

Factors affecting baseline quality of life in two international adjuvant breast cancer trials

J Bernhard, C Hürny, AS Coates, HF Peterson, M Castiglione-Gertsch, RD Gelber, E Galligioni, G Marini, B Thürlimann, JF Forbes, A Goldhirsch, H-J Senn, C-M Rudenstam for the International Breast Cancer Study Group (IBCSG)

Summary Quality of life (QL) is used to assess treatments in clinical trials but may be influenced by other factors. We analysed the impact of biomedical, sociodemographic and cultural factors on baseline QL indicators in two International Breast Cancer Study Group trials. Patients with stage II breast cancer were randomized within 6 weeks of primary surgery to various adjuvant treatments. They were asked to assess five indicators of QL at baseline. QL forms were available for 1231 (83%) of the 1475 premenopausal and 989 (82%) of the 1212 post-menopausal patients, who were from nine countries and spoke seven languages. Culture (defined as language/country groups) had a statistically significant impact on baseline QL measures. Premenopausal patients with poor prognostic factors showed a tendency to report worse QL, with oestrogen receptor status as an independent predictor for mood ($P = 0.0005$). Older post-menopausal patients reported better emotional wellbeing ($P = 0.002$), mood ($P = 0.002$), and less effort to cope ($P = 0.0009$) compared with younger post-menopausal patients. Co-morbidity, type of surgery, treatment assignment and sociodemographic factors showed a statistically significant impact in post-menopausal patients only. Cultural and biomedical factors influenced baseline QL and should be considered when evaluating the impact of treatment on QL in international breast cancer clinical trials.

Keywords: quality of life; breast cancer; cross-cultural issues; language; international trial

The methodology of international cancer clinical trials is constantly being improved and adapted as clinical questions evolve. The most recent step in this evolution is the inclusion of patient-rated quality of life (QL) as an end point for treatment comparison.

Social and cultural factors are an integral part of any individual's estimation or judgement of QL. The principles of QL assessment, however, have been established mostly within regional or national settings. Evaluating these social and cultural factors has only recently received attention, particularly in cancer clinical trials involving participants from multiple cultures (Hürny et al. 1992). The influence of such factors on cancer treatment comparisons based on QL is uncertain, and methods to adjust for them have rarely been discussed (Bernhard et al. 1996; Cella et al. 1996). We wished to examine the impact of social and cultural as well as biomedical factors, such as co-morbidity and prognostic factors at diagnosis, on patients' self-report of the experience of beginning treatment.

We examined three specific hypotheses. Based on prior experience in the Group, we expected substantial heterogeneity of baseline QL in the various language/cultural groups; we expected worse baseline QL with worse prognostic factors, both because perception of these factors may colour the information given to the patient and because worse QL had previously been reported among patients with receptor-negative tumours (Razavi et al. 1990), and we expected worse baseline QL scores in patients living alone or only with children, based on the social support paradigm.

We therefore analysed the relationship between biomedical, sociodemographic and cultural factors and five indicators of components of QL recorded at baseline assessment in two international adjuvant breast cancer trials (Hürny et al. 1996a). This investigation identified covariates which need to be considered when interpreting baseline QL and evaluating the influence of treatment factors on QL in international breast cancer clinical trials.

METHODS

The trials

Between July 1986 and April 1993, two International Breast Cancer Study Group (IBCSG) trials examined similar questions of timing and duration of adjuvant cytotoxic therapy for patients with node-positive operable breast cancer. In trial VI, we randomized 1475 eligible premenopausal and perimenopausal patients in a 2×2 factorial design to receive three or six initial cycles of chemotherapy using oral cyclophosphamide, intravenous methotrexate and 5-fluorouracil (CMF), with or without three later single cycles of reintroduction CMF administered at 3-month intervals. At the same time, 1212 eligible post-menopausal patients were randomized in IBCSG trial VII. All post-menopausal patients received 20 mg of tamoxifen daily for 5 years. Tamoxifen alone was compared with chemo-endocrine therapy, adding three initial cycles of CMF, three delayed CMF cycles administered at months 9, 12 and 15 or both early and delayed CMF. Eligibility criteria have been reported (International Breast Cancer Study Group, 1996, 1997). The randomization in both trials was stratified by institution, type of surgery and oestrogen receptor (ER) status. The participating institutions from nine countries are listed in the Appendix.

Members of the International Breast Cancer Study Group are listed in the Appendix.

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Correspondence to: A Coates, Department of Medicine, University of Sydney, Royal Prince Alfred Hospital, Camperdown NSW 2050, Australia

QL assessment

The QL form included five indicators of components of health-related QL especially relevant in adjuvant breast cancer patients (Hürny et al. 1992). Physical wellbeing, mood, appetite (Priestman and Baum, 1976; Coates et al. 1987) and perceived adjustment to chronic illness (PACIS) (Hürny et al. 1993) were assessed with single-item linear analogue self-assessment (LASA) scales, previously validated in several cancer populations (Coates et al. 1983; Coates et al. 1990; Butow et al. 1991). An additional assessment of emotional wellbeing used the 'Befindlichkeitsskala' (Bf-S), a psychometrically characterized 28-item adjective checklist (Zerssen, 1976; Zerssen, 1986). The relationship between the mood LASA and the Bf-S has been reported elsewhere (Hürny et al. 1996b). QL forms were translated into the seven required main languages by professional translators, pilot tested by physicians and patients in the relevant centres and adjusted in the light of their feedback to ensure not only linguistic, but also conceptual, equivalence. The LASA translations were further checked by an independent 'forward-backward' translation procedure.

In accordance with prior validated use of these instruments, patients were asked to fill in the scales referring to different time frames. The LASA scales for physical wellbeing, mood and appetite were related to the 'entire period since your last full clinical assessment', while the Bf-S was related to the 'present state or the way you feel now'. The time frame of the PACIS was not specified.

The protocols required that adjuvant therapy began within 6 weeks of surgery and that patients completed the baseline QL questionnaire on, or as close as possible to, day 1 of adjuvant therapy, before the administration of treatment. The actual timing with respect to surgery and the time at which the patient received information about her tumour varied according to the institution and the individual case. Overall, of the 1724 patients who received initial chemotherapy, 1421 patients (82%) completed the QL questionnaire either exactly as required (1052 patients: 61%) or before (369 patients: 21%), while 303 patients (18%) completed the questionnaire later.

Language/cultural, biomedical and sociodemographic factors

Biomedical factors investigated were age (for premenopausal and perimenopausal women, age was grouped as under 45 or 45 and older; for post-menopausal women, age was grouped as under 60 or 60 and older); oestrogen receptor (ER) and progesterone receptor status (negative vs positive, defining positive as 10 fmol mg⁻¹ cytosol protein or greater); extent of primary surgery (total mastectomy vs conservative surgery plus radiotherapy); presence of concomitant chronic disease; treatment assignment; number of positive axillary nodes; and clinical tumour size (≤ 2 cm vs > 2 cm). For this analysis we used clinical tumour size, as it was expected to be more relevant to patients' perceptions than pathological measurements. Sociodemographic factors investigated were marital status (married, divorced or separated, widowed, single); living situation (alone, with spouse or partner, with children, with others); employment status (full or part time, housewife, unemployed, other); occupation (housewife or retired, self-employed, white collar/upper level management, white collar/subordinate and blue collar); educational level (none/primary, secondary, tertiary, and also by total years grouped as 0-5, 6-7, 8-9, 10-12, more than 12); and reported income level (grouped simply as below average,

Table 1 Number of patients and institutions according to trial and cultural group

Cultural group		Number of institutions	Number of patients	
Country	Language		Trial VI	Trial VII
Australia/New Zealand	English	6	315	187
South Africa	English	1	43	49
Switzerland	French	3	63	54
Switzerland/Germany	German	6	203	166
Switzerland	Italian	1	42	57
Italy	Italian	3	157	164
Slovenia	Slovenian	1	138	97
Spain	Spanish	1	49	20
Sweden	Swedish	1	221	195
Total	9	7	22 ^a	1231

^aOne Swiss institution is represented in both the Swiss German and the Swiss Italian cultures.

Table 2 Mood means according to culture (sorted by mean trial VI value)

Country, Language	LASA anchors ^a	Trial VI		Trial VII	
		n	Mean ^b (95% CI)	n	Mean ^b (95% CI)
Slovenia, Slovenian	Srečna Nesrečna	130	54.6 (48.9, 60.0)	87	68.4 (62.4, 74.0)
Sweden, Swedish	Lycklig Otycklig	221	62.9 (58.9, 66.6)	194	66.5 (62.4, 70.4)
Switzerland/ Germany, German	Glücklich Unglücklich	196	70.8 (67.1, 74.3)	155	71.8 (67.5, 75.7)
Spain, Spanish	Feliz Desdichada	49	71.7 (64.1, 78.4)	20	76.9 (65.4, 86.1)
Italy, Italian	Buono Pessimo	156	74.2 (70.2, 77.9)	162	73.9 (69.9, 77.6)
Switzerland, French	Bon Mauvais	63	74.1 (67.7, 79.8)	52	82.0 (75.9, 87.2)
Australia/ New Zealand, English	Happy Miserable	309	77.9 (75.4, 80.4)	184	81.6 (78.4, 84.5)
South Africa, English	Happy Miserable	43	79.3 (72.2, 85.3)	49	81.7 (75.3, 87.1)
Switzerland, Italian	Buono Pessimo	42	83.8 (77.4, 89.1)	57	84.4 (79.0, 89.1)

^aPatients were asked to mark a cross on a 100-mm line to rate mood overall for the entire period since their last full clinical assessment. Higher scores reflect better mood. ^bTransformed mean as described in Statistical methods.

average, above). Culture was defined by nine broad language/country groupings (English/Australia or New Zealand; English/South Africa; French/Switzerland; German/Switzerland or Germany; Italian/Switzerland; Italian/Italy; Slovenian/Slovenia; Spanish/Spain; Swedish/Sweden), recognizing that in these data language is inextricably associated with culture. German-speaking patients from Switzerland and Germany were combined because there were only 14 from Germany.

Table 3 Summary of the impact of biomedical factors on baseline QL measures in trial VI and VII (two-sided *P*-values)

	Emotional wellbeing (Bf-S)		Mood		Physical wellbeing		Appetite		Adjustment (PACIS)	
	VI	VII	VI	VII	VI	VII	VI	VII	VI	VII
<i>Non-tumour related factors*</i>										
Age: 60 + (VII)		0.002		0.002						0.0009
Chronic disease: no						0.02				
Treatment assignment: less chemotherapy								0.007		
<i>Tumour related factors*</i>										
ER status: positive			0.0005							
Progesterone receptor status										
Number of positive nodes: fewer positive nodes		0.01	0.003	0.05						0.0008
Tumour size										
Type of surgery: mastectomy				0.006						

*Category of factor associated with higher QL scores.

Table 4 Emotional wellbeing, mood and adjustment means according to age in post-menopausal patients (trial VII)

QL scale	Age	<i>n</i>	Mean* (95% CI)	<i>P</i>
Emotional wellbeing (Bf-S)	< 60	432	75.9 (73.9, 77.8)	0.002
	60+	510	80.0 (78.3, 81.6)	
Mood	< 60	434	72.1 (69.6, 74.5)	0.002
	60+	526	77.1 (75.0, 79.0)	
Adjustment (PACIS)	< 60	437	64.5 (61.7, 67.2)	0.0009
	60+	532	70.5 (68.2, 72.7)	

*Transformed mean as described in Statistical methods.

Statistical methods

The LASA scales were scored by measuring in millimetres from 0 to 100, with higher numbers reflecting better QL, and the scores for the Bf-S were transformed to have the same range and interpretation. We used a transformation (the square root of 100 minus these scores) in all analyses, since this transformation approximated a normal distribution and stabilized the variances, but all results are reported in the 0 to 100 scale (100 minus the squares of the estimated means of the transformed scores). Because the square root transformation approximates a symmetric distribution, these 'transformed means' are approximate estimates of medians. Analyses of variance (ANOVA) were used to test for associations between baseline QL measures and various cultural, biomedical and sociodemographic factors. We previously showed that language had a significant influence on the QL scores obtained

from our instruments (Hürny et al. 1992). Therefore, for this analysis we grouped patients into the nine language/country groups listed above and assessed each of the biomedical and sociodemographic factors controlling for culture but not for the other factors, fitting a separate ANOVA model for each of the five QL measures within each of the two trials. In addition, we investigated interactions between selected factors that we had found to be associated with baseline QL. We report transformed means standardized to the overall distribution of cultures within each trial. No adjustment was made for multiple comparisons; two-sided *P*-values were used as descriptive statistics to identify associations in the observed results.

As previously shown, baseline QL scores can vary with time from start of chemotherapy (Hürny et al. 1994). In this analysis,

controlling for timing when testing the significance of culture did not change our conclusions. We did not control for timing when testing for biomedical and sociodemographic factors, because we expected that the effects of timing would be independent of these factors: overall, the proportion of the variance explained by timing was small.

RESULTS

Description of the sample

Baseline QL assessments were completed by 1262 (86%) of the 1475 trial VI patients and by 1008 (83%) of the 1212 trial VII patients. Compliance rates varied considerably among institutions, from 58% to 100% in trial VI and from 59% to 100% in trial VII. Excluded from this investigation were 50 patients from four countries who did not complete the QL form in the primary language of their region of their country (31 from trial VI, 19 from trial VII). Table 1 shows the culture groups, along with the number of institutions and the number of patients included in each.

Cultural factors

Overall, cultural factors had the strongest impact on baseline QL and affected all five measures in both trials ($P < 0.0001$ for all, except for appetite and physical wellbeing in trial VII, which were $P = 0.05$ and 0.003 respectively). For example, Table 2 shows the means of the mood scale according to culture. The pattern of mood scores across culture groups was similar within the two trials.

Two of the languages were used in more than one country, allowing for comparisons between countries within the same language. QL scores for English-speaking patients from Australia/New Zealand were similar to those for English-speaking patients from South Africa (Table 2). In contrast, Italian-speaking patients from northern Italy reported substantially lower mood scores than those from the adjoining southern part of Switzerland ($P = 0.01$ in trial VI, $P = 0.002$ in trial VII; Table 2). All other QL scales showed differences in the same direction, although not all of the differences were statistically significant.

Overall, the variance explained by these cultural factors was modest. It ranged from 3% (Bf-S, physical wellbeing) to 8% (mood) in trial VI (premenopausal and perimenopausal patients), and from 2% (physical wellbeing, appetite) to 6% (mood, PACIS) in trial VII (post-menopausal patients).

Biomedical factors

After controlling for cultural effects, biomedical factors also had an impact on the QL measures, as summarized in Table 3. The mood and adjustment scales were most responsive to these factors. The effects of tumour and non-tumour related biomedical factors were different in the two trials.

Age had a significant impact in post-menopausal patients only. Older patients (60+ years) reported better emotional wellbeing ($P = 0.002$) and mood ($P = 0.002$), and less effort to cope ($P = 0.0009$) compared with younger post-menopausal patients (Table 4). Although older patients were more likely to have total mastectomies (71% for patients under 55 years to 79% for patients 65 years and older), the age effect was independent of type of primary surgery.

Presence of concomitant chronic disease was associated with a tendency to worse physical wellbeing in post-menopausal patients

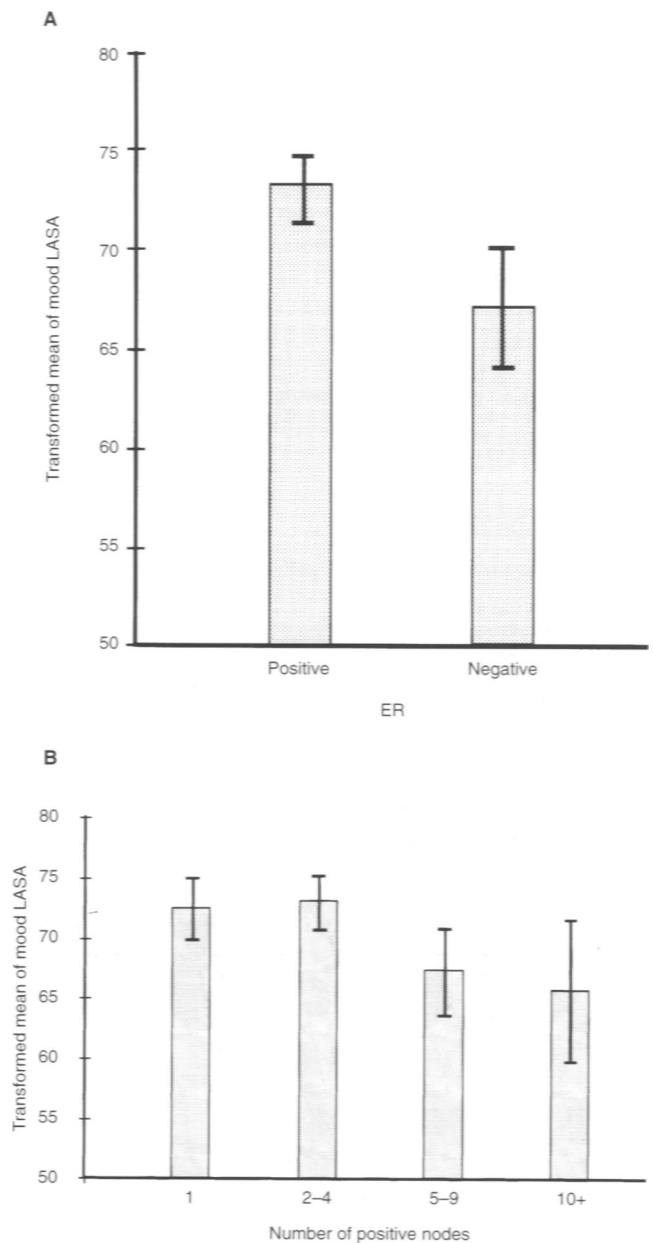


Figure 1 Impact of tumour factors on mood scores in premenopausal patients. (A) Transformed mean mood score by ER status. (B) Transformed mean mood score by number of positive nodes

(no co-morbidity: mean = 79.7; with co-morbidity: mean = 76.2, $P = 0.02$). As expected, co-morbidity was more prevalent in post-menopausal (33%) than premenopausal (13%) patients. Type of surgery had an impact on mood in post-menopausal patients only. Those treated with mastectomy reported better mood scores than those treated with conservation plus radiotherapy (76.1 vs. 70.8, $P = 0.006$). An effect of systemic adjuvant treatment assignment was observed in trial VII. Patients assigned to receive tamoxifen only reported better appetite (mean = 88.3) than those who were to undergo additional early (mean = 82.7), late (mean = 83.6), or early and late chemotherapy (mean = 84.5, $P = 0.007$).

In general, patients whose tumours had characteristics associated with poorer prognoses reported worse QL. Premenopausal

patients with ER-negative tumours reported worse mood than those with ER-positive tumours (67.2 vs. 73.0; $P=0.0005$). Higher numbers of positive nodes were associated with worse mood in both premenopausal ($P=0.003$) and post-menopausal patients ($P=0.05$) and with worse emotional wellbeing in post-menopausal patients ($P=0.01$); adjustment was negatively affected by status in premenopausal patients only ($P=0.0008$). ER status and number of positive nodes were both independent predictors of mood in premenopausal patients ($P=0.0004$ for ER status adjusted for number of positive nodes; $P=0.002$ for number of positive nodes adjusted for ER status). The association with ER status was seen in eight of the nine cultural subgroups ($P\leq 0.05$ for French/Switzerland and Spain); the difference was small and not statistically significant in the one subgroup in which the direction of the difference was the opposite (Italy). Figure 1 shows mean mood scores according to ER status and number of positive nodes in all premenopausal patients.

Sociodemographic factors

Sociodemographic factors were significantly associated with QL in post-menopausal, but not premenopausal, patients. Married and separated or divorced post-menopausal patients reported better emotional wellbeing (Bf-S) than those who were widowed or single (mean of married = 79.2, separated/divorced = 80.1, widowed = 75.3, single = 75.0; $P=0.05$). Living alone was associated with poorer emotional wellbeing (mean = 75.3) than living with others (mean for women living with spouse or partner = 78.9, with children = 77.3, with other = 83.4; $P=0.05$). Living alone or with children was associated with worse appetite than living with spouse, partner or other (mean for women living alone = 81.8, with children = 83.2, with spouse or partner = 85.8 with other = 88.4; $P=0.05$). Post-menopausal women with either little formal schooling or with extensive education reported worse adjustment than women with levels in between (mean for 0–5 years = 67.1, 6 or 7 years = 66.5, 8 or 9 years = 69.0, 10–12 years = 70.6, more than 12 years = 59.4; $P=0.04$).

Country differences within language

We also investigated whether or not there was a differential impact of biomedical and sociodemographic factors on global QL indicators between different countries within the same language group. Mood and adjustment were analysed separately in the two English-speaking groups (South Africa and Australia/New Zealand) within each trial and in the two Italian-speaking groups (Italy and Switzerland) within each trial. Although some differences were observed, there were no consistent patterns, suggesting that these factors have a similar impact on patient self-estimation within language groups. They do not explain the overall difference in mood between Italian-speaking patients from Italy and Italian-speaking patients from Switzerland.

DISCUSSION

Individual patients' baseline QL scores vary considerably within cancer clinical trials. They are highly predictive of the level of subsequent QL assessments and therefore relevant for investigating treatment-related changes. We analysed how biomedical, sociodemographic and cultural factors affected baseline scores of two large-scale adjuvant breast cancer trials (Hürny et al. 1996a)

and now report these associations in more detail. This information will be useful for investigators in determining which additional variables need to be assessed in breast cancer clinical trials.

Cultural factors

This investigation has confirmed and substantially extended our previous report (Hürny et al. 1992) that cultural and language factors affect patient-rated QL and, therefore, need to be considered in cross-cultural trials, although their contribution to the total variance in QL scores is modest. Although it remains possible that these findings are due to imperfect translation, we believe this is unlikely given the thorough multistep translation procedure which was used.

Before concluding that there are 'true' cultural differences, we should also consider institutional factors and the possibility of selective recruitment of patients with different characteristics, or differences in patient care in the various cultures. This may account for the differences seen between the Italian-speaking Swiss and the patients from northern Italy. The participating hospitals in Italy are larger, the waiting rooms are more crowded, and patients may feel more anonymous at the beginning of treatment than in the Swiss outpatient clinics. Also, the generally higher QL scores in Switzerland compared with Slovenia may reflect true overall socioeconomic differences between the two countries. It is also possible that systematic differences among cultures in the degree and method of doctor-patient communication about the details of the tumour and its treatment may underlie part of the observed cultural differences in QL.

On the other hand, in the case that patients from different cultures report similar QL scores (e.g. English-speaking patients from Australia/New Zealand and South Africa), this similarity may hide true cultural differences in perceptions, attitudes and habits. Although these differences are not relevant for overall treatment comparisons, in subgroup analyses an isolated interpretation of either symptoms or any aspect of QL without regard to the institutional, social and cultural context could be misleading (Hürny et al. 1993).

In summary, the overall differences among the investigated cultures probably reflect cultural differences in patients' response to disease and treatment sequelae, such as a tendency to stoic self-control or exasperated emotional expression in particular cultures. This is especially relevant for highly 'subjective' concepts such as 'coping' (PACIS), but was also seen in appetite, a relatively concrete sensation.

Biomedical factors

Age had an effect on QL in post-menopausal patients only. Post-menopausal patients under 60 reported worse emotional and adjustment scores than older patients. To our knowledge, the role of age in the adjustment to diagnosis and treatment has not been reported separately within menopausal status groups (Vinokur et al. 1990; Ganz et al. 1993; Mor et al. 1994), except in one study in which increased anxiety was observed in patients in their fifties treated by mastectomy (Maraste et al. 1992).

Co-morbidity was much more frequent in post-menopausal patients. It had a weak negative impact on physical wellbeing in both trials, but was significantly associated with physical wellbeing only in post-menopausal patients.

Extent of surgery was a significant factor associated with mood in post-menopausal patients, with patients who had had total mastectomies reporting better mood scores. At the start of adjuvant therapy, emotional distress is characterized by anxiety rather than depression (Maraste et al. 1992). A total mastectomy could have relieved anxiety regarding disease progression in these patients (Fallowfield et al. 1990), whereas in premenopausal patients other factors, such as concerns about body image, may dominate. Radiotherapy was given only after breast conservation, and followed chemotherapy. Its anticipation might have contributed to increased anxiety in the group treated by breast conservation. Other reports do not suggest a relationship between extent of surgery and either psychological distress or physical dysfunction at this early phase of recovery from surgery (Kiebert et al. 1991; Ganz et al. 1992; Pozo et al. 1992). The relationship between ER status and mood is in agreement with the finding reported by Razavi (1990), but has not been confirmed by other groups (Hislop and Kan, 1990; Maunsell and Brisson, 1990; Rosenqvist et al. 1993; Tjemsland et al. 1995). It may reflect either an intrinsic interaction between emotional processes and the endocrine system in premenopausal patients or the psychological impact of the physician having communicated to the patient information regarding her prognosis (Roberts et al. 1994). Interestingly, the association between ER status and perceived adjustment, which is not a pure emotional concept but has also a strong cognitive component, was not significant. On the other hand, the relationship between number of positive nodes and both emotional measures and adjustment may reflect patients' response to having received information regarding nodal involvement and its prognostic significance. The exact procedure and timing of patient information may have varied among and even within institutions. These issues cannot be further clarified with our data. Nevertheless, this finding is intriguing and warrants further study, especially in regard to treatment effects on QL and to biomedical outcome (Coates et al. 1992; Hüry, 1993).

The effect of treatment assignment on appetite in post-menopausal patients is probably an anticipatory effect. Patients were informed about the allocated treatment before completing the QL form. Patients assigned to receive tamoxifen only reported better baseline appetite scores than those assigned to receive late chemotherapy only. As reported in the analysis of the impact of treatment on subsequent QL in these trials (Hüry et al. 1996a), anticipation of treatment plays a role in patients' perception of QL.

Overall, biomedical factors showed little impact on baseline QL. Because treatment trials are stratified by major biomedical prognostic factors, they are primarily relevant for subgroup comparisons. Our findings contrast with those of a smaller investigation of 109 newly diagnosed breast cancer patients, which found no significant association between patient-rated rehabilitation needs and axillary node status, type of surgery or receipt of chemotherapy (Ganz et al. 1990). It is not clear whether this difference is due to the different QL measures (global indicators vs specific problem evaluation) or due to the different study contexts. In our study, mood and adjustment, those measures most closely reflecting patients' 'subjective' experience, were the most sensitive to biomedical factors.

Sociodemographic factors

Sociodemographic factors showed a relatively weak association with baseline QL, which was seen in post-menopausal patients

only. Overall, we found no major effect of these factors on QL. However, these factors have been shown to predict survival in breast (Karjalainen and Pukkala, 1990; Schrijvers et al. 1995) and other cancers, and we suggest that in large-scale international trials at least one indicator of socioeconomic status (e.g. educational level) be recorded.

Further investigations

More information is needed about the perception and understanding of cancer and its treatment in various cultures. The question of how interactions among cultural, social and biomedical factors affect QL in cancer clinical trial settings warrants further study, not just for baseline scores, but also for QL during treatment and follow-up. In addition, the generalizability of the effect of biomedical interventions on QL should be investigated within international clinical trials.

Only a modest part of the variance in QL scores was explained by the factors investigated. In contrast, individual psychosocial factors, such as stressful life events before diagnosis (Maunsell et al. 1992), history of depression (Maunsell et al. 1992), attitudes (Carver et al. 1994) and social support (Irvine et al. 1991) have been reported to be substantially associated with patients' adjustment. Their impact as covariates in evaluating treatment effects on QL could not be investigated in the present study.

Conclusions

Cultural factors have a substantial impact on baseline QL measures, although they explain only a small percentage of the total variance. They need to be considered when evaluating the influence of treatment on QL in international breast cancer clinical trials. Various biomedical factors have a less pronounced but tangible impact. Their effects are different in premenopausal compared with post-menopausal patients.

ABBREVIATIONS

ANOVA, analysis of variance; Bf-S, Befindlichkeitsskala; CMF, combination chemotherapy using oral cyclophosphamide plus intravenous methotrexate and 5-fluorouracil; ER, oestrogen receptor; IBCSG, International Breast Cancer Study Group; LASA, linear analogue self-assessment; PACIS, perceived adjustment to chronic illness scale; QL, quality of life

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APPENDIX

International Breast Cancer Study Group: participants and authors trials VI, VII

Coordinating Center Bern, Switzerland	M Castiglione, A Goldhirsch (Studies Coordinators), K Geiser, A Berlinger, G Egli (Data-Management) R Maibach, R Pedowski
Statistical Center Harvard School of Public Health and Dana-Farber Cancer Institute, Boston, MA, USA	R Gelber (Group Statistician), K Price, H Peterson, M Zelen, S Gelber, A O'Neill
Quality of Life Office Bern, Switzerland	J Bernhard, Ch Hürry, H Gusset
Pathology Office Institute of Cancer Research, Royal Cancer Hospital, Sutton, UK	B Gusterson, R Bettelheim, R Reed
Data Management Center Frontier Science and Technology Research Foundation Amherst, NY, USA	M Isley, R Hinkle

Auckland Breast Cancer Study Group, Auckland, New Zealand	RG Kay, VJ Harvey, CS Benjamin, P Thompson, A Bierre, M Miller, B Hochstein, A Lethaby, J Webber	University of Sydney, Dubbo Base Hospital and Royal Prince Alfred Hospital, Sydney, Australia	MHN Tattersall, A Coates, F Niesche, R West, S Renwick, J Donovan, P Duval, R J Simes, A Ng, D Glenn, RA North, J Beith, RG O'Connor, M Rice, G Stevens, J Grassby, S Pendlebury, C McLeod, M Boyer, A Sullivan, J Hobbs
Centro di Riferimento Oncologico Aviano, Italy	D Crivellari, S Monfardini, E Galligioni, A Veronesi, A Buonadonna, S Massarut, C Rossi, E Candiani, A Carbone, R Volpe, M Roncadin, M Arcicasa, GF Santini, F Villalta, F Coran, S Morassut	European Institute of Oncology, Milan, Italy	A Goldhirsch, G Martinelli, U Veronesi, A Luini, R Orecchia, G Viale, M Colleoni, F Nolè, F Peccatori, A Costa, S Zurrida, P Veronesi, V Sacchini, V Gallimberti
Spedali Civili & Fondazione Beretta, Brescia, Italy	G Marini, E Simoncini, P Marpicati, A Barni, P Grigolato, L Morassi	Ospedale Infermi, Rimini	A Ravaoli, D Tassinari, G Oliverio, F Barbanti, P Rinaldi, E Pini, G Drudi
Groote Schuur Hospital, Cape Town, Rep. of South Africa	DM Dent, A Gudgeon, E Murray, P Steynor, J Toop	Ospedale S Eugenio, Rome, Italy	M Antimi, M Minelli, V Bellini, R Porzio, E Pernazza, G Santeusano, LG Spagnoli
West Swedish Breast Cancer Study Group, Göteborg, Sweden	CM Rudenstam, A Wallgren, S Ottosson-Lönn, R Hultbom, G Colldahl-Jäderström, E Cahlin, J Mattsson, S Holmberg, S Jansson, L Ivarsson, O Ruusvik, LG Niklasson, S Dahlin, G Karlsson, B Lindberg, A Sundbäck, S Bergegårdh, H Salander, C Andersson, M Heideman, Y Hessman, O Nelzén, G Claes, T Flamhult, JH Svensson, P Liedberg	Ospedale S Bortolo, Vicenza, Italy	M Magazu, V Fosser, P Morandi, G Scalco, M Balli, M Gion, S Meli, G Torsello
General Hospital Gorizia, Italy	S Foladore, L Foghin, G Pamich, C Bianchi, B Marino, A Murgia, V Milan	Toronto Sunnybrook Regional Cancer Centre Toronto, Canada	K Pritchard, D Sutherland, C Sawka, G Taylor, R Choo, C Catzavelos, K Roche
Sandton Oncology Center Johannesburg, South Africa	D Vorobiof, M Chasen, G Fotheringham, G de Muelenaere, B Skudowitz, C Mohammed, A Rosengarten	SAKK (Swiss Group for Clinical Cancer Research): Inselspital, Bern	MF Fey, E Dreher, H Schneider, S Aebi, K Buser, J Ludin, G Beck, H Bürgi, A Haenel, JM Luthi, R Markwalder, HJ Altermatt, M Nandedkar
The Institute of Oncology, Ljubljana, Slovenia	J Lindtner, D Erzen, E Majdic, B Stabuc, A Plesnicar, R Golouh, J Lamovec, J Jancar, I Vrhoved, M Kramberger	Kantonsspital, St. Gallen	HJ Senn, B Thürlimann, Ch Oehlschlegel, G Ries, M Töpfer, U Lorenz, O Schittknecht, B Späti
Madrid Breast Cancer Group, Madrid, Spain	H Cortés-Funes, D Mendiola, C Gravalos, Colomer, M Mendez, F Cruz Vigo, P Miranda, A Sierra, F Martinez-Tello, A Garzon, S Alonso, A Ferrero, C Vargas	Ospedale San Giovanni, Bellinzona	F Cavalli, O Pagani, H Neuenschwander, W Müller, L Bronz, C Sessa, G Martinelli, M Ghielmini, P Luscieti, E Passega, T Rusca, P Rey, J Bernier, S Martinoli, E Pedrinis, G Losa, T Gyr, L Leidi, G Pastorelli, A Goldhirsch
Anti-Cancer Council of Victoria, Melbourne, Australia	J Collins, P Gregory, P Kitchen, S Hart, S Neil, M Henderson, I Russell, T Gale, M Pitcher, R Snyder, R McLennan, M Schwarz, I Burns, M Green, R Basser, R Drummond, A Rodger, G Richardson, J McKendrick, M Chipman	Kantonsspital, Basel	R Hermann, JF Harder, O Köchli, U Eppenberger, J Torhorst
Royal Adelaide Hospital, Adelaide, Australia	I Olver, A Robertson, P Gill, ML Carter, P Malycha, E Yeoh, G Ward, ASY Leong, J Lommax-Smith, D Hoosfall, R D'Angelo	Hôpital des Cadolles, Neuchâtel	D Piguet, P Siegenthaler, V Barrelet, RP Baumann
Sir Charles Gairdner Hospital, Nedlands, Western Australia	M Byrne, G van Hazel, J Dewar, M Buck, D Ingram, G Sterret	Kantonsspital, Luzern	R Joss
Australian New Zealand Breast Cancer Trials Group (ANZ BCTG) Mater Hospital Waratah, Newcastle, Australia	JF Forbes, J Stewart, D Jackson, R Gourlay, J Bishop, C Flower, A Wilson, S Cox, S Ackland, A Bonaventura, C Hamilton, J Denham, P O'Brien, M Back, S Brae, A Price, Muragasu, H Foster, D Clarke, R Sillar, V Clarke, S Brew	Kantonsspital, Zürich	B Pestalozzi, C Sauter, V Engeler, U Haller, U Metzger, P Huguenin, R Caduff
		Centre Hôpitalier Universitaire, Lausanne	L Perey, S Leyvraz, P Anani, F Gomez, D Wellman, G Chapuis, P De Grandi, P Reymond, M Gillet, JF Delaloye
		Hôpital Cantonal, Geneva	P Alberto, H Bonnefol, P Schäfer, F Krauer, M Forni, M Aapro, R Egeli, R Megevand, E Jacot-des-Combes, A Schindler, B Borisch, S Diebold
		Kantonsspital Graubünden, Chur	F Egli, P Forrer, A Willi, R Steiner, J Allemann, T Rüedi, A Leutenegger, U Dalla Torre
		Swiss Cancer League, Bern, Switzerland	U Metzger, W Weber, G Noseda