol 1983; 62: 635–641.
7. Cohen J, Cullen J, Martin L. Psychosocial aspects of cancer. New York: Raven Press; 1982.
8. Glanz K. Psychosocial impact of breast cancer: a critical review. Ann Behav Med 1992; 14: 204–212.
9. Irvine D. A critical review and meta-analysis of the literature investigating psychosocial adjustment in breast cancer Ottawa: Health Canada; 1996.
10. Scheid V, Buzdar AU, Smith TL, Hortobagyi GN. Clinical course of breast cancer patients with osseous metastasis treated with combination chemotherapy. Cancer 1986; 58: 2589–2593.
11. Coleman RE, Rubens RD. Bone metastases and breast cancer. Cancer Treat Rev 1985; 12: 251–270.
12. Rojas MP, Telaro E, Russo A, Fossati R, Confalonieri C, Liberati A. Follow-up strategies for women treated for early breast cancer. Cochrane Database Syst Rev 2000: CD001768.
13. WHO. ICF-International Classification of Functioning, Disability and Health. Geneva: WHO Library; 2001.
14. Cieza A, Brockow T, Ewert T, Amman E, Kollerits B, Chatterji S, et al. Linking health-status measurements to the international classification of functioning, disability and health. J Rehabil Med 2002; 34: 205–210.
15. Dickersin K, Scherer R, Lefebvre C. Identifying relevant studies for systematic reviews. BMJ 1994; 309: 1286–1291.
16. Hurny C, Bernhard J, Bacchi M, van Wegberg B, Tomamichel M, Spek U, et al. The Perceived Adjustment to Chronic Illness Scale (PACIS): a global indicator of coping for operable breast cancer patients in clinical trials. Swiss Group for Clinical Cancer Research (SAKK) and the International Breast Cancer Study Group (IBCSG). Support Care Cancer 1993; 1: 200–208.
17. Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: reliability, validity, and guidelines. J Clin Oncol 1984; 2: 187–193.
18. McDowell I, Newel C. Measuring health. A guide to rating scales and questionnaires. 2nd edn. New York: Oxford University Press; 1996.
19. Salek S. Compendium of Quality of Life Instruments. Chichester: Wiley; 1999.
20. Gazet JC, Ford HT, Coombes RC, Bland JM, Sutcliffe R, Quilliam J, et al. Prospective randomized trial of tamoxifen vs surgery in elderly patients with breast cancer. Eur J Surg Oncol 1994; 20: 207–214.
21. Salvadori B, Celio L, Oriana R, Bajetta E. Adjuvant oophorectomy versus CMF in premenopausal node-positive breast cancer: long-term results of an experience at the Milan Cancer Institute. Tumori 2000; 86: 258–259.
22. Rutqvist LE, Cedermark B, Glas U, Johansson H, Rotstein S, Skoog L, et al. Randomized trial of adjuvant tamoxifen in node negative postmenopausal breast cancer. Stockholm Breast Cancer Study Group. Acta Oncol 1992; 31: 265–270.
23. Rutqvist LE, Pettersson D, Johansson H. Adjuvant radiation therapy versus surgery alone in operable breast cancer: long-term follow-up of a randomized clinical trial. Radiother Oncol 1993; 26: 104–110.
24. Weber RF. Basic content analysis. Newbury Park: Sage Publications; 1990.
25. Fowble B, Schwaibold F. Local-regional recurrence following definitive treatment for operable breast cancer. St. Louis: Mosby Year Book; 1991.
26. Watson M, Greer S, Young J, Inayat Q, et al. Development of a questionnaire measure of adjustment to cancer: The MAC scale. Psychological Medicine 1988; 18: 203–209.
27. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. J Clin Oncol 1993; 11: 570–579.
28. Sprangers MA, Groenvold M, Arraras JI, Franklin J, te Velde A, Muller M, 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: 2756–2768.
29. Levine MN, Guyatt GH, Gent M, De Pauw S, Goodyear MD, Hryniuk WM, et al. Quality of life in stage II breast cancer: an instrument for clinical trials. J Clin Oncol 1988; 6: 1798–1810.
30. Schag CA, Ganz PA, Heinrich RL. CAncer Rehabilitation Evaluation System – short form (CARES-SF). A cancer specific rehabilitation and quality of life instrument. Cancer 1991; 68: 1406–1413.
31. Brady MJ, Cella DF, Mo F, Bonomi AE, Tulsky DS, Lloyd SR, et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. J Clin Oncol 1997; 15: 974–986.
32. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, 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: 365–376.

33. Morrow GR, Lindke J, Black P. Measurement of quality of life in patients: psychometric analyses of the Functional Living Index-Cancer (FLIC). Qual Life Res 1992; 1: 287–296.
34. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measurig depression. Arch Gen Psychiatr 1961; 4: 561–571.
35. Spielberger CD, Gorsuch RL, Lushene RE. STAI Manual for the State-Trait Anxiety Inventory Palo Alto, CA: Consulting Psychologists Press; 1969.
36. Rosenberg. Socienty and the adolescent self-image. Princeton, NJ: Princeton University; 1965.
37. Sarason IG, Sarason BR, Shearin EN, et al. A brief measure of social support: Practical and theoretical implications. J Soc Pers Relationships 1987; 4: 497–510.
38. Goldberg D. Manual of general health questionnaire. Windsor: National Foundation for Educational Research; 1978.
39. Hunt SM, McEwen J, McKenna SP. Measuring health status: a new tool for clinicians and epidemiologists. J R Coll Gen Pract 1985; 35: 185–188.
40. de Haes JC, van Knippenberg FC, Neijt JP. Measuring psychological and physical distress in cancer patients: structure and application of the Rotterdam Symptom Checklist. Br J Cancer 1990; 62: 1034–1038.
41. Mc Nair PM, Lorr M, Droppleman L. Manual for the profile of mood states. San Diego: Educational and Industrial Testing Services; 1971.
42. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361–370.
43. Watson M, Pruyn J, Greer S, van den Borne B. Locus of control and adjustment to cancer. Psychol Rep 1990; 66: 39–48.
44. Eysenck HJ, Eysenck SBG. Manual of the Eysenck Personality Scales (EPS Adult). London: Hodder and Stoughton; 1991.
45. Mesters I, van den Borne H, McCormick L, Pruyn J, de Boer M, Imbos T. Openness to discuss cancer in the nuclear family: scale, development, and validation. Psychosom Med 1997; 59: 269–279.
46. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. Psychosom Med 1979; 41: 209–218.
47. Mishel MH. The measurement of uncertainty in illness. Nurs Res 1981; 30: 258–263.
48. Carley KM. Content analysis. In: Asher RE, ed. The encyclopedia of language and linguistics. Edingburgh: Pergamon Press; 1990.
49. Palmquist ME, Carley KM, Dale TA. Two applications of automated text analysis: Analyzing literature and non-literary texts. In: Roberts D, ed. Text analysis for the social sciences: methods for drawing statistical inferences form texts and transcripts Hillsdale, NJ: Lawrence Erlbaum Associates; 1997.