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PSYCHOSOCIAL EFFECTS OF TREATMENTS FOR BREAST CANCER:
A TWO-YEAR FOLLOW-UP STUDY

Volume 1 (Main text)

ANDREW VINCENT MARK HUGHSON, MB CHB, DPM, MRCPSYCH

A thesis in two volumes submitted for the MD degree of the University of Glasgow, based on research conducted in Glasgow at the Victoria Infirmary, Gartnavel General Hospital and the University Departments of Psychological Medicine and Clinical Oncology

May 1989
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I owe an enormous debt to the patients who repeatedly allowed me to interview them, mostly at home, despite the arduous treatment many were receiving, and to my family for tolerating my frequent absences in connection with the project.
SUMMARY

In this thesis the psychosocial morbidity of treatment for breast cancer — in particular, adjuvant chemotherapy and radiotherapy after mastectomy — is examined. However, factors other than postoperative treatment which contribute to morbidity are considered, and the opportunity is taken to compare different ways of measuring psychosocial morbidity.

A relationship between psychosocial morbidity and breast cancer has long been recognised, but only recently has it been the subject of reliable, systematic investigation. Reliable studies conducted shortly before work for this thesis began showed that prior to breast biopsy and following mastectomy, a substantial minority of patients — perhaps as many as a quarter — experienced psychological morbidity of clinical degree. However, it was not clear how much of the pre-operative morbidity was specific to impending surgery for breast disease. Also, it had been suggested that post-operative radiotherapy increased psychological morbidity after mastectomy, but there were no quantitative data to confirm this belief. Hence the precise contribution of mastectomy and radiotherapy to post-operative morbidity was uncertain. There was little information in the literature on what factors other than treatment influenced liability to morbidity. The psychosocial effects of adjuvant chemotherapy after mastectomy had not been reported.
Using reliable observer and self rating scales, answers to the following main questions were sought.

(1) Does psychosocial morbidity prior to breast biopsy exceed that prior to routine surgery? What factors independently predict morbidity?

(2) What is the extent of psychosocial morbidity in patients allocated to adjuvant chemotherapy, and how does it compare with the morbidity in patients receiving post-operative radiotherapy?

(3) Does post-operative radiotherapy cause more psychosocial morbidity than no further treatment?

(4) What is the extent of morbidity in a sample of patients with "early" breast cancer receiving several types of treatment, and what factors independently predict morbidity?

(5) Compared with observer scales, how well do self rating scales perform in patients treated for breast cancer?

The results were respectively as follows.

(1) Psychosocial morbidity was compared in 91 patients awaiting breast biopsy and 30 patients awaiting elective cholecystectomy. The breast biopsy group was subdivided into patients proving to have cancer and those with benign disease. Contrary to expectation, the highest levels of morbidity occurred in patients with benign disease. Such patients may be a self-selected, anxiety-prone subset of all patients with benign disease. Patients
with cancer had levels of anxiety and depression similar to those in the cholecystectomy control group. However, subdivision of the cancer group by age showed there was a marked excess of anxiety in cancer patients aged 45 or less. Independent predictors of morbidity in the cancer group were age and a previous psychiatric history.

(2) Psychosocial morbidity was compared over two years in 74 patients with stage II breast cancer randomized to three forms of treatment after mastectomy: a three-week course of post-operative radiotherapy; a year of adjuvant chemotherapy (cyclophosphamide, methotrexate and 5-fluorouracil — CMF); and radiotherapy followed by CMF. At one and three months after surgery, there were no significant differences among the groups. At six months, in the groups allocated to chemotherapy, there was a significant excess of social morbidity, and several patients were subject to conditioned reflex nausea and vomiting. At one year, the patients allocated to chemotherapy (alone or after radiotherapy) showed significant excesses of depression, anxiety and social dysfunction compared with those treated with radiotherapy alone. Conditioned reflex symptoms increased markedly in the second six months of chemotherapy and persisted for up to a year thereafter.

Thus adjuvant chemotherapy had its main psychological impact during the second six months of treatment. Much of this morbidity could be prevented, without compromising survival, if courses of treatment were restricted to six months.

(3) Psychosocial morbidity was compared in 47 patients receiving post-operative radiotherapy and 39 receiving no further treatment
after mastectomy. One month after surgery, there were no significant differences in morbidity between the two groups; knowledge of impending radiotherapy did not seem to increase emotional distress. At three months, there were significant excesses of somatic symptoms and social dysfunction in patients who had completed radiotherapy. At six months, a significant excess of somatic symptoms persisted in the radiotherapy group. Up to half of these patients found that the treatment was very unpleasant. However, in the year after surgery there was never a significant excess of depression or anxiety in the radiotherapy group. Radiotherapy sometimes provoked anxiety, but some patients seemed reassured by the fact of receiving further treatment and having regular contact with the clinic staff. Patients on no further treatment did not have the opportunity to be reassured in this way.

(4) Psychosocial morbidity was measured over two years in 90 patients with stage I or II breast cancer. Depression and anxiety of clinical degree were found to be less frequent than in previous studies, affecting around 10% of patients rather than around 20%. However, patients aged under 50 showed higher morbidity compared with those aged 50 or above, and compared with matched control subjects with benign disease. The main independent predictors of morbidity at one year after surgery were age, neuroticism, emotional distress one month after surgery, and treatment with chemotherapy. Together, these predictors explained about a third of the variance in psychological morbidity; further work is needed to define more precisely those patients at risk.

(5) When compared with observer ratings, the principal self rating
scales used in this study, namely the general health questionnaire and the Leeds depression and anxiety scales, were found to be valid measures of psychosocial morbidity in patients receiving treatment for breast cancer. They would probably be valid for early cancers in other sites, and provide useful and economic measures of morbidity.
DECLARATION

I declare that I am the author of this thesis, and that it is, unless otherwise stated, my own work. It has not previously been submitted or accepted for a higher degree. I have consulted the references cited.

I began work for this thesis in 1977, when I was Senior Registrar in Psychiatry, Greater Glasgow Health Board. From 1979-1981, I was funded by the Cancer Research Campaign, and was Research Assistant and Honorary Senior Registrar in the Department of Psychological Medicine, University of Glasgow. During 1981-1982 I continued the project while Consultant Psychiatrist at Dykebar Hospital, Paisley.

I received valuable advice on the design of the project from Dr A F Cooper, Consultant Psychiatrist, Leverndale Hospital, Glasgow, and from Professor M R Bond and Mr Malcolm Adams of Glasgow University's Department of Psychological Medicine. However, the final responsibility for the design was my own.

I collected data for the project from 1977 to 1982, interviewing 195 patients, mostly in their own homes, and usually on several occasions over a period of up to two years. A further 42 patients included in the project were mostly interviewed by my colleague Dr A F Cooper. It was logistically impossible for me to assess all these additional patients at the same time as my own, but including them meant that the precision of the results could be improved. Dr Cooper interviewed occasional patients of mine when I was on leave, and I reciprocated for patients whom he had
originally seen. We assessed 16 patients jointly for a reliability study. I also interviewed a further 81 patients who, for various reasons, were not included in the project. In all I conducted 946 interviews, and Dr Cooper 126.

I coded much of the data obtained for computer analysis, but in 1982 I contracted encephalomyelitis and subsequently had clerical help in coding the remainder of the data and entering it on the Glasgow University ICL 2988 mainframe computer. Thereafter I personally analysed data at the computer terminal, using the Statistical Package for Social Sciences (SPSS-X). I also analysed much data by hand and using a statistical calculator and a statistical package on a microcomputer. The particular analyses undertaken were my own decision.

Much of the material in this thesis was originally published in the form of four abstracts, seven papers and a contribution to a book. I wrote the early drafts of all but one of the papers, but they were refined in the light of comments by Dr Cooper and two surgical colleagues, Mr Colin McArdle and Mr David Smith. Some of the papers were changed further after suggestions by journal referees. These comments and suggestions have influenced parts of the thesis.

G.V. Mark Hughes 24 May 1989
PREFACE

A relationship between psychosocial morbidity and breast cancer has long been recognised, but only recently has it been the subject of reliable, systematic investigation. Reliable studies conducted shortly before work for this thesis began showed that prior to breast biopsy and following mastectomy, a substantial minority of patients — perhaps as many as a quarter — experienced psychological morbidity of clinical degree. However, it was not clear how much of the pre-operative morbidity was specific to impending surgery for breast disease. Also, it had been suggested that post-operative radiotherapy increased psychological morbidity after mastectomy, but there were no quantitative data to confirm this belief. Hence the precise contribution of mastectomy and radiotherapy to post-operative morbidity was uncertain. There was little information in the literature on what factors other than treatment influenced liability to morbidity. The psychosocial effects of adjuvant chemotherapy after mastectomy had not been reported.

Using reliable observer and self rating scales, an attempt is made in this thesis to answer the following main questions.

(1) Does psychosocial morbidity prior to breast biopsy exceed that prior to routine surgery? What factors independently predict morbidity?

(2) What is the extent of psychosocial morbidity in patients allocated to adjuvant chemotherapy, and how does it compare with the morbidity in patients receiving post-operative radiotherapy?
(3) Does post-operative radiotherapy cause more psychosocial morbidity than no further treatment?

(4) What is the extent of morbidity in a sample of patients with "early" breast cancer receiving several types of treatment, and what factors independently predict morbidity?

(5) Compared with observer scales, how well do self rating scales perform in patients treated for breast cancer?

Insofar as the available data permit, the opportunity is also taken to examine the effects of recurrent disease, the mechanisms whereby psychosocial morbidity might be produced, and how it might be prevented.
CHAPTER 1:

HISTORICAL INTRODUCTION AND REVIEW OF THE LITERATURE

Historical introduction
Breast cancer was recognised in the time of Hippocrates, who was born around 460 BC. Treatment by mastectomy seems to have evolved because surgeons of the day recognised that an untreated breast cancer could ulcerate and fungate, causing much pain and distress. On the other hand surgeons were often reluctant to operate, since the patient could die of surgery, itself very painful.1

Thus Henri de Mondeville, surgeon during the years 1285-1314 to two kings of France (Phillipe le Bel and Louis le Hutin) distinguished between "palliative" treatment (for example diet and purgation) and "curative" treatment. The latter comprised surgery, cautery or the use of "médicines corrosives" to destroy the tumour. He recommended that in deciding the treatment, the surgeon should consider the patient's capacity to tolerate pain and heat: a primitive recognition of the relevance of psychological factors to treatment choice.2

The early forms of mastectomy were crude. In one sixteenth century operation two enormous needles to which cords were attached were pushed through between the breast and the underlying muscle. Once the two cords were in place under the breast, their four ends were tied together in front of it and pulled. The breast was thus drawn away from the chest wall to be cut off with a large knife. Cautery was then applied, though some bleeding might be allowed in the
belief that bad humours — in particular black bile — would be released.³

This belief in an association between cancer and the body humours had started in Greek times. For example, Paul of Aegineta wrote: "For cancers are formed by black bile overheated; and if particularly acrid, it is attended with ulceration."⁴ Black bile (melancholy) was also linked with mood, and according to Leshan, Galen believed that cancer was commoner in melancholic women than in sanguine women.⁵ *

Later medical writers — for example Walshe, Paget, Gendron and Snow — also believed in a link between temperament and proneness to cancer.⁶ However, other eminent clinicians did not seem to share this opinion. The Scottish surgeon John Hunter, in a careful review of possible causes of cancer, made no mention of emotional factors⁶ nor do they feature as causes in the writings of Sir Benjamin Brodie — an authority on breast cancer who described sero-cystic disease.⁷

The nineteenth century French surgeon Velpeau dismissed emotional factors as causes of breast cancer: "In short, my observations authorise me to say, that no organic constitution, no state of health, general or habitual, affords protection from cancer; there is no ground for seeking here the predisposing cause of the

*However, scrutiny of the Latin translation of the complete works of Galen (Galeni C, Opera Omnia. Kühn DCG ed. Vols 1-20. Leipzig: Cnobloch, 1821-1833) suggests that Galen did not state this belief directly. Rather, he believed in an association between black bile and cancer, especially of the breast (volume 11, page 139); and also in an association between black bile and melancholic mood (see, for example, volume 8, pages 177–8).
disease. I may say as much of the moral condition; sadness, grief, uneasiness of mind absolutely play no part in the production of cancer; and if one does take any notice of it, it is rather to humour the patient, than to satisfy a scientific requirement."

The emotional consequencies of mastectomy in the postoperative period are little evident in the writings of these authors, perhaps because clinical practice was so different from now. Before anaesthesia, antisepsis and modern histology became available, mastectomy tended to be performed late in the course of the breast cancer, if at all. Some surgeons were apparently reluctant to operate in patients of a melancholic disposition.9 Brodie warned against surgery in "those women... with a hysterical nervous system, a small pulse, and cold hands and feet..."10 Much distress arose from unoperated local disease invading adjacent structures, ulcerating and becoming infected. In patients undergoing surgery, terror of the operation with its inevitable pain and high risk of death, may well have overshadowed the effects of loss of the breast. In many cases the breast would have been destroyed or grossly disfigured prior to mastectomy. In those who survived surgery, removal of a fungating growth might have improved, relatively speaking, the quality of life.

A moving account of mastectomy without anaesthesia is given by the English novelist Fanny Burney (1752-1840) in a letter written in 1811 to her sister Esther.11

There was much deliberation among her medical advisers as to whether an operation should be performed. "M Dubois [an eminent Paris surgeon, Fanny Burney having married a Frenchman] gave me a prescription to be pursued for a month... but uttered so many charges to me to be tranquil, & to suffer no uneasiness, that I could not but suspect there was room for terrible inquietude."
Finally a decision was reached that she be operated on by M Larrey (shortly to become Napoleon's surgeon-in-chief). Told she would get only two hours notice of surgery, she nonetheless had to wait: "After sentence thus passed, I was in hourly expectation of a summons to execution; judge, then, my surprise to be suffered to go on full 3 Weeks in the same state!"

On the day of the operation she was given a wine cordial, in the hope of making her somnolent, while a team of seven men, dressed in black, assembled. "M Dubois placed me on the Mattress, & spread a cambric handkerchief over my face. It was transparent, however, & I saw through it, that the bed was instantly surrounded by the 7 men & my nurse. I refused to be held; but when, Bright through the cambric, I saw the glitter of polished steel... I closed my eyes... relinquishing all watching, all resistance... this resolution once taken, was firmly adhered to, in defiance of a terror that passes all description, & the most torturing pain. Yet — when the dreadful steel was plunged into the breast — cutting through veins — arteries — flesh — nerves — I needed no injunction not to restrain my cries. I began a scream that lasted uninterruptedly during the whole time of the incision — & I almost marvel that it rings not in my Ears still so excruciating was the agony. When the wound was made, & the instrument was withdrawn, the pain seemed undiminished, for the air that suddenly rushed into those delicate parts felt like a mass of minute but sharp & forked poinards, that were tearing the edges of the wound — but when again I felt the instrument — describing a curve — cutting against the grain, if I may so say, while the flesh resisted in a manner so forcible as to oppose & tire the operator... then, indeed, I thought I must have expired.

"...I concluded the operation was over — Oh no! presently the terrible cutting was renewed — & worse than ever, to separate the bottom, the foundation of this dreadful gland from the parts to which it adhered... I then felt the knife rackling against the breast bone — scraping it... M Dubois pointed to some further requisition — & again began the scraping!"

"...My dearest Esther, not for Weeks, but for Months I could not speak of this terrible business without nearly again going through it! I could not think of it with impunity! I was sick, I was disordered by a single question — even now, 9 months after it is over, I have a head ache from going on with the account! I dare not revise, nor read, the recollection is still so painful"

"When all was done... my strength was so diminished that I was obliged to be carried... & then I saw my good Dr Larry [sic], pale as myself, his face streaked with blood, & its expression depicting grief, apprehension, & almost horror."

The operation notes stated that all the roots of the cancer had been removed and there was high hope of success. Fortunate to escape post-operative infection, Fanny Burney lived almost forty years longer (but possibly the tumour was not really malignant).

Because mastectomy struck terror, there had long been interest in non-surgical methods, which could be thought of as "topical
chemotherapy". Thus Velpeau stated: "A cutting operation has always occasioned so much alarm, that practitioners have never abandoned the idea of curing tumours without it... Two circumstances militate in favour of caustics in the eyes of the public. First, patients are less terrified of them; second, their action is less painful than that of a cutting instrument. Upon this subject, however, the unfortunate patients are deceived. No species of caustic can destroy a tumour of the breast, without occasioning acute and long continued pain... The agony... is in some cases so violent, I have known patients find it more painful than a cutting operation to which they may previously have submitted with much dread... It cannot be denied, however, that caustics do possess some advantages. As they do not give the idea of an operation, they are less terrifying to the patients, and their application will be permitted much more cheerfully, and with infinitely less effort than the knife... No definite judgment can be given as to the real value of caustics in practice."12

Examples of caustics included butter of antimony, Vienna paste (mixture of lime and potash), caustic potash, nitric and sulphuric acids, zinc and gold chlorides, and arsenic paste.

The advent of anaesthesia, allowing developments in surgery, stopped the use of caustics. The radical mastectomy, removing the axillary lymph nodes and pectoralis major muscle, was proposed by Bernard Peyrihle in 1774 and a century later adopted by Halsted.13 The idea was to rid the patient of every possible trace of cancer, preventing further spread. Radical mastectomy remained the standard operation for more than 50 years after the turn of the century, despite pioneering work in the 1930s by Geoffrey Keynes,
who showed that treatment of the cancer with interstitial radium needles and conservation of the breast whenever possible did not compromise survival. Keynes was well aware of the adverse psychological effects of radical mastectomy, referring to it as a hideous mutilation. Why Keynes's methods were not more widely adopted at the time is unclear. However, simple mastectomy followed by radiotherapy became common after McWhirter showed it was as effective as radical mastectomy.

It is now accepted that radical treatment of local disease does not prevent metastatic spread. In many cases of "early" breast cancer, especially if the axillary nodes are involved, micrometastases already exist at the time of diagnosis. From the point of view of survival, extensive local treatment is thus a case of locking the stable door after the horse has bolted. This has led to the use of systemic treatments: hormonal manipulation or adjuvant chemotherapy. Agents such as cyclophosphamide, methotrexate, 5-fluorouracil, vincristine and doxorubicin were found to induce remission in some cases of advanced breast cancer. Combinations of drugs were more effective than single agents. Such combinations, labelled "adjuvant chemotherapy", have been used in "early" breast cancer in the hope of destroying any micrometastases before they can develop into overt systemic disease. The most widely recognised régime of adjuvant chemotherapy has been "CMF": cyclophosphamide, methotrexate and 5-fluorouracil. The nature of the local treatment being unimportant for survival, there has been greater emphasis on less mutilating surgery; radical mastectomy is seldom performed nowadays, and "lumpectomy" is commoner.
REVIEW OF THE LITERATURE

In this review, the literature will be examined prior to May 1977, when work for the thesis began. However, occasional references will be made to publications after that date, for example research presented as a preliminary communication in 1977 but not published in full until later.

Studies of the psychosocial consequences of breast cancer will be divided into two broad categories: the mainly qualitative, and the mainly quantitative. Qualitative studies will refer usually to unstandardized, uncontrolled observations, on samples of patients which are often ill-defined. Quantitative studies are those using standardized measures on well-defined samples, usually with a control group. There is naturally some overlap between the categories. Some studies classed as mainly qualitative contain much numerical data, but are regarded as qualitative because it is difficult to draw general conclusions from them. However, the two categories enable a rough chronological sequence to be maintained. Most of the "mainly qualitative" studies were published before the early 1970's and most of the "mainly quantitative" were published thereafter.

Much of the literature on psychosocial aspects of breast cancer is conceptually heterogeneous. However, after the various studies have been described and criticized, their results will be drawn together and summarized under several headings.

Early uncontrolled qualitative studies

The first attempt to study systematically the psychological
The consequences of breast cancer appears to be that of Renneker and Cutler in 1952. The former a psychoanalyst and the latter a surgeon, they sought to "correlate the status of current surgical treatment with applicable psychoanalytic knowledge of behaviour." Fifty patients operated on by the second author were interviewed. It is not clear how they were selected, no demographic data were given, and there was no control group. The authors focused on the "dual psychological conflict facing a woman with breast cancer": (1) adjustment to breast mutilation; (2) adjustment to invasion by a potentially fatal disease. The authors noted frequent post-mastectomy depression, characterised by anxiety, insomnia, depressive attitudes, occasional ideas of suicide and feelings of shame and worthlessness. "One can say that these women mourn the loss of their breast. They are concerned with what their husbands, or men in general, will think of them in their new mutilated state. Feminine pride has been severely damaged. They are faced with the problem of changing the mind's picture of their body image to one with a unilateral breast, or none at all."

Renneker and Cutler emphasised the psychological, sexual, and maternal significance of breasts. They wrote: "...when we examine the situation critically we see that the breasts are the only positive evidence of femaleness." After this extraordinary statement they exhorted surgeons to "understand that the primary emotional reaction connected with disease of the breast is usually not a fear of cancer or death, but is rather the shocking feeling that the basic feminine role is in danger."

The women in this study were classed as "mature" or "neurotic." A "mature" woman "accepted her breasts, good or bad, with a
A "neurotic" woman was "masculine, frigid or superficially sexual in an exaggerated fashion." Her sexuality was "fused with guilt." She might "overvalue" her breasts. If so, she might show extreme depression after mastectomy. Apart from "neurotic" women, those most liable to show marked reactions were young women of childbearing age. Older married women with children would show milder reactions.

Some of these opinions were questionable, inferential judgments rather than observations. On the other hand, Bard and Sutherland (1955) were less influenced by the preconceptions of psychoanalysis. They studied patients derived from two sources: those undergoing radical mastectomy (n=20, age range 20-58 years); and mastectomy patients who had been referred to a psychiatric consultation service (number and age range not stated). Exactly how these patients were chosen for inclusion in the study is unclear. There was no control group. Notwithstanding, this work was important. The authors provided a sensible and believable account of the psychological consequences of breast surgery, based on detailed and perceptive interviews.

Bard and Sutherland found that discovery of a breast lump frequently provoked fear and anxiety. Excessive fear might cause denial of the possibility of serious illness, leading to delay in treatment. When told that surgery was necessary, all women were shocked, terrified, numb, panicky or stunned. Some were afraid they would die during the operation. However, the "primary source of anxiety" probably lay in "an enormous fear of cancer and all its implications." This anxiety might be due to the consequences for the patients' families, such as children being left without a
mother. On the other hand many patients expressed fears of
deformity or disfigurement, some saying they would prefer death to
mastectomy. This was because mastectomy would affect not just
sexual relationships, but self-esteem and the ability to dress
naturally.

Following operation, many patients experienced transient relief at
being alive, followed by anxiety, anger, resentment or dependence.
On discharge home they feared their families and friends would be
horrified at having to deal with a mutilated person. Any problem
with the wound, for example infection, was seen as ominous. Trauma
to the wound or to the opposite breast, from knocks received in a
crowd or from sexual intercourse, engendered fears of serious
consequences such as further and more extensive surgery. Minor
depressions were common, often manifest as irritability,
nervousness, lack of patience and being difficult to live with.
Post-operative care of the wound served to remind the patients of
their deformity, and thereafter dressing and undressing
constituted a "dreaded emotional crisis" for most women. Some said
they were "half man, half woman." Many lost sexual desire, feeling
unattractive to their husbands, and some slept in a darkened room.
Outside home, many tried to conceal having undergone the
operation. A few were devastated and became chronically depressed.

Bard and Sutherland carefully emphasised the need to understand
the patient in the context of her own personal circumstances. For
example, to the casual observer two patients might appear equally
hostile or resentful. One such patient was angry because she was a
self-sufficient person who disliked having to depend on others
during her stay in hospital. Another was angry because she
believed her aspiration biopsy had caused a benign lesion to turn malignant.

This study contained the patients' verbatim statements, which illustrated anxieties and concerns more vividly than formal rating scales. A patient who feared that normal daily activity after her operation might be harmful commented, "You treat yourself like a soft-boiled egg. You might break your shell at any moment." Another who feared her children would notice her deformity said, "If I told them about it, they might take a morbid interest. You know kids are sadists that way. The way they stare at cripples, for instance. They don't mean to be that way, curiosity makes them be that way, but they are very sadistic."

The authors noted that mastectomy might pose a real threat to marriages, especially if already unhappy. Husbands might show anxiety, guilt or rage. They might be appalled by the wound and prolong invalidism by being over-protective.

Bard and Sutherland disagreed with Renneker and Cutler's opinion that the patient's main problem was protecting her breast, rather than protecting her life. They criticized Renneker and Cutler for dividing women into the "mature" and "neurotic." This was because "mature" women seemed to be those who coped with mastectomy and "neurotic" women those who did not: a circular argument. Bard and Sutherland regarded this classification of women's personalities as moralistic and lacking in meaning. Perhaps surprisingly they were unable to confirm the finding of Renneker and Cutler that exaggerated emotional reactions occurred in younger women still able to bear children and milder reactions in married
postmenopausal women who had borne children.

Despite its limitations of method, the work of Bard and Sutherland was notably open-minded and free of unhelpful jargon. Many of its findings have since been confirmed.

In a related paper, Bard attempted to predict those patients who would show psychogenic invalidism following radical mastectomy. (This was really a quantitative paper, but belongs here historically.) Bard studied 20 patients with no previous history of surgery or of psychiatric consultation, who were free of menopausal symptoms. The precise source of the sample was not stated, but presumably it coincided partly with that of the previous paper. Shortly before surgery, Bard sought to measure the personality factor of dependence, which he thought might predict invalidism. Dependence was defined as "a basic personality component expressed in the solicitation of support and protection from those regarded as powerful and nurturant. Its presence is further defined as the extent to which a patient has been unable to free herself from maternal control." He used three techniques to assess dependence: a focused interview covering personal, inter-personal and sexual history, the Rorschach Ink Blot Test, and a modification of the Thematic Apperception Test. Independent psychologists then evaluated the projective tests for evidence of dependence, and a psychiatrist evaluated the interview data. Summaries of the three components for each patient were prepared and then ranked by two judges on a dependence scale ranging from 1 to 20. Similarly, six to 10 weeks after surgery, a further focused interview took place and an independent psychotherapist scrutinized it for evidence of invalidism, basing his opinion on
"the quality of depression, weakness, social participation and motor activity." Two judges then ranked the psychotherapist's summary to provide a 1 to 20 invalidism score.

This elaborate procedure resulted in surprisingly high inter-rater reliability, though there was some doubt as to whether the projective tests actually measured dependence. These tests failed to predict invalidism at the five per cent level of significance. However, dependence as assessed from the focused interview was significantly associated with invalidism (r=0.5). This was a good study for its day, with careful attention to reliability. However, since Bard seems to have conducted both the pre- and postoperative interviews, bias could still have occurred despite the independent assessors.

Bard and Waxenberg also sought to predict invalidism in these patients from the Cornell Medical Index (CMI), which, like the other procedures, was administered before surgery and between six and 10 weeks thereafter. The CMI has three components: physical symptoms, general medical symptoms, and mood and feeling. Pre-operative scores on the first two of these correlated significantly with postoperative invalidism; scores on mood and feeling failed to do so. Despite the significant correlations, prediction of invalidism in individual patients was, disappointingly, no better than chance. However, there was a high correlation (r=0.88) between the pre- and postoperative mood and feeling scores.

In 1963, Quint published a paper based on interviews with 21 women admitted over a six week period to a university hospital for
With the exception of one refusal, these women appear to have been consecutive cases of stage I and II breast cancer. They told the author their views on "the three basic changes which this operation initiates. First, it precipitates a period of shock and unexpected events. Second, it leaves a change in body appearance. Third, it mars the future by the prospect of shortened life and the possibility of slow, painful death." The article contained some moving verbatim accounts of the women's experiences. The author noted that patients in hospital were shocked and that the real impact of mastectomy did not occur until they had gone home. Then agitation, upset, exhaustion and "blue spells" set in. The period of upset tended to be longer if there were wound problems. Personal appearance was a major preoccupation for some, especially those who had had big breasts, and there were difficulties with prostheses. However, the uncertain future was a greater concern.

Like that of Bard and Sutherland, Quint's study was notable for sensitive and perceptive interviewing. Given the unselected sample, it is perhaps unfortunate that no measure of the frequency of problems was given, other than the author's overall impressions.

In the same year, Adsett published a paper entitled "Emotional reactions to disfigurement from cancer therapy." This paper did not present data; it reflected the author's reading and clinical practice. He believed that in the breast-conscious American society, some women who had undergone mastectomy would project onto their husbands their own loss of self-esteem, even if the husbands were supportive. This would lead to unrealistic fears of
having disrupted the marital relationship. Adsett suggested that a nurse could help a woman to adapt to the loss of her breast by "continuous contact with the patient as well as providing a woman figure with which the patient can identify and use as an object for her reality testing." However, he quoted no evidence in support of this rather convoluted statement. Overall, this paper did not advance knowledge, but it anticipated the use of nurse counsellors.

Slightly more informative was a chapter by Eisenberg and Goldenberg (1966), who described an evaluation of "quality of survival" in breast cancer. "It was the intent of this study to evaluate the ability and capacity of the patient to resume her pre-operative responsibilities whether it meant returning to outside work or to her household chores." The study concerned physical performance more than mood. The patients were identified from the Connecticut Cancer Registry. Of 606 patients, 234 were not available for interview. Of those 234, 125 were excluded arbitrarily because they were older than 70 years, 104 were notified too late to enter the study, and a handful had died or moved house. Of the 372 remaining, 120 were excluded because they or their physicians refused. Finally, 252 were interviewed, of whom 91% had radical mastectomies, and the remainder "limited surgery." Ninety-five patients underwent postoperative radiotherapy. The patients were interviewed twice within a period of 18 months, but the timing of the first interview in relation to surgery was not clear.

Results were reported in terms of lymphoedema, arm movement, activity and attitude status. Arm swelling occurred in 173 women
(69%), and was severe in 16 (6%). Just over half of all patients had limitations of arm movement which tended to improve with time. Half the patients had resumed their usual activities by the time of the first interview, and 92% by the second interview. The "attitude status" was "good" if the patient had no complaints, "fair" if she had some complaints, and "poor" if she "expressed to a great extent her unhappiness about the whole episode." On this basis, 54% of patients were said at initial interview to have had good attitudes, 42% fair and 4% poor. At follow-up, however, only 43% had good attitudes, 57% fair and 1% poor.

These definitions of attitude might be thought to provide more information about the attitudes of the investigators than about those of the patients. Clearly the patients' distress could not have been judged properly on the basis of voiced complaints. So Eisenberg and Goldenberg's study contributed little to the understanding of the psychological state of mastectomy patients.

Postal questionnaire studies

In the early 1970s, several postal questionnaire studies were published. Although easy to administer, they had definite drawbacks. These included poor response rates, limitations on what could be asked because of lack of personal interaction, and ignorance of the reliability of information obtained. Even so, some researchers managed to compound these errors with further avoidable ones, principally a failure to define the origin and nature of the samples studied and the time since surgery.

The study of Torrie (1970) demonstrates these problems. Torrie
posted a questionnaire to an unstated number of women who had undergone mastectomy throughout the United Kingdom. He received replies from 1400 drawn from 368 hospitals, but failed to report how the original sample was selected, what the response rate was, which patients dropped out, nor the time elapsing since mastectomy. Notwithstanding, the survey showed that some women with breast cancer faced serious problems. Nearly half of the women wrote that the operation had not been clearly explained. Too often, information appeared to have been given in an offhand, insensitive way. After the operation, many women had been upset by the scar, and the provision of prostheses had sometimes been very unsatisfactory. Although relationships with husbands had often become closer, several husbands had reacted badly to the mutilation and had sought out other women. There had not been enough information on how to make love following a mastectomy. Depression had occurred in 83.5% of the women. Half of these had become depressed within a week and mood disturbance had lasted from one month to a year.

Sixty-two per cent of Torrie's sample had received radiotherapy, and nearly half reported they had been adversely affected. "Radiotherapy seemed the worst part of the treatment for most of the women; they did not understand it, were unprepared, and received no explanation of the procedure..."

In such a poorly defined survey, the figures had little meaning, but there could be no doubt that serious problems could occur after mastectomy and radiotherapy, and that well-designed systematic studies were needed. However, in the same year another disappointing postal study was published.
Schottenfield and Robbins (1970) used a questionnaire to survey retrospectively the quality of survival among patients who had undergone radical mastectomy. Quality of survival was defined in terms of the patients' ability to work, perform normal activities and care for themselves. There were no direct assessments of mood. The data were obtained by sampling a population of 5472 Caucasian women operated on between 1949 and 1962. A patient sample of 826 was obtained, partly by random sampling and partly from lists of attenders at follow-up clinics. Of these 653 (79%) responded to the authors' postal questionnaire. The time since operation was very variable — up to 15 years. Forty-four per cent of the women were found to be employed full-time or part-time, 54% not employed but performing normal daily activities and two per cent unable to function without help. Seven per cent of the sample had returned to their normal activities within seven to 12 months of mastectomy, and a further seven per cent after one year. Five years after operation 16% of survivors were unable to work or perform normal daily activities, at 10 years 9% and at 15 years 12%. At five years performance status was significantly lower in those who had presented with regional disease than in those who had presented with local disease, but at 10 and 15 years differences between these two groups were no longer statistically significant.

The authors believed that the survey would "personalise, in a most gratifying way, the follow-up of cancer patients." They thought that if physical deformity, functional disability and psychological stress were to be prevented in the cancer patient, a comprehensive rehabilitation program must be provided. They did
not however state how psychological stress might be defined, how its extent might be demonstrated, nor how a rehabilitation programme might be shown to prevent it. Their results have limited application: selection bias may have occurred despite a large sample; in the absence of a control group it is difficult to interpret the information presented; the methods of assessment were superficial. At best, their results showed that radical mastectomy could not be universally devastating in its effects.

In 1977 Winick and Robbins reported what they optimistically described as an evaluation of the Memorial Hospitals' PMRG (Post Mastectomy Rehabilitation Group) program. The program, based at the Sloan-Kettering Cancer Center in New York City, was presumably developed as a result of the work of Schottenfield and Robbins (1970) described in the preceding paragraphs. It comprised four or five days of exercises intended to prevent physical complications, and discussions on emotional and psychological anxieties with a social worker and a volunteer.

Eight hundred and sixty three out of about 1700 patients who had undergone mastectomy at the Memorial Hospital between 1970 and 1974, and who had attended the PMRG program, were studied. Of the 1700 about 1400 filled in a questionnaire posted by the authors. Of the 1400, only 963 completed more than a few questions. The authors decided to omit the 437 who did not finish the questionnaire. What happened to some 800 patients who did not respond to or complete the questionnaire was not recorded. Furthermore, there was no information on those patients who did not attend the PMRG program; the proportion of actual attenders was therefore unknown.
Hence the data obtained were almost certainly biased and of doubtful general validity. The authors' findings that younger patients appeared to resume normal activities sooner than older patients, and that extensive surgery resulted in delayed return to work are plausible enough. However, their data on emotional stress are almost impossible to interpret. On the basis of the patients' responses to open ended questions, the authors divided emotional distress into two categories: none or minimal, and moderate or severe. Only 406 (47%) of their sample of 863 patients gave information on emotional distress, and of the 406, 13% experienced moderate or severe symptoms as judged by the authors. Perhaps surprisingly, distress appeared to be less severe in younger patients. The authors commented: "...the fact that only 52 patients (13%) indicated experiencing moderate or severe stress is sufficient to judge the PMRG program 'clinically significant' and a major accomplishment in mastectomy rehabilitation." This conclusion was totally unjustified. It was all the more surprising since the authors in the next sentence stated that a comparison group who did not have rehabilitation after mastectomy would have been desirable.

The conclusion from this study has to be similar to that of the Schottenfield and Robbins paper: merely that after mastectomy not all patients become very upset emotionally. The data on prevalence and on the effect of age on emotional adjustment were potentially too biased to be trustworthy.

In contrast, Craig, Comstock and Geiser (1974) took the precaution of using control subjects in their questionnaire study of quality
of survival in breast cancer. They focused on adjustment to mastectomy in the long term. Most of their cases had been diagnosed more than five years previously, and none less than nine months previously. The cases (n=134) were identified from a county cancer registry likely to detect over 90% of those treated in the local county hospital, which covered a well-defined catchment area. The control subjects were obtained from census data. There were, in fact, two control groups, both matched by age and sex with the breast cancer patients. The second control group was also matched by neighbourhood with the cancer patients. This was because the authors feared a bias due to an effect of geographical location on hospital use and indices of disability. In the event the fears were unfounded and the two control groups were merged (total n=260). The women in the study received a postal questionnaire which asked them to rate themselves on physical health, employment, happiness and depression. The completion rate for questionnaires, helped by follow up interviews in those not immediately responding, was high: about 90% for patients and 80% for control subjects.

On the whole, psychological morbidity seemed low, with little or no difference between the cases and the control subjects. Only six per cent of cases and 3% of controls chose the term "unhappy" to describe their "attitude". Notwithstanding, 21% of cases and 20% of controls reported symptoms of depression. Only five women in the entire study reported a "pessimistic attitude to life"; notably, three of the five had recurrent breast cancer and died shortly after the survey. The main finding was a slight excess of physical disability and a tripling of mortality in patients with breast cancer. This was one of the better-conducted questionnaire
surveys, and strongly suggested that breast cancer was not usually associated with major psychological upset in the long term. However, the meaning of the questions asked was too imprecise; their range was insufficient to detect subtle psychological effects of mastectomy.

In fact, an uncontrolled study from Australia (Buls et al, 1976) showed that certain problems did persist in the long term. A single observer interviewed 100 women presenting consecutively to a follow-up surgical clinic. The time since mastectomy was very variable: up to 11 years. Radical mastectomy was the commonest operation and 84% of the patients had received postoperative radiotherapy. Mastectomy had a serious and lasting effect. One third of patients experienced anxiety and embarrassment due to the absent breast and this proportion did not diminish with time. Arm oedema, which affected about half the patients, may have contributed to the cosmetic anxieties, and absent or poor advice on prostheses undoubtedly did so. Surprisingly, only three patients reported sexual difficulties, and the authors mentioned no adverse psychological effects of radiotherapy.

However, in the United States Peck (1972) had meantime reported his uncontrolled observations on a series of 50 patients undergoing radiation therapy. The sample was selected at random from patients with health insurance who were suffering from a variety of neoplasms in the chest, throat, pelvis or reticuloendothelial system. The most frequent diagnosis was carcinoma of the breast (n=18). Not all patients had been informed they had cancer, but most inferred the diagnosis from being given radiotherapy. All 18 patients who had undergone mastectomy thought
that the operation was definite evidence of cancer.

The principal emotional reactions to having cancer were depression and anxiety. In 41 patients (81%) anxiety was moderate to severe. Guilt and anger were also common. Four patients had suicidal ideas related to cancer. Peck noted that patients occasionally denied their illness, but more often they acknowledged it but denied that it was life-threatening. Other mental mechanisms noted were displacement (worrying about other people rather than about themselves) and identification with the physician (being involved in the fight against the disease).

The specific role of radiotherapy in inducing depression or anxiety was not discussed in this paper, but Peck and Boland (1977) devoted a subsequent paper to the emotional reactions to radiation treatment of a further series of 50 patients. The composition of the sample was similar to that of the previous series, although only 11 patients suffered from breast cancer. Forty-two patients had potentially curable cancer, but in the remaining eight treatment was only palliative. In fact, a third of the sample died within three years of the study. The patients were interviewed before and after radiotherapy. There was no control group, but the interviews were detailed.

Initially the patients were found to have little idea as to the nature and duration of their treatment. Most thought that receiving radiotherapy was "bad news", and feared it might be physically damaging or might induce cancer. Fears of burns, pain and scarring were common. At this pre-treatment interview, over half of the sample were judged by the authors to be depressed or
anxious. As in the previous paper, depression and anxiety were not clearly defined.

Some of the patients were treated with cobalt, whilst others were treated by the Betatron, a large noisy machine. One week after treatment, those patients who had had to lie under the Betatron reported that the experience was frightening. Some had been distressed by seeing dying patients. The majority of patients were now judged to be depressed or anxious, but not severely so. A few patients were angry because the treatment had made them feel worse.

This study, though uncontrolled, provided definite evidence that radiotherapy could induce emotional distress; but it was unclear to what extent distress occurred in the patients with breast cancer.

Meantime, in the United Kingdom, Lyon had commenced prospective research on psychological problems in 100 women with breast cancer of whom all received radiotherapy. Unfortunately he failed to publish the full results of what appears to have been a well-designed study. A patchy review of his findings can be found in a chapter on the management of psychological problems in breast cancer.35 There was no information on the precise source of the sample. Thirty-eight per cent of the patients had not undergone mastectomy; presumably some patients must have had advanced disease.

Measures of morbidity included the Eysenck personality inventory, the Beck depression inventory and a visual analogue scale. The
patients had high scores on the Eysenck personality inventory "lie" scale. This suggested some were "faking good." Nonetheless, 11% of the patients were judged by the Beck inventory to have been moderately or severely depressed. During the course of radiotherapy, the visual analogue scale showed that mood was initially low, possibly because of uncertainty as to what was to come. Mood then lifted slightly, but thereafter declined steadily until the end of the course of treatment, especially in patients who had undergone mastectomy. Thirteen per cent of the total sample expressed thoughts of suicide during radiotherapy, mostly at the beginning of the course. So this study suggested a strong association between depression and treatment of breast cancer with radiotherapy; fortunately there were no actual suicide attempts.

However, it was the unexpected suicides of three of his patients that prompted Ervin, a surgeon, to interview in depth 12 patients, chosen mostly at random, on whom he had operated over the preceding 10 years. These suicides were not related to radiotherapy, and Ervin concluded that mastectomy was a devastating experience in which emotional suffering far outweighed physical suffering. "Initially the woman sees herself mutilated and repulsive, desexed, and suffering from a disease which can only end in a lingering and lonely death." He recommended a policy of scrupulous honesty tempered with hope, with acknowledgement of emotional problems. This paper showed intuitive wisdom even though there was virtually no quantitative data or formal evaluation.

In 1978 Jamison and her colleagues published two reports on psychosocial aspects of mastectomy, one describing the woman's perspective and the other the man's perspective. In the former
paper, a sample of 41 women was obtained from two sources: a self-help recovery group (Women for Women) and the American Cancer Society. The authors acknowledged that the sample was biased. The degree of bias cannot be determined since the authors did not state how the patients were selected from the two sources. However, since the mean age of the sample was 52.7 years and 80% of the patients were married, it may not have been seriously biased with respect to age and marital status. The women were seen at a mean of 22 months (median=10 months) after mastectomy, and completed several questionnaires. Sixty per cent judged that their post-mastectomy emotional adjustment was excellent or very good, 23% that it was good, seven per cent that it was adequate and 10% that it was poor. A quarter had experienced suicidal ideation after mastectomy, and a third had increased their use of tranquillizers. Several had consumed more alcohol. Those with suicidal ideation had high Eysenck Personality Inventory neuroticism scores. Over half the women reported phantom breast sensations, usually painful but occasionally erotic. A fifth to a quarter had experienced sexual problems such as decreased desire for intercourse, lack of orgasm or a general deterioration in sexual relationships. On the other hand, occasional improvements in sexual relations occurred. Younger women had significantly poorer adjustment to mastectomy.

To determine the effect of mastectomy on men, Wellisch et al. sent questionnaires to the husbands or partners of another sample of women contacted through Women for Women and the American Cancer Society. The response rate was only 15%. Around the time of the women's operations, a third of these men had lost their appetite, and about two fifths reported sleep disturbance or impaired work
performance. Over a third thought that the sexual relationship with their partners had been spoiled by the operation. Twenty percent of the men had not seen their partners naked after mastectomy.

In these two papers, biased sampling and poor response rates made the detailed figures unconvincing. However, the finding that younger age predicted morbidity was interesting, given so few previous attempts to define predictors. One such attempt was reported by Cobliner, a psychotherapist. In an impressionistic study, he interviewed personally some 300 patients with early breast or gynaecological malignancies. There was almost no information on the source or precise nature of the sample — not even the numbers with each type of cancer. Nor were there any details of how morbidity was assessed. Notwithstanding, he felt able to identify several factors which seemed to influence successful adjustment to these cancers. They included a high self-image, a positive image of femininity which suffered little or no change as a result of the disease and its treatment, a high level of faith in the clinic, the doctors and the treatment, the ability to tell worries to a confidante, good relations with other people, a satisfying occupation, and success in coping with problems in the past.

There was no empirical support for these findings. Some of the factors might be regarded as manifestations of good adjustment, rather than their causes. However, there is an element of common sense in the essence of his thesis: namely, that well adjusted people can be expected to cope well.
Psychosocial effects of chemotherapy.

A literature search in 1977 failed to show any study of the psychosocial effects of chemotherapy after mastectomy. Bonnadonna and his co-workers, the pioneers of adjuvant chemotherapy with cyclophosphamide, methotrexate and 5-fluorouracil (CMF) for early breast cancer, maintained the treatment was well tolerated. In 1976 they reported the results of a randomized study in which, after radical mastectomy, 207 women were given CMF and 179 control subjects no further treatment. They stated: "The quality of life during CMF was, in general, good. It can be approximately estimated that less than 10 per cent of patients showed a lowering of performance status as a result of prolonged administration of CMF... Seventeen patients refused to complete the chemical treatment more for psychological reasons than because they were severely affected by toxic manifestations." Unfortunately, after this passing comment, they made no further reference to the "psychological reasons".

There was little information on the psychosocial effects of chemotherapy in general. Bond (1967) in a detailed and extensive monograph on chemotherapy in the treatment of advanced malignant disease, reported that mental depression was a side effect of treatment with vinblastine. However, mood disturbance was not implicated as a complication of the many other chemotherapeutic agents reviewed, including cyclophosphamide, methotrexate and 5-fluorouracil, although their unpleasant physical side effects were well documented. At that time methotrexate had been used as a single agent for nearly 20 years and the other two for over five years. Indeed Bond noted that chemotherapy sometimes produced
short-term subjective (as well as objective) improvement — subjective benefit being based on clinical impression rather than on any detailed measurement. He emphasised that candidates for chemotherapy should be carefully selected; this policy might have prevented mood upset.

Two years later, in a text on cytotoxic drugs in the treatment of cancer, one author commented that alkylating agents — for example, mustine hydrochloride — administered to the upper part of the body might cause toxic effects on the brain, including "deafness, general depression and inability to concentrate". Depression was not reported as a side effect of the other drugs reviewed.

After the introduction of combined chemotherapy, for example to treat blood cancers and lymphomas, Whitehead (1975) stated in a letter to the New England Journal of Medicine that the nausea and vomiting induced by such regimes had received insufficient attention. He made two pertinent observations: that some patients vomited before their treatment; and that some could become deeply depressed or even suicidal. He appears not to have recognised pre-treatment vomiting as a Pavlovian conditioned response, stating it attested to "the abhorrence with which [the patients] regard the treatment".

In the same year Burge and colleagues reported on quality and quantity of survival in acute myeloid leukaemia. They said that the quality of life was improved as a result of less aggressive chemotherapy. However, quality of life was assessed solely by an observer's global five-point rating based on length of time in
hospital, physical symptoms and ability to work or lead a normal life. Since there was no assessment of quality of life in control patients treated with more aggressive chemotherapy, the basis of the authors' statement of an improvement is not clear.

Priestman and Baum (1976) were aware of the need for controlled studies, and described the use of linear analogue scales to assess quality of life in patients with advanced breast cancer treated with chemotherapy and with endocrine treatment. This preliminary methodological paper, which showed the linear analogue scales to be reliable, did not provide a clear statement about quality of life on the two régimes.

Conclusions from the "mainly qualitative" studies

Clearly many of the above studies on the psychosocial effects of treatment for breast cancer had serious drawbacks. These can be classified under several headings.

(1) Definition and selection of subjects

Samples need to be defined precisely, with a clear indication of their origins and any methods used to select them. Possible biases in selection must be considered. Many studies failed to provide such information; perhaps some investigators thought this was unimportant. Very seldom were there any references to consecutive patients. Where patients were clearly not consecutive, often the method of selection was not defined; bias cannot be ruled out. Also, the exact nature of the disease and its treatment was sometimes unclear. Authors usually stated the nature of primary
surgical treatment (for example, radical mastectomy), but often did not give enough information on the stage of the cancer, or on what proportion of patients received additional treatment such as postoperative radiotherapy. Metastatic breast cancer could be expected to have different psychological effects from early cancer, and extra treatment to influence morbidity. These problems tended to be worse in postal questionnaire studies.

(2) Experimental design

Most of the research cited was retrospective, or at least partly so. This might have caused bias in the recall of information. Too often the timing of assessments in relation to treatment was not stated. Often the samples consisted of a cross section of patients who had undergone mastectomy over the previous few years. Thus some patients would have been seen shortly after surgery, but others not until months or years later. The psychosocial effects of a serious illness like breast cancer could be expected to vary with time. The mixing of results from different time periods makes it hard to distinguish the early and late consequences of treatment.

Few studies had control groups. To what extent are control groups needed?

Certain experiences — for example loss of the breast — are virtually unique to breast cancer. Thus controlled studies might be unnecessary to understand matters such as feelings of mutilation, phantom sensations and problems with prostheses.
The need for control groups is much clearer in studies concerned principally with mood disturbance and social dysfunction, which occur also in people not suffering from breast cancer. Even so, careful interviewing (for example in work of Bard and Sutherland\textsuperscript{22} or of Peck\textsuperscript{33} \textsuperscript{34}) may be sufficient to show causal connections between psychosocial upset and treatment for breast cancer. Control groups could give a spurious air of respectability, for example in a postal questionnaire study too superficial in content. However, absence of control groups causes serious difficulty in judging the extent of psychosocial morbidity.

(3) Inadequate methods of assessment.

Assessments of psychosocial morbidity need to be valid and reliable. Perhaps the simplest form of validity is face validity. The questions asked have to be relevant and comprehensive. At another level, if a criterion of validity can be defined, the assessments should be sensitive and specific. In practice there are no absolute criteria of psychosocial morbidity; the "gold standard" of validity is usually taken to be the administration of a reliable interview schedule by an experienced psychiatrist or other suitably trained professional. Put another way, validity becomes partly a matter of consensus opinion. On this basis sensitivity and specificity have practical meaning only when another method of assessment — for example a questionnaire — is compared with the results of an observer interview.

Much of the research described above fell down on several of these criteria. Some of it was superficial in content, failing to tap relevant information. Even in studies where interviewing was good,
the reliability of information obtained was not considered. Where questionnaires were used, generally their reliability was not checked and since they were not validated against observer assessments, sensitivity and specificity were unknown.

In spite of these limitations, what conclusions can be drawn from the "mainly qualitative" studies?

Firstly, the discovery of a breast lump might induce feelings of shock, depression and anxiety along with fears of death and mutilation. Mastectomy might cause depression, anxiety, irritability, anger or guilt. Occasionally depression might be very severe or chronic, with or without ideas of — or even actual — suicide. By its mutilating effect mastectomy might damage feminine self-concept. Sexual difficulties might lead to marital problems, including rejection by the husband. On the other hand improvement in marital and sexual relationships was sometimes reported. Loss of the breast might cause serious problems with dressing, aggravated by an inadequate prosthesis. Embarrassment might lead to social withdrawal.

Most of the studies in which post-operative radiotherapy was mentioned suggested that it increased psychological distress. The effect of chemotherapy on mood was unclear.

The studies reviewed so far did not allow a precise statement on the extent of the morbidity, although clearly not all women were seriously affected. Whether certain subgroups of women were prone to morbidity was largely unknown. Opinion was divided as to
whether morbidity was greater in older or in younger women. Bard had found that dependent personalities were prone to morbidity, but his concept of dependence was complex. He also found a relationship between Cornell Medical Index scores and "invalidism", too weak to be of practical value. Impressionistic research suggested that morbidity was higher in women who were badly adjusted generally, but hard evidence was lacking. The duration of the morbidity was also unclear. What evidence there was suggested that mastectomy was not usually associated with major mood upset in the long term. However, some research suggested that problems with body image and sex might be long-lasting.

Other psychological effects included concerns about possible recurrence of the cancer and death. Innocent aches and pains might wrongly be attributed to recurrent cancer, causing anxiety. There was disagreement as to whether loss of the breast or possible death was the main cause of morbidity.

The stress associated with breast cancer might lead to the use of mental defence mechanisms. Denial of the presence of cancer appeared to be the commonest mechanism. Although it might prevent or reduce psychological morbidity, it might also cause delay in seeking treatment.

Mainly Quantitative Studies

During the 1970's, the need for more clearly defined, reliable studies was increasingly recognised; some of the earlier reports in this period described psychological problems in the period
Studies focusing on pre-operative morbidity

One such study was the paper by Katz and colleagues (1970) entitled "Stress, distress and ego defenses — Psychoendocrine response to breast biopsy." Thirty women awaiting breast biopsy, of whom 22 proved to have cancer, were studied. Whether or not these patients were consecutive was not stated. Nineteen came from a hospital clinic and the remainder from private physicians. The methods of quantifying distress were somewhat unusual, though previously documented. The authors used a score of "defensive adequacy." Defensive adequacy had three components: affect, functional disruption, and impairment of defensive "reserve". Affect was scored on a scale from -6 through 0 to 6. Negative scores denoted pleasant emotions, and positive scores unpleasant emotions. The other two components were scored from 0 to 6, higher scores meaning greater impairment. The three scores were then added together to form a "total psychiatric score." The authors also identified the patients' main defence mechanisms. Finally they measured hydrocortisone production, by injecting a tracer of hydrocortisone labelled with radioactive carbon 14.

Interviews with the patients were tape recorded to allow assessments by independent raters. Inter-rater reliability proved to be satisfactory, but was lowest for defensive reserve. Although there were no control subjects, the authors thought that most of the women did not show significant defensive breakdown. This opinion was partly supported by the patients' hydrocortisone production being within the normal range; there was a significant,
albeit modest, correlation between levels of hydrocortisone production and total psychiatric scores. The main defence mechanisms identified were displacement, projection, denial with rationalization, hope and prayer, stoicism-fatalism, and a mixture of defences. The first two mechanisms mostly failed to protect against morbidity; denial with rationalization was a more effective defence, but led to delay in obtaining medical advice.

Although this paper showed careful attention to reliability, possible bias in the selection of subjects, the unusual method of quantifying psychiatric upset together with the absence of control subjects cause some difficulty in interpreting the results. However, the authors' comments to the effect that despite the threat posed by breast biopsy, many patients coped, seem reasonable. Likewise the defence mechanisms outlined are convincing — unlike the ethical justification for giving radioisotopes, which the authors chose not to discuss.

A controlled study of psychological morbidity prior to breast biopsy was reported in 1975 by Schonfield. His main purpose was to show whether life experiences influenced the development of breast cancer. In consecutive Hebrew-speaking Israeli women, the Holmes-Rahe schedule of recent experience failed to show higher scores in 27 women who proved to have cancer than in 85 with benign disease. In fact the opposite trend was seen: the benign group scored significantly higher for recent events requiring major or minor adjustment. The patients also completed the Institute of Personality and Ability Testing (IPAT) anxiety scale. The cancer patients aged 42 or less showed a significant excess of anxiety compared with the benign group. Schonfield thought that
this was because loss of the breast was more important to younger patients. Depression was not measured.

In 1975 Greer and his research group at the Faith Courtauld Unit for Human Studies in Cancer started to publish a series of papers based on 160 consecutive patients who underwent breast biopsy. This work was of major importance because the sample was unbiased and the researchers used reliable measures of morbidity, notably the Hamilton depression rating scale. The patients were interviewed preoperatively and then followed up for two years.

The first of these studies provided information on morbidity in the period prior to breast biopsy. Depression as measured by the Hamilton scale appeared to be about as frequent in the 91 patients who subsequently proved to have benign disease as in the 69 found to have cancer. It was seldom of clinical degree: only 3% of cancer patients and 2% of control subjects scored 20 or more on the Hamilton depression scale. A further 4% of cancer patients and 3% of controls scored between 16 and 20, which suggested to the authors a clinically mild depressive state. Ninety three per cent of cancer patients and 95% of controls scored from 0 to 15. Anxiety was not measured. However, the main purpose of this work was to examine patterns of emotional expression in patients with breast cancer compared with control subjects with benign disease. Drawing on the methodology of David Kissen, who had reported that men with lung cancer had poor outlets for emotional discharge, Greer and colleagues found that women with breast cancer showed a longstanding personality trait of abnormal emotional expression. Compared with patients with benign disease, they showed abnormal expression or suppression of anger. Abnormal suppression was
commoner than abnormal expression.

In a companion paper published in the same year, investigating delay in consultation, Greer and colleagues noted that denial of illness was prominent in women with breast cancer who delayed seeing their doctors. The findings of both these preoperative papers had obvious theoretical and practical relevance.

This early work of Greer and his co-workers can be criticised because the authors might not have been truly "blind" to the diagnosis of cancer or benign disease, even though they did not seek out the probable diagnosis in advance. The cancer patients were older on average than those with benign disease. Also, in many cases, the patients' surgeons must have known the likely diagnosis. This knowledge might have been communicated verbally or non-verbally to the patients, and non-verbally from the patients to the researchers. In a paper on methodology, the authors themselves acknowledged that such biases could occur.

Morbidity in general surgical samples

None of the above preoperative papers compared morbidity in patients undergoing breast biopsy with that in patients undergoing routine surgery. Some of the morbidity prior to breast biopsy might not have been due to the threat of breast cancer, but simply to the threat of being admitted to hospital and undergoing surgery. Several mainly qualitative studies had drawn attention to anxiety in general surgical patients. For example, fears of the anaesthetic, of pain after or even during surgery, and of death were described. In one study, however, it was suggested that
occasional patients might actually welcome surgery as a pleasant change from hard work and poverty.52

In the late 1960's and early 1970's quantitative studies of anxiety in general surgical patients were undertaken by Spielberger and his research associates. In one of the early studies to be published by that group, twenty six male patients undergoing major surgery (precise operations not stated) completed Spielberger's state-trait anxiety inventory (STAI) 18-24 hours before surgery, and again three to nine days after surgery.55 Mean anxiety state scores were significantly higher before surgery than post-operatively. Trait anxiety, reflecting a personality characteristic, did not change significantly. These results were confirmed in a larger series of 56 male patients by Auerbach, who included an extra assessment at 48 hours after surgery. State anxiety at 48 hours was only slightly less than before surgery; during convalescence there was again a marked decline.56 In a further study of 59 male surgical patients, Martinez-Urrutia obtained similar results.57

Subsequently, Chapman and Cox studied a mixed sex sample in which 10 males and 34 females underwent routine abdominal surgery. (These patients in fact served as a control group for kidney donors and recipients.) The patients completed the STAI before surgery and on days one and three thereafter. Results for the abdominal surgery sample seemed to contradict Spielberger's results: there was a trend on day one for anxiety and depression to be higher than on the day before surgery, and on day three these symptoms were of similar intensity as prior to surgery. Sex did not influence the results.58 However, the post-operative
assessment of Chapman and Cox was at three days exactly rather than the three to nine days in Spielberger's study.  

Taken together, the results of these studies suggested that major surgery provoked excess anxiety before operation, but that anxiety did not decline immediately afterwards. Rather it fell (presumably to baseline levels) several days after operation.

Studies focusing on post-operative morbidity

In a further paper from the Faith Courtauld Unit, Morris, Greer and White (1977) followed up the 69 patients with cancer (stage I and II) and the 91 with benign disease for two years after operation. They measured mood (depression), and marital, sexual, interpersonal and work adjustment. Personality was measured with the Eysenck personality inventory. Depression (score of 10 or more on the Hamilton scale) occurred in 11 of 63 (17%) of cancer patients at three months after operation. At 12 months the prevalence was 12 of 53 (23%) and at two years 10 of 45 (22%). In patients with benign disease the corresponding prevalences were 7/85 (8%), 10/75 (13%) and 5/65 (8%). The trend towards more depression in the cancer patients compared with those with benign disease was not statistically significant except at two years.

There was also a trend towards more sexual problems in the cancer patients. At three months, 8 (18%) of the cancer patients experienced changes for the worse, compared with 4 (6%) of those with benign disease. This difference was statistically significant, but by two years there were no significant
differences: 10 (32%) of the cancer group reported changes for the worse, compared with 14 (27%) of the benign group. About a tenth of both groups reported changes for the better. The authors believed that some of these sexual difficulties reflected the problems of middle age rather than the effects of breast cancer.

There were no significant changes in overall marital adjustment, but more cancer patients than benign controls reported a long-lasting improvement in interpersonal relationships. Work adjustment deteriorated in cancer patients, especially in the first three months after operation. Thereafter some improvement occurred, so that by two years 71% of the mastectomy group had regained their preoperative work status. There was no work deterioration in the benign group.

An interesting feature of this study was an attempt to classify patients' psychological responses to diagnosis. Five categories — denial, fighting spirit, stoic acceptance, anxious/depressed acceptance and helpless/hopeless — were distinguished. These categories were not entirely stable over time; stoic acceptance became increasingly common.

Two predictors of morbidity emerged from this work. Patients still "stressed" by mastectomy at two years had higher preoperative scores on the Hamilton depression scale and on the neuroticism scale of the Eysenck personality inventory.

Certain comments can be made about this study. In their preoperative paper, Morris and Greer used a threshold of above 20 to define moderate to severe morbidity on the Hamilton depression scale, and a score of 16 to 20 to define mild
depression. In their postoperative paper,\textsuperscript{69} they reduced the threshold for depression to 10 or above. Had they continued to use a threshold of 20 or above, very little depression would have been evident, with no significant differences between cancer and control groups. This suggests that the depression reported in their post-operative paper was mild in degree and less than that seen in many psychiatric patients. Their use of the undefined term "stressed" seems in keeping with this view.

Also, the cancer and benign disease groups differed in age. The mean age of the cancer patients was 58 years, and that of the benign group 48 years. In theory, some of the observed differences might have been due to age rather than to breast cancer. To overcome this problem, the authors stated they used a technique of looking at change within each patient group, using patients as their own controls, and observing and comparing changes for better or worse in the two groups. However, this technique could not have removed an effect of age. Instead, the authors might have reported the association between age and morbidity in the cancer group and then in the benign group. Had an effect of age been demonstrated, the groups could have been analysed after subdivision by age.

The findings of Morris and colleagues on work adjustment and predictors of morbidity had been anticipated partly in a small study by Schonfield of 42 patients attending a radiotherapy clinic.\textsuperscript{60} These patients, of whom all had been in full time employment, suffered from several types of malignancy, but 18 had breast cancer. Nine patients (21\%) had not returned to work by nine months after surgery; compared with those back at work they had shown at the time of radiotherapy significant morale loss and
Impaired well-being on the Minnesota Multiphasic Personality Inventory, and high covert anxiety on the IPAT scale. However, numbers were too small for a specific statement about the patients with breast cancer.

The study of Maguire and his co-workers, reported in 1975 and 1976 but more fully in 1978, used age matching to overcome the problem of age differences between cancer and control groups. Reliable observer rating scales were used to assess several aspects of morbidity, notably depression, anxiety and sexual dysfunction. These scales were used by Brown and Harris in their classic studies of depression in women in London. The interviews in Maguire's study were tape recorded to allow independent checking of ratings. Symptoms were classed as absent, mild, moderate or severe.

Two hundred and one women attending breast clinics were included in the study: consecutive patients due to undergo breast biopsy and a one in five sample of women who did not require biopsy. One hundred and seventeen proved to have cancer. Of these, 96 were interviewed at three to four months and one year after operation. The remainder had died, were too ill, had moved house or refused to be seen. Eighty of 84 control patients with benign disease were seen at the same time intervals. Because of the differences between patients and control subjects with respect to age, social class and marital status, subsamples were taken: 75 cancer patients aged 65 or less who were free from recurrent disease and 50 patients with benign disease who matched those in the mastectomy sample for the variables cited. All but six of the 75 cancer patients underwent simple or modified radical mastectomy.
Results for the preoperative period showed that after discovery of disease and prior to attending the breast clinic, a substantial minority of women in both groups experienced moderate to severe depression or anxiety. Anxiety of this degree occurred in 23% of those who proved to have cancer and 26% of those with benign disease. For depression the corresponding figures were 13% and 12%. After the patients had attended the clinic, the prevalence of anxiety rose slightly to 27% in the cancer patients but fell to 15% in patients with benign disease. Depressive symptoms showed a similar, less marked trend. Minor degrees of anxiety or depression were very common in all patients and also tended to fall in patients with benign disease after they had attended the clinic.

At both four and 12 months after surgery, there was significantly more anxiety and depression in cancer patients than in the benign control group. Twenty-one per cent of the cancer patients experienced moderate or severe anxiety at four months, and 19% at one year. For depression the corresponding figures were 27% and 21%. In the control subjects the highest prevalence of morbidity was 12% for moderate to severe depression at four months. For clinical depression at one year, and clinical anxiety at both four months and one year, the prevalences in the benign group were all 8%. In a preliminary report, Maguire had noted that morbidity was greater in younger cancer patients, but actual data to support this observation were not given.61

Sexual problems in the cancer patients were commoner than mood disturbance. At four months, 40% had moderate to severe sexual difficulties. At one year, the prevalence remained high at 33%. In
the benign group the corresponding percentages were 12% and 8%.

Sixty-two (85%) of the cancer patients underwent postoperative radiotherapy. The authors believed it might have contributed to psychiatric morbidity. Patients associated it with a worse prognosis, and some said it made them exhausted and even lower in spirits. Radiotherapy also seemed to induce anxiety. However, since only 13 patients did not receive radiotherapy, it was not possible formally to prove that mood disturbance was commoner in patients who had received radiotherapy than in those who had not.

The authors found that psychological and sexual morbidity was often unrecognised or untreated. It was suggested that specially trained nurses, social workers or volunteers might help these patients.

This was a well-designed and clearly written study. However, the results applied to patients aged 65 or less and free of recurrent disease.

"The fallacy in postmastectomy depression" was the sceptical title of a North American controlled study by Worden and Weisman (1977). The authors set out to examine whether depression was specific to loss of the breast per se, using a different control group from Morris or Maguire. They compared 40 women with newly diagnosed breast cancer with 50 fresh cases of women with other cancers, namely Hodgkin's disease, malignant melanoma and cancer of the colon. Both groups appear to have consisted of virtually consecutive patients. Refusal to participate was said to be uncommon, but the number refusing was not given. The patients were
seen on six occasions over a period of six to eight months. Mood was measured by the profile of mood scales (POMS), and by a clinical rating. Other assessments included self-esteem, predominant concerns (health, religion, work, money, family, friends, self-appraisal, and existential concerns), coping strategies, and the degree to which problems had been resolved.

The results were perhaps surprising. Levels of depression were remarkably similar in the women with breast cancer and in those with cancer in other sites. Twenty per cent of patients with breast cancer were judged to show the clinical syndrome of depression, lowered self esteem, increased health concern, and loss of energy, compared with 18% of women with other cancers. In both groups, those with lowered self esteem tended to show persistent health concerns, many social problems with difficulty in resolving them, and low ego strength. This pattern of results suggested a vulnerability to distress in general, rather than to mastectomy of itself. The authors believed that a specific postmastectomy syndrome occurred in a minority of women only.

These results formed part of a wider study of the psychological effects of a variety of cancers in 163 patients of both sexes. In this wider study the following factors were found to be associated with vulnerability to emotional distress: pessimism, a past history of depression, family problems, marital problems, low social class, and having little support. Religious observance was associated with decreased vulnerability, possibly because of its correlation with being older, conventional and having strong roots in the community.
In their mastectomy patients Worden and Weisman did not find body image problems to be common, but they did not ask about them unless prompted by the patients. This was to avoid biasing the results by suggesting that such problems might exist. Possibly this was a case of throwing the baby out with the bathwater. The research of Bard and Sutherland,2 of Morris et al55 and of Maguire62 strongly suggests that had specific enquiry been made, more patients would have voiced concerns about body image. Hence some of the morbidity of mastectomy might have been missed. However, Worden and Weisman pointed out that patients in the control group also reported body image problems due to lymphoedema, skin grafting or colostomy.

On the other hand, Ray (1977) in a careful study comparing 30 matched pairs of patients who had undergone mastectomy or cholecystectomy 18 months to five years previously, specifically sought out the effects of breast loss.67 She interviewed these patients on a single occasion lasting up to two hours. They completed depression and anxiety scales developed by Costello and Comrey, a self-esteem scale devised by Rosenberg, and several other scales which measured social warmth, social abrasiveness, social attractiveness, introversion-extraversion and body cathexis. For the body cathexis scale the patients rated their physical attractiveness with respect to 15 body parts, the total score being the sum of the individual scores. Surprisingly, this scale did not include an item about breasts. However, Ray encouraged the patients to talk freely about the effect of their illness and mastectomy.

She found that the mastectomy group were significantly more
depressed and anxious than the cholecystectomy group, tended to have lower self-esteem and described themselves as more introverted in their behaviour. There were no significant differences on the other scales. Ray thought that her findings reflected concerns about both the loss of the breast and possible recurrence of cancer. Despite the lack of significant differences between groups on the body cathexis scale (which may have been due to the absence of items about breasts), Ray found that 16 of the 30 in the mastectomy group were seriously concerned about disfigurement. They used terms such as "no longer a full woman" or even described the operation as "obscene".

This study therefore suggested that mastectomy had a long term effect on mood as well as on body image, but the matched design could have led to slight bias. The cancer and control groups were matched for age and time since operation. Matching for age, which was performed because mastectomy patients are on average older than cholecystectomy patients, might have caused her mastectomy group to be younger than usual. Indeed the oldest mastectomy patient was aged only 65. The other selective factor in this study was exclusion of patients with recurrent disease or physical deformity. This illustrates a common methodological difficulty. Selection and matching performed for very good scientific reasons, namely precision and the avoidance of confounding factors, may limit the generality of the conclusions.

A partial explanation of the difference in body image problems reported by Worden and Weisman and by Ray may be found in the work of Polivy.68 Using a standard questionnaire, Polivy compared body image problems in three groups: mastectomy patients, patients
found on biopsy to have benign disease and general surgical controls. The surgical control subjects showed little change in either body image or total self image. The benign group experienced a decline in body and self image immediately after surgery. The most interesting result was that the breast cancer patients reported no such decline until several months after mastectomy. Polivy attributed this delay in acknowledging body image problems to massive denial.

Polivy did not assess mood in this study, except to note that mastectomy patients expressed more fears of death or mutilation than the other groups. In a review article, however, she made the important observation that patients might deny not just the presence of cancer, but also the presence of anxiety.

The non-expression of anxiety was also noted in a study published by Margarey et al in 1977. This concerned the influence of psychosocial factors firstly on delay in reporting breast symptoms, and secondly on the practice of breast self-examination. Ninety consecutive women admitted to a hospital in New South Wales, Australia, for breast biopsy were interviewed on videotape. Ten of the videotapes were used, along with earlier data, for a pilot study to develop operational definitions of some psychological factors. These included the use of ego defence mechanisms, the extent of anxiety and depression expressed verbally and non-verbally, and interpersonal support received. On the whole the various measures proved reliable when the videotapes were rated by independent observers. The patients also completed the Spielberger Anxiety Inventory, Millimet's Manifest Anxiety-Defensiveness Scale and the depression scale of the Minnesota
Multiphasic Personality Inventory. However, only 43 patients completed all the scales; no adequate explanation was given for so much missing data. Some of the videotapes were technically flawed and only 64 were available for the main study.

The data were examined by correlational methods, including multiple regression analyses. Unfortunately, the numbers of patients available for each analysis, and the actual levels of morbidity, were not reported. The authors found that 43.4% of the variance in delay was explained by the use of denial and suppression, the non-use of intellectualization, the absence of anxiety reported verbally, the presence of anxiety shown non-verbally, and the presence of depression reported verbally.

In view of the seemingly large amount of missing data, the results should be viewed with caution. However, the relationship between delay and denial was similar to that previously noted by Greer, and the absence of anxiety reported verbally by patients who showed anxiety was striking. This result together with Polivy's observations suggested that in patients under threat of cancer, denial of anxiety might prevent the full extent of that symptom from being detected by rating scales.

Conclusions from the "mainly quantitative" studies

Pre-operative morbidity

Four papers discussed pre-operative morbidity. All agreed on its presence, but not on its extent. Pre-operative depression as defined by Maguire and colleagues was much commoner than
depression as defined by Greer and Morris. In the latter study, levels of morbidity appeared similar in patients with benign disease and those with cancer. In Maguire's study, while morbidity was similarly high in the benign and cancer groups prior to attendance at the outpatient clinic, thereafter it was significantly lower in patients with benign disease. This result was partly in accord with that of Schonfield who showed that morbidity was higher in cancer patients (but only those aged 42 or less) than in patients with benign disease.

To some extent the differing results of these studies must have reflected varying design, patient selection factors, and definitions of morbidity. The one constant finding in the above three papers was that only a minority of patients experienced morbidity of clinical degree. This finding was also in accord with the fourth paper: the uncontrolled observations of Katz et al. However, the size of this minority remained in some doubt, and none of these researchers showed whether patients about to undergo breast biopsy were more or less upset than those about to have routine surgery.

Post-operative morbidity

Post-operatively, agreement was greater. Having redefined clinical depression as a Hamilton score of 10 or above, Morris et al found that the prevalence of postoperative depression varied from 17 to 23%. Maguire et al found that the prevalence of moderate to severe depression varied from 21 to 27% and anxiety from 19 to 21%. Worden and Weisman's figure for depression was 20%. So the prevalences of clinical symptoms, as defined by these authors,
were similar: about a fifth to a quarter of patients being affected. One could conclude, as for the pre-operative period, that morbidity of clinical degree affected only a minority of patients after mastectomy; and that the size of this minority depended partly on thresholds to define morbidity, and perhaps also on the influence of postoperative radiotherapy, which many patients on whom these figures were based received.

Both Maguire and Morris found that morbidity persisted beyond four months (respectively up to one year and up to two years) and Ray's study suggested that depression and anxiety lasted up to five years.  

There was some disagreement about the extent of problems with body image, but probably up to half of patients were upset by disfigurement — possibly more. The prevalence of sexual problems varied from 18% in the study of Morris et al to 40% in that of Maguire et al. (However, the denominator in the latter study included only those who were sexually active and aged 65 or less.) Morris et al thought that some of the sexual problems might reflect middle age rather than mastectomy.

Morris and colleagues found that work status was still impaired in nearly a third of patients at two years after mastectomy.

Predictors of morbidity

In the quantitative studies, about the only definite information on predictors of emotional morbidity was the finding of Morris et al (published in fact shortly after work for this thesis began)
that high pre-operative depression scores and high Eysenck neuroticism scores predicted those patients liable to be "stressed" by mastectomy. However, Weisman's finding in a mixed group of cancer patients (including breast), that vulnerability to morbidity was associated positively with pessimism, a past history of depression, family problems, marital problems, low social class, and having little support, but negatively with religious observance, is relevant. The qualitative studies had already suggested that women who were dependent and poor copers were prone to morbidity.

The effect of age on morbidity — about which there had been disagreement in the qualitative studies — was not examined in the quantitative studies, with one exception: Maguire's observation (not however supported by a formal analysis of data) that younger women were more liable to be distressed.

Effects of further treatment after mastectomy

Only one further treatment — postoperative radiotherapy — was examined in the "mainly quantitative" research. Maguire et al. agreed with the "mainly qualitative" studies, that radiotherapy might increase emotional distress. Morris et al reported that radiotherapy did not influence morbidity at two years after mastectomy, but did not describe its more immediate effects.

There were no quantitative studies in the literature on the psychosocial effects of other forms of postoperative treatment such as oophorectomy or adjuvant chemotherapy. There was little information on the effects of recurrent disease and its treatment.
Scope of this thesis

This review of the literature has highlighted several areas where knowledge was lacking or incomplete. Not all could be explored, given constraints on both clinical material and time, but information was sought in the following areas.

The psychosocial effects of further treatments: adjuvant chemotherapy and postoperative radiotherapy.

Effects of recurrent disease.

In both the preoperative and postoperative periods:

Precise levels of morbidity, using both observer rating scales and self rating scales as a check on possible observer variation in defining morbidity.

Predictors of morbidity.

Finally, it was of interest to examine the performance of self rating scales in detecting psychosocial morbidity in patients undergoing treatments for breast cancer. Self rating scales, if satisfactory, could save both time and expense in future studies.

The precise questions asked have been stated in the Preface; the methods of addressing them are discussed in the next chapter.
Design of study

For each of the questions asked in the Preface, the following comparisons were made among groups of patients.

(1) *Does psychosocial morbidity prior to breast biopsy exceed that prior to routine surgery? What factors independently predict morbidity?*

Here psychosocial morbidity was compared in consecutive patients under the age of 70 awaiting breast biopsy with that in consecutive women aged under 70 awaiting elective cholecystectomy. The patients undergoing breast biopsy were subdivided into those proving subsequently to have cancer and those with benign disease. Within the breast biopsy groups, an attempt was made to find independent predictors of morbidity, using demographic and other data to be described later.

Elective cholecystectomy was chosen as a control operation because it was commonly performed on women of similar age to those undergoing breast biopsy. Other control operations, for example varicose veins and hernia repair, were considered, but rejected both because turnover of patients undergoing these operations was low and because the waiting time for admission was far longer than for breast biopsy.
What is the extent of psychosocial morbidity in patients allocated to adjuvant chemotherapy, and how does it compare with the morbidity in patients receiving post-operative radiotherapy?

The starting point for this question was a randomized trial of adjuvant chemotherapy in stage II breast cancer.

(In stage I disease, the cancer appears to be confined to the breast. In stage II disease, it has spread to the axillary lymph nodes; although disease cannot be demonstrated elsewhere, micrometastases are very often present at the time of diagnosis. Adjuvant chemotherapy is intended to destroy these micrometastases before they enlarge and kill the patient.)

The design of this trial is shown in figure 2-1. Consecutive patients under the age of 70 with histologically proved stage II breast cancer underwent simple mastectomy and axillary clearance and were allocated at random to:

(i) a three week course of radiotherapy to chest wall and local lymph nodes;
(ii) a year’s course of adjuvant chemotherapy;
(iii) radiotherapy followed by chemotherapy.

The chemotherapy régime was based on that of Bonadonna in Italy,18 except that all drugs were given intravenously. Cyclophosphamide (300 mg/m) methotrexate (40 mg/m) and 5-fluorouracil (600 mg/m) were administered at the outpatient clinic on days one and eight of consecutive 28 day cycles. Treatment was started within six
weeks of mastectomy and continued until recurrence or for one year. Patients allocated to combined radiotherapy and chemotherapy began their course of radiotherapy four to six weeks post-operatively and chemotherapy was started four to six weeks after completion of radiotherapy.

Post-operative radiotherapy was conventional orthovoltage treatment: 15 fractions over three weeks to chest wall, axilla, infra- and supraclavicular fossae, and internal mammary region (average tumour dose 3.7 Gy).

This trial had been set up at the Victoria Infirmary in Glasgow by Mr C S McArdle and colleagues to examine the effect of adjuvant chemotherapy on quantity of both disease-free survival and overall survival in stage II breast cancer. A few patients at Gartnavel General Hospital who attended the oncology clinic of Professor K C Calman also entered the trial. It was thought important to examine quality of survival as well as quantity.

(3) Does post-operative radiotherapy cause more psychosocial morbidity than no further treatment?

Two groups in the chemotherapy trial received postoperative radiotherapy. Since patients with stage I cancer attending the Victoria Infirmary received no further treatment after mastectomy, they could serve as a control group to assess the psychosocial effects of radiotherapy. Ideally these patients on no further treatment would have had stage II cancer. An ideal sample was not available, since local opinion was that patients with stage II cancer should receive further treatment, but differing stages of
disease could be allowed for in the interpretation of results. The only selection criteria for the stage I patients studied was that, like the stage II group, they should be a consecutive series, aged under 70 and free of second cancers.

(4) What is the extent of morbidity in a general sample of patients with "early" breast cancer receiving several types of treatment, and what factors independently predict morbidity?

The inclusion of patients with stage I disease meant there would be a large group of consecutive patients with stage I or II breast cancer, receiving several treatments. The advantage of a large, general sample was that it would allow a fairly precise population estimate of the extent of morbidity in patients with "early" breast cancer, to compare with the results of other workers, and also would provide enough patients to examine predictors of morbidity. Results for patients at risk of psychological trouble would be more reliable and have wider application if derived from a general sample rather than from subgroups.

Control subjects without cancer were desirable to confirm whether morbidity in the cancer patients was higher than expected. Patients already seen prior to surgery could also serve as control groups after surgery: consecutive patients aged under 70 who, following breast biopsy, were found to have benign disease; and consecutive women aged under 70 who had undergone elective cholecystectomy.
(5) How well do self rating scales perform in patients treated for breast cancer?

A sample of breast cancer patients with reasonably high prevalences of morbidity was needed to address this question of validity; but until prevalences were known, the precise sample could not be predicted. This matter is discussed below in the section on the statistical analysis of the validity study, and also in chapter 7.

Timing of psychosocial assessments

Pre-operative assessments took place on the afternoon or evening prior to the day of surgery.

The timing of postoperative psychosocial assessments was partly dictated by the design of the chemotherapy trial. Assessments were made at one, six, 13, 18 and 24 months after operation (figure 2-1). This allowed morbidity to be measured prior to follow-up treatment, after radiotherapy, midway through the course of chemotherapy, shortly before completion of chemotherapy, and 5 and 11 months after completion of chemotherapy. The cancer patients were interviewed at all these times. The original intention was to see the control patients with benign disease at the same time intervals. However, there was insufficient time available to carry out the many interviews required, and some patients with benign disease were not keen to be interviewed repeatedly. As a compromise they were seen at one, three and 13 months. The cholecystectomy group was seen at three months only, by which time much of the physical recovery from surgery seemed
likely to have occurred.

Patients on chemotherapy were reviewed as close as possible to day 28 of each treatment cycle. This was the time in the cycle when physical toxicity was least, since about three weeks had elapsed since the previous injection. The purpose of this timing was to minimize confusion between physical and psychological symptoms. For a similar reason, radiotherapy patients were interviewed two to three weeks after completion of treatment.

**Measures of morbidity used**

The measurement of psychosocial morbidity in patients undergoing breast surgery and further treatment presented certain problems. Ideally, assessment of patients would have been blind, but treatment received could not be concealed from the interviewer. The possibility of tape-recording interviews, editing them in such a way that all references to further treatment were removed, and having the edited tapes rated by independent assessors was considered. However, it was rejected as impracticable. Despite this, observer assessments were considered essential, even if potentially biased. Self rating scales were also desirable, as a check on possible observer bias.

**Observer scales**

When the study was planned (1977), Dr Peter Maguire was asked for his advice on observer scales. The previous year he had published preliminary findings of his mastectomy study. In this work he had used the same scales (at that time unpublished) as
Brown and Harris in their study of the social origins of depression in women. Dr Maguire kindly provided the author with nine relevant scales and definitions of morbidity. These scales were subsequently published by Brown and Harris. Since they had been used successfully both in women in the community and in women with breast cancer, they were the obvious choice. They are as follows:

- **depressed mood**;
- **fears/anxiety/worry**;
- **under activity**;
- **drive (appetite and sex)**;
- **sleep**;
- **socially unacceptable behaviour**;
- **effect on day-to-day routine**;
- **employment or housework/child care**.

For most of the scales there were four possible ratings: 0=absent, 1=mild, 2=moderate and 3=severe. However, the two drive scales (appetite and sex) had seven-point scales which allowed for ratings of increased drive as well as reduced drive.

Certain features of the present study affected the way in which these scales were used. Account had to be taken of the many physical symptoms likely to be experienced by patients receiving treatment such as chemotherapy. Some symptoms, for example loss of appetite or lack of energy, were potentially ambiguous because they could denote either psychological distress or physical malaise. For ratings of depression or anxiety, somatic symptoms
such as gastro-intestinal dysfunction were discounted. On the other hand, the under activity scale normally referred only to symptoms of presumed psychological origin — for example, depressive retardation. In patients receiving radiotherapy or chemotherapy, it might be impossible to know whether under activity was caused by change in mood or treatment received. Thus in the assessment of under activity the cause was ignored, and ratings could reflect symptoms of physical origin, psychological origin, or both. The same was true for ratings of day-to-day routine and of problems with employment and housework.

It seemed likely that few, if any, patients would report increased sex drive after mastectomy, and therefore the seven-point sex scale was changed to a four-point loss of libido scale. Maguire had changed this scale in the same way.\textsuperscript{61-63} To simplify matters further, the seven-point appetite scale was not used, so that all scales remaining had a range of 0-4. The original definitions of the scale points are given in Appendix 1.

Ratings of loss of libido were made only in married or cohabiting patients. Loss of libido was thought important in those without sexual partners, but would have been difficult to measure. Problems in measuring precise baseline levels of sexual desire led to a decision to include in ratings of loss of libido married patients who were no longer sexually active. Inevitably, a rating of zero in such patients might mean that sexual appetite, though unchanged, was low.

There were still rather many observer scales, and sleep ratings did not seem essential, except for the validity study (chapter 7).
Otherwise they have not been included in the presentation of results. In the interests of clarity or brevity, the remaining scales are often referred to by alternative names, as follows (original names in brackets):

- depression (depressed mood);
- anxiety (anxiety/fears/worry);
- lethargy (under activity);
- loss of libido (sex);
- irritability (socially unacceptable behaviour);
- routine/social dysfunction (effect on day-to-day routine);
- work (employment or housework/child care).

Ratings covered the month prior to each assessment. A reliability study was conducted, comparing ratings of 16 patients by two observers: the author and his colleague Dr A F Cooper. The author interviewed the first patient in the presence of Dr Cooper and thereafter, for successive patients, the observers exchanged roles. However, in the case of six patients the second observer could not be present. He therefore rated a tape recording of the other observer's interview. Full details of the results obtained are given in Appendix 2. There were few disagreements between raters and none was greater than one scale point. The extent of agreement was assessed by the unweighted version of Cohen's Kappa. The respective values of Kappa for depression, anxiety, irritability, loss of libido, lethargy, social dysfunction, (house)work and insomnia were 0.68, 0.74, 0.67, 1.0, 0.81, 0.85, 0.90 and 0.79. Inter-rater reliability was therefore satisfactory.

The above method almost certainly resulted in greater agreement.
than would have been obtained from separate interviews by the two observers. Separate interviews were tried in one patient, but afterwards she objected very strongly. Already very worried prior to breast biopsy, she was confused by being interviewed twice. The author believed it would have been unethical to pursue the matter further in these patients.

Observer assessments were also used for physical symptoms. A simple arbitrary physical symptom score was devised based on the presence or absence of several relevant symptoms in the month prior to assessment. These included anorexia, nausea, vomiting, irritation of mucous membranes, hair loss, complete alopecia, skin reaction, pain, arm swelling, and significant other symptoms. One point was allotted for each symptom present, and the score was the sum of the points. "Irritation of mucous membranes" included symptoms such as mouth ulcers and cystitis due to chemotherapy, and oesophagitis due to radiotherapy. An example of a "significant other symptom" would be dyspnoea caused by lung metastases.

In patients receiving post-operative treatment, the presence of conditioned reflex nausea and vomiting was noted. (Patients subject to treatment-induced nausea and vomiting often developed conditioned reflex symptoms in response to previously neutral stimuli such as the smell of the hospital, as will be described in later chapters.)

In joint assessments of 12 patients the author and Dr A F Cooper both agreed completely as to the presence or absence of physical and conditioned reflex symptoms. This was hardly surprising, given
that the severity of individual symptoms was not recorded. Rating their severity would have been desirable, but the more detailed reliability study needed would probably have stretched the goodwill of the patients too far. In any case, summing the points for each physical symptom to provide an overall score gave an indication of the severity of physical problems.

Although formal standardized observer assessments were essential for reliability, by their very fixed nature they might miss important topics. Therefore, six months after surgery, cancer patients were asked open-ended questions. The questions were always the same: How do you feel about your illness? How do you feel about the mastectomy? How do you feel about your treatment? Immediate replies were recorded verbatim. In addition, patients who had received radiotherapy followed by chemotherapy were asked how the two forms of treatment compared. At any of the assessments, spontaneous comments were noted.

Self rating scales

Self rating scales (Appendix 3) had to be sufficiently sensitive to detect minor degrees of morbidity. Scales such as those of Beck and Zung, often used in patients with severe depressive illnesses, might not have been sensitive enough. The general health questionnaire was chosen because it had been widely used and was known to be valid and reliable in detecting morbidity in general practice and in outpatient clinics. Although likely to be suitable for patients with breast cancer, it had potential drawbacks.

Firstly, it contained somatic and social items. Cancer patients
free of psychological symptoms might endorse these items solely on account of physical illness or physical treatment. As a result their scores on the questionnaire would increase and they might wrongly be classified as psychiatrically ill. This was known to occur in physically ill inpatients. Secondly, when the study was started the general health questionnaire did not provide separate scores for depression and anxiety.

However, it was clear that the problem of misclassification could be reduced by using the 36-item version of the general health questionnaire in which items concerned with physical illness had been removed. In the event this version was not used because new subscales of the general health questionnaire became available in 1978, as detailed below.

To provide separate scores for depression and anxiety, an additional measure, the Leeds scales for the self assessment of depression and anxiety, was included. The general versions of the two Leeds scales were chosen as they were designed to measure the degree of depression and anxiety in patients with a variety of diagnoses. Most of the items in the Leeds scales were purely psychic in content, unlike many in the general health questionnaire.

The Leeds scales were modified slightly because they measured very recent mood, whereas the general health questionnaire measured mood over the previous few weeks. With the agreement of Dr Snaith, their designer, the wording of the Leeds scales was altered to refer to the previous few weeks. This was similar to the time period applied to the observer scales.
A year after the study began, a version of the general health questionnaire was published containing four subscales derived by principal components analysis. The subscales were: somatic symptoms, anxiety and insomnia, social dysfunction, and severe depression. All but the social dysfunction subscale had been validated against clinical assessments. The severe depression subscale contained items purely psychic in content, namely ideas of worthlessness, hopelessness and suicide; there were no somatic items. The anxiety/insomnia scale was mainly psychic in content, although arguably insomnia might sometimes be caused by physical complaints. However, it was clear that these subscales overcame many of the problems of misclassifying patients with purely physical complaints and they provided separate measures of depression and anxiety. They were used extensively in the data analysis.

There were recognised threshold scores to define morbidity for most of these self rating scales. The standard 60-item version of the general health questionnaire had scores ranging from 0 to 60, with a score of 12 or above to indicate clinically significant morbidity. However, this threshold was obtained from a general practice sample. Scores on each Leeds scale ranged from 0 to 18. For both depression and anxiety, the recommended threshold for clinical morbidity was a score of 7 or above.

There were no recognised threshold scores for the four subscales of the general health questionnaire. These were determined from comparisons of observer and self ratings obtained during the course of the study, as described in chapter 7. Threshold scores
to define clinical morbidity were found to be: somatic symptoms 6/7; anxiety and insomnia 6/7; social dysfunction 7/8; severe depression 2/3. The analysis to be reported in chapter 7 also suggested that the threshold score for the 60 item version of the general health questionnaire should be doubled to 24 for the detection of definite cases (observer depression or anxiety rating of two or more).

Two other self rating scales were used: the Eysenck Personality Inventory (EPI), and the Mill Hill synonyms test of verbal intelligence. There had been suggestions that cancer patients might differ in personality from the general population, and the influence of personality and intelligence on adjustment to cancer was of interest. Verbal intelligence rather than performance intelligence was measured since the former seemed less likely to be affected by physical problems caused by cancer or its treatment. Also, verbal intelligence seemed relevant for the understanding of cancer and its implications.

Patients normally completed the EPI (form A) at one month after surgery, and the Mill Hill scale at three months. The Mill Hill score was converted into an intelligence quotient according to the method of Peck. It was impossible to be certain that the EPI scores, especially the neuroticism score, would not be influenced by current mental state. The possibility of specifically asking patients to fill in the EPI to reflect their usual selves was considered. Kendell and DiScipio had found that such instructions reduced neuroticism and introversion scores in depressed psychiatric inpatients, when compared with the scores obtained without the instructions. However, changing the EPI in this way
might have inhibited comparisons with other research on cancer patients in which no change had been made. Also, the breast cancer outpatients would not generally be so depressed as psychiatric inpatients. The instructions were left unchanged and in practice the majority of patients seemed to take the inventory to refer to their normal selves.

Proforma

A proforma was devised, covering basic information (for example age, social class, marital status, menstrual status, work status) plus certain other items which might influence morbidity (e.g. delay between finding the breast lump and attending the outpatient clinic, time on the waiting list, education, knowledge of family members or friends with breast cancer, past history of serious illness, past psychiatric history, religious observance, living alone). Details of the proforma and necessary definitions of items are given in Appendix 4. Several of these measures were fairly crude, but seemed likely to be reliable. Ideally a fuller assessment of personal and social functioning would have been made. For example, a measure of the intensity of religious conviction would have been better than defining religious observance merely by whether the patient attended church more than once a month. A good marriage or good social support might protect against morbidity, but valid and reliable assessment of the quality of marriage or social support would have been complex. The patients already had many questionnaires to fill in, and to maintain their co-operation the amount of information sought had to be limited.
Location of interviews

In Maguire's study interviews took place in the patients' homes, to encourage free discussion. Likewise the author saw patients at home whenever possible. Home interviews proved to be essential for the regular follow-up of patients who otherwise would have been reviewed seldom or not at all in the outpatient department; their co-operation had to be secured. Interviews in hospital were often difficult because of lack of a suitable room or because the patients had to see other doctors or undergo tests. However, some patients had to be assessed at the hospital: for practical reasons, those seen prior to surgery; those who preferred to be seen at the hospital; and some of those who seemed to accept the study only if their surgeons approved there and then. Often great care was needed to ensure that the arrangements for interviews were adequate. Most interviews lasted about an hour, with a range from about half an hour to four hours.

Statistical notes

Numbers of patients required

There was no definite way of knowing the numbers of patients needed. In a comparison of two groups, knowledge of the standard deviation would allow calculation of the number of patients necessary to show a mean difference of clinically relevant size at a given level of significance. However, use of the standard deviation was open to question with skewed data such as general health questionnaire scores. Also, the definition of a clinically
relevant difference was very much a matter of opinion, though even a large difference in psychological morbidity seemed less important than, say, a 5% difference in long-term survival.

Size of postoperative stage II sample

In practice the critical factors influencing sample size were time available and the need to obtain, in the post-operative period, as many stage II patients as possible, since unlike the stage I patients they would be randomized into three smaller groups. The randomized trial of chemotherapy in stage II cancer had been running for nearly a year when the psychological study began, and over 40 patients had been recruited. This suggested that over the following two years a further 80 stage II patients would enter the trial, and allowing for a few refusals, at least 70 of these would enter the psychological study. This would mean 20 or more in each of the three randomized groups. A psychologist with extensive statistical knowledge — Mr Malcolm Adams — advised that 20 patients in each group was the minimum number required. In fact the "vanishing sample phenomenon" occurred. It took over three years, not two, for the 80 or so patients to materialise. With a two-year follow-up, this meant that data collection lasted more than five years.

Additional stage II sample

In anticipation of the problem of numbers, a further stage II sample was obtained. Forty-four patients who had already entered the chemotherapy trial were seen for the first time at 13 months after mastectomy, when many were completing a year's treatment.
Although early interviews were missing in these patients, the information obtained proved valuable. It allowed a more precise estimate of the psychological effects of chemotherapy and helped comparisons of the performance of the observer and self rating scales.

Since the author was fully occupied collecting data prospectively from the time of surgery, he was unable to interview all the additional stage II patients. His colleague Dr A F Cooper very kindly saw most of them.

Size of stage II sample receiving radiotherapy.

With a sample of around 70 stage II patients seen from one month onwards, at least 20 patients would be allocated to radiotherapy alone. However, a further 20 or so patients would receive radiotherapy followed by chemotherapy. Their chemotherapy would start after the three month assessment. Therefore, by combining the radiotherapy alone patients with those allocated to radiotherapy plus chemotherapy, at least 40 patients could be assessed before and after radiotherapy. This would have the advantage of increasing statistical power in the comparison with stage I patients on no further treatment. The only drawbacks would be: (1) the radiotherapy plus chemotherapy patients would have to be excluded from the analysis at six months; (2) since patients in that group would know about the impending chemotherapy, conceivably their mood might thereby be affected.

In the light of the results obtained (chapters 4 and 5), the size of the radiotherapy sample was in fact doubled in this way.
Size of postoperative stage I sample

Scrutiny of records showed that roughly equal numbers of stage I and II patients were treated over a given period. However a stage I sample equal to the stage II sample (over 70 patients) was too large to be followed up in the time available. A sample of 40 stage I patients was therefore identified, which seemed large enough for comparisons with stage II patients receiving radiotherapy. There would still be a consecutive general sample of 80 or more patients with stage I or II breast cancer.

Size of control groups and of pre-operative cancer sample

There were far more patients with benign disease than with cancer. In theory a very large benign control group was possible, but again there would have been insufficient time available for follow up. On the other hand patients with benign disease would be younger than those with cancer, so that analysis of results by age was indicated. Thus around 40 control patients with benign disease seemed necessary, to allow them to be divided by age into subgroups of reasonable size.

For a similar reason, in the preoperative period, a sample of around 40 patients with stage I or II cancer was aimed at. To achieve this aim without introducing selection bias, it seemed that the previously decided number of around 40 patients with benign disease would have to be greatly exceeded. This was because benign disease was much commoner than cancer, and the diagnosis was often uncertain until after frozen section biopsy. In some
patients, however, younger age, the clinical nature of the lesion, or both, made a diagnosis of cancer most unlikely. Therefore, after obtaining the desired consecutive sample of 40 patients with benign disease, the author decided to omit preoperative interviews in patients in whom cancer was improbable. This policy worked well; the number of redundant interviews of patients with benign disease was kept to a minimum and no case of cancer was missed.

For statistical reasons it subsequently proved necessary in the post-operative period to obtain a few more patients with benign disease. For practical reasons they had to be recruited pre-operatively. A further eight consecutive patients with benign disease were assessed before surgery and one month thereafter. Because of the pattern of results which was emerging (to be described in chapter 6), it was not thought necessary to follow up the final eight beyond one month.

The cholecystectomy patients were on average closer in age to the cancer patients than were the benign group. It was decided to study a sample of 30 consecutive patients being admitted for surgery.

Data analysis

Data analysis was governed by two main principles. The first was the avoidance of repeated significance testing, such that "significance" might arise by chance alone. The second was not losing relevant information in pursuance of the first. Several groups of patients were analysed over a two year period. A multi-group repeated measures analysis of variance seemed to have
many advantages: comparisons amongst groups and within groups, measurement of interactions, statistical control by the use of covariates, and avoidance of spurious significance. The main drawback was the need for constant numbers within each group over time. Losses to follow-up occurred as a result of deaths and refusals. Deaths occurred mainly in the radiotherapy-alone group. Equal numbers over time could have been achieved only by excluding such patients, or by the dubious process of substituting group means for missing scores. Exclusion of patients who had died would have meant excluding them following relapse, a likely period of suffering. Hence important information would have been lost. Furthermore, much of the data was either of nominal type, or, if interval, markedly skewed. Thus violation of underlying statistical assumptions was possible.

Therefore, the alternative method of performing separate cross-sectional analyses for each time interval was chosen. As a result, no available data were left out. To reduce the risk of spurious statistical significance, analyses were confined largely to comparisons that were of clinical interest; the data were not "combed" for every significant difference. Where possible, tests which allowed for multiple comparisons were chosen.

Data in the chemotherapy trial were analysed on an intention-to-treat basis. All patients were included in the analysis of results regardless of whether they had relapsed or failed to complete chemotherapy. This was so that the results could guide practical decision-making by the clinician.

The main statistical tests used were as follows: for comparisons
among groups, $X^2$ tests, Fisher exact probability tests, one-way (parametric) analysis of variance, Kruskal-Wallis analysis of variance, $t$-tests and Mann-Whitney $U$-tests; for comparisons within groups, paired $t$-tests, McNemar's $X^2$ test for correlated proportions, Cochran's $Q$ test, Friedman analysis of variance and the binomial test. Two-tailed tests were preferred, except where previous research strongly suggested the likely direction of a difference. Thus one tailed tests were used in comparisons of the psychosocial effects of radiotherapy with those of no additional treatment. Further details are given in the appropriate chapters.

Predictors of morbidity were determined by stepwise multiple regression analysis. Variable entry and removal were determined by the default criteria in the Statistical Package for Social Sciences (SPSS-X): a probability of 0.05 for variable entry and 0.1 for variable removal. Plots of residuals were examined to check the adequacy of models, and transformations used if indicated. Results are reported as $R^2$ and adjusted $R^2$. $R^2$ is the proportion of variation in a dependent variable explained by a combination of independent (predictor) variables. $R^2$ varies from 0 to 1; the higher its value, the more successful is prediction. Adjusted $R^2$ is a more realistic estimate of the value of $R^2$ which might be obtained in the population from which the sample was drawn.
Methods in the validity study.

Criteria of morbidity

In the validity study the aim was to compare the performance of the general health questionnaire, its subscales, and the two Leeds scales with valid criteria of morbidity.

In the absence of some physical or biochemical marker, the generally accepted criterion of "caseness" is the judgement of a clinical psychiatrist or trained interviewer using a reliable interview schedule. In the present context, the definition of a "case" seemed arbitrary. If a patient enduring severe side effects from chemotherapy felt very depressed, would she be a "case" or would she be showing an entirely understandable reaction to enormous stress? Also, symptoms such as retardation which might aid case definition were ambiguous in patients with severe physical symptoms.

Consideration was given to applying well-known definitions of caseness which either were available when the study began or shortly afterwards: for example the Feighner criteria, or the Brown and Harris criteria. However, Feighner's definitions of caseness depended partly on ambiguous somatic symptoms, and would not have been suitable unless modified. Brown and Harris defined caseness by saying that "a psychiatrist would not be surprised to see [the woman] in an outpatient clinic". Caseness could be judged by comparing with "anchoring examples" — that is, typical case histories. However, more precise definitions seemed necessary in the present study. Given that definition of a case of depression
or anxiety would have to concentrate on "psychic" symptoms, the simplest method seemed to be one based on degree of morbidity; the following working definitions were adopted.

To examine the validity of the 60-item and 28-item versions of the General Health Questionnaire an observer rating of 2 or more for depression or anxiety was chosen as the criterion for caseness (figure 2-2). This seemed appropriate for scales designed as non-specific case detectors. The observer under activity scale was used to validate the somatic symptoms subscale. In the patients studied the under activity scale was really a global estimate of fatigue rather than a direct measure of somatic symptoms, but seemed likely to reflect feelings of physical dysfunction. The observer depression scale was used to validate the severe depression subscale. On the under activity and depression scales, the criterion chosen for caseness was a score of 2 or above.

The other two subscales of the general health questionnaire measure anxiety/insomnia and social dysfunction. Although the former scale is often used as a measure of anxiety alone, strictly speaking it should be validated against ratings of both anxiety and insomnia. Therefore observer ratings of anxiety and of insomnia were summed to form a seven-point scale to validate the anxiety/insomnia subscale.

The impairment of day-to-day routine observer scale covers social dysfunction and so might have been used on its own to validate the social dysfunction subscale. However, the latter subscale contains items concerned with the performance of tasks or usual activities. Its content was thought to be reflected more accurately by
comparing it with combined observer ratings of day-to-day routine and of performance at work and household tasks. Thus to validate the social dysfunction subscale, scores on the impairment of day-to-day routine scale and the (house)work/child care scale were summed to form a second seven-point scale.

On each of the combined observer scales, a score of 2 or above was again chosen to define caseness.

Validation of the two Leeds scales was more straightforward. An observer depression rating of two or above was used to validate the Leeds depression scale, and an anxiety rating of two or above for the Leeds anxiety scale.

Statistical methods in the validity study

Firstly, correlation co-efficients between observer ratings and self ratings were computed. Correlation coefficients are often used to estimate validity, although it is easy to obtain a statistically significant correlation co-efficient even if classification is poor. Since distributions of the data were skewed, Spearman non-parametric rank order co-efficients were preferred, although for comparison with other work, the Pearson co-efficients were sometimes also calculated. In practice the two co-efficients tend to give very similar results.

For a more precise estimate of the performance of the scales and subscales, sensitivities and specificities were calculated. During the course of the study, the method of receiver operating characteristic (ROC) curve analysis became increasingly popular as
an elegant way of summarizing the effects on classification of
different thresholds of morbidity. In chapter 7 the data are
presented in this form. Used originally to examine observer
variation in detecting radar signals, ROC curves are plots of
sensitivity (on the y-axis) versus (on the x-axis) the false
positive rate (=1-specificity) for every possible threshold score.
Thus an ROC curve shows the discriminating power of the
questionnaire at every possible threshold of morbidity. If the
discrimination is no better than chance, the ROC curve follows the
straight line $y=x$ rising diagonally from the origin. The area
under this line is 0.5. If discrimination is better than chance,
the curve is bowed upwards above the straight line. A perfect ROC
curve would reach right up to the point on the y-axis where
sensitivity is 100%, the false positive rate 0% and the area under
the curve 1.0. In practice this ideal is not achieved. Examination
of the ROC curve allows a decision to be made about the optimal
threshold for morbidity for a given purpose.

Item analyses allowed a more detailed examination of the
performance of the general health questionnaire. Goldberg has
described the method in his Maudsley monograph. An item analysis
shows how well each item of the questionnaire detects different
degrees of morbidity. Certain items might prove to be redundant.
If so, a modified version of the questionnaire might be considered
for use in breast cancer patients.

An example of an item analysed by the method used by Goldberg is
shown below. It shows the percentages of normals, of patients with
mild symptoms and of cases with given GHQ scores. According to the
usual method of scoring, a GHQ score of 2 or 3 means that the item
is endorsed.

<table>
<thead>
<tr>
<th>GHQ score</th>
<th>Gradient</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Have you been feeling run down</td>
<td>Normal</td>
</tr>
<tr>
<td>and out of sorts?</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Case</td>
</tr>
</tbody>
</table>

This item performs well. Less than 10% of normals endorse it, most "cases" endorse it, while an intermediate number of patients with mild symptoms do so. The gradient is the difference between the percentages of normals and cases endorsing the item. For this item the gradient is therefore \((88-8) = 80\).

Ideally several degrees of morbidity rated by observers — for example absent, mild, moderate and severe — would be differentiated by the items of the questionnaire. In practice observers may not be able to agree about all these categories. Thus in the original item analysis of the general health questionnaire Goldberg decided to use three categories only: absent, mild and severe. Patients falling between these categories were excluded. In the present study too few patients were available to allow exclusions. As in the example above, three categories of morbidity were used: absent, mild and "case." "Mild" meant an observer rating of one, while "case" was defined as an observer depression or anxiety rating of two or above. This method would not be expected to give as good discrimination as one which excluded patients who could not definitely be placed in a given group.

Since the Leeds scales are scored differently from the general health questionnaire, the above method of item analysis is not
appropriate. Items in the Leeds scales were analysed by calculating the correlation coefficients between observer ratings of depression and anxiety and relevant items. This was the method used by Snaith et al in the development of the Leeds scales.76

Ideally a validity study would be purpose designed, using a sample known to have a reasonable prevalence of morbidity — for example 30%. A low prevalence of morbidity might make the validity co-efficients unreliable. In the present work, the validity study, being an extension of the main study of the effects of different treatments, had to capitalize on existing data. Although previous work suggested that prevalences of 20% or more could be expected, it was soon apparent that levels of morbidity were often low. A sample of patients with adequate prevalences of depression, anxiety, somatic and social symptoms had to be found. In the event the sample which came closest to this requirement proved to be those stage II patients allocated to chemotherapy alone or combined with radiotherapy, at 13 months after operation, as will be described in chapter 7.

Effect of age on Leeds anxiety scores

A supplementary question which arose during the study will also be examined in chapter 7: the effect of age on Leeds anxiety scores. When designing the Leeds scales, Snaith and his colleagues began with a large pool of possible items. An item analysis was then undertaken to remove those correlated with demographic factors such as age and social class. Therefore the final versions of the two Leeds general scales should not have shown any correlations with age.
However, in a cross-validation study, Snaith and colleagues found an unexpected, significant negative correlation between Leeds anxiety scores and age. On this basis they recommended that in comparing anxiety levels in different age groups, the scores of older patients should be weighted as follows: age <30, add 0 to score; age 30-39, add 1 to score; age 40-49, add 2 to score; age 50-59, add 3 to score; age 60+, add 4 to score. The authors suggested that people became less anxious as they grew older.76

Where allowance for age is necessary in this thesis, the age correction factor has not, however, been applied. In chapter 7 it is shown that in control subjects (benign breast and cholecystectomy) there were no significant correlations between age and uncorrected Leeds anxiety scores; indeed application of the correction factor led to significant positive correlations with age. Thus the age correction factor seemed of dubious validity — perhaps not surprisingly since the significant negative correlation with age noted by Snaith and colleagues should not have arisen in the first place.

In subsequent chapters age is allowed for either by subdividing treatment groups by age, or by constructing matched pairs.
CHAPTER 3:
PSYCHOSOCIAL MORBIDITY PRIOR TO BREAST BIOPSY

The aims of the research reported in this chapter were: (1) to determine how specific to breast surgery is pre-operative psychological morbidity, by comparing women undergoing breast biopsy with those undergoing routine elective surgery; (2) within patients awaiting breast surgery, to identify those most vulnerable to emotional distress.

The selection of patients has been described in chapter two. Three groups of patients were studied: those undergoing frozen section biopsy who proved to have cancer; those who proved to have benign disease; and those awaiting elective cholecystectomy.

Interviews took place on the afternoon or evening prior to the day of surgery, but since the patients were also interviewed after surgery, scores obtained on the Eysenck personality inventory and the Mill Hill test of verbal intelligence were available for most of them. Where appropriate, these scores were also used in the analysis of results.

The cancer patients were older, on average, than those with benign disease. However, the two breast biopsy groups were not matched by age, since the resultant selected groups would not be representative samples of the populations from which they were drawn. Within the two breast biopsy groups, the relationship between age and ratings of psychological distress was examined. Comparisons were then made according to age group. Multiple regression analysis was used in the hope of identifying those
breast biopsy patients most prone to psychological distress. In the cholecystectomy group, associations between physical symptom scores and ratings of psychological morbidity were explored.

RESULTS

Forty-three consecutive patients with benign disease and 48 consecutive patients with cancer were asked to participate in this part of the study. Four in the benign group were excluded (two refused, one did not speak English and one was mentally handicapped). Four cancer patients also refused (Appendix 5), leaving samples of 39 and 44 respectively. A further eight consecutive patients with benign disease were subsequently recruited (this was done mainly to increase the size of the benign group after surgery — see chapter 6). However, these extra patients gave a final sample of 47 in the benign group before surgery. Of 30 women awaiting elective cholecystectomy, none refused to take part.

Table 3-1 illustrates the age differences amongst the three groups. Mean age was lowest for patients with benign disease, intermediate for cholecystectomy patients, and highest for breast cancer patients. Otherwise demographic data for the three groups were similar. The benign group tended to have higher Eysenck personality inventory neuroticism scores than the other groups, though differences were not significant. There was no association between age and Eysenck neuroticism scores in any of the groups.

Table 3-2 shows the results of the observer scales prior to operation. Patients with benign disease were significantly more depressed and irritable than patients with cancer or gall-bladder
disease. The benign group also tended to show more anxiety and loss of libido. The cholecystectomy group showed a trend towards greater lethargy than the other groups. Social dysfunction tended to be higher in the cholecystectomy and benign groups compared with the cancer group.

A similar pattern was seen on the self rating scales (table 3-3). Patients with benign disease were more anxious and depressed than the cancer or cholecystectomy patients, although the differences were not statistically significant. However, the cholecystectomy patients had significantly more somatic symptoms than the other groups. Both they and the benign breast patients showed more social dysfunction than the cancer patients.

The cancer and benign disease patients were then subdivided into two groups: those aged 45 or under and those aged 46 or above (tables 3-4 and 3-5). Cancer patients aged 45 or under were very significantly more anxious, and showed significantly more loss of libido, than cancer patients aged 46 or above. They tended to be more depressed and irritable. In contrast, benign disease patients aged 46 or above tended to be more depressed and had significantly greater social dysfunction, than those aged 45 or under.

Mean physical symptom scores were 0.93 (range=0-4) for the cholecystectomy patients, but only 0.07 and 0.09 for the cancer and benign groups respectively \(p<0.0001\). Table 3-6 shows the nonparametric correlation coefficients between physical symptoms and observer and self rating scales in the cholecystectomy group. All correlations were positive. On observer ratings, correlations were significant mainly for scales with little or no psychic
content. However, on self ratings, there was a significant
correlation between physical symptoms and Leeds anxiety scores.

Prediction of morbidity

Several stepwise multiple regression analyses were performed in
the breast biopsy patients. Independent variables were age, social
class, marital status, work status, previous history of serious
illness, previous psychiatric history (that is, having received
psychotropic medication prior to discovery of breast disease),
religious observance, education, time from discovery of breast
lump to outpatient clinic, time on the waiting list, living alone,
and knowledge of friends or relatives with breast cancer. The
dependent variables were scores on the general health
questionnaire, and on the Leeds depression and Leeds anxiety
scales.

Analyses were performed first for patients with benign disease,
but none of the independent variables predicted morbidity.
Positive results emerged in the cancer group. Table 3-7 shows the
correlation matrix for the 44 cancer patients. Time on the waiting
list (mean=5.3 weeks) was the only variable associated with
increased morbidity as measured by the general health
questionnaire ($r=0.34; \ p=0.025$). There were no predictors of Leeds
depression scores. However, two variables independently predicted
Leeds anxiety scores (table 3-8): age, and a previous history of
having received psychotropic medication. Together, they accounted
for a quarter of the variance ($R^2=0.25$; adjusted $R^2=0.22; \ p<.003$).
Time on the waiting list just failed to reach significance as a
third independent predictor of anxiety.
SUMMARY OF RESULTS: CHAPTER 3

In patients awaiting cholecystectomy, somatic symptoms and social dysfunction were prominent, and there was a significant association between physical symptoms and anxiety.

Patients who proved to have benign disease had the highest levels of psychological morbidity. Social dysfunction was also prominent in this group.

Patients who proved to have cancer, considered as a whole, did not appear to have more symptoms than the cholecystectomy control group.

Within the cancer group, however, patients age 45 or less had high levels of psychological morbidity. Multiple regression analysis showed that a previous history of psychological upset made a further, independent contribution to pre-operative anxiety in the cancer patients.
CHAPTER 4:
THE PSYCHOSOCIAL EFFECTS OF ADJUVANT CHEMOTHERAPY

In this chapter the psychosocial effects of adjuvant chemotherapy are compared with those of radiotherapy. Patients with stage II cancer were randomized to receive radiotherapy, adjuvant chemotherapy or radiotherapy followed by chemotherapy (figure 4-1).

RESULTS

Seventy-nine patients were invited to participate in this part of the study. Five (four in the combined radiotherapy/chemotherapy and one in the chemotherapy alone group) refused to do so (Appendix 5). Of the 74 patients remaining, 24 were allocated to receive radiotherapy, 27 to receive chemotherapy and 23 to receive combined therapy. The treatment groups were similar in respect of age, social class, marital status and previous psychiatric history (table 4-1). During the course of the study, six patients refused further psychiatric interviews (table 4-2). A further six patients refused to continue chemotherapy but agreed to further interviews. Four patients developed local regional recurrence and 15 (20%) disseminated disease. Nine (38%) of the 24 radiotherapy patients had died by 24 months, compared with only six of 50 (12%) in the two chemotherapy groups (p<0.03). Table 4-3 gives sample sizes at each time interval after operation.
Psychological symptoms

Prevalences of symptoms are shown as the percentages of patients scoring above threshold scores for morbidity. In the case of the observer scales, barcharts (figures 4-2 to 4-12) show the percentages with a score of one or above. Barcharts for the self rating scales show the percentages scoring above the relevant threshold for morbidity (these thresholds are discussed further in chapter 7). The actual numbers of patients scoring above the threshold are also given, at the base of each bar.

The prevalences of depression, anxiety and behaviour upset (irritability) measured by the observer scales are illustrated in figure 4-2. The prevalences of depression and anxiety at one month following mastectomy in the radiotherapy-alone group were 33% and 38% respectively, both falling to 14% at one year. The prevalences of anxiety and depression in the two chemotherapy groups were similar at one, three and six months. At 13 months, however, there was an excess of depression (p<0.1), and a significant excess of anxiety (p<0.05) in the chemotherapy groups.

At one month the prevalence of behaviour upset in the radiotherapy group was 13%, and 22% in both the chemotherapy groups. At one year, the prevalence in the radiotherapy group was only 5% compared with 25% and 27% in the two chemotherapy groups. This difference was nearly significant (p<0.07, using Fisher's exact probability test with the two chemotherapy groups combined, because of small expected frequencies).

At 18 months, prevalences of depression, anxiety and irritability
fell in the two chemotherapy groups, but there was an apparent increase in morbidity in the radiotherapy-alone group. However, examination of individual scores showed that virtually all the morbidity in that group occurred in patients with systemic relapse. All five patients with systemic disease scored positively for depression or anxiety, compared with none of the disease-free survivors (p<0.001). Only one of the five was still alive at 24 months.

Figure 4-3 shows the prevalences of morbidity as measured by the 60-item general health questionnaire and two of its subscales — anxiety/insomnia and severe depression. Figure 4-4 shows prevalences on the Leeds depression and anxiety scales. The pattern is similar to that seen on the observer scales. There were no significant differences among groups up to six months after surgery. At 13 months on the 60-item general health questionnaire, on the anxiety/insomnia subscale and on the Leeds anxiety scale, there was a trend towards more morbidity in the two chemotherapy groups compared with the radiotherapy group, though differences were not significant. However, on both the severe depression subscale and the Leeds depression scale, there was a significant excess of morbidity in the two chemotherapy groups (using Fisher's exact probability test with data from the two chemotherapy groups combined, because of small expected frequencies).

In the second year, prevalences measured by the self rating scales generally fell. There was no clear rise in morbidity in the radiotherapy group at 18 months, but two of the five radiotherapy patients with systemic relapse had felt too ill to complete self rating scales.
Somatic and social problems

Figure 4-5 shows the observer ratings of under activity, routine upset and work/housework problems. The pattern on all three scales is similar. At one and three months after operation, there were no significant differences among groups. At both six and 13 months, morbidity in the radiotherapy group was lower than in the two chemotherapy groups. On the routine upset scale, these differences were statistically significant. In the second year, morbidity in the chemotherapy groups lessened. However, at 18 months in the radiotherapy group, there appeared to be a slight peak in morbidity, similar to that seen on the observer depression, anxiety and behaviour scales.

Results of the somatic and social dysfunction subscales of the general health questionnaire are shown in figure 4-6. As with the observer scales, there were no significant differences among groups up to three months. At six months, the radiotherapy patients tended to show more morbidity relative to the other groups than they did on the corresponding observer scales. However, at 13 months, results were similar to the observer scales: both chemotherapy groups experienced more morbidity than the radiotherapy group. Using 3 by 2 $\chi^2$ tests, these differences were not significant, but when the results for social dysfunction were re-analysed by Kruskal-Wallis analysis of variance, the differences were significant at less than the 5% level. In the second year morbidity was mostly lower than during the first year.
Loss of libido

In figure 4-7 loss of libido is seen to be similarly distributed among the three treatment groups.

Results for larger cohort of patients

Since an additional series of stage II patients had been seen for the first time at 13 months, it was of interest to merge it with the preceding sample to provide results for a larger group of 112 patients. Table 4-4 shows the demographic data for the additional patients and table 4-5 the new sample sizes at the three time intervals during the second year.

Results for the larger cohort are shown in figures 4-8 to 4-12. On the whole they confirmed those from the smaller cohort. Results at 13 months for the 60-item general health questionnaire and for the observer under activity scale became statistically significant.

Population estimate of degree of morbidity associated with chemotherapy.

The larger sample gave an opportunity to estimate the theoretical extent of morbidity in the population from which it was drawn. Since the two groups allocated to chemotherapy were, by one year, essentially similar, they were merged for this purpose. Of 76 patients allocated chemotherapy alone or after radiotherapy, 15 (20%) scored 2 or more on the observer depression scale. The 95% confidence intervals were 11-29%. The proportions classified as depressed by both the severe depression subscale of the general
health questionnaire and the Leeds depression scale were identical: 28%, with 95% confidence intervals of 18-38%.

So in round terms around a quarter of patients intended to complete chemotherapy at 13 months after operation were clinically depressed. This percentage would have been marginally higher had those patients not completing chemotherapy been excluded.

In the radiotherapy alone group, the prevalences of depression were very low at 13 months: 6% of 36 patients scored 2 or more on the observer scale; none scored above the threshold on the severe depression subscale and only 3% above the threshold on the Leeds depression scale. These prevalences were too low to allow the calculation of valid confidence intervals. (For example, the "95% confidence intervals" for 6% of a sample of 36 were -2% to 14%).

Further information on levels of morbidity, based on a sample of mixed stage I/II patients, is given in Chapter 6.

**Conditioned reflex symptoms.**

In the cohort of patients allocated chemotherapy (alone or after radiotherapy) who were first seen at 13 months after mastectomy, it was found that several had felt sick or vomited before their injection of chemotherapy. After repeated drug-induced nausea and vomiting, they had begun to feel sick or vomit in response to previously neutral stimuli, such as the sight or smell of the hospital and medical equipment such as syringes or needles. As will be discussed further in chapter 8, these symptoms appeared to arise from a classical Pavlovian conditioning process. In the
cohort first seen at 13 months, the occurrence of conditioned reflex symptoms was not recorded systematically and figures for their prevalence would probably be an underestimate. However, the stage II patients seen prospectively from one month onwards were always asked about conditioned reflex symptoms; the prevalences reported below should therefore be accurate.

Three months after operation two patients who had received radiotherapy alone and three receiving chemotherapy alone were experiencing conditioned reflex nausea without vomiting. Thereafter this problem ceased in patients who had received radiotherapy alone. At six months in both groups allocated to chemotherapy 15 of 46 (33%) patients had conditioned reflex nausea and six (13%) conditioned reflex vomiting. At 13 months, in those 46, the prevalence of conditioned reflex nausea and vomiting had risen considerably, the corresponding figures being 27 (59%) (p<.002) and 16 (35%) (p<.01). Furthermore, conditioned reflex symptoms persisted beyond cessation of treatment. At 18 months, 11 of 41 (27%) had conditioned reflex nausea and three (7%) conditioned reflex vomiting. Even at 24 months, seven of 39 (18%) still had conditioned reflex nausea.

As in the cohort first seen at 13 months, the conditioned stimulus was most often something in the hospital environment, but anything associated with the administration of chemotherapy might subsequently of itself induce nausea or vomiting. One woman vomited when she saw a member of the clinic staff in a shop. Other stimuli included clothes worn or perfume used whilst attending for treatment, or the mere thought of treatment. Where possible patients sought to avoid experiencing such stimuli again. A year
after completing treatment, a 31-year-old patient talked of her "sick coat". She had worn it during treatment, but now it was hidden at the back of her wardrobe, to stop her feeling sick again. Another patient who had completed chemotherapy tried to remove what she experienced as the nauseous smell of the hospital from some of her clothes by washing them repeatedly. After her attempts had failed she threw the clothes away.

Physical symptom scores

Physical symptom scores among groups (table 4-6) were similar up to three months after operation, but at six and 13 months were significantly higher (p<0.001) in the two chemotherapy groups. At 18 months the trend was reversed (p<0.1), reflecting systemic relapse in the radiotherapy-alone group.

Relationship between mood and physical symptoms

To what extent were the anxiety and depression of chemotherapy associated with physical symptoms? This question was examined in the 40 patients who actually completed the chemotherapy course. Inclusion of the six who did not finish treatment (and who experienced very few dysphoric or physical symptoms) would have obscured the meaning of any correlations found. Table 4-7 shows the Spearman correlation coefficients between ratings of mood and physical symptoms in these 40 patients at 13 months after mastectomy. Coefficients were first calculated for the total physical symptom score and then for the commoner individual physical symptoms, namely nausea, vomiting, irritation of mucous membranes, and alopecia.
There were modest positive correlations between all ratings of mood and the total physical symptom score, and also between mood and nausea. None was statistically significant. However, correlations between ratings of mood and vomiting, and between mood and irritation of mucous membranes, tended to be larger and several were significant. In contrast, correlations between ratings of mood and alopecia were all negative. Indeed the negative correlation between observer anxiety and alopecia was just significant at the five per cent level.

**Relationship between mood and conditioned reflex symptoms**

There were several positive correlations between mood and conditioned reflex symptoms (table 4-8). For conditioned nausea the correlations were larger than for conditioned vomiting. All but one of the correlations with nausea, but only one of those with vomiting, were significant.

An association between mood and conditioned reflex symptoms might merely reflect two other associations: that between mood and physical symptoms; and the inevitable association between conditioned reflex symptoms and physical symptoms (conditioned symptoms being dependent on pre-existing nausea and vomiting). A comparison was therefore made between the nine patients who had nausea or vomiting without any conditioned reflex symptoms, and the 29 patients who had nausea or vomiting combined with either conditioned reflex symptom (tables 4-9 and 4-10).

Table 4-10 shows that despite the small numbers, there was a
strong trend for the patients who had conditioned reflex symptoms to have greater mood disturbance than those who did not. This trend was statistically significant for the Leeds depression and anxiety scales. The two groups did not differ significantly in age. (In chapter six it will be shown that there was a significant negative correlation between age and morbidity at 13 months.)

Other correlates of conditioned reflex symptoms.

Thus both mood and the length of time on treatment were related to conditioned reflex symptoms. Were any other patient variables significantly associated with liability to conditioned reflex symptoms? A search for additional correlates, by cross-tabulations and breakdown of demographic and other background data (see proforma) with conditioned reflex nausea and vomiting was negative. In particular, no relationship could be shown with Eysenck Personality Inventory scores. The mean (SD) Eysenck neuroticism score in patients without conditioned symptoms was 9.3 (4.7); in those with conditioned symptoms it was 8.9 (5.7). For extraversion the corresponding figures were 10.9 (2.7) and 11.1 (3.6).

Other correlates of mood disturbance.

Mood disturbance in patients receiving chemotherapy was associated positively with physical symptoms, except for hair loss. What other factors influenced liability to mood disturbance?

The examination of this question is deferred until chapter 6, where predictors of morbidity at 13 months after mastectomy are
examined in a larger sample of 79 stage I and II patients. (The multiple regression analyses reported in chapter 6 show that the main independent predictors of morbidity at 13 months were age, Eysenck neuroticism scores, previous scores on the questionnaires measuring mood, and treatment with chemotherapy.)

Patients' opinions of their treatment.

The patients' responses to the question "How do you feel about your treatment", recorded verbatim at the six month assessment, are given in Appendix 6. Clearly there were more adverse comments about chemotherapy than about radiotherapy. One patient stated that chemotherapy was the worst thing that had ever been thought up. She said that the clinic had been nicknamed "Belsen" because chemotherapy made people look like the victims of a Nazi concentration camp.

Patients in the combined radiotherapy/chemotherapy group were asked to compare the two forms of treatment. All but two of the 23 patients were already in no doubt that the adverse effects of chemotherapy were worse than those of radiotherapy (p<.001 — binomial test). Of the two patients who did not think that chemotherapy was worse, one said that the two treatments were about equal and the other that radiotherapy was worse. By 13 months, however, the latter patient had become depressed and reversed her previous opinion about the two treatments.
Other observations.

A few patients on chemotherapy reported that they felt low for a few days after each injection. This feeling did not always last long enough to qualify for a depression rating of 1.

Chemotherapy was the only treatment to induce suicidal thoughts, which usually occurred at the point in the treatment cycle when physical toxicity was maximal. Such thoughts were not persistent. With the exception of one patient with a long history of endogenous depression antedating mastectomy, no patient required admission to a psychiatric ward.

Several patients reported that in the days preceding each visit to the chemotherapy clinic they became anxious because they feared further conditioned reflex symptoms.

On the other hand some patients derived a sense of security from the fact of getting treatment and regular check-ups at the clinic. For that reason, some had mixed feelings about stopping treatment.

While loss of libido was not significantly different among the three treatment groups, three patients on chemotherapy reported unaccustomed pain on intercourse which they related to the treatment. This problem seemed to stem from the adverse effect of chemotherapy on mucous membranes. Two patients reported anxieties about contraception, being afraid they might conceive a child malformed by chemotherapy.
SUMMARY OF RESULTS: CHAPTER 4

Psychosocial symptoms were assessed over two years in a randomized trial of three forms of treatment following mastectomy for Stage II breast cancer. The treatments were: (1) three weeks of radiotherapy; (2) one year of adjuvant cyclophosphamide, methotrexate and 5-fluorouracil; (3) radiotherapy followed by chemotherapy. Analysis of the results on an intention-to-treat basis showed no appreciable differences among groups in depression or anxiety at one, three and six months after operation. However, at six months significantly more patients allocated to chemotherapy reported disturbance of their daily routine.

At 13 months, patients who had been allocated to chemotherapy (alone or after radiotherapy) showed significantly more depression, anxiety and social dysfunction than control patients treated with radiotherapy alone. About a quarter of patients in the two chemotherapy groups were clinically depressed. Conditioned reflex nausea and vomiting increased markedly during the second six months of chemotherapy, and persisted for up to a year thereafter.

Mood disturbance was significantly more likely to occur in patients subject to drug-induced vomiting and irritation of mucous membranes. However, alopecia was not associated with increased mood disturbance. There was a positive association between mood upset and conditioned reflex nausea and vomiting.

Mood disturbance also seemed linked to systemic recurrence of cancer.
CHAPTER 5:
THE PSYCHOSOCIAL EFFECTS OF POSTOPERATIVE RADIOTHERAPY

In this chapter the psychosocial effects of radiotherapy after mastectomy are investigated. Psychosocial morbidity in patients with stage II breast cancer who received post-operative radiotherapy was compared with that in patients with stage I cancer who received no further treatment after mastectomy.

In chapter 2 it was pointed out that to increase statistical power, the stage II patients who received radiotherapy and those who received radiotherapy followed by chemotherapy were merged for comparison with the stage I patients. A possible drawback was that morbidity in the radiotherapy followed by chemotherapy group might have been affected by knowledge of impending chemotherapy. However, the results reported in chapter 4 showed that at one and three months, morbidity did not differ significantly in the patients who received radiotherapy alone and those who had chemotherapy in addition. Therefore it seemed justifiable to merge the groups in this way, and to refer to the combined group as the "radiotherapy group". Obviously, the patients who went on to receive chemotherapy had to be excluded from the analysis after the three month assessment.

RESULTS

Forty-three stage I and 51 stage II patients were invited to participate in this section of the study. Four in each group refused to do so (Appendix 5). Table 5-1 shows that the demographic and other background data for the two groups were
Tables 5-2 and 5-3 show the scores on the observer and self rating scales at one and three months after operation for patients allocated to radiotherapy or to no further treatment. At one month, prior to treatment, there were only minor differences between the two groups, none of which was significant. At three months, patients who had completed radiotherapy two to three weeks previously showed significantly higher observer scores for lethargy (p<0.001) and routine upset (social dysfunction) (p<0.04) than those not so treated. They also scored significantly higher on the general health questionnaire p<0.04) and on its somatic symptoms subscale (p<0.05). They tended to score higher on the social dysfunction subscale (p<0.07).

At six months, observer ratings showed that the marked trend towards excess lethargy in patients who had received radiotherapy was maintained (table 5-4). These patients scored higher on the general health questionnaire (p<0.04) and on the somatic symptom subscale (p<0.04) (Table 5-5). Neither observer nor self ratings demonstrated any excess of anxiety or depression in the radiotherapy group.

By 13 months, the trend towards excess lethargy and somatic symptoms in patients treated with radiotherapy had stopped. Although there were no significant differences between groups on any of the scales, there was a slight trend towards more anxiety and depression in patients not given radiotherapy.

Physical symptom scores (Table 5-6) were similar at one month
after operation, but at three months were markedly higher in the radiotherapy group (p<0.001). Thereafter there were no significant differences between the groups.

To determine whether psychological morbidity in the radiotherapy group at three months was associated with physical symptoms, Spearman correlation coefficients between ratings of morbidity and physical symptom scores were calculated (table 5-7). All but one of the coefficients were positive, but only three approached significance on two tailed tests: those with behaviour upset, with the somatic symptom subscale of the general health questionnaire, and with the social dysfunction subscale. All three were significant using one tailed tests. However, the scattergram of the physical symptom score with behaviour upset showed that the positive correlation was largely due to the influence of a single outlying point, namely a patient with a behaviour score of 2 and a physical symptom score of 6. There were no such influential points in the scattergrams of physical symptoms with somatic symptoms and social dysfunction. Thus there was no convincing relationship between physical symptoms and ratings of mood; rather, physical symptoms seemed to be associated with somatic and social dysfunction.

**Conditioned reflex symptoms**

Two patients who had felt sick during radiotherapy experienced conditioned reflex nausea on re-entering the treatment centre. In both patients this symptom was mild and short-lived; neither had conditioned reflex vomiting.
Patients' opinions of their treatment.

The verbatim responses of the radiotherapy patients to the question, "How do you feel about your treatment?" are given in Appendix 6. Five of 23 patients described radiotherapy as having been "very severe", "very unpleasant", "very rough", "horrible" and "terrible".

Some patients told the author that they had been frightened by the radiotherapy machine. Two stated they could never go through the treatment again. A few had been distressed by seeing patients with advanced cancer. One patient feared radiotherapy might cause long-term physical harm.

However, at least half of the 23 had no particular complaints about their treatment. Reassurance by the radiographers seemed to have allayed the fears of some of them. One patient said she felt insecure after completing her treatment because she was no longer getting frequent check-ups. Psychological upset associated with radiotherapy was mostly short lived but occasionally resulted in increased ratings of anxiety at three months.

Most non-radiotherapy patients interpreted their lack of post-operative treatment favourably, but there were exceptions. A few became anxious in the context of not receiving further treatment. For example, one patient feared her illness was too serious to justify any further intervention. She experienced acute anxiety leading to a panic attack which she interpreted as a sign of metastatic disease. Unlike the radiotherapy patients, she attended the outpatient clinic only every six months and several weeks elapsed before she was reassured.
SUMMARY OF RESULTS: CHAPTER 5

Psychosocial morbidity was compared in 47 patients who received post-operative radiotherapy and 39 who received no further treatment after mastectomy.

One month after operation, prior to radiotherapy, there were no significant differences between the two groups on any of the measures of psychosocial morbidity.

At three months, patients who had completed radiotherapy had significantly more somatic symptoms and social dysfunction than those not so treated. At six months the radiotherapy group continued to show more somatic symptoms. A year after operation, there were no significant differences between groups.

Several patients receiving radiotherapy were seriously upset by their treatment. While somatic symptoms were the main problem, some patients experienced anxiety, usually short-lived. This anxiety was not associated with physical symptoms and appeared to stem partly from environmental factors in the radiotherapy department. However, occasional node negative patients, who were seen infrequently after surgery, were not reassured in the absence of post operative treatment and also became anxious. Overall, results failed to confirm that depression and anxiety were commoner in patients who received radiotherapy than in those who received no further treatment.
In this chapter psychosocial morbidity is examined in more detail in a consecutive sample of 90 patients with stage I or II breast cancer. This more general sample comprised firstly: 39 patients with stage I cancer, who served as the control group for the radiotherapy study reported in chapter 5; secondly, 51 patients with stage II cancer. The latter group consisted of the first 51 of the 74 patients in the chemotherapy study reported in chapter 4. The final 23 of the 74 were excluded because after the first 51 the author had stopped recruiting new patients with stage I cancer. If the final 23 had been included, the sample would not have been drawn from a truly consecutive series of patients with stage I/II breast cancer.

The aims of the more detailed analysis were:

(1) To obtain more precise estimates of the levels of morbidity over a two-year period. This would allow comparisons with the results of other researchers who had studied samples of stage I and II breast cancer.

(2) To seek factors contributing independently to morbidity in this group. An association between chemotherapy and psychological morbidity has already been shown. If other factors contributed to morbidity, patients liable to problems could perhaps be identified.
Handling of control groups.

Before these analyses, a decision was necessary on how to allow for the age differences between the cancer patients and those with benign or gall bladder disease, already noted in chapter 3 (pre-operative results). In particular, the age difference between the cancer and benign groups was unexpectedly large (difference between means = 15.9 years). Although the method of analysis by age could be different from that reported in chapter 3 — the benign group was now a control group instead of an experimental group — it was thought important to avoid any method which selected a biased subsample of the cancer patients. Such bias would obscure estimates of levels of morbidity. Subject to this constraint, two main methods were considered for the cancer/benign comparison.

The first was to examine the effect on age in the cancer and benign groups separately, by scattergrams and correlation coefficients, and make appropriate allowance for the results obtained. The second was by constructing matched pairs, a method which would increase statistical sensitivity. To avoid bias in the cancer group, this matching could be done by selecting only from the benign group.

However, no final decision was made until some preliminary analysis had been undertaken. The original pre-operative sample of patients with benign disease had comprised 39 patients. Of these 34 agreed to be seen at one and three months, and 30 at 13 months.

Firstly, levels of morbidity in the benign group were compared at
the three assessments (tables 6-1 and 6-2). On all measures there were no significant differences in morbidity with time. Next the correlation coefficients between age and and the various measures of morbidity were calculated (table 6-3). None of these was significant, except for an isolated correlation between age and the observer rating of (house)work problems. These results suggested: (1) a single assessment in the benign group would have been sufficient; (2) since mood disturbance in the benign group did not vary with age, depression and anxiety in cancer patients of any age could be compared with that in the benign group.

However, the latter conclusion was not altogether justified because the age difference between the benign and cancer patients was so large. There were few patients aged over 50 in the benign group, and since a majority of cancer patients were aged over 50, a comparison between them and the benign group was of dubious validity. The same problem (too few older patients in the benign group) also affected attempts to construct matched pairs by selecting patients solely from the benign group.

One solution would have been to recruit more patients with benign disease, but to allow enough matches for the older cancer patients, a very large sample would need to have been screened. So a compromise solution was adopted. The cancer patients were split into those aged 50 or above (n=59) and those aged under 50 (n=31). A further eight consecutive patients with benign disease were recruited, giving a total of 42 at one month after surgery. It was then possible to extract from the 42 a subsample of 31 patients which matched the cancer patients aged under 50 for age, social class and marital status. Matching was exact for marital status,
within five years for age, and within one point on the Registrar General's 5-point scale for social class.

This solution meant there were no matches for the older cancer patients. However, the subdivision of the cancer patients by age meant that the older cancer patients could be compared with the younger cancer patients.

Since the cholecystectomy patients were closer in age to the cancer patients, it seemed reasonable simply to establish that within the cholecystectomy group there were no significant correlations between age and morbidity (table 6-4) and then compare that group as it stood with the cancer patients. (The correlation coefficient for age with Leeds depression scores (0.37) approached significance, with a probability of 0.06. However, inspection of the relevant scattergram showed that the coefficient was inflated by a single outlying point; correlations for the two other measures of depression were negligible.)

Results for the cancer group.

Of the 90 cancer patients who agreed to help with this part of the study, 11 died and 11 refused further follow-up over the two years. One of the 90 was unavailable at the one-month interview but was included subsequently. On two occasions, patients felt too ill to complete self-rating scales. The 51 patients with stage II disease received post-operative radiotherapy (n=17), a year's course of adjuvant chemotherapy (n=22) or a combination of both (n=12); the 39 with Stage I disease received neither.
The mean (SD) age of the 90 cancer patients was 53.7 (10.4) years. Sixty-nine (77%) were married, 2 (2%) divorced, 13 (14%) widowed and 6 (7%) never married. Thirty-four (38%) were drawn from social classes I and II, 44 (49%) from social class III and 12 (13%) from social classes IV and V. Twenty-one (23%) gave a history of treatment for nervous complaints from their general practitioner, and a further 5 (6%) reported previous treatment by a psychiatrist. Demographic data for the benign and cholecystectomy groups have already been given in chapter 3.

Overall morbidity in the cancer patients.

Results were first calculated to show the proportion of all cancer patients with clinical depression and anxiety (namely observer ratings of two or above) at all assessments (table 6-5). No more than 8% of patients were clinically depressed or anxious at any time in the two years after mastectomy, with the exception of clinical anxiety at one month (15%). Likewise the upper 95% confidence limits never exceeded 14%, except for 22% in the case of anxiety at one month. Clinical morbidity was very low in the second year.

Minor morbidity (observer ratings of 1) was common. The prevalences of minor depression at 1, 3, 6, 13, 18 and 24 months were respectively 32%, 24%, 13%, 20%, 15% and 13%. For minor anxiety, the corresponding figures were 21%, 19%, 19%, 27%, 19% and 13%.
Effects of age on morbidity.

Table 6-6 shows results of all the observer scales at one month. Here the cancer patients are subdivided into those aged under 50 (n=31, mean age=41.6) and those aged 50 or above (n=58, mean age=60.2). The former group is compared with 31 matched control subjects with benign disease.

Psychological symptoms — depression, anxiety and irritability — were significantly commoner in cancer patients aged under 50 compared with the control subjects with benign disease and also compared with cancer patients aged 50 or above. Loss of libido was more severe than mood disturbance, being especially common in younger cancer patients. However, about a fifth of married patients aged 50 or above reported total loss of sexual appetite following mastectomy.

The pattern of results for non-psychic symptoms, namely under activity, change in daily routine (social dysfunction) and problems with work and household tasks was different. Whilst the younger cancer patients had more problems than the matched controls, there were no significant differences between the two cancer age groups. The older cancer patients showed a trend towards more serious problems with work and household tasks.

Results of the self rating scales at one month (table 6-7) were similar to those of the observer scales. On the 60-item General Health Questionnaire, the cancer patients aged under 50 scored significantly higher than the matched controls, and higher than the older cancer patients. The same pattern of scores (high
morbidity in the younger cancer patients compared with the matched controls and compared with the older cancer patients) occurred on the Leeds depression scale and on both measures of anxiety. Differences for anxiety were statistically significant, or nearly so, using two-tailed tests.

Results of the social dysfunction subscale also resembled closely the observer findings. The younger cancer patients scored very significantly higher than the benign group but both groups of cancer patients had high scores.

At three months (tables 6-8 and 6-9), the younger cancer patients continued to score significantly higher on measures of depression and anxiety, compared with the older cancer patients, but again there were no significant differences for non-psychic symptoms (under activity, routine and work upset, and somatic symptoms). Loss of libido was significantly commoner in younger cancer patients.

These tables also show morbidity in the cholecystectomy group. On the whole levels of depression and anxiety in this group were lower than in the younger cancer patients, and comparable with levels in the older cancer group.

At six months (tables 6-10 and 6-11) the pattern was similar to that at three months, although for purely psychic symptoms, differences between the younger and older cancer patients were significant only on the observer depression and the Leeds anxiety scale. There was also a significant excess of somatic symptoms in the younger cancer patients.
The effect of age on several of the measures of morbidity was still evident at 13 months (tables 6-12 and 6-13). There was a trend towards more depression in the younger cancer patients. The cancer patients aged under 50 showed significantly more anxiety than those aged 50 or above. However, there were no clear differences in symptoms of clinical degree (observer ratings of 2 or above). Sexual problems, though less common than at one month, remained an important source of morbidity.

The full results at 18 and 24 months, subdivided by age, are shown in tables 6-14 to 6-17. At 18 months (tables 6-14 and 6-15) all measures of depression or anxiety, except the Leeds depression scale, continued to show a strong trend (significant or nearly so) towards greater morbidity in the younger patients. However, by 24 months this trend was confined to measures of anxiety.

Unlike depression and anxiety, loss of sexual appetite continued to be prominent in the second year after operation. At 18 months in married patients, 23% of those aged under 50 and 10% of those aged 50 or above reported moderate to severe loss of libido; at 24 months the corresponding figures were 21% and 10%. The first of these age differences was statistically significant.

**Effects on employment.**

At the time of mastectomy, 36 of the original 90 patients had paid employment (24 full-time and 12 part-time). The extent to which they resumed work is shown in table 6-18. The category "full hours" refers to those patients who had resumed, or virtually
resumed, their usual pre-operative working hours. "Reduced hours" refers to patients whose usual working hours were cut substantially (for example, by half).

The full hours category includes certain patients on chemotherapy who were usually off work on their injection day, and often the following day. Generally employers helped them by rescheduling work to fit in with the twice monthly chemotherapy injections, and overall their working time was little affected, if at all. It seemed best to include them in the full hours category.

Table 6-18 shows that by 6 months, most patients had resumed work, and of these only a few had had to reduce their normal working hours substantially. At 18 and 24 months, about four fifths of patients were working, none with reduced hours. One patient was not working because her employer's factory had closed down, and another who for some time had been thinking of giving up work decided to do so after her operation. Otherwise, it was clear that treatment for breast cancer had directly caused loss of work.

Independent predictors of morbidity at 13 months

Several stepwise multiple regression analyses were performed to determine more precisely the factors contributing independently to morbidity at one year. The independent variables included age, social class, marital status, work status, previous history of serious illness, previous psychiatric history, religious observance, education, intelligence, knowledge of friends or relatives with breast cancer, follow-up treatment received and scores on self rating scales at one month after operation. The
dependent variables were scores on the General Health Questionnaire, on its subscales, and on the Leeds depression and anxiety scales at one year. Seventy-nine patients completed these scales. The correlation matrix is shown in table 6-19.

Table 6-20 shows the results of the multiple regression analyses obtained using the default criteria in the Statistical Package for Social Sciences (SPSS-X). In these analyses the variables were untransformed, with a probability of 0.5 for variable entry and 0.1 for variable removal. The main predictors of morbidity at one year after mastectomy appeared to be scores on the self rating scales at one month, Eysenck neuroticism scores, age and treatment with chemotherapy. Prediction seemed best for depression and anxiety.

However, inspection of plots of residuals showed that for the 60-item general questionnaire and two of its subscales (somatic symptoms and severe depression), the distribution of the residuals deviated from normality (figures 6-1 to 6-3). During the study it had become apparent that scores on the 60-item GHQ and these two subscales often had a positive skew. This was especially so in the case of the severe depression subscale.

The anxiety/insomnia and social dysfunction subscales usually had distributions quite close to normality, but the distribution of residuals for the social dysfunction subscale was not ideal (figure 6-4).

Accordingly, the regression analyses for the 60-item general health questionnaire and the somatic symptoms, severe depression
and social dysfunction subscales were repeated after transformation of the dependent variables. For the 60-item questionnaire and its somatic symptoms subscale, scores were transformed by adding one and then calculating the Naperian logarithms. (Adding one avoided the problem of the logarithm of zero.) The behaviour of the residuals improved (figures 6-5 and 6-6).

In the case of the severe depression subscale, standard transformations (square root, addition of one followed by taking Naperian logarithms, common logarithms or reciprocals) had only a marginal influence on the distribution of the residuals. However, a more extreme transformation, namely taking the fourth root, seemed reasonably effective (figure 6-7).

The peaked distribution of residuals for the social dysfunction subscale was also somewhat resistant to standard transformations; the least unsatisfactory was adding one and taking Naperian logarithms (figure 6-8).

The results for the regression analyses using the transformed dependent variables are given in table 6-21. On the whole the transformations improved the models. In the case of the 60-item general health questionnaire, three extra predictive variables (Eysenck neuroticism, treatment with chemotherapy and verbal intelligence) entered the equation, and the proportion of variance explained almost doubled. An extra variable (treatment with chemotherapy) also entered the equation for social dysfunction, though the increase in variance explained was small. There were no new variables in the equation for somatic symptoms, but again a
slight increase in variance explained. Results for the severe depression subscale were essentially unchanged.

The final regression equations are set out in table 6-22. The coefficients for the independent variables were positive, with two main exceptions: those for age and social class. However, in the equation predicting the 13 month Leeds depression score, there was a counter-intuitive negative sign in front of the one month GHQ-60 score. Likewise in the equation for the 13 month severe depression score, the one month Leeds anxiety score had a negative sign. These two negative signs occurred despite adequate tolerances for the relevant independent variables. In both cases they were the last variables to enter the equation and their omission would have had only a minor effect on the variance explained. Inspection of residual plots and partial plots for the final equations suggested there were no serious violations of the assumptions of homogeneity of variance and linearity in the models.

These analyses therefore confirmed that the consistent predictors of psychosocial morbidity continued to be the ratings of morbidity at one month, Eysenck neuroticism scores, age and treatment with chemotherapy.

SUMMARY OF RESULTS: CHAPTER 6

Psychosocial morbidity was examined in 90 consecutive patients aged under 70 with Stage I or II breast cancer. In the two years after mastectomy, the prevalences of depression and anxiety of clinical degree were low: under 10%, except for clinical anxiety at one month (15%). Confidence intervals showed that the
prevalences of clinical morbidity in the population from which the sample was drawn were probably under 15%, except that anxiety at one month might have been as high as 22%. However, cancer patients aged under 50 showed significantly higher prevalences compared with cancer patients aged 50 or above and compared with matched control subjects with benign breast disease. Social and work problems were common at all ages. Sexual problems were more severe than mood disturbance. Patients at risk of mood disturbance one year after operation could be predicted by combinations of age, Eysenck neuroticism scores, self ratings of mood at one month after operation, and whether or not they were receiving chemotherapy.
CHAPTER 7:
PERFORMANCE OF THE SELF RATING SCALES

This chapter contains an analysis of the performance of the self rating scales used in this study: the general health questionnaire and its subscales; and the Leeds general scales for the self assessment of anxiety and depression. These scales are compared with observer ratings.

As outlined in chapter 2, a sample with reasonably high prevalences of morbidity (depression, anxiety, somatic symptoms and social dysfunction) had to be found. The sample closest to this ideal was the series of stage II patients (reported in chapter 4) who were completing (or were intended to complete) chemotherapy at 13 months after operation.

There were 45 patients allocated to chemotherapy alone or combined with radiotherapy who had been followed up prospectively from one month onwards and who completed self rating scales at 13 months. However, an additional 30 similar patients had been assessed for the first time at 13 months, mostly by Dr A F Cooper, allowing a total sample of 75 to be used.

RESULTS

The mean age (SD) of the 75 patients was 51.2 (11.0) years. Fifty (67%) were married, 2 (3%) separated or divorced, 10 (13%) widowed and 13 (17%) never married. The social class distribution was: I - 2 (3%); II - 26 (35%); III - 36 (48%); IV - 7 (9%); V - 4 (5%). Nineteen (25%) reported previous treatment for psychological
symptoms by their general practitioner, and a further 3 (4%) had been treated by a psychiatrist. Forty-eight of the 75 patients were interviewed by the author and 27 by Dr A F Cooper.

**Results for the general health questionnaire**

Table 7-1 shows the Spearman rank-order correlation coefficients between observer scores and the general health questionnaire and its subscales.

Figure 7-1 shows the Receiver Operating Characteristic (ROC) curves for the 60-item and 28-item general health questionnaire scales. Since the ROC curves are bowed considerably above the diagonal, both versions of the questionnaire performed much better than chance. The areas under the curves, found by counting 1mm squares on graph paper, were 0.97 (60-item) and 0.98 (28-item).

Since ROC curves are subject to sampling variation, standard errors were calculated for the plotted points. Each point has two standard errors, one in the horizontal plane and the other in the vertical plane. Some of the percentages corresponding to these points (for example 0% and 100%) were either too small or too large for meaningful standard errors. However, examples of more valid standard errors were 9.0% in the vertical plane and 3.7% in the horizontal plane for the point where sensitivity was 87% and false positive rate 8%. Likewise where sensitivity was 80% and the false positive rate 3%, the standard errors were 10.7% (vertical) and 2.2% (horizontal). The other standard errors which could reasonably be measured were of similar size. Standard errors in the vertical plane were larger than those in the horizontal plane.
because the sample of cases (15) was smaller than that of non-cases (60).

Some of the sensitivities and specificities corresponding to these ROC curves are shown in tables 7-2 and 7-3. On the General Health Questionnaire 60-item scale, with a threshold score of 12 or above to define morbidity, sensitivity was 100% but specificity only 76% (table 7-2). Doubling the threshold score to 24 or above caused the sensitivity to fall to 87% but the specificity to rise to 97%.

For the 28-item version of the General Health Questionnaire (table 7-3) doubling the threshold score to 10 or above gave the best discrimination between cases and non-cases.

Figures 7-2 and 7-3 show the ROC curves for the four subscales of the General Health Questionnaire. Although the curves deviate considerably from the diagonal, those for the somatic symptoms subscale and the social dysfunction subscale seem less close to the ideal than those for the anxiety/insomnia or severe depression subscales. The areas under the ROC curves were 0.82 (somatic symptoms), 0.90 (anxiety/insomnia), 0.85 (social dysfunction) and 0.81 (severe depression).

Table 7-4 shows sensitivities and specificities corresponding to the ROC curves for the subscales. As defined by the observer ratings, there were 22 cases of under activity (somatic symptoms), 23 of anxiety and insomnia, 27 of social dysfunction and 14 of depression. A cut-off score of 6/7 discriminated between cases and non-cases on both the somatic symptoms subscale and on the anxiety and insomnia subscale. The cut-off score for the severe depression
subscale was 2/3, and for the social dysfunction subscale 7/8. For both the anxiety/insomnia and severe depression subscales, sensitivity and specificity were satisfactory. For the other two subscales specificity was somewhat low, and could not be improved without losing sensitivity.

Item analysis of the general health questionnaire

The full item analysis of the general health questionnaire is set out in Appendix 8. Three items were found to be poor discriminators among groups. They were numbers 5 ("pains in head"), 6 ("tightness or pressure in head") and 19 ("frightening or unpleasant dreams").

It was also clear that many items did not discriminate very well between normal patients and those with minor morbidity. If poor discrimination is defined arbitrarily as a difference of less than 10% in the proportions of normals and those with minor morbidity endorsing a given item, then in 21 items discrimination was poor. These items were the three already cited plus numbers 8 ("afraid of collapse in public place"), 21 ("managing to keep busy and occupied"), 27 ("managing as well as most people in your shoes"), 31 ("feeling warmth and affection for those near to you"), 32 ("finding it easy to get on with people"), 34 ("afraid to say anything to people in case you made a fool of yourself"), 36 ("capable of making decisions about things"), 38 ("dreading everything you have to do"), 40 ("couldn't overcome your difficulties"), 46 ("able to face up to your problems"), 48 ("feeling people were looking at you"), 52 ("life entirely hopeless"), 53 ("hopeful about own future"), 54 ("reasonably
happy, all things considered"), 57 ("thought of the possibility that you might make away with yourself"), 58 ("couldn't do anything because your nerves were too bad") 59 ("wishing you were dead and away from it all") and 60 ("found that the idea of taking your life kept coming into your mind").

This list includes five of the seven items of the severe depression subscale. The remaining items in the list did not seem to show a particular pattern, except that several concerned relationships with other people.

Eight items were endorsed by more than 10% of normals. These were numbers 1 ("perfectly well and in good health"), 2 ("in need of a good tonic"), 7 ("been able to concentrate on whatever you're doing"), 9 ("having hot or cold spells"), 10 ("perspiring (sweating) a lot"), 15 ("been feeling mentally alert and wide awake"), 16 ("feeling full of energy") and 22 ("taking longer over the things you do"). Only the last two of these were endorsed by more than 15% of normals.

Differentiation between normals and cases was better. Only 13 items (numbers 5, 6, 13, 19, 31, 34, 48, 51, 52, 56, 57, 58 and 60) had gradients of less than 40. These items included six of the seven in the severe depression subscale. However, all items of the severe depression subscale had a gradient of at least 20, and four had a gradient of more than 35.
Results for Leeds scales

Table 7-5 shows sensitivities, specificities and false positive rates for the Leeds depression and anxiety scales. As defined by observer ratings, there were 14 cases of depression and seven of anxiety. The recommended cut-off score of seven or above for both scales did not need to be changed.

Table 7-6 shows several correlation coefficients: observer ratings of depression with Leeds depression total score and with Leeds depression items; observer ratings of anxiety with Leeds anxiety total score and with Leeds anxiety items. All coefficients were highly significant.

For depression the correlation coefficient with the item on appetite was low. For anxiety the correlations with the items on anxiety out of the house and with palpitations ("butterflies") were also low.

Effect of age on the Leeds anxiety scale.

In chapter 2, Snaith's recommendation that in comparing Leeds anxiety levels in different age groups, the scores of older patients be weighted, was discussed. In all the results presented so far, unweighted Leeds anxiety scores were used. In chapter 6, where the effect of age on morbidity was examined, the pattern of the unweighted Leeds anxiety scores closely resembled that of the two other measures of anxiety: observer ratings and the anxiety/insomnia subscale of the general health questionnaire. For that reason alone it seemed better not to use the age correction.
factor.

However, a stronger reason was that in both control groups after surgery, the correlations between age and unweighted Leeds anxiety scores were not significant. In the benign group at one and three months, the values of Spearman's rho were 0.06 (n=42) and 0.04 (n=34). In the cholecystectomy group at three months, the value was 0.11 (n=26). After the scores had been weighted by the age correction factor, the three coefficients all became significantly positive: respectively 0.34 (p<0.03), 0.34 (p<0.05) and 0.45 (p<0.03).

SUMMARY OF RESULTS: CHAPTER 7

The performance of the General Health Questionnaire as a case detector was assessed in 75 patients allocated to chemotherapy for early breast cancer. The questionnaire and its subscales were found to be valid when compared with observer ratings. The misclassification rate of the 60-item version of the questionnaire was lowest when the standard threshold score for clinical morbidity was doubled to 24. It was lowest for the 28-item version when the threshold score was doubled to 10. Suggested threshold scores for clinical morbidity for the subscales are: anxiety and insomnia subscale 6/7; severe depression subscale 2/3; somatic symptoms subscale 6/7; and social dysfunction subscale 7/8.

The performance of the Leeds general scales for the self assessment of depression was also examined in the same patients. The recommended threshold scores (6/7 for both depression and anxiety) appeared to be satisfactory.
Morbidity prior to breast biopsy

The results reported in chapter 3 lend some support to the belief that breast biopsy patients are more vulnerable than general surgical patients to pre-operative morbidity. It was notable, however, that patients with cancer, considered as a whole, did not seem more anxious or depressed than control patients who had undergone cholecystectomy. Patients with benign disease appeared to be the most distressed. However, when cancer patients were subdivided by age, a marked excess of anxiety was evident in those patients aged 45 or less. Multiple regression analysis confirmed the strong negative relationship between age and anxiety in cancer patients, and showed that a previous history of psychological upset made a further, independent contribution to pre-operative anxiety.

Some of these results were unforeseen. While anxiety was anticipated in both the cancer and benign groups, the author expected firstly that it would be of lesser degree in patients with benign disease, of whom fewer faced a definite threat of early death; and secondly that in both groups anxiety levels would be higher in younger patients, for whose families premature death would be especially serious. The finding that in the benign group anxiety was high and did not decline with age suggested that a proportion of this anxiety was not due to admission for breast biopsy, but to some other characteristic of the patient sample.
The benign group was a consecutive series of patients with benign lumps, and was likely to have been adequately representative of patients presenting with benign lumps to their general practitioners, who could be expected to refer all of them to outpatient clinics. However, a bias towards anxiety in patients attending clinics could have occurred if these patients possessed personality traits such as anxiety or hypochondriasis which would render them more liable to notice lumps or to consult their doctors. A high Eysenck neuroticism score would be in keeping with this view. A less likely explanation would be that the patients were not self-selected and that there was an association between benign breast disease and anxiety due to factors other than knowledge of a breast lump. Conceivably, neuro-endocrine factors in the hypothalamus or pituitary might predispose to both benign breast disease and anxiety. Alternatively, anxiety through a neuro-endocrine mechanism might actually increase the size of benign breast lesions and make them clinically apparent.93

The variable results of some of the early controlled studies have been discussed fully in chapter 2. Greer and Morris found similar levels of depression in patients found to have cancer and those with benign disease. Anxiety was not measured. However, in a more recent study of similar patients, Morris et al, using the Spielberger self rating scale, showed that anxiety was slightly higher in patients with benign disease (n=43) than in patients with cancer (n=21).94 In the cancer group, anxiety was notably low in younger patients — the exact opposite of the results of the present study. The authors suggested that a greater threat to life and a greater awareness of cancer among younger patients might provoke the psychological defence of denial, so that anxiety would
not be manifest. However, they thought this explanation was unlikely, since it was not clear why denial should only occur in younger cancer patients. But equally there seems no reason why the low anxiety in the present series of older cancer patients should have been due to denial.

Maguire et al found that in the period between attendance at the outpatient clinic and breast biopsy, distress was significantly higher in cancer patients than in those with benign disease. Schonfield found an excess of anxiety only in those cancer patients aged 42 or less.\(^{66}\)\(^ {63}\)

On the other hand, in a series of 56 consecutive patients Wirsching (1982) found that anxiety was significantly higher in patients with benign disease than in those with cancer, the cancer group experiencing little or no anxiety.\(^ {55}\) In the same year Gottesman and Lewis reported that mean pre-operative scores for depression and anxiety were virtually identical in 15 patients with early breast cancer and 15 women undergoing elective surgery.\(^ {96}\) The results of these two studies resemble those of the author.

Of interest is the recent finding of Hughes et al that patients attending a breast clinic and proving to have benign disease had experienced an excess of depression in the previous year, compared with those with cancer and also when compared with the general population.\(^ {93}\) Depression in their benign group was associated with recent life events and social difficulties. The authors concluded that the somatic complaints of patients with benign breast disease might be secondary to psychiatric disorder. The present results
are consistent with this finding. The benign group, like theirs, also showed a trend towards excess social dysfunction.

The positive associations between physical symptom scores and ratings of psychosocial morbidity in the cholecystectomy group require comment. Correlations between symptoms such as vomiting or pain and, for example, lethargy are to be expected since all are associated with chronic cholecystitis. The significant correlation between physical symptoms and general health questionnaire scores might also be due, at least in part, to the many somatic and social items in the questionnaire. However, the significant association between physical symptoms and Leeds anxiety scores cannot be so explained because there are no somatic items in that scale. It is possible that anxious patients are more liable to report nausea, vomiting and pain, but it is more likely that physical symptoms provoke anxiety. Certain patients reported spontaneously that bouts of pain made them frightened. Hence physical distress may have contributed to some of the anxiety prior to admission for gall-bladder surgery. This possibility seems to have received little attention in previous research.87 98 Anxiety due to physical distress would decrease differences in anxiety scores between cholecystectomy and breast biopsy patients, since the breast biopsy patients experienced negligible physical upset. In keeping with previous work, a few cholecystectomy patients expressed fears of the anaesthetic or other physical procedures, and two were afraid they might have cancer; but malaise and fatigue were much more striking clinically than anxiety or depression.

Thus results in the pre-operative period were not entirely
clearcut. However, manifest ps malignant disease is a frequent
awaiting biopsy of malignant lesions may be less common than was
sometimes been supposed. Despite the interval section procedure,
which may provoke more anxiety than the needle biopsy which is
replacing it, most cancer patients aged over 65 (numerically a
large group) did not report serious morbidity. In the minority —
those aged 45 or less — it remains to be confirmed whether needle
biopsy would reduce the marked excess of anxiety.

Results for the benign group supported the belief that patients
presenting with benign breast disease may be especially liable to
psychological morbidity. If so, these patients might not be an
ideal control group in the post-operative period.

The cholecystectomy control group, chosen because it would provide
reasonable numbers of female patients who had not been on the
waiting list for a prolonged period, was imperfect. Although these
patients were regarded as "cold" cases, the degree to which
several of them would experience malaise and pain was not
anticipated; pain may have increased anxiety slightly. However, no
group would be ideal in controlling for the effects of routine
surgery.

Psychosocial effects of adjuvant chemotherapy

Whether adjuvant chemotherapy actually achieved its aim of
improving survival was until recently uncertain. A meta-analysis
of the results of clinical trials of adjuvant chemotherapy in some
10000 patients has now shown that it reduces early deaths in
postmenopausal patients by about one sixth and in premenopausal
patients by about one third. Clearly, however, the effect on survival is modest; many patients die despite the treatment. Hence its psychosocial effects continue to be relevant.

Recent reports on the psychosocial effects of chemotherapy

When this thesis was started, there were no published reports on the psychological effects of adjuvant chemotherapy after mastectomy. Preliminary results of the thesis, showing a significant excess of depression in chemotherapy patients a year after surgery, were published in abstract form in 1979 and 1980. Subsequently, two randomized controlled studies from the United Kingdom, likewise providing a single estimate of morbidity during treatment, also suggested that adjuvant chemotherapy was associated with increased emotional distress.

Palmer and colleagues found that nine of 24 (37%) patients who had completed a six month course of five-drug chemotherapy reported severe disruption to their lives compared with two of 21 (9%) receiving the single agent chlorambucil. Twenty-nine per cent of those who had received the five-drug combination said that the treatment was unbearable or could not be gone through again.

Maguire and colleagues judged that 20 of 26 (77%) patients receiving cyclophosphamide, methotrexate and 5-fluorouracil (CMF) for one year had experienced anxiety or depression compared with 9 of 18 (50%) having no treatment, and that of 15 receiving melphelan, four (27%) had experienced anxiety and five (33%) depression. Some of these patients, who were assessed by reliable interview methods at three and 12-18 months after
mastectomy, received psychiatric treatment during a counselling project. It is not entirely clear whether the results obtained were based on the three month assessment, when the patients would still be receiving chemotherapy, or on that at 12-18 months, when treatment would be complete — or, indeed, whether the results were calculated in some other way. These two studies caused doubts to be expressed as to whether adjuvant chemotherapy could be justified.103 105

In the United States, adjuvant chemotherapy has been more widely adopted as routine treatment. Probably for that reason, quantitative controlled studies of its psychological effects were lacking until very recently.10 However, in an uncontrolled study based on a single structured interview, Meyerowitz and colleagues (1979) noted that in 50 breast cancer patients undergoing adjuvant treatment with CMF, up to 80% experienced emotional distress, and up to 88% behavioural disruption, in five life areas: marriage and family, sex, financial situation, general activity level and work-related activity level.106 In a follow-up study of 35 of these patients, the authors found that patients took on average 6.4 months to "return to their old selves".107

A more recent uncontrolled study of similar patients by Knobf (1986) also suggested that distress persisted beyond treatment. Of 78 patients (a selected sample drawn from private oncology practices and from a university hospital clinic) those who had finished treatment were more upset by loss of the breast and about the uncertainty of survival than those still receiving chemotherapy. Knobf suggested that a delayed reaction to loss of the breast and a loss of security from receiving treatment might
be responsible. Some support for this opinion comes from the early results of a controlled study by Cassileth and colleagues (1986) comparing self-rated anxiety levels in 68 mastectomy patients randomised to CMF plus prednisolone (CMFP), or to observation only. Assessments over one year showed no significant differences between the two groups, but there was a trend towards higher anxiety levels in patients not given adjuvant treatment. The authors thought that allocation to observation only might induce anxiety, whilst active treatment might have a placebo effect. The results are not altogether comparable with other studies of the psychological effects of CMF, since steroid hormones may affect mood, and levels of depression were not reported. However, the trend towards anxiety in patients given no further treatment is similar to that found in Maguire's chemotherapy study and consistent with the results for the stage I patients reported in chapter 5.

One other study from the United States seemed to suggest that morbidity in patients with breast cancer treated with adjuvant chemotherapy was low. Silberfarb and colleagues (1980) reported that early morbidity in such patients was less than in those treated with radiotherapy. The authors wondered if chemotherapy might induce psychological morbidity at a later stage in treatment. However, reliable conclusions cannot be drawn from this study because the chemotherapy sample comprised only seven patients.
Conditioned reflex symptoms

Recently conditioned reflex nausea and vomiting have also been described by North American researchers. However, before this work is discussed, a question arises: were the pre-treatment nausea and vomiting experienced by patients in the present study genuine conditioned reflex symptoms?

These symptoms only occurred after a variable duration of post-treatment nausea or vomiting. They became more frequent with repeated exposure to chemotherapy injections, but less frequent after chemotherapy was stopped. Sometimes they generalized to stimuli outwith the hospital, for example the smell of organic chemicals similar to those used in the hospital. They could occur in response to the thought of treatment. These patterns fit with classical Pavlovian conditioning: the unconditioned stimulus being the administration of CMF (leading to nausea or vomiting) and the conditioned stimulus being anything just before its administration — usually the sight or smell of the immediate surroundings. Second order conditioned stimuli and generalization are a natural sequel.

However, it could be argued that anticipatory nausea was merely a manifestation of anxiety rather than a conditioned response. But the author found that patients seemed able to distinguish between the kind of nausea they might experience in response to anxiety, and the kind of anticipatory nausea they recognised was peculiar to chemotherapy treatment, and took account of this in recording conditioned symptoms.
In the first of the North American reports, Neese and colleagues studied patients receiving chemotherapy for lymphomas. They found that the prevalence of conditioned reflex nausea was related to dose and duration of chemotherapy. Subsequently, Morrow studied 225 patients receiving several regimes of chemotherapy for a variety of cancers. Anticipatory nausea or vomiting occurred in 47%, a prevalence of 21%. Morrow used the word "anticipatory" rather than "conditioned reflex" to avoid implications about cause, but thought that a conditioning mechanism was likely. Multiple regression analysis showed that independent predictors of conditioned reflex symptoms were: the severity of post-treatment nausea and vomiting; the length of time from the treatment pulse to the point at which post-treatment symptoms were most severe; and treatment with cisplatin. In contrast to the results of Neese and colleagues, and those of the author, Morrow believed that if patients developed conditioned reflex symptoms, they would do so within four months of starting treatment.

One recent study has described conditioned reflex vomiting in patients receiving CMF for breast cancer. Wilcox and colleagues compared the incidence of this symptom in patients randomized to low dose and high dose CMF in a clinical trial. They found that 59% of 22 patients on high dose CMF had anticipatory vomiting compared with only 14% of 29 on low dose CMF. The pooled incidence was therefore 33%. Those who developed post-treatment vomiting before the fourth cycle of treatment were significantly more likely to develop conditioned reflex symptoms eventually. Anticipatory vomiting was commoner when post-treatment vomiting was severe. However, not all patients entering the clinical trial were included by the authors and symptoms were recorded.
retrospectively, based on notes made by clinic staff. Thus the incidences reported may not be strictly accurate.

Comment on the present study: psychosocial effects of chemotherapy

In the present study, repeated assessments over two years allowed a detailed review of the psychosocial cost of CMF. There were no significant differences among treatment groups up to three months after mastectomy, but by six months patients on chemotherapy alone or in combination had suffered more upset to their daily routine than those treated with radiotherapy alone, and conditioned reflex symptoms were common. Those receiving combined therapy were already almost unanimous that chemotherapy was the more unpleasant treatment.

Adjuvant chemotherapy had its main psychosocial impact during the second half of intended treatment. Depression, anxiety, social dysfunction and conditioned reflex symptoms peaked at one year, even though over a tenth of patients did not complete CMF. Conditioned reflex symptoms continued beyond the first year. Depression may also have persisted in minor degree. However, most patients allocated chemotherapy escaped systemic relapse in the second year. Unlike the radiotherapy-alone patients, they were spared much of the emotional and physical distress associated with recurrent disease.

(Although in the radiotherapy group patients with recurrent cancer were significantly more distressed than those free of disease, a precise estimate of the morbidity due to recurrent disease would require a larger patient sample. However, Silberfarb and
colleagues, comparing patients with breast cancer at three phases of the disease — initial treatment, first recurrence and final illness — found a significant excess of depression at first recurrence compared with the other two phases. More recently, Hopwood has reported that at least a third of patients presenting with advanced breast cancer may have psychological morbidity amenable to treatment.

The peak of psychological morbidity during the second half of CMF, and some of the after-effects, could almost certainly be prevented if courses of treatment were restricted to about six months. Since Bonadonna and colleagues have shown recently (1985) that six months of adjuvant CMF is probably as effective as 12, there seems little justification at present for longer courses of CMF.

Several questions remain unanswered. While psychological morbidity could be greatly reduced by shortening courses of chemotherapy, it is unclear whether the lifetime psychological cost to the patient due to adjuvant chemotherapy would thereby become similar to that due to radiotherapy alone. The precise lifetime cost could only be determined by indefinite follow-up of a very large series of patients. Much would depend on the varying effects and timing of relapses, further treatments and deaths after the first two years. These matters are complex. Although the present study and that of Silberfarb and colleagues show, not surprisingly, that recurrent disease is distressing, treatment given for systemic relapse may sometimes reduce morbidity. Thus Baum and colleagues (1980) found that chemotherapy given for systemic relapse enhanced well-being, despite physical toxicity, provided remission occurred. The psychological effects of chemotherapy may vary
according to the stage of disease at which it is prescribed.

Significantly more patients died in the radiotherapy-alone group compared with the two chemotherapy groups. Given that the object of the study was to determine the psychosocial cost of allocation to follow-up treatment, those who believe that death is not the end of experience might want to consider metaphysical questions: does death stop any further suffering? Is it better to be dead than miserable from chemotherapy?

Such questions can only be considered theoretically (one could hardly employ a medium as research assistant!) If it were assumed that the dead patients all had "average ratings of morbidity", including them in the analyses would not change the results — the analyses would be valid as performed. If they were assumed to have no morbidity whatsoever (the after-life either being non-existent or consisting of eternal happiness), the results might be different but not the conclusions since there would still be less morbidity in patients allocated to radiotherapy alone compared with the chemotherapy groups. Only if it were assumed that after death the radiotherapy-alone patients had suffering above average might the conclusions be different.

These considerations might seem farcical, but death and its meaning were treated very seriously by some of the patients. Two women in the radiotherapy alone group who knew they were dying told the author that they had lost their religious faith. Others re-examined their beliefs about death and after-life.

At a more tangible level, the study did not address the
psychosocial cost of chemotherapy to the patients' families. There could be no doubt that family members were often upset by the effects of chemotherapy on the patients, and sometimes also by seeing them die despite a year of arduous treatment. But whether the total amount of morbidity in the relatives of those treated with chemotherapy would be higher than in the relatives of those treated with radiotherapy (who tended to die sooner) is unclear. In theory this question, at least, is answerable, but practical measurement would be difficult.

Mechanisms whereby psychological morbidity developed.

What features of the chemotherapy régime caused patients to become depressed or anxious? The design of the study does not allow formal scientific answers, but there are certain pointers.

Depression and anxiety were associated with certain physical symptoms, especially vomiting and irritation of mucous membranes. This association might be interpreted in several ways. Firstly, patients with mood disturbance might be more likely to notice, experience or report physical symptoms. Secondly, unpleasant physical symptoms might induce reactive mood change. Thirdly, physical symptoms and mood change might have a common cause, namely the metabolic changes induced by chemotherapy. Chemotherapy might affect the brain either directly or through some intermediate metabolic disturbance. In either case the mood change would be endogenous.

The first explanation — increased sensitivity to physical symptoms — does not seem an important mechanism. If mood change
made patients more likely to report physical problems, one would have to explain why they should report vomiting and irritation of mucous membranes but not hair loss.

However, it would not be surprising if vomiting and irritation of mucous membranes — both very unpleasant symptoms — induced reactive mood change. Some patients said that post-treatment vomiting was emotionally upsetting. Alopecia also seems sufficiently unpleasant to induce mood change; yet the two were not positively related. But mostly the patients were warned about hair loss, which unlike vomiting is not debilitating, and good wigs were provided.

(There was a single negative association between hair loss and mood, significant at the five per cent level, which is hard to explain, but possibly in the context of many significance tests, it was really a chance finding.)

Conditioned reflex symptoms also seemed to be a source of distress, greater than that associated with nausea or vomiting alone. Conditioned reflex symptoms and their relation to mood are discussed more fully below.

Was there any pointer to metabolically-induced mood change? Occasionally patients reported feeling depressed in the days immediately after each injection. Although this could be interpreted as a depressive reaction to attending the clinic, these patients seemed to recognise that this mood change had a different quality compared with how they ordinarily felt when depressed. This suggested it had an organic basis. Recently Devlen
and colleagues have reported a similar finding in patients receiving chemotherapy for malignant lymphoma; they also thought an organic mechanism might have been responsible.\textsuperscript{119}

How might chemotherapeutic agents induce organic mood change?

The basic metabolic principles of CMF therapy are reasonably clearcut. After conversion to active metabolites, cyclophosphamide acts as an alkylating agent which probably exerts its effect by cross-linking, within cells, the two strands of deoxyribose nucleic acid (DNA). It may also damage DNA in other ways. Methotrexate inhibits the synthesis of folic acid, while 5-fluorouracil, a fraudulent pyrimidine, interferes with nucleic acid synthesis. Hence cell proliferation is inhibited in three different ways. However, the detailed metabolism of these drugs is complex, and much is not understood.\textsuperscript{120}

The induction of vomiting by these drugs — a subject which has been studied in some detail — illustrates some of this metabolic complexity. Firstly, the three drugs vary not only in their emetic potency — cyclophosphamide being the most potent, followed by 5-fluorouracil and then by methotrexate — but also in the onset time and the duration of vomiting. Secondly, there are several neural pathways (probably involving several neurotransmitters) whereby these drugs stimulate the vomiting centre in the brain stem. Their action on the vomiting centre cannot be explained solely in terms of stimulation of the chemoreceptor trigger zone (on the surface of the medulla at the area postrema) and subsequent transmission of impulses via dopaminergic neurones to the vomiting centre. Other inputs to the vomiting centre — for
example, from the gut and from the forebrain, may be relevant. Histamine, cholinergic substances and enkephalins may be implicated as neurotransmitters in the emetic actions of cytotoxic drugs. Furthermore, additional pathways must exist to mediate nausea and its autonomic accompaniments.\textsuperscript{121}

Given the seemingly wide range of actions of cytotoxic drugs and their metabolic derivatives in the brain stem and elsewhere, it is easy to imagine that they might somehow upset neurotransmitters concerned with mood, albeit perhaps indirectly. Brain stem disturbance due to encephalitis or motor neurone disease is a well-recognised cause of emotional lability. However, large numbers of neurotransmitters are now recognised.\textsuperscript{122} Their potential interactions are so complex that it is extremely difficult to make any definitive statement on the neurochemical basis of mood, farless speculate on how chemotherapy might upset the balance.

Nonetheless, methotrexate is known to have a direct effect on brain cells. Although only 1-2\% of plasma methotrexate enters the brain, depletion of folic acid has been found in the brain cells of both humans and animals treated with prolonged low-dose methotrexate.\textsuperscript{120} Deficiency of folic acid has been linked to depression in humans, although the direction of the association and its specificity to depression rather than to other psychiatric illnesses must remain in some doubt.\textsuperscript{123-126}

Other organic mechanisms may be relevant, for example the release of cell breakdown products into the circulation. More recently, Dykes and her colleagues have shown, in the same chemotherapy
trial which was the basis of this thesis, that there was an excess of certain viral infections in the patients treated with chemotherapy. Subclinical viral infection could cause depression.

Treatment with CMF also depresses ovarian function. Hormonal disturbance might upset mood either metabolically or psychologically in that premenopausal patients knew that their periods had stopped and might not return. This might partly explain why psychological morbidity tended to be greater in patients aged under 50.

Although many of the above comments are speculative, both endogenous and reactive factors seem relevant to mood change associated with adjuvant chemotherapy. Their precise nature and contribution are very hard to disentangle, and must be the subject of future research.

The relation between mood and conditioned reflex symptoms

There appeared to be an association between mood and conditioned reflex symptoms which was independent of the corresponding physical symptoms. Patients with conditioned reflex nausea or vomiting showed greater mood disturbance than those with drug-induced nausea or vomiting but no conditioned reflex symptoms. However, this result has to be viewed with some caution. Since the severity of drug-induced nausea and vomiting was not recorded, the patients with conditioned reflex symptoms might have had more severe drug-induced symptoms than those without conditioned reflex symptoms. In this case the true association
would be that between mood and severity of drug-induced symptoms.

Indeed the studies of Morrow and of Wilcox and colleagues, \(^{112, 113}\) quoted above, showed that conditioned reflex symptoms were more likely if post-treatment nausea or vomiting was severe. Nonetheless, an independent association between mood and conditioned reflex symptoms is not ruled out in the present study. Some patients were very upset by conditioned reflex symptoms which, unlike the corresponding drug-induced symptoms, seemed to them to imply the social stigma of being mentally unsound. Also, some clearly became anxious in anticipation of conditioned reflex symptoms.

Patients often had mixed feelings about attending the chemotherapy clinic. On the one hand they sought, and often obtained, reassurance about their disease from the clinic staff; but on the other hand the same staff also administered the very unpleasant treatment. This may have been a source of emotional conflict. In some ways their position is analogous to that of the dogs in Pavlov's laboratory who were rewarded with food after seeing a circle but got nothing after seeing an ellipse. When the circle and the ellipse were progressively altered until the dogs could not distinguish between them — that is, the stimulus was ambiguous — they showed great distress. \(^{115}\) Clinic staff may have become an ambiguous stimulus for the patients, though there must be some doubt about extrapolating from experimental neuroses in dogs to humans.

Overall, it seems that conditioned reflex symptoms probably had at least some direct effect on mood. However, underlying mood
disturbance might affect susceptibility to conditioned reflex symptoms, and a combination of mechanisms is possible.

It was of interest that there was no relation between Eysenck personality inventory scores and liability to conditioned reflex symptoms. Eysenck once maintained that introverts were more readily conditioned than extraverts. However, in the light of criticism by other researchers, he later modified this theory: introverts would condition more readily than extraverts provided three requirements were met. Firstly, a partial (intermittent) reinforcement schedule should be used. Secondly, the unconditioned stimulus had to be weak. Thirdly, the interval between the conditioned and unconditioned stimulus had to be less than half a second. These provisos attempted to take account of relative differences in postulated "excitation" and "inhibition" in the brains of introverts and extraverts. In the present study, the first of these requirements may partly have been met because some patients attended the hospital for checks without necessarily receiving chemotherapy. Probably the third requirement was met but not the second because an injection of drugs seems a strong stimulus.

However, the lack of association between introversion and conditioned reflex nausea and vomiting tends to confirm that Eysenck's earlier theory needed qualification.
Psychosocial effects of radiotherapy

In chapter 2 it was concluded that studies prior to 1978 strongly suggested that radiotherapy after mastectomy was associated with increased psychological morbidity. More recent research has tended to confirm this finding. Forester and colleagues studied 200 men and women undergoing radiotherapy for a variety of tumours. They did not say how many had cancer of the breast. About half were treated by the betatron — a large noisy machine — while the rest were treated by the much quieter linear accelerator. Dysphoric mood as measured by Spitzer's Schedule for Affective Disorders was marked in both groups initially. Thereafter it became less in those treated by the linear accelerator but increased in the betatron group. Differences in diagnosis between groups did not account for this result; as in the study of Peck and Boland, reported in chapter 2, the patients were frightened of the betatron.

More directly relevant is the paper of Holland and colleagues who studied 20 patients undergoing six weeks of radiotherapy after mastectomy for stage II breast cancer. There were no control subjects, but detailed assessments of mood were made before treatment, during treatment and towards its completion. Depression and hostility were found to increase significantly during treatment — as in Forester's patients treated by the betatron. Anxiety about mutilation decreased significantly. The authors thought that the increase in dysphoria in their patients might be due to factors other than the treatment machine. They suggested it might be a reaction to the side effects of treatment, such as anorexia and fatigue, or else stem from the prospect of no longer
being reassured from receiving treatment and being monitored closely by the clinic staff, after completion of radiotherapy.

Shortly afterwards Silberfarb and colleagues published a paper (already referred to in the discussion on chemotherapy) of which the main purpose was to compare morbidity at different stages of breast cancer: primary treatment, first recurrence and final illness. However, 14 of the primary treatment group received post-operative radiotherapy. The authors reported that the radiotherapy patients experienced distress specific to that treatment (for example from being forced to confront cancer by attending the radiotherapy centre).

These papers and some of the research cited in chapter 2 therefore suggested that radiotherapy might induce morbidity in the following ways: (1) via frightening machines; (2) by physical side effects; (3) by forcing patients to think about cancer or to contemplate lack of continuing support after treatment. However, support during treatment might reduce morbidity.

Comment on the present study: effects of radiotherapy

In the present study the first and third of these mechanisms clearly operated in some patients; but there was no convincing connection between the side effects of radiotherapy and mood.

The design of the study also enabled the psychological effects of the prospect of radiotherapy to be assessed. One month after mastectomy, more than a third of all patients reported depression, anxiety or social dysfunction, and well over half some degree of
lethargy or inability to work. However, there were no significant differences on any of the measures of psychosocial morbidity between those patients who were due to receive radiotherapy and those who were not. Knowledge of impending treatment did not seem to cause excess morbidity.

Although the findings reported in chapter 5 leave no doubt that the ensuing radiotherapy caused psychological morbidity in a minority of the patients studied, there was at three months no significant excess of depression or anxiety in the radiotherapy group compared with the no treatment group. However, at three months (two to three weeks after completing treatment) almost two thirds of the radiotherapy group were found on observer ratings to have been lethargic over the previous few weeks, compared with less than a third of the control group. Nearly half of the radiotherapy patients had experienced routine upset compared with just over a third of those who did not receive radiotherapy. Results of the self rating scales were in keeping with those of the observer ratings.

There were likewise no significant differences in depression or anxiety at six and thirteen months. Whilst the available sample of patients treated with radiotherapy was smaller from six months onwards, it was of sufficient size to demonstrate that a significant excess of somatic symptoms persisted at six months.

Could the excess of somatic symptoms observed at three and six months in patients treated with radiotherapy have been a psychological rather than a physical effect of treatment? While psychological stress might induce somatic symptoms even in the
absence of overt depression or anxiety, there seems no reason why patients treated with radiotherapy should be any more likely to manifest psychological stress as somatic symptoms than patients not so treated. Thus the excess of somatic symptoms probably had a physical basis. For similar reasons, the excess of social dysfunction noted at three months in radiotherapy patients seems unlikely to have been psychogenic. Nearly all the radiotherapy patients had to travel to hospital five days every week and often to restrict other activities because of physical symptoms. That their daily routine was disrupted is hardly surprising.

Since patients treated with radiotherapy all had Stage II cancer, whilst those not so treated had Stage I cancer, results might conceivably reflect severity of disease rather than treatment with radiotherapy. However, this possibility seems unlikely. Stage II disease might affect patients in two main ways. Firstly, the patients might realise that their disease had a relatively poor outlook. Secondly, there is a remote chance that an excess of micrometastases could alter mood physiologically. In either case, increased depression or anxiety would seem likely. Yet in spite of this potential bias, no excess of psychological morbidity was found in Stage II patients.

The failure to show that radiotherapy induced an excess of depression or anxiety at any time in the first year after operation was unexpected. Could it have been due to inadequate statistical power? Conceivably, larger samples might have shown differences, but results suggest that any such differences would have to be small. Because the hypothesis tested was that radiotherapy would induce more psychological morbidity than no
further treatment, one-tailed significance tests were used. These are twice as sensitive as two-tailed tests. Moreover, the tests picked up the differences in somatic and social symptoms fairly consistently, but never any differences in depression or anxiety. This suggests that if there were any real differences in mood they would be less important than those in somatic or social dysfunction. Continuing somatic discomfort up to six months after operation did not appear to induce significant emotional upset in the radiotherapy patients, despite suggestions that fatigue induced by radiotherapy might be an important source of emotional distress.63 131

Another possible reason for the lack of differences in mood might be the timing of assessments. The three month observer assessments, which covered the preceding month, did not normally include the first week of the radiotherapy course. Ideally, an extra assessment a few days after radiotherapy had started, and a corresponding assessment in the no further treatment group, would have been made; but it is very doubtful if the patients, especially those in the control group, would have tolerated being seen more often. Furthermore, the self rating scales covered the previous "few weeks". From the comments patients made while filling in these questionnaires, it was clear that fear at the beginning of radiotherapy was sometimes reflected in the three month general health questionnaire and Leeds scores.

The most plausible explanation for the lack of differences in mood may be anxiety associated with not receiving further treatment. Occasional stage I patients feared that mastectomy alone might be an inadequate treatment. In contrast, certain radiotherapy
patients seemed to gain a sense of security from the mere fact of getting further treatment. The patients who did not receive radiotherapy were seen infrequently at the surgical outpatient clinic. While many attended the hospital a few days after discharge to have stitches removed or have a prosthesis fitted, usually their next appointment was not until six months after mastectomy. Unlike the radiotherapy patients, they had little opportunity to be reassured by professional staff in the weeks after operation. Had a mastectomy nurse counsellor been available, they might have shown less morbidity than the radiotherapy patients.

The absence of an appreciable excess of depression or anxiety in those treated with radiotherapy should not detract from the fact that up to half the patients found that radiotherapy was a very unpleasant form of treatment which caused persisting somatic symptoms and temporary social disruption. On this basis, and given that its only function is to prevent local recurrence, there is a strong case for careful thought before radiotherapy is prescribed after mastectomy. A recent survey of surgical practice showed that some surgeons were more likely than others to prescribe radiotherapy. Thus sometimes it may be given more as a routine than as a result of careful individual assessment of the risk of local recurrence and of the patient's wishes after informed discussion of the treatment options.

Moreover, strictly speaking the results obtained apply only to a three week course of radiotherapy after mastectomy. An excess of depression or anxiety might have emerged had the course of treatment been longer — as in the study of Holland et al.
patients treated by breast conservation, a five or six week course of radiotherapy is usual, the total dose being higher — about 5000 rads. In the recent Cancer Research Campaign trial of breast conservation, Fallowfield and her colleagues thought that such radiotherapy might have caused mood disturbance. (These authors also commented that patients in the conservation group sometimes became anxious because they feared that the conserved breast had not been adequately treated.) Caution is also needed in extrapolating the results of the present study to radiotherapy given for other types of cancer, where the dose of radiotherapy might again be different. Furthermore, mood may be influenced not just by the treatment per se, but also by the patients' beliefs and expectations, by the treatment setting and by relationships with the clinic staff.

Levels of morbidity

The results reported in chapter 6 showed that levels of depression and anxiety of clinical degree (ratings of 2 or 3) in the mixed stage I/II sample were lower than expected — generally less than half those reported in the early British and American controlled studies of similar patients, and less than the more recent figure of 18% obtained by Hughes in an uncontrolled study. Examination of confidence intervals showed it was very unlikely that the prevalences of clinical depression or anxiety would have exceeded 14% in the population from which the sample was drawn, except in the period immediately after operation, prior to any further treatment.

Could the low prevalences of depression and anxiety have been due
to factors other than treatment for breast cancer? Although this study used the same observer scales as that of Maguire, ratings might have been conservative, despite satisfactory reliability. However, morbidity assessed by the self rating scales was also low. The upper age limit (69) in the present study was higher than in that of Maguire (65). Thus relatively more patients with low scores were included. There were few areas of marked social deprivation in the catchment area of the hospital. There may have been little background morbidity associated with social problems.

In view of these low prevalences, two recent reports are of interest. The first, in the United States, was by Bloom and her colleagues of the Psychological Aspects of Cancer Study Group. In a large multicentric study, patients with early breast cancer, patients with benign breast disease, cholecystectomy patients and healthy women were assessed on four occasions over a year. The authors concluded that their mastectomy patients experienced more post-surgical distress than the control subjects, but that the results did not support the belief that mastectomy was followed by severe psychiatric sequelae in psychologically healthy women. Patients with a previous history of having used major psychoactive drugs, those with recurrent breast cancer or concurrent physical illness and those whose physicians did not give approval were among those excluded from the study. The main purpose of some of these exclusions was to avoid factors which might confound the specific effects of breast cancer and its treatment.

Detailed comparisons between the present study and that of Bloom and colleagues are limited because of this large proportion of exclusions, and because the measures of morbidity (derived by
principal components analysis) were different. The multivariate analyses used by Bloom and her co-workers had the advantage of reducing the chances of spurious statistical significance, but the derived scales — for example "psychopathology" (mainly paranoid and obsessional symptoms) and "psychosocial impairment" (depression and social rôle) — do not correspond to the usual clinical concepts. Indeed Bloom and colleagues stated that the statistical analysis of their data reduced accuracy in determining the status of an individual patient.

The second report was Dean's study in Edinburgh. Dean, using Spitzer's Research Diagnostic Criteria, found that three months after operation 17.7% of her mastectomy patients had minor depressive disorder but only 9.7% major depressive disorder, whilst at one year the corresponding percentages were 18.2% and 4.5%. Anxiety was even less prevalent: at three and 12 months general anxiety disorder was present in only 0.9% and 4.5% of patients respectively. Minor depression was significantly commoner than in a matched community sample, but there were no significant differences for major depression. The clinical case rate, determined by Dean's own judgment that the patient was clinically ill plus fulfilment of either the Research Diagnostic Criteria for major depressive disorder or the Feighner criteria for depression or anxiety, was 10% at three months and 5% at 12. Dean thought that the lower rates compared with earlier British studies were probably due to differing diagnostic criteria, but did not rule out a genuinely lower prevalence in her East of Scotland sample. She suggested that morbidity might have been low because her patients had undergone a two-stage diagnostic procedure which allowed preoperative counselling.
However, the prevalence of clinical morbidity in the author's West of Scotland sample was very similar to that observed by Dean, despite the one-stage frozen section procedure. Like Dean, the author found that few of the patients regarded themselves as psychiatrically ill. While occasionally severe, symptoms of clinical degree were usually short-lived, lasting weeks rather than months, unless reactivated by prolonged chemotherapy or recurrent disease. The main exception was loss of sexual interest, which tended to persist. The prevalences of serious sexual problems in the patients were much higher than those for depression and anxiety. Both Maguire and Dean also found that sexual problems were conspicuous after mastectomy. Subdivision of the cancer patients by age showed that psychological and sexual morbidity as measured by many of the scales were significantly commoner in patients aged under 50. This confirms Maguire's clinical impression, based on an unselected sample, that morbidity was higher in younger patients. The findings of previous researchers — that morbidity was either unassociated with or positively associated with age — may well have resulted from selective sampling and unstandardized methods of assessment.

In the present study it is not certain to what extent the effect of age on mood — in particular anxiety — was specific to treatment for breast cancer. Levels of anxiety, especially in the second year, were often so low that they may largely have reflected baseline levels in the community. In a recent review, Kay reported that the prevalence of anxiety in older people in the...
community was lower than in younger people.\textsuperscript{138} Had there been enough older control subjects in the present study, the specificity of the age effect might have been clearer. However, in the light of the results reported in chapter 3, patients with benign disease may not be an ideal control group and it might be better to use a random community sample.

Whilst sexual problems were very prominent in younger cancer patients, a substantial minority of older cancer patients reported severe loss of libido. It might be thought that loss of libido in older patients was due to age rather than to the effects of treatment for breast cancer. Again the dearth of older patients with benign disease prevented a matched comparison with the older cancer group. Morris and colleagues found that a surprisingly large proportion of middle-aged patients with benign breast disease experienced sexual difficulties over a two year period.\textsuperscript{59} However, in the older cancer patients the loss of interest in sex was usually sudden. The patients often attributed it to mutilating surgery, although other factors such as further treatment (radiotherapy or chemotherapy) or the feeling that sex was not very important in the context of cancer were sometimes relevant. It would be unreasonable to conclude that treatment for breast cancer had no causative effect on sexual appetite in the older patients. Even if loss of libido would have occurred eventually in this group, treatment for breast cancer must have brought it forward in time.

For social and work problems, there were no consistent differences between younger and older patients. Since the older cancer patients had fewer psychological symptoms than the younger cancer
patients, they may have had fewer social difficulties of psychic origin. However, they appeared to take longer to recover physically from surgery and follow-up treatment. This may explain why there were no clear differences between the age groups.

It could be argued that the results would have been different had the patients been treated by breast conservation or mastectomy and reconstructive surgery rather than by mastectomy alone. Although such techniques may confer very important advantages such as greater freedom with clothes and avoidance of feelings of disgust when undressing, the evidence that they actually reduce depression, anxiety and sexual problems appears to be conflicting.\textsuperscript{13-14} Dean showed that breast reconstruction with a simple subpectoral prosthesis reduced psychological morbidity at three months after surgery, though not at a year.\textsuperscript{13} However, published work has so far failed to show that breast conservation reduces depression or anxiety.\textsuperscript{13-14} Certainly the prevalences of serious mood disturbance in the author's patients could not have been very much lower, especially in the second year after surgery, and suggest that most patients cope amazingly well, even if the surgical procedure is not ideal.

**Prediction of morbidity**

The multiple regression analyses showed that morbidity at a year could be predicted independently by factors such as age, Eysenck neuroticism, scores on self rating scales at one month and treatment with chemotherapy. That younger patients with previous evidence of emotional lability were vulnerable fits with common sense.
Two results were less expected. Verbal intelligence emerged as a significant independent predictor of the (transformed) 60-item general health questionnaire score. Possibly higher intelligence leads to mood upset because of greater insight into the uncertain future in breast cancer. Social class was associated with social dysfunction, but the direction of the association was interesting. Higher social class was correlated with greater social dysfunction. Women of higher social class might be more socially inhibited by mutilating surgery, or alternatively more ready to report the social effects of the operation. However, since each of these results emerged in only one of the equations, they should be treated with caution, unless confirmed in another series of patients.

Indeed all the predictive factors require validation in other samples, even though the use of adjusted $R^2$ rather than $R^2$ makes some allowance for sampling variation. But age, one month mood scores, Eysenck neuroticism and treatment with chemotherapy emerged repeatedly in the analyses, Such internal consistency suggests they may be true predictors. Furthermore, some of the findings of other researchers are similar. Morris and colleagues found that morbidity was predicted by preoperative Eysenck neuroticism scores and ratings of depression; more recently Hughes showed that it was predicted by scores on the 60-item General Health Questionnaire. Dean (1987) found that the patients' preoperative mental state independently predicted morbidity 3 months after operation, along with further treatment received and the quality of the patient's marital relationship.
The percentages of variance explained by the predictive equations, although very reasonable for this type of data, do not allow the exact identification of those patients likely to be helped by interventions such as counselling.\textsuperscript{44-47} However, extra vigilance in the follow-up of younger cancer patients with high scores on measures of psychological morbidity around the time of operation, especially if they are receiving chemotherapy, seems prudent.

The validity study.

Criteria of validity: severity of illness

The \textit{ad hoc} criteria of caseness used in this study, and the reasons for their use, have been described in chapter 2. On the face of it, the definitions of caseness were different from those used by Brown and Harris,\textsuperscript{64} but was this really so?

For a woman to qualify as a "case", Brown and Harris stipulated that "a psychiatrist would not be surprised to see [the woman] in an outpatient clinic". To be judged a (non-specific) "case" in the present study, a score of 2 or 3 for either depression or anxiety was needed. However, most cases scored 2. The author would not have been surprised if some patients scoring 2 had been referred to a psychiatric clinic. Indeed on occasion they were so referred. Seldom was the severity such that in-patient care might have been indicated. Patients scoring 1 could usually function reasonably well despite symptoms, rather like some of the borderline cases of Brown and Harris. Examples of ratings are given in appendix 7.

So the range of psychiatric illness seen in the present study
tended to be less than that in psychiatric practice, and probably of comparable degree to that observed by Brown and Harris in women in the community.

Comparisons with the self rating scales

The results of the validity study suggested that the general health questionnaire functioned reasonably well in patients undergoing chemotherapy following mastectomy. For the 60-item version of the questionnaire, a higher threshold score of at least 20 seemed necessary to identify definite cases, and for the 28-item version, a threshold of at least 10. There seemed to be little to choose between the performance of the two versions.

The threshold of 10 or above for the 28-item questionnaire was close to that obtained by Bridges and Goldberg (12 or above) in neurological inpatients.92 These patients were also subject to somatic and social symptoms and so the threshold appropriate for general practice had to be raised.

The anxiety/insomnia and the severe depression subscales appeared to perform adequately with the suggested threshold scores. The other two subscales (somatic symptoms and social dysfunction) performed fairly well. However, the threshold for the somatic symptom subscale should be viewed with some caution since the validating criterion was not a direct measure of somatic symptoms.

Goldberg originally derived these subscales by principal components analysis. He validated three of them against observer ratings, but had no observer ratings to compare with the social
dysfunction subscale, and did not suggest threshold scores."

However, one recent study has provided threshold scores for two of the subscales of the general health questionnaire: anxiety/insomnia and severe depression. For the former subscale Aylard and colleagues suggested a score of 5 or above as the threshold for definite morbidity. This is 2 points lower than the author's of 7 or above. Their threshold score for definite morbidity on the severe depression subscale (4 or above) is only 1 point above the author's. As they emphasised, however, it is unrealistic to expect a sharp distinction between health and pathology.

That some of the thresholds were close to those of others suggested that the observer ratings were reasonably accurate. However, there was one interesting discrepancy between observer and self ratings. Despite a careful interview one patient denied any psychological symptoms, and therefore was given observer ratings of zero. She also restricted discussion of her illness. Yet on the general health questionnaire, she endorsed many items concerned with psychological distress. When asked about this, she obliquely but convincingly acknowledged she had experienced the symptoms she had endorsed. Thus she was really a "false positive." The conventional rule that the performance of a self rating scale is judged by the "gold standard" — administration of a reliable interview schedule by an experienced psychiatrist — was in this case turned on its head: the "gold standard" was the self rating scale, not the observer rating. Denial of illness and psychological symptoms face to face but not on paper may be uncommon, but the extent to which it occurs in patients with cancer should be investigated further. In a study of another
subject where denial is prominent, namely alcoholism, Lucas and colleagues found that patients admitted to a greater consumption of alcohol when interrogated by a computer than when interviewed by a psychiatrist.\(^4\)\(^9\)

Recently (1988), in a paper describing the development of computerized assessments for minor psychiatric disorder, Lewis et al have commented: "... using a human interviewer introduces the problem of inter-observer variation.... In the traditional validity study, a questionnaire is compared with an interview, regarded as an error free 'gold standard.' Disagreement between interview and questionnaire is then an inevitable result of using an interview as the criterion in a validity test that assumes it is error-free. It is, therefore, difficult to sustain the argument that questionnaires, such as the GHQ, are less valid or accurate at detecting minor psychiatric disorder because they are self-report."\(^1\)\(^5\)\(^0\) On this basis the traditional comparison of a self rating scale with an observer assessment is an unduly severe test of validity.

**Comments on the item analysis**

Although the results discussed above pointed to the validity of the standard general health questionnaire and its subscales in the patients studied, an improved version might have been possible based on the items which were found to be the best discriminators of psychological morbidity.

The expectation that patients with purely physical problems might endorse somatic and social items, causing them to be poor
discriminators of psychological upset, was partly confirmed. Three items in the somatic symptoms subscale (1, 2 and 9) were endorsed by over 10% of normals. One item in the social dysfunction subscale (22 — talking longer over things) was endorsed by 22% of normals. Item 16 (lack of energy) was endorsed by 25% of normals, but is not part of the 28-item questionnaire or the subscales.

Two items in the somatic symptoms subscale (5 and 6, concerned with pains, tightness and pressure in the head) were endorsed by too few patients in any category to be good discriminators of psychological morbidity. Overall, therefore, items in the somatic symptom subscale could not be thought of as a good case discriminators. However, four items in the social dysfunction subscale were good discriminators, consistent with Goldberg's observation that social items may compare favourably with the more traditional ones (measuring depression or anxiety directly).74

The item analysis seemed disappointing in that about half of the 60 items were poor discriminators of differing degrees of psychological morbidity. However, this result has to be seen in context. As noted in chapter 2, the item analysis could not have been expected to give as good discrimination as one which excluded patients with intermediate degrees of disturbance. Furthermore, the range of severity in the sample studied was smaller than in that studied by Goldberg to select items for the original general health questionnaire.74 Goldberg had three grades of severity: normal, mild and severe. His mild cases were drawn from a psychiatric outpatient clinic, the definition of severity being: "mildly ill — needs some psychiatric help. Quite all right as an out-patient." Goldberg's severe cases had to be in-patients on the
The mild cases in the present study were not usually in need of psychiatric help and often had little or no impairment of their day-to-day functioning and relationships with other people. Hence one could not expect them always to endorse items concerned with problems in interpersonal relationships and daily functioning. Most "cases" had ratings of 2 (moderate) rather than 3 (severe), and only one, with a history of endogenous depression antedating mastectomy, was admitted to a psychiatric ward. Thus only a small percentage of "cases" would have been expected to endorse items concerned with severe disturbance, for example those in the severe depression subscale. Viewed in this context, the questionnaire performed surprisingly well. Better discrimination would be likely in samples with a wider range of disturbance.

Technicalities aside, the existing questionnaire and its subscales worked well in practice. The results of chapter 5 (psychosocial effects of radiotherapy) showed that the subscales of the general health questionnaire discriminated successfully between, on the one hand, somatic symptoms and social symptoms and, on the other hand, depression and anxiety. Also, in chapter 4 (effects of chemotherapy) the severe depression subscale gave results very similar to those of the Leeds depression scale.

Hence it seems premature to recommend a shorter version of the questionnaire for cancer patients on the basis of the item analysis. Results from any item analysis are subject to sampling variation. Other, larger samples might give different results. Furthermore, if all the apparently poor items were excluded, most
of the items measuring severe depression would disappear. The range of the questionnaire might thereby be restricted such that it would not detect severe depression — a problem which should not be missed even if uncommon in a given patient population. Finally, as Snaith has observed, there is already a surfeit of scales; careful analysis of the performance of existing scales in varying circumstances should precede the creation of new scales.

So unless further item analyses in larger and more heterogeneous samples of cancer patients under many different conditions (for example, at different stages of disease and with different treatments) showed a consistent pattern of poor discrimination, then the existing questionnaire and its subscales seem a better option than a modified questionnaire. Although the results were for patients treated for breast cancer, the questionnaire and its subscales would seem likely to perform adequately in patients receiving similar types of treatment for early cancers in other sites. What then is the best way of using the existing questionnaire?

The 28-item version of the questionnaire, which contains all four subscales, may be preferable to the 60-item version because cancer patients often have to undergo many investigations, may tire easily and so be unable or unwilling to concentrate for long. If either version were the sole means of identifying cases, it might be best to opt for specificity by using a high threshold score and thereby improving classification. However, a high threshold may not be desirable in cancer patients free of physical symptoms because sensitivity might be reduced. If comparisons of mood were
to be made between cancer patients with few physical symptoms and those with many, the anxiety/insomnia and severe depression subscales, which avoid ambiguous somatic symptoms, could be analysed separately. The thresholds for these subscales should not need changing according to the presence or absence of physical symptoms (although this would need formal proof).

On the other hand if trained interviewers were available a good strategy might be to leave the standard 60-item and 28-item thresholds unchanged — i.e. to opt for sensitivity. The burden of interviewing could thereby be much reduced with little risk of missing cases, regardless of the presence of physical symptoms.

The Leeds scales

Both Leeds scales seemed to perform adequately with the standard threshold of seven or above, despite the possible influence of physical symptoms. This result is not altogether surprising since neither Leeds scale is heavily loaded with items liable to be endorsed by patients with purely physical distress. The Leeds scales have been largely superceded by the Hospital anxiety and depression (HAD) scales, in which such items have been deliberately avoided.\(^{52}\)

General comments

The Leeds scales (and probably also the closely related Hospital Anxiety and Depression scale) would therefore seem a good option to measure mood in cancer patients. The general health questionnaire has the advantage of additional measures of somatic and social dysfunction. However, scales specifically designed for
cancer patients, or at least for those with physical illness, might be a better option. Several such scales have been developed in recent years — for example the PAIS (psychosocial adjustment to illness) scale, the Rotterdam scales, and purpose-designed linear analogue scales or diary cards. Not all have been comprehensively validated, but such scales are likely to cover more topics relevant to cancer patients. Scales borrowed from other contexts do not measure items such as the reaction to an operation scar. However, an argument in favour of scales validated in other contexts (for example, psychiatry, general practice or medical clinics) is that the scores obtained by cancer patients — provided that they can be shown to be valid — can be compared with the levels of morbidity which have become familiar in these other contexts. Hence it may be easier to judge the severity of symptoms in cancer patients. Perhaps the best solution in cancer patients is to include both general scales (with items applicable to nearly everybody) and specific scales (with items especially relevant to cancer patients) — provided, of course, that the patient is not over-burdened with questions.

Clearly self rating scales have limitations such as the ability of patients to complete them. (In cancer patients this problem may stem from severe physical illness rather than severe psychiatric illness). Even fit patients need careful explanation of the purpose of the scales, encouragement to complete them and careful checking that they have done so. However, self rating scales have the advantage of freedom from observer bias in an area of medicine where the nature of the treatment can seldom be disguised from the investigator. Since they also cost much less than observer interviews, they have a valuable place in the assessment of the cancer patient.
Conclusions

Psychosocial morbidity has been emphasised in several circumstances: before breast biopsy (in patients with benign disease and in younger cancer patients); during chemotherapy (especially the second six months of treatment); to a lesser extent during radiotherapy; and after recurrence of cancer.

However, a common factor which has emerged in both the present study and in the work of others is that not receiving further treatment may provoke anxiety. The mere fact of receiving treatment may have a placebo effect, which may counteract any adverse psychological effects of that treatment. Such a placebo effect may have offset the anxiety due to a three-week course of radiotherapy, but was clearly insufficient to counteract the adverse psychological effects of a year of intensive chemotherapy.

The placebo effects of receiving treatment merit greater attention in future research. It would be useful if they could be recorded formally and quantified. They may well vary from one treatment centre to another, depending on the degree of support available. Since many trials of cancer treatments have to be multicentric, there is an excellent opportunity to find out whether this is so. The placebo effects may also vary with the stage of the disease; this too could readily be investigated. It should not be difficult to compare, say, the psychosocial effects of radiotherapy given immediately after breast surgery to prevent local recurrence with those of radiotherapy delayed until recurrence. In the latter case radiotherapy might be more reassuring than frightening.
Studies comparing the psychosocial effects of the oestrogen-receptor blocking agent tamoxifen with those of other postoperative treatments might also help to clarify the placebo effect. Tamoxifen appears to be well tolerated, without obvious harmful psychological effects. If so, it becomes a placebo, psychologically speaking. It would be especially interesting to discover if morbidity in stage I patients treated with tamoxifen was less than in those on no further treatment.

Further work is theoretically desirable to clarify and quantify the mechanisms — both physiological and psychological — whereby treatments such as radiotherapy and chemotherapy induce psychological morbidity. However, the problems of designing adequate scientific experiments to disentangle the various mechanisms would be enormous or even impossible both practically and ethically. Research to provide even partial answers would almost certainly take years, by which time more effective and less toxic anti-cancer treatments would probably be available.

Rather than spend money on understanding precisely the pathophysiology of depression associated with the present-day CMF régime, it would seem better to spend it developing anti-cancer drugs without emetic potential. Failing that, money would be well spent on developing drugs to abolish the almost universal post-treatment nausea and vomiting. Conditioned reflex symptoms would then disappear completely. Since the results reported suggest that some of the mood disturbance stems from nausea and vomiting (especially if accompanied by conditioned symptoms), depression and anxiety would probably decrease also. Not only
would there be great benefit for nearly all patients, but the rôle of nausea and vomiting in inducing mood disturbance would become clearer.

However, nausea and vomiting remain common. From a practical standpoint, how might the psychosocial morbidity associated with postoperative treatments be reduced, using existing knowledge?

*Reducing the psychosocial morbidity of postoperative treatments*

Several suggestions have been made. In controlled experiments, behavioural methods have successfully reduced the prevalence and severity of conditioned reflex nausea and vomiting. The techniques, all of which involve learning to relax, include: systematic desensitization; hypnosis with guided imagery (descriptions of pleasant, tranquil scenes); progressive muscle relaxation training with guided imagery; and biofeedback with muscle relaxation training and guided imagery.156 157 These are given once the patient has begun to develop conditioned symptoms. Ideally they would be given prophylactically before the onset of conditioned symptoms, but attempts to identify patients at risk have not had much success. Similar techniques would very probably be valuable in patients experiencing acute anxiety or panic under radiotherapy machines. With the increasing use of breast conservation, more patients are likely to undergo adjuvant radiotherapy.

Treatment with tetracyclic antidepressant drugs and cognitive therapy have been recommended to relieve depressive symptoms in cancer patients,158 159 but to what extent such treatment
alleviates depression due specifically to chemotherapy is unclear. The value of counselling by nurses or other professionals is debatable, but psychological symptoms due to misconceptions about a particular treatment might be helped. In patients receiving no postoperative treatment, nurse counsellors might compensate for the absence of a placebo effect of treatment. Nurse counsellors are likely to use cognitive methods, even if not formally defined as such; adjuvant psychological therapy, developed by Greer's research group, is more formally based on both cognitive and behavioural techniques. Further work is needed to determine the effect of these interventions on the morbidity of postoperative treatments.

However, such methods are unlikely to be effective in all patients, and moreover some of them require extra resources which often will not be forthcoming. The simplest way to avoid the morbidity of post-operative treatment is to reduce such treatment to the absolute minimum without compromising survival. (However, the possible placebo effects of receiving treatment should be kept in mind.) Postoperative radiotherapy could probably be omitted in many patients, though sometimes it will be impossible to predict the likelihood of local recurrence. The value of adjuvant chemotherapy in postmenopausal patients is small; in this group psychosocial morbidity should be preventable by prescribing tamoxifen instead. However, adjuvant chemotherapy remains valuable in premenopausal patients with positive axillary nodes; in these patients, treatment should last no more than six months.

Finally, there is probably an irreducible minimum of psychological morbidity which will not disappear until fully effective cures
become available. No one can totally remove the threat and sense of loss which treatment for breast cancer may induce, and indeed it may not be desirable to suppress normal grief reactions. The main aim must be to reduce unnecessary distress, by avoiding over-zealous treatment, and by directing support to those who wish it, need it and can be shown, by proper scientific evaluation, to be helped by it.
REFERENCES


FIGURE 2-2 — Validation of scales: criteria for caseness.

Depression

Anxiety

Under Activity

Depression

Anxiety

Insomnia

Routine upset

Work/housework

general health questionnaire
(60-item and 28-item)

Either score ≥ 2

either score ≥ 2

score ≥ 2

score ≥ 2

sum of scores ≥ 2

sum of scores ≥ 2

somatic symptoms

severe depression

anxiety and insomnia

social dysfunction

2
<table>
<thead>
<tr>
<th></th>
<th>Cancer (n=44)*</th>
<th>Benign (n=47)*</th>
<th>Cholecystectomy (n=30)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at operation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>53.4 (11.0)</td>
<td>37.5 (11.2)</td>
<td>46.8 (12.6)+</td>
</tr>
<tr>
<td><strong>Social class</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I+II</td>
<td>14 (31.8)</td>
<td>11 (23.4)</td>
<td>10 (33.3)+</td>
</tr>
<tr>
<td>III</td>
<td>23 (52.3)</td>
<td>24 (51.1)</td>
<td>12 (40.0)</td>
</tr>
<tr>
<td>IV+V</td>
<td>7 (15.9)</td>
<td>12 (25.5)</td>
<td>8 (27.7)</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>32 (72.7)</td>
<td>37 (78.7)</td>
<td>23 (76.7)+</td>
</tr>
<tr>
<td>Divorced</td>
<td>2 (4.5)</td>
<td>3 (6.4)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Widowed</td>
<td>7 (15.9)</td>
<td>2 (4.3)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Unmarried</td>
<td>3 (6.8)</td>
<td>5 (10.6)</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td><strong>Previous psychiatric</strong></td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>30 (68.2)</td>
<td>34 (72.3)</td>
<td>20 (66.7)+</td>
</tr>
<tr>
<td>G.P.</td>
<td>10 (22.7)</td>
<td>10 (21.3)</td>
<td>10 (33.3)</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>4 (9.1)</td>
<td>3 (6.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><strong>E.P.I. score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extraversion</td>
<td>10.9 (3.7)</td>
<td>10.7 (3.6)</td>
<td>12.1 (3.7)</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>9.6 (5.4)</td>
<td>11.5 (5.3)</td>
<td>10.3 (5.6)</td>
</tr>
</tbody>
</table>

*For E.P.I. scores, numbers were 43, 42 & 26 respectively. +p<0.0001. §Not significant (X² tests). §Married v. unmarried. †Some v. none.
### TABLE 3-2 — Observer scales: numbers (percentages) scoring above 0.

<table>
<thead>
<tr>
<th>Rating</th>
<th>Cancer n=44</th>
<th>Benign n=47</th>
<th>Cholecystectomy n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>13 7 0 (45)</td>
<td>15 11 0 (55)</td>
<td>3 3 0 (20)*</td>
</tr>
<tr>
<td>Anxiety</td>
<td>23 7 1 (70)</td>
<td>24 15 0 (83)</td>
<td>16 3 0 (63)</td>
</tr>
<tr>
<td>Irritability</td>
<td>12 1 0 (30)</td>
<td>20 5 0 (53)</td>
<td>7 1 0 (27)†</td>
</tr>
<tr>
<td>Libido loss‡</td>
<td>4 4 1 (29)</td>
<td>5 8 0 (35)</td>
<td>6 0 0 (26)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>17 1 0 (41)</td>
<td>12 9 1 (47)</td>
<td>14 3 0 (57)</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>6 2 0 (18)</td>
<td>9 2 0 (29)</td>
<td>10 0 0 (33)</td>
</tr>
<tr>
<td>Inability to work</td>
<td>6 1 0 (16)</td>
<td>7 5 0 (26)</td>
<td>7 2 0 (30)</td>
</tr>
</tbody>
</table>

*p<0.01; †p<0.03 (for some v. no morbidity: X² tests with 2 d.f.)
†Married patients: sample sizes 31, 37 and 23 respectively.

### TABLE 3-3 — Scores on self rating scales.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Cancer n=44</th>
<th>Benign n=47</th>
<th>Cholecystectomy n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (inter-quartile range)</td>
<td>Median (inter-quartile range)</td>
<td>Median (inter-quartile range)</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>6.5 (2-18)</td>
<td>14.0 (5-24)</td>
<td>11.5 (4-20)</td>
</tr>
<tr>
<td>Subscales</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>4.0 (2-8)</td>
<td>5.0 (3-7)</td>
<td>7.0 (4-10)*</td>
</tr>
<tr>
<td>Anxiety &amp; insomnia</td>
<td>6.5 (2-11)</td>
<td>10.0 (6-12)</td>
<td>7.0 (3-10)†</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (6-8)</td>
<td>7.0 (7-10)</td>
<td>7.5 (7-10)†</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.0 (0-3)</td>
<td>1.0 (0-3)</td>
<td>0.0 (0-2)</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>3.0 (1-6)</td>
<td>4.0 (2-8)</td>
<td>4.0 (3-6)</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>6.0 (2-10)</td>
<td>8.0 (5-10)</td>
<td>6.0 (4-8)</td>
</tr>
</tbody>
</table>

*p<0.03; †p=0.05; ‡p=0.1 (Kruskal-Wallis analysis of variance)
TABLE 3-4 — Observer scales in breast biopsy patients: numbers (percentages) scoring above 0, according to age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Cancer</th>
<th>Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;46 n=12</td>
<td>&gt;46 n=32</td>
</tr>
<tr>
<td>Rating &gt;0</td>
<td>No (%)</td>
<td>No (%)</td>
</tr>
<tr>
<td>Depression</td>
<td>7 (58)</td>
<td>13 (41)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>12 (100)</td>
<td>19 (59)*</td>
</tr>
<tr>
<td>Irritability</td>
<td>5 (42)</td>
<td>8 (25)</td>
</tr>
<tr>
<td>Libido loss</td>
<td>6 (60)</td>
<td>3 (14)†</td>
</tr>
<tr>
<td>Lethargy</td>
<td>5 (42)</td>
<td>13 (41)</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>2 (17)</td>
<td>6 (19)</td>
</tr>
<tr>
<td>Inability to work</td>
<td>2 (17)</td>
<td>5 (16)</td>
</tr>
</tbody>
</table>

*p=0.013; †p=0.03; *p=0.002 (Fisher tests). $p<0.1 (X^2$ test with Yates's correction).

TABLE 3-5 — Scores on self rating scales, according to age: medians and interquartile ranges.

<table>
<thead>
<tr>
<th>Age</th>
<th>Cancer</th>
<th>Benign</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;45 n=12</td>
<td>&gt;46 n=32</td>
</tr>
<tr>
<td>Scale</td>
<td>Median(IQR)</td>
<td>Median(IQR)</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>4.0 (3-11)</td>
<td>5.5 (0-17)</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>4.5 (2-6)</td>
<td>4.0 (2-8)</td>
</tr>
<tr>
<td>Anxiety &amp; insomnia</td>
<td>10.0 (7-14)*</td>
<td>5.5 (2-10)</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (6-8)</td>
<td>7.0 (7-8)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.5 (0-3)</td>
<td>0.0 (0-3)</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>4.5 (3-6)†</td>
<td>2.0 (0-6)</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>9.5 (7-12)§</td>
<td>4.5 (1-7)</td>
</tr>
</tbody>
</table>

*p<0.03; †p<0.05; †p<0.07; §p<0.01 (Kruskal-Wallis ANOVA)
TABLE 3-6 — Spearman correlation coefficients between physical symptom scores and observer and self ratings in cholecystectomy patients.

<table>
<thead>
<tr>
<th>Observer ratings</th>
<th>Self ratings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>General Health Questionnaire .45†</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Somatic symptoms .32</td>
</tr>
<tr>
<td>Irritability</td>
<td>Anxiety and insomnia .28</td>
</tr>
<tr>
<td>Libido loss</td>
<td>Social dysfunction .21</td>
</tr>
<tr>
<td>Lethargy</td>
<td>Severe depression .01</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>Leeds depression .34</td>
</tr>
<tr>
<td>Inability to work</td>
<td>Leeds anxiety .41†</td>
</tr>
</tbody>
</table>

*p<0.01; †p<0.05
### TABLE 3-7 — Lower triangle correlation matrix in breast cancer patients (n=44) (decimal points omitted)

<table>
<thead>
<tr>
<th></th>
<th>1.</th>
<th>2.</th>
<th>3.</th>
<th>4.</th>
<th>5.</th>
<th>6.</th>
<th>7.</th>
<th>8.</th>
<th>9.</th>
<th>10.</th>
<th>11.</th>
<th>12.</th>
<th>13.</th>
<th>14.</th>
<th>15.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Social class</td>
<td>17</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Marital status</td>
<td>12 03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Relig. observance</td>
<td>27* -08 -06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Delay to clinic</td>
<td>21 -02 -17 11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>6. Waiting list time</td>
<td>-02 -20 -23 -13 -03</td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Past med. history</td>
<td>35† 23 12 03 -10 -12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Past psych. history</td>
<td>14 13 19 -13 -13 -10 19</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Breast ca. friends</td>
<td>-18 16 -11 -02 -14 -16 02 -07 -03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. Work</td>
<td>-34* -04 09 -20 -11 -13 -07 03 15 06 05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. Living alone</td>
<td>37† 27* -59† -04 -09 -07 -02 06 28* 27* -21 -15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14. GHQ-60 score</td>
<td>-17 -05 01 07 -04 34* -10 05 04 -10 04 07 -13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15. Leeds depression</td>
<td>-20 -07 21 15 11 23 -06 23 -10 -16 28* -01 -29* 70†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16. Leeds anxiety</td>
<td>-41† -06 11 07 -12 20 -06 22 -15 -10 30* 12 -28* 72† 68†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* p<0.05; † p<0.01

### TABLE 3-8 — Results of multiple regression analysis after entry of two significant independent predictors

**Variables entered: age; past psychiatric history***

Multiple R=0.50 R²=0.25  
Adjusted R²=0.22

**Analysis of variance**

<table>
<thead>
<tr>
<th></th>
<th>DF</th>
<th>Sum of squares</th>
<th>Mean square</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regression</td>
<td>1</td>
<td>131.10</td>
<td>131.10</td>
<td>8.689</td>
<td>.0052</td>
</tr>
<tr>
<td>Residual</td>
<td>42</td>
<td>633.69</td>
<td>15.09</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>SE B</th>
<th>Beta</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-.175</td>
<td>.052</td>
<td>-.455</td>
<td>-3.335</td>
<td>.0018</td>
</tr>
<tr>
<td>Past psych. history</td>
<td>2.574</td>
<td>1.221</td>
<td>.288</td>
<td>2.108</td>
<td>.0412</td>
</tr>
<tr>
<td>Constant</td>
<td>14.592</td>
<td>2.830</td>
<td></td>
<td>5.157</td>
<td>.0000</td>
</tr>
</tbody>
</table>

Next variable nearest to entry into equation = time on waiting list, with p for entry of 0.10

***Absent coded 0; present coded 1"

FIGURE 4-2 — Percentages of patients with depression, anxiety and behaviour upset on observer scales.

Observer rated depression: % scoring >1

Observer rated anxiety: % scoring >1

Observer rated behaviour upset: % scoring >1

*p<0.1 (X^2 test with 2 df)

*P=0.07 (Fisher exact test with groups C and RC combined)
Figure 4-3 — Percentages of patients with morbidity on the general health questionnaire and the anxiety/insomnia and severe depression subscales.

GHQ 60-item: % scoring ≥12

<table>
<thead>
<tr>
<th>Months</th>
<th>X</th>
<th>3</th>
<th>6</th>
<th>13</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>51</td>
<td>31</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>13-24</td>
<td>44</td>
<td>38</td>
<td>13</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

Anxiety/insomnia subscale: % scoring ≥7

<table>
<thead>
<tr>
<th>Months</th>
<th>X</th>
<th>3</th>
<th>6</th>
<th>13</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>51</td>
<td>31</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>13-24</td>
<td>44</td>
<td>38</td>
<td>13</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

Severe depression subscale: % scoring ≥3

<table>
<thead>
<tr>
<th>Months</th>
<th>X</th>
<th>3</th>
<th>6</th>
<th>13</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>51</td>
<td>31</td>
<td>12</td>
<td>11</td>
<td>9</td>
<td>11</td>
</tr>
<tr>
<td>13-24</td>
<td>44</td>
<td>38</td>
<td>13</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

*P<0.03 (Fisher exact test with groups C and RC combined)

Figure 4-4 — Percentages of patients with morbidity on the Leeds depression and anxiety scales.

Leeds depression: % scoring ≥7

<table>
<thead>
<tr>
<th>Months</th>
<th>X</th>
<th>3</th>
<th>6</th>
<th>13</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>25</td>
<td>24</td>
<td>24</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>13-24</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*P<0.03 (Fisher exact test with groups C and RC combined)

Leeds anxiety: % scoring ≥7

<table>
<thead>
<tr>
<th>Months</th>
<th>X</th>
<th>3</th>
<th>6</th>
<th>13</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12</td>
<td>25</td>
<td>24</td>
<td>24</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>13-24</td>
<td>24</td>
<td>24</td>
<td>24</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
FIGURE 4-5 — Percentages of patients with under activity, routine upset and work/housework problems on observer scales.

Observer rated under activity: % scoring ≥1

Observer rated routine upset: % scoring ≥1

Observer rated (house)work problems: % scoring ≥1
FIGURE 4-6 — Percentages of patients with morbidity on the somatic symptoms and social dysfunction subscales of the general health questionnaire.

FIGURE 4-7 — Percentages of patients with loss of libido.
FIGURE 4-8 — Percentages of larger cohort of patients with depression, anxiety, behaviour upset or loss of libido on observer scales.

![Depression: % ≥1](#)  Anxiety: % ≥1

![Radiotherapy (R)](##)  Chemotherapy (C)  Radio+chemo (RC)

% ≥1

No ≥ 1 Months 13 18 24 13 18 24

*p=0.1; 1p<0.05 (Χ^2 tests with 2 df)

FIGURE 4-9 — Percentages of larger cohort of patients with morbidity on the general health questionnaire and the anxiety/insomnia and severe depression subscales.

6 H Q 60-item: % ≥12

% ≥12

No ≥ 12 Months 13 18 24

*p<0.05 (Χ^2 test with 2 df)

Anxiety/insomnia: % ≥7  Severe depression: % ≥33

% ≥

No ≥ cut-off Months 13 18 24 13 18 24

*p=0.01 (Χ^2 test with 2 df)
FIGURE 4-10 — Percentages of larger cohort of patients with morbidity on the Leeds depression and anxiety scales.

Leeds depression: $\% \geq 7$
Leeds anxiety: $\% \geq 7$

- Radiotherapy (R)
- Chemotherapy (C)
- Radio+chemo (RC)

*P < 0.04 ($\chi^2$ test with 2 df)

FIGURE 4-11 — Percentages of larger cohort of patients with underactivity, routine upset and work/housework problems on observer scales.

Under activity: $\% \geq 1$
Routine upset: $\% \geq 1$
(House)work problems: $\% \geq 1$

*P < 0.02 ($\chi^2$ test with 2 df)
FIGURE 4-12 — Percentages of larger cohort of patients with morbidity on the somatic symptoms and social dysfunction subscales of the general health questionnaire.

Somatic symptoms: % ≥ 37 Social dysfunction: % ≥ 8

Radiotherapy (R)
Chemotherapy (C)
Radio+chemo (RC)

No 2 cut-off

Months 13 18 24 13 10 24

*p = 0.002 (X² test with 2 df)
TABLE 4-1 — Patient characteristics (chemotherapy study).

<table>
<thead>
<tr>
<th></th>
<th>Radiotherapy (n=24)</th>
<th>Chemotherapy (n=27)</th>
<th>Radio+chemo (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>52.7 (12.3)</td>
<td>55.2 (11.2)</td>
<td>49.4 (10.7)</td>
</tr>
<tr>
<td>Social class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>1 (4)</td>
<td>0</td>
<td>2 (9)</td>
</tr>
<tr>
<td>II</td>
<td>5 (21)</td>
<td>8 (30)</td>
<td>10 (43)</td>
</tr>
<tr>
<td>III</td>
<td>14 (58)</td>
<td>13 (48)</td>
<td>9 (39)</td>
</tr>
<tr>
<td>IV</td>
<td>3 (13)</td>
<td>4 (15)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>V</td>
<td>1 (4)</td>
<td>2 (7)</td>
<td>1 (4)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>14 (58)</td>
<td>19 (70)</td>
<td>16 (69)</td>
</tr>
<tr>
<td>Divorced</td>
<td>2 (8)</td>
<td>0</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Widowed</td>
<td>5 (21)</td>
<td>6 (22)</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Never married</td>
<td>3 (13)</td>
<td>2 (7)</td>
<td>3 (13)</td>
</tr>
<tr>
<td>Previous psychiatric treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>16 (67)</td>
<td>21 (78)</td>
<td>14 (61)</td>
</tr>
<tr>
<td>G.P.</td>
<td>6 (25)</td>
<td>4 (15)</td>
<td>9 (39)</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>2 (8)</td>
<td>2 (7)</td>
<td>0</td>
</tr>
</tbody>
</table>

TABLE 4-2 — Numbers of patients who refused further interviews or further chemotherapy, relapsed, or died during study.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
<th>Combined treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agreed to participate</td>
<td>24</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>Refused further interviews</td>
<td>1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Refused further chemotherapy</td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>(but not further interviews)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Systemic*</td>
<td>10</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Died</td>
<td>9</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

*A few patients who developed systemic relapse died before they could be re-interviewed.
### TABLE 4-3 — Numbers of patients receiving each type of treatment during study.

<table>
<thead>
<tr>
<th>Months since surgery</th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
<th>Combined treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>23</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>24*</td>
<td>23</td>
</tr>
<tr>
<td>13</td>
<td>21†</td>
<td>24*</td>
<td>22</td>
</tr>
<tr>
<td>18</td>
<td>18†</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>24</td>
<td>14</td>
<td>19</td>
<td>20</td>
</tr>
</tbody>
</table>

*Sample size one less for self rating scales as one patient felt too depressed to complete them.
†Sample size two less for self rating scales as patients felt too ill physically to complete them.

### TABLE 4-4 — Patient characteristics: additional sample first seen at 13 months.

<table>
<thead>
<tr>
<th></th>
<th>Radiotherapy (n=15)</th>
<th>Chemotherapy (n=15)</th>
<th>Radio+chemo (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>55.5 (9.9)</td>
<td>50.6 (11.8)</td>
<td>50.5 (9.0)</td>
</tr>
<tr>
<td>Social class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>4 (27)</td>
<td>6 (40)</td>
<td>4 (25)</td>
</tr>
<tr>
<td>III</td>
<td>8 (53)</td>
<td>7 (47)</td>
<td>10 (63)</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>1 (7)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>V</td>
<td>3 (20)</td>
<td>1 (7)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>9 (60)</td>
<td>9 (60)</td>
<td>9 (56)</td>
</tr>
<tr>
<td>Divorced</td>
<td>1 (7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Widowed</td>
<td>2 (13)</td>
<td>1 (7)</td>
<td>3 (19)</td>
</tr>
<tr>
<td>Never married</td>
<td>3 (20)</td>
<td>5 (33)</td>
<td>4 (25)</td>
</tr>
<tr>
<td>Previous psychiatric treatment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11 (73)</td>
<td>12 (80)</td>
<td>11 (69)</td>
</tr>
<tr>
<td>G.P.</td>
<td>3 (20)</td>
<td>3 (20)</td>
<td>3 (19)</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>1 (7)</td>
<td>0</td>
<td>2 (12)</td>
</tr>
</tbody>
</table>
TABLE 4-5 — Numbers of patients receiving each type of treatment from 13 months: combined cohort.

<table>
<thead>
<tr>
<th>Months since surgery</th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
<th>Combined treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>36*</td>
<td>39†</td>
<td>37</td>
</tr>
<tr>
<td>18</td>
<td>32*</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>24</td>
<td>27</td>
<td>31</td>
<td>35</td>
</tr>
</tbody>
</table>

*Sample size two less for self rating scales as patients felt too ill physically to complete them.
†Sample size one less for self rating scales as one patient felt too depressed to complete them.

TABLE 4-6 — Mean scores for physical symptoms

<table>
<thead>
<tr>
<th>Months since surgery</th>
<th>Radiotherapy</th>
<th>Chemotherapy</th>
<th>Combined treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
</tr>
<tr>
<td>3</td>
<td>3.2</td>
<td>3.4</td>
<td>3.1</td>
</tr>
<tr>
<td>6</td>
<td>0.4 *</td>
<td>3.8</td>
<td>3.6</td>
</tr>
<tr>
<td>13</td>
<td>0.7 *</td>
<td>3.7</td>
<td>3.8</td>
</tr>
<tr>
<td>18</td>
<td>1.3 †</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>24</td>
<td>1.0</td>
<td>0.1</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*p<0.001; †p<0.1 (Kruskal-Wallis test on differences among groups)

TABLE 4-7 — Spearman correlation coefficients of ratings of mood with physical symptoms (total score and key individual symptoms).

<table>
<thead>
<tr>
<th>Mood scales</th>
<th>Physical symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total score</td>
</tr>
<tr>
<td>Observer depression</td>
<td>0.22</td>
</tr>
<tr>
<td>Observer anxiety</td>
<td>0.12</td>
</tr>
<tr>
<td>GHQ Anxiety/insomnia</td>
<td>0.17</td>
</tr>
<tr>
<td>GHQ Severe depression</td>
<td>0.25</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>0.19</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>0.11</td>
</tr>
</tbody>
</table>

*p<0.05; †p<0.02
### TABLE 4-8 — Spearman correlation coefficients of ratings of mood with conditioned reflex symptoms.

<table>
<thead>
<tr>
<th>Mood scales</th>
<th>Conditioned reflex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nausea</td>
</tr>
<tr>
<td>Observer depression</td>
<td>0.33*</td>
</tr>
<tr>
<td>Observer anxiety</td>
<td>0.40*</td>
</tr>
<tr>
<td>GHQ anxiety/insomnia</td>
<td>0.26</td>
</tr>
<tr>
<td>GHQ severe depression</td>
<td>0.31*</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>0.36*</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>0.37†</td>
</tr>
</tbody>
</table>

*P<0.05; †P<0.02

### TABLE 4-9 — Relationship of nausea, vomiting, and conditioned reflex (CR) nausea and vomiting.

<table>
<thead>
<tr>
<th>Drug-induced symptom</th>
<th>No CR symptoms</th>
<th>CR nausea</th>
<th>CR nausea+vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>No nausea</td>
<td>7*</td>
<td>1†</td>
<td>—</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6</td>
<td>9</td>
<td>17</td>
</tr>
</tbody>
</table>

*Five of the seven stopped chemotherapy before 13 months
†Stopped chemotherapy at 9 months
TABLE 4-10 — Relationship between mood, nausea/vomiting, and conditioned reflex nausea/vomiting.

<table>
<thead>
<tr>
<th></th>
<th>Nausea or vomiting</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-conditioned reflex (n=9)</td>
</tr>
<tr>
<td></td>
<td>Conditioned reflex (n=29)</td>
</tr>
<tr>
<td>Mean (SD) age</td>
<td></td>
</tr>
<tr>
<td>Observer ratings</td>
<td>Score  No (%)</td>
</tr>
<tr>
<td>Depression</td>
<td>0  7 (78)  12 (41)</td>
</tr>
<tr>
<td></td>
<td>'&gt;1 2 (22)  17 (59)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0  7 (78)  11 (38)</td>
</tr>
<tr>
<td></td>
<td>'&gt;1 2 (22)  18 (62)</td>
</tr>
<tr>
<td>GHQ subscales</td>
<td>Median (interquartile range)</td>
</tr>
<tr>
<td></td>
<td>Non-conditioned reflex</td>
</tr>
<tr>
<td>Anxiety/insomnia</td>
<td>4 (2.5-5.5)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0 (0-1.5)</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>2 (0.5-4)</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>2 (0-3.5)</td>
</tr>
<tr>
<td></td>
<td>Conditioned reflex</td>
</tr>
<tr>
<td></td>
<td>6 (2-11.5)</td>
</tr>
<tr>
<td></td>
<td>1 (0-6)</td>
</tr>
<tr>
<td></td>
<td>4 (2-9.5)</td>
</tr>
<tr>
<td></td>
<td>4 (2.5-9)</td>
</tr>
</tbody>
</table>

*p<0.05; †p<0.02
TABLE 5-1 — Patient characteristics (radiotherapy study).

<table>
<thead>
<tr>
<th></th>
<th>None (n=39)</th>
<th>Radio (n=47)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at operation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>53.9 (9.5)</td>
<td>51.1 (11.5)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Social class</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I+II</td>
<td>15 (38.4)</td>
<td>18 (38.3)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>20 (51.3)</td>
<td>23 (48.9)</td>
<td>n.s.</td>
</tr>
<tr>
<td>IV+V</td>
<td>4 (10.3)</td>
<td>6 (12.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>32 (82.0)</td>
<td>30 (63.8)</td>
<td></td>
</tr>
<tr>
<td>Divorced</td>
<td>1 (2.6)</td>
<td>4 (8.5)</td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>5 (12.8)</td>
<td>7 (14.9)</td>
<td>n.s.*</td>
</tr>
<tr>
<td>Never married</td>
<td>1 (2.6)</td>
<td>6 (12.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Previous psychiatric</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>28 (71.8)</td>
<td>30 (63.8)</td>
<td></td>
</tr>
<tr>
<td>G.P.</td>
<td>10 (25.6)</td>
<td>15 (31.9)</td>
<td>n.s.†</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>1 (2.6)</td>
<td>2 (4.3)</td>
<td></td>
</tr>
<tr>
<td><strong>E.P.I. score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extraversion</td>
<td>11.5 (3.8)</td>
<td>10.5 (3.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>9.9 (5.0)</td>
<td>8.5 (5.4)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Verbal I.Q.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>105.3 (11.5)</td>
<td>101.2 (11.2)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

*χ² test on married versus unmarried. †χ² test on some versus none.
TABLE 5-2 — Comparisons between treatment groups on observer ratings at one and three months: scores above 0.

<table>
<thead>
<tr>
<th>Months since mastectomy</th>
<th>1</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Depression</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>12 2 (37) 38 n.s.</td>
<td>7 2 (24) 38 n.s.</td>
</tr>
<tr>
<td>Radio</td>
<td>14 3 1 (38) 47</td>
<td>12 2 (30) 46</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>13 2 (39) 38 n.s.</td>
<td>7 4 (29) 38 n.s.</td>
</tr>
<tr>
<td>Radio</td>
<td>8 5 3 (34) 47</td>
<td>7 4 (24) 46</td>
</tr>
<tr>
<td><strong>Irritability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>34 4 (11) 38 n.s.</td>
<td>32 5 1 (16) 38 n.s.</td>
</tr>
<tr>
<td>Radio</td>
<td>39 7 1 (17) 47</td>
<td>38 7 1 (17) 46</td>
</tr>
<tr>
<td><strong>Libido</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>4 5 5 (45) 31 n.s.</td>
<td>5 3 3 (34) 32 n.s.</td>
</tr>
<tr>
<td>Radio</td>
<td>3 4 9 (52) 31</td>
<td>2 6 7 (48) 31</td>
</tr>
<tr>
<td><strong>Lethargy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (Under activity)</td>
<td>12 7 (50) 38 n.s.</td>
<td>8 3 (29) 38 &lt;0.001</td>
</tr>
<tr>
<td>Radio</td>
<td>21 6 2 (62) 47</td>
<td>18 12 (65) 46</td>
</tr>
<tr>
<td><strong>Routine upset</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>12 2 (37) 38 n.s.</td>
<td>6 2 (21) 38 &lt;0.04</td>
</tr>
<tr>
<td>Radio</td>
<td>13 4 1 (38) 47</td>
<td>12 6 (39) 46</td>
</tr>
<tr>
<td><strong>Inability to work</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>14 9 (61) 38 n.s.</td>
<td>10 1 (29) 38 n.s.</td>
</tr>
<tr>
<td>Radio</td>
<td>17 9 (55) 47</td>
<td>11 6 (37) 46</td>
</tr>
</tbody>
</table>

*One Stage I patient could not attend the one month interview & another the three month; one Stage II patient refused the three month interview.
†One-tailed test comparing proportions with some and no morbidity.
§Married/cohabiting patients only.
TABLE 5-3 — Comparisons between treatment groups at one and three months: self rating scales

<table>
<thead>
<tr>
<th>Months since mastectomy</th>
<th>1</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scale</strong></td>
<td><strong>Therapy</strong></td>
<td><em><em>Median (inter-quartile range) n</em> p†</em>*</td>
</tr>
<tr>
<td>General health</td>
<td>None</td>
<td>4.0 (1-12)</td>
</tr>
<tr>
<td>questionnaire</td>
<td>Radio</td>
<td>5.0 (2-15)</td>
</tr>
<tr>
<td><strong>Subscales</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>None</td>
<td>3.0 (1-5)</td>
</tr>
<tr>
<td>symptoms</td>
<td>Radio</td>
<td>3.0 (2-6)</td>
</tr>
<tr>
<td>Anxiety and insomnia</td>
<td>None</td>
<td>3.0 (0-7)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>3.0 (1-7)</td>
</tr>
<tr>
<td>Social</td>
<td>None</td>
<td>7.5 (7-9)</td>
</tr>
<tr>
<td>dysfunction</td>
<td>Radio</td>
<td>8.0 (7-10)</td>
</tr>
<tr>
<td>Severe</td>
<td>None</td>
<td>0.0 (0-1)</td>
</tr>
<tr>
<td>depression</td>
<td>Radio</td>
<td>0.0 (0-1)</td>
</tr>
<tr>
<td>Leeds</td>
<td>None</td>
<td>1.0 (0-3)</td>
</tr>
<tr>
<td>depression</td>
<td>Radio</td>
<td>2.0 (1-5)</td>
</tr>
<tr>
<td>Leeds</td>
<td>None</td>
<td>4.0 (1-7)</td>
</tr>
<tr>
<td>anxiety</td>
<td>Radio</td>
<td>3.0 (0-7)</td>
</tr>
</tbody>
</table>

*See Table 5-2
†One-tailed probability using the Mann-Whitney U-test.
TABLE 5-4 — Comparisons between treatment groups on observer ratings at six and 13 months: scores above 0.

<table>
<thead>
<tr>
<th>Months since mastectomy</th>
<th>6</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Score</td>
<td>Score</td>
</tr>
<tr>
<td><strong>Rating</strong></td>
<td><strong>Therapy</strong></td>
<td><strong>1</strong></td>
</tr>
<tr>
<td>Depression None</td>
<td>None</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>1</td>
</tr>
<tr>
<td>Anxiety None</td>
<td>None</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>2</td>
</tr>
<tr>
<td>Irritability None</td>
<td>None</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>1</td>
</tr>
<tr>
<td>Libido None</td>
<td>None</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>1</td>
</tr>
<tr>
<td>Lethargy None (Under activity)</td>
<td>None</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>4</td>
</tr>
<tr>
<td>Routine None</td>
<td>None</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>1</td>
</tr>
<tr>
<td>Inability None to work</td>
<td>None</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>2</td>
</tr>
</tbody>
</table>

*Patients randomised to chemotherapy after three months excluded; one Stage I patient refused the 13 month interview; two Stage II patients died after six months.

†One-tailed test comparing proportions with some and no morbidity.

*Married/cohabiting patients only.
<table>
<thead>
<tr>
<th>Months since mastectomy</th>
<th>6</th>
<th>13</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scale</strong></td>
<td><strong>Median (inter-quartile range)</strong></td>
<td><strong>n</strong>*</td>
</tr>
<tr>
<td>General health</td>
<td>None</td>
<td>0.0 (0-4)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>2.0 (0-12)</td>
</tr>
<tr>
<td><strong>Subscales</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic</td>
<td>None</td>
<td>2.0 (1-4)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>4.0 (1-8)</td>
</tr>
<tr>
<td>Anxiety and insomnia</td>
<td>None</td>
<td>3.0 (1-6)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>3.0 (1-7)</td>
</tr>
<tr>
<td>Social</td>
<td>None</td>
<td>7.0 (7-7)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>7.0 (7-8)</td>
</tr>
<tr>
<td>Severe</td>
<td>None</td>
<td>0.0 (0-1)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>0.0 (0-0)</td>
</tr>
<tr>
<td>Leeds</td>
<td>None</td>
<td>1.0 (0-3)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>2.0 (0-3)</td>
</tr>
<tr>
<td>Leeds</td>
<td>None</td>
<td>2.5 (1-6)</td>
</tr>
<tr>
<td></td>
<td>Radio</td>
<td>2.0 (0-6)</td>
</tr>
</tbody>
</table>

*See Table 5-4; also at 13 months two patients felt too ill to complete self rating scales.
†One-tailed probability using the Mann-Whitney U-test.
TABLE 5-6 — Physical symptoms in treatment groups: median scores and interquartile ranges

<table>
<thead>
<tr>
<th>Months since mastectomy</th>
<th>Therapy</th>
<th>Median (IQR) n*</th>
<th>Median (IQR) n*</th>
<th>Median (IQR) n*</th>
<th>Median (IQR) n*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>0.0 (0-1) 38</td>
<td>0.0 (0-0) 38</td>
<td>0.0 (0-0) 38</td>
<td>0.0 (0-0) 37</td>
</tr>
<tr>
<td>3</td>
<td>Radio</td>
<td>0.0 (0-1) 47</td>
<td>3.0 (2-4) 46</td>
<td>0.0 (0-1) 23</td>
<td>0.0 (0-1) 21</td>
</tr>
</tbody>
</table>

*For explanation see Tables II to IV.
†p<0.0001 (one-tailed probability using the Mann-Whitney U-test).

TABLE 5-7 — Spearman correlation coefficients between physical symptom scores and rating scales in radiotherapy patients at three months.

<table>
<thead>
<tr>
<th>Observer ratings</th>
<th>rho</th>
<th>p*</th>
<th>Self ratings</th>
<th>rho</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>.15</td>
<td>.33</td>
<td>General health questionnaire</td>
<td>.19</td>
<td>.21</td>
</tr>
<tr>
<td>Anxiety</td>
<td>.02</td>
<td>.87</td>
<td>Somatic symptoms</td>
<td>.27</td>
<td>.07</td>
</tr>
<tr>
<td>Irritability</td>
<td>.27</td>
<td>.07</td>
<td>Anxiety and insomnia</td>
<td>.04</td>
<td>.77</td>
</tr>
<tr>
<td>Libido loss</td>
<td>.17</td>
<td>.36</td>
<td>Social dysfunction</td>
<td>.25</td>
<td>.09</td>
</tr>
<tr>
<td>Under activity</td>
<td>.00</td>
<td>1.00</td>
<td>Severe depression</td>
<td>.17</td>
<td>.27</td>
</tr>
<tr>
<td>Routine upset</td>
<td>.58</td>
<td>.24</td>
<td>Leeds depression</td>
<td>.14</td>
<td>.35</td>
</tr>
<tr>
<td>Inability to work</td>
<td>.58</td>
<td>.11</td>
<td>Leeds anxiety</td>
<td>.01</td>
<td>.96</td>
</tr>
</tbody>
</table>

*Two-tailed
### TABLE 6-1 — Observer scales in benign group: scores above 0.

<table>
<thead>
<tr>
<th>Months after surgery</th>
<th>One (n=34)</th>
<th>Three (n=34)</th>
<th>13 (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating</td>
<td>1 2 3 %&gt;0</td>
<td>1 2 3 %&gt;0</td>
<td>1 2 3 %&gt;0</td>
</tr>
<tr>
<td>Depression</td>
<td>5 1 0 (18)</td>
<td>6 0 0 (18)</td>
<td>2 1 0 (10)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6 1 0 (21)</td>
<td>6 1 0 (21)</td>
<td>4 0 0 (13)</td>
</tr>
<tr>
<td>Irritability</td>
<td>4 0 0 (12)</td>
<td>2 0 0 (6)</td>
<td>2 0 0 (7)</td>
</tr>
<tr>
<td>Libido loss*</td>
<td>2 0 0 (8)</td>
<td>1 1 0 (8)</td>
<td>1 0 0 (5)</td>
</tr>
<tr>
<td>Under activity</td>
<td>7 3 0 (29)</td>
<td>6 1 0 (21)</td>
<td>4 1 0 (17)</td>
</tr>
<tr>
<td>Routine upset</td>
<td>1 0 0 (3)</td>
<td>3 0 0 (9)</td>
<td>1 0 0 (3)</td>
</tr>
<tr>
<td>Work problems</td>
<td>1 1 0 (6)</td>
<td>2 0 0 (6)</td>
<td>2 0 0 (7)</td>
</tr>
</tbody>
</table>

*Married/cohabiting patients: sample sizes 26, 26, 22 respectively
Changes in scores on all scales not significant (Cochran's Q tests comparing some versus no morbidity over the three time intervals).

### TABLE 6-2 — Self rating scales in benign group: median scores and interquartile ranges

<table>
<thead>
<tr>
<th>Months after surgery</th>
<th>One (n=34)</th>
<th>Three (n=34)</th>
<th>13 (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scale</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>General health</td>
<td>2.0 (0-7)</td>
<td>0.0 (0-6)</td>
<td>0.0 (0-1)</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>4.0 (2-5)</td>
<td>2.0 (1-4)</td>
<td>0.0 (0-7)</td>
</tr>
<tr>
<td>Anxiety &amp; insomnia</td>
<td>5.0 (2-6)</td>
<td>3.0 (1-7)</td>
<td>3.0 (1-7)</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (7-7)</td>
<td>7.0 (7-7)</td>
<td>7.0 (7-7)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.0 (0-2)</td>
<td>0.0 (0-1)</td>
<td>0.0 (0-1)</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>1.5 (0-5)</td>
<td>1.5 (0-4)</td>
<td>1.0 (0-3)</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>3.0 (1-7)</td>
<td>2.5 (0-5)</td>
<td>3.0 (0-7)</td>
</tr>
</tbody>
</table>

Changes in scores on all scales not significant (Friedman analysis of variance).
### TABLE 6-3 — Benign breast group: correlations between age and scores on rating scales (n=34)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Spearman rho</th>
<th>Scale</th>
<th>Spearman rho</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>0.07</td>
<td>General health questionnaire</td>
<td>-0.01</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-0.10</td>
<td>Somatic symptoms</td>
<td>-0.21</td>
</tr>
<tr>
<td>Irritability</td>
<td>0.03</td>
<td>Anxiety &amp; insomnia</td>
<td>0.01</td>
</tr>
<tr>
<td>Libido loss*</td>
<td>0.07</td>
<td>Social dysfunction</td>
<td>-0.10</td>
</tr>
<tr>
<td>Under activity</td>
<td>0.20</td>
<td>Severe depression</td>
<td>0.08</td>
</tr>
<tr>
<td>Routine upset</td>
<td>0.31</td>
<td>Leeds depression</td>
<td>0.15</td>
</tr>
<tr>
<td>Work problems</td>
<td>0.34†</td>
<td>Leeds anxiety</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Married/cohabiting patients only: sample size=26.
†p=0.052

### TABLE 6-4 — Cholecystectomy patients at three months: correlations between age and scores on rating scales (n=26*)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Spearman rho</th>
<th>Scale</th>
<th>Spearman rho</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>0.08</td>
<td>General health questionnaire</td>
<td>0.05</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.15</td>
<td>Somatic symptoms</td>
<td>0.04</td>
</tr>
<tr>
<td>Irritability</td>
<td>0.12</td>
<td>Anxiety &amp; insomnia</td>
<td>0.12</td>
</tr>
<tr>
<td>Libido loss†</td>
<td>0.09</td>
<td>Social dysfunction</td>
<td>0.21</td>
</tr>
<tr>
<td>Under activity</td>
<td>0.17</td>
<td>Severe depression</td>
<td>0.06</td>
</tr>
<tr>
<td>Routine upset</td>
<td>0.15</td>
<td>Leeds depression</td>
<td>0.37</td>
</tr>
<tr>
<td>Work problems</td>
<td>0.26</td>
<td>Leeds anxiety</td>
<td>0.11</td>
</tr>
</tbody>
</table>

*Four of the original 30 patients refused to be seen after surgery.
†Married/cohabiting patients only: sample size=21.
**TABLE 6-5** — Clinical depression and anxiety on observer scales in cancer patients: numbers, percentages and 95% confidence intervals (CI).

<table>
<thead>
<tr>
<th>Months after mastectomy</th>
<th>Score $\geq 2$ No (%) CI</th>
<th>Score $\geq 2$ No (%) CI</th>
<th>Score $\geq 2$ No (%) CI</th>
<th>Score $\geq 2$ No (%) CI</th>
<th>Score $\geq 2$ No (%) CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=89)</td>
<td>7 (8) 2-14% 6 (7) 1-13% 4 (5) 0-10% 6 (7) 2-14% 1 (1) *</td>
<td>31 0 (3) 0.003 15 2 1 (10) 0.008 13 4 0 (7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (n=86)</td>
<td>13 (15) 8-22% 7 (8) 2-14% 5 (6) 1-11% 2 (2) *</td>
<td>40 0 (0) 0.013 8 4 3 (23) 0.07 11 5 1 (10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (n=85)</td>
<td>7 0 (0) 0.04 10 1 0 (36) 0.01 6 0 0 (10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 (n=81)</td>
<td>2 0 (0) 0.001 7 7 6 (48) 0.001 2 2 8 (24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 (n=73)</td>
<td>7 2 0 (7) 0.14 12 3 1 (13) 0.20 20 10 0 (17)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24 (n=68)</td>
<td>1 0 0 (0) 0.001 12 2 1 (10) 0.53 19 5 0 (9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Percentages were too low for valid confidence intervals.

**TABLE 6-6** — Observer scales at one month: numbers of patients with morbidity and percentages with clinical symptoms (score of 2 or above)

<table>
<thead>
<tr>
<th>Matched Benign</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=31</td>
</tr>
<tr>
<td>Rating</td>
<td>1 2 3 $\geq 2$ px</td>
</tr>
<tr>
<td>Depression</td>
<td>3 1 0 (3) 0.003</td>
</tr>
<tr>
<td>Anxiety</td>
<td>4 0 0 (0) 0.013</td>
</tr>
<tr>
<td>Irritability</td>
<td>3 0 0 (0) 0.04</td>
</tr>
<tr>
<td>Libido loss‡</td>
<td>2 0 0 (0) 0.001</td>
</tr>
<tr>
<td>Under activity</td>
<td>7 2 0 (7) 0.14</td>
</tr>
<tr>
<td>Routine upset</td>
<td>1 0 0 (0) 0.001</td>
</tr>
<tr>
<td>Inability to work</td>
<td>1 0 0 (0) 0.001</td>
</tr>
</tbody>
</table>

*Benign compared with cancer aged <50 years; some versus no morbidity.
‡Cancer aged <50 years compared with cancer aged >50 years; some versus no morbidity.
§Married/cohabiting patients only: sample sizes 27,27,42 respectively.
<table>
<thead>
<tr>
<th>Scale</th>
<th>Matched benign</th>
<th>Cancer</th>
<th>Cancer</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=31</td>
<td>Age&lt;50</td>
<td>Age&lt;50</td>
<td>Age&gt;50</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>1.0 (0-4)</td>
<td>0.005</td>
<td>7.0 (2-23)</td>
<td>0.12</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>4.0 (2-5)</td>
<td>0.62</td>
<td>4.0 (2-7)</td>
<td>0.29</td>
</tr>
<tr>
<td>Anxiety and insomnia</td>
<td>5.0 (2-6)</td>
<td>0.09</td>
<td>6.0 (2-11)</td>
<td>0.004</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (6-7)</td>
<td>0.005</td>
<td>8.0 (7-10)</td>
<td>0.82</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.0 (0-2)</td>
<td>0.52</td>
<td>0.0 (0-2)</td>
<td>0.23</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>1.0 (0-4)</td>
<td>0.21</td>
<td>2.0 (0-5)</td>
<td>0.49</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>2.0 (0-6)</td>
<td>0.08</td>
<td>5.0 (2-9)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Benign versus cancer aged <50 years.
†Cancer aged <50 years versus cancer aged >50 years.
TABLE 6-8 — Observer scales at three months: numbers of patients with morbidity and percentages with clinical symptoms (score of 2 or above)

<table>
<thead>
<tr>
<th>Scale</th>
<th>Cholecystectomy</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age&lt;50</td>
<td>Age ≥50</td>
</tr>
<tr>
<td></td>
<td>n=26</td>
<td>n=29</td>
</tr>
<tr>
<td>Rating</td>
<td>1 2 3</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Depression</td>
<td>5 3 0 (12)</td>
<td>8 4 0 (14)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6 2 0 (8)</td>
<td>9 3 1 (14)</td>
</tr>
<tr>
<td>Irritability</td>
<td>3 0 0 (0)</td>
<td>8 2 0 (7)</td>
</tr>
<tr>
<td>Libido loss†</td>
<td>3 0 0 (0)</td>
<td>4 7 6 (48)</td>
</tr>
<tr>
<td>Under activity</td>
<td>10 5 0 (19)</td>
<td>6 8 0 (28)</td>
</tr>
<tr>
<td>Routine upset</td>
<td>4 1 0 (4)</td>
<td>2 6 0 (21)</td>
</tr>
<tr>
<td>Inability to work</td>
<td>6 0 0 (0)</td>
<td>6 3 0 (10)</td>
</tr>
</tbody>
</table>

*Cancer aged <50 years compared with cancer aged ≥50 years; some v. no morbidity
†Married/cohabiting patients only: sample size 21,27,43 respectively

TABLE 6-9 — Self rating scales at three months: median scores and interquartile ranges

<table>
<thead>
<tr>
<th>Scale</th>
<th>Cholecystectomy</th>
<th>Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age&lt;50</td>
<td>Age ≥50</td>
</tr>
<tr>
<td></td>
<td>n=26</td>
<td>n=29</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>2.5 (0-10)</td>
<td>5.0 (0-23)</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>2.0 (1-6)</td>
<td>4.0 (2-7)</td>
</tr>
<tr>
<td>Anxiety/insomnia</td>
<td>4.0 (1-8)</td>
<td>6.0 (3-11)</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (6-9)</td>
<td>7.0 (7-9)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.0 (0-3)</td>
<td>1.0 (0-3)</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>2.0 (1-4)</td>
<td>4.0 (2-6)</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>4.5 (0-5)</td>
<td>4.0 (2-9)</td>
</tr>
</tbody>
</table>

*Cancer aged <50 years versus cancer aged ≥50 years.
TABLE 6-10 — Observer scales at six months: numbers of cancer patients with morbidity and percentages with clinical symptoms (score of 2 or above)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Age &lt;50</th>
<th>Age &gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=29</td>
<td>n=56</td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td>6 3 0 (10)</td>
<td>5 1 0 (2)</td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>9 2 0 (7)</td>
<td>7 2 1 (5)</td>
</tr>
<tr>
<td><strong>Irritability</strong></td>
<td>5 1 0 (7)</td>
<td>4 0 0 (0)</td>
</tr>
<tr>
<td><strong>Libido loss†</strong></td>
<td>6 5 4 (33)</td>
<td>3 0 5 (12)</td>
</tr>
<tr>
<td><strong>Under activity</strong></td>
<td>10 2 0 (7)</td>
<td>12 5 0 (9)</td>
</tr>
<tr>
<td><strong>Routine upset</strong></td>
<td>7 2 0 (7)</td>
<td>10 1 0 (2)</td>
</tr>
<tr>
<td><strong>Inability to work</strong></td>
<td>4 1 0 (3)</td>
<td>8 2 1 (5)</td>
</tr>
</tbody>
</table>

*Χ² test: some versus no morbidity.
†Married/cohabiting patients only: sample sizes 27 and 42.

TABLE 6-11 — Self rating scales in cancer patients at six months: median scores and interquartile ranges.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Age&lt;50</th>
<th>Age&gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=29</td>
<td>n=55</td>
</tr>
<tr>
<td><strong>General health questionnaire</strong></td>
<td>5.0 (0-14)</td>
<td>1.0 (0-5)</td>
</tr>
<tr>
<td><strong>Somatic symptoms</strong></td>
<td>4.0 (2-8)</td>
<td>3.0 (1-5)</td>
</tr>
<tr>
<td><strong>Anxiety/insomnia</strong></td>
<td>5.0 (1-10)</td>
<td>3.0 (1-6)</td>
</tr>
<tr>
<td><strong>Social dysfunction</strong></td>
<td>7.0 (7-9)</td>
<td>7.0 (6-8)</td>
</tr>
<tr>
<td><strong>Severe depression</strong></td>
<td>0.0 (0-2)</td>
<td>0.0 (0-1)</td>
</tr>
<tr>
<td><strong>Leeds depression</strong></td>
<td>2.0 (1-6)</td>
<td>2.0 (1-3)</td>
</tr>
<tr>
<td><strong>Leeds anxiety</strong></td>
<td>5.0 (2-9)</td>
<td>2.0 (0-4)</td>
</tr>
</tbody>
</table>

*Mann-Whitney test
TABLE 6-12 — Observer scales at 13 months: numbers of cancer patients with morbidity and percentages with clinical symptoms (score of 2 or above)

<table>
<thead>
<tr>
<th>Age &lt;50</th>
<th>Age &gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=29</td>
<td>n=52</td>
</tr>
<tr>
<td>Rating</td>
<td>1 2 3</td>
</tr>
<tr>
<td>Depression</td>
<td>9 3 0 (10)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>15 0 0 (0)</td>
</tr>
<tr>
<td>Irritability</td>
<td>5 2 0 (7)</td>
</tr>
<tr>
<td>Libido loss†</td>
<td>5 4 6 (35)</td>
</tr>
<tr>
<td>Under activity</td>
<td>11 5 0 (17)</td>
</tr>
<tr>
<td>Routine upset</td>
<td>7 1 0 (3)</td>
</tr>
<tr>
<td>Inability to work</td>
<td>3 3 0 (10)</td>
</tr>
</tbody>
</table>

*Some versus no morbidity.
†Married/cohabiting patients only: sample sizes 26 and 37.

TABLE 6-13 — Self rating scales in cancer patients at 13 months: median scores and interquartile ranges.

<table>
<thead>
<tr>
<th>Age&lt;50</th>
<th>Age&gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=29</td>
<td>n=51</td>
</tr>
<tr>
<td>Scale</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>12.0 (0-20)</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>5.0 (2-9)</td>
</tr>
<tr>
<td>Anxiety/insomnia</td>
<td>6.0 (3-11)</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (7-10)</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.0 (0-3)</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>4.0 (1-6)</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>5.0 (2-8)</td>
</tr>
</tbody>
</table>

*Mann-Whitney test
TABLE 6-14 — Observer scales at 18 months: numbers of cancer patients with morbidity and percentages with clinical symptoms (score of 2 or above)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Age &lt;50</th>
<th></th>
<th></th>
<th>p</th>
<th>Age ≥50</th>
<th></th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=28</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>%≥2</td>
<td>n=45</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>(0)</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>(11)</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Irritability</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>(0)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Libido loss†</td>
<td>6</td>
<td>4</td>
<td>2</td>
<td>(23)</td>
<td>0.01</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Under activity</td>
<td>7</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>(11)</td>
<td>8</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Routine upset</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>(7)</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Inability to work</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>(4)</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*X² (Fisher exact†) tests: some versus no morbidity.
†Married/cohabiting patients only: sample sizes 26 and 31.

TABLE 6-15 — Self rating scales in cancer patients at 18 months: median scores and interquartile ranges.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Age&lt;50</th>
<th></th>
<th></th>
<th>p</th>
<th>Age≥50</th>
<th></th>
<th></th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=28</td>
<td>Median</td>
<td>(IQR)</td>
<td>p</td>
<td>n=45</td>
<td>Median</td>
<td>(IQR)</td>
<td>p</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>4.0 (0-12)</td>
<td>0.02</td>
<td></td>
<td></td>
<td>0.0 (0-4)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>4.5 (2-8)</td>
<td>0.02</td>
<td></td>
<td></td>
<td>2.0 (1-5)</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety/insomnia</td>
<td>5.5 (2-8)</td>
<td>0.03</td>
<td></td>
<td></td>
<td>3.0 (1-5)</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (6-8)</td>
<td>0.88</td>
<td></td>
<td></td>
<td>7.0 (6-7)</td>
<td>0.88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.5 (0-1)</td>
<td>0.09</td>
<td></td>
<td></td>
<td>0.0 (0-1)</td>
<td>0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leeds depression</td>
<td>2.0 (0-4)</td>
<td>0.93</td>
<td></td>
<td></td>
<td>2.0 (1-3)</td>
<td>0.93</td>
<td></td>
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</tr>
<tr>
<td>Leeds anxiety</td>
<td>4.5 (1-7)</td>
<td>0.07</td>
<td></td>
<td></td>
<td>2.0 (0-7)</td>
<td>0.07</td>
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</tbody>
</table>

*Mann-Whitney test
### TABLE 6-16 — Observer scales at 24 months: numbers of cancer patients with morbidity and percentages with clinical symptoms (score of 2 or above)

<table>
<thead>
<tr>
<th>Rating</th>
<th>Age &lt;50</th>
<th>Age &gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=25</td>
<td>n=43</td>
</tr>
<tr>
<td>Depression</td>
<td>1 2 3 %2</td>
<td>1 2 3 %2</td>
</tr>
<tr>
<td></td>
<td>5 0 0 (0)</td>
<td>4 1 0 (2)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8 1 0 (3)</td>
<td>1 0 0 (0)</td>
</tr>
<tr>
<td>Irritability</td>
<td>1 0 0 (0)</td>
<td>1 0 0 (0)</td>
</tr>
<tr>
<td>Libido loss†</td>
<td>4 4 1 (21)</td>
<td>2 0 3 (10)</td>
</tr>
<tr>
<td>Under activity</td>
<td>6 0 0 (0)</td>
<td>8 1 1 (5)</td>
</tr>
<tr>
<td>Routine upset</td>
<td>4 0 0 (0)</td>
<td>4 2 0 (5)</td>
</tr>
<tr>
<td>Inability to work</td>
<td>2 0 0 (0)</td>
<td>2 2 0 (9)</td>
</tr>
</tbody>
</table>

*Χ² tests: some versus no morbidity.
†Married/cohabiting patients only: sample sizes 24 and 30.

### TABLE 6-17 — Self rating scales in cancer patients at 24 months: median scores and interquartile ranges.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Age&lt;50</th>
<th>Age&gt;50</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=25</td>
<td>n=43</td>
</tr>
<tr>
<td>General health questionnaire</td>
<td>2.0 (0-7)</td>
<td>0.075</td>
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<tr>
<td>Somatic symptoms</td>
<td>4.0 (2-6)</td>
<td>0.51</td>
</tr>
<tr>
<td>Anxiety/insomnia</td>
<td>5.0 (2-8)</td>
<td>0.16</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>7.0 (7-8)</td>
<td>0.83</td>
</tr>
<tr>
<td>Severe depression</td>
<td>0.0 (0-2)</td>
<td>0.30</td>
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<tr>
<td>Leeds depression</td>
<td>2.0 (1-5)</td>
<td>0.72</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>5.0 (1-8)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

*Mann-Whitney test*
TABLE 6-18 — Numbers (percentages) resuming work.

<table>
<thead>
<tr>
<th>Months after mastectomy</th>
<th>1</th>
<th>3</th>
<th>6</th>
<th>13</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full-hours*</td>
<td>6 (17)</td>
<td>15 (44)</td>
<td>23 (72)</td>
<td>11 (79)</td>
<td>21 (78)</td>
<td>22 (88)</td>
</tr>
<tr>
<td>Reduced hours</td>
<td>1 (3)</td>
<td>2 (6)</td>
<td>4 (13)</td>
<td>3 (10)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Not back at work</td>
<td>29 (80)</td>
<td>17 (50)</td>
<td>5 (16)</td>
<td>6 (20)</td>
<td>6 (22)</td>
<td>3 (12)</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>34</td>
<td>32</td>
<td>30</td>
<td>27</td>
<td>25</td>
</tr>
</tbody>
</table>

*See text.
| 16 | | -36† -12 | -11 -19 -15 | 23* 10 07 16 | 15 12 00 -19 23* | 27* 17 -12 -10 -06 -03 | -08 14 -09 -06 -01 00 09 | -03 -40† 04 05 03 27* -17 -06 | -16 -42† 11 11 -13 -06 -12 23* 41† | -32† 00 20 -15 02 00 -02 23* 01 13 | -14 03 09 10 01 01 05 -02 07 08 04 | -28* -26* -04 04 -09 -08 -11 -02 10 17 02 09 | -48† -17 02 14 -16 -04 -24* -05 13 08 -03 11 81† | -19 -12 -06 -04 -02 -01 -15 06 04 18 00 13 49† 45† | -17 -10 05 -08 -09 00 01 -08 00 06 -02 14 70† 58† | -04 -25* -14 -08 -06 -02 -08 15 18 14 04 80† 51† | -20 -12 09 04 -03 -11 -22* -09 04 03 -17 11 67† 73† | -30† -10 11 02 -06 03 -18 -10 15 05 -07 01 73† 79† | -31† -15 19 11 10 03 00 -04 02 00 12 25* 26* 29† | -40† -10 19 10 -06 -03 -04 -02 09 -04 01 18 30† 48† | -32† -05 19 00 00 -02 -08 -16 -02 -09 11 19 12 25* | -24* 00 14 15 06 04 00 00 08 -01 11 28* 19 20 | -12 -25* 13 -04 12 01 01 02 07 06 13 19 24* 16 | -26* -02 08 04 08 04 02 -14 -09 -21* -02 21 26* 38† | -33† -11 09 00 -07 10 -08 -16 06 -05 02 08 25* 44† | -13 02 04 -16 -01 14 -06 -06 11 -17 -02 -06 42* 42† | -12 01 25† -06 -12 -07 00 10 -21 01 09 01 -12 -14 | 21 -36† -02 00 08 -05 10 10 34† 40† -05 -18 15 00 |

*p < 0.05; †p < 0.01 (two-tailed)
TABLE 6-20 — Independent predictors of morbidity at 13 months after mastectomy in 79 patients (GHQ-60 = 60-item General Health Questionnaire).

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Predictors</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHQ-60</td>
<td>Leeds depression at one month; age</td>
<td>0.18</td>
</tr>
<tr>
<td>Somatic symptoms</td>
<td>Eysenck neuroticism; chemotherapy treatment</td>
<td>0.20</td>
</tr>
<tr>
<td>Anxiety/insomnia</td>
<td>Anxiety/insomnia at one month Eysenck neuroticism; age</td>
<td>0.34</td>
</tr>
<tr>
<td>Social dysfunction</td>
<td>Social class; Leeds depression at one month</td>
<td>0.13</td>
</tr>
<tr>
<td>Severe depression</td>
<td>GHQ-60 score at one month; Leeds depression at one month; Eysenck neuroticism; age</td>
<td>0.29</td>
</tr>
<tr>
<td>Leeds depression</td>
<td>GHQ-60 score at one month; Leeds depression at one month; Eysenck neuroticism; age</td>
<td>0.39</td>
</tr>
<tr>
<td>Leeds anxiety</td>
<td>Eysenck neuroticism; age</td>
<td>0.37</td>
</tr>
</tbody>
</table>

TABLE 6-21 — Independent predictors of morbidity at 13 months after mastectomy in 79 patients, after transformation of dependent variables. (GHQ-60 = 60-item General Health Questionnaire).

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Predictors</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log_e (GHQ-60+1)</td>
<td>Leeds depression at one month; Eysenck neuroticism; verbal intelligence quotient; age; chemotherapy treatment</td>
<td>0.34</td>
</tr>
<tr>
<td>Log_e (Somatic symptoms+1)</td>
<td>Eysenck neuroticism; chemotherapy treatment</td>
<td>0.23</td>
</tr>
<tr>
<td>Log_e (Social dysfunction+1)</td>
<td>Social class; Leeds depression at one month; chemotherapy treatment</td>
<td>0.15</td>
</tr>
<tr>
<td>4(Severe depression)</td>
<td>GHQ-60 score at one month; Leeds depression at one month; Eysenck neuroticism; age</td>
<td>0.28</td>
</tr>
</tbody>
</table>
TABLE 6-22 — Regression equations to predict morbidity at 13 months.

**Dependent variable untransformed**

- **Anxiety/Insomnia** = 6.97 + .18(1/12 anxiety/insomnia) + .26(Eysenck neuroticism) - .10(age)
- **Leeds Depression** = 0.37 + .61(1/12 Leeds depression) + .18(Eysenck neuroticism) - .07(1/12 GHQ60 score + 1.11(chemotherapy treatment*))
- **Leeds Anxiety** = 5.13 + .33(Eysenck neuroticism) - .08(age)

**Dependent variable transformed**

- Loge (GHQ-60 +1) = -.32 + .12(1/12 Leeds depression) + .06(Eysenck neuroticism) - .04(age) + .74(chemotherapy treatment*) + .02(verbal intelligence quotient)
- Loge (Somatic symptoms +1) = .82 + .06(Eysenck neuroticism) + .45(chemotherapy treatment*)
- Loge (Social dysfunction +1) = 2.27 + .02(1/12 Leeds depression) - .09(social class) + .12(chemotherapy treatment*)
- 4/ (Severe depression) = 1.02 + .11(1/12 Leeds depression) + .05(Eysenck neuroticism) - .07(1/12 Leeds anxiety) - .02(age)

*The term "chemotherapy treatment" can be replaced by its code of 1.*
Figure 6-1 — Histogram of standardized residuals for 60-item GHQ

<table>
<thead>
<tr>
<th>Observed</th>
<th>Expected</th>
<th>SD</th>
<th>(* = 1 Case) (:. = Normal Curve)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>.06</td>
<td>&gt;3.00</td>
<td>*</td>
</tr>
<tr>
<td>1</td>
<td>.12</td>
<td>3.00</td>
<td>*</td>
</tr>
<tr>
<td>0</td>
<td>.31</td>
<td>2.67</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>.70</td>
<td>2.33</td>
<td></td>
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<tr>
<td>0</td>
<td>1.44</td>
<td>2.00</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>2.64</td>
<td>1.67</td>
<td>*</td>
</tr>
<tr>
<td>7</td>
<td>4.33</td>
<td>1.33</td>
<td><strong>;</strong>*</td>
</tr>
<tr>
<td>6</td>
<td>6.37</td>
<td>1.00</td>
<td>********;</td>
</tr>
<tr>
<td>3</td>
<td>8.39</td>
<td>.67</td>
<td>*</td>
</tr>
<tr>
<td>4</td>
<td>9.90</td>
<td>.33</td>
<td>**</td>
</tr>
<tr>
<td>12</td>
<td>10.46</td>
<td>.00</td>
<td>*********<strong>;</strong></td>
</tr>
<tr>
<td>17</td>
<td>9.90</td>
<td>-.33</td>
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</tr>
<tr>
<td>16</td>
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<td>-.67</td>
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<td>**</td>
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<tr>
<td>2</td>
<td>4.33</td>
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<td>2.64</td>
<td>-1.67</td>
<td>*</td>
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<td>-2.00</td>
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<td>-2.33</td>
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</tbody>
</table>

Figure 6-2 — Histogram of standardized residuals for somatic symptoms subscale.

<table>
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<th>Observed</th>
<th>Expected</th>
<th>SD</th>
<th>(* = 1 Case) (:. = Normal Curve)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
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<td></td>
</tr>
<tr>
<td>1</td>
<td>.06</td>
<td>&gt;3.00</td>
<td>*</td>
</tr>
<tr>
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<td>.12</td>
<td>3.00</td>
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<td>.71</td>
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</tr>
<tr>
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<td>1.46</td>
<td>2.00</td>
<td>*</td>
</tr>
<tr>
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<td>1.67</td>
<td>**;</td>
</tr>
<tr>
<td>3</td>
<td>4.39</td>
<td>1.33</td>
<td>**;</td>
</tr>
<tr>
<td>4</td>
<td>6.45</td>
<td>1.00</td>
<td>****</td>
</tr>
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<td>8.50</td>
<td>.67</td>
<td>**;</td>
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<tr>
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<td>10.02</td>
<td>.33</td>
<td>********;</td>
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<td>******<strong>;;</strong></td>
</tr>
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<td>******<strong>;;</strong></td>
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<tr>
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<tr>
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<td>4.39</td>
<td>-1.33</td>
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<td>2.67</td>
<td>-1.67</td>
<td>*</td>
</tr>
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<td>-2.00</td>
<td></td>
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<td>-2.67</td>
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<tr>
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<td>.12</td>
<td>-3.00</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>.06</td>
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<td></td>
</tr>
</tbody>
</table>
### Figure 6-3 — Histogram of standardized residuals for severe depression subscale.

<table>
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<th>Expected n</th>
<th>SD</th>
<th>(* = 1 Case) (: = Normal Curve)</th>
</tr>
</thead>
<tbody>
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<tr>
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<td>2.67</td>
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</tr>
<tr>
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<td>.70</td>
<td>2.33</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.44</td>
<td>2.00</td>
<td>;***</td>
</tr>
<tr>
<td>1</td>
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<td>1.67</td>
<td>*</td>
</tr>
<tr>
<td>1</td>
<td>4.33</td>
<td>1.33</td>
<td>*</td>
</tr>
<tr>
<td>0</td>
<td>6.37</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>8.39</td>
<td>.67</td>
<td>;******</td>
</tr>
<tr>
<td>17</td>
<td>9.90</td>
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<td>;<strong><strong><strong><strong>;</strong></strong></strong></strong></td>
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<tr>
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<td>10.46</td>
<td>.00</td>
<td>;*****<em><strong>;</strong></em></td>
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<tr>
<td>18</td>
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<td>;<strong><strong><strong><strong>;</strong></strong></strong></strong></td>
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<tr>
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<td>;*****<em><strong>;</strong></em></td>
</tr>
<tr>
<td>5</td>
<td>6.37</td>
<td>-1.00</td>
<td>;****</td>
</tr>
<tr>
<td>6</td>
<td>4.33</td>
<td>-1.33</td>
<td>**<strong>;</strong></td>
</tr>
<tr>
<td>1</td>
<td>2.64</td>
<td>-1.67</td>
<td>*</td>
</tr>
<tr>
<td>0</td>
<td>1.44</td>
<td>-2.00</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>.70</td>
<td>-2.33</td>
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### Figure 6-4 — Histogram of standardized residuals for social dysfunction subscale.

<table>
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### Figure 6-5 — Histogram of standardized residuals for 60-item GHQ after transformation by Naperian logarithms.

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### Figure 6-6 — Histogram of standardized residuals for somatic symptoms subscale after transformation by Naperian logarithms.

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Figure 6-7 — Histogram of standardized residuals for severe depression subscale after fourth root transformation.

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Figure 6-8 — Histogram of standardized residuals for social dysfunction subscale after transformation by Naperian logarithms.

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Figure 7-1 — ROC curves: GHQ-60 (●—●) and GHQ-28 (○—○)

Figure 7-2 — ROC curves: somatic symptoms (●—●) and anxiety/insomnia (○—○)
Figure 7-3 — ROC curves: social dysfunction (●—●) and severe depression (○—○)
TABLE 7-1 — Correlation coefficients between observer ratings and general health questionnaire.

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<th>Observer rating (range)</th>
<th>Spearman rho*</th>
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<td>GHQ-60 Caseness</td>
<td>GHQ-60 Caseness (0-1)</td>
<td>0.72</td>
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<td>GHQ-28 Caseness</td>
<td>GHQ-28 Caseness (0-1)</td>
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<td>Somatic symptoms</td>
<td>Under activity (0-3)</td>
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<td>Anxiety/insomnia</td>
<td>Anxiety/insomnia (0-6)</td>
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</tr>
<tr>
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<tr>
<td>Severe depression</td>
<td>Depression (0-3)</td>
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*p<0.001 for all coefficients

TABLE 7-2 — Validity coefficients of 60-item GHQ at different threshold scores.

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<th>16+</th>
<th>17+</th>
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TABLE 7-3 — Validity coefficients of 28-item GHQ at different threshold scores.

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<td>100</td>
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<td>100</td>
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<td>80</td>
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### TABLE 7-4 — Validity coefficients of subscales of the GHQ at different threshold scores.

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<td><strong>Anxiety/insomnia</strong></td>
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<td>40</td>
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<td>77</td>
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<tr>
<td>Sensitivity</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
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<td>86</td>
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<td>50</td>
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<td>36</td>
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<td>Specificity</td>
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<td>97</td>
<td>97</td>
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<td>97</td>
</tr>
</tbody>
</table>

### TABLE 7-5 — Validity coefficients of Leeds scales at different threshold scores.

| Threshold | 0+ | 1+ | 2+ | 3+ | 4+ | 5+ | 6+ | 7+ | 8+ | 9+ | 10+ | 11+ | 12+ | 13+ | 14+ | 15+ | 16+ | 17+ |
|-----------|----|----|----|----|----|----|----|----|----|----|------|------|------|------|------|------|------|------|------|
| **Leeds depression** | | | | | | | | | | | | | | | | | | | | |
| Sensitivity | 100 | 100 | 100 | 100 | 100 | 93 | 86 | 79 | 71 | 50 | 36 | 36 | 29 | 29 | 14 | 14 | 14 | 0 |
| Specificity | 0 | 18 | 33 | 46 | 59 | 72 | 79 | 85 | 90 | 90 | 92 | 97 | 100 | 100 | 100 | 100 | 100 | 100 |
| % False positive | 100 | 92 | 67 | 54 | 41 | 28 | 21 | 15 | 10 | 10 | 8 | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Leeds anxiety** | | | | | | | | | | | | | | | | | | | | |
| Sensitivity | 100 | 100 | 100 | 86 | 86 | 86 | 86 | 86 | 57 | 57 | 57 | 43 | 43 | 29 | 29 | 14 | 14 | 14 | 0 |
| Specificity | 0 | 18 | 28 | 44 | 57 | 86 | 76 | 79 | 84 | 84 | 84 | 88 | 93 | 97 | 97 | 100 | 100 | 100 |
| % False positive | 100 | 82 | 72 | 56 | 43 | 35 | 24 | 21 | 16 | 16 | 16 | 12 | 7 | 3 | 3 | 0 | 0 | 0 | 0 |
TABLE 7-6 — Leeds depression and anxiety scales: correlations of total scores and item scores with observer ratings of mood.

<table>
<thead>
<tr>
<th>Self ratings</th>
<th>Observer depression (0-3)</th>
<th>Observer anxiety (0-3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leeds depression total score</td>
<td>0.75</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Depression items</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. I wake early and then sleep badly for the rest of the night</td>
<td>0.47</td>
<td>0.48</td>
</tr>
<tr>
<td>3. I feel miserable and sad</td>
<td>0.71</td>
<td>0.58</td>
</tr>
<tr>
<td>5. I have lost interest in things</td>
<td>0.68</td>
<td>0.58</td>
</tr>
<tr>
<td>7. I still enjoy the things I used to</td>
<td>0.45</td>
<td>0.58</td>
</tr>
<tr>
<td>9. I feel life is not worth living</td>
<td>0.59</td>
<td>0.58</td>
</tr>
<tr>
<td>10. I have a good appetite</td>
<td>0.36</td>
<td>0.36</td>
</tr>
<tr>
<td>Leeds anxiety total score</td>
<td>0.62</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Anxiety items</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. I get very frightened or panic feelings for apparently no reason at all</td>
<td>0.48</td>
<td>0.43</td>
</tr>
<tr>
<td>4. I feel anxious when I go out of the house on my own</td>
<td>0.36</td>
<td>0.28</td>
</tr>
<tr>
<td>6. I get palpitations or a sensation of 'butterflies' in my stomach</td>
<td>0.30</td>
<td>0.31</td>
</tr>
<tr>
<td>8. I feel scared or frightened</td>
<td>0.58</td>
<td>0.57</td>
</tr>
<tr>
<td>11. I am restless and can't keep still</td>
<td>0.49</td>
<td>0.45</td>
</tr>
<tr>
<td>12. I am more irritable than usual</td>
<td>0.49</td>
<td>0.50</td>
</tr>
</tbody>
</table>
APPENDIX 1:

OBSERVER SCALES

Copies of these scales were kindly provided by Dr Peter Maguire. Names of scales as supplied: Depressed mood, Anxiety/fears/worry, Under activity, Appetite, Sex, Sleep, Change in behaviour, Change in routine, Housework/work.

DEPRESSED MOOD

A. Crying
   Feeling miserable
   Looking miserable, unable to smile or laugh
   Feelings of hopelessness about the future
   Suicidal thoughts
   Suicidal attempt
   Increased morbid interest — not associated with worry

1 — Minor

B. i) occasional crying
   ii) occasional periods of feeling miserable, which is a clear departure from how the person normally looks, or occasionally complains of feeling miserable (should last more than 2 or 3 minutes and occur several times per day)

C. 2 — Moderate

b. i) frequent crying (e.g. would burst into tears for no apparent reason while watching T.V. These episodes occurred nearly every night, but interspersed with periods of appearing perfectly all right)
   ii) frequently looks miserable — rarely smiles or laughs and often complains of feeling miserable/unhappy for a week or more (e.g. for a whole week felt life had become "a real struggle" and unable to smile or laugh)
   iii) holds ideas of hopelessness about the future (but less strongly and persistently than "3" — see below)
   iv) occasional serious suicidal ideas without plan (with other signs of depressive mood change) — or minor self inflicted injury (not dangerous to life) e.g. scratching arms

C. 3 — Marked

B. i) continual or almost continual crying
   ii) so depressed seems to have no feelings at all, shows no emotion in response to anything
   iii) strongly holds ideas of hopelessness about the future,
or all of the time; e.g. would prefer to be dead, doesn't want to get better — believes there is no future and that nothing can help him

iv) depressive stupor

v) frequent suicidal ideas without plan (with other signs of depressive mood change); or occasional with plan (e.g. decided to attempt suicide — planned to use potassium cyanide which was readily available in her laboratory — and took a flat by herself specifically for the attempt).

vi) suicidal attempt or serious self-inflicted injury (e.g. setting fire to clothes) with other signs of depressive mood change

C. Felt miserable and hopeless. Depression very marked in the morning, but present throughout the day. He cried at least twice a week in private. Unable to smile or laugh. Suicidal thoughts.

Complained future was bleak — that there was no future. This feeling lasted longer than a week. Complained strongly of depression and she cried for part of every day. Felt the end was coming. Finally broke down in doctor's surgery, saying she couldn't go on living.

ANXIETY/FEAR/WORRY

A. Psychosomatic accompaniments
   Tenseness/anxiety
   Specific worry
   Panic attacks
   Phobias

1 — Minor

B. i) some increased anxiety, tenseness, specific worry anxious worry (i.e. diffuse/free-floating), or one of its somatic accompaniments e.g. palpitations, cold sweats, recent unusual bowel irregularity, indigestion, headaches lasting for 2 or 3 days

   ii) phobias which cause some anxiety unless avoids situation

C.

2 — Moderate

B. i) very frequent (several times a week) worry, tenseness, anxiety or one of above psychosomatic symptoms (e.g. had diarrhoea which remained constant for 12 weeks)

   ii) infrequent acute attacks of worry tenseness or anxiety — but short of panic

   iii) very infrequent panic attacks
iv) phobia(s) producing much anxiety unless avoids situation

C. Worried a lot about his job and the possibility of failing. Had occasional diarrhoea, palpitations or sweating. Felt very tense and anxious — paced up and down. Got rather anxious when having to meet people. Anxiety present most days of the week.

3 — Marked

B. i) continual and severe tenseness, anxiety etc. (e.g. rigid and nervous all week before admission)

ii) frequent and severe anxiety attacks (e.g. (1) on several occasions woke in the night and thought heart had stopped — couldn't breathe (2) had several "bad turns" when thought going to have a stroke, felt faint, frightening thoughts went round in head. Felt something awful going to happen — became "all worked up") N.B. Not panic attacks because not acted on

iii) panic attacks (unless very infrequent)

iv) phobias of such severity cause panic attack unless avoids situation

C. Complained of occasional diarrhoea, palpitations and sweating. Some worry and tenseness about his work. Became increasingly anxious about meeting people. On frequent occasions had to get up and leave room because he felt panicky.

UNDER ACTIVITY/RETARDATION

A. Slowness of thinking/speech
   Slowness of action i.e. retardation
   Feeling tired/complains no energy/getting up late/falling asleep in chair
   Stupor

1 — Minor

B. i) has occasional and unusual periods of tiredness

ii) some unusual difficulty in carrying on work or leisure activity because of tiredness

iii) some unusual difficulty in getting up in the morning

iv) some trouble with muddled/inconclusive thinking but not due to thought disorder

C.

2 — Moderate

B. i) frequently feels tired, several things are too much of an effort
ii) stops carrying out several activities e.g. hobbies. Tends to sit around doing nothing or watching T.V. rather than be involved with usual interests

iii) or keeps on with usual work or leisure activities but finds great difficulty in doing them as well as — or at same pace as used to

iv) great difficulty in getting up in the morning, often stays in bed later or goes to bed during day

C. After birth of baby felt very tired. Things became too much of an effort. Felt had no energy — did things very slowly. Lost interest in knitting and crochet. Sat around doing nothing much of the time. But managed to keep on looking after baby (a high 2 — nearly a 3)

3 — Marked

B. i) almost everything becomes too much of an effort — continually feels tired

   ii) stops practically all activities — hobbies, work, housework (practically all rôle functioning interrupted). Spends all time, or almost all time, sitting around doing nothing

   iii) frequently stays in bed all day

C.

DRIVE (APPETITE)

A. Appetite up
   Appetite down

N.B. Scale points differ from other scales in clinical section
   Nil = point 3 on scale

1 — Minor (Point 2 or 4 on scale)

B. i) some loss of appetite (e.g. felt a little "off" food: no meal refusal, but ate slightly less)

   ii) some increased hunger

2 — Moderate (Point 1 or 5 on scale)

B. i) considerable loss of appetite

   ii) considerable increase in appetite. Eats much more at, and in between meals

3 — Marked (Point 0 or 6 on scale)

B. i) complete or almost complete refusal of food and/or drink

   ii) eats all or almost all before him
DRIVE (SEX)

A. Sex up
   Sex down

N.B. Scale points differ
   Nil = 3 on 0 to 6 scale

1 — Minor (Point 2 or 4 on scale)

B. i) some loss of interest in sex
   ii) some increase of interest in sex

2 — Moderate (Point 1 or 5 on scale)

B. i) considerable loss of interest in sex
   ii) considerable increase of interest in sex

3 — Marked (Point 0 or 6 on scale)

B. i) complete or almost complete refusal of sex

SLEEP

A. Difficulty in getting off
   Waking early
   Waking during night — getting off again

1 — Minor (where total sleep is not more than one hour less than usual)

B. i) difficulty in getting off to sleep, waking up early, or waking during night and getting off again
   ii) some disturbance because of occasional nightmares

2 — Moderate

B. i) total sleep usually 2 hours less than before (e.g. unable to get to sleep before 3 a.m. for over a week — but as on holiday able to sleep much later in the mornings
   ii) frequent nightmares

3 — Marked

B. i) total sleep usually 3 hours less than before (e.g. (1) complained that he lay awake for "hours" — variable number — before getting off to sleep. Also waking in early morning at about 4 a.m. — but eventually able to get back to sleep again. (2) awoke at about 5 a.m. each morning for 12 weeks — even though taking sedation — and was unable to return to sleep)
SOCIALLY UNACCEPTABLE BEHAVIOUR

A. Irritability
   Verbal attacks
   Violence/destructive behaviour
   Odd/bizarre behaviour

1 — Minor

B. i) increased irritability
   ii) for women, crying occasionally in "public", i.e. before
       friend or close relatives
   iii) minor infringements of social manners, causing some
        annoyance
   iv) some screaming and shouting at home; verbal attacks on
       others if provoked
   v) occasionally knocking things about in the house
   vi) minor infringement of the law (shop-lifting, driving) on
       one occasion

C.

2 — Moderate

B. i) for men, crying occasionally in "public"; for women, crying
    often in "public"
   ii) causing embarrassment by being rude or offensive, picking
       quarrels etc.
   iii) frequent screaming and shouting at home. Frequent
       unprovoked verbal attacks
   iv) occasional unprovoked physical attacks
   v) "odd" behaviour (e.g. on 3 different occasions ran out of
       house and spent night in Waterloo Station)
   vi) minor infringements of the law on several occasions,
       without apparent motive

C.

3 — Marked

B. i) for men, crying often in public
   ii) falling out persistently with friends, relatives, neighbours
   iii) frequent unprovoked outbursts of shouting and screaming in
        one day
   iv) making physical attacks on others, with apparent intention
       of doing them serious harm
v) very strange behaviour, e.g. partial undressing, urinating, walking naked etc. in public

vi) major offence without apparent motive

vii) if done in public, serious self-inflicted injury (other than suicidal attempt) such as burning of skin, pushing a hand through a window, etc.

C.

EFFECT ON DAY-TO-DAY ROUTINE

A. Being less talkative/not answering back
Avoids seeing friends and relatives/draws the curtains loses interest in things (work, hobbies, family)/sitting around doing nothing
Appearance
Decisions

1 — Minor

B. i) slightly less talkative

ii) some decrease in desire to see/speak to friends, relatives etc.

iii) some decrease in pursuit of hobbies, leisure activities and accomplishments of usual jobs around the house; or leaves them unfinished or not done properly

iv) some loss of interest in appearance

v) some difficulty in making decisions; affects usual activity to some degree — e.g. avoids going shopping when can

C.

2 — Moderate

B. i) much less talkative than usual, frequently doesn't answer when spoken to

ii) considerable decrease in desire to see/speak to friends, relatives etc. (e.g. (1) only occasionally consents to visit friends, then shows discomfort (2) often refuses to answer 'phone or doorbell)

iii) considerable decrease in pursuit of hobbies, leisure activities and (for men) enthusiasm for doing jobs around the house

iv) spends part of each day in bed (gets up very late, etc.)

v) considerable loss of interest in appearance (e.g. hair, shaving, washing, make-up)

C.
3 — Severe

B. i) extremely withdrawn and retarded, virtually at a standstill
   ii) neglect of self care
   iii) loss of interest in all activities; shuns contact with people

IMPACT ON EMPLOYMENT (for men/women) & HOUSEWORK & CHILD CARE (for women)

A. Employment and/or housework/child care
   Impaired performance
   Stopping work

1 — Minor

B. Some fall-off in performance

2 — Moderate

B. For employment or housework:
   Definite fall-off in quality of performance or some time off/or amount done

3 — Marked

B. Largely stopped activities
APPENDIX 2:

RELIABILITY STUDY.

**TABLE A2-1 — Inter-rater reliability for depression and anxiety**

<table>
<thead>
<tr>
<th>Cooper</th>
<th>Depression</th>
<th>Hughson</th>
<th>Anxiety</th>
</tr>
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<tbody>
<tr>
<td>Rating</td>
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<td>4 0 3 1</td>
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<td>3</td>
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<td>0 0 0 0</td>
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<td>16 9 5 0</td>
<td>16 9 5 0</td>
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<tr>
<td>Kappa</td>
<td>0.74</td>
<td>0.68</td>
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</table>

**TABLE A2-2 — Inter-rater reliability for irritability and loss of libido**

<table>
<thead>
<tr>
<th>Cooper</th>
<th>Hughson</th>
<th>Irritability</th>
<th>Loss of libido*</th>
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<tbody>
<tr>
<td>Rating</td>
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<td>0 1 2 3 Total</td>
<td>0 1 2 3 Total</td>
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<td>3</td>
<td>0 0 0 0</td>
<td>0 0 0 3 3</td>
<td>0 0 0 3 3 0</td>
</tr>
<tr>
<td>Totals</td>
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<td>16 8 1 0 3</td>
<td>12 8 1 0 3 12</td>
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<tr>
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*Married/cohabiting patients only
TABLE A2-3 — Inter-rater reliability for under activity and routine upset

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<th>Rater</th>
<th>Cooper</th>
<th>Hughson</th>
<th>Cooper</th>
<th>Hughson</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating</td>
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<td>Under activity</td>
<td>Routine</td>
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<td>Total</td>
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</tr>
<tr>
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<td>0</td>
<td>1</td>
<td>1</td>
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<tr>
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<td>Kappa</td>
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<td>0.85</td>
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</table>

TABLE A2-4 — Inter-rater reliability for (house)work and insomnia

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<th>Cooper</th>
<th>Hughson</th>
<th>Cooper</th>
<th>Hughson</th>
</tr>
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<tbody>
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<td>Rating</td>
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<td>(House)work</td>
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<td>(House)work</td>
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<td>Kappa</td>
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<td>0.79</td>
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</table>
APPENDIX 3:

SELF RATING SCALES

GENERAL HEALTH QUESTIONNAIRE

Please read this carefully

We should like to know if you have had any medical complaints, and how your health has been in general, over the past few weeks. Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about recent complaints, not those you had in the past.

It is important that you try to answer ALL THE QUESTIONS.

Thank you very much for your co-operation.

HAVE YOU RECENTLY

<table>
<thead>
<tr>
<th>Question</th>
<th>Better than usual</th>
<th>Same as usual</th>
<th>Worse than usual</th>
<th>Much worse than usual</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Been feeling perfectly well and in good health?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Been feeling in need of a good tonic?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>3. Been feeling run down and out of sorts?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>4. Felt you are ill?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>5. Been getting any pains in your head?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>6. Been getting a feeling of tightness or pressure in your head?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>7. Been able to concentrate on whatever you're doing?</td>
<td>Better than usual</td>
<td>Same as usual</td>
<td>Less than usual</td>
<td>Much less than usual</td>
</tr>
<tr>
<td>8. Been afraid you were going to collapse in a public place?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
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<tr>
<td>9. Been having hot or cold spells?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
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<tr>
<td>10. Been perspiring (sweating) a lot?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>11. Found yourself waking early and unable to get back to sleep?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
</tr>
<tr>
<td>12. Been getting up feeling your sleep hasn't refreshed you?</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
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<tr>
<td>Question</td>
<td>Not at all</td>
<td>No more than usual</td>
<td>Rather more than usual</td>
<td>Much more than usual</td>
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<td>13. Been feeling too tired and exhausted even to eat?</td>
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<td>14. Lost much sleep over worry?</td>
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<td>15. Been feeling mentally alert and wide awake?</td>
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<td>16. Been feeling full of energy?</td>
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<td>17. Had difficulty in getting off to sleep?</td>
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<tr>
<td>18. Had difficulty in staying asleep once you are off?</td>
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<td>19. Been having frightening or unpleasant dreams?</td>
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<td>20. Been having restless, disturbed nights?</td>
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<td>21. Been managing to keep yourself busy and occupied?</td>
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<td>22. Been taking longer over the things you do?</td>
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<td>23. Tended to lose interest in your ordinary activities?</td>
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<tr>
<td>24. Been losing interest in your personal appearance?</td>
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<td>25. Been taking less trouble with your clothes?</td>
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<td>26. Been getting out of the house as such as usual?</td>
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<td>27. Been managing as well as most people would in your shoes?</td>
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<td>28. Felt on the whole you were doing things well?</td>
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<td>29. Been late getting to work or getting started on housework?</td>
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<td>30. Been satisfied with the way you've carried out your tasks?</td>
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<tr>
<td>Question</td>
<td>Rating Options</td>
<td></td>
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<td>-------------------------------------------------------------------------</td>
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<tr>
<td>31. Been able to feel warmth and affection for those near to you?</td>
<td>Better than usual</td>
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<td></td>
<td>About same as usual</td>
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<td></td>
<td>Less well than usual</td>
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<td></td>
<td>Much less well</td>
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<tr>
<td>32. Been finding it easy to get on with people?</td>
<td>Better than usual</td>
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<td></td>
<td>About same as usual</td>
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<td>Less well than usual</td>
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<td></td>
<td>Much less well</td>
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<tr>
<td>33. Spent much time chatting to people?</td>
<td>More time than usual</td>
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<td></td>
<td>About same as usual</td>
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<td>Less than usual</td>
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<td></td>
<td>Much less than usual</td>
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<tr>
<td>34. Kept feeling afraid to say anything to people in case you made a fool of yourself?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Rather more than usual</td>
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<td></td>
<td>Much more than usual</td>
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<tr>
<td>35. Felt you are playing a useful part in things?</td>
<td>More so than usual</td>
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<td></td>
<td>Same as usual</td>
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<td></td>
<td>Less useful than usual</td>
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<td></td>
<td>Much less useful</td>
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<tr>
<td>36. Felt capable of making decisions about things?</td>
<td>More so than usual</td>
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<td></td>
<td>Same as usual</td>
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<td></td>
<td>Less so than usual</td>
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<td></td>
<td>Much less capable</td>
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<tr>
<td>37. Felt you're just not able to make a start on anything?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Much more than usual</td>
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<tr>
<td>38. Felt yourself dreading everything you have to do?</td>
<td>Not at all</td>
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<tr>
<td></td>
<td>No more than usual</td>
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<td>Rather more than usual</td>
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<td>Much more than usual</td>
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<td>39. Felt constantly under strain?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Much more than usual</td>
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<td>40. Felt you couldn't overcome your difficulties?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Much more than usual</td>
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<tr>
<td>41. Been finding life a struggle all the time?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Rather more than usual</td>
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<td>Much more than usual</td>
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<tr>
<td>42. Been able to enjoy your normal day-to-day activities?</td>
<td>More so than usual</td>
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<td></td>
<td>Same as usual</td>
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<td>Less so than usual</td>
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<td></td>
<td>Much less than usual</td>
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<td>43. Been taking things hard?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Rather more than usual</td>
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<td></td>
<td>Much more than usual</td>
<td></td>
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<tr>
<td>44. Been getting edgy and bad-tempered?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Rather more than usual</td>
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<td></td>
<td>Much more than usual</td>
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<tr>
<td>45. Been getting scared and panicky for no good reason?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Rather more than usual</td>
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<td></td>
<td>Much more than usual</td>
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<tr>
<td>46. Been able to face up to your problems?</td>
<td>More so than usual</td>
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<tr>
<td></td>
<td>Same as usual</td>
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<td></td>
<td>Less able than usual</td>
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<td></td>
<td>Much less able</td>
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<tr>
<td>47. Found everything getting on top of you?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Much more than usual</td>
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<tr>
<td>48. Had the feeling that people were looking at you?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<td>Much more than usual</td>
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<tr>
<td>49. Been feeling unhappy and depressed?</td>
<td>Not at all</td>
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<td></td>
<td>No more than usual</td>
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<tr>
<td>Question</td>
<td>Degree of Agreement</td>
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<td>50. Been losing confidence in yourself?</td>
<td>Not at all</td>
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<td>51. Been thinking of yourself as a worthless person?</td>
<td>Not at all</td>
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<tr>
<td>52. Felt that life is entirely hopeless?</td>
<td>Not at all</td>
<td></td>
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<tr>
<td>53. Been feeling hopeful about your own future?</td>
<td>More so than usual</td>
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<tr>
<td>54. Been feeling reasonably happy, all things considered?</td>
<td>More so than usual</td>
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<tr>
<td>55. Been feeling nervous and strung-up all the time?</td>
<td>Not at all</td>
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<tr>
<td>56. Felt that life isn't worth living?</td>
<td>Not at all</td>
<td></td>
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<tr>
<td>57. Thought of the possibility that you might make away with yourself?</td>
<td>Definitely not</td>
<td></td>
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<tr>
<td>58. Found at times that you couldn't do anything because all your nerves were too bad?</td>
<td>Not at all</td>
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<tr>
<td>59. Found yourself wishing you were dead and away from it all?</td>
<td>Not at all</td>
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<tr>
<td>60. Found that the idea of taking your life kept coming into your mind?</td>
<td>Definitely not</td>
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</tbody>
</table>
Please indicate how you have been feeling in the last few weeks, by underlining the correct response to each of the following items.

| 1. I wake early and then sleep badly for the rest of the night | Yes | definitely | Yes | sometimes | No not | such | at all |
| 2. I get very frightened or panic feelings for apparently no reason at all | Yes | definitely | Yes | sometimes | No not | such | at all |
| 3. I feel miserable and sad | Yes | definitely | Yes | sometimes | No not | such | at all |
| 4. I feel anxious when I go out of the house on my own | Yes | definitely | Yes | sometimes | No not | such | at all |
| 5. I have lost interest in things | Yes | definitely | Yes | sometimes | No not | such | at all |
| 6. I get palpitations or a sensation of 'butterflies' in my stomach | Yes | definitely | Yes | sometimes | No not | such | at all |
| 7. I still enjoy the things I used to | Yes | definitely | Yes | sometimes | No not | such | at all |
| 8. I feel scared or frightened | Yes | definitely | Yes | sometimes | No not | such | at all |
| 9. I feel life is not worth living | Yes | definitely | Yes | sometimes | No not | such | at all |
| 10. I have a good appetite | Yes | definitely | Yes | sometimes | No not | such | at all |
| 11. I am restless and can't keep still | Yes | definitely | Yes | sometimes | No not | such | at all |
| 12. I am more irritable than usual | Yes | definitely | Yes | sometimes | No not | such | at all |
APPENDIX 4:

PROFORMA

DATE SEEN:

NAME:
ADDRESS:

TELEPHONE:

GENERAL PRACTITIONER:

SURGEON:

PROJECT NUMBER:

HOSPITAL NUMBER:

DATE OF BIRTH:

DATE OF OPERATION:

AGE AT OPERATION:

DATE SEEN BY SURGEON:

RELIGION
Protestant=1
Catholic=2
Jewish=3
Other=4
None=5

CHURCH ATTENDANCE
Frequent (more than once a month)=1
Infrequent (less than once a month)=0

TIME FROM DISCOVERY OF BREAST TROUBLE TO BEING SEEN BY SURGEON (weeks):

TIME FROM OUTPATIENT CLINIC TO OPERATION (weeks):

PREVIOUS ILLNESS:

None/minor illness=0
Significant illness=1

Examples of minor illnesses: influenza, uncomplicated appendicectomy, diagnostic dilatation and curettage of uterus.

Examples of significant illness: diabetes, symptomatic tuberculosis, major surgery

PREVIOUS PSYCHIATRIC HISTORY

None=0

Treatment from general practitioner only=1
(E.g.: minor tranquillizers for "nerves")

Treatment from psychiatrist=2
HISTORY OF BREAST DISEASE

Breast cancer in family: absent=0; present=1
Breast cancer in friends: absent=0; present=1

PERSONAL HISTORY
School leaving age
Minimum=1
Minimum+1=2
Minimum+2=3
Minimum+3=4 etc.

Further education
None=0
College=1
University=2

CURRENT EMPLOYMENT (exact description)

None=0
Part-time=1
Full-time=2

PREVIOUS EMPLOYMENT

IF MARRIED, HUSBAND'S EMPLOYMENT (exact description)

SOCIAL CLASS: (I=1) (II=2) (III=3) (IV=4) (V=5):

MARRIAGE
Presently married=1
Divorced/separated=2
Widowed=3
Never married=4

Pregnancies (and number of surviving children):

Domestic situation
Living alone=1
Not living alone=0

Domestic roles, social activities, interests:

RECENT MEDICATION
Drugs before discovery of breast trouble:

Drugs since discovery of breast trouble:

Psychotropic drugs taken since discovery of breast trouble=1
No psychotropic drugs taken since discovery of breast trouble=0
MENSTRUAL STATUS
Periods in past two years: premenopausal=1
No periods in past two years: postmenopausal=2

KNOWLEDGE EXPRESSED ABOUT POSSIBLE CANCER
No clear statement=0
Indirect but clear reference to possibility of cancer=1
(E.g.: "A friend had it - it went to her liver and she died")
Direct statement=2
(E.g.: used the word "cancer" or "malignant")

SPONTANEOUS COMMENTS
APPENDIX 5:

REFUSALS, EXCLUSIONS AND LOSSES TO FOLLOW-UP

Refusals to take part in study

Stage II patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class*</th>
<th>Further treatment†</th>
<th>Reasons given for refusal</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>Widowed</td>
<td>III</td>
<td>C</td>
<td>&quot;I'm too nervous&quot;</td>
</tr>
<tr>
<td>47</td>
<td>Married</td>
<td>II</td>
<td>RC</td>
<td>&quot;I don't like questionnaires&quot;</td>
</tr>
<tr>
<td>48</td>
<td>Married</td>
<td>III</td>
<td>RC</td>
<td>No reason given. Subsequently this lady became depressed while on chemotherapy. Her general practitioner contacted her surgeon because of this, but she refused to see a psychiatrist.</td>
</tr>
<tr>
<td>40</td>
<td>Married</td>
<td>IV</td>
<td>RC</td>
<td>&quot;I've too much on my hands with the children and everything.&quot; This patient, who seemed very tense and defensive, subsequently defaulted from follow-up treatment.</td>
</tr>
<tr>
<td>44</td>
<td>Married</td>
<td>III</td>
<td>RC</td>
<td>&quot;Enjoyed talking to you but I don't want to take part.&quot; This patient seemed well adjusted and later to tolerate the treatment very well.</td>
</tr>
</tbody>
</table>

Stage II patients in additional cohort first seen at 13 months.

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class*</th>
<th>Further treatment†</th>
<th>Reasons given for refusal</th>
</tr>
</thead>
<tbody>
<tr>
<td>49</td>
<td>II</td>
<td>RC</td>
<td></td>
<td>&quot;I certainly don't want to take part.&quot; This patient was adamant she would have as little as possible to do with those treating her.</td>
</tr>
<tr>
<td>55</td>
<td>III</td>
<td>RC</td>
<td></td>
<td>Not known</td>
</tr>
</tbody>
</table>

*Social class for refusals was usually obtained from information in the surgical case notes. It may therefore be slightly inaccurate.

†C=Chemotherapy; RC=Radiotherapy+chemotherapy.
### Stage I patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class*</th>
<th>Further treatment†</th>
<th>Reasons given for refusal</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>Married</td>
<td>II</td>
<td></td>
<td>&quot;Don't like questionnaires.&quot; Past history of nervous trouble treated by her GP.</td>
</tr>
<tr>
<td>64</td>
<td>Married</td>
<td>III</td>
<td></td>
<td>No reason given, but friendly with immediately preceding patient.</td>
</tr>
<tr>
<td>45</td>
<td>Married</td>
<td>II</td>
<td></td>
<td>&quot;I don't like surveys.&quot;</td>
</tr>
<tr>
<td>59</td>
<td>Married</td>
<td>III</td>
<td></td>
<td>No reason given.</td>
</tr>
</tbody>
</table>

### Patients with benign disease

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Reason given for refusal</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>Married</td>
<td>II</td>
<td>&quot;It's very wrong that you're seeing me and being a psychiatrist.&quot;</td>
</tr>
<tr>
<td>42</td>
<td>Married</td>
<td>IV</td>
<td>&quot;I'm too nervous&quot;. This patient, thought to have a large cancer, felt too upset to talk about anything. (In fact she had a giant fibroadenoma.)</td>
</tr>
</tbody>
</table>

**Cholecystectomy group: no refusals.**

### Exclusions

Two patients, both in the benign group, had to be excluded. One could not speak English, and the other had mental handicap.

### LOSSES TO FOLLOW UP

#### Stage II patients

**Deaths: radiotherapy patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>38</td>
<td>Married</td>
<td>III</td>
<td>6 months</td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>Widowed</td>
<td>II</td>
<td>13 months</td>
<td></td>
</tr>
<tr>
<td>62</td>
<td>Married</td>
<td>III</td>
<td>13 months</td>
<td>Died of biliary carcinoma</td>
</tr>
<tr>
<td>41</td>
<td>Single</td>
<td>III</td>
<td>18 months</td>
<td></td>
</tr>
<tr>
<td>63</td>
<td>Married</td>
<td>IV</td>
<td>6 months</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>Married</td>
<td>III</td>
<td>18 months</td>
<td></td>
</tr>
<tr>
<td>62</td>
<td>Divorced</td>
<td>III</td>
<td>13 months</td>
<td>At 13 months too ill for self ratings</td>
</tr>
<tr>
<td>Age</td>
<td>Marital status</td>
<td>Social class</td>
<td>Time last interviewed</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>----------------</td>
<td>--------------</td>
<td>-----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>43</td>
<td>Widowed</td>
<td>IV</td>
<td>18 months</td>
<td>At 18 months too ill for self ratings</td>
</tr>
<tr>
<td>38</td>
<td>Married</td>
<td>V</td>
<td>18 months</td>
<td>At 18 months too ill for self ratings</td>
</tr>
</tbody>
</table>

Deaths: chemotherapy patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td>Widowed</td>
<td>IV</td>
<td>18 months</td>
<td></td>
</tr>
<tr>
<td>35</td>
<td>Married</td>
<td>III</td>
<td>13 months</td>
<td></td>
</tr>
<tr>
<td>68</td>
<td>Widowed</td>
<td>II</td>
<td>1 month</td>
<td>Died suddenly of myocardial infarct</td>
</tr>
</tbody>
</table>

Deaths: radiotherapy + chemotherapy patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>66</td>
<td>Single</td>
<td>II</td>
<td>13 months</td>
<td>Died following surgery for primary cancer of transverse colon</td>
</tr>
<tr>
<td>51</td>
<td>Married</td>
<td>II</td>
<td>6 months</td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>Married</td>
<td>III</td>
<td>13 months</td>
<td></td>
</tr>
</tbody>
</table>

Deaths: Stage I patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>Married</td>
<td>III</td>
<td>Before surgery</td>
<td>Died following investigation of renal failure.</td>
</tr>
<tr>
<td>56</td>
<td>Married</td>
<td>III</td>
<td>13 months</td>
<td></td>
</tr>
</tbody>
</table>

Refusals to continue in study

**Radiotherapy patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>Divorced</td>
<td>III</td>
<td>1 month</td>
<td>Said she was &quot;too nervous&quot; to continue. Part of her nervousness stemmed from a very real delay in being notified of her radiotherapy appointment. Seen briefly at one year; said she was a lot better</td>
</tr>
</tbody>
</table>

**Chemotherapy patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>Married</td>
<td>III</td>
<td>18 months</td>
<td>Angry and in pain after developing spinal secondaries</td>
</tr>
<tr>
<td>63</td>
<td>Married</td>
<td>III</td>
<td>13 months</td>
<td>Too depressed to continue. At six and 13 months was too depressed to complete self rating scales</td>
</tr>
<tr>
<td>Age</td>
<td>Marital status</td>
<td>Social class</td>
<td>Time last interviewed</td>
<td>Comment</td>
</tr>
<tr>
<td>-----</td>
<td>----------------</td>
<td>--------------</td>
<td>-----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>66</td>
<td>Married</td>
<td>II</td>
<td>18 months</td>
<td>Appeared to want to deny illness</td>
</tr>
<tr>
<td>58</td>
<td>Married</td>
<td>III</td>
<td>3 months</td>
<td>Said she was annoyed because her husband's GP had stopped his clofibrate. Thought this was very wrong — not pleased with doctors</td>
</tr>
<tr>
<td>59</td>
<td>Widowed</td>
<td>V</td>
<td>1 month</td>
<td>Limited intellect. Had great difficulty with self rating scales. Didn't want any more of it.</td>
</tr>
</tbody>
</table>

**Radiotherapy + chemotherapy patients**
None

**Stage I patients**

- 59 Married III 6 months Probably refused because didn't want to think about her illness. Relapsed at a year and died before 18 months
- 67 Married III 6 months Husband developed cancer of colon; patient felt it was too much all at once

**Patients with benign disease**

- 30 Married III Before surgery Husband didn't approve
- 45 Married V Before surgery Afraid that husband wouldn't approve
- 39 Divorced III Before surgery Living with parents; agreed to be seen in principle, but said that parents didn't like confidential surveys. It did not prove possible to arrange an interview.
- 32 Married III Before surgery On staff of hospital; understandably didn't want to divulge confidential information to someone she might meet at work
- 19 Single IV Before surgery "My father doesn't like surveys"
- 26 Married III 3 months Appeared to be staying elsewhere; never at home
- 45 Married III 3 months Ostensibly impossible to fix suitable time; obviously not keen
<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>Married</td>
<td>II</td>
<td>3 months</td>
<td>Moved house</td>
</tr>
<tr>
<td>64</td>
<td>Widowed</td>
<td>II</td>
<td>3 months</td>
<td>Not well physically; family felt it would be too much for her</td>
</tr>
</tbody>
</table>

**Cholecystectomy patients**

<table>
<thead>
<tr>
<th>Age</th>
<th>Marital status</th>
<th>Social class</th>
<th>Time last interviewed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>47</td>
<td>Married</td>
<td>II</td>
<td>Before surgery</td>
<td>Would only agree to follow-up by post but didn't return forms</td>
</tr>
<tr>
<td>41</td>
<td>Married</td>
<td>V</td>
<td>Before surgery</td>
<td>No reason given</td>
</tr>
<tr>
<td>53</td>
<td>Single</td>
<td>III</td>
<td>Before surgery</td>
<td>No reason given</td>
</tr>
<tr>
<td>61</td>
<td>Married</td>
<td>II</td>
<td>Before surgery</td>
<td>Not keen to be seen at home; husband has alcohol problem</td>
</tr>
</tbody>
</table>

Comment on refusals and losses to follow-up.

Had the missing data from refusals and losses to follow-up been available, would the results have been affected? The main positive finding in the thesis was an excess of psychological morbidity in patients treated with chemotherapy (alone or after radiotherapy). No stage II patient who received radiotherapy alone refused to take part. In the two chemotherapy groups, psychological factors appeared relevant in three of the five patients who would not participate. One felt too nervous to take part, another became depressed, and another probably had many psychosocial problems. Therefore, had scores for the five been available, it seems most unlikely that psychosocial morbidity would have fallen in the chemotherapy groups; indeed, it might well have risen.

On the other hand, a further five patients who received chemotherapy dropped out later. However, for three of them
observer scores were available up to 13 months. One of the three, with a long history of endogenous depression, was unable to complete the self rating scales at 13 months; had she done so, she would undoubtedly have had very high scores. In the two cases lost before 13 months, the effect on scores is harder to judge, but proportionately would have to be small. The 59 year-old lady of limited intellect seemed to cope surprisingly well with chemotherapy, according to the clinic staff.

The effect of the excess of deaths in the radiotherapy group on the conclusions is discussed in chapter 8.

In the stage I group, one of four the refusals had a known past history of treatment for nervous complaints. Again a significant reduction in morbidity in the stage I group seems unlikely, had scores for the four been available.

There were two refusals in the benign group before surgery. One of the two was spoken to only briefly, but showed very obvious distress. The other was seen at greater length, and was certainly somewhat anxious. Pre-operative morbidity in the benign group would not have fallen, had scores for the two been included.

Several patients in the benign group dropped out later: nine of the 39 intended to be followed up over a year. In particular, the level of morbidity in the benign group at 13 months might be questionable. After considering the previous ratings of the individual patients who dropped out, the author thought that morbidity in the benign group might have been marginally higher at 13 months, but essentially the same at one month.
In the cholecystectomy group the only problem was missing data for four of 30 patients at three months after operation. The pre-operative 60-item general health questionnaire scores of the four were 0, 8, 9 and 26. The last of the four had an observer rating of one for anxiety (the high GHQ score partly reflected physical symptoms); the others showed no psychological morbidity. There was nothing to suggest that their post-operative scores would have been unusual.
APPENDIX 6:

REACTIONS TO TREATMENT

At the six month interview, patients' opinions of adjuvant treatment were sought. The same question, "How do you feel about your treatment?" was asked of each patient. The following were the immediate verbatim replies, classified according to treatment received.

Radiotherapy-alone patients

"After I got the radiotherapy I felt very secure — They're going to give me checks. Then insecurity — I don't think anybody is bothering here. I'm just a number. I've seen so many different doctors."

"I found it very good."

"I think everybody did all they could. The team in radiotherapy were very nice and very kind."

"I think I've had wonderful treatment, son. I've been treated like a queen."

"Very good, Everything is very good. They were all very kind. It never really got me down."

"The only thing I always say... They were very kind and helpful."
"The operation's nothing, but radium's terrible — mentally as well as physically. It's a very severe treatment."

"I found it was all right. I didn't find it bad. It was the travelling. It was awful in the bad weather."

"I felt bored by having to stay in hospital for three weeks — it was awful to bear. I could have travelled with my son in the morning. The treatment itself was no problem."

"Very severe. It made me very nervous. The travelling to and fro and the big things on top of me. I said to somebody I'd go through the operation again but not the treatment."

"It gets me down going back every time. The radiotherapy is the lesser of the evils. It's very unpleasant but it's better than chemotherapy..." [This patient had not undergone chemotherapy, but had observed the effects of chemotherapy on other patients.]

"Horrible. I didn't like the radium treatment at all. They don't give you confidence. The machines go burst. I have a fear of radiation. I feel in this country they feel a little extra doesn't matter."

"It was a bit tiresome when I went but I felt quite good after it. I'd recommend anybody to go."

"It's very rough on you."
"I could never go through that again. It terrified me. I had to get Valium. My nerves went for me. I got very scared. That Friday [her first day of treatment] that machine was just like a monster to me. I was cold, shaky and crying. On Monday I couldn't take it. As soon as I got up, my nerves started because I knew I had to go under that machine. The following Friday, I went under it but I was a total wreck. I had pins and needles all over me. I couldn't relax at all."

"I felt quite squeamish but otherwise it wasn't too bad."

"Quite honestly, at the time, it's quite traumatic to go through: the fear of the unknown. Once you have experienced it, it's not too bad. It's behind you in the past and life goes on."

"I'm glad it's over. That's all one can say about it. I hope it's successful."

"Well, I felt it was necessary and the treatment itself was nothing at all. My biggest problem was the vomiting." [This patient's radiotherapy had exacerbated a pre-existing oesophageal stricture.]

"Well, there's really nothing in the treatment, but it's the after-effects. It burned under my arm."

"That therapy... well, I was all right getting it."

"I was quite happy with the radiotherapy."
Chemotherapy-alone patients

"It's all right. Sometimes you're sick with it, but you have no pain. I've lost weight. Last September I said to my husband, 'I'll never go through with it.' It's better now. I'm looking forward to stopping the treatment. I'm counting the months."

"I'm not bad — not so bad as some of them. I've often said I'm not going back. I think it would be foolish, now I've had all this done."

"I haven't been back. I said I'm not taking any more. One injection and all my hair fell out. I thought they might have told me that. Two hours after each injection, I was flat on my back. My doctor had to give me injections for sickness. I stopped eating for two weeks: liquids only. I felt they could kill me. I said I'm taking a chance and I'm not having them. Having no hair was worse than getting over the operation. I couldn't go outside the door for a month."

"I just hate it. It would take very little to stop you going. You really have to push yourself to come."

"Well, I don't like it at all."

"I feel horrible about the treatment. I wish I didn't have to take it. At the same time I'll go through with it. The day after it, I say, 'That's the last time. I'll no take any mair'. I hate it."

"Ach well, it has the sort of side effects. I also appreciate it's
for my own good; so I'm perfectly willing to take the treatment. When you're feeling rough, you think to yourself, 'I wonder how much more I can take.'"

"You've just got to take it: there's nothing else for it. I hope everything is all right once I've finished the injections. The cure is worse than the disease."

"I think the treatment has done me quite well. At first I felt I wouldn't go for it. It becomes part of your life. I say I just have to go. I think it's been quite good."

"I could put it lucidly. It makes me terribly ill. It makes me sick. The two weeks running of injections: that nearly kills me."

"You see, of course I don't like the treatment because of the side effects, but I must suffer the side effects if the treatment is going to prevent any further trouble."

"It's horrible."

"I don't like the treatment: that's one thing I don't like."

"Well, I don't really care for it. I feel if it's necessary then that's it. I used to think, 'What will happen at the end of the injections?' They'll do their best, whatever it is."

"The injections make me feel very frightened."

"If I didn't have a good husband or a good daughter, I couldn't
carry on with these injections. I've everything to live for. If I didn't get these injections, it might be worse for myself. I know these injections are for your own good. See, so far as cooking meals... tomorrow they won't have a cooked meal because I can't stand the smell of it. See the night before... I get tensed up. I feel the taste of the injection going right up — horrible sensation."

"I dread these days [injection days]. There is no other word. I suppose it's because the whole thing is sort of humiliating as much as anything. The last three weeks I was sick with the thought of them. I thought I was a strong-willed person but there's nothing I can do about it. It's horrible. The sickness is horrible — in front of a doctor and other women. On Thursday [the day after her injection] I have a day off. I crawl from the bed to the bathroom. But I am coping with them. Does that make sense? I'll go on with them to the end of the course."

"I find this is a big thing, this waiting around. That to me is the biggest bore of the whole lot. It's like two weeks in the month. It involves really the day you go to hospital and the day after. I'm always sick. I've been told my scan is clear. I'm very thankful."

"Horrible. I wish I could stop it. When I was coming here, I thought it was a lot of tablets, and that was me finished. I do hate it. I dread every Tuesday [day before injection]."

"As soon as I walk into the waiting room, you feel this terrible squeamishness coming on. At home, you think of it and you become
squeamish. It's tiresome and I'd sooner not have it. But every
time my husband says it's essential you have it, I could be a lot
worse."

"Well, I'm not fond of it actually, but, touch wood, compared with
the other women, I'm not too bad, really. I get that squeamish
feeling but I've not been sick."

"I know it's got to be done but I don't like it. Sometimes I'm
awful depressed. It's not me. I could just sit and let the whole
place fall about me."

"You want me to tell you? Absolutely horrible. I could put it
stronger. I think the treatment is ghastly. Hellish."

"I've just got to put up with it because I know it's better safe
than sorry. It's reassuring. It's always different people giving
the treatment. Some are more expert than others at doing
injections. They are always very kind and understanding."

Radiotherapy plus chemotherapy patients.

"It doesn't make me feel any better, I can tell you. After the
operation I felt a lot better. After three weeks, I was beginning
to feel normal again, and thereafter I was back to square one."

"I suppose the injections were more successful than the
radiotherapy. At the beginning of the injections I lacked energy.
It's not so bad now."
"I know it's to do me good. I'm not shying away from it."

"It's very debilitating and I'm very weak and unable to do anything. I'm sick and very exhausted. I start to recover on the Saturday."

"I can understand getting that radium treatment but the injections... I can't see how they can make you better when they pull you down. I wouldn't mind at all if it was definitely doing good. He [her surgeon] said it was in case there were any cancerous cells. I certainly don't relish the idea of a whole year like this."

"I feel all right. The only thing I'm thinking about is it's bound to do me good. I don't like going for treatment. I'd rather go to the radiotherapy than to the injections. Definitely, yes."

"You ask yourself, 'Is it all worth it?' You don't have a clue if it's doing you any good. When they turn round and say you should have the injections, but they don't really know, you begin to wonder about the treatment. When I'm feeling fine and I'm going to be made ill, I think I must be going daft in the head or something. But then you think, 'The doctors know best.'"

"What can you say about something which makes you feel pretty miserable. It's the length of time. Before you start it seems a very long time. It doesn't seem so long now."

"If this is got to be, I'll just have to take it and suffer it. When you're sick, you feel as if you are going to die. The
radiotherapy was a walkover compared with this."

"All right, really. I don't think I've got really anything to complain about. It's just going for the injections. Once I'm there I'm fine. The injections upset me more than the radiotherapy."

"I feel that it's marvellous that I'm getting it. I really do. I know it's helping me. It's for my benefit, not for theirs. That's the way I feel about it."

"The treatment is so atrocious that it's taken up all my thoughts. All my aggression has been taken up with the treatment. I think it's the most atrocious thing that has been ever thought up. The effect is very distressing. Radiotherapy was over in three weeks. It's much worse than the effects of radiotherapy."

"I hate it. Oh, I hate it. I dread it, doctor. I keep thinking they'll say I don't need 12 months. I just hate it. I think it's because of the sickness and weakness in my legs. Whenever you walk into the hospital... See the smell of the hospital: this treatment affects your sense of smell. Certain perfumes I now scunner at. Every fortnight after the treatment, I say to myself, 'How will I ever get through it?' You feel you're getting better and then you're back to square one. The operation and the radiotherapy was a walkover to me, but this chemotherapy... It's an awful afternoon. It's a nerve-racking afternoon because you're uptight before you go and you're sick and vomiting going home."

"I don't like the injections. I'm frightened of the needle. I hate it. I didn't like the radiotherapy but it wasn't so bad."
"Well at the present time it's not too bad. This is my three week break in treatment. In my treatment week I've been dreadful: no energy at all and dizzy — not dizzy — my balance. I spent one and a half days in bed. I could just sleep all the time. I haven't been out this week because I couldn't trust myself to keep my balance."

"I feel I'm getting better — making a bit of progress. Sometimes after the injections I have a feeling of sickness."

"I didn't feel frightened with the radiotherapy. I didn't feel sick until the end. This treatment now is different. I'm terrified. Not about the actual side effects — the sickness and the vomiting — but they have the most awful job getting the blood out of me and the drugs into me. That's what really scares me."

"I'm fine with chemotherapy. The biggest problem is a sort of nausea. The other thing is dry skin. It's quite unpleasant. I'd say it's easier than the radiotherapy." [This patient was one of only two receiving combined therapy who, at the six month assessment, thought that chemotherapy was less unpleasant than radiotherapy. By the end of her chemotherapy, however, she had become clinically depressed, and thought chemotherapy was worse than radiotherapy.]

"I've no complaints — nothing but the best attention from everyone. I had no problems with radiotherapy." [This patient should have received chemotherapy subsequently, but wasn't so informed until the day she was due to start treatment. She refused
chemotherapy, partly because she hadn't been warned about it, but mainly because she had heard of another patient who had experienced severe vomiting.

"It takes over your whole life. I don't understand how it does. It does on occasion make you feel extremely depressed... I have never had this in my whole life. This seems a different thing entirely — like a big black thing — you couldn't get out of it."

"See when I go for these injections — they ask me how I feel. I say fine. I could be dying. I could be dying but I say fine. I just freeze. I just want to get out... They smile and ask, 'How are you?' You think to yourself, 'You know bloody well how I feel, you bastard.' I'd make them take the injections themselves and see how they like that. I wouldn't feel sorry for them. They're so cheerful and you feel like saying, 'Go to hell. Get the f--- out of here.' You're feeling so bad... it's a horrible feeling."

"I don't try to think too much about it. I don't like it. The thing I feel about it is... I'm not ill; the treatment makes me feel ill. If it wasn't for the treatment I'd be back at work. Sometimes I feel it's a lost year."

"Fine. I mean if it's going to help me, I ought to take my treatment — if it's going to prolong my life."
APPENDIX 7:

ILLUSTRATIVE CASE HISTORIES

These histories, chosen mainly on the basis of positive features, illustrate ratings of morbidity.

Case no: 003

Date first seen: 6 October 1977 (day before mastectomy).
Age at operation: 38.
Stage II breast cancer. Randomized to radiotherapy.

Married with three children aged 8, 13 and 16. Former severe alcoholic, totally abstinent over previous six years. Husband also recovered alcoholic. She now works as social work assistant. Member of Alcoholics Anonymous. Out at all hours to help alcoholics. Previous physical and mental health otherwise good. "Pretty happy-go-lucky" by nature. Good family life.


morning in bed, hardly sleeps at night. "When I came out of hospital, all the props were removed. I was like a rag doll. I cried all the time for a solid week. I felt that my clothes were those of a dead person. I felt someone had died. The emotional thing was terrible... a fantastic feeling of fear... complete loneliness."

Three month interview, after radiotherapy. All ratings zero, except sex rating of 2 (definite loss of interest but beginning to pick up thanks to husband's support). GHQ-60 score: 0. Leeds depression score: 1 Leeds anxiety score: 0. "I've no fear of whether anything may happen or not. Anything can happen to anybody. It doesn't worry me. I have faith in God — a standby for me." Being treated with radiotherapy had also given her a sense of security.

Six month interview. Again very emotional (depression 1, anxiety 2, behaviour 2; GHQ-60 score 49; Leeds depression 12, Leeds anxiety 9). Suspects (correctly) that has cancer in other breast. Missing support from radiotherapy unit. At surgical outpatient clinic feels she is "just a number."

How do you feel about your illness? "When I got the one breast removed, I felt very optimistic. Recently when I feared about the other one going, I felt I was doomed. The relatives I've had have died from cancer."

How do you feel about the mastectomy? "It in no way bothers me as far as my appearance is concerned. I can go to parties and dances. I feel pretty repulsive as far as my sexuality is concerned."
13 months. Has died in hospital, after second mastectomy and course of chemotherapy.

Comment. Despite past history of alcoholism, had been well adjusted emotionally before developing breast cancer. Some anxiety before surgery, but very severe emotional reaction immediately afterwards. Much calmer after radiotherapy, but then increasingly worried — with good reason — about recurrent disease. Her history shows that receiving treatment may reassure and reduce psychological morbidity.

Case no: 032

Date first seen: 26 February 1979 (one month after mastectomy).
Age at operation: 51.
Stage II breast cancer. Randomized to chemotherapy alone.

Married with two children aged 10 and 12. Works as part-time clerkess. Husband nurse and part-time chiropodist. Past history of thoracoplasty for tuberculosis. No other serious illness. Never had treatment for nervous complaints, but thinks she is a worrier.
No family problems.

One month. Observer ratings: all zero. GHQ-60 score: 0. Leeds depression score: 0. Leeds anxiety score: 0.

Three month interview (after two months of chemotherapy). Observer ratings: depression 1, anxiety 1, sex 1. Other observer ratings zero. GHQ-60 score: 7. Leeds depression score: 1. Leeds anxiety score: 5. Depressed last weekend and generally a bit worried.
Gives another lady a lift to chemotherapy injections. "Taking her in the car depresses me; the minute I see her she feels sick. She talks all the time about illness. I told her she was lucky not to have had illness up till now... Sometimes you think about the injection and the nausea comes over you again. Butterscotch relieves the sickness." Not yet back at work, but wants back.

Six month interview. Back at work. ("The best thing I ever did.") Observer ratings: all zero except sex 1 ("not so important as before"). GHQ-60 score: 0. Leeds depression score: 1. Leeds anxiety score: 3. Vomiting before her chemotherapy injections as well as after them. "I get a rotten taste in my mouth... and the smell — just when you come in that door. Maybe next week I'll try eau de Cologne..."

_How do you feel about your illness?_ "Well, I feel it was... the worst time was before going into hospital. If there was anything there it would be the major operation. Since then, after it's all over, you realise it was nothing. It could be a lot worse... if they said there was nothing more they could do for you."

_How do you feel about the mastectomy?_ I don't think about it too much. You're given an appliance. You don't really want to look at yourself... My husband said it was fortunate it was a neat wound. I don't think it's neat at all."

13 month interview (just before last two chemotherapy injections). Observer ratings: depression 2, anxiety 1, sex 1, under activity 1, behaviour 1, routine 1, housework 1. GHQ-60 score: 51. Leeds depression score: 9. Leeds anxiety score: 10. Still vomiting
before and after injections. Takes perfume with her to counteract
the smell of leather in the car, which makes her feel sick. Has a
wig for hair loss. "After I saw Mr Mack for an X-ray recently I
thought I had TB as well. I wished I would just sleep away."
Occasional suicidal ideation. Pretty miserable much of the time.
Very tired and run down. Rather tense and irritable. Sleeping
badly: losing a couple of hours a night. Thinks she is eating too
much; describes it as "comfort eating". On Triptafen Minor.

18 month interview (5 months off chemotherapy). All observer
ratings zero. GHQ-60 score: 0. Leeds depression and anxiety
scores: both 1. Felt sick going back to chemotherapy clinic
recently. "Even the doctor's white coat made me feel sick. I felt
it coming in waves... but I feel better than I've felt for a long
time... these injections... they really made me feel dreadful... I
think it was going back to work which saved my life."

24 month interview. All observer ratings zero. GHQ-60 and Leeds
anxiety scores both zero. Leeds depression score: 1. Still feels
sick going up to the clinic. But generally well: "To come out of
the Victoria and get a good report — it's like getting a pot of
gold."

Comment. Although she described herself as a worrier, her
personality did not seem in any way unusual. Coped very well with
mastectomy and early part of chemotherapy course. Severe
conditioned reflex nausea and vomiting in second half of
chemotherapy course, with conditioned nausea persisting during
second year. Clinically depressed by the end of the chemotherapy
course, recovering after chemotherapy was stopped.
Case no: 064

Date first seen: 26 June 1980 (one month after mastectomy).

Age at operation: 42.

Stage II breast cancer. Randomized to radiotherapy followed by chemotherapy.

Divorced, with son aged 21 and daughter aged 19. Left school at 16. Later passed Higher English and took secretarial course. Now runs a large pub. Comes across as a competent and intelligent person. However, says she has always been bothered with depression and nerves, especially if under pressure, and has sometimes had treatment for nerves from her GP. No psychiatric referrals. Normally a sociable person who mixes easily. Good physical health in the past. Five years ago she had cosmetic surgery to enlarge both breasts (bilateral implants).

One month interview. Observer ratings. Depression 1, anxiety 0, activity 1, behaviour 0, routine 1, work 1. GHQ-60 score: 22. Leeds depression score: 9. Leeds anxiety score: 1. Felt low and "down" for a week during month after surgery. A bit tired after working and shopping. Went back to work one week after operation. Enthusiasm for work and leisure activities slightly impaired.

Three month interview. Observer ratings all zero. GHQ-60 score: 1. Leeds depression score: 2. Leeds anxiety score: 1. Moderate side effects of radiotherapy, mainly sickness, sore throat and skin reaction. However, coped well and continued working, albeit with
some time off, despite treatment. Back full time now and doing everything as usual.

Six month interview. Observer ratings all zero. GHQ-60 score: 2. Leeds depression score: 2. Leeds anxiety score: 4. Says she's fine with chemotherapy, though has slight nausea before as well as after injections. Thinks chemotherapy is less severe than radiotherapy (the only patient to think so at six months).

How do you feel about your illness? "I'll tell you the God's truth, doctor. I don't think about it. I just cut off. It's my way of handling it. I just don't think about it."

How do you feel about the mastectomy? "Again, doctor — maybe mentally I just don't think about it. It's a terrible psychological thing — an attack on femininity. I quite deliberately shut off. I'd be really upset. I'm hoping to have a reconstruction done."

13 month interview. Observer ratings: depression 2, anxiety 1, activity 2, behaviour 1, routine 1, work 1. GHQ-60 score: 43. Leeds depression score 14. Leeds anxiety score 14. Feeling very low. Quite definitely depressed. Sometimes pretty bad. Fleeting suicidal thoughts. Very little energy. GP has put her on "librium" at night because of poor sleep. Looks a different person compared with six months. Has lost her usual liveliness and enthusiasm. Seems withdrawn. Physically lacks lustre. Skin and hair look dry. Recognises a very definite change in herself, which she attributes to chemotherapy. Now thinks that chemotherapy is a lot worse than radiotherapy. Conditioned reflex nausea persists.
18 month interview. Observer ratings all zero. GHQ-60 score: 1. Leeds depression score: 1. Leeds anxiety score: 0. "I'm feeling better than ever." No further conditioned reflex nausea.

24 month interview. Zero scores on all observer ratings, GHQ-60 and both Leeds scales.

Comment. This patient, though generally competent, recognised she had some underlying liability to depression and anxiety under stress. She showed a mild psychological reaction during the month after mastectomy, but at three and six months seemed to have recovered emotionally, perhaps by use of the mental mechanism of denial. But at the end of chemotherapy, she was clinically depressed. She made a complete recovery after chemotherapy was stopped.

Case no: 141

Date first seen: 25 July 1978 (day before mastectomy).
Age at operation: 41.
Stage I breast cancer. No further treatment after mastectomy.

Married with three sons aged 9, 11 and 12. Eldest son has epilepsy, well controlled. Works as teacher — happy enough but would prefer part-time work, which is not available. Also husband gave up job as bank accountant after 25 years to join a small shipping firm which then folded up. He is now out of work; this causes some worry. Otherwise no particular problems. She has had no serious illnesses and no psychiatric history. However, probably
somewhat anxious by nature.

Pre-operative ratings: depression 0, anxiety 1, sex 2. Other ratings zero. GHQ-60 score: 6. Leeds depression score: 4. Leeds anxiety score 10. There has been a lot of uncertainty about the nature of the breast lump. Originally told it was "breast mouse", but now surgeon's doubt has caused some increased anxiety, but no acute worry or panic.

One month interview. Ratings: depression 0, anxiety 2, under activity 1, sex 2, behaviour 0, routine upset 1, housework 1. GHQ-60 score: 6. Leeds depression score: 4. Leeds anxiety score: 10. "The second day home was a panic day. In hospital it was a different atmosphere. I weathered it pretty well. A lady I know had a mastectomy two years ago. She couldn't look at herself. I said, 'I'm not going to go home and find myself like that'.... On Thursday I really panicked. I couldn't put my finger on anything. Fortunately the children were away and my husband was at home. He's a very calm and reassuring person. It was a very unpleasant day. I felt I was losing my grip. It was a totally new experience. I practically took off. It was irrational." Worried about a mole on the side of her face. Might be something dreadfully wrong. Cried one day (not enough to rate a "1" for depression).


Now emerges that while in hospital she became friendly with another lady who also underwent mastectomy. Like herself, this
lady had no further treatment, but died of lung involvement only a few weeks after discharge from hospital. Began to wonder why she herself had no further treatment. Thought it might mean that nothing further could be done for her. Became very anxious, acutely so at times, with sensations of breathlesses. Began to believe that breathlessness meant lung involvement. Entered vicious spiral of increased anxiety and breathlessness and had panic attack which forced her to go out of the room.

Six month interview. Feeling better. Back at work. Reassured about health by GP. Ratings: all zero except sex=1. GHQ-60 score 5; Leeds depression score 5, Leeds anxiety score 9.

How do you feel about your illness? "I didn't consider I was ill prior to it."

How do you feel about the mastectomy? "The bulk of the time I don't think about it."

13 month interview. Again somewhat anxious and also feeling low. "I started getting pains at the other side. The doctor says it's tension." Observer ratings: depression 1, anxiety 1, activity 1, sex 1; remainder zero. GHQ-60 score: 2. Leeds depression score 7. Leeds anxiety score 8.

18 month interview. Discomfort in other breast persists and had quite a lot of pain down other side and upper arm. "It's worrying me." Had a panic attack which forced her to open the window and lean out because felt she couldn't breathe properly. Less enjoyment of activities. Observer ratings: depression 0, anxiety
2, sex 1, routine 1, remainder zero. GHQ-60 score: 4. Leeds depression score: 4. Leeds anxiety score: 10.

24 month interview. "...up and down. When I started getting this pain off and on I really was a coward." Still a bit anxious and feels tired all the time, but doing everything. Observer ratings: depression 0, anxiety 1, activity 1, sex 1, remainder zero. GHQ-60 score: 5. Leeds depression score: 7. Leeds anxiety score: 11.

Comment. Her history shows that not receiving further treatment may be misconstrued and cause anxiety leading to panic. She was seen as an outpatient only every six months, allowing fears about cancer to build up in between times. Might have been helped by counselling. GHQ scores often surprisingly low in view of observer ratings and Leeds anxiety scores. This is probably because she has an anxious personality and GHQ measures symptoms present more than usual rather than absolute levels.
### APPENDIX 8:

**ITEM ANALYSIS OF GENERAL HEALTH QUESTIONNAIRE**

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<th>GHQ 2</th>
<th>GHQ 3</th>
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<td>6. Been getting a feeling of tightness or pressure in your head?</td>
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<td>7. Been able to concentrate on whatever you're doing?</td>
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<td>12. Been getting up feeling your sleep hasn't refreshed you?</td>
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<td>13. Been feeling too tired and exhausted even to eat?</td>
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<td>16. Been feeling full of energy?</td>
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<td>17. Had difficulty in getting off to sleep?</td>
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<td>18. Had difficulty in staying asleep once you are off?</td>
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<td>30. Been satisfied with the way you've carried out your tasks?</td>
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<td>31. Been able to feel warmth and affection for those near to you?</td>
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<td>32. Been finding it easy to get on with people?</td>
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<td>33. Spent much time chatting to people?</td>
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<td>36. Felt capable of making decisions about things?</td>
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<td>37. Felt you're just not able to make a start on anything?</td>
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<td>38. Felt yourself dreading everything you have to do?</td>
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<td>41. Been finding life a struggle all the time?</td>
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<td>48. Had the feeling that people were looking at you?</td>
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<td>50. Been losing confidence in yourself?</td>
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<td>52. Felt that life is entirely hopeless?</td>
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<td>53. Been feeling hopeful about your own future?</td>
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<td>54. Been feeling reasonably happy, all things considered?</td>
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<td>55. Been feeling nervous and strung-up all the time?</td>
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<td>56. Felt that life isn't worth living?</td>
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<td>57. Thought of the possibility that you might make away with yourself?</td>
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<td>58. Found at times that you couldn't do anything because your nerves were too bad?</td>
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<tr>
<td>59. Found yourself wishing you were dead and away from it all?</td>
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<tr>
<td>60. Found that the idea of taking your life kept coming into your mind?</td>
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