Psychosocial factors and the risk of developing breast cancer:

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Executive summary

This review examines the relationship between psychosocial factors and the development of breast cancer in women.

The notion that cancer might be related to stress or emotional factors is as old as the history of recorded medicine. Over the past few decades, however, there has been a renewed interest in the relationship between mind and body, as complex interrelationships between the immunological, endocrine and nervous systems have been delineated. There is now ample evidence that stress can induce disturbances in immune system competency, and that impaired immune function can predispose to malignant growth. While these data do not prove conclusively that stress causes cancer, they do corroborate clinical and epidemiological observations in the area. Finally, there are many anecdotal reports of women expressing their belief that ‘stress’ or ‘depression’ contributed to the development of their breast cancer.

This report presents an overview of the available published research into psychosocial predictors of developing breast cancer, and focuses on three main areas:

- Stressful life events;
- Short-term coping with life events/social support; and,
- Long-term emotional and personality factors.

Although these factors are clearly interrelated, they have rarely been measured together.

Methods

Extensive computerised literature searching using key words, hand searching of bibliographies and author searches were used to identify research papers. Pre-determined inclusion criteria were used to determine eligibility of each article for inclusion in this review. Seventy-one papers were excluded and thirty-eight were included on this basis. In addition, seven methodological articles and thirteen review papers were included. Data were abstracted using a standardised data abstraction and quality assessment format (see Appendix 8) to accurately record relevant aspects of methodology and results.
Limitations of the literature

Much of the data published before the late 1980s were obtained from methodologically flawed studies. Assessments of psychological factors were generally made after a diagnosis of cancer was given, and so a distinction between cancer-related and pre-morbid factors could not be made. Some studies addressed this problem by interviewing women considered to be at risk of having breast cancer (e.g., when attending for a mammogram or breast biopsy) before they knew their diagnosis. It is possible however, that the women who were subsequently diagnosed with breast cancer had more cues before testing that a cancer diagnosis was likely (because of their age, a family history of breast cancer or physical symptoms), than those with benign disease.

Moreover, few early papers dealt adequately with non-psychosocial factors that may both independently and interactively affect risk of developing breast cancer. The most important of these is age. Older women have had more time to experience severe life events, and may be more depressed; they may also be less emotionally volatile. Data obtained from studies in which age and other known predictors were not taken into account, are difficult to interpret.

Results

1 Life events

Twenty-five papers examined life events. Several of these papers represent reanalyses of data presented by the same research group in earlier reports. A decision was made to include the most recent analyses that adjusted for age (and other factors, if possible).

Life events, as they have been assessed in the past, do not appear to be associated with significant breast cancer risk. The majority of studies reported no differences between cancer patients and controls, in the number of life events experienced. Papers using one particular scale, the Brown and Harris life events and difficulties scale (LEDS) to assess life events, reported an association between severe life events and breast cancer risk. However, the only other papers that found an association between significant life events and breast cancer risk have significant design flaws.

Although the weight of evidence would appear not to support any association between life events and breast cancer risk, few studies were rigorous.
2 Short-term coping with life events and social support

Eighteen papers have examined short-term coping with life events and eleven are included in this review. The evidence for the influence of short-term coping with life events and the development of breast cancer is scanty and inconsistent. It is unlikely that this factor plays a significant role in determining breast cancer risk. The notion that social support reduces the impact of stressful life events is not supported.

3 Long-term emotional and personality factors

Sixteen papers exploring the impact of long-term emotional and personality factors on the development of breast cancer were included. None of the studies were conducted in Australia and it may not always be appropriate to generalise the findings to this setting.

- Emotional repression/alexithymia/low type A behaviour

The evidence for the impact on breast cancer risk of emotional repression particularly of anger, is uncertain. Five out of thirteen studies reported a negative effect; however, the majority of these studies did not directly measure repression of anger, but rather related issues such as self-awareness and the absence of a type A personality. Most of the eight studies that reported positive results had serious design flaws.

- Chronic anxiety and depression

Few studies have measured negative emotions and life events together, so it is difficult to tease out their independent and interdependent effects. Evidence for a link between breast cancer and chronic anxiety and depression is very poor. Only one of nine studies reported a positive finding (non-significant) and then only in one subgroup of patients who may have picked up cues from their doctors.

- Other personality features

Investigations of general personality factors have not produced promising results. Only two of seven studies reported significant findings. Extroversion/introversion, authoritarianism, dependence, external locus of control, religiosity, commitment and a tendency to behave in socially desirable ways were unrelated to breast cancer risk. Anti-emotionality (mistrust of feelings) was associated with a small increase in risk in one poorly reported study. Another study noted that women with excessive self-esteem, unresolved recent grief and a hysterical disposition were more likely to develop breast cancer, although these psychological ratings were based on
subjective judgements with no inter- or intra-rater reliabilities reported.

**Conclusion**

Evidence for a relationship between psychosocial factors and risk of breast cancer is weak. Perhaps the strongest predictors demonstrated are emotional repression, especially of anger, and the loss of a significant other. However, the majority of studies do not support even these associations. In addition, as none of the research reviewed was undertaken in Australia, the relevance to local conditions must be questioned.

Although Australian women should be reassured that the available evidence does not support a major role for psychosocial factors in the development of breast cancer, they should also know that few studies have been sufficiently rigorous to definitively rule out a minor role. Both the conceptualisation of an association and the selection of research methods need considerable refinement.

The role of psychosocial factors in breast cancer management has not been examined in this review. This question will be the subject of an additional report from the NHMRC National Breast Cancer Centre.

**Recommendation**

Research in this area will not be advanced unless:

- well-validated, standardised, measurement tools are available which assess the inter-relatedness of stressful events and personality characteristics;
- comparison populations are well-selected; and,
- age and other known risk factors are accounted for in the design and analyses.
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## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>AES</td>
<td>Anger Expression Scale</td>
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<tr>
<td>BMI</td>
<td>Body Mass Index</td>
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<td>BUPA</td>
<td>well women’s clinic (London)</td>
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<td>CECS</td>
<td>Courtauld Emotional Control Scale</td>
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<td>CI</td>
<td>confidence interval</td>
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<td>CSI</td>
<td>Coping Strategies Inventory</td>
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<tr>
<td>GHQ</td>
<td>General Health Questionnaire</td>
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<td>IPAT</td>
<td>Institute Personality Ability Testing</td>
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<td>IPSO</td>
<td>French Institute of Psychosomatic Medicine</td>
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<tr>
<td>LEDS</td>
<td>Life Events and Difficulties Scale</td>
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<tr>
<td>MAS</td>
<td>Manifest Anxiety Scale</td>
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<td>MeSH</td>
<td>MedLine search heading</td>
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<tr>
<td>MMPI</td>
<td>Minnesota Multiphasic Personality Inventory</td>
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<td>OR</td>
<td>odds ratio</td>
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<td>PDS</td>
<td>Personality Deviance Scale</td>
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<tr>
<td>RR</td>
<td>relative risk</td>
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<tr>
<td>SAQ-N</td>
<td>Self-assessment Questionnaire-Nijmegan</td>
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<tr>
<td>SDS</td>
<td>Social Desirability Scale</td>
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<tr>
<td>SQ</td>
<td>symptom questionnaire</td>
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<td>SRRS</td>
<td>Social Readjustment Rating Scale</td>
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<tr>
<td>STAI</td>
<td>State-trait Anxiety Inventory</td>
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<tr>
<td>STPI</td>
<td>State-trait Personality Inventory</td>
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<tr>
<td>STPS</td>
<td>State-trait Personality Scale</td>
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<td>TAS</td>
<td>Toronto Alexithymia Scale</td>
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1 Background

This review examines the relationship between psychosocial factors and the development of breast cancer in women. The NHMRC National Breast Cancer Centre aims to provide up to date information based on systematic reviews of the published data to women and health professionals, on potential risk factors for breast cancer. Psychosocial factors have been identified and targeted as an important review topic.

The notion that cancer might be related to stress or emotional factors is as old as the history of recorded medicine (Rosch 1984). Galen’s treatise on tumours, *De Tumoribus*, noted that melancholy women were much more susceptible to cancer than other females. In 1701, the English physician, Gendron, emphasised the effects of ‘disasters of life as occasion much trouble and grief’ in the causation of cancer. Such concepts were replaced in the 20th century by the search for external explanations of illness. This approach was based on the ideas of the 17th century French philosopher, Rene Descartes, who espoused a reductionistic view of the body in which the mind, or spirit, was viewed as a distinctly separate and unrelated entity from the mechanistic body.

Over the past few decades, however, there has been a renewed interest in the relationship between mind and body, as our understanding of the complex interrelationships between the immune, endocrine and nervous systems has increased. There is now ample evidence that stress can induce disturbances in immune system competency, and that impaired immune function can predispose to malignant growth (Morley et al 1991, Rabin et al 1989). While these data do not prove conclusively that stress causes cancer, they do corroborate clinical and epidemiological observations in this area. Finally, there are many anecdotal reports of women expressing their belief that they believe that ‘stress’ or ‘depression’ contributed to the development of their breast cancer (Brinton et al 1995).

Reviewed papers are referenced in the text of this report, and are listed alphabetically in Appendix 1. Non-reviewed papers are indicated numerically in the text and listed numerically in the References.
1.1 Definition of terms

The literature on psychosocial precursors to breast cancer focuses on three main areas:

- Stressful life events;
- Short-term coping with life events/social support; and,
- Long-term emotional and personality factors.

Several authors have suggested that chronic elevated levels of negative emotions and somatic stress, perhaps caused by stressful events that are mediated by ineffective coping mechanisms, may contribute to the development of cancer. These concepts have been presented in many different ways by the various investigators. The definitions provided below represent the most common ways in which these terms have been used.

a) Stress is defined as a somatic reaction to any environmental event that is perceived by an individual to demand increased coping efforts. This event may be seen as positive (e.g., a birth) or negative (e.g., loss of a spouse). The extent to which individuals perceive the event as exceeding their coping resources, the coping responses utilised and the amount of social support available, will all mediate to the stress response. There is disagreement concerning whether the total number of stressful life events, the types of life events (e.g., loss or financial difficulty) or the intensity of stress experienced, are important in causing cancer. Most investigators have tried to count the number and type of stressful events, and to obtain an objective or subjective rating of their intensity. Some investigators have combined an assessment of the total number of life events experienced with an assessment of the severity of their impact and/or their significance to the individual.

b) Because human behavioural and physiological reactions to life events vary widely, depending on how the event is perceived and handled, several authors have suggested the value of studying an individual’s coping response to stress, rather than to document the number and nature of life events. The inability to cope with stress has been viewed as being the crucial element among psychosocial factors purported to influence breast cancer risk. Hilvarki-Clarke (1994) has developed a model in which coping strategies mediate between the number of stressful events, their significance, the person’s personality style and breast cancer risk. It is thought to be the ability to cope with stressors that determine the extent of neuroendocrine and immunologic disturbance.
Coping has most commonly been explored in terms of characteristic
short-term responses to stress (for example, active problem solving or
denial). Some investigators have attempted to classify coping
strategies in terms of the methods used or their effectiveness in
moderating stress. The most common classification has been between
‘problem focused’ and ‘emotion focused’ coping strategies with
problem focused strategies regarded as the more effective (Lazarus et
al 1984). Social support has infrequently been explored as a
moderator, or ‘buffer’ of stress (Wheaton 1985). This has been
measured either directly (by rating the degree of support received for
each stressful event) or indirectly (eg by measuring the quality of the
marital relationship or degree of loneliness).

c) The influences of a wide variety of long-term emotional and
personality factors on responses to stress (and the development of
breast cancer) have also been explored in the literature. Some studies
try to identify a chronic anxious or depressive disposition, others
follow the work conducted in cardiovascular disease in defining a
‘cancer’ prone (type C) personality type. The predictor of cancer most
frequently explored has been an emotionally repressive response style
or ‘alexithymia’ (literally, an inability to describe one’s emotions).

Although these areas are clearly interrelated, they are rarely measured
together, and the reviewers felt a separate consideration of each would
simplify the literature review.

1.2 Methodological issues

The majority of studies in this field have used a limited prospective or
case control design. One or two studies are prospective. Each design
has advantages and disadvantages which are discussed below.

1.2.1 Prospective studies

Prospective studies evaluate predictive factors in healthy subjects who
are followed for a number of years until a substantial percentage of the
sample develop cancer. This design circumvents the need to evaluate
whether psychological effects are the result of knowing or suspecting
one has cancer, or are due to cancer-induced somatic changes even
when conscious awareness of the cancer is absent. Such fore-
knowledge may contribute to psychological states such as anxiety and
depression, and also selectively bias recall of the number and intensity
of life events. Unfortunately, psychosocial hypotheses are usually
added on to prospective studies that have primary hypotheses
concerning physical factors. Because these studies are not designed
specifically to examine psychosocial factors, the design phase seldom includes careful consideration of psychosocial scales.

### 1.2.2 Limited prospective studies

Limited prospective studies are those in which the number of subjects required to obtain sufficient cases for analysis, is sharply limited by the selection of women known to be at risk of developing cancer. Women attending for mammography or biopsy are included before the diagnosis is known to either the patient or interviewer. Subsequently, when the diagnosis is clarified, psychological differences between cases and normal controls are explored. Limited prospective studies are always hospital or clinic-based, as the eligible study population includes women undergoing breast biopsy. Therefore, these studies may not always capture a representative group of individuals with a particular disease.

Limited prospective studies are much cheaper and less time-consuming to run than prospective studies, and so allow the inclusion of more refined and accurate measures and stratification of cancer type. In addition, both prospective and limited prospective studies evaluate subjects under the same conditions, the former in a relatively anxiety-free situation, the latter in the very anxiety-inducing situation of awaiting a diagnosis.

Although it is assumed that all subjects investigated in prospective studies are being examined under the same conditions, the *a priori* probability of being diagnosed with breast cancer is not the same for all women undergoing a biopsy. Age, a past history of breast cancer and current symptoms may also affect the probability of identifying a malignant rather than a benign lesion. These differences may lead women to anticipate the results of their biopsy with considerable accuracy (Geyer 1992), making the claims to unbiased, blinded assessment of psychological states and stress open to question.

Interestingly, Geyer (1992) found that although women who correctly suspected they had cancer also had a more depressed mood, mood was not associated with the number and types of life events reported by the women. This single study suggests that recall biases may not occur as a result of knowledge of the diagnosis.

### 1.2.3 Case control studies

Case control studies compare subjects with cancer with healthy controls. Their advantage is that subjects can be accrued very quickly, and that controls may be matched on important factors, such as age and socio-economic status. Because of the small numbers, more intensive evaluations may be economically feasible (such as
physiological measures). Several comparison groups may be used, such as well women, women who were screened and found to have benign disease or healthy breast tissue and/or women undergoing different forms of surgery. The latter group are included to control conditions that induce anxiety and illness. However, case control studies still suffer from the methodological weaknesses described above: psychological differences may be due to the pre-existing cancer and knowledge of diagnosis.

1.2.4 Other methodological issues

Potential confounders

The epidemiology of breast cancer is well elucidated (Kelsey 1990) and although knowledge is incomplete, a number of risk factors have been consistently identified. In particular, age, age at menarche, age at menopause, family history, breast feeding history and body mass index (BMI) have repeatedly been identified as influencing a woman’s risk of breast cancer. It is important that the design or analysis controls for these factors.

Differences in number of life events or psychological state being confounded by age, which is highly prognostic of breast cancer. Older women having had more time to experience severe life events, and may be more depressed; they may also be less emotionally volatile. Several authors have also argued that if psychosocial factors play a role in the initiation of cancer, then this role may be most evident in younger subjects for whom the disease process is presumably less influenced by long-term exposure to environmental risk factors, and to age-related deterioration of the immune system (Temoshok & Heller 1984).

Choice of cases and controls

The choice of cases and controls is also important. It is preferable that cases and controls are assessed under conditions as identical as possible, so observable differences can clearly be attributed to psychological history and/or state. In some studies, controls are chosen from women with benign breast disease; in others from those with normal breast tissue. While those with benign breast disease may be better matched in terms of pre-biopsy symptoms and suspicions of cancer, these women are at an increased risk of developing breast cancer at a later stage. Women shown at biopsy or by mammogram to have normal breast tissue, however, are less likely to suspect cancer and may, therefore, differ from cases in the degree of bias introduced into reports of life events or psychological state. Because of the differences between these control groups, it is essential that they be clearly identified. If both groups are included in a study, then the data
should be reported separately. Similarly, if cases are collected from different sources (for example, from women about to undergo breast biopsy, mammography or a routine check-up) then the data should be reported separately. Each source is accompanied by different anxieties and expectations, which may affect outcome measures.

1.3 Aims and objectives of review

This report presents an overview of the available published research into psychosocial predictors of developing breast cancer. In each of the three areas described above, an attempt was made to:

- identify all relevant articles;
- assess the sources of bias in each study;
- examine the suitability of studies for pooling data; and,
- summarise the available evidence about the effects of psychosocial factors on breast cancer risk and, where possible, to produce summary estimates of effect.
2 Methods

2.1 Literature search strategy

2.1.1 Identification of relevant studies

A computerised CD rom search of the Australian and overseas literature published between 1966 and 1996 was conducted to identify relevant studies examining the psychosocial factors that may predispose women to breast cancer. A cut-off date of 1970 was subsequently used, since literature prior to this date was often based on psychological theory and measures no longer considered valid.

CD rom data bases searched included: MedLine, PsychInfo, NEJM, Cinahl, and Cancerlit. The key words or MeSH used included: breast neoplasms, depression, bereavement, behaviour mechanisms, cancer personality, causality, divorce, emotions, emotions affect, general adaptation syndrome, life events, life-style loss, personality, psychological stress, psychoneuroimmunology, psycho-physiology, psycho-social, social-psychology, type C personality and stress.

When articles were obtained, key words were re-checked, and bibliographies hand searched. Articles which presented literature reviews and validation of measurement tools were obtained for reference. Primary workers in the field were identified and CD rom data base searches using author fields were conducted.

Abstracts that did not give a clear summary of the paper were not excluded at this stage, so as to minimise the exclusion of relevant studies.

2.1.2 Criteria for the inclusion and exclusion of articles identified in the literature search

Studies were considered eligible for inclusion in the analysis if they:

- had as an outcome the diagnosis of breast cancer (Stages 1 or 2);
- included the assessment of one or more psychosocial risk factors;
- used either a prospective, limited prospective or case control design with at least one comparison group of healthy women, or women with benign breast disease;
were published in a peer-reviewed journal, or otherwise in the public domain in a peer acceptable form (e.g., a government report);

- were published after 1970; and,

- were printed in English.

If studies did not fully meet the detailed inclusion criteria, the review team used their expert knowledge to decide whether or not the data were suitable, based upon a consensus decision.

Articles were excluded from the review if they:

- were single case reports;

- were letters, news items or commentaries;

- assessed psychosocial factors in coping with treatment, prognosis, or relapse;

- assessed psychosocial/psychological factors in cancer in general and not breast cancer in particular;

- were conference abstracts not subsequently found to be published in a peer-reviewed journal;

- were conference proceedings; and/or,

- were published prior to 1970.

This process resulted in the identification of three population-based case control studies, twenty-seven limited prospective studies, two nested case control studies, six hospital-based case control studies, seven measurement articles and thirteen reviews. A list of these articles is included as Appendix 1. Seventy-one papers were excluded for the reasons listed above. A list of these articles is included as Appendix 2.

Papers published before 1970 were excluded on the basis of several methodological considerations: a) the studies were generally based on psychoanalytic theory and used measurement tools no longer considered reliable or valid, b) they were primarily uncontrolled, with inadequate descriptions of the sample.

Restricting the literature review to papers written in English is not expected to substantially bias the results. Several papers originally published in other languages were later translated and published in English and were, therefore, included in the review. Fifteen articles, primarily in German, French and Italian were not included.

Restricting the search to studies in which breast cancer patients were the majority of cases meant that the results could be reasonably applied to breast cancer. However, this also meant that results from studies that may have had application to breast cancer were not
considered. The conclusions drawn may have been different were these studies included. As the majority of studies in this field have focused on breast cancer, the reviewers believe that it is unlikely that substantial differences would be found.

2.2 Review of the literature

2.2.1 Data abstraction

Data were extracted using a standardised data abstraction and quality assessment form, developed by the project team to accurately record relevant aspects of methodology and results (see Appendix 3). Data extracted concerned:

- study design;
- aspects likely to influence the validity and generalisability of results;
- variations in measurement tools and procedures that may determine the validity of meta-analysis;
- actual results;
- a description of the strengths and weaknesses of each paper; and,
- a recommendation for exclusion or inclusion of a paper in the review.

Articles were reviewed by two experts in the area. Disagreements between reviewers were noted and criteria for resolving differences were developed. Where a consensus agreement could not be achieved, the more conservative rating (negative) was used.

2.2.2 Criteria for exclusion of articles developed during the review process

During the review process, a set of quality assessment rules was developed (see Section 2.2.3). Studies were excluded if they had one serious design flaw (usually selection bias) or if they had several less serious design flaws that the reviewers felt compromised the study. Where disagreement occurred between reviewers the more conservative assessment (exclusion) was adopted.

Serious design flaws included:

- an inappropriate control group was used, such as hospital staff, for comparison with women with breast cancer (case control studies) or with those undergoing a biopsy (limited prospective studies).
If data were also available using an appropriate concurrent control group (eg women with benign disease who had undergone a biopsy), the paper was included (eg Fox, 1994). If insufficient information was provided to determine whether the control group was appropriate, the paper was included but its quality score reflected this uncertainty. One exception to this rule was made in the case of the Cooper series (1986, 1989, 1992, 1993), which used an inappropriate control group, because the reviewers felt that there were aspects of this substantial body of work not included elsewhere in the literature;

- an unacceptably low response rate was reported with differential refusal rates between cases and non-cases;
- the interviewer was not blinded to case status where subjective ratings were made; and,
- breast cancers were not separated from other cancers in reporting the data.

Less serious design flaws included:

- the statistical analysis was not described or could not be inferred;
- strategies for reducing recall bias were not employed in case control studies, or in limited prospective designs where the cancer patients had been warned of their likely diagnosis;
- the psychological measures were not validated; and,
- the data were not adjusted for potential confounders, especially age.

Multiple publications from the same data source were reviewed to determine which publication presented the data in the most suitable manner for inclusion in this review. Publications that used a subset of cases with an appropriate control group, with some attempt at adjustment for age, were more likely to be included than papers examining all cases of breast cancer, with no attempt to adjust or using heterogeneous, inappropriate control groups.

### 2.2.3 Quality assessment

During the review process, each study was assessed for quality using the standard form (see Appendix 3). The quality assessment, designed to be brief and focused, was based upon previously published scales and checklists (English et al 1995, Longnecker 1994, Oxman 1994).
The key features of the quality assessment were:

- definition of case status and representativeness of cases and controls or cohort;
- data collection procedures including equality of exposure ascertainment for all subjects and attempts to eliminate recall bias; and,
- response rates or adequacy of follow-up.

Thus, the priority of quality assessment was to detect systematic errors (i.e. bias), occurring within the studies included in the reviews. To compare study quality, a weighted quality assessment score was calculated for each study. Firstly, each question in the quality assessment was given a response score ranging from one to six. The highest score (i.e. six), was given when the paper provided adequate details of measures taken by the investigators to reduce systematic errors, and the lowest score (i.e. one) when no information was provided, or the study did not sufficiently account for the relevant variable.

Each question was also weighted (range one to three) according to the relative importance of each variable to the study outcome and effect measures. The greatest weight (i.e. three), was given to the representativeness of the study population and compatibility in data collection. The final quality score was a weighted response score (i.e. response score multiplied by the weight).

Holman et al. (1996) reported that the scoring of study quality was unhelpful in deciding which studies to exclude in a review since, for example, a study could score highly but still have a major flaw. Thus, studies were not excluded from this review on the basis of a quality assessment score; however, each study had to achieve the minimal acceptable standard (see exclusion criteria, Section 2.1.2).
3 Results

3.1 Overall description of the literature

Overall, there is a paucity of large-scale, well designed empirical studies that have been performed in this field. Many of the studies employed small sample sizes, using convenience samples of indeterminate bias. Cases and controls from different sources were sometimes combined, making the data impossible to interpret. Comparison groups were frequently selected from different source populations than the cases (eg Cooper, Cooper and Faragher, 1989). An interesting example of this comes from a case control study by Bandyopadhyay, Chattopadhyay, Ghosh and Brahmachari (1987) in which psychological test results of ten breast cancer patients were compared with those of normal females ‘selected randomly from central Calcutta’. The comparison of life stress experienced or personality characteristics between women admitted to hospital in a particular city for a biopsy and a control group of women in a different city attending a primary care facility, raises many questions about the possibility for selection bias.

When details are provided about these comparison populations, clearly they differ in many ways from the cases. Although the papers generated by Cooper and his group provide the clearest example of this design flaw, many other researchers have used inappropriate control groups, without providing sufficient detail to allow the examination of potential bias (eg Forsen, 1991). Response rates were rarely reported and in the limited prospective studies, few attempts were made to assess the extent to which women suspected their diagnosis.

The data were rarely adjusted for potential confounders, particularly age. Few of the papers examining the association between personality factors and breast cancer risk dealt adequately with confounders. For example, in the papers reviewed, the age difference between a case group and comparison group was often substantial (Cooper papers), without appropriate adjustment being made in analysis. When age adjustment was made, it usually took the form of stratified presentation of data (Schonfield, 1975) using such broad categories that residual confounding is likely. Few of the additional well characterised risk factors for breast cancer are even measured, let alone adjusted for in analysis. Multivariate analysis is used
infrrequently to provide an estimate of the independent effects of psychosocial factors on breast cancer risk, although the more recent papers such as that by Roberts, Newcomb, Trentham-Deitz and Storer (1996) have examined the independent effects of psychosocial factors on breast cancer risk.

Measures were sometimes idiosyncratic and psychometric data were not reported (see Appendix 4). Finally, the statistics were sometimes poorly designed and often poorly presented. These deficiencies mean that it is impractical to perform meta-analyses of the data in each of the three main topic areas.

However, to mitigate this rather bleak report, the more recent studies show a marked improvement, with several excellent papers providing a clear description of the methodology and sample, using multivariate analysis with adjustment for confounders and presenting a thoughtful discussion of the results (eg Roberts, Newcomb, Trentham-Deitz and Storer, 1996).

The complete results of studies included in this review are provided in Appendix 6, the major findings in Appendix 7 and the weighted quality assessment scores in Appendix 7.

3.2 Life events

Investigators examining the association between stressful life events and breast cancer risk have used different scales based on either checklists developed specifically for the purposes of their research (Greer and Morris, 1975 and Snell and Graham, 1971), or on standardised methods well described in psychological literature (Holmes, Rahe 1967, Brown et al 1977). Both approaches have their limitations. The use of standardised checklists may facilitate comparisons among papers, however, the relevance of the individual items and of their weighting requires examination in the population being studied. In addition, the standardised checklists seldom provide the opportunity for an individual woman to describe the importance that each event actually holds. On the other hand, although the life event scales developed specifically for particular research projects may reflect the values and experiences of the population being investigated, the use of these idiosyncratic scales reduces the comparability between papers and makes a quantitative synthesis of research data impossible.

Checklist assessments of life events usually separate the events themselves from the individual’s perception of that event. In addition, checklists are criticised because they do not ensure that all study participants share a common standard for interpreting the judgement.
words within the scales (eg ‘serious illness’) nor can it be assumed that events on the list are independent (eg divorce may be associated with financial difficulties) (Monroe, Roberts 1990).

3.2.1 Life events scales

Holmes-Rahe social readjustment rating scale (SRRS) (Holmes and Rahe, 1967)

This scale was developed in order to combine an assessment of the number and type of stressful life events that have occurred in the past, with an assessment of their importance as determined by the time necessary to adjust to each event. The two North Americans who developed the scale examined a ‘sample of convenience’ using a list containing life events based on observations in clinical practice. The 394 subjects in this sample were predominantly young (206 less than 30 years of age and 51 greater than 60 years of age), third generation American, middle class (323), white (363) and Protestant (241). Males and females were approximately equally represented in the sample. The defined subgroups in the sample had relatively high agreement in the rank order and scoring of the items in the scale. The study population gave weights to events relative to the 500 that was assigned to marriage. The authors themselves state that ‘these events pertain to major areas of dynamic significance in the social structure of the American way of life’. The relevance of this checklist and its weightings to other cultures and indeed to North American culture in the 1990s is open to question.

Subsequent investigators using the SRRS generally use the standard rank order and weightings provided by Holmes and Rahe. Study participants check items on the inventory that they acknowledge have occurred; therefore it is possible that one individual’s interpretation of what constitutes a ‘severe’ illness may differ from another individual’s interpretation of the same construct.

Life events and difficulties scales

Brown and Harris (1978, 1979) developed a scale designed to assess life events and their role in the aetiology of depression, with a focus on the role of loss events (eg widowhood or divorce) and the strength of emotion that such experiences would evoke. The meaning of the events was seen as being important, although the scale itself rather than the study participants, provides a standardised assessment of the meaning to be ascribed to particular events. The standard assessment is based on contextual information provided by study participants. A list of thirty-eight classes of events involving change was developed, and a detailed reference guide to assist in the interpretation of the meaning of particular events was included. The reliability and validity
of this life events instrument was assessed among schizophrenic patients. The LEDS relies on the skill, sensitivity and training of an interviewer to evoke information about events that have occurred in study subjects' lives, using standard questions and probes. Brown and Harris acknowledge that although this approach is likely to lead to more standardised assessment of life events for research purposes, it presumes that events have the same meaning for all subjects, for example, divorce is treated as a major stressful life event although it may be a cause for much relief for some individuals.

Although Brown and Harris distinguish between 'provoking agents' (events that can either provoke the onset of disease or influence its course) and 'vulnerability agents' (events that can increase the impact of the 'provoking agents'), the distinction is not always considered by other researchers.

Other scales

Cooper and his team (Cheang and Cooper, 1985) in England developed a Likert scale for life events assessing the stressfulness of each event to the individual. Although many items are in common with the SRRS, in-depth interviews with English women highlighted a number of important events that did not appear on the Homes-Rahe scale. In addition, weightings varied substantially between the American and the English sample. Their scale was seen to be more appropriate for the women in the population they were studying.

Twenty-five papers examined life events. Several of these papers were reanalyses of data presented by the same research group in earlier reports. A decision was made to include the latest analysis that adjusted for age (and other factors if possible), in which it was possible to separate data from appropriate and inappropriate controls.

Two papers were excluded from consideration for this review because they had used inappropriate control groups, reported data selectively and/or had small sample sizes with confounding by age (Ippoliti, Natalia and Pozzi et al, 1991 and Choroto, 1994).

No published work was identified which examined the risk of breast cancer using Henderson's 'life events scale' developed for Australian populations (Henderson et al 1981).

3.2.2 Holmes-Rahe SRRS and its variants

All the papers to be discussed in this section except Fox, Harper and Hyner (1994), used variants of the SRRS rather than the original scale (see Appendix 4). Schoenfield (1975) used a poorly-described sample of thirty-three non-hospitalised Israelis to assign weights to the scale; Priestman, Priestman and Bradshaw (1985) used the Cochrane and
Robertson (1973) inventory adapted from the SRRS; Roberts, Newcomb, Trentham-Dietz and Storer (1996) developed an abbreviated version of the SRRS that was tested on women similar to the study population, and Forsén (1991) used both the SRRS and a modified version that focused on events which occurred in the six years prior to diagnosis. Edwards, Cooper and Pearl et al (1990) used a forty-two item scale developed by Cheang and Cooper (1985) in England. This section will discuss all papers using SRRS either in its original form or in a modified form. The research by Cooper and colleagues will be dealt with separately although their scale was derived from that of Holmes and Rahe. These papers describe research undertaken in the UK, USA, Finland and Israel.

**Limited prospective studies**

The three limited prospective studies were based on very different populations. Fox, Harper and Hyner (1994) report the results of the analysis of questionnaires completed by 826 women (less than 50% of those approached), presenting for mammograms at a specialist breast centre. As fifty-two of the seventy-two women with breast cancer had previous breast cancer, results will be reported for the incident cases only. After adjusting for age, BMI, family history, menopausal status, menstrual history and parity, the mean difference in the SRRS did not differ significantly between the incident cancer group and the other study groups. The means did vary, however, (cancer: 241 ± 27.7, normals: 175 ± 12.9) and an analysis of individual items revealed that a higher proportion of the incident cancer group had experienced the death of a spouse or close family member within the two years prior to diagnosis (60% versus 27% in the normal group). As the analysis of individual items was not adjusted for age or any other confounders, it is difficult to interpret this result.

Schonfield (1975) examined 112 women (twenty-seven subsequently found to have cancer and eighty-five with benign tumours) undergoing a breast biopsy in five different hospitals in Tel Aviv, and dealt with confounding and ethnic background by stratification resulting in small subgroups divided by age (≤ 42 years and ≥ 43 years) and place of birth (European-American and African-Asian). Using an analysis of variance to examine life change unit scores for the three years prior to diagnosis, Schonfield reported that women with benign tumours had higher scores than those with breast cancer. The items dealing with loss and separation such as death of a spouse or divorce, were analysed separately although these data were not presented. It was stated that there were no significant differences were detected in these events between the cases and controls.
Edwards, Cooper and Pearl et al (1990) reported the results of an investigation of 1,052 women receiving a breast examination and mammogram at the University of Virginia Medical Centre. The study population included a sample of women both with breast symptoms and those who were asymptomatic; all women received a breast examination and a mammogram. Although it is not stated in the paper, it is unlikely that they all underwent a biopsy. There were 597 women with normal breasts, 505 women with benign breast disease, seventy-one with pre-cancerous growths such as hyperplasia and seventy-nine with breast cancer. Factor analysis was used to identify eight subscales of life events. After controlling for age and history of breast cancer, none of the eight life events scales predicted diagnosis. A subsequent analysis examined both the occurrence of events and their severity by summing items and examining each event separately. Although a number of individual items such as surgery or greater threat of job loss was significant, the authors appropriately interpret these data from exploratory analyses cautiously.

**Case control studies**

The three case control studies varied in quality. Priestman, Priestman and Bradshaw (1985) examined one hundred women with breast cancer and one hundred women with benign disease attending three surgical clinics over a three-month period, and a convenience sample of one hundred women drawn from a combination of paramedical and ancillary staff and members of the general public. No differences were reported in the mean number of stressful life events or the severity of these events between any of these groups.

Forsén (1991) examined eighty-seven women with newly diagnosed breast cancer and controls matched by age, sex, language and parity. No details were provided on the source of controls. Differences were reported in the mean life events scores for both the twelve months and the six years prior to diagnosis. In particular, more loss events were reported in the cancer group although this difference was not significant. Multivariate analysis adjusting for anxiety, depression, marital status, education and social class confirmed that life event scores for the twelve months preceding diagnosis, and sustaining an important emotional loss were significant predictors of breast cancer risk. The only known risk factors for breast cancer accounted for in this study were age and parity. Although cases and controls were matched for these factors, there is no indication that an appropriate matched analysis was undertaken.

A well designed population-based, case control study (Roberts, Newcomb, Trentham-Dietz and Storer, 1996) examined 258 women with newly diagnosed breast cancer and 614 controls randomly selected via drivers’ licenses for women younger than 65, and through
the United States Health Care Financing Administration for women aged over 65. All participants were aged between 50 and 79.
Frequency-matching was used to control for age. An abbreviated version of the SRRS, which only included items relevant to older women, was pilot-tested. Reliability testing among thirty-five cases and thirty-five controls six months after the original interview, showed 83% agreement between the responses. The reported odds ratios were adjusted for age, age at first birth, parity, family history of breast cancer, BMI, and age at menarche. There were no differences in the overall number of events or the experience of losses. In the analysis of differences in the experience of individual items in the scale, controls reported the death of a close friend more than cases (odds ratio (OR) = 0.72, 95% confidence interval (CI) 0.52-1.00).

3.2.3 Cooper studies

The series of papers produced by Cooper and his colleagues (Cheang and Cooper, 1985; Cooper, Cooper and Faragher, 1989; Cooper and Faragher, 1992; Cooper and Faragher, 1993 and Faragher and Cooper, 1990) present a challenge to the reviewer. All papers, bar the paper by Cheang and Cooper (1985), refer to the same study population of 1,324 women attending a surgical outpatient clinic in one city, 272 women attending a breast screening clinic in a second city, and 567 women attending a primary health care facility in a third city. This latter group of women were included as normal controls. The first two groups of women were classified according to whether they had cancer, cysts, benign breast disease or normal breasts and were interviewed prior to receiving their final diagnosis. Thus it would appear that this is a limited prospective study. The women attending the primary health care facility, however, did not undergo a diagnostic procedure and their inclusion as controls provides the disadvantages (and advantages) of a case control study. Normal women from the clinic populations were combined in analysis, with the 567 women attending the primary health care facility. There was potential for confounding by age, occupation, smoking status, alcohol use and reproductive history. Information was not presented on other confounders such as personal and family history of breast cancer. Data from these papers will be discussed only where it is possible to examine the results in the surgical outpatient group alone, excluding findings from 'normal' controls that included 567 women attending the primary health care facility.

In the first paper of the series (Cheang and Cooper, 1985), the data presented were either the pilot phase of the later research or an analysis of the first 163 participants. In this study, 121 women admitted to hospital for a breast biopsy were interviewed on the day
before the operation. An additional forty-two healthy controls were selected 'randomly' from a well woman clinic. The assessment of stressful life events was based on recall of events that had occurred two years before the discovery of the breast lump or before the interview (for the healthy controls). The forty-eight separate life events were scaled by an additional twenty-five women undergoing a breast biopsy. Scores from ten to one were allocated to events in order of severity with ten being allocated to the death of a husband and one to a wedding anniversary. Unadjusted data only are presented; the authors claim that there was only a minor difference in age between the unusually young cancer group (mean age 50.5), and women who were cancer-free (mean age 48). Women with breast cancer reported more life events and more stressful life events than the cancer-free women (p < 0.01). In addition, 98% of the women with cancer reported experiencing at least one loss and/or illness event compared with 71% of the non-cancer women (p = 0.002). As there is no adjustment for age and no assessment of the potential for confounding by other risk factors for breast cancer, these results should be interpreted cautiously. The scale developed for this study formed the basis of the larger study reported in the later papers.

Life events are examined in three additional papers from this research group (Cooper, Cooper and Faragher, 1989 and Cooper and Faragher, 1993). Data from the 1989 paper are discussed as they were presented in a manner facilitating the examination of results for the surgical outpatient clinic groups separately from the well woman clinic control group, and they were adjusted for age.

The forty-eight life event items were examined with the frequencies separated from the perceived severity scores. Although it was claimed that the data were age-adjusted, differences are consistent with unadjusted, or incompletely adjusted data. For example, the control group who were younger reported more work-related problems, more difficulties with children, and more new loans or mortgages than the cancer group. Conversely, the cancer group reported more births of grandchildren, deaths of close friends and retirement. An examination of the experienced severity of each life event revealed that although there were few differences in the incidence of events, reported severity of the events was greater in the cancer group than in the other groups. These patterns were not however consistent over all forty-eight items.

This substantial body of work from one research group and the 1989 paper in particular provides little supporting evidence for an association between life events and breast cancer risk. The choice of comparison groups and approach to analysis limits the validity of this work. In addition, the authors appear to highlight single differences in
the examination of a forty-eight item list rather than examine overall patterns.

3.2.4 Brown and Harris LEDS

Two limited prospective studies (Geyer 1991, 1993, and Chen, David and Nunnerley et al, 1995) used this scale although data are presented in a manner that limits their direct comparison.

The study population used in Geyer’s 1991 paper was also the basis for his later report (in 1993), in which data were presented on ninety-two women (74% of all who were eligible), thirty-three of whom were diagnosed with malignant disease, fifty-nine diagnosed with benign disease, and on an additional control group of twenty women admitted for gallstone surgery. After noting the age differences between his groups, Geyer used regression techniques to adjust for differences in age distribution and family history. The most severe life events, those associated with loss, were more common in the cancer group.

Although there was no difference between benign and malignant groups in family history of disease, there was an interaction between severe life events and family history in determining breast cancer risk. The adjusted regression coefficients, presented without standard errors or tests of significance, demonstrated a stronger association between life events (r = 0.28) and breast cancer than between age and breast cancer (r = 0.19).

Chen, David and Nunnerley et al (1995) examined seventy-two women referred for examination of breast lesions following mammographic screening and a second group of forty-seven symptomatic women undergoing biopsies; forty-one were diagnosed with cancer and seventy-eight with benign disease. A number of confounding factors were reported including age, marital status, menopausal status, age at menarche, age at birth of first child, alcohol use and family history. The adjusted odds ratio for severely threatening events was very high at 15.00 although the confidence interval was wide (3.74 to 60.44). Moderate threatening events that were experienced as important by the study participants were also associated with increased risk of breast cancer (OR_{adjusted} 9.70; 95% CI 2.45-38.17). This association was seen in both the screened and symptomatic samples.

These intriguing papers using the LEDS indicate avenues for additional research. Not only are they of a higher quality (see Appendix 7) than most of the other papers reviewed, they also use a measurement tool which attempts to capture a more complex conceptualisation of life events than is the case with simple checklists. Although the data are not presented in a way which facilitates the
calculation of a summary effect measure, they suggest that severe or severely threatening life events may be associated with increased breast cancer risk. It is also worthy of note that these studies were undertaken in different countries, the UK and in Germany, suggesting that the LEDS may be a useful measurement tool beyond the culture in which it was developed.

### 3.2.5 Scherg papers (based on Bahnson et al)

Scherg and colleagues published three papers (1981, 1987, 1988) examining life events and breast cancer risk using a modification of a questionnaire developed by Bahnson and Bahnson (1979). The life events component of the questionnaire was designed to measure reluctance to admit life events rather than the experience of life events themselves.

The earliest paper (Scherg, Cramer and Blohmke, 1981) reports a limited prospective study based on 3,306 women attending a gynaecological screening clinic at Heidelberg University. Matched pair analyses were undertaken on one hundred cases and one hundred symptom-free healthy controls (matched for age, social class and 'family status'), and sixty-nine of the cases matched for age with sixty-nine women with benign breast disease. Analyses were further stratified by age (50, 51-70 years). Although no data are presented on total life events, the authors report that cases experienced the loss of a close relative in the past three years more often than healthy controls (46% versus 31%). This is counter to the expectations of the authors who had hypothesised that cancer patients would recall fewer events. Cases also claimed to be more bothered by war and postwar experiences; this is particularly apparent in the older age group. As these were the only results reported, it is difficult to assess whether the overall pattern of experiences supports a role for stressful life events.

Scherg (1989) later noted that the control group in his 1981 report included a larger proportion of symptom-free women attending the clinic for screening, while the cases were mainly women following up the detection of a breast lump. In the later analysis, data were presented for seventy-five case control pairs under 70 years of age who were matched for age (within three years) and reason for consultation. Only the women with benign disease were included in the comparison group. Conditional logistic regression analyses for five scales were presented. Prior war experience was a significant predictor of breast cancer risk ($p = 0.007$) although the strength of association was reduced when fear of breast cancer (assessed prior to biopsy) was included ($p = 0.02$). The results for the life events scale, which included a fifteen-item checklist, were not reported as they were not significant.
The third paper in this series (Scherg and Blomcke, 1988) reported a case control analysis including the same study population and additional subjects. Test results were compared for 125 incident cancer cases, seventy-seven prevalent breast cancer cases, 306 women with cancer at other sites, and 1,563 controls who underwent the same diagnostic tests and were cancer-free. Many analyses combine the three cancer groups. The only table presenting life events separately for the different case groups and the control group did not adjust for age. Such adjustment is necessary as the controls were on average, ten years younger than the cases. Compared with controls, the incident breast cancer cases reported no differences in the death of a father or mother but considerable differences in the loss of a spouse (35.2% versus 18.1%) and the experience of war trauma (81% versus 65.6%). Such results are consistent with age confounding.

These papers present limited, inconsistent data on an association between life events and breast cancer. War and postwar experiences appear to be more common in breast cancer cases in all analyses of the data. When there was appropriate adjustment for age and a suitable comparison group (Scherg, 1987), no association was found with any other life events.

3.2.6 Interviews and other scales

Limited prospective studies

In a limited prospective study of sixty-nine women later found to have cancer and ninety-one women with benign breast disease (Greer and Morris, 1975), a structured interview was used to assess the ‘occurrence of major stressful events’ in the five years before diagnosis. Although the controls were significantly younger than the women with cancer, no adjustment or stratification for age was reported. There were no differences either in the total number of stressful life events experienced (data not shown in the paper) or in the number of loss events. Two subsequent reports of these data were excluded as they reported results of a subset of participants (Bageley, 1979) or were more limited in the detail reported (Greer and Morris, 1978). A briefly described limited prospective study (Schwarz and Geyer, 1984) used a non-standardised, structured interview to assess stress among eighty-one women undergoing a biopsy. Among the seventy-six women included in a path analysis, the experience of loss was not associated with breast cancer risk.

Case control studies

The data presented in the two case control studies, using a brief questionnaire or a structured interview, also failed to provide evidence supporting an association (Snell and Graham, 1971, and Brémont,
Kune and Bahnson, 1986). Snell and Graham’s large study based on 352 women with breast cancer and a control group of 670 women with cancer and non-neoplastic diseases, was published twenty-six years ago. Participants were interviewed about experiences in the five years preceding diagnosis. Brémond, Kune and Bahnson (1986) used a structured interview with a single question concerning stressful life events, in their study of fifty women with breast cancer and one hundred disease-free controls (age-matched within five years) selected from the same clinic. Among women aged 44 and younger (of whom there were fourteen cases and twenty-one controls) the reported odds ratio (from an unmatched analysis), for having had a ‘serious psychological shock during the past five years’ was 4.33 (95% CI 1.2-16). Among women aged 45 and older the odds ratio was 1.09 (95% CI 0.4-2.9) and for the total population it was 2.01 (95% CI 0.94-4.3). The rationale for age stratification was not discussed and may well have been opportunistic. In addition, this case series included a substantial proportion of young women (28% were aged 44 and younger) an unusually young group of women to have breast cancer. Neither of these case control studies assessed the severity of life experiences.

3.2.7 Population based case control studies (record linkage studies)

Ewertz (1986) and Kvikstad, Vatten, Tretli and Kvinsland (1994) used population data available from Denmark and Norway, respectively, to link cancer incidence records with population registry data describing the marital status of the population. The Danish study (Ewertz, 1986) reported the marital status of 1,792 newly diagnosed breast cancer cases and 1,739 controls based on an age-stratified random sample of the population. Data from the Central Population Register showed no differences in marital status, length of widowhood or time from divorce to diagnosis. Kvikstad et al (1994) included 4,491 incident cases of breast cancer over a twenty-four year period and 44,910 cancer-free controls who were frequency matched by age to the cases. Adjustment was made for age at first birth and parity. Widowhood was not associated with increased risk while the odds ratio for divorce indicated a negative association with breast cancer (0.83, 95% CI 0.75-0.92). These two studies provide an unbiased assessment of a very limited measure of life events and stress.
3.2.8 Life events summary

Life events, as they have been assessed in the past, do not appear to be associated with breast cancer risk. The majority of studies reported no differences between cancer patients and controls in the number of life events experienced. The papers using the Brown and Harris Leds to assess life events reported an association between severe events (explicitly described as loss events in the Geyer papers but not described in detail by Chen et al, 1995) and breast cancer risk. Although appropriate adjustment for confounding is a feature of both research groups, Chen included more factors in the multivariate analysis. The only other papers that found an association between life events and breast cancer risk received very low quality ratings. The Scherg paper identified an association between war experiences but not with other measures of life events.

Work using the Brown and Harris scale, a more complex scale to administer than those reported in the other studies, should be replicated in other settings. These findings may reflect a more accurate assessment of life events using this scale or may represent systematic error.

Although the weight of evidence appears not to support an association between life events and breast cancer risk, few studies have been of a sufficiently high quality (see Table 1). Any additional research should use well-validated tools which assess complexity as well as number of life events. Careful consideration must also be given to the choice of comparison populations and adjustment for age, as well as for other known risk factors for breast cancer. The results of studies exploring the impact of life events on the development of breast cancer are summarised in Table 1.
Table 1
Summary of results of studies examining life events and breast cancer risk

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Scale</th>
<th>Weighted Quality score</th>
<th>Study type</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geyer, 1993</td>
<td>Brown-Harris</td>
<td>93%</td>
<td>Limited prospective</td>
<td>✓</td>
</tr>
<tr>
<td>Greer, 1975</td>
<td>Interview</td>
<td>92%</td>
<td>Limited prospective</td>
<td>—</td>
</tr>
<tr>
<td>Chen, 1995</td>
<td>Brown-Harris</td>
<td>91%</td>
<td>Limited prospective</td>
<td>✓</td>
</tr>
<tr>
<td>Edwards, 1990s</td>
<td>SRRS (Cooper)</td>
<td>90%</td>
<td>Limited prospective</td>
<td>—</td>
</tr>
<tr>
<td>Roberts, 1996</td>
<td>SRRS</td>
<td>87%</td>
<td>Population case-control</td>
<td>—</td>
</tr>
<tr>
<td>Ewertz, 1966</td>
<td>Registry linkage</td>
<td>86%</td>
<td>Population case-control</td>
<td>—</td>
</tr>
<tr>
<td>Scherg, 1987</td>
<td>Bahnson</td>
<td>85%</td>
<td>Limited prospective</td>
<td>✓</td>
</tr>
<tr>
<td>Schonfeld, 1975</td>
<td>SRRS</td>
<td>86%</td>
<td>Limited prospective</td>
<td>—</td>
</tr>
<tr>
<td>Kvikstad, 1994</td>
<td>Registry linkage</td>
<td>83%</td>
<td>Population case-control</td>
<td>—</td>
</tr>
<tr>
<td>Priestman, 1985</td>
<td>SRRS</td>
<td>83%</td>
<td>Case-control</td>
<td>—</td>
</tr>
<tr>
<td>Schwarz, 1984</td>
<td>Questionnaire</td>
<td>79%</td>
<td>Limited prospective</td>
<td>—</td>
</tr>
<tr>
<td>Fox, 1994</td>
<td>SRRS</td>
<td>78%</td>
<td>Limited prospective</td>
<td>—</td>
</tr>
<tr>
<td>Cooper, 1989</td>
<td>Cheang &amp; Cooper²</td>
<td>73%</td>
<td>Limited prospective</td>
<td>—</td>
</tr>
<tr>
<td>Snell, 1971</td>
<td>Interview for SLE</td>
<td>77%</td>
<td>Hospital case-control</td>
<td>—</td>
</tr>
<tr>
<td>Brémont, 1986³</td>
<td>Single question</td>
<td>66%</td>
<td>Hospital case-control</td>
<td>—</td>
</tr>
<tr>
<td>Forsén, 1991</td>
<td>SRRS</td>
<td>49%</td>
<td>Hospital case-control</td>
<td>✓</td>
</tr>
<tr>
<td>Cheang, 1985</td>
<td>Cheang &amp; Cooper</td>
<td>47%</td>
<td>Limited prospective</td>
<td>✓</td>
</tr>
</tbody>
</table>

¹ No association for life events, positive association for war trauma.

² The attribution of the source of the scale is not made in Cooper (1989). In examining all the papers from this research group, we have inferred that the scale was developed by Cheang and Cooper and refined by other members of the research team.

³ A significant association between life events and breast cancer risk was found for women under 45 years of age.

3.3 Coping with life events

An acceptance in the psychiatric literature that stressful life events make only a small contribution to the explanation of variance in psychiatric disorders led to an examination of the potential role of intervening variables, such as coping and social support, that may modify the effects of these events (Dohrenwend, Dohrenwend 1974). In this section of the review, coping strategy is defined as a short-term response to a stressful life event rather than a long-term response style. Seventeen papers examined coping with life events; eleven are
included in this review. Papers were excluded for the reasons specified in Appendix 5.

Other papers were excluded for the following reasons:

1. Cooper and Faragher (1993) was not presented in a way that permits a comparison between women with breast cancer and appropriate control groups.

2. Choroto (1994) was excluded from consideration for the review because inappropriate control groups were used, data were reported selectively, a small sample size was used, and data were confounded by age.

3. The paper by Wirsching, Stierlin and Hoffman et al (1982) was excluded because data were not presented in a usable way and there was confounding by age and knowledge of diagnosis was evident.

4. Greer (1978, 1979) was excluded as more detailed data were contained in his 1975 paper.

3.3.1 Coping strategies inventory and variants

Three papers which assessed coping with life events were based on the Folkman and Lazarus (1980) sixty-eight item coping strategies inventory (CSI). Chen, David and Nunnerley et al (1995) used a seventy-two item adaptation while Edwards, Cooper and Pearl et al (1990), used a thirty-eight item version known as the ways of coping checklist developed by a team led by Cooper in the UK (Cooper and Faragher, 1992).

Folkman and Lazarus (1980) developed their scale after examining the ways in which a sample of one hundred, mainly white, American men and women aged 45-64, who were participating in a population-based study of health (Alameda County studies), dealt with stressors over a twelve month period. Coping was defined 'as the cognitive and behavioural efforts made to master, tolerate, or reduce external and internal demands and conflicts among them'. Respondents were asked to indicate whether they used each of sixty-eight coping strategies when faced with specific stressful situations. These strategies were derived from theoretical work completed by one of the authors (Lazarus, 1966), and the coping literature. Items were divided into problem-focused and emotion-focused categories to differentiate between strategies that serve to deal with the source of the stress (problem-focused coping) and those that regulate stressful emotion (emotion-focused coping).
In the paper by Edwards, Cooper and Pearl et al. (1990) (see Section 2.2), no association was found between breast cancer risk and either the four coping scales developed from the thirty-eight items, or the individual coping items. In an additional analysis to determine whether coping was an effect modifier of the association between stress and disease, no significant association was identified. All analyses adjusted for age and history of breast cancer. The ways of coping checklist used in this study was borrowed from the research by Cooper and his group (see Section 3.2.1).

The checklist, described in Cooper and Faragher (1992) was developed by asking ‘a series of individuals’ to describe methods used to cope with stressful events, and a checklist was subsequently generated using the most commonly reported thirty-six items. No additional information was provided on the population used to develop this scale. Few differences were detected in their large limited prospective study particularly when data were age-adjusted. Approximately one hundred and thirty significance tests were performed to detect differences between the four study groups, for each of the thirty-six individual items and for the mean factor scores for five factors derived from the individual items in the checklist (denial, internalisation, externalisation, emotional outlet and anger), and for crude and age-adjusted frequencies. This paper provided strong evidence for the need to age-adjust data as there was a very strong relationship between age and the use of coping strategies (older women used far fewer strategies), but no evidence for a role for coping strategies in influencing the risk of breast cancer. The authors claim that there was some weak evidence for an association between coping strategies and breast cancer risk, as women with breast cancer always used fewer strategies than normal women even when the data were age adjusted. They did not, however, use fewer strategies than women with cysts or benign disease who were the more appropriate controls.

Chen, David and Nunnerley et al. (1995) (see Section 2.2) also found little support for the role of coping mechanisms. However, among women who had experienced a severe life event in the five years before diagnosis, those who coped with stress by confronting it and working out a plan to deal with the problem were at higher risk. This result should be interpreted with caution as there is no indication that the researchers had an a priori hypothesis about the role of coping strategies in this particular subgroup. In a multivariate analysis adjusting for age, family history, menopausal status, personality, tobacco and alcohol use and experience of severely threatening or important moderately threatening events, being problem focused was associated with a five-fold increase in risk (OR = 5.12; 95% CI 1.46-17.89). It is unclear how this reported odds ratio relates to the implied
effect modification between severe life events and ways of coping
with these events. The authors note that their finding runs counter to
their prediction that women with increased risk of breast cancer are
less likely to actively confront their problems. They speculate that a
confrontational approach may not be of benefit when a woman is
faced with a severely stressful event, such as the death of a relative or
serious illness in the family, over which she has little control.

3.3.2 Other approaches to the assessment of coping
strategies

Most of the studies examining an association between coping
strategies and breast cancer risk have not used standardised
measurement tools which can be readily compared. Individual
researchers have developed questions to include in a battery of
assessments of personality type and stress. Few researchers report the
validity or the reliability of their questionnaires.

A German psychological instrument (Kuhl, 1980) designed to measure
‘action control’ or women’s reactions to stress was used in a limited
prospective study (Schwarz and Geyer, 1984). There was no
association between action control and cancer. In their case control
study, Brémond, Kune and Bahnson (1986) asked study participants
whether they generally slept well, and whether they used sleeping pills
or tranquilisers regularly. No differences were reported between cases
and controls. Bahnson also influenced Scherg’s limited prospective
study (Scherg, 1987) in Germany. A questionnaire developed by
Bahnson was used to examine the association between a number of
psychosocial scales and breast cancer risk. Although Scherg did not
state that any of the scales were included expressly to assess coping
strategies, an assessment of a tendency to adapt to the outside world,
to be oriented towards social and religious norms (commitment), or to
attempt to give socially desirable responses may be seen as assessing
an approach to coping. In the conditional logistic regression analysis
of the age-matched cases and controls, cases were more likely to score
highly on social desirability and commitment scales, and these
associations were increased after adjustment for fear of breast cancer
\(p = 0.04\) and \(p = 0.073\) respectively. There was some evidence for an
interaction between commitment and fear of breast cancer and
between social desirability and age.

3.3.3 Social support

Standardised measurement scales have not been used for the
assessment of social support in any of the papers reviewed. Cooper
and his English team (1986, 1993) used a social support inventory to
determine the number of people to whom a woman could turn for
support and her relationship with each of these individuals. Total amount of social support was the same between the groups, although cancer patients used their parents less and their children more than control subjects. This finding is consistent with a confounding effect by age. Edwards, Cooper and Pearl et al (1990) used the same social support inventory in their North American research. Neither the total amounts of social support nor individual sources of support were significant predictors of breast cancer risk. The availability of social support did not interact with stressful life events scores in predicting diagnosis.

In his paper based on the work of Brown and Harris, Geyer (1991, 1993) regarded social support as modifying the effect of stressful life events. His approach to the assessment of social support is not described in detail; it was rated on a five-point scale for events described as long-term threats. As ‘life events’ and ‘lack of social support’ were highly correlated, social support was excluded from the model. Geyer notes that many stressful life events (eg loss of a partner) inevitably lead to a decline in social support, further complicating an examination of the independent role of social support in mediating between stress and cancer.

3.3.4 Coping with life events and social support summary

The evidence on coping with life events is scanty and inconsistent. It is unlikely that coping plays a significant role in determining breast cancer risk. This review examined the construct of social support only in the context of research on stress (or life events) or on personality characteristics and breast cancer risk. A significant relationship between social support and breast cancer risk was not found in the studies reviewed; however, the reviewers are not able to comment on the vast literature concerning social support, which was beyond the scope of the current review.

3.4 Long-term emotional and personality factors

Sixteen papers exploring the impact of long-term emotional and personality factors on the development of breast cancer, with adequate design and analysis characteristics, were identified (see Appendix 6). The majority of papers explored the impact of:

- an alexithymic, or repressive coping style;
- chronic anxiety/depression; and,
- various related personality features.
The following discussion is, therefore, organised under these headings.

There was high variability in the study design, the range of measurement tools used and the statistics reported. The reviewers concluded that a meta-analysis would not be possible.

The majority of papers (eight of sixteen) were conducted in UK or USA cities. Five were published in Europe (France, Italy, Germany, Holland), one in Israel, one in Greece and one in India. It may not always be appropriate to generalise these findings to the Australian setting.

3.5 Emotional repression / alexithymia / low type A behaviour

Emotional repression may represent a risk factor in cancer because the degree of somatic stress experienced may be abnormally augmented or prolonged by these typical responses to stress. Several studies have reported a link between a repressive coping style and increased physiological arousal (Anderson 1981).

Prospective studies

Two prospective case control studies have been reported in this area. Hahn and Petitti (1988) used data from the Walnut Creek contraceptive drug study (a prospective study begun in 1969), 8,932 women who completed the Minnesota multiphasic personality inventory (MMPI) (90% response rate) were followed up through computer-stored hospital discharge records to ascertain the development of breast cancer. 117 breast cancer patients first diagnosed after entering the study and confirmed by biopsy were identified. Differences in group means on the MMPI scales for depression, repression/sensitisation and lying were analysed. No significant differences were found in univariate or multivariate analyses on the depression and repression/sensitisation subscales. While breast cancer patients had slightly elevated scores on the lie scale (p < 0.05) the authors suggest that this is unlikely to be of clinical significance, and should be interpreted with caution given the large sample size. The authors argue that significant results reported in limited prospective and case control studies may be due to the effects of cancer patients knowing or suspecting their diagnosis. However, it is also possible that the MMPI repression/sensitisation subscale was not detecting the same psychological characteristics as those reported in these latter studies.
Bleiker et al (1996) sent personality questionnaires, together with an invitation to a screening unit, to all women over the age of 43 in the Dutch city of Nijmegen (nearly 30,000 residents). 9,705, or 34% responded, including 131 women who were later diagnosed with breast cancer for the first time. Six age-matched controls per case were selected from amongst the women who did not develop breast cancer. The self-assessment questionnaire-Nijmegen (SAQ-N) was especially constructed for use in this study to assess traits (rather than states), and was composed of eleven well validated scales (such as the Spielberger trait anxiety scale). Cronbach’s alpha and test-retest reliability for the scales ranged from 0.67 to 0.92 (alpha) and 0.59 to 0.82 (reliability). Logistic regression, controlling for somatic factors such as family history, early menarche, late menopause, overweight and parity, was used to predict case versus control status. The expression or suppression of emotion was found not to be related to breast cancer risk; however, one psychological factor, anti-emotionality (an absence of emotional behaviour or a mistrust of one’s own feelings) was found to be weakly associated with breast cancer. While significantly contributing to the model, the OR for this variable was only 1.19 and the authors themselves noted that an OR of 1.2 is at the limits of reliability for an epidemiologic study. However, the same result was obtained in a second analysis using a different age-matched control group, and in a third analysis that excluded women who had a palpable tumour at diagnosis close to the time of questionnaire completion.

3.6 Psychiatric interviews measuring suppression of anger and other feelings

Limited prospective studies

Greer and his colleagues developed a structured interview schedule for measuring expression of anger and other feelings during the 1970s. Greer and Morris acknowledged the limitations of a subjective interview rating, but believed that important insights could be gained through a properly conducted clinical interview. They suggested the development of more rigorous, explicit criteria for ratings and that interviews be taped. This interview schedule was used in a single study, that was re-analysed and reported in two other papers. In a later study, the improvements described above were incorporated into the procedure.

Greer and Morris (1975, 1978) approached one hundred and sixty women attending for breast biopsy and obtained an excellent response rate (96%). The women were interviewed, and completed several personality questionnaires. Sixty-nine women were later diagnosed
with breast cancer and ninety-one women were found to have benign
disease. In an age adjusted nonparametric analysis, women with breast
cancer who were younger than 50, were more likely to be extreme
suppressors or extreme expressers of emotion (especially anger)
(\(p < 0.001\)) than those with benign disease. Subsequent work focused
on repression only even though the original observations were related
to broad notions of a lack of psychological wellness.

Bageley (1979) re-analysed a subsample of the above series (one
hundred and thirteen women), forty-five of whom were later
diagnosed with breast cancer and sixty-eight with benign disease. In
an analysis controlling for menopausal status and age, women with
cancer were more likely to repress feelings (\(p < 0.01\)). Repression was
also associated with reduced hostility, as reported on the Caine and
Foulds (1967) hostility scale, suggesting some concurrent validity.

Morris, Greer, Pettingale and Watson (1981) interviewed seventy
patients attending for breast biopsy (93% response rate). The
interviews were conducted by one interviewer, and were audiotaped
and transcribed. Eight tapes used in the standardisation procedure and
twelve tapes with technical difficulties were excluded from the
analysis, leaving fifty patients, seventeen with breast cancer and
thirty-three with benign disease. The transcripts were analysed to
produce a standardised ordinal rating scale with six points ranging
from extreme suppression to extreme expression of anger. Interviews
were then rated independently by three blind raters. Inter-rater
reliability for the anger ratings was very high (Kendall’s coefficient of
concordance 0.91, \(p < 0.001\)). Mean expression of anger ratings for
cancer patients were significantly lower than for those women with
benign disease (\(p < 0.01\)). When the analysis was stratified by age
group, only the 40–49 age group approached significance (\(p = 0.08\))
for this variable. Numbers were so small in the remaining cells,
however, that interpretation of the data was difficult.

3.6.1 The Courtauld emotional control scale

Two limited prospective studies used the Courtauld emotional control
scale (CECS). This is a twenty-one item scale developed by Watson
and Greer (1983) to measure more objectively the extent to which
individuals report controlling their reactions when each of anger,

anxiety and depression is experienced. The measure has good internal
reliability and test-retest reliability and initial evaluations suggest
good concurrent and face validity. The CECS has a moderate inverse
correlation with the anger subscale of the Spielberger et al (1985)
state-trait personality scale (STPS) and a moderate inverse correlation
with the Bortner type A behaviour scale (Bortner, Rosenman 1967).
Thus, people high on control as measured by the CECS, report less anger and exhibit fewer type A behaviours.

Grassi and Cappellari (1988) interviewed seventy-six women admitted for breast lump biopsy (100% response rate). Patients completed the CECS within two days of hospitalisation and the symptom questionnaire (SQ) (Kellner 1976), a scale measuring anxiety, depression, hostility and somatic symptoms, on the evening before breast lump biopsy. Subsequently, forty-one subjects were diagnosed with breast cancer and thirty-five with benign breast disease. The groups were comparable on all demographic characteristics except for age: cancer patients were significantly older. Clinical symptoms that were considered highly suggestive of cancer pre-operatively (eg nipple or skin retraction, nipple discharge) were present in a comparable percentage of the two groups. Thus, the results were not likely to reflect differential expectations of having cancer. Cancer patients reported significantly greater self-control on all three subscales of the CECS (p < 0.05) and significantly less hostility prior to biopsy (p < 0.05). However, the analysis did not control for age or other known predictors of breast cancer.

These results support the hypotheses that the psychological profiles of breast cancer patients are characterised by inhibition of emotions and the tendency to present as compliant and eager to please under stressful and threatening circumstances. However, the results may have been confounded by age or other breast cancer predictors.

Fox (1994) invited 2,000 women awaiting mammograms to participate in a study exploring psychosocial predictors of breast cancer. Only 41% of women completed the questionnaires (measures of stress and social support and the CECS), which may have introduced significant selection bias into the study. Both patients and interviewers had no certain knowledge of the diagnosis. Subsequently, twenty women were diagnosed with breast cancer, 488 with benign breast disease and 266 with normal breast tissue. Fifty-two women had had a previous breast cancer and were not considered in this report. Analysis of the group differences adjusted for age, BMI, family history, menopausal status, childbirth status and total menses, showed that women with breast cancer reported significantly greater control over emotions (p < 0.0001) than healthy controls or women with benign disease. However, results need to be viewed in the light of possible selection bias.

3.6.2 The Toronto alexithymia scale

The Toronto alexithymia scale (TAS) (Taylor et al 1985) consists of twenty-six items measuring the ability to identify and communicate feelings, amount of daydreaming and preference for focusing on
external versus internal events. Thus, it focuses more on self-awareness than repression of feelings, although there appears to be a link between these concepts. The TAS correlates positively with the anger-in and negatively with the anger-out subscales of the anger expression scale (AES) (Taylor et al 1985). Test-retest reliability was not reported. The scale has adequate internal reliability (Cronbach’s alpha = 0.75).

Anagnostopoulous, Vaslamatzis, Markidis et al (1993) used the TAS and the personality deviance scale (PDS) (Bedford, Foulds 1978), a measure of hostility, in a study of psychosocial predictors of breast cancer. They interviewed 448 women (response rate = 92%) attending breast screening centres in Athens, prior to diagnosis. Due to the length of the assessment battery, the TAS was given only to a random subset of one hundred women. In the overall sample there were 180 cases of breast cancer, 112 women with benign disease and 156 women with healthy breast tissue. Unfortunately, we are not told the distribution of cases/non-cases in the one hundred women who completed the TAS. In a multivariate analysis adjusting for most potential confounders, only one psychological variable was significant: low denominatory attitudes. Breast cancer patients were less likely to think badly of people. However, breast cancer patients did not differ significantly from controls in their expression of hostile or other feelings. The authors concluded that the results supported the idea of a type C personality predisposition to cancer, but not an alexithymic one.

### 3.6.3 The questionnaire of repression

This instrument is based on the manifest anxiety scale (MAS) (Taylor 1933) and the Marlow-Crowne (Crowne & Marlowe 1964) social desirability scale (SDS). Subjects are divided into repressors (low on anxiety and high on defensiveness), and non-repressors (all other score combinations). This measure has been shown to be associated with low levels of reported negative emotions and tendencies for blocking, avoidance and denial. It differs from the above measures in focusing on repression of anxiety, rather than on anger and other feelings.

Kreitler, Chiatchik and Kreitler (1993) gave the repression questionnaire to seventy-two women awaiting a biopsy (response rate 79%), thirty-two of whom were diagnosed post-operatively with breast cancer and forty with no cancer. A further control group of twenty-six women awaiting surgery for a variety of surgical interventions unrelated to the diagnosis or treatment of malignancy was included. The women completed the questionnaire two to three days prior to surgery and again one to two days after surgery. No significant differences were found between the groups prior to
psychosocial factors and the risk of developing breast cancer

surgery; however, after surgery the number of repressors in the malignancy group increased significantly more than in other groups. Thus, the authors suggest that repression may represent a response to, and not a cause of, cancer. However, this small study must have had very limited power to detect differences between groups.

3.6.4 Psychosocial questionnaire of Bahnson and Bahnson

This questionnaire uses a number of scales, several of which are relevant to the repression of emotion hypotheses (Bahnson & Bahnson 1979). They include measures of suppression of anger, external control, pattern A behaviour, and social desirability. Psychometric data on the scales were not presented.

Scherf, Cramer and Blohmke (1981) asked 3,036 women attending a gynaecologic clinic to complete the psychosocial questionnaire before receiving a diagnosis. 87% of the sample completed the questionnaire. One hundred age-matched cases and healthy controls, and sixty-nine age-matched cases and women with benign disease, were identified. Cancer patients showed significantly more suppression of anger in the 20-50 age group (if anything, the trend was reversed in the 50-70 age group). This finding supports those of Greer and Morris (1975, 1978) who found a distinction in anger expression only in younger women with cancer. Overall, the authors reported that the psychosocial questionnaire discriminated poorly between groups.

3.6.5 Bortner type A scale

The Bortner type A scale consists of fourteen bipolar adjectives (eg never rushed-always feel rushed), rated on an eleven-point scale centred at zero and ascending to five in both directions (Bortner & Rosenman 1967). One item directly addresses emotional repression. It is hypothesized that cancer patients will have low scores on the type A scale. Thus it represents an indirect measure of repression.

Faragher and Cooper (1990) administered the Bortner type A scale, amongst others, to 1,596 women attending one of two clinics for specialist evaluation, after complaining to their general practitioners of breast lumpiness or tenderness (response rate not reported). An additional sample was collected from 567 women attending the BUPA centre in London for a general medical check-up. Since more women in the former group were likely to have cancer, and to be more anxious during testing, this sampling strategy would bias the results towards finding a significant difference between the groups. Unfortunately, the authors do not separate out the BUPA group in the analysis, so that it is difficult to interpret the data. On the assumption, however, that most
women in the BUPA group had normal breast tissue, some conclusions can be drawn by excluding the normal controls, and comparing cases with patients with benign breast disease. Cooper et al (1986, 1989, 1992, 1993) reported results from this data series in a number of articles, some of which separated out the normal controls and some of which did not. The same methodological problem is present in other studies in which Cooper was a co-author (e.g. Cheang et al, 1985).

Of the 1,596 women in the study group, 171 were later diagnosed with cancer, 155 with cysts, 1,110 with benign breast disease and 727 with normal breast tissue (Faragher et al, 1990). Faragher and Cooper conducted a factor analysis of the Bortner type A scale, yielding four factors: time consciousness, personal drive, satisfaction/contentedness and interpersonal relationships. In an age-adjusted analysis, groups were significantly different on the total score and on all four factors; however, cancer and benign groups differed significantly only on the fourth factor, indicating that cancer patients had a tendency to suppress feelings, and had few interests that involved personal relationships outside of their home and work environments. However, the authors noted that although this difference was statistically significant, the mean difference was only 1.2 points, and probably of little clinical importance.

Cheang and Cooper (1985) gave the Bortner type A scale to 121 patients admitted for a breast biopsy (response rate not reported) and to forty-two healthy patients randomly selected from a well women clinic. While the overall scores on the Bortner scale were not significantly different, seven individual items, including the one addressing emotional repression, distinguished the cancer group from one of the control groups (not stated). However, analyses were not adjusted for age or other potential confounders, and because at least one of the control groups contained the BUPA group (women attending a well women’s clinic), no conclusions could be drawn from this result.

Edwards, Cooper, Pearl et al (1990) gave the Bortner type A scale, amongst others, to 1,052 women (90% response rate) attending for breast examination and mammography. Unfortunately, this sample combined women attending for a routine examination and women referred by their physicians after a lump was detected. Since more women in the latter group were likely to have cancer, and to be more anxious during testing, this sampling strategy would bias the results towards finding a significant difference between groups. However, neither the total score nor individual items on this scale discriminated between groups. The authors concluded that the type A scale may not be appropriate for this setting.
Case control studies

One hospital based case control study has been reported in this area. Watson, Pettingale and Greer (1984) compared psychological and autonomic responses in thirty breast cancer patients diagnosed on average twenty-seven months earlier, with twenty-seven normal controls who had recently attended a breast screening clinic, matched for social class and marital status. Response rates were not reported. All subjects were exposed to three videotapes, two stressful and one neutral, presented in random order. Patients completed three personality inventories before watching the videos: the CECS measure of emotional repression, the state-trait personality inventory (STPI) (measuring trait anger and anxiety) and the Marlowe-Crowne scale. Two measures of autonomic arousal were taken before and during the procedure: heart rate and skin resistance responses. Women were also asked to indicate how angry, anxious or sad they felt at different points throughout the procedure, on linear analogue scales. After watching each videotape, the women were asked to rate how disturbing they found the video and whether they had tried to hide their feelings whilst watching.

Breast cancer patients were significantly more likely to report a tendency to repress anger ($p < 0.05$) and to respond to stress with a repressive coping style ($p < 0.001$). The breast cancer group appeared to experience more anxiety and disturbance but were more likely to inhibit their reactions in response to the stress tapes. There were no differences between the groups in autonomic arousal, but within the breast cancer group, increased electrodermal activity was associated with a tendency to respond to stress using a repressive coping style. While the authors acknowledged that these differences may have been a result of the cancer, they also suggested that since most patients were assessed more than two years after diagnosis, it was unlikely that their responses were significantly influenced by stress related to a cancer diagnosis.

3.6.6 Emotional repression summary

In summary, the evidence for the impact of emotional repression, particularly of anger, is uncertain, but intriguing. The results are summarised in Table 2. Five out of thirteen studies reported a negative result; however, the majority of these studies were not directly measuring repression of anger, but rather related issues such as self-awareness and the absence of a type A personality.

However, only four of the studies reporting a positive result were adjusted for age. In one of these four studies, the response rate was very poor, perhaps introducing significant sample bias. In another
two, anger repression was associated with breast cancer only in patients younger than 50, however, as there are important differences between pre- and post-menopausal onset disease, this result does not invalidate the study. Clearly there is a need for confirmatory evidence, exploring subsets of cancer patients with measures specifically targeting emotional repression.

For the field to be advanced, there needs to be a standardisation of measures so that different studies can be more readily compared. Scales more directly measuring repression of emotions, particularly anger (such as the CECS) appear to be most sensitive. Measures of general alexithymia appear to be less sensitive. The relationship between breast cancer and type A personality has not been supported and should be abandoned. It is also essential that future studies adjust for age and other confounders.

3.7 Chronic anxiety and depression

Several authors have suggested that chronic elevated levels of negative emotions may contribute to the development of cancer. This may be because a negative response style enhances the stressful impact of life events, or because negative emotions are a proxy measure of stress. Alternatively, anxiety and depression may have an independent effect on the development of cancer. Few studies measure negative emotions and life events together, so it is difficult to tease out these interrelationships.

Prospective studies

Using data from the Walnut Creek contraceptive drug study (described in Section 3.4.1), Hahn and Petitti (1988) found no significant differences between breast cancer patients and healthy women using the MMPI depression subscale (Sobel & Worden 1979).

Limited prospective studies

Non-significant differences between patients and controls on anxiety and depression have been reported by:

- Greer and Morris (1975, 1978) with the Hamilton (1967) rating scale of depression;
- Schonfield (1975) using the MMPI subscale of severe depressive symptoms (Sobel & Worden 1979);
- Grassi and Cappellari (1988) using the symptom questionnaire for anxiety and depression;
- Jasim, Le, Marty et al (1990) using a psychosomatic interview for both anxiety and depression; and,

Scherg, Cramer and Blohmke (1981) using the psychosocial scale (described in Sections 3.2.5 and 3.4.1) found non-significant differences in anxiety, in the direction opposite to that hypothesised: benign patients had slightly higher anxiety scores than cancer patients. Similarly Morris, Greer, Pettingale and Watson (1981) found that benign patients scored significantly higher on trait anxiety, as measured on the state-trait anxiety inventory (STAI) inventory.

Only one study has reported positive findings. Schonfield (1975) using the Institute personality ability testing (IPAT) scale measuring covert and overt anxiety (Cattell & Steer 1963) found that cancer patients under 45 years of age had higher covert anxiety \( (p < 0.10) \) than age-matched benign patients. No significant differences were observed in overt anxiety. The authors suggested that younger patients may have picked up cues from their doctor that the diagnosis was likely to be cancer.

**Case control studies**

Only one case control study is reported in this area. Bleiker et al (1996) (described in Section 3.4.1) found that neither anxiety and depression nor their inverse optimism, were related to breast cancer risk.

### 3.7.1 Chronic anxiety and depression summary

The evidence for a link between breast cancer and chronic anxiety and depression is very poor. Of nine studies in this area, using a wide array of measures, only one reported a non-significant positive finding in women under 42 years of age. The authors suggested that these patients may have picked up cues from their doctor that the diagnosis was likely to be cancer. Given the established status of most of the scales used, it appears clear that there is no relationship between anxiety and depression and subsequent breast cancer. A summary of the results is presented in Table 2.

### 3.8 Other personality features

Investigations of general personality factors related to breast cancer have not produced promising results. All studies have one in this category used a limited prospective design. A number of studies (Bagoley, 1979; Chen, David, Nunnerley et al, 1995; Greer and Morris, 1975, 1978, and Priestman, Priestman and Bradshaw, 1985) reported non-significant results using the Eysenck personality
inventory, a questionnaire with excellent psychometric properties that assesses extroversion/introversion (Eysenck & Eysenck 1964).

Scherg, Cramer and Blohmke (1981) reported no differences between groups in social desirability, authoritarianism, dependence, external control, religiosity and commitment, although their questionnaire was not validated. Similarly, in a single study reanalysed and reported in several articles, Greer and Morris (1975, 1978) and Bageley (1979) found no difference between groups in hostility and general adjustment, based on a combination of psychiatric interview and questionnaires.

Only two studies reported significant findings. In a large case control study, Bleiker et al (1996) (described in Sections 3.4.1 and 3.4.3) observed a small increase in cancer risk (19%) in women who were less likely to trust their feelings or let their behaviour be influenced by emotions.

Jasim, Le, Marty et al (1990) studied seventy-seven women awaiting breast biopsy (a response rate of 50%). They were interviewed by a psychosomatician from the French Institute of Psychosomatic Medicine (IPSO). The authors reported no significant differences in demographic and disease variables between responders and non-responders, except that non-responders were more likely to have smaller and multifocal tumours. Responders and non-responders also comprised similar proportions of breast cancer patients, which means that the study results were unlikely to be biased, despite the high refusal rate. Of the responders, eighteen patients were found to have breast cancer and fifty-nine a benign breast disease.

Both patient and interviewer were blind to the diagnosis. The physicians concerned were instructed not to give the patient any information about the presumed nature of the tumour. The psychosomatic interview took approximately one hour and was based on the psychosomatic theory developed by Marty (1983). According to Marty’s theory, the capacity to allay serious psychological trauma in response to stress is determined by the individual’s fundamental mental structure which can be classified as either psychotic, poorly-organised neurotic or well-organised neurotic. These constructs were not clearly defined by the authors. After classifying the woman’s mental structure and noting recent symptomatology, the psychosomatician allocated her to a high- or low-risk breast cancer group. Unfortunately, the interviews were not taped and no data on inter- or intra-rater reliabilities were presented.

In a multivariate analysis adjusted for age at interview, family history, age at first delivery and parity, women with a poorly organised neurosis or psychosis had a relative risk (RR) of 17.8, \( p < 0.009 \), with
a 95% confidence interval of 1.2-infinity. More specifically, women with excessive self-esteem (RR = 10), unresolved recent grief (RR = 7.5) and a hysterical disposition (RR = 8.2) were more likely to develop breast cancer. The psychosomatician’s risk allocation was correct in seventeen of the nineteen cases and twenty-three of the fifty-eight non-cases (p < 0.02). The authors argue that in-depth interviews are better able to identify the essential elements of mental functioning than paper and pencil questionnaires.

These results are intriguing, but require replication in a larger study with better reporting of inter- and intra-reliability of ratings.

3.8.1 Other personality features summary

Only two of seven studies in this field reported significant findings. Extroversion/introversion, authoritarianism, dependence, external locus of control, religiosity, commitment and a tendency to behave in socially desirable ways were found to be unrelated to the development of breast cancer. Anti-emotionality (mistrust of feelings) was found to be associated with a very small increased risk of breast cancer in one study, but as the reviewers were able to obtain only a summary of this paper, they could not comment on the validity of these findings. It is interesting, however, that one of the few positive findings in this group of studies used a measure related to alexithymia. One study reported a significant relationship between impaired mental state (psychosis or neurosis) and the development of breast cancer. Specifically, women with excessive self-esteem, unresolved recent grief and a hysterical disposition were more likely to develop breast cancer. This result is hard to interpret within the context of other findings. A woman with an hysterical disposition and excessive self-esteem appears unlikely to be emotionally repressive. However, the ratings of mental state were based on subjective judgements with no inter- or intra-rater reliabilities reported. Replication of the study findings with improved validation of the ratings and a fuller description of the criteria used are required, before such a conclusion can be accepted.
### Table 2

**Summary of the link between long-term emotional and personality factors and the development of breast cancer**

<table>
<thead>
<tr>
<th>Study type/author</th>
<th>Quality score</th>
<th>Repression/alexithymia</th>
<th>Anxiety/depression</th>
<th>General personality factors</th>
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<tr>
<td><strong>Prospective studies</strong></td>
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<tr>
<td>Hahn &amp; Pettit (1988)</td>
<td>74</td>
<td>P &lt; 0.05</td>
<td>n.s.*</td>
<td>n.s.*</td>
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<td><strong>Limited prospective studies</strong></td>
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<tr>
<td>Grassi &amp; Cappellari (1988)</td>
<td>93</td>
<td>p &lt; 0.05</td>
<td>n.s.</td>
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<td>Kreitler, Chiatchik &amp; Kreitler (1993)</td>
<td>93</td>
<td>n.s.</td>
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<tr>
<td>Greer &amp; Morris (1975, 1978)</td>
<td>92.5</td>
<td>p &lt; 0.01*</td>
<td>n.s.*</td>
<td>introversion, hostility adjustment: n.s.*</td>
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<td>Bageley (1979)</td>
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<tr>
<td>Edwards, Cooper, Pearl et al (1990)</td>
<td>90</td>
<td>n.s.</td>
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<tr>
<td>Scherg, Cramer &amp; Blohmke (1981)</td>
<td>90</td>
<td>p &lt; 0.05</td>
<td>n.s.</td>
<td>social desirability, authoritariansim, dependence, external control, religiosity and commitment: n.s.*</td>
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<td>Schonfield (1975)</td>
<td>85</td>
<td></td>
<td>n.s.*</td>
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<td>Morris, Greer, Pettingale &amp; Watson (1981)</td>
<td>83</td>
<td>p &lt; 0.01</td>
<td>n.s.*</td>
<td>low derogatory attitudes, p &lt; 0.05* hostility, self-confidence, dependence, n.s.</td>
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<td>Anagnostopoulos, Vasilimitzis, Markidis et al (1993)</td>
<td>80</td>
<td>n.s.*</td>
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<tr>
<td>Faragher &amp; Cooper (1990)</td>
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<td>p &lt; 0.05</td>
<td></td>
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<tr>
<td>Fox (1994)</td>
<td>78</td>
<td>p &lt; 0.0001*</td>
<td></td>
<td>n.s.*</td>
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<td>Jasim, Le, Marty et al (1990)</td>
<td>71</td>
<td>n.s.</td>
<td></td>
<td>neurosis, p &lt; 0.01*</td>
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<td>Cheang &amp; Cooper (1985)</td>
<td>47</td>
<td>n.s.</td>
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<td><strong>Case control studies</strong></td>
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<td>Priestman, Priestman &amp; Bradshaw (1985)</td>
<td>83</td>
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<td>neurosis, introversion, n.s. *</td>
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<tr>
<td>Watson, Pettingale &amp; Greer (1984)</td>
<td>66</td>
<td>p &lt; 0.05</td>
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* age-adjusted
3.9 Conclusion

Evidence for a relationship between psychosocial factors and breast cancer is weak. Any links between psychosocial factors and breast cancer are likely to be small, related to a variable or variables not well operationalised in studies to date, or applicable to a limited subset of breast cancers. Perhaps the strongest predictors demonstrated are emotional repression, especially of anger, and the loss of a significant other. However, the majority of studies did not support even these associations. As few of the studies have been of very high quality, additional research using well validated tools that assess complexity as well as the number of life events appears warranted. Careful consideration must be given to the choice of comparison populations and adjustment for age as well as other known risk factors for breast cancer.
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