

Psychological Distress in Cancer Patients Attending the European Institute of Oncology in Milan

A. Brédart^a F. Didier^a C. Robertson^b E. Scaffidi^a D. Fonzo^a A. Costa^c
A. Goldhirsch^d P. Autier^b

^aPsycho-Oncology Research Unit, ^bDivision of Epidemiology and Biostatistics, ^cTraining and Communication Unit and ^dDepartment of Medical Oncology, European Institute of Oncology, Milan, Italy

Key Words

Hospital Anxiety and Depression Scale (HADS) · Depressive disorder, major · Anxiety disorder, generalised · Interventions, psychosocial, psychiatric

Abstract

Background: The determination of the extent and specific features of the psychological distress to be expected in a cancer centre may influence the choice of interventions to be implemented for addressing these problems. This study was aimed at estimating the prevalence of psychological distress in patients attending a second reference cancer centre in Milan (Italy), and at identifying associated factors. **Patients and Methods:** 190 consecutive patients were assessed within 3 days of hospital discharge using the Hospital Anxiety and Depression Scale. **Results:** Major depressive disorders or generalised anxiety disorders were estimated in 16% of the patients. Only 2 of these patients were referred to the psycho-oncology unit, hence the psychological distress of many patients was not considered during their hospital stay. In the multiple regression analysis, independent predictors of psychological distress were female gender, experience of disturbance in family and social life due to illness, nausea and vomiting, and perception of being in a poor state

of health ($R^2 = 0.31$, p value < 0.001), while physical functioning, fatigue and pain, significant factors in univariate analysis ($p < 0.05$), sociodemographic and clinical factors were not predictors. **Conclusion:** The psycho-oncology team should focus on helping doctors and nurses identify the patients' psychological problems, dealing with them or making a referral.

Copyright © 1999 S. Karger AG, Basel

Introduction

The occurrence of mood disorders in oncology has to be given serious attention because these disorders may further damage patients' quality of life and impair their ability to adhere to treatment or make decisions that ultimately influence their chance of survival [1]. In oncology, mood disorders essentially denote adjustment, major depressive or anxiety disorders. According to the fourth edition of *Diagnostic and Statistical Manual of Mental Disorders* [2], adjustment disorders refer to maladaptive reactions, either emotional (anxious or depressed mood) or behavioural (decline in occupational functioning, social activities, or in relationships with others) that manifest as a result of a stressful event. Adjustment disorder is considered when stressful events, namely the communication

KARGER

Fax + 41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 1999 S. Karger AG, Basel
0030-2414/99/0574-0297\$17.50/0

Accessible online at:
www.karger.com/journals/ocl

Anne Brédart
Psycho-Oncology Research Unit
European Institute of Oncology
Via Ripamonti 435, I-20141 Milan (Italy)
Fax +39 02 57 489 208, E-Mail abredart@ieo.it

of diagnosis or relapse, induce maladaptive reactions that persist over 7–14 days [3]. Major mood disorders, either depressive or anxiety disorders, encompass more intense, numerous and lasting anxious or depressive symptoms in comparison to adjustment disorders. Mood disorders are psychiatric syndromes, while psychological distress refers to a continuum of emotional symptoms varying in severity.

A diagnosis of cancer, its treatment and associated side effects may cause considerable psychological distress. Different studies conducted during the last decades have revealed that mood disorders were highly prevalent in oncology: figures ranged from 2 to 46% for anxiety, from 6 to 42% for depressive and from 32 to 52% for adjustment disorders, depending on sample characteristics (e.g. stage of disease, out- or inpatients), mode of data collection (e.g. interviews vs. self-assessment) or diagnostic criteria (e.g. cutoff scores for determining pathological cases) [4–14].

Different factors, either psychosocial (e.g. lower socioeconomic status, poor social support, history of psychological problems, accumulation of stress) or medical (e.g. more physical symptoms, more advanced cancer at diagnosis), have been proposed for identifying patients at greater risk of difficulties in coping with cancer [13]. Enhanced knowledge of these risk factors may influence the choice of interventions to be implemented for addressing patients' difficulties [15].

This survey took place during the first year of operation of a Psycho-Oncology Unit at the European Institute of Oncology (EIO) in Milan, where at that time no recommendation for psychological or psychiatric referral had yet been established. The aim of this study was to estimate the prevalence of the major depressive disorder or generalised anxiety disorder in cancer patients attending the different departments of this oncology hospital, and to identify factors associated with psychological distress. This should help to determine the type and availability of personnel making up the psycho-oncology team as well as to select the activities to be developed.

Patients and Methods

Patients

Between August 1997 and March 1998, a consecutive series of about 6 patients per week were recruited from all EIO departments. They were invited to complete the 'Hospital Anxiety and Depression Scale' (HADS) [16] within 3 days before hospital discharge. The EIO is a specialised oncology centre accredited for care and treatment coverage by the Italian National Health Service and a referral cancer centre for the whole of Italy.

Instruments

The HADS is a brief self-report measuring scale composed of 14 four-level Likert scale items assessing symptoms of anxiety (tension, fear, worries, restlessness, panic) and depression (loss of pleasure, loss of interest, sadness, slowing down, pessimism). It has been shown to be valid and effective in screening large, diverse cancer patient populations, in order to identify who is most likely to require psychiatric or psychosocial interventions [5–8]. Total HADS scores range from 0 to 42. An elevated total score means intense anxiety or depressive symptoms.

In a validation study comparing HADS scores and psychiatric disorders established on the basis of clinical interviews using DSM-III criteria, an optimal threshold score of 14 was chosen for discriminating between no disorder and generalised anxiety disorder or major depressive illness [8]. At a score of >14, it had a sensitivity of 80%, specificity of 76% and a positive predictive value of 41%. Thus 2/5 patients scoring over 14 would be true cases.

Sociodemographic data (age, gender, educational level, socio-economic status, distance of residence to EIO, mode of health care payment) and clinical data (stage of illness, time since diagnosis, being on or off treatment, length of hospital stay at time of assessment) were recorded through medical records. Physical, social, role functioning, symptoms (nausea, fatigue, pain) and health status perception were assessed as potential predictors of psychological distress, using the QLQ-C30 [17]. To minimise patients' burden, only a subsample of the population (n = 116) was consecutively administered this last questionnaire. The QLQ-C30 is composed of multi-item scales and single item measures, ranging in score from 0 to 100. A high score for a functional scale and for health status perception represents a healthy level of functioning or quality of life, whereas a high score for a symptom scale corresponds to a high level of symptomatology.

Physical functioning refers to a patient's ability to perform self-care, mobility or physical activities, social functioning to his experience of disturbance in family life and social activities. This may cover feelings of a lack of practical or emotional support and a loss of affiliation. Role functioning means freedom from limitations in performing a job or housework. Health perception is measured by the patient self-rating his current physical condition and quality of life.

Statistics

In a univariate analysis, levels of psychological distress determined by HADS threshold scores of 14 were compared according to the different sociodemographic and clinical factors, using Mantel χ^2 for trend [18]. On the QLQ-C30 scales raw scores were dichotomised into 'no problem' versus 'slight/considerable problems', using a 33 or 67 cutoff for the symptoms or functional scales, respectively. Multiple regression analysis was performed using HADS total scores and QLQ-C30 scale scores as continuous variables, and including the statistically significant variables in univariate analysis. Backward procedure was adopted for selecting the important predictors [19].

Results

Two-hundred and twenty patients were approached. The response rate was 86%. Nonparticipation was due to fear of the questionnaire administrator of burdening the

Table 1. Patients' characteristics

	Respon- dents (n = 190)	NR to HADS (n = 30)	NR to QLQ-c30 (n = 100)
<i>Age, years</i>			
Median	56	56	56
Range	22–87	22–77	22–87
<i>Gender</i>			
Male	55 (29)	6 (20)	22 (22)
Female	135 (71)	24 (80)	78 (78)
<i>Geographical origin</i>			
Milan	47 (25)	6 (20)	23 (23)
Northern Italy (except Milan)	77 (41)	9 (30)	43 (43)
Central/Southern Italy	66 (35)	15 (50)	34 (34)
<i>Diagnosis</i>			
Not yet established	7 (4)	2 (7)	1 (1)
Breast cancer	89 (47)	11 (37)	54 (54)
Gastric cancer	11 (6)	4 (13)	8 (8)
Lung cancer	21 (11)	1 (3)	9 (9)
Colon cancer	14 (7)	4 (13)	7 (7)
Head and neck cancer	6 (3)	2 (7)	2 (2)
Lymphoma	6 (3)	1 (3)	3 (3)
Gynaecological cancer	15 (8)	4 (13)	6 (6)
Others	21 (11)	3 (10)	10 (10)
<i>Disease stage</i>			
Not yet established	39 (21)	6 (20)	25 (25)
Solid tumour			
Local	35 (18)	8 (27)	28 (28)
Locoregional	37 (20)	3 (10)	5 (5)
Metastasis	73 (38)	8 (27)	35 (35)
Non-solid tumour	3 (2)	1 (3)	2 (2)
No information	3 (2)	4 (13)	5 (5)
<i>Time since diagnosis, months</i>			
Median	2	4	2
Range	0–231	0–112	0–126
<i>Treatment status</i>			
On treatment	157 (83)	28 (87)	75 (75)
Off treatment	33 (17)	4 (13)	25 (25)
<i>Length of hospital stay, days</i>			
Median	5	6	4
Range	0–60	3–20	0–60

Values in parentheses represent percentage. NR = Non-respondents.

patient (13%) or patient refusal (1%). Respondents did not differ from nonrespondents with regard to clinical and sociodemographic data. Hence these results may be considered to be representative of the patients attending our Oncology Institute.

Table 2. Psychological distress according to HADS and sociodemographic parameters

	HADS ≤ 14	HADS > 14
<i>Gender***</i>		
Male (n = 55)	44 (80)	11 (20)
Female (n = 135)	72 (53)	63 (47)
<i>Age**</i>		
≤ 50 (n = 71)	51 (72)	20 (28)
50–65 (n = 73)	36 (49)	37 (51)
> 65 (n = 46)	29 (63)	17 (37)
<i>Geographical origin¹</i>		
Milan (n = 47)	25 (53)	22 (47)
Northern Italy (except Milan) (n = 77)	49 (64)	28 (36)
Central/Southern (n = 66)	42 (64)	24 (36)
<i>Financial resources¹</i>		
Breadwinner (n = 90)	62 (69)	28 (31)
<i>Sickness/disability/</i>		
unemployment (n = 17)	7 (42)	10 (59)
Pensioner (n = 42)	22 (52)	20 (48)
Housewife/students (n = 36)	22 (61)	14 (39)
Other (n = 5)		

Values in parentheses represent percentage.

** p < 0.01; *** p < 0.001 (Mantel χ^2 for trend).

¹ Non-significant.

Median age of the sample was 56 years (range 22–87) and 135 (71%) of the subjects were female. The frequency of specific malignancies and disease stages reflected the typical activities of the EIO (table 1). Median Karnofsky performance status [20] was 90 (range 40–100). Seventy-four (34%) of the patients presented an HADS score > 14. Considering that the positive predictive value of an HADS score > 14 is 41%, among our patients 30 (16% of the overall sample) would be true cases of a major depressive disorder or generalised anxiety disorder.

Univariate Analysis

There was a higher proportion of patients with an HADS score > 14 (51%) in the 50–65 age category as compared to younger and older age and a significantly higher proportion of female than male patients scored > 14 (table 2). Other sociodemographic parameters, i.e. marital status, socio-economic status, distance to care location and mode of health care payment, were not statistically associated with HADS levels of psychological distress.

Objective clinical parameters were not related to categories of psychological distress (table 3), whereas a higher

Table 3. Psychological distress according to HADS and illness-related parameters

	HADS ≤ 14	HADS > 14
<i>Present disease status</i>		
Solid tumour		
Local (n = 35)	18 (51)	17 (49)
Locoregional (n = 37)	24 (65)	13 (35)
Metastatic (n = 73)	44 (60)	29 (40)
Other (n = 45)		
<i>Time since diagnosis</i>		
Less than 1 year (n = 144)	89 (62)	55 (38)
More than 1 year (n = 43)	25 (58)	18 (42)
No information (n = 3)		
<i>Present treatment status</i>		
On treatment (n = 157)	95 (61)	62 (40)
Off treatment (n = 33)	21 (65)	12 (36)
<i>Length of hospital stay</i>		
Less than 5 days (n = 110)	68 (62)	42 (38)
More than 5 days (n = 69)	42 (61)	27 (39)
Outpatient (n = 11)		

Values in parentheses represent percentage. Comparisons are nonsignificant.

proportion of elevated HADS scores was observed in patients with problems of physical functioning, social functioning or having pain, nausea and vomiting and fatigue (table 4). Psychological distress increased significantly in patients perceiving themselves to be in a poor state of health: 30 (81%) patients who perceived themselves to be in good health had an HADS score <15 compared to 7 (19%) >14, while 3 (33%) patients who perceived themselves to be in poor health had an HADS <15 compared to 6 (67%) >14.

Multivariate Analysis

In the full model with all the significant univariate variables age, physical functioning, fatigue and pain had no significant effect on HADS scores adjusting for the other variables. The best regression model explaining the association between anxiety and depression scores and the influencing factors combine perception of health status, social functioning, nausea and vomiting, and gender ($R^2 = 0.31$, p value <0.001) (table 5). HADS scores increase with problems in social functioning, nausea and vomiting, and decrease with perception of a healthier condition. Female patients have higher anxiety and depression scores.

Table 4. Psychological distress according to HADS and general cancer symptoms and functional status (EORTC QLQ-C30)

	HADS ≤ 14	HADS > 14
<i>Physical functioning**</i>		
No problem (n = 76)	56 (74)	20 (26)
Slight/considerable (n = 40)	18 (45)	22 (55)
<i>Role functioning¹</i>		
No problem (n = 55)	39 (71)	16 (29)
Slight/considerable (n = 59)	33 (56)	26 (44)
<i>Social functioning***</i>		
No problem (n = 70)	53 (76)	17 (24)
Slight/considerable (n = 46)	21 (46)	25 (54)
<i>Fatigue**</i>		
No problem (n = 48)	38 (79)	10 (21)
Slight/considerable (n = 68)	36 (53)	32 (47)
<i>Nausea and vomiting*</i>		
No problem (n = 90)	62 (69)	28 (31)
Slight/considerable (n = 26)	12 (46)	14 (54)
<i>Pain**</i>		
No problem (n = 66)	49 (74)	17 (26)
Slight/considerable (n = 50)	25 (50)	25 (50)
<i>Financial impact¹</i>		
No problem (n = 72)	49 (68)	23 (32)
Slight/considerable (n = 44)	25 (57)	19 (43)
<i>Health status perception**</i>		
Poor (n = 9)	3 (33)	6 (67)
Average (n = 69)	41 (59)	28 (41)
Good (n = 37)	30 (81)	7 (19)

Values in parentheses represent percentage.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ (Mantel χ^2 for trend).

¹ Non-significant.

Referral to the Psycho-Oncology Unit

Looking at the activity report of the Psycho-Oncology Unit, only 2 out of the 74 patients presenting HADS scores suggesting psychological distress in this survey were referred for psychological help. The medical and nursing staff was aware of the availability of that service, however no specific criteria had yet been divulged to help them screen for psychological distress.

Discussion

In a sample of 190 consecutive cancer patients, 34% of the patients presented an HADS score >14, estimating the number of patients suspected of suffering from major

Table 5. Multiple regression: dependent variable HADS total scores

Model and variables	Regression coefficient	SE	p value
<i>Model 1</i>			
Constant	19,542	5.914	0.001
Age	2.666×10^{-2}	0.047	0.572
Female vs. male	3.541	1.333	0.009
Physical functioning ¹	4.600×10^{-3}	0.037	0.900
Social functioning ¹	-6.525×10^{-2}	0.029	0.025
Fatigue ²	-5.900×10^{-3}	0.034	0.861
Nausea and vomiting ²	4.892×10^{-2}	0.026	0.067
Pain ²	-5.904×10^{-3}	0.027	0.828
Health perception ³	-0.102	0.034	0.004
<i>Final model</i>			
Constant	20.400	2.388	0.000
Female vs. male	3.493	1.297	0.008
Social functioning ¹	-6.023×10^{-2}	0.026	0.022
Nausea and vomiting ²	4.627×10^{-2}	0.025	0.063
Health perception ³	-9.768×10^{-2}	0.030	0.002

Residual standard errors for model 1 = 6.32 and for final model = 6.22.

¹ Scale going from 0 (poor functioning) to 100 (excellent functioning).

² Scale going from 0 (no problem) to 100 (considerable problems).

³ Scale going from 0 (very poor) to 100 (excellent).

depressive disorder or generalised anxiety disorder at 16% of the overall sample.

Compared with the original Derogatis et al. [4] study, this proportion is higher (16 vs. 8%), but with another Italian study using the WHO Classification of Mental and Behavioural Disorders criteria (ICD-X) for diagnosing psychiatric disorders, the proportion of estimated major depressive disorders or generalised anxiety disorders is equivalent (16 vs. 16%) [10].

Thus, a large proportion of patients (34%) were presenting an HADS score justifying at least further psychological evaluation. However, considering the activity report of the Psycho-Oncology Unit of the EIO, only 2 of these patients were referred to the Psycho-Oncology Unit. This is particularly alarming considering that early maladjustment to cancer has been found to predict depressive symptoms 1 year after a cancer diagnosis [21]. At start of a psycho-oncology clinical service, doctors and nurses need help in identifying emotional disturbance in their patients in order to initiate appropriate referral.

Practical aids such as short checklists for the regular assessment of patients' psychological symptoms as well as

guidelines for referral should be provided. For example, specific depressive symptoms such as anhedonia, guilt, suicidal thoughts or hopelessness have to be pointed out to clinicians [22]. The number, intensity and duration of symptoms indicate the type of psychosocial or psychiatric intervention. Adjustment disorders may be dealt with on the ward by doctors and nurses thanks to case discussions with a consultant, while major mood disorders need complementary psychopharmacological and/or psychotherapeutic interventions. Other psychosocial interventions have been proposed to prevent affective disorders [23]. Providing adequate and coherent medical information while offering reassurance and empathy may reduce the development of mood disorders in cancer patients [24]. Teaching programmes designed to improve doctors' communication skills are now being evaluated [25].

Since nurses are usually in daily contact with patients, they should also be able to monitor patients' physical, psychological or social problems and initiate appropriate referrals. In addition, prevention of emotional disturbance also requires more specific programmes directed to patients at higher psychological risk, either because of undergoing highly stressful therapeutic procedures or because of personal predisposing characteristics.

Since our evaluation was performed only once, we do not have any information on the course of patients' psychological distress. Within several months, patients off treatment overall may regain their emotional equilibrium without specialist intervention. However, timely psychological interventions may help overcome the acute emotional distress experienced in the diagnostic and treatment phase leading to a more satisfactory dealing with the immediate requests of cancer therapy, namely the choice of treatment or coping with side effects.

As in other studies, psychological morbidity was found to be associated with physical symptoms and functioning. However, the disease stage was not significantly related to psychological distress, but in this sample the level of the Karnofsky performance status was high and the levels of symptoms low (QLQ-C30 dyspnea, nausea and vomiting, and diarrhoea). Independent predictors of psychological distress were patients' perception of disturbance in social functioning, nausea and vomiting, and perception of being in a poor state of health. This is in part reflected in the research mentioned above where 2 out of 4 predictors of depressive symptoms 1 year after cancer diagnosis were poor social support and performance status [21]. In our young and mostly female sample, these factors played a dominant role.

Only 31% of the HADS score variance was explained by the variables included in the multiple regression mod-

el. The remaining unexplained variance may be related to more specific factors that were not investigated in this patients group which was heterogeneous with regard to the type of diagnosis and disease stage.

The patients' perception of being in a poor state of health and nausea and vomiting were significantly related to psychological distress. This underlines how the physical condition and the psychological distress overlap in this sample. It further shows the importance of checking the adequacy of the patients' knowledge and comprehension of their own illness status and prognosis. Misperception may eventually be corrected although more generally patients may need counselling for coping with the loss of unrealistic hope for cure and for envisaging more appropriate treatment perspectives. The deterioration of social functioning that weighed importantly on psychological distress could be dealt with by enhancing the emotional support given to patients. Moreover, patients experiencing nausea and vomiting should also be the focus of more intense psychological help.

To conclude, this study adds new evidence of the need for improving the management of psychological distress in cancer patients. Attenuating the burden of cancer disease and its treatment on the quality of life is an objective of oncology care. Psychosocial interventions should aim at enhancing detection of emotional distress and preventing the development of psychopathological reactions. Doctors and nurses require both direct help on the ward and specialised training for identifying the patients' psychological problems, dealing with them or making decisions for referral. Complementary programmes provided by the psycho-oncology team should be set up for cancer patients at a higher risk of poor adjustment to cancer.

Acknowledgements

This work was supported by a grant from the American-Italian Cancer Foundation and from the European Institute of Oncology Foundation.

References

- 1 Ford S, Fallowfield L, Lewis S: Can oncologists detect distress in their out-patients and how satisfied are they with their performance during bad news consultations? *Br J Cancer* 1994; 70:767-770.
- 2 American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 4. Washington, American Psychiatric Association, 1996.
- 3 Massie MJ, Holland JC: Overview of normal reactions and prevalence of psychiatric disorders; in Holland JC, Rowland JH (eds): *Handbook of Psychooncology: Psychological Care of the Patient with Cancer*. New York, Oxford University Press, 1990, pp 273-282.
- 4 Derogatis LR, Morrow GR, Fetting J, Penman D, Piasefsky S, Schmale AM, Henrichs M, Carnicke CLM Jr: The prevalence of psychiatric disorders among cancer patients. *JAMA* 1983; 249:751-757.
- 5 Razavi D, Delvaux N, Farvacques C, Robaye E: Screening for adjustment disorders and major depressive disorders in cancer in-patients. *Br J Psychol* 1990;156:79-83.
- 6 Razavi D, Delvaux N, Brédart A, Paesmans M, Debusscher L, Bron D, Stryckmans P: Screening for psychiatric disorders in a lymphoma out-patient population. *Eur J Cancer* 1992; 28A:1869-1872.
- 7 Hopwood P, Howell A, Maguire P: Screening for psychiatric morbidity in patients with advanced breast cancer: Validation of two self-report questionnaires. *Br J Cancer* 1991;64: 353-356.
- 8 Ibbotson T, Maguire P, Selby P, Priestman T, Wallace L: Screening for anxiety and depression in cancer patients: The effects of disease and treatment. *Eur J Cancer* 1994;30A:37-40.
- 9 Cull A, Stewart M, Altman DG: Assessment of and intervention for psychosocial problems in routine oncology practice. *Br J Cancer* 1995; 72:229-235.
- 10 Morasso G, Costantini M, Baracco G, Borreani C, Capelli M: Assessing psychological distress in cancer patients: Validation of a self-administered questionnaire. *Oncology* 1996;53:295-302.
- 11 Chaturvedi SK, Chandra PS, Channabasavanna SM, Anantha N, Reddy BKM, Sharma S: Levels of anxiety and depression in patients receiving radiotherapy in India. *Psychooncology* 1996;5:343-346.
- 12 Aass N, Fosså SD, Dahl AA, Moe TJ: Prevalence of anxiety and depression in cancer patients seen at the Norwegian Radium Hospital. *Eur J Cancer* 1997;33:1597-1604.
- 13 Berard RMF, Boermeester F, Viljoen G: Depressive disorders in an out-patient oncology setting: Prevalence, assessment, and management. *Psychooncology* 1998;7:112-120.
- 14 Roth AJ, Kornblith AB, Bael-Copel L, Peabody E, Scher HI, Holland JC: Rapid screening for psychological distress in men with prostate carcinoma: A pilot study. *Cancer* 1998;82:1904-1908.
- 15 Harrison J, Maguire P: Predictors of psychiatric morbidity in cancer patients. *Br J Psychiatry* 1994;165:593-598.
- 16 Zigmond AS, Snaith RP: The Hospital Anxiety and Depressive Scale. *Acta Psychiatr Scand* 1983;67:361-370.
- 17 Aaronson NK, Ahmedzai S, Bergman B, et al: The European Organisation 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.
- 18 Mantel N: Chi-square test with one degree of freedom: Extensions of the Mantel-Haenszel procedure. *J Am Stat Assoc* 1963;58:690-700.
- 19 SPSS Base 7.5. Chicago, SPSS, 1997.
- 20 Karnofsky DA, Burchenal JH: The clinical evaluation of chemotherapeutic agents in cancer; in MacLeod CM (ed): *Evaluation of Chemotherapeutic Agents*. New York, Columbia University Press, 1949, pp 191-205.
- 21 Grassi L, Malacarne P, Maestri A, Ramelli E: Depression, psychosocial variables and occurrence of life events among patients with cancer. *J Affect Disord* 1997;44:21-30.
- 22 Passik SD, Dugan W, McDonald MV, Rosenfeld B, Theobald DE, Edgerton S: Oncologists' recognition of depression in their patients with cancer. *J Clin Oncol* 1998;16:1594-1600.
- 23 Maguire P: Psychosocial interventions to reduce affective disorders in cancer patients: Research priorities. *Psychooncology* 1995;4:113-119.
- 24 Fallowfield LJ: Giving sad and bad news. *Lancet* 1993;341:476-478.
- 25 Fallowfield L, Lipkin M, Hall A: Teaching senior oncologists communication skills: Results from phase I of a comprehensive longitudinal program in the United Kingdom. *J Clin Oncol* 1998;16:1961-1968.