

**PSYCHOSOCIAL VARIABLES
IN THE DEVELOPMENT
OF BREAST CANCER**

**MELANIE ANNE PRICE
BSc (HONS)**

**A thesis submitted in fulfillment
of the requirements for the degree of**

DOCTOR OF PHILOSOPHY

Department of Psychological Medicine

Faculty of Medicine

University of Sydney

May 2002

Abstract

There is widespread community belief that stress or depression contributes to the development of cancer, although the empirical evidence is equivocal. The strongest psychosocial predictors for developing breast cancer are recent highly threatening life events and emotion suppression, particularly anger. Although the available evidence does not support a major role for psychosocial variables in the development of breast cancer, few studies have been of sufficient quality to state definitively that they do not.

This thesis examined a semi-prospective cohort of women recalled following routine breast screening on a range of psychosocial variables thought to be associated with the development of breast cancer. The aim was to tease apart the components of "stress" and to examine the interaction between these components in relation to the risk of developing breast cancer. The first part of this study examines the features of Temoshok's (1987) Cancer Prone Personality. Breast cancer subjects are compared with three control groups: women diagnosed with normal breast tissue, women diagnosed with benign or cystic breast tissue without requiring a biopsy, and a third group of women with benign breast tissue who require biopsy confirmation. No evidence is found to support a direct role for personality in the development of breast cancer.

The second part of this study examines life event stress and stress related variables in a subgroup of the sample, those women undergoing fine needle biopsy. The Hilakivi-Clarke et al. (1993) model of psychosocial variables in the development of breast cancer is used to examine the interactions between recent life event stress, and a number of specific vulnerability factors, coping style, emotional control and poor social support. Methodological features of this study include the use of an objective investigator-based instrument to assess the severity of recent life events (LEDS), a large community based sample of asymptomatic women and extensive control of somatic risk factor variable. The results of this study support the theory that life event stress alone is not important in the development of breast cancer, rather, it is the interaction between highly threatening life events and an absence of an intimate social support, which is an independent risk factor for breast cancer.

Presentation of Thesis

This thesis is presented as a series of published manuscripts. The first two chapters contain a review of the literature, introducing the research rationale, aims, hypotheses, methodology and approach to data analysis. Chapters Three, Four and Five contain the following manuscripts. The candidate is the principle author of each of these papers.

Chapter Three: "Predictors of breast cancer in women recalled following screening" published in the Australian and New Zealand Journal of Surgery in 1999, Volume 69, pages 639-646.

Chapter Four: "The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part 1-The Cancer Prone Personality" published in Cancer Volume 91(4), pages 679-685, 2001.

Chapter Five: "The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part 2 - Life Event Stressors, Social Support, Defense Style, and Emotional Control and Their Interactions" published in Cancer Volume 91(4), pages 686-697, 2001.

The final chapter provides a summary and conclusions of the research findings, limitations and suggestion for the direction of future research.

Preface

The study presented in this thesis represents research undertaken by the candidate in conjunction with other researchers in the Department of Psychological Medicine of the University of Sydney at Royal North Shore Hospital, Sydney, Australia, The Department of Surgery at Royal North Shore Hospital and Northern Sydney and Lower Central Coast BreastScreen, NSW, Australia. Ethics approval was granted by the University of Sydney and the Royal North Shore Hospital Medical Research Ethics Committee.

The candidate was involved in all aspects of the study, and was responsible for coordinating the study under the supervision of Professor Christopher Tennant, and associate supervision of Associate Professor Phyllis Butow, Associate Professor Ross Smith and Professor Stewart Dunn. This study was made possible by funding received from the National Health and Medical Research Council of Australia.

The original contributions of the candidate include:

Study Design: The candidate was responsible for the study sample including all women recalled following breast screening, rather than focusing only on women undergoing biopsy. The candidate was also responsible for the final selection of the specific psychosocial questionnaire measures and for compiling questions related to established risk factor variables, in conjunction with other researchers.

Data collection, entry and analyses: The candidate was responsible for all aspects of data collection, entry and analyses. The candidate conducted the majority of data collection and entry. The candidate was solely responsible for the hypotheses and models used within this thesis. All data presented in this thesis were analysed by the candidate under the guidance of Professor Christopher Tennant and Associate Professor Butow.

Manuscripts: The candidate was the principle author of the manuscripts presented in this thesis, responsible for the conceptualisation and the interpretation of the data, under the supervision of Professor Christopher Tennant and Associate Professor Phyllis Butow.

Acknowledgments

I am indebted to Professor Christopher Tennant for his supervision of this study and thesis. I would like to thank Professor Tennant for providing the opportunity to learn and participate in the field of life event stress research, and for his unfailing enthusiasm and encouragement. My thanks also to Ms Kathy Palmer for her early training in life event stress procedures, and to Dr Ethelle Bennett for her expertise, encouragement and unfailing advice regarding all aspects of life event stress research and analyses.

I would like to thank my associate supervisors Associate Professor Phyllis Butow, Associate Professor Ross Smith and Professor Stewart Dunn for their expertise, guidance and encouragement throughout the project.

I am most especially grateful to Associate Professor Phyllis Butow for her quiet confidence, advice, encouragement and support, particularly during the hard times, without which this thesis would have remained unfinished.

I would also like to thank my colleagues within the Department of Psychological Medicine - Dr Catherine McMahon for being a mentor and friend, Ms Susan Kennedy for her work on the project, for her friendship and support, and Ms Alison Cornish for her enthusiastic participation in the thankless task of data cleansing, for her optimism and thoughtfulness.

This research would not have been possible without the cooperation and support of all the staff at the assessment clinic of the Northern Sydney and Lower Central Coast BreastScreen, NSW, at Royal North Shore Hospital and to the women themselves.

And finally, I am grateful to my family and friends for their enduring support, patience and encouragement. I am most indebted to my partner Martin, who never doubted. To my sister Sandi and my best mate Cath, thank you for always being there.

Table of Contents

Abstract.....	ii
Presentation of Thesis	iii
Preface.....	iv
Acknowledgments	v
Table of Contents.....	vi
Appendices	x
Table of Tables	xi
Table of Figures.....	xii
List of Abbreviations	xiii
CHAPTER 1: INTRODUCTION	1
Established Risk Factors for Developing Breast Cancer.....	3
<i>Incidence</i>	3
<i>Sociodemographics</i>	3
<i>Genetic and Familial Breast Cancer</i>	3
<i>Breast Disease</i>	4
<i>Reproductive and Endogenous Hormonal Factors</i>	4
<i>Exogenous Hormonal Factors</i>	5
<i>Lifestyle Factors</i>	5
Psychosocial Risk Factors for Developing Breast Cancer	7
<i>Historical Anecdotes and Early Studies</i>	7
<i>Life Event Stress</i>	10
Empirical Findings	11
Non standardised interviews and scales	11
Checklist approach	13
Case-control studies.....	13
Limited prospective studies	15
Summary of Checklist Approach	16
Life Events and Difficulties Schedule (LEDS).....	16
Prospective Studies	18
Population Record Linkage Studies	19
Summary of life event stress.....	20
<i>Emotional Suppression</i>	23

Definitions	24
Empirical Evidence	25
Retrospective studies	25
Limited prospective studies	25
Prospective studies	27
Related Concepts	28
Alexithymia	28
Type A	29
Emotional suppression summary	29
<i>General Personality</i>	31
<i>Anxiety and Depression</i>	34
<i>Coping Styles</i>	37
<i>Social Support</i>	40
<i>Summary and Conclusions of Psychosocial Research</i>	41
Methodological Considerations	42
<i>Atheoretical Approach</i>	42
<i>Research Design</i>	43
<i>Control Group</i>	44
<i>Confounders</i>	44
<i>Time Frame</i>	45
<i>Measuring Stress</i>	45
Research Aims	46
Hypotheses	49
Presentation of Thesis	50
CHAPTER 2: METHOD	51
Sample and Study Design	51
Participants	51
Procedure	52
Measures	52
<i>Questionnaire Measures</i>	52
Part 1: Demographic and Somatic Risk Factors	52
Figure 2: Diagnostic procedures, diagnostic categories, study groups and components	53
Part 2: Psychosocial Questionnaires	54

Defense Style	55
Locus of Control of Behaviour.....	56
Self-Esteem	56
Emotional Expression and Control.....	57
Trait Anxiety	58
State Anxiety and Depression	58
<i>Interview Measures</i>	59
Life Events and Difficulties Schedule	59
Interview Schedule for Social Interaction	62
<i>Diagnosis of Breast Disease</i>	63
<i>The Sample</i>	63
<i>Non-Participation Bias</i>	64
<i>Study Groups</i>	65
<i>Study Components</i>	65
<i>Approach to Data Analysis</i>	65

**CHAPTER 3: ESTABLISHED RISK FACTORS FOR BREAST
CANCER.....72**

Summary	73
Introduction	73
Methods.....	74
Results.....	75
Discussion	83
Summary	87
References	87

CHAPTER 4: CANCER PRONE PERSONALITY 93

Abstract	94
Introduction	94
Methods.....	95
Results.....	97
Discussion	102
References	104

**CHAPTER 5: LIFE EVENTS, COPING, PERSONALITY, SOCIAL
SUPPORT AND THEIR INTERACTIONS..... 107**

Abstract..... 108

Introduction..... 108

Material and methods..... 110

Subjects..... 110

Procedure..... 111

Measures..... 111

Diagnosis of Cancer..... 113

Statistics..... 113

Results..... 114

Sample Characteristics..... 114

Acute Stressors..... 117

Chronic Stressors..... 118

Cumulative Stressors..... 118

Vulnerability Factors..... 119

Interactions..... 121

Potential Confounders..... 122

Discussion..... 125

References..... 128

CHAPTER 6: SUMMARY AND CONCLUSIONS..... 134

Established Risk Factors for Breast Cancer..... 134

Sociodemographic Variables..... 135

Family History of Breast Cancer..... 135

Benign Breast Disease..... 135

Reproductive factors..... 135

Exogenous Hormonal Factors..... 136

Lifestyle Factors..... 136

Summary..... 136

Psychosocial Risk Factors..... 137

The Cancer Prone Personality..... 137

Life Event Stress..... 139

Life Event Stress and Vulnerability Factor Interactions..... 140

Summary..... 142

<i>Strengths</i>	143
<i>Limitations</i>	144
<i>Future Direction</i>	145
REFERENCES	146

Appendices

Appendix I: Research Information Letter	A-1
Appendix II: Consent Form.....	A-3
Appendix III: Demographic and Somatic Risk Factor Questionnaire	A-4
Appendix IV: Defense Style Questionnaire	A-7
Appendix V: Locus of Control of Behaviour	A-10
Appendix VI: Self Esteem.....	A-11
Appendix VII: Emotional Expression and Control.....	A-12
Appendix VIII: Trait Anxiety.....	A-13
Appendix IX: Hospital Anxiety and Depression	A-14
Appendix X: Life Events and Difficulties Schedule.....	A-16
Appendix XI: Examples of Life Events	A-21
Appendix XII: Interview Schedule for Social Interaction.....	A-22
Appendix XIII: Predictors of breast cancer in women recalled following screening	A-23
Appendix XIV: The role of psychosocial factors in the development of breast cancer:	
Part 1 – The cancer prone personality.....	A-31
Appendix XV: The role of psychosocial factors in the development of breast cancer:	
Part 2 – Life events, coping, personality, social support and their interactions.....	A-38
Appendix XVI: Epidemiological evidence for a relationship between life events, coping style, and personality factors in the development of breast cancer.....	A-50

Table of Tables

Table 1: Studies examining life event stress and breast cancer development	21
Table 2: Studies examining emotional suppression and breast cancer development.....	30
Table 3: Studies examining general personality and breast cancer development.....	33
Table 4: Studies examining depression or anxiety and breast cancer development	36
Table 5: Studies examining coping styles and breast cancer development	39
Table 6: Summary of psychosocial questionnaires	54
Table 7: Comparison of assessment clinics attendees and study participants	64
Table 8: Coefficients for planned contrasts between groups.....	66
Table 9: Distribution of demographic variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)	76
Table 10: Distribution of family history of breast cancer and reproductive variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)	78
Table 11: Distribution of exogenous hormonal variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI).....	81
Table 12: Distribution of alcohol and cigarette consumption, body mass index and body mass index by menopausal status for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)	82
Table 13: Demographic and somatic risk variable for the breast cancer group and non cancer control groups	99
Table 14: Mean scores (SD) and univariate F-tests for group differences on psychological variables between breast cancer and non cancer control groups	101
Table 15: Demographic and risk factor variables for breast cancer.....	115
Table 16: Number of subjects reporting at least one acute stressor for each severity rating of long term threat in the two year period prior to interview.....	117
Table 17: Number of subjects reporting at least one chronic stressor for each severity rating (long term threat) in the two year period prior to interview	118
Table 18: Weighted scores for acute and chronic stressors in the two year period prior to biopsy.....	119
Table 19: Descriptives for “vulnerability factors”, Wald statistic, Odds Ratios and corresponding 95 % Confidence Interval	120
Table 20: Wald χ^2 statistic, Odds Ratios and corresponding 95 percent confidence	

intervals for interaction terms between vulnerability and major stressor
variables predicting breast cancer diagnosis..... 121

**Table 21: Final Multiple Logistic Regression Model for Predictors of Breast
Cancer 124**

Table of Figures

Figure 1: Hilakivi-Clarke et al. (1993) model of psychosocial factors in the
development of breast cancer 47

Figure 2: Diagnostic procedures, diagnostic categories, study groups and
components 53

List of Abbreviations

BMI	Body Mass Index
CECS	Courtauld Emotional Control Scale
CI	Confidence Interval
EPI	Eysenck Personality Inventory
EPQ	Eysenck Personality Questionnaire
GHQ	General Health Questionnaire
HAD	Hospital Anxiety and Depression scale
HDRS	Hamilton Depression Rating Scale
LEDS	Life Events and Difficulties Schedule
LEI	Life Event Inventory
MMPI	Minnesota Multiphasic Personality Inventory
ns	not significant
OR	Odds Ratio
RR	Relative Risk
SAQ-N	Self Assessment Questionnaire-Nijmegen
SRRS	Social Readjustment Rating Scale

CHAPTER 1: INTRODUCTION

The notion that cancer might be related to stress or emotional factors can be traced back to around 200AD when Galen noted that melancholy women were much more susceptible to cancer than other females (Rosch, 1993). In the first half of this century the search focused on external explanations for illness, influenced by Descartes, who viewed the mind as a distinctly separate and unrelated entity from the mechanistic body. A renewed interest in the mind-body relationship over the past three decades parallels our increasing understanding of the complex interrelationships between the immunological, endocrine and nervous systems.

There is mounting evidence that stress can disturb many areas of the immune system and that impaired immune system function predisposes to malignant growth (Rabin, Cohen, Ganguli, Lysle, & Cunnick, 1989; Morley, Benton, & Solomon, 1991; Olf, 1999). There is also evidence of considerable individual differences in the response of the immune system to stress and these differences appear to be determined by the way individual responds to stress and other personal resources (Ursin, 1993). However, it is unclear whether psychosocial factors impact directly on endocrine, immune and nervous systems or indirectly by affecting behaviours such as diet, exercise, sleep etc which themselves have links to endocrine and immune functioning (Baltrusch, 1991; Hall, 1998; Baum, 1999).

There have been many articles published regarding psychosocial factors and cancer, some focusing on life event stress, others on the cancer prone personality traits, some covering psychosocial factors in disease onset, and some on disease outcome, while others are more theoretical in nature (Grossarth-Maticek, Kanazir, Schmidt, & Vetter, 1982; Greer & Watson, 1985; Temoshok, 1987; Baltrusch, 1988; Gross, 1989; Baltrusch, 1991; Eysenck, 1991; Levenson, 1991; Bryla, 1996; McGee, Williams, & Elwood, 1996; Burke, 1997). However, there has been little integration of these disparate areas, with comparisons made between multiple cancer sites and discussing both factors affecting onset and progression of the disease. While possible, it seems unlikely that any single psychosocial factor, or set of factors, will be related in the same fashion to the onset of all cancers or that any set of psychosocial factors will be of similar importance in different stages of the disease (McGee et al., 1996).

The focus of this thesis is the role of psychosocial variables in the development of breast cancer. Breast cancer is a biologically diverse, hormonally sensitive disease and since "stress" is involved in activation of the endocrine system, as well as the immune system, it seems likely that psychosocial factors may potentially play a greater role in cancer of the breast than at other sites.

Greer and Watson (1985) describe a Type C behaviour pattern, incorporating the suppression of emotional responses, particularly when angry, a defensive response to stress, being compliant and unassertive. In situations of stress, this Type C behaviour pattern breaks down, increasing rather than reducing the threat associated with life event stress. Similarly, Temoshok (1987) describes a Cancer Prone Personality that predisposes an individual to developing cancer. The features of this personality are a repressive style of coping, difficulty in expressing emotions and a tendency towards helplessness and hopelessness. Both Greer and Watson (1985) and Temoshok (1987) concur that these traits attributed to the Type C personality or coping style are stress related and that the core feature, the control or suppression of negative emotions, has biological consequences.

Hilakivi-Clarke, Rowland, Clarke, & Lippman (1993) have developed a model in which the interaction between life event stress, personality and social support alters an individual's ability to cope with stress. An individual's capacity to contend with stress, moderates neuroendocrine and immune functioning, that in turn mediates breast cancer risk. In this model, the presence of stress alone not important, rather it is the significance of life event stress to an individual, coupled with an individual's ability to cope with the stressor. According to this model, an individual's personality characteristics and social support mediate an individual's ability to cope.

Together, these models provide an avenue for explaining clinical and epidemiological observations in this area, as well as the anecdotal reports of women who believe that "stress" or "depression" was a factor in the development of their cancer (Baghurst, Baghurst, & Record, 1992; Brinton, Malone, Liff, & Schoenberg, 1994). To begin this review, a brief overview of the disease and established risk factors is presented, followed by a review of the evidence for psychosocial factors in the development of breast cancer. The focus is given to the psychosocial factors thought to be related to the development of breast cancer; namely life event stress, social support, personality, coping style and affect. These areas are clearly interrelated and although they are at times measured together, rarely are their interactive effects examined. Each domain is considered separately and where possible their interrelationships are discussed.

Established Risk Factors for Developing Breast Cancer

Incidence

Breast cancer is the most common cancer in women in developed countries with an estimated 790,000 cases worldwide in 1990 and approximately one million new cases currently diagnosed each year (Forbes, 1997). The incidence of breast cancer varies substantially between countries and is more prevalent in affluent countries (Kelsey & Berkowitz, 1988). The lifetime risk of breast cancer in Australian women is 1 in 12, similar to other developed countries (Kricker & Jelfs, 1996; Taylor & Boyages, 2000; Taylor & Boyages, 2001).

Sociodemographics

There are a number of well established and putative risk factors for breast cancer. The biggest risk factors for developing breast cancer are being female and increasing age (Vogel, 1996). Breast cancer in males is relatively rare and the incidence of breast cancer is approximately one hundred times higher in females (Kelsey, 1993). The rate of breast cancer increases strongly up to the age of menopause when the rates continue to rise with age but more slowly (Kelsey, 1993; Kricker & Jelfs, 1996). Unlike most illnesses, breast cancer is associated with higher socioeconomic status, often reflected by level of education (Heck & Pamuk, 1997; Tavani, Braga, La Vecchia, Negri, Russo, & Francheschi, 1997). Education itself, however, is unlikely to increase breast cancer risk, but may be reflecting greater exposure to breast cancer risk factors (Heck & Pamuk, 1997).

Genetic and Familial Breast Cancer

Inherited genetic breast cancers account for only a small percentage cases and these cancers most often associated with an early age of onset (Henderson, 1993; Slattery & Kerber, 1993; Bondy, Lustbader, Halabi, Ross, & Vogel, 1994). A family history of breast cancer is an independent risk factor for breast cancer, although for most the increase in risk is small (Henderson, 1993; Anton-Culver, Kurosaki, Taylor, Gildea, Brunner, & Bringman, 1996). A two to three fold increase in risk is associated with having a first degree relative with breast cancer (Henderson, 1993; Anton-Culver et al., 1996; Pharoah, Day, Duffy, Easton, & Ponder, 1997). The risk is slightly higher for women whose relative was diagnosed at a younger age or had bilateral disease (Slattery & Kerber, 1993; Pharoah et al., 1997). A positive family history of breast cancer, however, does not indicate the nature of the underlying risk factor, because genetic, environmental and lifestyle factors can cluster together in families (Becher & Chang-Claude, 1996).

Breast Disease

Biopsy confirmed benign breast disease has been associated with a modest increased risk of subsequent breast cancer (Kelsey, 1993). Recent evidence suggests that any increase in risk may be associated with specific types of benign disease, such as atypical hyperplasia, that may be a precursor for breast cancer (Kelsey & Berkowitz, 1988; Bodian, 1993; Colditz, 1993; Henderson, 1993).

Reproductive and Endogenous Hormonal Factors

A number of risk factors related to life time exposure to sex steroids are considered to play an etiological in breast cancer (Colditz, 1993; Hankinson, Colditz, Manson, Willett, Hunter, Stampfer, & Speizer, 1997). These include age of menarche (commencement of menstruation), age of first full term pregnancy, parity (number of full term pregnancies), length of lactation and age at menopause.

Early onset of menarche has long been associated with a higher risk of breast cancer (Kelsey, Gammon, & John, 1993; Vogel, 1996). Some evidence suggests age of menarche is a more important predictor of breast cancer in premenopausal women, while other evidence supports claims that it is a weak risk factor for all age groups (Harris, Lippman, Veronesi, & Willett, 1992; Talamini, Franceschi, La Vecchia, Negri, Borsa, Montella, et al., 1996). A difficulty in assessing the risk associated with age of menarche is inaccuracy of recall particularly in older women (Kelsey et al., 1993).

Breast changes associated with pregnancy are thought to protect breast tissue against carcinogens (Harris et al., 1992; Kelsey et al., 1993). The younger a woman's age at the birth of her first child, the lower her risk of breast cancer, with a first pregnancy before age twenty providing a significant reduction in risk (Kelsey et al., 1993; Talamini et al., 1996; Vogel, 1996). In contrast, a first child after age thirty significantly increases breast cancer risk to a level similar or higher than having no full term pregnancies, that is approximately two fold (Harris et al., 1992).

Independent of age at birth of first child, the number of full term pregnancies (parity) also affects breast cancer risk (Harris et al., 1992; Kelsey et al., 1993). Women without children (nulliparous) women have a 1.2-1.7 increase in risk of breast cancer compared with women with children. Risk decreases with an increase in number of children, the relative risk of breast cancer associated most prominently in women with three or more full term pregnancies (Kelsey et al., 1993).

While breast cancer is more common in postmenopausal women, later onset of menopause has been associated with an increased risk of breast cancer (Kelsey & Berkowitz, 1988; Pathak & Whittemore, 1992; Kelsey et al., 1993; Vogel, 1996). This risk has been attributed to prolonged exposure to hormones (Kelsey et al., 1993) and risk of breast cancer for menopause after age 55 years is twice that of women whose menopause occurs under 44 years (Henderson, 1993; Talamini et al., 1996; Tavani et al., 1997).

Exogenous Hormonal Factors

Most individual studies provide little evidence to support a significant change in risk of breast cancer with oral contraceptive use (Stanford, Brinton, & Hoover, 1989; Malone, Daling, & Weiss, 1993; Newcomb, Longnecker, Storer, Mittendorf, Baron, Clapp, Trentham-Dietz, & Willett, 1996; Hankinson et al., 1997). However, reanalysis of data from 54 epidemiological studies confirms a small but significant increase in breast cancer risk (Relative Risk (RR)=1.07) with ever using oral contraceptives (Collaborative Group on Hormonal Factors in Breast Cancer, 1996).

More controversial are claims of an increased risk of breast cancer associated with the use of hormone replacement therapy (HRT). Recent reanalysis of data from 51 epidemiological studies confirmed a relative risk of breast cancer of 1.14 for ever use, with a modest but significant trend of increasing risk with each year of use (Collaborative Group on Hormonal Factors in Breast Cancer, 1997). The relative risk of breast cancer associated with use for more than four years was 1.35, however the associated increase in risk declines by five years after stopping.

Lifestyle Factors

The relationship between obesity and breast cancer varies according with menopausal status (Deslypere, 1995). There is a modest increase in risk of breast cancer (RR=1.2-1.5) with increased body weight, particularly in postmenopausal women, (Taioli, Barone, & Wynder, 1995; Ballard-Barbash & Swanson, 1996; Hunter, Spiegelman, van den Brandt, Folsom, Goldbohm, Graham, et al., 1997). Conversely, heavier premenopausal women are significantly less likely to develop breast cancer (RR=0.4-0.6) (Taioli et al., 1995; Ballard-Barbash & Swanson, 1996). The increase in risk of breast cancer in obese postmenopausal women has been attributed to the hormone estradiol stored in adipose tissue entering the circulation (Potischman, Swanson, Siiteri, & Hoover, 1996).

Epidemiological evidence also supports a modest dose response association between alcohol consumption and breast cancer, detected with consumption of as little as one drink per day (Katsouyanni, Trichopoulou, Stuver, Vassilaros, Papadiamantis, Bournas, et al., 1994; Longnecker, Paganini-Hill, & Ross, 1995; Levi, Pasche, Lucchini, & La Vecchia, 1996). The relative risks associated with one, two or three drinks per day are 1.1, 1.2 and 1.4 respectively (Longnecker, 1994). These results have been replicated across countries with varied social customs related to alcohol intake including the Netherlands (van den Brandt, Goldbohm, van' t Veer, 1995), Switzerland (Levi et al., 1996), Spain (Martin-Moreno, Boyle, Gorgojo, Willett, Gonzalez, Villar, et al., 1993) and North America (Gapstur, Potter, Sellers, & Folsom, 1992). The mechanism by which alcohol consumption might influence breast cancer risk is unclear, although it is possibly due to the effect of hormone level.

Consensus on the relative importance of individual risk factors, the magnitude of each, and their relevance to different age groups is rare. Opinion also varies as to how well established risk factors explain the incidence of breast cancer. Madigan, Ziegler, Benichou, Byrne, and Hoover (1995) estimate that forty one percent of US breast cancer cases can be explained by later first birth, nulliparity, family history and higher socioeconomic status. Tavani et al. (1997) estimate that higher education, older age at first birth, nulliparity, older age at menopause, hormone replacement therapy and family history can account for 56 percent of cases in Italy. However, the Netherlands Cancer Registry and the American Cancer Society claim that recognised risk factors can account for as little as 25 percent of breast cancer cases (Seidman, Stellman, & Mushinski, 1982; Kelsey & Berkowitz, 1988; Bleiker, van der Ploeg, Hendriks, & Ader, 1996).

It is therefore possible that psychosocial factors may contribute to the risk of developing breast cancer. While psychological variables need not be causal agents in tumour development, nor even necessary or sufficient for promoting tumour growth, Greer and Watson (1985) suggest that in some individuals psychological factors contribute to the promotions of certain tumours through their interactions with biological homeostatic mechanisms.

Psychosocial Risk Factors for Developing Breast Cancer

The empirical evidence relating to the role of psychosocial variables in the development of breast cancer is reviewed and discussed in this section. While various psychosocial factors purported to play a role in the development of breast cancer are related, often studies have focused on a particular domain. Differences in methodology and measures employed across studies precludes the presentation of meta-analysis. Instead, the evidence is considered under the headings of life event stress, emotion suppression, general personality, anxiety and depression, coping style and social support; within each section the studies are organised according to the strength of the study design, from the methodologically weakest to the strongest. Where possible, the interrelationships between these domains are discussed. However, to begin, a brief historical overview sets the scene for the growth of empirical research relating to psychosocial factors in the development of breast cancer.

Historical Anecdotes and Early Studies

Throughout history observations regarding the nature of a person who develops cancer, while varying in time and location, have remarkably consistent themes. Two themes dominate, loss and emotional repression. In 1701 Gendron, a Physician, noted women with depression and high anxiety were more prone to cancer (Bahnsen, 1980). Guy (1759), a Surgeon, observed a common pattern of malignancies in women with “hysteric and nervous complaints”, those who were “dull, phlegmatic and melancholic”, as well as those who had experienced “such Disasters in Life, as occasion much trouble and Grief” (in Kowal, 1955). Walsh, a Professor of Pathological Anatomy, in his 1846 treatise pronounced “... that it would be vain to deny that facts of a very convincing character, in respect of the agency of the mind in the production of this disease (cancer), are frequently observed”. He concluded that “mental misery, sudden reversal of fortunes and habitual gloominess” were common causes of carcinoma (in Kowal, 1955).

In 1854 Amussat asserted that “The influence of grief appears to me to be in a general way, the most common cause of cancer...” (in Kowal, 1955). Sir James Paget, described as an outstanding medical mind of the 19th century, noted “...deep anxiety, deferred hope, and disappointment, are quickly followed by the growth or increase of cancer, that we can hardly doubt that mental depression is a weighty addition to the other influences that favour the development of the cancerous constitution” (Kowal, 1955). Clinical case studies are still being offered in support of dramatic loss, grief and depression precipitating the onset of breast cancer (Biondi, 1996).

The first systematic examination of stress and cancer development was reported in 1883. In a series of 250 consecutive cancer patients, Snow reported 156 (62.4%) had experienced "immediate antecedent troubles", usually very poignant in nature such as the loss of a near relative (LeShan, 1959). Evans (1926) employed Jungian psychotherapy to examine the emotional history of one hundred patients who developed cancer, concluding that the typical cancer patient suffered the loss of an important emotional relationship prior to onset and was unable to find an effective outlet for the resultant psychic energy (LeShan, 1959). Foque (1931) described the history of his cancer patients as including "great crises, grave depressive afflictions, profound mourning, and all the sad emotions which have prolonged repercussions ... you can see in the patients prolonged and silent sorrow without the release of sobs and tears" (in LeShan, 1959).

Bacon, Renneker and Cutler (1952) formulated a psychosomatic profile of women with cancer of the breast reporting several behavioural characteristics common to these patients. These included a masochistic character, inhibited sexuality and motherhood, an inability to deal appropriately with anger or hostility, and an unresolved conflict with their mother.

With the employment of standardised instrumentation and the inclusion of control groups, LeShan and Worthington (1956) advanced research in this field. The Worthington Personal History Interview was employed to study 250 cancer patients and 150 age-equivalent healthy controls. The conclusions drawn from the projective tests and interviews identified four characteristic distinguishing cancer patients from controls. Patients were more likely to have suffered the loss of a major emotional relationship prior to signs of the tumour, and furthermore, within this relationship they had been able to express their emotions easily. Patients with cancer tended to have a blockage in their expression of hostile feelings. The cancer patients also displayed self-dislike and a lingering unresolved tension with one parent.

While agreeing that loss and depression may precede cancer, Bahnson and Bahnson (1966) suggest these emotional states might be necessary but not sufficient for cancer development. Influenced by psychoanalytical theories, they hypothesised that persistent use of denial and repression predisposes the individual to somatic manifestations of discharge of conflict. Using a variety of methods to assess the ego defenses, cancer patients were compared to normal controls. The results indicated cancer patients displayed a tendency for denial and repression. When angry, cancer patients reported that they would not blow up, shake or tremble, and would not get depressed or get angry with themselves. Rather they would usually try to think about more pleasant things and would rather stay friendly with people.

In one of the first studies in this area to focus on a specific cancer site, Kissen and Eysenck (1962) specifically tested the hypothesis that denial and repression (or suppression) of negative feelings are more common in cancer patients, in a sample of patients admitted to hospital for diagnosis and treatment of chest complaints. Patients subsequently diagnosed with lung cancer scored significantly lower on neuroticism, interpreted as being consistent with a diminished outlet for emotional discharge. This association between a poor emotional outlet and the diagnosis of lung cancer was replicated by Kissen (1966) who also reported higher mortality rates in lung cancer patients with a poor emotional outlet than those with a good emotional outlet.

Life Event Stress

“Mrs Emerson, upon the Death of her Daughter, underwent Great Affliction, and perceived her Breast to swell, which soon after grew Painful; at last broke out in a most inveterate Cancer, which consumed a great Part of it in a short Time. She had always enjoyed a perfect state of Health.” (Guy, 1759, in Kowal, 1955).

The concept of stress is not easily defined, but in the broadest sense, stress can be defined as an event or demand requiring a response, an adjustment or change, and in the process consuming resources (such as physical, mental, emotional among others) to deal with it. Variety in the approach to examining stress is largely dependent on the way in which it is defined or operationalised. While some examine the subjective internalised experience, most focus on life events, the external conditions experienced by an individual, an objective condition.

Life events are discrete occurrences of daily life, either physical and/or psychological in nature, that disrupt or threaten to disrupt normal life activities (Brown & Harris, 1978). An event may be seen as positive (eg a birth) or negative (eg loss of a spouse). The impact of such events or the resulting “stress” is dependent upon the intensity of the event and an individual’s resources to adapt to the event, such as coping style and social support (Tennant, Langeluddecke, & Byrne, 1985).

Assessment of life events is generally based on either standardized checklists or structured interview (Brown & Harris, 1978). There are a number of life event inventories, or checklists, that are similar in many respects, the most commonly used instrument being the Holmes and Rahe Social Readjustment Rating Scale (SRRS) (Holmes & Rahe, 1967). This checklist consists of 43 items events pertaining to areas of dynamic significance of life such as family, relationships, occupation, economics, residence, health and education. The common theme behind the events is that the occurrence usually requires adaptation or adjustment. The emphasis of this approach is that of change, rather than on psychological meaning or emotion. Each event is assigned a magnitude of readjustment relative to other events (weighting) and these weightings are summed to determine a “total life change” score. The checklist approach has been criticised for the limited range of experiences covered, and the lack of both specificity and sensitivity of event definition. Reliability has also been questioned, and concerns raised about the difficulty of ensuring events are independent of the disease in question, and the potential for reporting of events being influenced by mood or personality (Monroe & Roberts, 1990; Geyer, 1991; Geyer, 1993).

The Brown and Harris Life Events and Difficulties Schedule (LEDS) (1978) is an investigator based interview approach towards assessing life event stress and largely excludes these biases (Tennant, Smith, Bebbington, & Hurry, 1979). The semi-structured interview has been designed to elicit detailed descriptions of life events and chronic difficulties including information about the context in which they occurred. The focus of this approach is the strength of emotion that the experience of an event evokes. The meaning of the event for an individual is used to establish the degree of severity. Events and difficulties are independently rated on a number of stress dimensions, the principle dimension being threat or loss. Ratings are made according to comprehensive guidelines provided by the authors of the scale. This approach has been widely used, and is well validated and reliable (Tennant et al., 1979; Brown, 1982; Brown & Harris, 1989; Wethington, Brown, & Kessler, 1997).

Empirical Findings

Research relating to life events and/or stress in the development of breast cancer is reviewed, and where possible discussed in relation to other psychosocial variables. Studies are reviewed according to the approach taken to assess life event stress; non standardized interviews and scales, the checklist or inventory approach, studies using the LEDS, prospective studies using a range of measures and record linkage studies. The findings are summarized in Table 1.

Non standardised interviews and scales

Two limited prospective and two case-control studies used non-standardised structured interviews. Hypothesising that "social trauma" mediates breast cancer growth, Snell and Graham (1971) report the results of interviews with 352 breast cancer patients and 670 controls selected from a New York hospital. Stressful life events occurring within the previous five years were recorded. No differences were seen in the types of events experienced, the degree of closeness or kinship to the person involved, nor in subjective assessment of emotional upset experienced. Unfortunately, subjects with non-gynaecological cancer were included in the control group, limiting the interpretation of the study as stress has been linked to the development of other cancers (Goodkin, Antoni, & Blaney, 1986; Eysenck, 1988; Chorot & Sandin, 1994).

Greer and Morris (1975) interviewed 69 women with breast cancer and 91 women with benign breast disease prior to diagnosis. Subjects were asked about the occurrence and nature of stress during the period of the previous five years. Events causing "severe or

prolonged emotional distress" were recorded. No details were provided as to specific questions or prompts given to subjects. Benign controls were significantly younger than cases and no adjustment or stratification for age was reported. No differences were recorded in either the number of stressful life events or loss events.

Schwarz and Geyer (1984) briefly describe the use of a non-standardised, structured interview to assess stress among women undergoing a biopsy. The variables of interest were recent life events (time frame not indicated) and 'action control', described as an indicator of reaction to stress. Among the 76 women included in a path analysis, the experience of loss was not associated with breast cancer risk.

Brémond, Kune and Bahnson (1986) examined fifty women with breast cancer and one hundred age-matched controls from the same breast clinic. Women under age 45 with breast cancer reported having a "serious psychological shock during the past five years" more often than their age-matched controls (Odds Ratio (OR) 4.33, 95% Confidence Interval (CI) 1.2-16.0); there was no such relation for the total sample or for women over 45 years. No rationale was given for age stratification, and as the number of breast cancer cases under the age of 45 was small ($n=14$) this result may well have been opportunistic.

Scherg and Blohmke (1988) examined three specific types of traumatic events in relation to breast cancer risk (death of a parent in childhood, loss of spouse by death, divorce or separation, and the experience of traumatic events during World War II). The results are reported on a sample of 508 women attending a German clinic for breast examination, including 202 with breast cancer, and 1563 age stratified controls without cancer. There were no differences in the incidence of these selected life events between subjects with cancer of the breast and cancer at other sites. The results showed that subjects with cancer more often experienced the death of their mother before age 16 ($RR=1.7$), more often experienced the loss of a spouse ($RR=1.5$) and had experienced more war trauma events ($RR=1.3$) compared with non-cancer controls.

Checklist approach

Case-control studies

These six case-control studies vary in quality. Cheang and Cooper (1985) report a comparison of life event data collected on 121 women admitted to hospital for a breast biopsy and 42 "randomly" selected healthy controls. The authors developed a life event inventory specifically for this purpose with events scaled by a separate sample of pre-biopsy women. The 46 women subsequently diagnosed with breast cancer reported more life events and more stressful life events than the cancer-free women within the previous two years ($p < 0.01$). Ninety eight percent of cases reported at least one loss or illness event compared with 71 percent of the benign group ($p = 0.002$). However, only unadjusted data were presented, despite "minor" age differences between groups (mean age cases: 50.5 years; benign group: 48 years; healthy controls: 42 years), and other potential confounders were not considered. These results require cautious interpretation.

This same 48 item checklist (Cheang & Cooper, 1985) was administered to a mixed sample of 1,324 women attending a surgical clinic for breast symptoms, 272 women attending a breast clinic for breast symptoms and 567 asymptomatic women attending a primary health care facility (Cooper, Cooper, & Faragher, 1989; Cooper & Faragher, 1993). Subjects were divided into four groups, 171 diagnosed with breast cancer, 155 with cysts, 1,110 with benign breast disease and 727 with normal breast tissue. The breast cancer subjects reported fewer life events within the previous two years, but the events that did occur were rated by the subjects as having a greater impact. This result may be explained by differences in the types of events reported, with the cancer group more often had experienced the death of a close friend and illness related events.

However, despite claiming age-adjusted analyses, the results of the Cooper et al. (1989, 1993) study are consistent with incompletely adjusted data. The younger control groups experienced significantly more housing, work and relationship events, while the older cancer group reported more illness events and the loss of a close friend. Significant group differences for marital status, employment, alcohol and cigarette consumption were not included in analysis, and other risk factors such as family history and reproductive history were not considered. While the authors claim support for an increased incidence of recent bereavement associated with breast cancer, it is uncertain whether this effect is independent of age and other risk factors. The choice of comparison groups and approach to analysis limits the validity of this work, with the authors highlighting individual item differences rather than examining overall patterns.

Priestman, Priestman, and Bradshaw (1985) compared 100 women with breast cancer, 100 women with benign disease (both from surgical clinics) and a convenience sample of 100 healthy controls selected from among family and friends. A modified version of the SRRS was used to record events over the previous three years. No differences were reported between breast cancer patients and benign controls on the number of events reported or total "stress" scores. Age and other potential confounders were not considered and it was the healthy control group who scored higher for both number of stressful events and total stress score.

Forsén (1991) examined 87 women newly diagnosed with breast cancer and 87 controls matched on age and parity. Other potential confounders were not considered and no details were provided on the source of controls. The breast cancer group had significantly higher weighted life events scores for both twelve months (SRRS) and six years (modified SRRS) prior to diagnosis. Fifty-four percent of the cancer group experienced an important emotional loss within the previous two-year period compared to seven percent of controls. Multivariate analysis adjusting for anxiety, depression, marital status, education and social class confirmed that life event scores for the twelve months preceding diagnosis (RR=2.67, CI 1.13-6.30), and sustaining an important emotional loss (RR=5.02, CI 1.72-14.7), were significant predictors of breast cancer risk.

Ginsberg, Price, Ingram and Nottage (1996) report a case-control study of 98 cases and 98 controls randomly selected from electoral rolls, matched for age and place of residence. Adjusting for age at menarche, nulliparity, breast cancer history, exercise, body weight, BMI, smoking, alcohol and other dietary factors, women who scored in the highest quartile of life change scores for the past 10 years were 4.67 (CI 1.33-16.41) times more likely to have developed cancer. Life "change" scores for the most recent two year period, and life event "distress" scores for both the two and ten year periods showed non-significant trends of increased breast cancer risk.

These positive findings contrast to the result of a well designed population-based, case-control study of 258 newly diagnosed breast cancer cases and 614 randomly selected controls aged between 50-79 years (Roberts, Newcomb, Trentham-Dietz, & Storer, 1996). An abbreviated, age relevant version of the SRRS was used to examine life events for the previous five years. No differences were reported in the number of life events in the past five years, nor in the severity of events experienced. Reported odds ratios were adjusted for age, age at first birth, parity, family history of breast cancer, BMI, and age at menarche. No differences were seen in the number of events or experience of losses generally.

Limited prospective studies

The three limited prospective studies using the checklist approach on varied populations report varied results. Schonfield (1975) administered the SRRS scale to 112 women undergoing biopsy in five different Israeli hospitals. Confounders were dealt with by stratifying by the median age and place of birth. In contrast to expectation, the 85 women subsequently diagnosed with benign breast disease scored significantly higher for recent life change than the 27 diagnosed with breast cancer. When five specific loss items such as death of a spouse or divorce were examined separately (although the data were not presented), it was stated that there were no differences in these events between the cases and controls.

Fox, Harper, Hyner and Lyle (1994) administered the SRRS to 826 women presenting for mammograms at a specialist breast centre. Of these women, 52 had a prior diagnosis of breast cancer, 20 were later diagnosed with breast cancer, 488 with fibrocystic disease and 266 with "normal" results. After adjusting for age and other confounders, no significant differences were detected between new cases and the three control groups on SRRS scores. Individual item analysis revealed 60 percent of the newly diagnosed cancer group had experienced the death of a spouse or close family member within the past two years compared to only 27 percent of normal controls. However, the poor response rate (41%) as well as the failure to adjust for age or other confounders for individual item analyses limits the validity of this finding.

Edwards, Cooper, Pearl, de Paredes, Leary and Wilhelm (1990) investigated 1,052 women, including those with and without breast symptoms, all undergoing breast examination and mammography. Seventy-nine had breast cancer, 71 had pre-cancerous growths, 505 had benign breast disease and 397 normal breast tissue. The Cheang and Cooper (1985) checklist used in this study was specifically developed to assess life events in relation to the development of breast cancer and the scaling of events was done by a sample of pre-biopsy women. The inventory was used to record life events occurring in the previous two years and subjective ratings of the severity of each event on a 10-point likert-scale. The four diagnostic groups varied on prior history of cancer (including breast cancer) and this variable was subsequently controlled for in analyses. No differences were detected between the groups for the occurrence of events or for subjective severity ratings of events. Post-hoc factor analysis of the checklist yielded eight life event factors, none of which predicted a breast cancer diagnosis. Furthermore, coping style, personality Type A and social support did not moderate the relationship of stress and breast cancer.

Summary of Checklist Approach

The checklist inventory approach to assessing life events in relation to breast cancer development has produced inconsistent and at times contradictory results. Three semi-prospective studies failed to find any association between life event stress and breast cancer (Schonfield, 1975; Edwards et al., 1990; Fox et al., 1994). Of six retrospective studies, three report positive findings (Cheang & Cooper, 1985; Forsén, 1991; Ginsberg et al., 1996), one negative findings (Roberts et al., 1996), one that the cancer group experienced less events but reported them as subjectively more stressful (Cooper & Faragher, 1993) while another found healthy controls reported higher levels of life events stress (Priestman et al., 1985). Many of these studies focus on individual events rather than the overall picture that is the basis of the checklist approach. Variation in design, sample size, measures, and adequate consideration of potential confounders, add to the difficulty of interpreting conflicting results.

Life Events and Difficulties Schedule (LEDS)

Three studies have utilized the Brown and Harris (1978) Life Events and Difficulties Schedule (LEDS) to assess life event stress in relation to the development of breast cancer. Protheroe, Turvey, Horgan, Benson, Bowers and House (1999) report the results of a study of 332 women with suspicious breast lumps recruited from three breast clinics. One hundred and six women subsequently diagnosed with breast cancer and 226 women with benign disease were interviewed for life events occurring in the previous five years using the LEDS. Multivariate logistic regression analysis, controlling for age and other somatic risk factors, revealed no increase in the risk of breast cancer associated with severe life events or chronic difficulties. A major limitation in this case-control study was that 14 percent of subjects (30.2% of cancer subjects and 6.2% of benign subjects) were aware of their diagnosis prior to interview. No differences were reported in the number of severe events in those who knew or correctly guessed their diagnosis. While denial is an adaptive response to a breast cancer diagnosis, the potential impact of denial on the reporting of life events is unknown (Geyer, 1992). However, the LEDS method of assessing life events reduces the likelihood of this bias.

Chen, David, Nunnerley, Michell, Dawson, Berry, Dobbs & Fahy (1995) administered the LEDS to assess life event stress during the previous five years to a mixed sample including 72 women referred for examination following screening mammography and 47 symptomatic women undergoing biopsies. With a total sample of 119 women, 41 were later diagnosed with breast cancer and 78 with benign disease. The proportion of symptomatic and asymptomatic in each group was not reported. Coping strategies and personality traits were

also assessed as potential mediating factors. Forty-six percent of the breast cancer group and 19 percent of the benign control group reported at least one severely threatening event in the preceding five years. Life events rated as of important moderate threat were also found to be more common in the breast cancer group (48.8%) than the benign group (37.2%). Overall, there were no differences between the groups in the use of coping strategies.

Multiple logistic regression analysis, adjusting for age and other somatic risk factor variables, assessed life events and coping strategies in relation to breast cancer. The adjusted odds ratio for severely threatening events during the past five years was 15.00, although the confidence interval was wide (3.74-60.44). "Important moderately threatening" events were also associated with increased risk of breast cancer (OR=9.70, CI 2.45-38.17). While the data were not presented, the authors state these associations were seen in both the screened and symptomatic samples (Chen et al., 1995). Among women who had experienced at least one threatening event, those who confronted stress (problem focused coping) were at increased risk of breast cancer (OR=3.11, CI 1.18-8.19). Problem focused coping was also reported as increasing the risk of breast cancer in the multivariate analysis (OR 5.12, CI 1.46-17.89), although it is unclear if the interaction between life events and coping was included in this model. While these results provide support for a significant role for severely threatening life events in the development of breast cancer, the validity of combining two sources of women presenting to different clinics for different reasons is questionable. In addition the questionable adequacy of statistically adjusting for the large age range (20-70 years) in a small sample and the number of variables included in the final analysis reduce the strength of this result.

Geyer's (1991, 1993) study is a rarity in this field, growing from a strong theoretical basis and outlining a clearly defined set of hypotheses. Life events were conceptualised within a model of stress encompassing the influence of vulnerability factors. The Brown and Harris (1978) model of life events and illness, defines life events as provoking (causal or trigger) agents for disease, while acknowledging that other factors, called vulnerability factors, increase the impact of provoking agents on disease. According to this model, only the most threatening events would be expected to make a difference between the cancer group and controls.

Geyer (1991, 1993) reports the investigation of 92 women admitted to hospital for breast surgery. The LEDS was used to assess life events and difficulties experienced over eight years prior to presentation, acknowledging the long prodromal period between the initiation of breast cancer and clinical manifestation. Significant differences were apparent for life

events rated as severely threatening between 33 subjects later confirmed with breast cancer and 59 controls with benign breast disease. Forty-eight percent of the breast cancer group reported at least one event in this category compared with only 15% of the benign control group. Social support, hypothesized as a vulnerability factor, was highly correlated with the life events and necessarily excluded from analyses. Family history of breast cancer was included as a vulnerability factor. The results were presented as adjusted regression coefficients without standard errors or tests of significance. However, regression coefficients demonstrated a stronger association between severely threatening life events and breast cancer ($r=0.28$) (*sic*) and an interaction between severely threatening life events and family history ($r=0.24$) (*sic*), than between age and breast cancer ($r=0.19$) (*sic*) (Geyer, 1993). This study, although small, provides evidence for a role for severely threatening life events in the development of breast cancer and for family history of breast cancer as a vulnerability factor increasing the impact of life events.

The results of these three studies using the interviewer-based LEDS approach to assess life events in relation to the development of breast cancer are intriguing. Two small studies suggest a significant role for severely threatening life events, while a larger study, with both strengths and weaknesses, failed to replicate these findings.

Prospective Studies

A number of prospective studies have focused on specific, but varied types of stress. Jacobs and Bovasso (2000) prospectively examined parental death in childhood in a sample of 1533 women recruited into a mental health survey in 1980 and followed-up through 1994-1995. After controlling for age, family history of breast cancer and other risk factors, maternal death in childhood significantly increased the risk of breast cancer (OR=2.6, CI 1.6-4.4).

Achat, Kawachi, Byrne, Hankinson and Colditz (2000) examined job strain in 26,936 postmenopausal women participating in the Nurses' Health Study, in paid employment and without a history of cancer. The Karasek Job Content Questionnaire (Karasek & Theorell, 1990) was used to assess subjective evaluations of work characteristics including psychological workload and level of control. During the two years of follow-up 219 cases of breast cancer were identified. Controlling for age and other risk factors, no association between job strain and the development of breast cancer was observed.

Lillberg, Verkasalo, Teppo, Helenius and Loskenvuo (2001) prospectively examined the subjective appraisal of daily stress in a sample of 10,519 female twins participating in the Finnish Twin Cohort Study. Participants completed the Stress of Daily Activities (Lillberg et

al., 2001) questionnaire in 1975 and 1981. By 1996, 205 incident breast cancers were identified. After controlling for age and a number of other risk factors, as well as zygosity, there was no association between perceived stress of daily life and the development of breast cancer.

Population Record Linkage Studies

Two large population record-linkage studies have studied two major adverse life events, namely widowhood and divorce, objectively verified and linked to the incidence of breast cancer. These population-based studies have the advantage of avoiding sampling selection and recall bias by using information from registries.

Ewertz (1986) used Danish cancer incidence records and population registry data to match marital status in 1,782 breast cancer cases diagnosed within a twelve month period and 1,738 randomly selected age-stratified controls. One hundred and seventy five cases (9.8%) and 198 controls (11.4%) were widowed at the time of diagnosis and no association was found between length of widowhood and breast cancer risk. Similarly 154 (8.6%) of cases and 157 (9.0%) of controls were divorced at diagnosis and there was no association between the time of divorce and breast cancer.

Kvikstad, Vatten, Tretli and Kvinnsland (1994), using similar Norwegian registry data, report a population based nested case-control study of 4,491 breast cancer cases and 44,910 controls born between 1935 and 1954. Records of divorce and widowhood were completed up until five years prior to the cancer diagnosis, testing the hypothesis that these major life events occurring over a long prodromal period were related to breast cancer risk. Information was collected from the population census and from the cancer registry. One hundred and thirty cases (2.9%) and 1197 (2.7%) of controls were widowed and there was no association with breast cancer. Four hundred and eighty four cases (10.8%) and 5660 controls (12.6%) were divorced, and after controlling for age, age at first birth, parity and place of residence, divorced women compared with married women were significantly less likely to have developed breast cancer (OR=0.83, CI 0.75-0.92).

Summary of life event stress

The evidence for an association between life event stress and breast cancer risk is inconsistent and far from convincing. Two population-based record linkage studies found no evidence of a link between widowhood or divorce and breast cancer incidence. One prospective study reports a significant increase in risk of breast cancer associated with the childhood death of a parent. Job strain and daily hassles were not associated with breast cancer. The nine studies using checklists vary in quality and provide mixed results with four positive results, four negative results and one reporting, paradoxically, more events in the control group. Of four studies using non-standardised interviews, only one found an association between life events and breast cancer and only in younger women. Among the highest quality are two semi-prospective studies using the LEDES interview, a comprehensive method of estimating the degree of severity of stressor exposure, and superior to the checklist approach. Although sample sizes were small, results suggest that severely threatening life events may be associated with increased breast cancer risk, and that coping strategies may moderate the association. Of note, however, a larger case-control study using the LEDES approach failed to replicate these findings.

Table 1: Studies examining life event stress and breast cancer development

Design / Authors	Measures	Time Frame	Results*
<i>Case-Control Studies</i>			
Snell & Graham, 1971	Social Trauma	5 years	ns
Bremond et al., 1986	Non-standardised interview	5 years	ns (total sample) <45yrs (OR ^a =4.3; CI ^b 1.2-16.0)
Priestman et al., 1985	Cochrane & Robertson LEI ^c	3 years	ns
Cheang & Cooper, 1985	Cheang & Cooper LEI ^c	2 years	Life event scores (p<0.01) Loss/illness event (p=0.002)
Cooper et al., 1989, 1993	Cheang & Cooper LEI ^c	2 years	Less events but perceived as more severe*
Ginsberg et al., 1996	Tennant & Andrews LEI ^c	2 years 10 years	2 yrs ns* 10 yrs (RR ^e =4.67; CI ^b 1.33-16.4)*
Forsén, 1991	SRRS ^d SRRS ^d (modified)	1 year 6 years	RR ^e =2.7; CI ^b 1.1-6.3)* 6yrs Emotional loss (RR ^e =5.02, CI ^b 1.7-14.7)*
Roberts et al., 1996	SRRS ^d (modified)	5 years	ns*
Protheroe et al., 1999	LEDS ^f	5 years	ns*
<i>Semi-Prospective Studies</i>			
Greer & Morris, 1975	Psychiatric Interview	5 years	ns
Schwarz & Geyer, 1984	Non-standardised interview	not given	ns*
Edwards et al., 1990	Cheang & Cooper LEI ^c	2 years	ns*
Schonfield, 1975	SRRS ^d (modified)	3 years	Controls higher SRRS ^d scores (p<0.05)*

*age adjusted; ^aOdds Ratio; ^b95% Confidence Interval; ^cLife Event Inventory; ^dSocial Readjustment Ratings Scale ^eRelative Risk; ^fLife Events and Difficulties Schedule; ^gRegression coefficient.

Table 1 continued: Studies examining life event stress and breast cancer development

Design / Authors	Measures	Time Frame	Results*
<i>Semi-Prospective Studies (continued)</i>			
Fox et al., 1994	SRRS ^d	2 years	SRRS ^d ns* Death of spouse / family member
Scherg & Blohmke, 1988	Parental Death	Childhood	Death of Mother <16
	Widowhood/Divorce	Lifetime	(RR ^e =1.7)
	War Trauma	Childhood	Loss of Spouse (RR ^e =1.5) War Trauma (RR ^e =1.3)
Geyer, 1991, 1993	LEDS ^f	8 years	Severely threatening life events (r ^g =0.28)*
Chen et al., 1995	LEDS ^f	5 years	Severely threatening life events (OR ^a =15.0, CI ^b 3.7-60.4)*
<i>Prospective Studies</i>			
Jacobs & Bovasso, 2000	Parental death in childhood	Childhood	OR ^a =2.6, CI ^b 1.6-4.4*
Achat et al., 2000	Job strain	2 years	ns*
Lillberg et al., 2001	Daily hassles	20 years	ns*
<i>Record Linkage Studies</i>			
Ewertz, 1986	Widowhood / Divorce	Lifetime	ns*
Kvikstad et al., 1994	Widowhood / Divorce	Lifetime to 5	Widowhood (ns)*
		years pre-diagnosis	Divorce (OR ^a =0.83, CI ^b 0.75-0.92)*

*age adjusted; ^aOdds Ratio; ^b95% Confidence Interval; ^cLife Event Inventory; ^dSocial Readjustment Ratings Scale ^eRelative Risk; ^fLife Events and Difficulties Schedule; ^gRegression coefficient.

Emotional Suppression

“Let me speak to you regarding things of which you must be most aware. To get angry and shout at times pleases me, for this will keep up your natural heat; but what displeases me is your being grieved and taking all matters to heart. For it is this, as the whole of physic teaches, which destroys our body more than any other cause.” (Sassoli, Physician to patient, 1402, in LeShan, 1959).

Although the terminology varies, the concept of emotional suppression or repression or bottling up of one's emotions as a risk factor for cancer is a central theme in early research findings and continues as a dominant theme, both theoretically and empirically. Suppression of emotional responses appears in Greer and Watson's (1985) description of Type C behaviour, difficulty in expressing emotions appears as part of Temoshok's (1987) Cancer Prone Personality and a lack of an outlet for strong feelings and the failure to express such emotions features in Eysenck's (1991) Type I Cancer Prone Personality.

An inherent assumption in the hypothesis that the suppression or control of emotional responses results in physiological consequences that in turn affect the development of cancer, is that an individual's physiological response differs when emotions are expressed compared to when emotions are controlled (Gross, 1989). Some validity of the concept by means other than self-report has been reported by Pettingale, Watson and Greer (1984) who found that breast cancer patients were independently rated as being significantly less facially expressive than controls under stress conditions and were more likely to hide their feelings under stress. While no differences were detected in measures of autonomic arousal in this study (Watson, Pettingale, & Greer, 1984), Anderson (1981) found a significant negative correlation between subjective ratings of stress and physiological arousal.

There is some evidence to support the assumption that the tendency to suppress or express emotions is a trait characteristic. Bleiker, van der Ploeg, Ader, van Daal and Hendriks (1995) compared emotional expression and control variables in a community-based sample of 25 women before and after their breast cancer diagnosis and 825 controls without breast cancer. Eighteen months following diagnosis, breast cancer subjects scored significantly lower for emotional expression-out (defined as feelings being directed towards other people) and emotional control (defined as the control of outward expression of feelings) than their pre-diagnosis scores. There were no differences detected in these scores in control subjects. Interestingly, emotional expression-in, defined as feelings being held in or suppressed, was stable over time for all subjects. This result suggests that emotional expression-out and

emotional control are affected by a diagnosis of cancer and its consequences, but that emotional suppression is stable over time and situation.

However, Kreitler, Chaitchik and Kreitler (1993) suggest the opposite. This group employed the Weinberger, Schwartz and Davidson repression questionnaire (1979) that conceptualises anxiety as the basic element of repression, distinguishing between actual anxiety and anxiety disguised by defensiveness. Repressors were defined as scoring low on anxiety and high on defensiveness and non-repressors are all other score combinations. In a study of 72 Israeli women undergoing biopsy and 26 women awaiting non-cancer surgery, they found a significant increase in repression after surgery in the cancer group, indicating that repression may be a response to, not a cause of, cancer.

Definitions

Studying the role of emotional suppression in the development of breast cancer is complicated by variability in the terminology used to distinguish it, in the way it is defined and measured, and the meaning attributed to the concept. Greer and Morris (1975) focus on the behavioural aspects, defining "emotional suppressors" as individuals who had less than three times openly shown anger as an adult and nearly always bottled up other feelings. Watson and Greer (1983) refer to "emotional control", defining it as the extent to which individuals report controlling their emotional reactions. Fox et al. (1994) use repression to refer to what is being measured by the Watson and Greer Courtauld Emotional Control Scale (CECS) (1983), while Kreitler et al. (1993) use the Weinberger et al. definition of repression as the combination of low reported anxiety and high defensiveness (1979).

Empirical Evidence

Retrospective studies

Jansen and Muenz (1984) compared 69 breast cancer patients with two control groups, one group of 82 women with fibrocystic disease and a second group of 71 healthy controls, on a variety of personality and emotional variables. Over 35 percent of the cancer group kept anger in, compared to seven percent of the benign group and 15 percent of healthy controls. Younger women with cancer were comparable to the overall group, but 50 percent of the less educated younger women with cancer reported keeping anger in. Results suggest that "keeping anger in" is correlated to breast cancer regardless of age, but is more pronounced in younger, less educated women. Although these results appear to provide strong support for anger suppression being correlated with breast cancer, caution is required as each of these "traits" relied on a single forced choice question.

Brémond et al. (1986) also report higher suppression of emotions in 50 breast cancer patients compared to 105 age-matched benign breast disease controls. In a series of 23 biopsychosocial questions, two items showed significant group differences. Of interest here, the breast cancer group were significantly more likely to agree with the statement "it is best never to show your feelings to others", the difference most prominent in subjects older than 45 years. However, with 23 individual comparisons, several significant differences would be expected by chance. No rationale is provided for splitting the sample at this age and it may well have been opportunistic.

Limited prospective studies

Pioneering empirical examination of psychosocial variables in the development of breast cancer, Greer and Morris (1975) assessed 160 patients admitted to hospital for breast tumour biopsy as part of an interdisciplinary study. Sixty-nine were later confirmed to have breast cancer and 91 benign breast disease. The psychological assessment included an evaluation of the degree to which subjects concealed or expressed negative emotions, in particular anger. Extreme suppressors of emotions were defined as those who had less than twice in their adult lives openly showed anger and nearly always bottled up other emotions. Extreme expressors of emotions were those who had a history of frequent outbursts of anger and rarely concealed their emotions. Those in between these extremes were classified as normal.

The breast cancer group reported extreme suppression of negative emotions, particularly anger, compared to benign controls, with 47.8% of the cancer group reporting extreme suppression of anger compared with 15.4% of controls ($p < 0.001$) (Greer & Morris, 1975). Although less frequent, extreme expression of anger was also more common in the cancer

group (20.3%) in comparison to controls (9.9%). A similar pattern of differences was apparent with the release of other emotions, although the differences were not as marked. Age correlated with both cancer and suppression of emotions. When differences between breast cancer subjects and benign controls for the release of emotions were evaluated by age group, extreme suppression or extreme expression of anger was significantly higher in the cancer group only in women under 50 years of age. However, re-analysing an undefined subsample of these women, controlling for menopausal status and age, Bageley (1979) concluded that women with breast cancer were significantly more likely to repress feelings ($p < 0.01$).

Refining the above procedure Morris, Greer, Pettingale and Watson (1981) examined 50 women admitted to hospital for breast biopsy, 17 later confirmed as having breast cancer and 33 benign breast disease. Information as to the frequency with which they lost control of their emotions when angry was recorded, with the inter-rater reliability 0.91. Suppression of anger (defined as losing control in front of adults less than twice in adult life) was more common in the cancer group than benign controls ($p < 0.01$). However, adjusting for age, there was no difference in anger expression for women over 50 years and for women aged 40-49 years the difference was marginal ($p < 0.08$). With a small sample it is difficult to interpret these results conclusively. While the authors claim the result follows the same pattern as the Greer and Morris (1975) study, the claimed pattern of suppression of anger in breast cancer subjects is difficult to support with these data.

The Wirsching, Hoffmann, Stierlin, Weber and Wirsching (1985) examination of emotional suppression in 56 women prior to biopsy, was based on ratings made by both the interviewer and an independent assessor on a number of psychological dimensions. Ratings were made for remoteness, suppression of feelings, rationalizing attitude, anxiety, optimism, self-sufficiency, altruism and harmonizing behaviour. The breast cancer group were more likely to deny current emotional distress, were less anxious and more aloof compared to benign controls. The cancer group was also more rational, optimistic, self-sufficient and altruistic. The authors claim that these traits allowed a blind rater to correctly predict 83% of cancer patients and 71% of benign controls according to these ratings. However, no details are provided about age or other biological risk factors, and the number of variables examined in relation to the sample size introduces significant doubt as to the validity of this result.

In contrast, Scherg (1987) report negative findings in a semi-prospective study of 100 breast cancer cases and 100 age-matched healthy controls, and 69 breast cancer cases and 69 age-matched benign controls, from a sample of women attending a gynaecological clinic. Prior to

diagnosis, each subject completed a modified version of the Bahnsen and Bahnsen (1979) psychosocial questionnaire including scales for suppression of anger, external control, pattern A behaviour, and social desirability. Initial presentation of these data suggested that breast cancer patients were significantly more likely to suppress anger than both benign controls and healthy controls, but only in the 20-50 year age group (Scherg, Cramer, & Blohmke, 1981). However, subsequent presentation of these data controlling for the reason for presentation and fear of breast cancer, found no evidence to support differences between cases and controls in the suppression of anger (Scherg, 1987).

The Courtauld Emotional Control Scale (CECS) has been utilized in two limited prospective studies. The CECS was developed to evaluate the extent individuals control their reactions when angry, anxious and depressed, the items derived from prior interview-based studies of women undergoing breast biopsy (Watson & Greer, 1983).

Grassi and Cappellari (1988) administered the CECS and the Symptom Questionnaire (Kellner, 1976) (measuring anxiety, depression, hostility and somatic symptoms) in a sample of 76 women admitted to hospital for breast biopsy. Forty-one women later confirmed with breast cancer scored significantly higher on the total score for emotional control from the CECS than benign controls ($p=0.04$). Differences in sub-scale scores of the CECS individually assessing control of anger, anxiety and depression were marginal ($p=0.055$). The breast cancer group was significantly lower on state hostility scores ($p=0.02$). However, the analyses did not control for substantial age differences or other known predictors of breast cancer.

Fox et al. (1994) also report significantly higher scores on the CECS in 20 new breast cancer patients when compared with 266 women with normal breast tissue and 488 women with fibrocystic disease attending a mammography clinic. After adjustment for age and other known risk factors, sub-factor analysis revealed that this difference was primarily for anger and depression, while the breast cancer group varied from the normal group only on suppression of anxiety. However, the poor response rate (41%) greatly reduces the weight of this study.

Prospective studies

Two prospective studies have been reported in this area. Hahn and Petitti (1988) report on Minnesota Multiphasic Personality Inventory (MMPI) (Hathaway & McKinley, 1951) data collected from 8,932 women involved in a prospective contraceptive drug study commenced in 1969. Follow-up via computer-stored hospital discharge records in 1982 identified 117

biopsy confirmed breast cancers developed after study entry. Univariate and multivariate analyses failed to detect significant group differences on the repression/sensitisation subscales.

Bleiker et al. (1996) prospectively assessed trait personality in a community based study of Dutch women attending a breast screening program. The SAQ-N (van der Ploeg, 1989), a self-report questionnaire comprised of reliable and well validated psychological scales, was used to assess rationality, anti-emotionality, emotional expression-in, emotional expression out, and emotional control. Of the 9705 women completing the questionnaire (34% response rate), 131 were later diagnosed with breast cancer. Six age-matched normal controls per case were also selected. Logistic regression analyses, controlling for somatic factors such as family history, early menarche, late menopause, obesity and parity, were used to predict case versus control status. Emotional Expression and Control variables were not related to breast cancer risk. The only significant psychological factor predicting breast cancer was significantly higher anti-emotionality (OR=1.19 CI 1.05-1.35), defined as "an absence of emotional behaviour or a lack of trust in one's own feelings" (Bleiker et al., 1996).

Related Concepts

Alexithymia

Alexithymia is defined as "an inability to describe one's emotions" and is considered to be a personality trait (Todarello, La Pesa, Zaka, Martino, Lattanzio, 1989). Todarello et al. (1989) assessed alexithymia in a mixed sample of 200 women undergoing mammography for suspected carcinoma or screening. The 13 women subsequently diagnosed with breast cancer scored significantly lower on alexithymia, indicating an inability to verbalise or express their emotions. However, the small number of breast cancer cases, poor response rate (66%), failure to adjust for age, breast symptoms or other confounding variables limits to validity of this result.

These findings contrast to those of Anagnostopoulos, Vaslamatzis, Markidis, Katsouyanni, Vassilaros and Stefanis (1993) who examined women attending breast screening, including 180 later diagnosed with breast cancer, 112 with benign disease and 156 with healthy breast tissue. A random subset of 100 women (breakdown of diagnosis unclear) completed the Toronto Alexithymia Scale (TAS) (Taylor, Ryan, & Bagby, 1985). After adjusting for most potential confounders there were no group differences in alexithymia.

Type A

Type A behaviour is also related to the concept of emotional suppression and defined as an overt pattern of behaviour characterised by being hard driving, ambitious and time conscious and is contrasted to a Type B behaviour pattern characterised by being slower moving, less aggressive and more easy going (Bortner, 1969). Three studies have examined Type A behaviour in relation to breast cancer development. The details of these studies have been described earlier.

Cheang and Cooper (1985) assessed Type A behaviour using the Bortner scale (Bortner, 1969) in a sample of 121 women with breast disease prior to biopsy and 42 healthy clinic patients. No significant differences were detected between the groups in the overall pattern of Type A behaviour. Individual item analysis detected significant differences between the cancer group and controls, the distinguishing feature being the concealment of feelings, although individual item analyses are not displayed and the validity of this procedure is questionable. Faragher and Cooper (1990), factor analysing the Bortner type A scale, found breast cancer patients (n=171) tended to suppress feelings, and have few personal relationships outside of home and work, compared to 1110 women with benign disease. In contrast, Edwards et al. (1990), controlling for age and history of cancer, found no differences on the Bortner type A scale in 1052 women attending for breast examination and mammography.

Emotional suppression summary

The evidence for the impact of emotional suppression or control, in particular anger, on the development of breast cancer, is equivocal, but intriguing. A summary of study findings is displayed in Table 2. Two prospective studies reported negative results, although one study used a sub-scale of the MMPI based on a theoretical model currently not widely used and not directly assessing emotional suppression; the other possibly affected by sampling bias (response rate 34%). Five other studies reported negative results, including one assessing anger suppression, one repression, one alexithymia and two measuring Type A personality. Of the nine studies reporting positive results, only four were adjusted for age. Among the highest quality studies are three positive findings, including the two reporting a positive association with suppression of anger in women under age 50 years. These results highlight the necessity to adjust for age and other confounders, but also suggest that suppression may be a more important variable for younger women (possibly linked to the premenopausal hormonal profile). Scales directly measuring suppression or control of emotions, particularly anger, appear more sensitive than measures of general alexithymia and type A.

Table 2: Studies examining emotional suppression and breast cancer development

Design / Authors	Measures	Results*
<i>Case-control</i>		
Jansen & Muenz, 1984	Single Psychosocial Questions	Cancer subjects keep anger in*
Brémond et al., 1986	Single Bio-psychosocial Questions	Cancer subjects agree it is better never to show feelings to others*
Cheang & Cooper, 1986	Type A	ns
Faragher & Cooper, 1990	Type A	Cancer subjects suppress feelings
<i>Semi-prospective</i>		
Greer & Morris, 1975	Interview assessment of emotional suppression	Extreme expression or suppression in cancer subjects under 50 yrs*
Morris et al., 1981	Interview assessment of emotional suppression	Suppression of anger in cancer subjects under 50 yrs*
Wirsching et al., 1985	Interview assessment of emotional suppression	Cancer subjects deny current distress, more rational, altruistic & optimistic
Scherg, 1987	Suppression of anger, external control, pattern A & social desirability	ns*
Grassi & Cappellari, 1988	CECS ^a & Hostility	Cancer subjects higher CECS Cancer subjects lower hostility
Fox et al., 1994	CECS ^a	Cancer subjects higher CECS*
Kreitler et al., 1993	Repression	ns
Todarello et al., 1989	Alexithymia	Cancer subjects lower on alexithymia
Anagnostopoulos et al, 1993	Alexithymia	ns*
Edward et al., 1990	Type A	ns*
<i>Prospective</i>		
Hahn & Petitti, 1988	MMPI ^b repression	ns*
Bleiker et al., 1996	Emotional expression and control; anti-emotionality; rationality	Anti-emotionality high in breast cancer*

*age adjusted ^aCourtauld Emotional Control Scale ^bMinnesota Multiphasic Personality Inventory

General Personality

The investigation of general personality factors in relation to the development of breast cancer is based on the assumption that people who develop cancer have a specific premorbid personality structure that predisposes them to develop cancer and considers traits beyond emotional suppression. This area of enquiry has not produced promising results (Table 3).

Two limited prospective studies (Greer & Morris, 1975; Chen et al., 1995) and one case-control study (Priestman et al., 1985) have reported non-significant results for extroversion and neuroticism using the Eysenck Personality Inventory (EPI) (Eysenck & Eysenck, 1964). Morris et al. (1981) reported significantly lower neuroticism using the Eysenck Personality Questionnaire (EPQ) (Eysenck & Eysenck, 1975) in breast cancer patients compared with controls, but only in women in the 40-49 years age group.

The results regarding hostility have been mixed, with Greer and Morris (1975) reporting no significant differences, while Anagnostopoulos et al. (1993) reported a significant association between low denigratory attitudes towards others and breast cancer after controlling for age and other risk factors. Grassi and Cappellari (1988) also report breast cancer cases having significantly lower state hostility in comparison to benign controls in a sample of 76 women undergoing breast biopsy ($p=0.02$). However, significant differences in age and socio-economic status between the groups were not controlled for in analysis, nor were other risk factor variables for breast cancer considered.

Three other studies report significant findings. Scherg (1987), using a modified psychosocial questionnaire (Bahnon & Bahnon, 1979) assessed women attending a breast clinic, matched on age and reason for consultation, and controlling for "fear of breast cancer". Breast cancer subjects were less anxious and more committed to social and religious norms, while there were no differences for paranoid sensitivity, authoritarianism, dependence, external control, or somatic symptoms (Scherg, 1987). Bleiker et al. (1996) (described earlier) 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.

Some intriguing results come from a semi-prospective study examining psychosomatic characteristics in 77 women awaiting breast biopsy (18 cancers, 59 benign disease), classified as psychotic, poorly organised neurotic or well organised neurotic (Jasmin, Le, Marty, Herzberg, & Psycho-Oncology Group, 1990). Multivariate analysis adjusted for age, family history, age at first delivery and parity found women with a poorly organised neurosis or psychosis were at increased risk of breast cancer ($RR=17.8$, $p<0.009$). 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. However, the psychosomatic classifications are not well defined and no inter-rater reliability data were presented. Consequently, it is difficult to assess the importance of these findings.

In summary, there is little consistency in the results for general personality traits in relation to breast cancer development. Extroversion/introversion, authoritarianism, rationality, dependence, external locus of control, religiosity and commitment have been found to be unrelated to breast cancer. Lower hostility has been associated with breast cancer in two out of three studies and anti-emotionality was found to result in a modest increase in breast cancer risk in one study. One study reported a significant relationship between impaired mental state (psychosis or neurosis) and the development of breast cancer. However, mental state ratings were based on subjective judgments and no inter-rater reliability was reported.

Table 3: Studies examining general personality and breast cancer development

Design / Authors	Measures	Results*
<i>Case-control</i>		
Priestman et al., 1985	EPI ^a	ns*
<i>Semi-Prospective</i>		
Greer & Morris, 1975	EPI ^a , hostility, social adjustment	ns*
Morris et al., 1981	EPQ ^b	ns*
Chen et al., 1995	EPI ^a	ns*
Scherg, 1987	Bahnon & Bahnon (1979) psychosocial questionnaire	More committed to social & religious norms. No differences for paranoid sensitivity, dependence, authoritarianism, external control*
Grassi & Cappellari, 1988	Symptom Questionnaire (Kellner, 1976)	Low state hostility (p=0.02)*
Jasmin et al., 1990	Psychosomatic Interview	Poorly organised neurosis or psychosis (RR ^d =17.8)*
Anagnostopoulos et al., 1993	Personality Deviance Scale (Bedford, 1978)	Low denigratory attitudes*
<i>Prospective</i>		
Bleiker et al., 1995	(SAQ-N) ^c	Antiemotionality (OR ^e =1.19)*
*age adjusted ^a Eysenck Personality Inventory ^b Eysenck Personality Questionnaire ^c Self Assessment Questionnaire-Nijmegen ^d Relative Risk ^e Odds Ratio		

Anxiety and Depression

“The cases are so frequent in which deep anxiety, deferred hope and disappointment are quickly followed by the growth and increase of cancer, that we can hardly doubt that mental depression is a weighty addition to the other influences favouring the development of the cancerous constitution.” (James Paget, 1870, in Greer, 1979).

Several authors have suggested that chronic levels of negative emotions may contribute to the development of cancer. It is possible that negative responses enhance the impact of stressful life events or that 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, life event stress and coping style together, so it is difficult to tease out these inter-relationships.

While there is a long history of anecdotal evidence linking depression and the development of cancer, implying a causal association, the empirical evidence is unconvincing. Often quoted in support of a relationship between depression and cancer are a number of longitudinal studies assessing depression or depressive symptoms at a single point in time and assessing subsequent cancer incidence. A recent meta-analysis of such data concluded that while both depression and cancer are common, the evidence for an association between depression and cancer is at best weak (McGee, 1994). Studies directly examining an association between depression and the development of breast cancer similarly provide little support for such a relationship (Table 4).

One case-control study reports significantly more depressive symptoms in the two years prior to onset of breast cancer symptoms in 87 breast cancer patients compared with age and parity matched control (Forsén, 1991).

A number of quasi-prospective studies have examined the association between depression and breast cancer using a variety of definitions, including trait depression, depressive illnesses, and current depressive symptoms as assessed by a range of measures. The results have been remarkably consistent. Greer and Morris (1975) found no differences on current levels of depressive symptoms or for a history of medically treated depressive illness within the previous five years in a sample of women undergoing breast biopsy. Similarly, Schonfield (1975) reported no differences in depressive tendencies as assessed by the MMPI (Hathaway & McKinley, 1951) in an Israeli sample of women undergoing biopsy. Chen et al. (1996) reported no significant differences between breast cancer cases and benign

controls on the General Health Questionnaire (GHQ). Jasmin et al. (1990) report no differences between breast cancer subjects and benign controls for latent depression, essential depression or acute depression as examined by an open-ended psychosomatic interview.

Aragona, Muscatello and Mesiti (1997) report the exception in a psychosomatic study of 149 women prior to diagnostic breast surgery. Although there were no differences on MMPI depression scores (Hathaway & McKinley, 1951) or the Hamilton Depression Rating Scale (Hamilton, 1967) between 108 breast cancer patients and 41 benign breast disease controls, significantly more of the cancer group (64%) than benign controls (24%) met DSM-III-R (American Psychiatric Association, 1987) criteria for a mild depressive disorder ($p=0.005$).

The three semi-prospective studies that have considered chronic or trait anxiety in relation to breast cancer development provide no evidence to support such a claim. Schonfield (1975) found no evidence for chronic anxiety as measured MMPI (Hathaway & McKinley, 1951). However, Scherg (1987) reported benign controls being characteristically more anxious than breast cancer cases, while Morris et al. (1981) report benign controls scored marginally higher on trait anxiety compared with breast cancer cases.

Two prospective studies have examined depression with respect to the development of breast cancer. The largest study administered the MMPI (Hathaway & McKinley, 1951) to 8932 women enrolled in the Walnut Creek Contraceptive Drug Study. This self-report measure assesses stable personality traits, including depression. Computer-stored hospital discharge records revealed 117 of these women had developed breast cancer in the subsequent 12-14 years. After adjusting for a number of confounding variables, no significant differences were detected for depression between the 117 women who developed breast cancer and healthy women (Hahn & Petitti, 1988).

Bleiker et al. (1996) similarly report negative results in a prospective study carried out in conjunction with a breast screening program. All women over 43 years of age in the Dutch city of Nijmegen were invited to attend breast screening and complete a self-report questionnaire encompassing well validated personality scales including trait measures of depression and anxiety (SAQ-N) (van der Ploeg, 1989). Of the 9705 respondents (34% response rate), 131 were later diagnosed with breast cancer and compared with 771 age-matched controls. Logistic regression analyses, controlling for a number of somatic risk factors, detected no differences between cases and controls for trait depression or trait anxiety (Bleiker et al., 1996).

In summary, the evidence of an association between depression and/or anxiety and the development of breast cancer is poor. Both prospective studies and four of the five semi-prospective studies reported no association between depression and breast cancer development. One study found that dysthymia, but not major depression, associated with breast cancer, and a case-control study has reported more depressive symptoms in the breast cancer group. Of four studies examining trait or chronic anxiety, three reported negative results, while one, contrary to expectation, found that the benign control group scored higher on trait anxiety than breast cancer cases.

Table 4: Studies examining depression or anxiety and breast cancer development

Design / Authors	Depression Measure	Results*	Anxiety Measure	Results*
<i>Case-control</i>				
Forsen et al., 1991	Depressive symptoms (2 yrs)	Higher in Ca pts	-	-
<i>Semi-prospective</i>				
Greer & Morris, 1975	Current symptoms	ns	-	-
	Depressive illness	ns		
Schonfield, 1975	MMPI ^a	ns	Chronic Anxiety	ns
Morris et al., 1981	-	-	Trait anxiety	ns
Scherg, 1987	-	-	Trait anxiety	Lower in cancer pts
Jasmin et al., 1990	Acute, essential, latent depression	ns	-	-
Chen et al., 1995	GHQ ^b	ns	-	-
Aragona et al., 1997	MMPI ^a / HDRS ^c	ns	-	-
	Dysthymia	Higher in Ca pts		
<i>Prospective</i>				
Hahn & Pettiti, 1988	MMPI ^a	ns	-	-
Bleiker et al., 1996	Trait Depression	ns	Trait Anxiety	ns

*age adjusted ^aMinnesota Multiphasic Personality Inventory ^bGeneral Health Questionnaire ^cHamilton Depression Rating Scale

Coping Styles

Folkman and Lazarus (1980) define coping as “the cognitive and behavioural efforts made to master, tolerate, or reduce external and internal demands and conflicts among them”. They distinguish between problem-focused coping that deals with the source of the stress and emotion-focused coping that regulates stressful emotion. Defense mechanisms are defined as “patterns of feelings, thought, or behaviours that are relatively involuntary and arise in response to perceptions of psychic danger. They are designed to hide or alleviate the conflicts or stressors that give rise to anxiety” (American Psychiatric Association, 1987). There is evidence to support the assumption that individual’s have some consistency in their pattern of coping (Folkman & Lazarus, 1980; Andrews, Singh, & Bond, 1993).

A distinctive style of coping is a central feature of the theorized Cancer Prone Personality. Greer and Watson (1985) describe a rigid and defensive behavioural style of responding to stress in which behavioural reactions are suppressed. Temoshok (1987) identifies a repressive coping style, in which personal needs are abrogated in favour of the needs of others, characterised by co-operative, unassertive, appeasing and accepting behaviour. While coping style has been suggested as a potential mediator in the relationship between stress and breast cancer risk (Bahnon, 1981; Watson et al., 1984), surprisingly few studies have directly examined individual differences in coping strategies (Table 5).

Earlier studies examined responses to stress, rather than coping style or coping strategies used to deal with stress. Greer and Morris (1975) interviewed 160 women prior to breast biopsy obtaining a history of recent life events and responses to those events. One third of the sample were reported to habitually react to stressors with denial and two thirds habitually faced stress realistically, although details of the interview process are scarce. No differences were detected between breast cancer cases and controls in their responses to stresses.

Schwarz and Geyer (1984) used a psychological instrument designed to measure “action control”, described as an indicator of reactions to stress, in a small limited prospective study of women undergoing biopsy. Among the 76 pre-biopsy women included in a path analysis, and adjusting for age and family history, there was no association between action control and breast cancer risk.

In contrast, Watson et al. (1984) and Pettingale et al. (1984) report significant differences in coping style in a sample of 30 breast cancer patients and 27 controls exposed to experimentally induced stressors in the form of video-taped material. Breast cancer patients scored significantly higher than controls for repressive coping style, as measured by the

Crowne-Marlowe (1960) scale of social desirability.

Wirsching et al. (1985) used an undefined semi-structured interview to rate 56 women undergoing breast biopsy on a number of psychological variables on the basis of explicit statements of the patients. The 18 women later diagnosed with breast cancer were rated as more optimistic, self-sufficient, avoidant of conflict and harmonising in the face of stress. The significance of these findings are difficult to interpret, given the lack of detail of both the interview and rating system, the small sample, multiple statistical comparisons and significant age differences between the groups.

Cooper and Faragher (1992) asked an undefined sample of 2163 women undergoing breast examination to describe methods used to cope with stressful events, creating a checklist of the 36 most commonly reported items based on the Ways of Coping Checklist (Folkman & Lazarus, 1980). Principle component analysis identified five factors, labeled as denial (avoidance strategies), internalise (use internal resources), externalise (maximizing use of social support), emotional outlet (outward expression of emotion such as tears or wishful thinking) and anger (outward expression of emotion via explosive and directed anger). Few differences were detected in their large case-control study after adjusting for age, despite some 130 tests of significance.

Edwards et al. (1990) used a 38 item version of the Ways of Coping Checklist (Folkman & Lazarus, 1980), in a sample of 1,052 women undergoing breast examination. Factor analysis produced four coping factors labeled maladaptive, denial/avoidance, seeking social support and venting. No differences were detected in breast cancer risk for either individual items or the four coping scales. Testing for an interaction effect, additional analysis revealed that coping did not modify the effect of life event stress on breast cancer risk, after adjusting for age and history of breast cancer.

Chen et al. (1995) employed the Coping Strategies Inventory (Tobin, Holroyd, & Reynolds, 1984) in 119 women undergoing biopsy. Contrary to their hypothesis, women who confronted stress by working out a plan to deal with the problem were at higher risk of breast cancer (OR=5.12; CI 1.46-17.89), independent of life events, and adjusted for age, family history, menopausal status, personality, tobacco and alcohol use. This group also reported a significant increase in breast cancer risk for women experiencing a severely threatening life event and confronting stress by focusing on the problem at hand (OR=3.1; CI 1.18-8.19). It is unclear, however, if this interaction was tested on the whole sample and/or in their multivariate model (Chen et al., 1995).

In summary, the evidence for an association between responses to stress or coping style and breast cancer is scant, inconsistent, and insufficient to derive a conclusion. Three of the seven studies described have reported positive findings, offering some support of an association between a repressive coping style and breast cancer, although the quality of some studies limits their credibility. Most intriguing is the result of a small but high quality study that reported confronting stress significantly increased the risk of breast cancer, a result contrary to expectation. Only two studies have considered the interaction of coping style and life event stress on breast cancer risk, one non-significant, and the other reporting a significant interaction between severely threatening events and dealing with stress by confronting it, although this interaction does not appear in the final multivariate model.

Table 5: Studies examining coping styles and breast cancer development

Design / Authors	Measures	Results*
<i>Case-control</i>		
Pettingale et al., 1984	Responses to stress	ns*
Cooper & Faragher, 1992	Ways of Coping Checklist	ns*
<i>Semi-prospective</i>		
Greer & Morris, 1975	Responses to life events	ns*
Schwartz & Geyer, 1984	Action control	ns
Wirsching et al., 1985	Responses to stress	Cancer group optimistic, self-sufficient, avoid conflict, harmonising
Edwards et al., 1990	Ways of Coping Checklist	ns*
Chen et al., 1995	Coping Strategies Inventory	Cancer group confront stress (OR ^a =5.12; 1.5-17.9)*

*age adjusted ^aOdds Ratio

Social Support

Social support is generally defined either structurally in terms of the number of individuals within one's social network, or functionally in terms of the availability of trusted individuals (Henderson, Duncan-Jones, Byrne & Scott, 1980; Bloom, Kang, & Romano, 1991). Most research examining the relationship between social support and breast cancer focuses on the role of support after diagnosis (Bloom, 1982; Funch, 1983; Neuling & Winefield, 1988; Zemore, 1989; Waxler-Morrison, Hislop, Mears, & Kan, 1991; Ell, Nishimoto, Mediansky, Mantell, & Hamovitch, 1992; Spiegel, 1992; Koopman, Hermanson, Diamond, Angell, & Spiegel, 1998; Kornblith, Herndon II, Zuckerman, Viscoli, Horwitz, Cooper, et al., 2001). Only four studies have considered social support in relation to the development of breast cancer, three of them in conjunction with life event stress.

Both Cooper, Davies Cooper, & Faragher (1986) and Edwards et al. (1990) used an unspecified inventory to assess the number of people an individual could turn to in a crisis and their relationship to that person. Cooper et al. (1986) found no differences in the number of supports available; differences in who was available for support were consistent with a confounding effect of age. Edwards et al. (1990) reported no differences in the number or relationship of social supports, nor did social support interact with life event scores in predicting diagnosis. Based on work by Brown and Harris (1978, 1989), Geyer (1991, 1993) proposed social support as modifying the effect of stressful life events. In his study, social support was rated for individual events, although the details are not clearly described. However, high correlation of "lack of social support" with "life events" precluded the inclusion of support in the model. Bleiker et al. (1996) used the Sarason Social Support Questionnaire (Sarason, Levine, Basham, & Sarason, 1983) to quantify the availability and satisfaction with social support and found no association with breast cancer risk.

Summary and Conclusions of Psychosocial Research

In general, the evidence for a relationship between psychosocial factors and breast cancer is weak, at times inconsistent and far from convincing. The strongest predictors are emotional suppression (especially of anger) and severely threatening life events, including the loss of a significant other. Although the available evidence does not support a major role for psychosocial factors in breast cancer development, few studies have been of sufficient quality to state definitively that such a role does not exist.

Few well designed studies report an association between life event stress and breast cancer. The exception are two small studies using the Brown and Harris LEDES that report severely threatening events predict breast cancer risk. These results suggest there may be some threshold for severity of stressors that is critical, rather than the number and type or the cumulative effect of minor stressors. The failure of studies isolating specific life changing events such as death of a spouse and divorce to find an association with breast cancer suggests that this selective approach of assessing life events may not be useful.

There is no evidence that social support, or chronic anxiety or depression affects breast cancer development. Similarly, general personality factors appear to be unrelated to breast cancer risk, the exception being one study showing rationality/antiemotionality slightly increasing breast cancer risk. Ten out of nineteen studies reported that suppression of emotions, particularly anger, is predictive of breast cancer, especially in younger women; however many of these had design flaws and no attempt has been made to integrate repression with life event data.

A significant weakness in this area of research is the essentially atheoretical approach to examining clearly interrelated psychosocial concepts in a multi-factorial disease such as breast cancer. Progression in the understanding of the role of psychosocial variables in breast cancer development and the mechanisms by which they exert their effects, requires the guidance of a model that acknowledges links with the endocrine, nervous and immune systems. Sufficient power to test such a model requires sample sizes considerably larger than most studies to date, essential for the interaction between variables to be explored, rather than simply measured concurrently. With little data available on the way in which the various independent but clearly interrelated psychosocial variables of life event stress, coping style, social support, affect and personality interact in relation to breast cancer development, examining these interactions would be a useful starting point.

Methodological Considerations

To some extent, inconsistencies reported in this field of research can be attributed to methodological limitations of many studies, although more recent studies have improved methodology. To date, many studies have reported on small sample sizes and convenience samples with indeterminate bias. Cases and controls from different sources were sometimes combined. Comparison groups were frequently selected from different source populations than the cases, making accurate data interpretation impossible. Data were rarely adequately adjusted for potential confounders, in particular age and few studies consider other well established risk factors. Multivariate analysis estimating the independent effect of psychosocial factors on breast cancer risk is rare, although more recent studies have improved methodology. It is therefore not surprising that this field of research has yielded inconsistent findings. Some of these limitations in design, sampling and measurement are discussed further below.

Atheoretical Approach

Few studies in this area have been guided by theoretical considerations when examining the relationship between psychosocial variables and breast cancer. Although theories such as the Cancer Prone Personality have grown from an attempt to explain the conflicting results of multiple studies, little research has been conducted as a direct attempt to test clearly defined theoretically based hypotheses. One exception is the Geyer (1991, 1993) study (described in detail in life event stress section) examining life event stress, conceptualized within a model of stress encompassing the influence of vulnerability factors and outlining a clear set of hypotheses to be tested.

The essentially atheoretical approach to examining clearly interrelated psychosocial concepts in a multi-factorial disease such as breast cancer is a significant weakness. Progression in the understanding of the role of psychosocial variables in breast cancer development and the mechanisms by which they exert their effects, requires the guidance of a model, which acknowledges links with the endocrine, nervous, and immune systems. Although the existing evidence linking psychosocial factors to breast cancer is inconclusive, theories proposed in an attempt to assimilate common themes from empirical findings regarding psychosocial variable and cancer, such as Greer and Watson (1985), Temoshok (1987) or Hilakivi-Clarke et al. (1993), have been rarely utilised or tested.

Research Design

While a prospective design is the ideal approach, averting many of the difficulties associated with the potential influence of a cancer diagnosis on retrospective reporting, the large sample sizes and prolonged time frame required to ensure adequate power, precludes its widespread use. The majority of studies to date have a limited prospective or case-control design. A limited prospective study is one in which the number of subjects required for analysis is limited by selecting those known to be at risk, such as women undergoing breast examination or breast biopsy. These studies are usually hospital-based with attendant sampling bias. Their strength, however, is in their capacity to evaluate psychological variables in subjects prior to confirmation of breast disease under similar conditions. Nevertheless the *a priori* probability of being diagnosed with breast cancer may not be the same for all participants, with some subjects correctly predicting their diagnosis prior to results being confirmed, particularly among those who have undergone examination prior to referral (Scherg, 1987).

Awareness of diagnosis introduces the potential for over-reporting of psychosocial variables such as life event stress in an attempt to explain their illness; alternatively repression or denial may result in minimization (Barraclough, 1996; Burke, 1997). Differences in anticipation of diagnosis have been found to influence self-report psychosocial data, and controlling for anticipation of diagnosis reduced previously reported differences between cases and controls (Scherg, 1987). Consistent with the claimed influence of "awareness" of diagnosis is the finding that post diagnosis repression and defensiveness increases (Kreitler et al., 1993).

The impact of suspected knowledge of diagnosis on the reporting of life event stress is less clear. Geyer (1992) found that women who correctly suspected their breast cancer diagnosis were more depressed prior to diagnosis; depression was not, however, associated with the reporting of life events, refuting the notion of recall bias. Despite the superiority of a limited prospective design in reducing biases, care is required to minimizing the likelihood of subjects suspecting their diagnosis ahead of time and to ensure all subjects are assessed under identical conditions.

Control Group

Related to the issue of design is the choice of an appropriate comparison group. While subjects with benign disease may undergo the same process of testing to confirm their diagnosis as those with breast cancer and thus share the same apprehensiveness, women with benign breast disease are also at greater ultimate risk of developing breast cancer than women without breast disease (Kelsey, 1993). However, the suggestion that a general population sample would be a more appropriate comparison than women with benign breast disease is also problematic. Differences in conditions of testing between groups may lead to any group differences being erroneously excessive (Greer, 1978). To guard against the potential biases that may be introduced via sampling, the source of both cases and controls need to be clearly identified and when collected from varying sources their data separately reported.

Confounders

A number of potential confounders in the form of well established risk factors ideally need to be considered in design and/or analyses. These include age, age at menarche, age at first full-term pregnancy, age at menopause, family history, and body mass index. Many studies have failed to adequately consider epidemiological factors that may confound results of psychological associations with cancer risk (Cella & Holland, 1988). The pathways by which psychological factors may influence breast cancer development are unclear, and may be direct by affecting the immune, nervous or endocrine system or indirect by behavioural means, such as diet, exercise or sleep. As a number of the psychosocial variables being examined in relation to developing breast cancer are also associated with established risk factors for the disease, the potential problem of confounding becomes apparent (Cella & Holland, 1988).

The most common difficulty is managing significant age differences between breast cancer cases and controls. While some studies attempt to adjust for age differences statistically, it is not always successful (McGee et al., 1996). This is evident in the Cooper et al. (1993) study where the significant group differences in the type and severity of life events were reported to increase the risk of breast cancer (detailed in life event stress section). However, the pattern of younger women experiencing more events and older women experiencing fewer events but of a more serious nature, such as illness and bereavement, is well documented as being related with age (George, 1989).

A family history of breast cancer, or more specifically the development of breast cancer in a

mother, sibling or child (or their death) is a significant life event. In these situations family history will be a major confounder.

Time Frame

Uncertainty as to the length of time between cancer initiation and clinical manifestation potentially complicates examination of psychosocial variables in relation to the onset of breast cancer. This issue is of particular importance in attributing a causal role for life event stress that occurs after the initiation of cancer. While the latent period of breast cancer development is estimated to be up to 18 years (Fox, 1978; Friberg & Mattson, 1997), the proposed relationship between life event stress and breast cancer appears to be associated with promoting tumour growth, rather than tumour initiation. Unless there is a critical time in tumour development in which the impact of stress is greater, presumably the longer the time frame studied, the stronger the association between life events and breast cancer.

Most studies have recorded life event stress within two to five years prior to clinical presentation. Recording of life events over extended time frames introduces a potential for error in recall details. The fall-off in reporting of events using the checklist approach rapidly decreases for periods greater than six months (Funch & Marshall, 1984). Recall of events via interview, such as the Life Event and Difficulties Schedule, however, has been reported as reliable for up to ten years (Brown & Harris, 1989). Methods of measuring life event stress are discussed below.

Measuring Stress

A variety of approaches have been used in this area of research to assess life event stress, with unequal success. The life event inventory approach used most often has had mixed and at times contradictory results. A major limitation of the inventory approach is its inability to distinguish between events of a trivial nature (Paykel 1983). However, the suggestion that life event stress may only be adequately examined by population record studies, comparing events of equal magnitude, avoiding contamination by recall and investigator related biases, is overly simplistic (Barraclough, 1996). Restricting the indication of stress to specific events such as widowhood and/or divorce does not allow antecedent factors such as the illness leading to death, or the degree of attachment to be included (Jones, Goldblatt, & Leon, 1984).

The LEDS provides a comprehensive approach of assessing life event stress, based on solid theoretical model acknowledging interactions with other psychosocial variables, and is

compatible with psychobiological models. It has already produced some consistency in results in the area of breast cancer development, and in other areas of research (Brown, 1981; Brown, Adler, & Bifulco, 1988; Tennant, Langeluddecke, Fulcher, & Wilby, 1988; Brown & Harris, 1989; Bennett, Beaurepaire, Langeluddecke, Kellow, & Tennant, 1991; Tennant, Palmer, Langeluddecke & Jones, Nelson, 1994; Tennant, 1994; Bennett, Tennant, Piesse, Badcock, & Kellow, 1998b).

Research Aims

The study presented in this thesis aims to examine the interactions between specific psychosocial variables and their role in the development of breast cancer. The psychosocial variables of interest are life event stress, personality, coping style, affect and social support.

The Hilakivi-Clarke et al. (1993) model provides a comprehensive approach for examining psychosocial variables within a model of stress and illness. The model proposes that the presence of stress itself is not the crucial factor in cancer development, rather the interaction between stressors, personality, and social support that alters an individual's ability to cope which in turn mediates breast cancer risk via alterations in neuroendocrine and immune functioning (Hilakivi-Clarke et al., 1993). This model not only allows, but also demands, that the interactive effects of various psychosocial variables be examined.

Other theories that have developed from an attempt to assimilate some of the themes from empirical findings regarding psychosocial variable and cancer are also of interest. Greer and Watson (1985) focus on Type C or cancer prone behaviour, possibly linked to the degree of emotional suppression and having an associated biological response. The model assumes that whatever the initial cause of cancer, tumour growth may be promoted by both the intrinsic properties of the tumour and homeostatic controls regulating cell growth and function. With no logical reason to exclude them, psychological factors are postulated as a part of the homeostatic control system. They hypothesize that in certain individuals, psychological factors contribute to cancer growth, via their interaction with biological systems. The central component of Type C behaviour is suppression of emotional responses, particularly when angry, and this behaviour pattern is proposed to increase autonomic arousal during stress.

Temoshok (1987) describes a "Cancer Prone Personality", predisposing some individuals to develop cancer and progress more quickly through its stages. The major components of the personality profile are specific personality traits of stoicism, niceness, perfectionism,

sociability, conventionality and rigid defensive controls; difficulty in expressing emotions and a tendency toward helplessness/hopelessness. The key feature of the Greer and Watson (1985) Cancer Prone Behaviour, emotional suppression, is incorporated in the Temoshok theory.

Although these models focus on different aspects of the psychosocial data, they are not incompatible. Specific features of the Cancer Prone Personality or Coping Style can be tested within the Hilakivi-Clarke et al. (1993) model. A number of specific hypotheses are proposed on the basis of past empirical research and tested according to the model proposed by Hilakivi-Clarke et al. (1993) displayed in Figure 1.

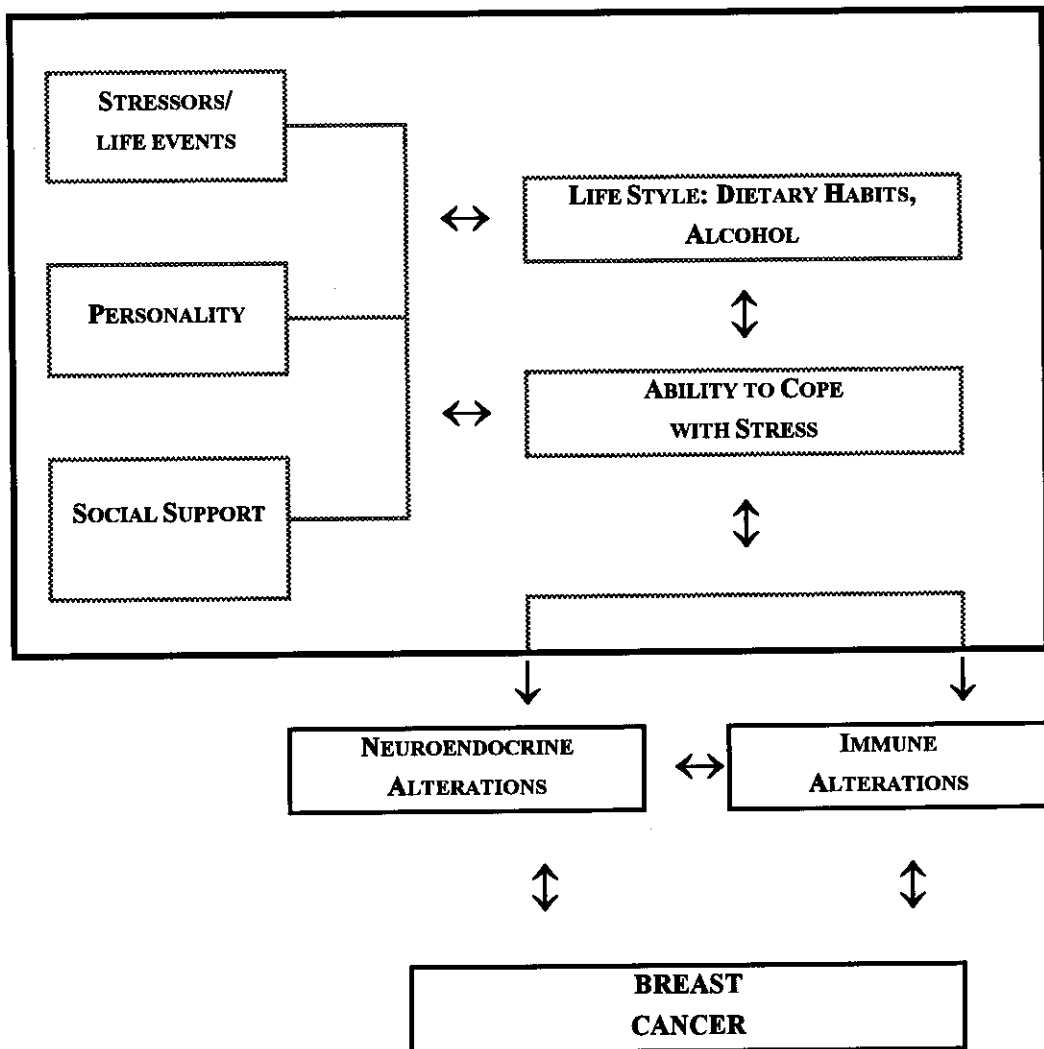


Figure 1: Hilakivi-Clarke et al. (1993) model of psychosocial factors in the development of breast cancer

While the Hilakivi-Clarke et al. (1993) model includes proposed neurohumoral and immune pathways via which psychosocial variables may exert their influence, an attempt to investigate these is beyond the scope of this thesis. The first step required, and the aim of the current study, is to ascertain whether psychosocial variables are associated with breast cancer development. This question is important, not only to clarify clinical and empirical observations, and community belief that stress or depression is a factor in the development of cancer, but because if such a link does exist, an opportunity may exist to intervene to reduce the risk or prevent the development of breast cancer.

In designing the study, particular effort has been made to address some of the methodological limitations identified in past research. Therefore, a semi-prospective design is employed, sampling from a community-based breast screening population sourced from one geographical and social area. Women with existing breast cancer or with breast symptoms prompting screening are excluded. Multiple psychosocial variables are examined simultaneously, using widely validated and reliable measures, including the Life Events and Difficulties Schedule to assess life event stress. A large sample size ensures adequate statistical power to test for the interaction between the psychosocial variables. Established risk factor variables are considered as confounding variables.

The study examines individual psychosocial variables in two related but separate domains, before their interrelationships are examined. Firstly, the psychological characteristics proposed by Temoshok's (1987) Cancer Prone Personality and Greer and Watson's (1985) Type C behaviour are examined as independent risk factors for breast cancer development. These characteristics include suppression or control for negative emotions, defense style or emotion focused coping style, locus of control or behavioural focused coping style, self esteem or trait depression, trait anxiety, state anxiety and depression. Secondly, on the basis of existing empirical evidence life event stress is examined as independent risk factors for breast cancer development. Thirdly, guided by the Hilakivi-Clarke et al. (1993) model, the interaction between, life event stress, coping style, emotional control, and social support, are examined in relation to breast cancer diagnosis.

Hypotheses

The hypotheses to be tested are:

Hypothesis 1: Particular trait personality variables are more common in women with breast cancer than women without cancer. Specifically:

- Type C Personality style is more common in breast cancer subjects, reflected by a less mature coping style, lower perceptions of personal control;
- Cancer subjects have more difficulty in expression of negative emotions, particularly anger, and will score higher on emotional expression directed inwards, higher control of emotions and lower external expression of emotions;
- A tendency toward helplessness or hopelessness is more common in cancer subjects, reflected by lower self esteem, lower trait anxiety, lower state anxiety and more common state depression.

Hypothesis 2: Life event stress, above a critical threshold of severity, increases the likelihood of breast cancer development. Specifically:

- life events or ongoing (chronic) difficulties independently rated as highly or severely threatening in nature will increase the risk of breast cancer development;
- life events or ongoing (chronic) difficulties independently rated at lower levels of threat have no independent effect on breast cancer risk.

Hypothesis 3: A more mature defense style acts as a buffer against the negative influence of life event stress on the risk of developing breast cancer. Specifically:

- More frequent use of a mature defense style will reduce the impact of life event stress on the risk of developing breast cancer;
- Less frequent use of a mature defense style will increase the impact of life event stress on the risk of developing breast cancer.

Hypothesis 4: Emotion suppression and control affects the impact of life event stress on the risk of developing breast cancer. Specifically:

- A tendency toward inward expression of emotions or higher levels of emotional control will increase the impact of negative life event stress on the risk of developing breast cancer;
- A tendency toward outward expression of emotions will reduce the impact of negative life event stress on the development of breast cancer.

Hypothesis 5: Social support is a vulnerability factor that moderates the impact of highly threatening or severely threatening life events and difficulties on the risk of developing breast cancer. Specifically:

- Good social support will buffer the impact of life event stress on the risk of developing breast cancer;
- Poor or absent social support will increase the impact of life event stress on the risk of developing breast cancer.

Presentation of Thesis

The study conducted for this thesis is presented as a series of published articles. Chapter 2 describes the research design and methodology of the study. Chapter 3 contains the first paper that presents data related to established risk factors for developing breast cancer. Chapter 4 contains the second paper presenting the data examining the trait characteristics of the Cancer Prone Personality. Chapter 5 contains the third paper presenting the data examining life event stress as an independent risk factor for developing breast cancer, and the interactions between life event stress, coping style, emotional expression and control, and social support, in relation to the development of breast cancer. Chapter 6 summarizes the result of the study, discusses limitations of the study and suggestions for future research.

CHAPTER 2: METHOD

Sample and Study Design

A semi-prospective design was employed enabling subjects to be assessed under similar conditions and avoiding the potential influence of a cancer diagnosis on the assessment of psychological data. The target population was a community based breast screening program. As part of the National Breast Screening Program, biennial mammography is recommended for women over the age of 50 years. BreastScreen NSW provides a standardized screening free of charge to all women over the age of 40 years. The screening program also ensured a community sample rather than a hospital or clinic sample, allowing a "normal" cohort for comparison, well matched geographically and socioeconomically and minimizing self-selection bias. Women attending screening were asymptomatic and therefore unlikely to "know" ahead of time they had cancer.

Participants

Women were recruited from the assessment clinics of the Northern Sydney and Lower Central Coast Breast Screening Program in New South Wales, Australia. These women had attended for routine breast mammography screening and were recalled for further testing on radiological grounds. Women aged between 50-69 years of age are actively recruited for screening from the electoral rolls and formed the bulk of the sample. Free mammograms, however, are available for all women over age 40 without referral. Approximately 10% of women screened during 1994-1997 were recalled for further testing. Ethics approval was given for this study from the University of Sydney and the Royal North Shore Hospital Medical Research Committee.

The inclusion criteria were:

- attendance for further assessment following routine breast screening;
- age 40 years or older;
- adequate command of the English language to complete questionnaire and interview.

The exclusion criteria were:

- a prior personal history of breast cancer;
- breast symptoms prompting screening;
- knowledge of test results;
- physical or psychiatric impairment inhibiting completion of questionnaire and/or interview

Procedure

On arrival at the clinic, women were provided with a written information leaflet, informing them of the study and inviting them to participate in research titled "Lifestyle Factors and Breast Health" (Appendix I). At the request of staff at the screening centre, direct reference to breast cancer was avoided, and "breast health" was used in its place.

Women spent between two to five hours at the clinic during which time further mammography, ultrasound, physical examination and fine needle biopsy were performed as indicated. Preliminary results were usually available by the end of the clinic. Between tests, women returned to a central waiting room. Utilising the waiting time, the women were individually invited to participate in the research. Participation involved a self-administered questionnaire taking approximately 25 minutes to complete and, for some, an interview. Women who required a needle biopsy to confirm diagnosis were approached for an interview once written consent for biopsy procedure was given and before test results were available. Figure 2 summarises the diagnostic procedures undertaken by the breast screening assessment clinic, the diagnostic categories, and the components of the psychosocial study that subjects were eligible to participate in. Written consent for participating in the research was obtained from all participants (Appendix II).

Measures

Questionnaire Measures

Part 1: Demographic and Somatic Risk Factors

Part one of the self-report questionnaire consisted of questions related to demographic variables and somatic risk factors (Appendix III). The demographic variables examined included age, marital status, level of education, past and present type of employment. Somatic variables examined included: family history of breast cancer; history of benign breast disease; parity; age at birth of first child; menopausal status; history of oral contraceptive use and current use of hormone replacement therapy; height and weight;

current alcohol consumption; past and present cigarette consumption.

<i>Breast Screening Assessment Clinic</i>		<i>Psychosocial Study</i>	
DIAGNOSTIC PROCEDURES	DIAGNOSIS/ STUDY GROUP	RISK FACTOR & PSYCHOSOCIAL QUESTIONNAIRE	LIFE EVENT & SOCIAL SUPPORT INTERVIEW
MAMMOGRAPHY &/OR ULTRASOUND &/OR PHYSICAL EXAMINATION → ↓	NORMAL BREAST TISSUE	✓	
	BENIGN/CYSTIC BREAST DISEASE		
↓ BIOPSY → ↓	BENIGN BREAST DISEASE	✓	✓
	BREAST CANCER		

Figure 2: Diagnostic procedures, diagnostic categories, study groups and components

Many of these questions related to distant events and a pilot study of this section of the questionnaire prompted the inclusion of a series of time frames or age ranges for subjects to select in response to these questions. This method of response was considered less taxing to complete and reduced completion time.

Part 2: Psychosocial Questionnaires

Part two of the questionnaire contained a number of psychosocial measures. These self-administered questionnaires were employed to assess three domains of Temoshok's (1987) Cancer Prone Personality:

- personality dimensions of defense style, locus of control of behaviour and self-esteem;
- emotional expression and control; and
- affect dimensions of trait anxiety, state anxiety and state depression.

The questionnaire measures used in this study are summarized in Table 6 and each questionnaire is provided in Appendix IV-IX. Each measure is described and discussed below.

Table 6: Summary of psychosocial questionnaires

Dimensions	Questionnaires and Factors
<i>Personality</i>	Defense Style Questionnaire (DSQ-40) (Andrews et al., 1993)
	Mature
	Immature
	Neurotic
	Locus of Control of Behaviour (LCB) (Craig, et al., 1984)
	Self-Esteem (Rosenberg, 1965)
<i>Emotional Expression and Control</i>	Emotional Expression & Control (EEC) (Bleiker et al., 1993)
	Emotional Expression-In
	Emotional Expression-Out
	Emotional Control
<i>Affect</i>	Trait Anxiety (Spielberger, et al., 1979)
	Hospital Anxiety & Depression (Zigmond & Snaith, 1983)
	State Anxiety
	State Depression

Defense Style

Defense mechanisms are “patterns of feelings, thoughts, or behaviours that are relatively involuntary and arise in response to perceptions of psychic danger. They are designed to hide or to alleviate the conflict or stressors that give rise to anxiety” (American Psychiatric Association, 1987). The Defense Style Questionnaire (DSQ-40) was employed to assess emotion-focused coping strategies (Andrews, Singh, & Bond, 1993). This 40-item self-report measure is designed to identify defense styles as defined by DSM-111-R.

The DSQ-40 yields scores for twenty individual defense mechanisms that constitute three higher order factor scores: mature defense style, neurotic defense style and immature defense style. Mature defense style comprises of four defense mechanisms, namely sublimation, humour, anticipation and suppression. Neurotic defense style embraces the defense mechanisms of undoing, pseudo-altruism, idealization and reaction formation. Immature defense style comprises of twelve defense mechanisms: projection, passive aggression, acting out, isolation, devaluation, autistic fantasy, denial, displacement, dissociation, splitting, rationalization and somatization.

Defense style is presumed to be a personality trait, stable over time and situation. The DSQ-40 has demonstrated internal consistency and temporal stability reflecting a trait measure. Cronbach α coefficients are 0.68, 0.58 and 0.80 for mature, neurotic and immature factors respectively. Test-retest correlations are 0.75, 0.78 and 0.85 for mature, neurotic and immature factors respectively. Construct validity has been confirmed by the capacity of the scale to distinguish between patients with anxiety disorders and controls. No gender differences are evident, but there is a tendency for increasing use of a mature defense style with age.

Individual defense mechanisms are represented by two items, scored on a likert scale from 1 (strongly disagree) to 9 (strongly agree). Scores for individual defense mechanisms are calculated by averaging the item scores, with a higher score reflecting greater use of a defense. Factor scores are then calculated by averaging the defense mechanism scores. Normative Australian data are available for the scale. The DSQ-40 has been useful in studies employing a stress and coping model in relation to physical and emotional health, including ischaemic heart disease (Tennant, Mihailidou, Scott, Smith, Kellow, Jones, et al., 1994), functional gut disorders (Bennett, Piesse, Palmer, Badcock, Tennant, & Kellow, 1998a), and psychological morbidity following disasters (Lewin, Carr, & Webster, 1998).

Locus of Control of Behaviour

Locus of Control is the perceived relationship between external events and an individual's behaviour, and the extent to which events are perceived to be under personal control (Craig, Franklin, & Andrews, 1984). An internal locus of control reflects an individual's belief that the relationship is attributed to personal effort, whereas an external locus of control attributes the relationship to luck or powerful others. The Locus of Control of Behaviour (LCB) scale was selected as a measure of problem-focused coping strategies (Craig et al., 1984).

The 14-item version of the LCB was employed, the original version modified by the removal of three items directly related to clinical anxiety (Andrews, 1990). Designed to assess perceived control over behaviour, this measure yields a single factor reflecting internal/external locus of control of behaviour. Construct validity of the single factor has been demonstrated in normal and clinical anxiety samples. LCB scores are independent of age and social desirability. The scale has internal consistency ($\alpha=0.79$) and the test-retest reliability at six months is 0.73.

Each item is scored on a likert scale from 0 (strongly disagree) to 5 (strongly agree). Six of the items are reverse scored prior to summing the 14 item scores to obtain a total score. A higher score indicates an external locus of control and a low score indicates an internal locus of control. Normative Australian data are available for the 14-item version of the LCB. This scale has been used in distinguishing different coping styles in patients with spinal cord injury (Hancock, Craig, Tennant, & Chang, 1993), in the study of voluntary blood pressure control (Hunyor, Bartrop, Craig, Cejnar, Liggins, Henderson, et al., 1991), stuttering (Craig et al., 1984) and myocardial ischaemia (Tennant et al., 1994).

Self-Esteem

Self-esteem refers to feelings of self worth, with high self-esteem reflecting feelings of being "good enough" and low self-esteem reflecting feelings of self-dissatisfaction or self-contempt (Rosenberg, 1965). Rosenberg's Self-Esteem Scale was used as a measure of trait depression (Rosenberg, 1965). This 10-item scale measures the self-acceptance aspect of self-esteem. Originally developed for use with adolescence, the Rosenberg Self-Esteem Scale is the most widely used measure of global self-esteem and the items on this instrument reflect a unidimensional factor (Shevlin, 1995).

Rosenberg's Self-Esteem scale has demonstrated internal consistency ($\alpha=0.92$) and a test-retest reliability of 0.85 over two weeks. Validity of the scale has been demonstrated by correlation with other measures of self-esteem, discrimination of depressed and non-

depressed subjects, and relationship to social and interpersonal consequences such as shyness, anxiety, participation and leadership (Rosenberg, 1965).

Items are rated on a 4-point likert scale ranging from 1 (strongly agree) to 4 (strongly disagree). Five items are reverse scored prior to total scores being calculated by summation of individual item scores. Total Self-Esteem scores range from 10-40, with lower scores reflecting higher self-esteem. This scale has been widely used in women with breast cancer and benign breast disease controls, both before and after diagnosis, as a predictor of psychological outcome and quality of life, and as a measure of coping with a cancer diagnosis (Curbow & Somerfield, 1991).

Emotional Expression and Control

The Emotional Expression and Control scale (EEC) was selected to assess the expression and control of negative emotions (Bleiker, van der Ploeg, Hendriks, Leer, & Kleijn, 1993). Emotional expression and control reflects the extent to which an individual reports controlling or expressing their emotions (Watson & Greer, 1983). Developed from the Watson and Greer (1983) measure of emotional control, the focus is on anger, anxiety and depression, and incorporates Spielberger's (1988) concept of anger expression which distinguishes between three components of anger expression: anger-in, anger-out and anger-control.

This 18-item self-report measure yields scores on three factors: emotional expression-in (EEI) which indicates expression of emotions to one's self; emotional expression-out (EEO) indicating expression of emotions toward others, and emotional control (EC) reflecting the extent of control over emotions (Bleiker et al., 1993). Each factor consists of three sub-scales that allow anger, anxiety and depression to be individually examined.

The relatively new scale was developed in the Netherlands on a sample of women participating in the population based breast screening program. Reliability has been demonstrated on this sample with Cronbach's α coefficients of 0.79, 0.86 and 0.86 for EEI, EEO and EC respectively. Test-retest reliability after two years was 0.65, 0.67 and 0.63 for EEI, EEO and EC respectively. Emotional Control is negatively correlated with trait anger, anxiety and depression indicating validity. Bleiker et al. (1993) reported significantly less emotional control in 112 newly diagnosed breast cancer patients compared to healthy controls, supporting the clinical relevance of the scale.

Items are scored on a 4-point likert scale assessing how respondents usually react, with

scores ranging from 1 (almost never) to 4 (almost always). Factor scores are the sum of individual item scores. Scores for the three factors range from 6-24 with a higher score reflecting more emotional expression in, more emotional expression out or more emotional control. Emotional Expression-Out is negatively correlated with age and Emotional Control is positively associated with age. Emotional Expression-Out is negatively correlated with Emotional Expression-In (-0.18) and Emotional Control (-0.23). Emotional Expression-In and Emotional Control are not significantly correlated.

The EEC scale has been used to study the effect of a breast cancer diagnosis on self-report personality measures (Bleiker et al., 1995), and to examine personality variables as risk factors for breast cancer (Bleiker et al., 1996). There are no normative Australian data available for this scale; however, the scale was developed on women undergoing routine breast screening in the Netherlands and comparable in age to the current study (Bleiker et al., 1993).

Trait Anxiety

Trait anxiety refers to a relatively stable emotional characteristic of anxiety proneness (Spielberger, Gorsuch, & Lushene, 1970). The 10-item sub-scale for trait anxiety from the State-Trait Personality Inventory (STPI) was selected to assess trait anxiety (Spielberger, Jacobs, Crane, Russell, Westberry, Barker, et al., 1979). Items refer to how a person generally feels and are rated on a four point likert scale from 1 (almost never) to 4 (almost always). Three items are reverse scored before item scores are summated for a total score. Total scores range from 10-40 with a higher score reflecting higher trait anxiety. The sub-scale is internally consistent ($\alpha=0.92$) and reliable (0.81) (Jacobs, 1988).

The trait anxiety sub-scale of the STPI has been used in the study of breast cancer (Pettingale et al., 1984), although not as widely as Spielberger et al's (1970) 20-item State-Trait Anxiety Inventory (STAI) (Morris et al., 1981; Scott, 1983; Pettingale et al., 1984; Levy, Herberman, Lippman, & d'Angelo, 1987; Neuhaus, Zok, Gohring, & Scharl, 1994). The 10-item trait anxiety sub-scale from the STPI was selected in preference to STAI primarily for its brevity.

State Anxiety and Depression

The Hospital Anxiety and Depression scale (HAD) (Zigmond & Snaith, 1983) was chosen to assess state anxiety and state depression. This measure was developed to assess clinically significant state anxiety and depression in hospital outpatients. Consisting of 14 items, seven for depression and seven for anxiety, any references to somatic symptoms that may be influenced by physical illness have been deliberately excluded. The concepts of anxiety and

depression in this measure are clearly distinguished.

This instrument has been widely validated and found to reliably identify clinically significant anxiety and depression as well as accurately measure the severity of both (Alyard, 1987). Cronbach α coefficients for cancer patients are high, $\alpha=0.93$ for anxiety and $\alpha=0.90$ for depression (Moorey, 1991). Correlations with clinician's ratings are 0.70 for depression and 0.74 for anxiety (Zigmond & Snaith, 1983).

Items refer to how the respondent has been feeling in the last week. Scoring of items range from (0) not at all to (3) mostly, definitely or very much. Items on each sub-scale are summed for a total score. A total score of 11 or more on either scale represents clinically significant mood disturbance. A score between 8 and 10 on either scale represents mild or borderline mood disturbance. The HAD has been widely used in outpatient clinics, hospitals and with breast cancer (Maraste, Brandt, Olsson, & Ryde-Brandt, 1992; Jellicic, Bonke, & Millar, 1993; Ellman & Thomas, 1995; Millar, Jellicic, Bonke, & Asbury, 1995).

Interview Measures

Life Events and Difficulties Schedule

The Life Events and Difficulties Schedule (LEDS) was used to assess the severity of life stressors (Brown & Harris, 1978). The interview is based on the theory that social and environmental changes (or anticipation of change) that threaten the most strongly held emotional commitments are the basis for the experience of severe stress (Wethington, et al., 1997). Stressors identified at interview are independently rated for severity of contextual threat with reference to relevant personal circumstances, but excluding the subjective reaction and emotional response to the stressor.

The interview consists of a series of questions covering a wide variety of stressors, including illness, bereavement, role relationship, crises or news, employment, finances, housing and marital relations. Subjects are encouraged to identify other sources of stressors not directly covered by the interview questions. Guidelines for probing positive responses are provided by the interview schedule, while allowing latitude for more detailed probing of responses to ascertain the likely severity of the emotional impact of a stressor (Wethington et al., 1997). The interview format is displayed in Appendix X.

Each event and difficulty is probed for details such as who was involved, the relationship of

the subject to the person involved (husband, child, friend, acquaintance), the duration of the stressor, the outcome, any changes that resulted from the event, the expectedness and the degree of control over the stressor, for example redundancy versus retrenchment. The timing of the event or difficulty in relation to other stressors is ascertained as accurately as possible.

The aim of the interview is to produce a clinical vignette, providing the context in which stressors occurred. This background information, such as age, marital status, family members and members of the current household and occupational status, is utilized in the rating of stressors. A narrative of each event and difficulty is constructed with reference to the circumstances in which it occurred but without reference to the emotional reaction to the stressor.

Central to the LEDS method of assessing life event stress is the rating of contextual threat. Contextual ratings of threat are based on the "likely response of an average person to an event occurring in the context of a particular set of biographical circumstances" (Brown & Harris, 1989, p24). These ratings therefore reflect what most people would be expected to feel as a result of an event or difficulty, rather than how an individual respondent reports to have felt.

For acute events, ratings of contextual threat are made at two points in time, allowing the immediate impact as well as the longer term implications to be reflected. Short-term threat relates to the day of impact, whereas long-term threat reflects the threat implied one week after its occurrence. Chronic difficulties are given only one rating of contextual threat, reflecting the ongoing level of threat.

Guidelines for rating the degree of severity of threat have been developed and documented for specific types of stressors and are contained in dictionaries produced by the authors. Examples of stressor ratings are provided according to the category of stressor, and the degree of severity, and outline the type and nature of information required to establish contextual ratings for a stressor (Wethington et al., 1997). This method avoids the contamination of subjective appraisal that is likely to be affected by the mood, personality, outcome of the stressor and cognitive restructuring.

Ratings are made by independent assessors, blind to both disease status and emotional response to the stressor. Each stressor is classified according to the following criteria:

Acute Event or Chronic Difficulty

A stressor is classified as an acute event if the duration of the event was less than six months, although the impact or consequences may be ongoing. Stressors that are continue for at least six months after onset are classified as chronic difficulties.

Category of Stressor

Each stressor is classified according to the nature of the stressor. Categories distinguished are: health of self, health of other, death, role relationship or interaction, crisis or news, employment, financial, marital. Stressors that involve more than one of these domains are classified according to the dominant category. Stressors not falling into one of these categories were classified as miscellaneous.

Dimensions of Stress

Acute events are given two ratings, one for 'short term threat' reflecting immediate impact and one for 'long term threat' reflecting the ongoing impact a week after the occurrence. Chronic difficulties are rated for ongoing 'threat'.

Severity of Stressor

Each stressor is rated on a scale from 0-5 (0=none, 1=mild, 2=moderate, 3=high, 4=severe, 5=extreme) for severity of impact. This range of severity ratings expands the original 4-point scale described by the authors by the addition of an extra point at each end of the range. The essence of the original 4-point rating scale was maintained as per the authors' definitions. The new categories used in this study were created for the following specific circumstances.

Firstly, at the low end of the scale, events such as a holiday or special celebrations were able to be included without necessarily allocating threat. Secondly, at the high end of the scale, extraordinary events or difficulties were able to be distinguished from severe but more common or expected events. Some examples of events rated at different levels of long term threat are provided in Appendix XI.

The original interview was maintained and has been demonstrated to be a reliable and valid method of collecting accurate information of events. The inclusion and exclusion criteria for events were maintained. The original rating categories were maintained and the new categories able to be combined with its nearest neighbour to obtain the original scale. The effect of expanding the rating scale for threat on the validity of the LEDS was assumed to be minimal and the Kappa coefficient for ratings of long term threat for this study was 0.92.

The LEDS is the most widely used interview assessment of life event stress and has been used in community samples and hospital samples, in the elderly, in people with psychiatric illness including schizophrenia, anxiety and depression, in studies of appendectomy, abdominal pain, gut disorders, heart disease, multiple sclerosis and breast cancer (Tennant, Langeluddecke, Fulcher, & Wilby, 1988; Brown & Harris, 1989; Bennett, et al., 1991; Geyer, 1991; Barraclough, Pinder, Cruddas, Osmond, Taylor, & Perry, 1992; Tennant, Palmer, Langeluddecke, Jones, & Nelson, 1994; Chen et al., 1995; Bennett, et al., 1998a; Bennett, et al., 1998b; Protheroe et al., 1999).

Reliability in the reporting of stressors is satisfactory, with 79 percent agreement between subjects and their relatives of events occurring within a 12 month period (Brown & Harris, 1978). There is also high agreement for severity ratings of events, with the same events reported by subjects and their relatives concurring in 91 percent of cases (Brown & Harris, 1989). Inter-rater reliability for contextual threat has been demonstrated to be consistently high, with agreement between nine individual raters for long-term threat between 70 and 90 percent for variously experienced raters (Tennant et al., 1979), while Brown and Harris (1989) report correlations of above 0.9.

The effectiveness of the LEDS method in promoting recall of life events over extended periods of time has been demonstrated. Over a period of 12 months, the fall-off in reporting of events is small and has been validated by cross-informant agreement (Brown & Harris, 1978). The fall-off of reporting of events over a ten year period was 5.8 percent and similar for both severe and non-severe events. The rate of fall-off for difficulties over a ten year period is similar at 5.1 percent.

Interview Schedule for Social Interaction

An abbreviated version of the Interview Schedule for Social Interaction (ISSI) was appended to the LEDS interview, probing the availability and quality of social supports (Henderson et al., 1980). This interview-based approach for assessing social support has established validity and reliability (Henderson et al., 1980). The sub-scales of the ISSI are internally consistent ($\alpha=0.67-0.81$), and test-retest correlations for the sub-scales are between 0.74-0.88 after four months.

Subjects were asked to provide a description of and an example of support from an intimate partner (if present) and a non-intimate support (Appendix XII). A vignette of each subject's social support network and the quality of intimate and non-intimate support, for both emotional and instrumental support, were presented to an independent rater for scoring.

Ratings for both emotional and instrumental support were made to reflect availability and quality of identified supports. A three point scale was used to differentiate adequacy of support; a 'good' rating reflected support generally available and comforting; an 'adequate' rating reflected support available but with some form of restriction and a 'poor' rating reflected limited availability and/or uncertainty in the quality of support.

Subjective appraisal of support was also recorded using a three point scale (poor, adequate, good) and subjective evaluation of change in support during the past two years was also recorded (better, worse, no change).

Diagnosis of Breast Disease

Results of the assessment procedure were obtained from the breast screening records. A breast cancer diagnosis was confirmed by histopathological results of breast tissue biopsy. Subjects who underwent biopsy and for whom no cancer was detected were classified as benign controls. Non-biopsy subjects were classified according to the final diagnosis given by the radiologist (normal tissue or benign breast disease with included cysts).

The Sample

During the period of data collection, 2821 women were eligible to participate in this research. Thirteen percent declined participation, citing a variety of reasons including no glasses, too nervous and no time. A further eight percent who agreed to participate were excluded from analyses due to incomplete questionnaires, primarily due to time restraints. The resulting sample included questionnaire data from 2224 subjects representing 79 percent of eligible subjects.

Of the 2821 women eligible to participate in the study, 848 underwent a fine needle biopsy and were invited into the interview component of the study. One hundred and eight women (12.7%) declined to participate and a further 48 women who initially agreed to participate later withdrew their consent for interview (6%), representing a response rate of 81.6%. Of the 692 women participating in the interview component, 176 (25.6%) were unable to be interviewed for logistical reasons, including receiving preliminary biopsy results prior to interview completion, leaving the clinic while another subject was being interviewed, and no private space being available for the interview. One woman diagnosed with lymphoma and one woman with an inconclusive diagnosis, were subsequently excluded from analyses. Consequently, five hundred and fourteen women were interviewed prior to biopsy results being available.

Non-Participation Bias

In an attempt to consider the degree of non-respondent and non-completion bias on the study sample, study participants are compared with characteristics of all women attending the screening program assessment clinics during the years the study was being conducted (Table 7). The mean age of both groups are comparable, 56.7 years for assessment clinic attendees compared with 56.1 years for study participants. Slightly less assessment clinic attendees underwent biopsy (23.3%) than study participants (27.6%), indicating that there may be some bias in the study sample towards this group of women. While this may suggest some study participation may have been biased towards those women who may have suspected their diagnosis ahead of time, the conformity in percentage of a breast cancer diagnoses negates this.

The percentages of women requiring biopsy who were later diagnosed with breast cancer are comparable (11% for clinic attendees and 13% for study participants) and the percentage of women undergoing biopsy later diagnosed with cancer is 13 percent in both populations. Overall these data indicate that while there may have been small participation bias with respect to women requiring biopsy, any bias does not appear to be related to knowledge of diagnosis. While acknowledging the possibility of respondent bias, a response rate of 87 percent, completion rate of 79 percent, and comparable percentage of breast cancer diagnoses for the population of assessment clinics and study participants over a comparable time frame, the potential for bias based on diagnosis is considered minimal.

Table 7: Comparison of assessment clinics attendees and study participants

	Assessment Clinic Attendees (1994-1996)	Study Participants (recruited Apr 94-Apr 97)
Age (mean years)	56.7	56.1
% requiring Biopsy	23.3	27.6
% diagnosed with Cancer	11.0	13.0
% biopsy with Cancer	47.2	47.2

Study Groups

Participants were allocated to one of four groups once final results of the assessment procedure were confirmed. The groups were defined according to diagnostic results of breast disease and procedures required for diagnosis. As there is continued debate as to the appropriateness of benign breast disease as a control group for breast cancer, a distinction was made between those diagnosed with "normal" breast tissue and those with "benign" or "cystic" breast disease. In order to further control for the potential influence of the biopsy procedure on reporting of psychosocial data, subjects with benign or cystic breast disease were separated according to the biopsy procedure.

Study Components

As previously described, there are two components in the study design, a set of self-administered questionnaires and an interview. All subjects recalled for further testing to the breast screening assessment clinic were invited to complete the questionnaires. The questionnaires consisting of items related to demographic and somatic risk factors, and a number of psychological questionnaires related to trait personality features, including coping style, emotional expression and control and affect. The first hypothesis, relating to features of the Cancer Prone Personality, is tested in the whole sample.

Ideally, all subjects would have participated in the interview component of the study, but time constraints inherent in the semi-prospective design and sampling from within a working assessment clinic setting, precluded this possibility. The interview component, used to obtain a detailed history of life event stress and social support, was therefore offered only to women who underwent fine needle biopsy. These women spent more time at the assessment clinic enabling the interview to be conducted prior to results being available and in undergoing the same diagnostic procedures, provided consistency in testing conditions. Hypotheses relating to life event stress data, and the interactions between life event stress and personality and social support variables, are therefore tested only in this subgroup of the sample.

Approach to Data Analysis

Demographic and somatic risk factor variables are mostly categorical in nature and defined according to existing empirical data. The primary presentation of the data in Chapter three, distinguishes between the breast cancer group and non-cancer controls. Multiple logistic regression analyses are used to predict group membership. The results are presented in terms of the odds ratio for breast cancer and the corresponding 95 percent confidence interval. In other analyses including these analyses, these variables are grouped according to the group

definitions used in individual analyses. (Logistic regression is discussed further below).

MANCOVA

The psychosocial questionnaire data collected on the whole sample is analysed using Multivariate Analysis of Covariance (MANCOVA). The aim is to compare the breast cancer group with three control groups: normal breast tissue controls, benign breast disease controls not requiring biopsy and benign breast disease control requiring biopsy. MANCOVA is used to examine differences between the four groups on the psychosocial scales, with selected demographic variables and somatic risk factor variables included as potential covariates. The contrast coefficients for the planned comparisons between the breast cancer group and each individual control groups are shown in Table 8. Multivariate analyses of the psychosocial measures are considered under three headings: personality, emotional expression and control, and affect.

Table 8: Coefficients for planned contrasts between groups

<i>Testing Conditions</i>	Groups			
	Non Biopsy		Biopsy	
<i>Final Diagnosis</i>	Normal Tissue (n=942)	Benign / Cystic (n=642)	Benign Biopsy (n=320)	Breast Cancer (n=285)
Comparison 1	1	0	0	-1
Comparison 2	0	1	0	-1
Comparison 3	0	0	1	-1

While logistic regression analysis is possible when there are more than two groups, this analysis is not available with the software SPSS accessible to the candidate (i.e. SPSS version 6.1.3) (SPSS Inc.). Instead multivariate analysis of covariance (MANCOVA) was utilized, allowing evaluation of mean differences among a set a dependent variables when there are two or more independent variables (groups). The null hypothesis in MANCOVA is that the population means are equal. MANCOVA deals with correlations among the dependent variables and the entire analysis is accomplished within the preset level for Type 1 error. This analysis also enables one or more covariates to be considered, allowing the mean differences in the dependent variables among the groups to be assessed after adjusting for differences in covariates (Tabachnick & Fidell, 2001).

One advantage of MANCOVA is that it allows planned comparisons between groups to be assessed (Tabachnick & Fidell, 2001). A second advantage is that the predictable variance associated with covariates is removed, adjusting group means to what they would be if all subjects were identical on covariates. However, there are a number of disadvantages. The first is that attribution of causality is not possible. Furthermore, care must be taken with the correlation of dependent variables, and correlation between dependent variables and covariates. The MANCOVA model has a number of assumptions including reliability of covariates, linearity between pairs of covariates, and covariates and dependent variables, homogeneity of regression, normality and homogeneity of variance.

The outcome variable of interest is the diagnostic grouping of subjects, and the variables of interest the psychological scales while adjusting for differences in somatic and demographic variables. However, in order to conduct MANCOVA to assess systematic group differences in the psychological variables, the diagnostic groupings were treated as the primary dependent variable, the somatic and demographic variables were treated as covariates, and the psychological variables were nominated as the outcome variables.

Selection of Covariates

Potential confounding variables and covariates were selected from among demographic and known risk factors for breast cancer were examined. The four groups were firstly compared on a number of demographic, medical and social risk factor variables. Variables correlated with psychological variables or judged to possibly influence psychological variables were identified for inclusion as covariates.

A confounder is defined as an extraneous variable that is associated with both the dependent and independent variables (Datta, 1993). A covariate is a variable significantly correlated with a dependent variable (Stevens, 1996). In non-experimental research such as the current study, variables on which the groups significantly differ can be statistically adjusted for by including these variables as covariates. Given the large sample size in the present study, up to 215 covariates could be included without adjustment becoming unstable (Stevens, 1996).

Variables considered as potential covariates were selected in two ways. Variables for which there were significant differences between groups were included as covariates on these grounds alone as a means for reducing initial differences between the groups. Secondly variables correlated with psychological variables, or judged to possibly influence psychological variables, or identified as potential risk factors for breast cancer on past empirical findings, were considered potential covariates. Each variable was then examined

for significant correlations with the psychosocial variables within individual groups.

As a result of this process the following variables were selected for inclusion as covariates and defined as follows:

1. Increasing age (continuous variable): age is an independent risk factor for breast cancer, the four groups were significantly different in age and correlated with many of the psychosocial variables.
2. Increasing level of education (continuous variable): level of education was not significantly difference across the four groups but was correlated with a number of the psychosocial variables, and therefore included as a covariate.
3. Family history of breast cancer (categorical variable): none, first degree relative diagnosed age 50+ years, first degree relative diagnosed age <50 years, unknown.
4. Age at onset of menopause (categorical variable): premenopausal, <45 years, 45-50 years, 50+ years, unknown.
5. Age at birth of first child (categorical variable): <29 years of age, 30+ years of age.
6. Parity (categorical variable): none, 1-2, 3+.
7. Body mass index (categorical variable): <25, 25+, unknown.
8. Oral contraceptive use (categorical variable): total use <1 year, used 1+years, unknown.
9. Daily alcohol consumption (categorical variable): no, yes, unknown.
10. History of benign breast disease (categorical variable): no, yes, unknown.
11. Current use of hormone replacement therapy (categorical variable): no, yes, unknown.

Testing of Assumptions

1. Absence of Outliers. For dichotomous variables univariate outliers were defined as those with less than 10 percent of the total sample in the smaller category (Tabachnick & Fidell, 2001). For continuous variables, univariate outliers were identified within each group using a cut off of a z-score $> |3.29|$, $p < 0.001$ (Tabachnick & Fidell, 2001). Outliers were checked to confirm accuracy of entry in the data file. In a large sample, a few standardized scores greater than 3.29 were expected (Tabachnick & Fidell, 2001). The number of univariate outliers in the sample was relatively small (53/24079 data points or 0.22%), 20 of these in the state depression variable.

State depression scores in a non-clinical sample would not be expected to follow a normal distribution. Therefore subjects were classified into non-cases (score 0-7), doubtful or mild cases (score 8-10) and clinical cases (score 11+) as defined by the authors of the scale (Zigmond & Snaith, 1983). Ninety-one percent of subjects were classified as non-cases, with 6.2 percent of subjects as doubtful or mild and only 2.8 percent classified in the clinical

depression range. Using this definition, even when subjects classified with either mild or clinical depression were combined, the state depression variable is a univariate outlier (Tabachnick & Fidell, 2001).

Rather than transform this variable that would later be difficult to interpret, or exclude this variable altogether, state depression scores were split into three groups according to thirtile scores. This resulted in subjects scoring less than two for state depression making up the reference group (no depression), scores of 2.0-3.99 were defined as low depression and scores of 4 or more redefined as high depression (rather than clinical depression). There were no differences detected between the groups for state depression scores ($\chi^2(6) = 4.04, p = 0.67$). This definition of state depression was used in multivariate analyses.

Univariate outliers on all other variables were examined and not considered so extreme as to suggest they were not part of the sample population. These cases were included in analyses; however, the impact of univariate outliers were reduced by modifying scores so that they remained deviant, but less deviant. Univariate outliers were assigned a raw score one unit larger or smaller than the next most extreme score for each variable (Tabachnick & Fidell, 2001). Using this technique, 24 of 53 data points identified as univariate outliers remained unchanged. Data were then explored for multivariate outliers in the four groups, defined as $p < 0.001$ for Mahalanonbis distance (Tabachnick & Fidell, 2001). This was achieved using linear regression. No multivariate outliers were identified.

2. *Absence of Multicollinearity and Singularity.* While the inclusion of covariates in analyses of non-experimental research is important to adjust for initial group differences and to eliminate systematic bias, the inclusion of highly correlated covariates (>0.8) removes much of the same error variance while including variables which are lowly correlated removes different portions of error variance (Stevens, 1996). The most highly correlated covariates were age and menopausal status ($\rho = 0.71$). As all the proposed covariates were correlated at less than 0.80, the set of ten covariates were considered unaffected by collinearity.

3. *Normality.* Normality of distribution was examined graphically for individual groups and was approximately normal for all dependent variables, except state depression (discussed above). According to Coakes and Steed (1997), with a sample size greater than 30 violation of this assumption is of little concern. On these grounds, multivariate normality was assumed.

4. *Homogeneity of Variance.* Homogeneity of Variance was tested using the Levene Test for

equality of variance. A p-value of less than 0.05 rejects the null hypothesis that group variances are equal. Where this assumption was violated, the F statistic for planned comparisons reported used separate variance estimates rather than pooled variance estimates (Stevens, 1996).

5. *Linearity*. Linear relationship between dependent variables and covariates was inspected by bivariate scatterplots. All were approximately linear.

6. *Homogeneity of Covariance*. Homogeneity of Covariance was tested by assessing homogeneity of regression hyperplanes since more than two covariates were used. This was tested using Wilk's lambda (Λ) with significance set at 0.05 (Stevens, 1996), the results allowing homogeneity of covariance to be assumed.

Logistic Regression

The interview data examining the life event stress and social support variable was collected only for those who underwent fine needle biopsy. The aim was to distinguish between those women with biopsy confirmed benign breast disease and those diagnosed with breast cancer. Multiple logistic regression analyses are used to examine individual variables and interactions in predicting group membership and to establish the direction of the effect. Univariate analyses of life event stress and social support variables are presented first, followed by the examination of interactive effects of life event stress with the hypothesized moderating or vulnerability variables (social support, defense style and emotional expression and control). Results for each variable are presented in terms of Odds Ratio for Breast Cancer with the corresponding 95 percent confidence interval.

Logistic regression analysis allows the prediction of a discrete outcome such as group membership from a set of variables that may be a mix of continuous, discrete, and dichotomous (Tabachnick & Fidell, 2001). Direct logistic regression also allows the evaluation of the contribution of a predictor variable to the outcome variable independently of other predictor variables in the equation. While relatively free from assumptions and restrictions, logistic regression is sensitive to extremely high correlations among predictor variables or multicollinearity. The effect of this will be apparent by the presence of high standard errors for parameter estimates.

The inclusion of additional predictor variables (or covariates) in a logistic regression provides a way of statistically adjusting for potential differences in their distributions, where

the covariate is not associated with the risk factor variable. An interaction is present when the association of a risk factor variable differs or varies depending on the level of a second variable, either a covariate or another risk factor variable. In this situation, the strength of the association or odds ratio estimate for one risk factor depends on the value of the second variable being specified. Estimation of odds ratio in the presence of interactions requires the correlation between the two variables to be accounted for.

An odds ratio is a measure of association estimating the likelihood of an outcome (eg breast cancer) being present among those with an independent variable (eg family history of breast cancer) compared with those without an independent variable (ie no family history of breast cancer) (Hosmer & Lemeshow, 1980). An odds ratio should be interpreted as the increase in likelihood of being in one categorical outcome (eg breast cancer rather than no breast cancer) when the value of the independent variable (family history) increases by one unit (Tabachnick & Fidell, 2001). An odds ratio greater than 1 reflects an increase in odds of an outcome (eg breast cancer) with a one unit increase in the independent or predictor variable (eg family history). For example an odds ratio of 1.5 indicates that the outcome (breast cancer) is 1.5 times (or 50% more likely) with a family history of breast cancer than without a family history of breast cancer. In other words, the odds of breast cancer for those with a family history of breast cancer are increased by 50 percent compared with those without a family history of breast cancer.

CHAPTER 3: ESTABLISHED RISK FACTORS FOR BREAST CANCER

This chapter contains the manuscript titled "Predictors of breast cancer in women recalled following screening" published in the Australian and New Zealand Journal of Surgery in 1999, Volume 69, pages 639-646.

The authors of this publication are Melanie A Price, Christopher C Tennant, Ross C Smith, Susan J Kennedy, Phyllis N Butow, Marjorie B Kossoff and Stewart M Dunn.

Changes have been made in response to examiners recommendations and therefore this chapter varies from the published version

A reprint version of this article is in Appendix XIII

The tables have been renumbered to maintain consistency within the thesis.

Summary

Established risk factors are associated with between 25-56% of breast cancer cases, but the relative importance and relevance to different age groups is unclear. This case-control study examines established risk factors in 298 women with breast cancer and 1926 women without breast cancer aged 40-87 and recalled for assessment following routine mammography. The cancer group were significantly older than the non cancer group ($F_{1,2222} = 107.6$, $p < 0.0001$). Obesity increased the odds of developing breast cancer (OR 1.48, CI 1.13-1.93). The breast cancer group were more likely to have ever used oral contraceptives (OR 1.50, CI 1.09-2.05) with women who used for over 10 years in total at highest risk (OR 1.73, CI 1.13-2.65). Daily consumption of alcohol was also associated with increased risk of developing breast cancer (OR 1.62, CI 1.13-2.33). Reproductive factors and a family history of breast cancer did not affect the odds of developing breast cancer and the reasons for these findings are explored. Results suggest that the effects of weight reduction in reducing post-menopausal breast cancer risk should be assessed.

Introduction

Breast cancer is the most common cancer in women in developed countries with an estimated 790,000 cases worldwide in 1990 and approximately one million new cases currently diagnosed each year.¹ Hormonal factors are generally considered to play an etiological role in breast cancer because of consistent association between reproductive factors and breast cancer.² Established risk factors for breast cancer include increasing age, older age at first birth, older age at menopause, nulliparity and high parity, family history and history of benign breast disease.²⁻⁵ Exogenous hormone therapy such as oral contraceptives and hormone replacement therapy increase breast cancer risk, although the risk diminishes with time.⁶⁻⁷ Evidence is increasing for a modest positive association between alcohol intake and breast cancer although a causal relationship has not been established.⁸⁻¹² Obesity is considered a risk factor for breast cancer in post-menopausal women, but protective in pre-menopausal women, although results are not universally consistent.¹³⁻¹⁷ Long periods of lactation have been reported as being protective against breast cancer, especially in pre-menopausal women.¹⁸⁻¹⁹

Consensus on the relative importance of individual risk factors, the magnitude of each, and their relevance to different age groups is rare. Opinion also varies as to how well established risk factors explain the incidence of breast cancer. Madigan et al.⁵ estimates 41 percent of US breast cancer cases can be explained by later first birth, nulliparity, family history and

higher socioeconomic status. Tavani et al.²⁰ estimate that higher education, older age at first birth, nulliparity, older age at menopause, hormone replacement therapy and family history can account for 56 percent of cases in Italy. However, the American Cancer Society claims that recognised risk factors can account for as little as 25 percent of breast cancer cases.³

Routine breast screening provides a unique opportunity to prospectively examine risk factors for the development of breast cancer in asymptomatic women at risk of breast cancer primarily because of their age. This case-control study investigates "established" risk factors for breast cancer in a cohort of older Australian women recalled for assessment following routine mammography.

Methods

The National Breast Screening Program commenced in Australia in 1993, actively recruiting women aged 50-69 from electoral rolls for screening mammography. Free mammograms, however, are available to all women over age 40. Women recalled for assessment to Northern Sydney and Lower Central Coast BreastScreen from April 1994 to April 1997 were invited to participate in research examining the role of psychosocial, demographic and somatic factors in breast cancer. Ethical approval was granted by the Royal North Shore Hospital Medical Research Ethics Committee. Screening rounds one and two were in progress during the period of this study. On arrival at the clinic, informed consent was sought, and consenting women completed a self-administered questionnaire while waiting for assessment. The questionnaire included items on demographics, reproductive history, hormonal variables, and several psychological questionnaires. [Psychosocial data will be reported separately].

Logistic regression analysis was used to distinguish between women with and without breast cancer for individual risk factors. Age was included as a confounder in all analyses. Where indicated, other confounders were also included in analysis, all variables being entered simultaneously. Analyses were performed using SPSS for windows (version 6.1.3).

Results

A total of 2,989 women were invited to participate in this research. The exclusion criteria were: prior personal history of breast cancer (39); Non-English speaking (93); physical or psychiatric impairment preventing completion of questionnaire (34). One woman diagnosed with lymphoma and one woman whose final diagnosis was outstanding were excluded from analysis. Thirteen percent declined participation and eight percent had incomplete questionnaires, resulting in 2224 (79 percent) questionnaires used in the final analysis. The final sample consisted of 298 (13 percent) breast cancer cases and 1926 (87 percent) controls including those who had no abnormality detected and those diagnosed with cysts or benign breast disease.

Demographic variables are summarised in Table 9. The age of our cohort ranged from 40-87 years with a mean age of 56.1 years. The cancer group was significantly older than the non cancer group with a mean age of 61.2 years (standard error (SE) ± 0.55) years and 55.3 years (SE ± 0.21) respectively ($F_{1,2222} = 107.6$, $p < 0.0001$). Fifteen percent of the cancer group were widowed compared to eight percent of the non cancer group; the difference non significant after controlling for age. We found a trend of increasing level of education and increasing risk of breast cancer, albeit non significant. The cancer group were more likely to be retired than in current employment, an effect diminishing with age, and there were no differences in type of work undertaken, past or present.

Seventy two percent of our cohort were Australian born. Women born outside of Australia were born in 63 different countries making individual comparison impossible. Instead, non Australian born women were allocated to an incidence group based on the relative incidence of breast cancer in women born in their country compared to that of Australian born women (lower, equivalent, higher, unknown). The relative incidence for each country was estimated from a tabulation of breast cancer cases by country of birth in New South Wales during 1987-1992.²¹ Most non Australian born women were born in countries with a similar incidence of breast cancer to Australia. No differences in risk of breast cancer were seen in non Australian born women compared to Australian born women (Table 9).

Table 9: Distribution of demographic variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n=298)^a No. (%)	Non cancer (n=1926)^a No. (%)	Odds ratio (95% CI) age adjusted
<i>Current Marital Status</i>			p=0.92
Married/Defacto	202 (68.9)	1426 (74.5)	1.00
Single/Never married	17 (5.8)	112 (5.9)	0.87 (0.50, 1.50)
Widowed	44 (15.0)	149 (7.8)	1.07 (0.71, 1.60)
Divorced	30 (10.2)	226 (11.8)	0.95 (0.63, 1.44)
<i>Level of Education</i>			p=0.24
Primary	10 (3.4)	70 (3.7)	1.00
3-4 years secondary	112 (38.1)	717 (37.6)	1.60 (0.78, 3.25)
5-6 years secondary	51 (17.3)	293 (15.4)	1.83 (0.87, 3.88)
Diploma/certificate	72 (24.5)	460 (24.1)	2.07 (0.99, 4.31)
University/college	49 (16.7)	368 (19.3)	2.02 (0.94, 4.31)
<i>Current Occupational Status</i>			p=0.48
Home employment	64 (21.8)	384 (20.1)	1.00
Full time work	69 (23.5)	567 (29.7)	1.14 (0.77, 1.69)
Part time work	50 (17.0)	489 (25.6)	0.92 (0.61, 1.39)
Seeking work/pension	3 (1.0)	44 (2.3)	0.45 (0.13, 1.54)
Retired	108 (36.7)	428 (22.4)	0.89 (0.62, 1.28)
<i>Type of work (past / present)^b</i>			p=0.89
Professional	5 (2.2)	41 (2.7)	1.00
Manager / small business	17 (7.6)	151 (10.1)	0.98 (0.34, 2.88)
Trade	81 (36.2)	538 (36.1)	1.21 (0.46, 3.23)
Clerical	78 (34.8)	461 (30.9)	1.17 (0.44, 3.12)
Semi skilled / unskilled	43 (19.2)	300 (20.1)	1.02 (0.37, 2.78)

^aNumbers for each variable do not add up to total due to missing values.

^bPaid employment only.

Table 9 continued: Distribution of demographic variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n=298) ^a No. (%)	Non cancer (n=1926) ^a No. (%)	Odds ratio (95% CI) age adjusted
<i>Country of Birth^c</i>			p=0.19
Australia	222 (74.7)	1372 (71.3)	1.00
Incidence < Australia ^d	2 (0.7)	34 (1.8)	0.44 (0.10, 1.85)
Incidence ~ Australia ^e	57 (19.2)	427 (22.2)	0.89 (0.64, 1.22)
Incidence > Australia ^f	9 (3.0)	65 (3.4)	1.05 (0.50, 2.17)
Incidence unknown c/f Australia ^g	7 (2.4)	27 (1.4)	2.44 (1.03, 5.82)

^aNumbers for each variable do not add up to total due to missing values.

^bPaid employment only.

^cIncidence rates by country of birth estimated from breast cancer cases in NSW during 1987-1992 (Kricke & Jelfs, 1996).

^dIncidence rates for breast cancer lower than Australian born women in women born in China, Estonia, Greece, Italy, Malta, Taiwan, Ukraine, Vietnam, Wales, Yugoslavia.

^eIncidence rates for breast cancer equivalent to Australian born women in women born in Austria, Bulgaria, Canada, Cyprus, Czechoslovakia, Denmark, Egypt, England, Finland, France, Germany, Hong Kong, Hungary, India, Indonesia, Iran, Iraq, Ireland, Israel, Lebanon, Netherlands, Norway, Philippines, Poland, Portugal, Romania, Scotland, South Africa, Spain, Sri Lanka, Sweden, Switzerland, Syria, Turkey, USA.

^fIncidence rates for breast cancer higher than Australian born women in women born in Malaysia, New Zealand, Singapore, USSR.

^gIncidence rates for breast cancer unknown compared to Australian born women in women born in Bolivia, Chile, Fiji, Japan, Kenya, Macau, Mauritius, Namibia, Papua New Guinea, Peru, Tanzania, Thailand, Tonga, Zimbabwe.

Maintaining consistency with the screening program, our definition of family history was restricted to women who had a mother, sister or daughter with breast cancer (Table 10). Eighteen percent of the cancer group and 14 percent of the non cancer group reported a positive family history. The odds ratio (OR) for developing breast cancer with a positive maternal history was 1.18 (95 percent confidence interval (CI) 0.73-1.92) and 1.03 (CI 0.62-1.77) for a sister with breast cancer. Sixteen women reported both mother and a sister with breast cancer and the odds ratio for breast cancer with this family history was non significant (OR 1.51, CI 0.41-5.57). Only nine women reported a daughter with breast cancer; the odds for developing breast cancer in this instance was 3.76 (CI 0.86-16.4).

Table 10: Distribution of family history of breast cancer and reproductive variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n=298) ^a No. (%)	Non cancer (n=1926) ^a No. (%)	Odds ratio (95% CI) adjusted for age	Odds ratio (95% CI) multivariate adjusted
Family history of breast cancer			p=0.40	p=0.49 ^c
None	231 (77.5)	1579 (82.0)	1.00	1.00
Mother (Father)	25 (8.4)	158 (8.2)	1.25 (0.79, 1.97)	1.18 (0.73, 1.92)
Sister	19 (6.4)	93 (4.8)	1.03 (0.61, 1.75)	1.03 (0.62, 1.77)
Daughter	5 (1.7)	4 (0.2)	3.97 (1.00, 15.7)	3.76 (0.86, 16.40)
Mother & Sister	3 (1.0)	13 (0.7)	1.55 (0.42, 5.70)	1.51 (0.41, 5.57)
Unknown	15 (5.0)	78 (4.1)	1.11 (0.62, 2.00)	1.29 (0.71, 2.34)
History of benign breast disease			p=0.55	p=0.49 ^d
No	231 (81.1)	1581 (83.8)	1.00	1.00
Yes	54 (18.9)	305 (16.2)	1.11 (0.80, 1.53)	1.12 (0.80, 1.57)
Age at first child			p=0.42	p=0.48 ^e
Nulliparous	36 (12.9)	260 (14.0)	1.00	1.00
<20 years	8 (2.9)	88 (4.7)	0.81 (0.36, 1.85)	0.95 (0.41, 2.18)
20-24 years	75 (27.0)	540 (29.0)	1.00 (0.65, 1.56)	1.06 (0.67, 1.67)
25-29 years	101 (36.3)	632 (34.0)	1.20 (0.67, 1.55)	1.25 (0.80, 1.95)
≥30 years	58 (20.9)	340 (18.3)	1.35 (0.65, 1.63)	1.45 (0.87, 2.42)
No. full pregnancies			p=0.67	p=0.34 ^e
None	36 (12.8)	264 (14.1)	1.00	1.00
1-2	132 (46.8)	913 (48.6)	1.20 (0.80, 1.80)	1.40 (0.87, 2.23)
≥3	114 (40.4)	701 (37.3)	1.16 (0.77, 1.76)	1.45 (0.87, 2.42)
No. incomplete pregnancies			p=0.58	p=0.50 ^e
None	161 (57.9)	1074 (57.7)	1.00	1.00
1	76 (27.3)	453 (24.3)	1.22 (0.90, 1.65)	1.25 (0.92, 1.71)
2	23 (8.3)	194 (10.4)	0.94 (0.58, 1.51)	0.95 (0.59, 1.54)
≥3	18 (6.5)	140 (7.5)	1.02 (0.60, 1.74)	1.03 (0.60, 1.76)

^aNumbers do not add up to total due to missing values. ^bKnown age of menopause only. ^cAge, age at first birth, parity, menopausal status. ^dAge, age at first birth, parity, family history, menopausal status. ^eAge, age at first child, parity, menopausal status, family history, education. ^fAge, age at first child, parity, body mass index.

Table 10 continued: Distribution of family history of breast cancer and reproductive variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n=298) ^a No. (%)	Non cancer (n=1926) ^a No. (%)	Odds ratio (95% CI) adjusted for age	Odds ratio 95% CI multivariate adjusted
<i>Lifetime lactation</i>			p=0.80	p=0.90 ^e
None	69 (25.7)	492 (27.0)	1.00	1.00
1-6 months	63 (23.5)	442 (24.3)	1.12 (0.77, 1.64)	1.09 (0.67, 1.75)
7-36 months	129 (48.1)	839 (46.0)	1.06 (0.77, 1.46)	1.03 (0.66, 1.61)
>36 months	7 (2.6)	49 (2.7)	1.48 (0.63, 3.49)	1.39 (0.55, 3.51)
<i>Menopausal Status</i>			p=0.04	p=0.05 ^f
Premenopausal	37 (12.4)	631 (32.8)	1.00	1.00
Postmenopausal	261 (87.6)	1395 (67.2)	1.59 (1.03, 2.44)	1.61 (1.00, 2.59)
<i>Age at Menopause^b</i>			p=0.47	-
<35 years	1 (0.6)	8 (1.0)	0.41 (0.05, 3.40)	
36-40 years	9 (5.2)	30 (3.6)	1.30 (0.57, 2.95)	
41-45 years	22 (12.8)	132 (16.0)	0.73 (0.43, 1.25)	
46-50 years	75 (43.6)	340 (41.2)	1.11 (0.77, 1.61)	
>50 years	65 (38.2)	315 (38.2)	1.00	

^aNumbers do not add up to total due to missing values. ^bKnown age of menopause only. ^cAge, age at first birth, parity, menopausal status. ^dAge, age at first birth, parity, family history, menopausal status. ^eAge, age at first child, parity, menopausal status, family history, education. ^fAge, age at first child, parity, body mass index.

There was a non significant but increasing trend between age at first birth and risk of breast cancer (Table 10). Compared to nulliparous women, those with their first birth under age 20 were less at risk of breast cancer while those with a first birth at 30 years and above were at increased breast cancer risk. There were no group differences in parity, incomplete pregnancies, history of lactation or history of benign breast disease.

Women currently menstruating were classified as pre-menopausal. Women with a history of a hysterectomy were considered pre-menopausal if currently aged less than 50 years (3%) and post-menopausal if currently aged 50 or more years (21.5%). Women with missing responses were also classified pre-menopausal if under age 50 years (1.3%) and post-menopausal if aged 50 years or more (3.6%). The cancer group were more likely to be post-menopausal than the non cancer group, with an odds ratio of 1.61 (CI 1.00-2.59) adjusted for

age, age at first child, parity and body mass index (Table 10). In women who had a known age at menopause, we found no differences between women with cancer and non cancer controls. Both groups were also similar in the current use of hormone replacement therapy (Table 11).

Sixty six percent of the cancer group and 73 percent of the non cancer group had ever used oral contraceptives (OC's). Ever use of OC's significantly increased the odds of breast cancer to 1.44 (CI 1.04-2.00, $p=0.03$), independent of age at first birth, parity, family history and level of education (Table 11). There was an inconsistent pattern of risk with age at first use; the only age range significantly increasing the risk of breast cancer was age 25-29 years (OR 1.78, CI 1.15-2.75, $p=0.01$). We found an increasing trend of breast cancer with length of OC use, significantly higher in women using OC's over 10 years in total (OR 1.73, CI 1.13-2.65, $p=0.01$).

A Body Mass Index (BMI) above 25 was more common in the cancer group independent of age (Table 12). Controlling for age, the odds of breast cancer in women with a BMI greater than 25 was significantly increased (OR 1.48, CI 1.13-1.93).

Alcohol consumption was examined by considering both the frequency of intake and average weekly consumption. The proportion of alcohol abstainers was similar in both groups, with a non significant trend for increased alcohol consumption associated with breast cancer (Table 12). Compared to non drinkers, daily alcohol consumption increased the odds of breast cancer to 1.62 (CI 1.13-2.33).

Table 11: Distribution of exogenous hormonal variables for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n=298) ^a No. (%)	Non cancer (n=1926) ^a No. (%)	Odds ratio (95% CI) adjusted for age	Odds ratio (95% CI) adjusted multivariate
<i>Current use of hormone replacement therapy</i>			p=0.68	p=0.63 ^b
No	181 (64.0)	1245 (65.8)	1.00	1.00
Yes	102 (36.0)	646 (34.2)	1.06 (0.81, 1.38)	0.93 (0.70, 1.25)
<i>Ever used oral contraceptive pill</i>			p=0.01	p=0.03 ^c
No	96 (34.2)	508 (26.9)	1.00	1.00
Yes	185 (65.8)	1378 (73.1)	1.50 (1.09, 2.05)	1.44 (1.04, 2.00)
<i>Age started oral contraceptives</i>			p=0.02	p=0.07 ^c
Never used	96 (35.3)	508 (27.9)	1.00	1.00
<25 years	57 (21.0)	693 (38.0)	1.44 (0.89, 2.35)	1.44 (0.88, 2.37)
25-29 years	54 (19.9)	333 (18.3)	1.85 (1.20, 2.83)	1.78 (1.15, 2.75)
30-34 years	26 (9.6)	169 (9.3)	1.10 (0.68, 1.79)	1.12 (0.69, 1.84)
35 + years	39 (14.3)	119 (6.5)	1.68 (1.09, 2.60)	1.54 (0.98, 2.41)
<i>Total years oral contraceptives</i>			p=0.12	p=0.19 ^c
Never used	96 (35.8)	508 (28.2)	1.00	1.00
<1 year	18 (6.7)	161 (8.9)	1.08 (0.62, 1.90)	1.11 (0.63, 1.96)
1-3 years	37 (13.8)	294 (16.3)	1.47 (0.94, 2.30)	1.32 (0.83, 2.09)
4-6 years	38 (14.2)	287 (15.9)	1.55 (0.99, 2.43)	1.53 (0.97, 2.42)
7-10 years	30 (11.2)	238 (13.2)	1.42 (0.88, 2.28)	1.36 (0.83, 2.22)
10+ years	49 (18.3)	315 (17.5)	1.77 (1.17, 2.68)	1.73 (1.13, 2.65)

^aNumbers for each variable do not add up to total due to missing values... ^bControlled for age, menopausal status, OC use, family history and education. ^cControlled for age, age first child, parity, family history and education.

Table 12: Distribution of alcohol and cigarette consumption, body mass index and body mass index by menopausal status for cancer and non cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n=298)^a No. (%)	Non cancer (n=1926)^a No. (%)	Odds ratio (95% CI) adjusted for age
<i>Amount of alcohol consumption</i>			p=0.17
None	62 (22.5)	400 (21.7)	1.00
<5 drinks/week	99 (35.9)	765 (41.4)	1.00 (0.71, 1.42)
5-10 drinks/week	72 (26.1)	413 (22.4)	1.30 (0.89, 1.89)
11-15 drinks/week	31 (11.2)	151 (8.2)	1.55 (0.95, 2.51)
>15 drinks/week	12 (4.3)	117 (6.3)	0.84 (0.43, 1.63)
<i>Frequency of alcohol consumption</i>			p=0.009
None	62 (22.1)	400 (21.5)	1.00
Occasional	64 (22.8)	498 (27.0)	0.98 (0.67, 1.44)
Weekly	65 (23.1)	549 (29.8)	1.01 (0.69, 1.48)
Daily	90 (32.0)	401 (21.7)	1.62 (1.13, 2.33)
<i>Total cigarettes ever smoked</i>			p=0.25
0-1 (thousand)	180 (65.0)	1188 (64.8)	1.00
1-100 (thousand)	38 (13.7)	319 (17.4)	0.90 (0.62, 1.32)
>100 (thousand)	59 (21.3)	325 (17.7)	1.27 (0.91, 1.75)
<i>Body mass index (BMI)</i>			p=0.004
BMI≤25	137 (51.9)	1122 (62.9)	1.00
BMI>25	127 (48.1)	663 (37.1)	1.48 (1.13, 1.93)

^aNumbers for each variable do not add up to total due to missing values.

Discussion

In our cohort of women recalled for further assessment following routine breast screening, the single most important risk factor identified for breast cancer was increasing age.¹⁶ Although the cancer group were more likely to be widowed, the older age of this group accounted for the difference. Age also accounted for the higher proportion of retirees in the cancer group. Type of employment was similar across our sample, but we found a non significant trend of higher level of education associated with increasing risk of breast cancer, consistent with previous reports.^{20, 22} Our cohort was drawn from one geographical area of Sydney which may explain the relative uniformity of sociodemographics. Most non Australian born women were born in countries with similar incidences of breast cancer to Australia and no group difference was detected.

A consistent finding in the literature is a two to three fold increase in risk of breast cancer associated with a first degree family history.^{5, 18, 23-27} This risk appears to be independent of reproductive factors.^{25, 28} In our cohort, the small number of women who had a daughter with breast cancer, or a sister and mother with breast cancer, were more likely to have developed breast cancer, although the trend was non significant. We did not detect any difference in risk of breast cancer in women reporting a mother or a sister with breast cancer. There are a number of possible explanations for family history not being a factor in our sample. Firstly, reliability of the data should be considered. With a participation rate of 79 percent, response bias is unlikely. As in most epidemiological studies we relied on self reported information and the accuracy of this information depends on both memory and knowledge. The few studies examining accuracy of self reported family history data confirm that information about breast cancer history in first degree relatives is usually reliable.²⁹⁻³⁰ Floderus et al.³¹ found a slight under-reporting by unaffected twins in a discordant twin study even for first degree relatives. Our information was collected before diagnoses were available, avoiding the possibility of recall bias and any tendency to under report would be similar in both groups.

A second possible explanation, and perhaps more likely, lies within our sample. Genetic breast cancers account for a small percentage of breast cancers and are usually associated with early onset.²⁴⁻²⁵ These women once diagnosed would not be included in our screening population. Our cohort was drawn from women over 40 years of age attending screening because of the risk of breast cancer associated with age and who were recalled for further assessment. Roseman et al. found that after age 45, the increased risk associated with a positive family history declined and for women over 60, those with a family history were not

at greater risk of breast cancer than women with no family history.³² Both Mettlin et al. and Sellers et al. report a reduced influence of family history on breast cancer risk in women over age 55 years compared to younger women.³³⁻³⁴ In our cohort, 73 percent were over age 50 and this may account for the lower than expected impact of family history. Our finding is consistent with a recent UK screening study that reported similar levels of family history (12 to 17 percent) to our cohort (14 to 17.5 percent) and found no independent impact of family history on breast cancer risk in women aged over age 55 years.¹⁶ Of interest to note were differences in family history within age groups in our cohort. Women in their 70's had a higher incidence of family history as would be expected with concurrently aging sisters and daughters. The incidence of family history for women in their 40's was similar to the older age groups, but the 40 to 49 year age group were more likely to report a mother than a sister with breast cancer. With women in their 40's self-referring for screening, it is not surprising that a high proportion of these women have a mother with breast cancer. The unanswered question is whether those with a family history of breast cancer are more likely to be recalled for further testing and therefore perhaps creating a bias in our sample for this variable.

There was also a general uniformity in reproductive history across our sample. Many studies indicate that a younger age at first birth reduces the risk of breast cancer independently of parity and other risk factors.^{13, 20, 35} We found a trend for increased risk of breast cancer with an older age at first birth and although not significant, the direction of the trend is consistent with previous findings. There were no differences between groups in parity, despite both nulliparity and high parity being previously reported as independent risks factors for breast cancer.³⁶ In our cohort 13.8 percent had no children and 37.7 percent of women had at least three children, therefore insufficient power is an unlikely explanation of these findings.

We found no evidence to support lactation protecting against breast cancer, a finding consistent with most Western studies.³⁷⁻³⁹ Most evidence for a protective role of lactation comes from Asian countries where breast feeding for a number of years is common practice.³⁹ Seventy five percent of our cohort breastfed, with an average duration of ten months. This is similar to figures from the United States but well below China, Japan and Taiwan where the average duration of lactation is over three years.³⁹ Less than three percent of our cohort breastfed for over three years making any protective effect of breastfeeding for long periods unlikely to be detected.

Seventy percent of our cohort were post-menopausal and breast cancer was more common in post-menopausal women, the difference attributable to the older age of our cohort and to the increasing risk of breast cancer with age. We found no difference in the age at onset of

menopause between groups. However, approximately 25 percent of our sample had a hysterectomy prior to or around the time of menopause, and therefore the age at onset of menopause unknown for these women, resulting in incomplete and potentially biased data, difficult to interpret with certainty.

A second potential confounder in assessing the onset of menopause and an independent risk factor is hormone replacement therapy. Individual studies provide mixed evidence for hormone replacement therapy affecting breast cancer risk.⁴⁰⁻⁴² However, a recent reanalysis of worldwide data on hormonal replacement therapy and breast cancer risk, reports an increased risk of 1.023 with each year of use, restricted to time of use and persisting up to five years after ceasing.⁷ Thirty four percent of our cohort were currently using hormone replacement therapy and we found no differences between the groups. Two limitations are important to note regarding our examination of HRT. The first is that we examined current use only, rather than ever use. The second limitation is inherent in our sample population and concerns both users and diagnosis rate. Women using HRT have been reported to have a slightly higher rate of recall following mammography, particularly after the first screening round, and a lower cancer detection rate at screening, due to the effect of HRT on breast density.⁴³

Where we did detect a significant difference was in history of oral contraceptive use. Women who had ever used OC's were 50 percent more likely to have developed breast cancer than women who had never used. There was a trend of increasing risk of breast cancer with duration of use, reaching significance in women who had used OC's for over ten years. In contrast, there was no linear pattern of risk associated with age at first use of OC's. We found women who first used OC's between the ages 25-29 years were at significantly higher risk of breast cancer compared to those who never used. Women who started OC's either under age 25 or over 29 years showed a non significant increase in risk compared to never users.

Previous individual studies report a slight or no increase in risk with early use and no association between length of use and breast cancer risk. In 1996 the Collaborative Group on Hormonal Factors in Breast Cancer⁶ reanalysed some 90% of worldwide data on oral contraceptives and breast cancer risk, reporting a small but significant increase in risk of breast cancer with ever oral contraceptive use. This increase in risk was most evident in current users, and detectable up to ten years after ceasing. The Collaborative Group also report that recent use, rather than age at first use or duration of use, was the best predictor of risk associated with OC's.

There are, however, a number of differences both in the nature of our cohort and with our results that suggests we should not assume consistency with the Collaborative Group. Firstly, the average age of our cohort is 56 years, an average seven years older than the Collaborative Cohort and equally it is seven years longer since their OC use. Secondly, 72 percent of our cohort reported ever using OC's, substantially higher than recent studies in Italy who report use in 14 to 18 percent,²⁶ 38 to 46 percent in the US,⁴⁴⁻⁴⁵ and the average of 40 percent ever use from past studies worldwide.⁶ Thirdly, the older age of our cohort has impacted on ever use, age at first use and duration of use, primarily due to the time when OC's were introduced for widespread use. For example, a woman now in her 70's would have been aged in her 30's when OC's were first available for general use, and therefore be less likely to have ever used, have been unable to start in early reproductive years and consequentially be less likely to have used for a long duration. In contrast, a woman now in her 40's potentially would have had access to OC's from her teen years. This is reflected in the rate of use, with 90 percent of women in their 40's compared to 25 percent of women in their 70's having ever used oral contraceptives.

This being the case, it is likely that the inconsistent trend of risk we found for age at first use and breast cancer risk is an artifact of our cohort. The number of women commencing OC use after the age of 30 years was small and they were more likely to be older women and therefore less likely to use OC's for long periods. Despite this, our data provides strong evidence that ever use of OC's significantly increases breast cancer risk, that is highest with a long duration of use, regardless of age, age at first birth, parity, family history of breast cancer and education. This is highlighted by the fact that older women most at risk of cancer and least likely to have used OC's demonstrated a significant OC effect as well as the younger women, least at risk of cancer but using OC's for long periods, demonstrating a significant OC effect. In contrast to the findings from the Collaborative group, our results suggest that the increase in risk of breast cancer associated with ever using OC's may persist long term after ceasing.

Our finding of a modest association between alcohol consumption and breast cancer is consistent with the growing body of evidence which suggests the two are related, although a causal relationship has yet to be established. Alcohol is thought to increase endogenous oestrogen levels, demonstrated by Reichman et al. in pre-menopausal women,⁴¹ although these findings are not universal⁴⁶ and the effect on hormonal levels in post-menopausal women is unclear.⁴⁷ A number of epidemiological studies provide support for a small positive association between alcohol intake and breast cancer^{9-12, 48-50} with as little as one glass a day increasing risk.^{8, 50} Some studies have found a dose response relationship⁵¹ while

others report a threshold effect.^{9, 46} Our findings suggest that frequency rather than amount is the important indicator of risk and are consistent with Katsouyanni et al.⁹ who reported that frequency of alcohol intake was more important than length of intake or early consumption.

Obesity and weight gain have been reported as risk factors for breast cancer particularly in post-menopausal women.¹³⁻¹⁷ Oestradiol levels are higher in obese women than in lean women⁵²⁻⁵³ and may be responsible for the increased risk for breast cancer.⁵⁴ Our findings add to the growing body of evidence for an increase in risk of breast cancer in overweight women.

Summary

Increasing age, obesity and ever use of oral contraceptives increase the odds of breast cancer in a population of women recalled for further testing following mammography screening. Daily alcohol consumption provided a modest increase in risk of breast cancer consistent with previous findings. These results should provide some reassurance for women over 40 that the unalterable variables of family history and reproductive factors do not substantially affect their risk of breast cancer and suggests that the effects of weight reduction should be assessed.

References

1. Forbes JF. The Incidence of Breast Cancer: The Global Burden, Public Health Considerations. *Sem Oncol* 1997; 24(suppl1):S1-20-S1-35.
2. Hankinson SE, Colditz GA, Hunter DJ, Manson JE, Willett WC, Stampfer MJ, et al. Reproductive factors and family history of breast cancer in relation to plasma estrogen and prolactin levels in postmenopausal women in the Nurses' Health Study (United States). *Cancer Causes Control* 1995; 6:217-224.
3. Seidman H, Stellman SD, Mushinski MH. A Different Perspective on Breast Cancer Risk Factors: Some Implications of the Nonattributable Risk. *Ca Cancer J Clin* 1982; 32(5):301-313.
4. La Vecchia C, Negri E, Franceschi S, Favero A, Nanni O, Filiberti R, et al. Hormone replacement treatment and breast cancer risk: a cooperative Italian study. *Br J Cancer* 1995; 72:244-248.
5. Madigan MP, Ziegler RG, Benichou J, Byrne C, Hoover RN. Proportion of Breast Cancer Cases in the United States Explained by Well-Established Risk Factors. *J Natl*

- Cancer Inst 1995; 87(22):1681-1685.
6. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996; 347:1713-27.
 7. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. *Lancet* 1997; 350:1047-59.
 8. Martin-Moreno JM, Boyle P, Gorgojo L, Willett WC, Gonzalez J, Villar F, et al. Alcoholic beverage consumption and risk of breast cancer in Spain. *Cancer Causes Control* 1993; 4:345-353.
 9. Katsouyanni K, Trichopoulou A, Stuver S, Vassilaros S, Papadiamantis Y, Bournas N, et al. Ethanol and breast cancer: an association that may be both confounded and causal. *Int J Cancer* 1994; 58:356-361.
 10. Longnecker MP, Paganini-Hill A, Ross RK. Lifetime Alcohol Consumption and Breast Cancer Risk among Postmenopausal Women in Los Angeles. *Cancer Epidemiol Biomarkers Prev* 1995; 4:721-725.
 11. Levi F, Pasche C, Lucchini F, La Vecchia C. Alcohol and Breast Cancer in the Swiss Canton of Vaud. *Eur J Cancer* 1996; 32A(12):2108-2113.
 12. Swanson CA, Coates RJ, Malone KE, Gammon MD, Schoenberg JB, Brogan DJ, et al. Alcohol Consumption and Breast Cancer Risk among Women under Age 45 Years. *Epidemiology* 1997; 8(3):231-237.
 13. Pathak DR, Whittemore AS. Combined Effects of Body Size, Parity, and Menstrual Events on Breast Cancer Incidence in Seven Countries. *Am J Epidemiol* 1992; 135(2):153-168.
 14. Taioli E, Barone J, Wynder EL. A Case-Control Study on Breast Cancer and Body Mass. *Eur J Cancer* 1995; 31A(5):723-728.
 15. Franceschi S, Favero A, La Vecchia C, Baron AE, Negri E, Dal Maso L, et al. Body size indices and breast cancer risk before and after menopause. *Int J Cancer* 1996; 67:181-6.
 16. Thomas E, Cade J, Vail A. Risk factor analysis of data from assessment clinics in the UK breast screening programme: a case-control study in Portsmouth and

- Southampton. *J Epidemiol Community Health* 1996; 50:144-148.
17. La Vecchia C, Negri E, Franceschi S, Talamini R, Palli D, Decarli A. Body mass index and post-menopausal breast cancer: an age-specific analysis. *Br J Cancer* 1997; 75(3):441-4.
 18. Yoo K-Y, Tajima K, Kuroishi T, Hirose K, Yoshida M, Miura S, et al. Independent Protective Effect of Lactation against Breast Cancer: A Case-Control Study in Japan. *Am J Epidemiol* 1992; 135(7):726-733.
 19. United Kingdom National Case-Control Study Group. Breast feeding and risk of breast cancer in young women. *BMJ* 1993; 307:17-20.
 20. Tavani A, Braga C, La Vecchia C, Negri E, Russo A, Franceschi S. Attributable risks for breast cancer in Italy: education, family history and reproductive and hormonal factors. *Int J Cancer* 1997; 70:159-163.
 21. Kricger A, Jelfs P. Breast cancer in Australian women 1921-1994. Australian Institute of Health and Welfare, Cancer Series No. 6 1996.
 22. Heck KE, Pamuk ER. Explaining the Relation Between Education and Postmenopausal Breast Cancer. *Am J Epidemiol* 1997; 145(4):366-72.
 23. Gapstur SM, Potter JD, Sellers TA, Folsom AR. Increased Risk of Breast Cancer with Alcohol Consumption in Postmenopausal Women. *Am J Epidemiol* 1992; 136(10):1221-31.
 24. Slattery ML, Kerber RA. A Comprehensive Evaluation of Family History and Breast Cancer Risk. The Utah Population Database. *JAMA* 1993; 270(13):1563-1568.
 25. Colditz GA, Willett WC, Hunter DJ, Stampfer MJ, Manson JE, Hennekens CH, et al. Family History, Age, and Risk of Breast Cancer. Prospective Data From the Nurses' Health Study. *JAMA* 1993; 270(3):338-343.
 26. La Vecchia C, Negri E, Franceschi S, Talamini R, Amadori D, Filiberti R, et al. Oral contraceptives and breast cancer: a cooperative Italian study. *Int J Cancer* 1995; 60:163-167.
 27. Hunter DJ, Spiegelman D, Adami H-O, van den Brandt PA, Folsom AR, Goldbohm RA, et al. Non-dietary factors as risk factors for breast cancer, and as effect modifiers of the association of fat intake and risk of breast cancer. *Cancer Causes Control* 1997; 8:49-56.
 28. Andrieu N, Clavel F, Auquier A, Le MG, Gairard B, Piana L, et al. Variations in the risk of breast cancer associated with a family history of breast cancer according to age

- at onset and reproductive factors. *J Clin Epidemiol* 1993; 46(9):973-980.
29. Anton-Culver H, Kurosaki T, Taylor TH, Gildea M, Brunner D, Bringman D. Validation of Family History of Breast Cancer and Identification of the BRCA1 and Other Syndromes Using a Population-Based Cancer Registry. *Genet Epidemiol* 1996; 13:193-205.
 30. Parent M-E, Ghadirian P, Lacroix A, Perret C. The Reliability of Recollections of Family History: Implications for the Medical Provider. *J Cancer Educ* 1997; 12(2):114-120.
 31. Floderus B, Barlow L, Mack TM. Recall Bias in Subjective Reports of Familial Cancer. *Epidemiology* 1990; 1:318-321.
 32. Roseman DL, Straus AK, Shorey W. A Positive Family History of Breast Cancer: Does Its Effect Diminish With Age? *Arch Intern Med* 1990; 150:191-194.
 33. Mettlin C, Croghan I, Natarajan N, Lane W. The association of age and familial risk in a case-control study of breast cancer. *Am J Epidemiol* 1990; 131(6):973-983.
 34. Sellers TA, Kushi LH, Potter JD, Kaye SA, Nelson CL, McGovern PG, et al. Effect of family history, body-fat distribution, and reproductive factors on the risk of postmenopausal breast cancer. *N Eng J Med* 1992; 326:1323-1329.
 35. Talamini R, Franceschi S, La Vecchia C, Negri E, Borsa L, Montella M, et al. The Role of Reproductive and Menstrual Factors in Cancer of the Breast Before and After Menopause. *Eur J Cancer* 1996; 32A(2):303-310.
 36. Kelsey JL, Gammon MD, John EM. Reproductive Factors and Breast Cancer. *Epidemiol Rev* 1993; 15(1):36-47.
 37. London SJ, Colditz GA, Stampfer MJ, Willett WC, Rosner BA, Corsano K, et al. Lactation and risk of breast cancer in a cohort of US women. *Am J Epidemiol* 1990; 132(1):17-26.
 38. Brinton LA, Potischman NA, Swanson CA, Schoenberg JB, Coates RJ, Gammon MD, et al. Breastfeeding and breast cancer risk. *Cancer Causes Control* 1995; 6:199-208.
 39. Michels KB, Willett WC, Rosner BA, Manson JE, Hunter DJ, Colditz GA, et al. Prospective assessment of breastfeeding and breast cancer incidence among 89 887 women. *Lancet* 1996; 347:431-436.
 40. Weinstein AL, Mahoney MC, Nasca PC, Hanson RL, Leske MC, Varma AO. Oestrogen Replacement Therapy and Breast Cancer Risk: A Case-Control Study. *Int J Epidemiol* 1993; 22(5):781-789.

41. Reichman ME, Judd JT, Longcope C, Schatzkin A, Clevidence BA, Nair PP, et al. Effects of Alcohol Consumption on Plasma and Urinary Hormone Concentrations in Premenopausal Women. *J Natl Cancer Inst* 1993; 85(9):722-727.
42. Newcomb PA, Longnecker MP, Storer BE, Mittendorf R, Baron J, Clapp RW, et al. Long-term Hormone Replacement Therapy and Risk of Breast Cancer in Postmenopausal Women. *Am J Epidemiol* 1995; 142(8):788-795.
43. Litherland JC, Evans AJ, Wilson ARM. The Effect of Hormone Replacment Therapy on Recall Rate in the National Health Service Breast Screening Programme. *Clin Radiol* 1997; 52:276-9.
44. Newcomb PA, Longnecker MP, Storer BE, Mittendorf R, Baron J, Clapp RW, et al. Recent oral contraceptive use and risk of breast cancer (United States). *Cancer Causes Control* 1996; 7:525-532.
45. Hankinson SE, Colditz GA, Manson JE, Willett WC, Hunter DJ, Stampfer MJ, et al. A prospective study of oral contraceptive use and risk of breast cancer (Nurses' Health Study, United States). *Cancer Causes Control* 1997; 8:65-72.
46. Dorgan JF, Reichman ME, Judd JT, Brown C, Longcope C, Schatzkin A, et al. The relation of reported alcohol ingestion to plasma levels of estrogens and androgens in premenopausal women (Maryland, United States). *Cancer Causes Control* 1994; 5:53-60.
47. Longnecker MP. Do Hormones Link Alcohol With Breast Cancer? *J Natl Cancer Inst* 1993; 85(9):692-693.
48. Rosenberg L, Metzger LS, Palmer JR. Alcohol Consumption and Risk of Breast Cancer: A Review of the Epidemiologic Evidence. *Epidemiol Rev* 1993; 15(1):133-144.
49. van den Brandt PA, Goldbohm RA, van' t Veer P. Alcohol and Breast Cancer: Results from the Netherlands Cohort Study. *Am J Epidemiol* 1995; 141(10):907-915.
50. Longnecker MP, Newcomb PA, Mittendorf R, Greenberg ER, Clapp RW, Bogdan GF, et al. Risk of Breast Cancer in Relation to Lifetime Alcohol Consumption. *J Natl Cancer Inst* 1995; 87(12):923-929.
51. Longnecker MP. Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. *Cancer Causes Control* 1994; 5:73-82.
52. Deslypere JP. Obesity and Cancer. *Metabolism* 1995; 44(9 (suppl 3)):24-27.
53. Potischman N, Swanson CA, Siiteri P, Hoover RN. Reversal of Relation Between

Body Mass and Endogenous Estrogen Concentrations With Menopausal Status. *J Natl Cancer Inst* 1996; 88(11):756-758.

54. Kelsey JL. Breast Cancer Epidemiology: Summary and Future Directions. *Epidemiol Rev* 1993; 15(1):256-263.

CHAPTER 4: CANCER PRONE PERSONALITY

This chapter contains the manuscript titled "The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part 1-The Cancer Prone Personality" published in Cancer Volume 91(4), pages 679-685, 2001.

The authors of this publication are Melanie A Price, Christopher C Tennant, Ross C Smith, Phyllis N Butow, Susan J Kennedy, Marjorie B Kossoff and Stewart M Dunn.

Changes have been made in response to examiners recommendations and therefore this chapter varies from the published version

A reprint version of this article is in appendix XIV

The table numbers have been renumbered to maintain consistency with the thesis.

Abstract

Background: Temoshok's "Cancer Prone Personality" theoretically predisposes some individuals to develop cancer and progress more quickly through its stages. *Methods:* This study examines the role of personality variables in 2,224 older women recalled for assessment following routine mammography breast screening. Using a semi-prospective design subjects completed self report measures of defense style, locus of control, emotional expression and control, self esteem, trait anxiety, and state anxiety and depression while waiting for medical examination. MANCOVA analysis was used to control for known risk factor variables and examine differences between three control groups (normal tissue controls, benign/cystic controls not requiring biopsy and benign biopsy controls) and 298 breast cancer subjects. *Results:* No differences were detected between breast cancer subjects and controls on measures of mature, immature and neurotic defense style, locus of control of behaviour, emotional expression-in, emotional expression-out and emotional control, self esteem, anxiety, or depression. *Conclusions:* We found no evidence to support an independent association between these personality measures and the development of breast cancer. Findings are discussed in the context of previous research.

Introduction

Despite limited empirical evidence of a role for psychosocial factors in the development of breast cancer, there is widespread belief to the contrary.¹⁻² While some researchers are satisfied the role of psychosocial variables in the development of breast cancer is negligible,³⁻⁴ others believe that the evidence to date has not been of sufficient quality to constitute a "fair test" of this hypothesis.⁵⁻⁷

One of the main factors studied and the focus of this report is that of personality. The "Cancer Prone Personality" theoretically predisposes some individuals to develop cancer and progress more quickly through its stages.⁸ The three components of this personality type are: (a) a distinctive coping style characterised by abrogating one's needs in favour of the needs of others; (b) difficulty in expressing emotions; and (c) an attitude of helplessness or hopelessness.⁸ The empirical evidence to support this theory in the case of breast cancer is equivocal. Much of the research focuses on emotional suppression or emotional control. Six out of thirteen studies in this area reported negative results.⁹⁻¹⁴ Of the seven studies reporting positive results,¹⁵⁻²¹ only two were adjusted for age; one of these had a very poor response rate,¹⁹ perhaps introducing significant sample bias while the other found anger repression was associated with breast cancer only in patients younger than 50 years.¹⁶

The current study examined the role of several personality variables including defense style and emotional expression and control, as well as recent life events and social support. The goal was to tease apart the components of "stress" and personality in a large sample, thus offering a fair test of a role for psychosocial variables in the development of breast cancer. The present paper reports our findings on three domains of the Type C personality style in relation to the development of breast cancer. Results of the accompanying data on life event stress and social support in a subset of this sample will be reported separately.

Methods

National Breast Screening commenced in Australia in 1993, actively recruiting women aged 50-69 for screening from electoral rolls. Free screening, however, is available to all women over age 40. Women attending the Northern Sydney and Lower Central Coast Breast Screening Program from April 1994 to April 1997 and who were recalled for assessment on radiological grounds, (ie an abnormal screening mammogram), were invited to participate in research examining the psychosocial factors in breast cancer development. Screening rounds one and two were in progress during the period of the study. The study was approved by the Royal North Shore Hospital Medical Research Ethics Committee.

On arrival at the clinic, consenting women completed a self-administered questionnaire while waiting for assessment. The assessment procedure could include mammography, physical examination, ultrasound and biopsy when indicated. The questionnaire included items on demographics, biological risk factors including reproductive history and hormonal variables, as well as several psychological questionnaires. These data are the focus of this paper. A subset of this sample, those requiring needle biopsy for a definitive diagnosis were interviewed for a history of recent life events, bereavement and social support prior to their test results being available; these data are reported separately in an accompanying paper. Results of the assessment procedure were subsequently established through the clinic records.

The inclusion criteria were: (a) attendance for assessment following routine breast screening; (b) age 40 years and older; and (c) adequate command of English. The exclusion criteria were: (a) prior history of breast cancer; (b) breast symptoms prompting screening; (c) knowledge of final assessment diagnosis; and (d) physical or psychiatric impairment inhibiting completion of questionnaire and/or interview.

Demographic and somatic risk factor variables were collected by self-report and included age, marital status, education, employment, family history of breast cancer, history of benign breast disease, parity, age at birth of first child, lactation, menopausal status, age at onset of menopause, oral contraceptive use, hormone replacement therapy, height, weight, alcohol and cigarette consumption.

Self-report questionnaires were used to examine the three domains of Temoshok's⁸ Cancer Prone Personality. Each questionnaire has accepted validity and reliability and has been used in similar populations.

(a) Coping Style: Emotion-focused coping was assessed by the Defense Style Questionnaire (DSQ-40).²² Defense style reflects a stable pattern of feelings, thoughts, or behaviours used to alleviate the conflict or stressors that give rise to anxiety.²³ Based on DSM-111-R definitions,²³ the 40-item measure yield scores for three defense styles: mature, neurotic and immature. Higher scores reflect greater use of a defense style. Problem-focused coping was measured by the Locus of Control of Behaviour (LCB) scale.²⁴ Designed to assess perceived control over behaviour, this 14-item measure yields a single factor reflecting internal/external locus of control of behaviour. A higher score indicates an external locus of control and a low score indicates an internal locus of control.

(b) Emotional Expression and Control: The Emotional Expression and Control scale (EEC) was used to assess the expression and control of negative emotions.²⁵ Developed from the Watson and Greer²⁶ measure of emotional control and Spielberger's concept of anger expression,²⁷ the focus is on self-reported expression and control of anger, anxiety and depression. The 18-item measure yields scores on three factors: emotional expression-in reflecting the expression of emotions to one's self; emotional expression-out reflecting the expression of emotions toward others, and emotional control reflecting the extent of control over emotions.²⁵ Higher scores respectively reflect more emotional expression in, more emotional expression out or more emotional control.

(c) Helplessness and Hopelessness: There is scant description of this dimension by Temoshok (1987) but the dimension of helplessness and hopelessness has grown primarily from studies implicating depression and anxiety and therefore the focus of examining this dimension has been trait and state depression and anxiety measures. Rosenberg's 10-item Self-Esteem scale measures the self-acceptance aspect of self-esteem and was used as a measure of trait depression.²⁸ Lower scores on this scale reflect higher self-esteem. Trait

anxiety was assessed using the sub-scale from Spielberger's State-Trait Personality Inventory (STPI).²⁹ The ten items refer to how a person generally feels and a higher total score reflects higher trait anxiety. The Hospital Anxiety and Depression scale (HAD)³⁰ assesses state anxiety and state depression. Excluding any reference to somatic symptoms, the 14 items refer to how the respondent has been feeling in the last week. Anxiety and depression in this measure are clearly distinguished, with scores greater than ten on either sub-scale reflecting clinically significant mood disturbance and scores between 8 and 10 representing borderline mood disturbance.

Multivariate analysis of covariance was performed using SPSS for windows 6.1.3. The psychological variables included in analysis were continuous and included: mature, immature and neurotic defense style, locus of control of behaviour, emotional expression-in, emotional expression-out, emotional control, self esteem, trait anxiety, state anxiety and state depression. Eleven variables were included as covariates: age, level of education, age at onset of menopause, first birth after age 29 years, parity, family history of breast cancer, history of benign breast disease, oral contraceptive use, current hormone replacement therapy, alcohol consumption and body mass index.

Results

A total of 2821 women were eligible to participate in this study. Thirteen percent of eligible women declined participation and a further eight percent had incomplete questionnaires, resulting in a total of 2,224 (79%) questionnaires available for the final analysis. Subjects were classified into four groups according to diagnosis and testing conditions. There were three control groups: normal tissue controls (n=947), benign or cystic lesions not requiring biopsy confirmation (n=644), benign lesions requiring biopsy confirmation (n=335); these groups were compared with breast cancer subjects (n=298).

No direct information was available for women declining to participate in the study. However, comparing our sample to the available statistics from the screening program assessment clinic, data on age, percentage of women requiring biopsy and percentage diagnosed with cancer during for the years 1994-1996 inclusive suggests minimal participation bias with respect to these variables. The mean age of women recalled for assessment was 56.7 years and the mean age of our sample was 56.1 years. The percentage of women recalled for assessment requiring needle biopsy was 23.3% compared with 28.5% of our sample. Eleven percent of women recalled were diagnosed with breast cancer

compared with 13.4% of our sample. Our higher percentage of subjects undergoing biopsy in comparison to assessment clinic attendees is consistent with women not requiring biopsy having less time to complete their questionnaire prior to the completion of medical assessment.

Demographic and somatic risk factor variables are summarized in Table 13. Our sample was aged between 40 to 87 years with a mean age of 56.1 years. The breast cancer group, with a mean age of 61.2 years, was significantly older than each of the three control groups ($p < 0.0001$). After controlling for age, there were no group differences for marital status, education, or employment.

Family history was defined as a first degree relative with breast cancer, distinguishing between a diagnosis before and after age 50 years; and group differences were non-significant ($p > 0.05$). No significant differences were detected for age at birth of first child, parity, age of onset of menopause, length of lactation or cigarette consumption. Normal tissue controls were less likely than the other groups to have previously had surgical removal of benign breast tissue ($p < 0.01$). Significant differences were detected between groups for menopausal status, oral contraceptive use, current use of hormone replacement therapy, daily alcohol consumption and body mass index (Table 13). Further details of these data are published elsewhere.³¹

Age, surgical removal of benign breast tissue, oral contraceptive use, current use of hormone replacement therapy, daily alcohol consumption and body mass index were selected as confounders on the basis of significant group differences. Age at onset of menopause (premenopausal/postmenopausal <40/41-45/46-50/50+/unknown), family history of breast cancer (none/ diagnosed 50+ years/ diagnosed <50 years/ unknown), first birth after age 29 years and parity (0, 1-2, 3+) were included as well documented correlates of breast cancer. Level of education was highly correlated with the majority of psychological variables and included as a covariate.

Table 14 displays group means for the eleven psychological variables. Using Wilk's criterion, these variables were not significantly different across the four groups ($F_{(33, 6479.36)} = 1.13, p = 0.28$). Results of univariate F-tests for individual variables controlling for covariates and confounders and other psychological variables are also shown in Table 14. To increase power, the three control groups were combined into one "non cancer" control group for comparison to the breast cancer group; this did not substantially change the findings.

Table 13: Demographic and somatic risk variable for the breast cancer group and non cancer control groups

Variable	Groups				Statistic
	Non Biopsy		Biopsy		
	Normal Tissue (n=947)	Benign/Cystic (n=644)	Benign Disease (n=335)	Breast Cancer (n=298)	
	N (%)	N (%)	N (%)	N (%)	
<i>Mean Age (SD) in years</i>	54.67 (9.16)	55.30 (8.54)	57.08 (9.91)	61.22 (9.43)	F=41.87, p<0.0001
<i>Current marital status</i>					$\chi^2(6)=23.60$
Married/Defacto	723 (76.7)	472 (73.6)	231 (70.2)	202 (68.9)	(p=0.005)
Single/Never married	50 (5.3)	39 (6.1)	23 (7.0)	17 (5.8)	
Widowed	65 (6.9)	50 (7.8)	34 (10.3)	44 (15.0)	
Divorced	105 (11.1)	80 (12.5)	41 (12.5)	30 (10.2)	
<i>Level of education</i>					$\chi^2(12)=11.9$
Primary	34 (3.6)	19 (3.0)	17 (5.2)	10 (3.4)	(p=0.45)
3-4 years secondary	357 (37.9)	230 (36.0)	130 (39.6)	112 (38.1)	
5-6 years secondary	147 (15.6)	93 (14.6)	53 (16.2)	51 (17.3)	
Diploma/certificate	212 (22.5)	170 (26.6)	78 (23.8)	72 (24.5)	
University/college	191 (20.3)	127 (19.9)	50 (15.2)	49 (16.7)	
<i>Family history of breast cancer</i>					$\chi^2(9)=16.71$
None	765 (80.8)	544 (84.5)	270 (80.6)	231 (77.5)	(p=0.053)
Diagnosed after age 50	79 (8.3)	43 (6.7)	16 (4.8)	29 (9.7)	
Diagnosed before age 50	58 (6.1)	31 (4.8)	31 (9.3)	22 (7.4)	
Unknown family history	45 (4.8)	26 (4.0)	18 (5.4)	16 (5.4)	
<i>History of benign breast disease</i>					$\chi^2(3)=13.18$
No	802 (86.6)	510 (80.1)	269 (83.3)	231 (81.1)	p=0.004
Yes	124 (13.4)	127 (19.9)	54 (16.7)	54 (18.9)	
<i>Age at birth of first child</i>					$\chi^2(12)=11.3$
Nulliparous	136 (14.7)	77 (12.3)	47 (15.1)	36 (12.9)	p=0.50
<20 years	48 (5.2)	28 (4.5)	12 (3.9)	8 (2.9)	
20-24 years	261 (28.3)	179 (28.6)	100 (32.2)	75 (27.0)	
25-29 years	308 (33.4)	231 (36.9)	93 (29.9)	101 (36.3)	
≥30 years	170 (18.4)	111 (17.7)	59 (19.0)	58 (20.9)	

^aNumbers for each variable may not add up to total due to missing values.

^bKnown age of menopause only

Table 13 (continued): Demographic and somatic risk variable for the breast cancer group and non cancer control groups

Variable	Groups				Statistic
	Non Biopsy		Biopsy		
	Normal Tissue (n=947) N (%)	Benign/ Cystic (n=644) N (%)	Benign Disease (n=335) N (%)	Breast Cancer (n=298) N (%)	
Parity					$\chi^2(6)=5.24$
Nulliparous	136 (14.6)	77 (12.2)	47 (15.1)	36 (12.8)	p=0.51
1-2	463 (49.7)	302 (47.9)	148 (47.0)	132 (46.8)	
≥3	333 (35.7)	252 (39.9)	119 (37.8)	114 (40.4)	
Menopausal Status					$\chi^2(3)=55.8$
Premenopausal	332 (35.1)	200 (31.1)	99 (29.6)	37 (12.4)	p<0.0001
Postmenopausal	615 (64.9)	444 (68.9)	236 (70.4)	261 (88.6)	
Age at Menopause^b					$\chi^2(6)=3.96$
<45 years	214 (35.7)	141 (32.5)	71 (34.8)	68 (28.9)	p=0.68
46-50 years	215 (35.8)	160 (36.9)	74 (36.3)	94 (40.0)	
>50 years	171 (28.5)	133 (30.6)	59 (28.9)	73 (31.1)	
Oral contraceptives					$\chi^2(3)=9.26$
<1 year in total ever	319 (35.8)	219 (35.8)	131 (43.5)	114 (42.5)	p=0.026
≥1 year total ever	571 (64.2)	393 (64.2)	170 (56.5)	154 (57.5)	
Hormone replacement therapy					$\chi^2(3)=10.81$
No current use	613 (65.6)	399 (62.5)	233 (73.0)	181 (64.0)	p=0.01
Current use	321 (34.4)	239 (37.5)	86 (27.0)	102 (36.0)	
Alcohol consumption					$\chi^2(9)=28.7$
None	181 (19.9)	147 (23.7)	69 (21.9)	61 (21.8)	p=0.0007
Occasional	227 (25.0)	178 (28.7)	93 (29.5)	64 (22.9)	
Weekly	278 (30.6)	176 (28.3)	95 (30.2)	65 (23.2)	
Daily	223 (24.5)	120 (19.3)	58 (18.4)	90 (32.1)	
Body mass index (BMI)					$\chi^2(3)=16.9$
BMI<25	555 (62.8)	394 (65.6)	173 (57.7)	137 (51.9)	p=0.0007
BMI≥25	329 (37.2)	207 (34.4)	127 (42.3)	127 (48.1)	

^aNumbers for each variable may not add up to total due to missing values.

^bKnown age of menopause only

Table 14: Mean scores (SD) and univariate F-tests for group differences on psychological variables between breast cancer and non cancer control groups

	Groups				Statistic
	Non Biopsy		Biopsy		
	Normal Tissue (n=947)	Benign/Cystic (n=644)	Benign Disease (n=335)	Breast Cancer (n=298)	
<i>Defense Style</i>					
<i>Mature</i>	6.24 (1.09)	6.28 (1.13)	6.27 (1.14)	6.37 (1.07)	$F_{(3,2209)}=0.05$, $p=0.99$
<i>Neurotic</i>	5.08 (1.13)	5.02 (1.13)	5.18 (1.20)	5.21 (1.14)	$F_{(3,2209)}=0.73$, $p=0.54$
<i>Immature</i>	3.63 (0.87)	3.60 (0.88)	3.69 (0.95)	3.69 (0.96)	$F_{(3,2209)}=2.08$, $p=0.10$
<i>Locus of Control of Behaviour</i>	21.48 (8.11)	20.61 (7.89)	21.76 (8.34)	21.96 (7.97)	$F_{(3,2209)}=1.62$, $p=0.18$
<i>Emotional Expression & Control</i>					
EE In	15.10 (4.08)	15.05 (4.06)	15.28 (4.49)	15.44 (3.88)	$F_{(3,2209)}=0.29$, $p=0.83$
EE Out	12.88 (3.43)	12.81 (3.12)	12.73 (3.52)	12.26 (3.01)	$F_{(3,2209)}=0.55$, $p=0.65$
Emotional Control	15.53 (3.79)	15.49 (3.77)	15.56 (4.16)	15.76 (3.62)	$F_{(3,2209)}=0.77$, $p=0.51$
<i>Self Esteem</i>	18.06 (4.60)	17.54 (4.65)	18.29 (4.74)	17.83 (4.29)	$F_{(3,2209)}=1.44$, $p=0.23$
<i>Trait Anxiety</i>	17.72 (4.85)	17.17 (4.68)	17.74 (5.17)	17.22 (4.60)	$F_{(3,2209)}=1.39$, $p=0.25$
<i>State Anxiety</i>	7.66 (3.99)	7.13 (3.78)	7.52 (4.14)	7.54 (3.76)	$F_{(3,2209)}=2.88$, $p=0.04$
<i>State Depression</i>	3.23 (2.90)	2.98 (2.65)	3.16 (2.97)	2.83 (2.44)	$F_{(3,2209)}=0.93$, $p=0.43$

* analysis controlled for age, education, age at onset of menopause (premenopausal /<45/46-50/50+/unknown), family history of breast cancer (none/aged 50+/aged<50/ unknown), first birth>29, parity (none/1-2/3+), BMI (<25/25+), oral contraceptives (<1 year total/>1 year), daily alcohol consumption, removal benign breast disease, current hormone replacement therapy.

Discussion

The current study employed a semi-prospective design to examine the three domains of Temoshok's⁸ Cancer Prone Personality in relation to the diagnosis of breast cancer in a community sample of older women recalled following routine breast screening. This method minimizes biases associated with hospital based sampling of symptomatic women and enabled standardization in assessment process and reporting. Women attending for similar breast screening have similar scores to community normative data for the EPQ and STAI.³²

With disagreement remaining as to the appropriate comparison group for breast cancer,^{4, 33} we distinguished between "normal" breast tissue controls and those with benign breast disease. As an added precaution against a potential impact of ongoing testing procedures during participation, we made a further distinction between those who did and did not undergo needle biopsy.

Controlling extensively for established risk factors for breast cancer, we found no evidence of an association between defense style, locus of control of behavior, self-esteem, trait or state anxiety or state depression and breast cancer in this large sample. Of particular note was the absence of association between breast cancer and emotional expression and control variables.

There are some findings from previous research offering support for emotional suppression, repression or control being associated with breast cancer. Both Grassi and Cappellari¹⁵ and Fox et al.¹⁹ report significantly higher emotional control in breast cancer patients. However, Greer and Morris¹⁶ found women with breast cancer under age 50 were more likely to be extreme suppressors or extreme expressors of emotion when compared with benign controls. Morris et al.¹³ reported less expression of anger in breast cancer patients than controls, although only the 40-49 age group approached significance ($p=0.08$). Similarly Scherg et al.¹⁷ found breast cancer patients showed significantly more suppression of anger, but in the patients aged 20-50 years.

It could be argued that our somewhat "older" sample (mean 56 years) may mask the importance of emotional control or suppression that may have an effect in younger women. However, in reanalysing our data for the 726 women aged between 40 to 50 years, we found no evidence for an association between emotional expression and control variables, or the other psychological variables, and breast cancer. Although the number of breast cancer subjects for comparison is small in this age group in the current study ($n=39$), the numbers

are not dissimilar to other studies reporting a positive association between emotional control or suppression and breast cancer.

However, the findings of the current study are consistent with those of Bleiker et al. in a large prospective study of a Dutch screening population that found no association between emotional expression and control and subsequent breast cancer diagnosis.¹⁰ With the largest series of breast cancer subjects in this area of research, we believe our study has sufficient power to detect small differences between groups.

The importance of controlling for established risk factor variables in the examination of potential psychological risk factors for breast cancer is undisputed, although the process of selecting adequate and appropriate combination of confounding variables is not precise. Although we considered a large number of risk factor variables, some limitations should be noted. Age at menarche was not included, primarily because the accuracy in recalling this in older women has been queried and there is some evidence this variable is more important in younger women.³⁴ We considered the history of benign breast disease in terms of surgical confirmation rather than prior breast biopsy, currently a more common method of diagnosing benign breast disease. In addition, the use of hormone replacement therapy was limited to current use, rather than including recent use, which has recently been identified as increasing breast cancer risk.³⁵

Although we employed a quasi-prospective design to examine a large asymptomatic community-based sample, the inherent limitations of this design can only be overcome with a truly prospective design. It is possible that the measures we have employed, although reliable and valid, may not be adequate to assess the concept of Type C personality. However, it may be more likely that the contribution of psychological factors in the incidence of breast cancer is small.³⁶⁻³⁷ If there is a premorbid cancer personality, the usefulness of examining personality alone, rather than in conjunction with stress, is questionable, given the two are fundamentally linked.³⁶

In conclusion, the findings of the current study do not support a direct role for personality in the development of breast cancer in older asymptomatic women attending a free community-based mammography screening program. It is possible that personality variables such as emotional control and defense style have no direct impact on the development of breast cancer, but are vulnerability factors that moderate the impact of life event stress on the development of breast cancer. We are exploring the latter hypothesis in our analysis of stressful life events.

References

1. Baghurst KI, Baghurst PA, Record SJ. Public perceptions of the role of dietary and other environmental factors in cancer causation or prevention. *J Epidemiol Community Health* 1992; 46:120-6.
2. Brinton LA, Malone KE, Liff J, Schoenberg JB. Re: "Should we consider a subject's knowledge of the etiologic hypothesis in the analysis of case-control studies?" *Am J Epidemiol* 1994; 140:1054-6.
3. Cassileth BR. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1996; 77(6):1015-6.
4. Barraclough J. Adverse life events and breast cancer. Other studies have found no association. *BMJ* 1996; 312(7034):845.
5. McGee R, Williams S, Elwood M. Are life events related to the onset of breast cancer? *Psychol Med* 1996; 26:441-7.
6. Burke MA, Goodkin, K. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1997; 79(5):1055-9.
7. Faragher MG, Cooper CL. 'Are life events related to the onset of breast cancer?' *Psychol Med* 1997; 27(2):497-8.
8. Temoshok L. Personality, coping style, emotion and cancer: toward an integrative model. *Cancer Surveys* 1987; 6:545-67.
9. Hahn RC, Petitti DB. Minnesota Multiphasic Personality Inventory-Rated Depression and the Incidence of Breast Cancer. *Cancer* 1988; 61:845-8.
10. Bleiker EM, van der Ploeg HM, Hendriks JH, Ader HJ. Personality factors and breast cancer development: a prospective longitudinal study. *J Natl Cancer Instit* 1996; 88(20):1478-82.
11. Kreitler S, Chaitchik S, Kreitler H. Repressiveness: cause or result of cancer? *Psychooncology* 1993; 2:43-54.
12. Edwards JR, Cooper CL, Pearl SG, de Paredes ESO, Leary T, Wilhelm MC. The relationship between psychosocial factors and breast cancer: some unexpected results. *Behav Med* 1990; 16(1):5-14.
13. Morris T, Greer S, Pettingale KW, Watson M. Patterns of expression of anger and their psychological correlates in women with breast cancer. *J Psychosom Res* 1981; 25(2):111-7.

14. Anagnostopoulos F, Vaslamatzis G, Markidis M, Katsouyanni K, Vassilaros S, Stefanis C. An investigation of hostile and alexithymic characteristics in breast cancer patients. *Psychother Psychosom* 1993; 59(3-4):179-89.
15. Grassi L, Cappellari L. State and trait psychological characteristics of breast cancer patients. *New Trends Experimental Clin Psychiatry* 1988; IV-N.2:99-109.
16. Greer S, Morris, T. Psychological attributes of women who develop breast cancer: a controlled study. *J Psychosom Res* 1975; 19(2):147-53.
17. Scherg H, Cramer I, Blohmke M. Psychosocial factors and breast cancer: a critical reevaluation of established hypotheses. *Cancer Detect Prev* 1981; 4:165-71.
18. Faragher EB, Cooper CL. Type A stress prone behaviour and breast cancer. *Psychol Med* 1990; 20(3):663-70.
19. Fox CM, Harper AP, Hyner GC, Lyle RM. Loneliness, emotional repression, marital quality, and major life events in women who develop breast cancer. *J Community Health* 1994; 19(6):467-82.
20. Cheang A, Cooper CL. Psychosocial factors in breast cancer. *Stress Med* 1985; 1:61-6.
21. Watson M, Pettingale KW, Greer S. Emotional control and autonomic arousal in breast cancer patients. *J Psychosom Res* 1984; 28(6):467-74.
22. Andrews G, Singh M, Bond M. The Defense Style Questionnaire. *J Nerv Mental Diseases* 1993; 181(4):246-56.
23. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders III Revised (DSM-III-R). Washington DC, 1987.
24. Craig A, Franklin J, Andrews G. A scale to measure locus of control of behaviour. *Br J Med Psychol* 1984; 57:173-80.
25. Bleiker EM, van der Ploeg HM, Hendriks JH, Leer JW, Kleijn WC. Rationality, emotional expression and control: psychometric characteristics of a questionnaire for research in psycho-oncology. *J Psychosom Res* 1993; 37(8):861-72.
26. Watson M, Greer S. Development of a questionnaire measure of emotional control. *J Psychosom Res* 1983; 27(4):299-305.
27. Spielberger CD. State-Trait Anger Expression Inventory, STAXI. Professional Manual. Odesa. FL: PAR, 1988.
28. Rosenberg M. Society and the adolescent self-image. Princeton, New Jersey: Princeton University Press, 1965.

29. Spielberger CD, Jacobs GA, Crane RS, Russell SF, Westberry L, Barker L, et al. Preliminary manual for the State-Trait Personality Inventory (STPI). Tampa, University of South Florida: Human Resources Institute, 1979.
30. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67:361-70.
31. Price MA, Tennant CC, Smith RC, Butow PN, Kennedy SJ, Kossoff MB et al. Predictors of breast cancer in women recalled following screening. *Aust N Z J Surg* 1999; 69:639-46.
32. Morris T, Greer S. Psychological characteristics of women electing to attend a breast screening clinic. *Clin Oncol* 1982; 8(2):113-9.
33. Barraclough J. Life events and the outcome of breast cancer. In: Lewis CE, O'Sullivan C, Barraclough J, eds. *The Psychoimmunology of Cancer: Mind and Body in the Fight for Survival?* Oxford: Oxford University Press, 1994; 213-27.
34. Kelsey JL, Gammon MD, John EM. Reproductive Factors and Breast Cancer. *Epidemiologic Reviews* 1993; 15(1):36-47.
35. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. *Lancet* 1997; 350:1047-59.
36. Fox BH. Premorbid Psychological factors as Related to Cancer Incidence. *J Behav Med* 1978; 1(1):45-133.
37. Fox BH. The role of psychological factors in cancer incidence and progression. *Oncology* 1995; 9(3): 245-53.

CHAPTER 5: LIFE EVENTS, COPING, PERSONALITY, SOCIAL SUPPORT AND THEIR INTERACTIONS

This chapter contains the manuscript titled "The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part 2 - Life Event Stressors, Social Support, Defense Style, and Emotional Control and Their Interactions" published in *Cancer* Volume 91(4), pages 686-697, 2001.

The authors of this publication are Melanie A Price, Christopher C Tennant, Phyllis N Butow, Ross C Smith, Susan J Kennedy, Marjorie B Kossoff and Stewart M Dunn.

Changes have been made in response to examiners recommendations and therefore this chapter varies from the published version

A reprint version of this article is in appendix XV

The tables have been renumbered to maintain consistency within the thesis.

Abstract

Background: The evidence supporting an association between life event stress and breast cancer development is inconsistent. *Methods:* 514 women requiring biopsy following routine mammographic breast screening were interviewed using the Brown and Harris Life Event and Difficulties Schedule (LEDS). Other psychosocial variables assessed included social support, emotional control and defense style. Biopsy results identified 239 women with breast cancer and 275 women with benign breast disease. Multiple logistic regression was used to distinguish between breast cancer subjects and benign breast disease controls on these psychosocial variables and their interactions. *Results:* Results reveal a significant interaction between highly threatening stressors and social support. Women experiencing a stressor objectively rated as highly threatening and were without intimate emotional social support had a nine-fold increase in risk of a breast cancer diagnosis. *Conclusions:* Although there was no evidence for an independent association between life event stress and breast cancer, there is strong evidence that social support interacts with highly threatening stressors to significantly increase the risk of breast cancer.

Introduction

Renewed debate regarding the association between stress and the development of breast cancer coincides with the recent publication of three studies, two reporting significant association between antecedent life events and breast cancer and a third which found no association.¹⁻³ The series of commentaries on the topic of "stress and the development of breast cancer" also reflect the inconsistency of research findings.⁴⁻⁸ Assessments of existing findings include the opinion that there is a "relatively minor" role for stress or emotional factors in the aetiology of breast cancer,⁴ that the question is clinically unimportant,⁵ that major life events in the presence of other psychosocial factors increase the risk of breast cancer,⁶ and that an adequate test of the hypothesis has yet to be achieved.⁷⁻⁸ Despite this, there is widespread belief in the community that stress is a risk factor for cancer,⁹ and in particular breast cancer.⁹⁻¹⁰

Population based studies examining widowhood and divorce have found no association with breast cancer.¹¹⁻¹² Early childhood losses or separation from parents have also been studied, some reporting no increased risk of breast cancer¹³ and others reporting a significantly higher risk of cancer (including breast cancer).¹⁴

The majority of life event studies have used event checklists, an approach prone to under-

reporting of events, bias by mood state,¹⁵⁻¹⁶ and "insensitivity" due to lack of specificity and contextual details.¹⁷ It is therefore not surprising that studies using this approach have yielded mixed results; four negative findings,^{2, 18-20} three positive findings,^{3, 21-22} and two in which the breast cancer group experienced significantly less stress than the control group.²³⁻²⁴

Use of the Life Events and Difficulties Schedule (LEDS)²⁵ to objectively assess life event stress has produced somewhat more consistent results. This interview enables precise event definition and encompasses contextual information in independent ratings of event severity. Two studies report that recent events rated as the highest category of severity of threat were 2-3 times more frequent in women diagnosed with breast cancer than in those with benign disease.^{1, 16} However, a recent study using this approach failed to replicate these findings.²⁶

However, the study of life events alone may be a somewhat incomplete approach. It may be that life event stressors when examined in conjunction with vulnerability factors such as coping style, emotional and behavioural patterns, and social support, will enable the relative impact of components of psychosocial "stress" to be teased apart.^{8, 27} Only a few studies assess these multiple factors,^{1, 16, 19, 28} perhaps due to the large samples required for sufficient power to adequately assess the interaction of these psychosocial variables.

A significant weakness in this area of research is the essentially atheoretical approach to examining clearly interrelated psychosocial concepts in a multi-factorial disease such as breast cancer, despite models being available.²⁹ Both Greer and Watson³⁰ and Temoshok³¹ describe a cancer prone personality, thought to predispose an individual to developing cancer. This personality is related to stress, purported to be maladaptive under conditions of prolonged or severe stress, increasing rather than reducing the impact of stressors;³⁰⁻³¹ however, life event stress and personality are rarely considered together.

Based on existing evidence, Hilakivi-Clarke et al. outline a comprehensive model in which life event stress, personality and social support influence an individual's ability to cope, which in turn mediates breast cancer risk via alterations in neuroendocrine and immune functioning.³² The crucial factor in this model is not the stressor, but the complex interaction between stressors, personality, and social support that affect an individual's ability to cope. This model is compatible with more general model of stress and illness.¹⁷ In the Brown and Harris model, life events are conceptualized as provoking agents for illness, influenced by specific vulnerability factors such as social support, proposed to increase the impact of life events and consequently the resulting stress and strain.

Although the potential benefits of social support on health, quality of life and immunity are well established,³³⁻³⁵ consideration of the role of social support in breast cancer has generally focused on its ability to mitigate the impact of diagnosis, adjustment to illness and prognosis.^{36, 41}

Only a few studies have considered social support in relation to the development of breast cancer. Bleiker et al. using an unspecified self-report measure of social support, reported no association with breast cancer.⁴² Cooper et al.²⁸ and Edwards et al.¹⁹ reported no differences in the number of social supports available in a crisis between breast cancer cases and controls. One of the few studies in this area with a theoretical basis employed the Brown and Harris model to examine the modifying effect of social support on stressful life events in breast cancer development.¹⁵⁻¹⁶ However, high correlation of "lack of social support" with "life events" precluded the inclusion of support in the model. To overcome the difficulty of assessing the components of stress, Tennant et al. have suggested that stress related variables, such as life events, social support, personality and coping should be assessed as distinct concepts.⁴³

The aim of the current study was to examine the role of antecedent life stressors, together with psychosocial "vulnerability" factors including social support, coping style and emotional control, in the diagnosis of breast cancer in asymptomatic women attending a community based mammographic breast screening program. This study design was chosen to minimise selection bias and enabled assessment to be carried out with both subjects and researchers blind to disease status.

Material and methods

Subjects

Eligible subjects were asymptomatic women requiring needle biopsy for diagnosis of breast disease following routine breast screening. Women attending the Northern Sydney and Lower Central Coast Breast Screening Program from April 1994 to April 1997 and who were recalled on radiological grounds, were invited to participate in research examining the psychosocial factors in breast cancer development. Participation involved completing a self-report questionnaire detailed below and fully reported separately. Life event stress and social support details were collected by personal interview. The ideal of interviewing all subjects was unfeasible; instead, a subset of the sample, those undergoing breast biopsy, were selected for interview. This group shared similar conditions of testing and were expected to experience similar apprehensiveness prior to diagnosis. This paper focuses on interview and

questionnaire data from women undergoing biopsy.

The inclusion criteria were: (a) undergoing breast biopsy following routine breast screening; (b) age 40 years and older; and (c) adequate command of English. The exclusion criteria were: (a) prior history of breast cancer; (b) breast symptoms prompting screening; (c) knowledge of results of biopsy; and (d) physical or psychiatric impairment inhibiting completion of questionnaire and/or interview.

Procedure

The complete assessment procedure, from mammogram to ultrasound, physical examination and biopsy, usually occurred on the same day. On arrival at the clinic, consenting women completed a self-administered questionnaire while waiting for assessment. After consenting to the biopsy procedure, subjects were interviewed prior to their test results being available. Approval for the study was granted by the Royal North Shore Hospital Medical Research Ethics Committee.

Measures

Demographic and somatic risk factor variables were collected by self-report and included age, marital status, education, employment, family history of breast cancer, history of benign breast disease, parity, age at birth of first child, lactation, menopausal status, age at onset of menopause, oral contraceptive use, hormone replacement therapy, height, weight, alcohol and cigarette consumption.

Self-report psychological questionnaires assessed features of the Cancer Prone personality. Emotion-focused coping was assessed using the DSQ-40 yielding scores for mature, immature and neurotic defense style.⁴⁴ Problem-focused coping was assessed by the Locus of Control of Behaviour (LCB) scale yielding a single factor reflecting internal/external locus of control.⁴⁵ The Emotional Expression and Control scale (EEC) measuring the expression and control of anger, anxiety and depression resulting in three factor scores: emotional expression-in, emotional expression-out, and emotional control.⁴⁶ Rosenberg's Self-Esteem scale measured the self-acceptance aspect of self-esteem.⁴⁷ Trait anxiety was assessed using the State-Trait Personality Inventory (STPI).⁴⁸ State anxiety and state depression was assessed using the Hospital Anxiety and Depression scale (HAD).⁴⁹ Detailed analysis of these data are reported separately.

An abbreviated version of the Henderson Social Support Interview Schedule was

administered to assess social support.⁵⁰ Independent ratings of intimate and non-intimate support for both emotional and instrumental support were made to reflect availability and quality. Ratings were made on a three point scale (poor, adequate, good) where a 'good' rating reflected support generally available and comforting; an 'adequate' rating reflected support available but with some form of restriction and a 'poor' rating reflected limited availability and/or uncertainty in the quality of support. Subjective appraisal of support was also recorded using this three point scale and subjective evaluation of change in support during the past two years was recorded (better, worse, no change).

The Bedford College Life Events and Difficulties Schedule (LEDS)²⁵ was used to collect details about life stressors occurring during the previous two years. This semi-structured interview allows details of life stressors and the context in which they occurred to be recorded. A vignette of each subject's personal circumstances and stressors was presented to independent raters, without reference to the subject's emotional responses or diagnosis. Of prime interest in this study was the ongoing impact of stressors reflected in the ratings of long-term "threat".

Long-term threat defines the degree of impact of a stressor a week after the occurrence. Severity of long-term threat was rated for each stressor on a five-point scale. Ratings were based on the criteria described and detailed examples provided by the authors of the schedule, with the addition of categories (none and extreme) to allow further distinction of stressors at the extremes. For example, the death of a spouse or child would be rated at the highest level of threat (extreme); the death of an elderly parent living in the same home would be rated a degree lower (severe); whereas the death of a parent-in-law not living in the same home but with regular contact would be rated another degree lower (highly threatening).

A distinction was made according to the duration of the stressor. Stressors were regarded as acute if less than six months in duration and chronic if continuing for 6 months or longer. Both acute and chronic stressors were categorized according to type (health of self, health of other, death, role/interaction, crisis/news, employment, financial, marital, miscellaneous).

Training of the interviewers and raters for this study was conducted by an expert in the field (CT). Interviews were conducted prior to results being available to either the subject or interviewer. The content of the interviews were rated independently with both the interviewer and rater blind to disease status. Inter-rater reliability for this study was 0.92.

The choice of time frame for assessment of stressors involved a difficult balance between the time period during which the impact of stressors is thought to influence tumour development, and that of optimising reliability in recalling life event stressors. The time from etiology to early detection of breast cancer is difficult to determine, but has been approximated at 18 years.⁵¹ Most reports suggesting a relationship between life event stressors and the diagnosis of breast cancer refer to a relatively short time frame, most commonly between two and five years, suggesting that any impact of stressors would be related to promoting tumour growth. Accuracy of recall using the checklist approach to examining life events rapidly decreases over six months particularly for less severe events, although the most severe events are least affected.⁵² However, using the LEDS approach, the fall-off in reporting of events is approximately five percent per year and is similar for severe and non-severe events.¹⁷ Given these data, a two year time frame for life events in our asymptomatic sample approximates the longer recall period of symptomatic women in previous studies, and ensures a high degree of reliability in recall.

Diagnosis of Cancer

Diagnosis of cancer was confirmed by histopathological results of breast tissue biopsy. Those without cancer were classified as benign controls.

Statistics

Data were analyzed using logistic regression to distinguish between subjects with breast cancer and control subjects with benign breast disease. Age was included as a confounder in all analyses. The final model included other confounders selected on both statistical and theoretical grounds.⁵³ All variables were entered simultaneously. Results are reported in terms of the Wald statistic, odds ratio and 95 percent confidence intervals. Variables were initially examined as "main effects". Interaction between the main effect variables were examined regardless of the individual significance of each main effect. All analyses were performed using SPSS for windows (SPSS Inc). Correlations are reported as Pearson's *r* for continuous variables and Spearman's *rho* for categorical variables. All *p*-values are two tailed.

Results

Sample Characteristics

Of 2,821 women recalled for assessment on radiological grounds following routine breast screening, 848 underwent needle biopsy and were invited to participate in this part of the study. One hundred and eight women (12.7%) declined to participate and a further 48 women initially agreeing to participate later declined to be interviewed (7%), representing a response rate of 80.3 percent. Of the 692 women participating, 176 (25.4%) were unable to be interviewed for logistical reasons including preliminary results of biopsy given to the subject prior to interview, leaving the clinic while the other subjects were being interviewed and no private space being available for the interview to be conducted. Five hundred and sixteen women were interviewed prior to results being available. One woman diagnosed with lymphoma and one woman whose final diagnosis was outstanding were excluded from analyses. Interview data were available for 239 women later confirmed to have breast cancer (46.5 percent) and 275 women diagnosed with benign breast disease (53.5 percent). Of all the women requiring biopsy following breast screening during 1994-1996 inclusive, 47.2% were diagnosed with breast cancer suggesting our sample is representative of our region. The benign to malignant biopsy ratio is consistent with other screening programs.⁵⁴⁻⁵⁷

The mean age of the cancer group was 61.3 years (SD 9.4), significantly older than benign controls with a mean age of 57.0 (SD 9.8), giving an odds ratio of 1.05 (95% CI 1.03-1.07). No differences were detected for marital status, occupational status, family history of breast cancer, history of benign breast disease, parity, age at menopause or obesity. There were increased odds of breast cancer with increasing level of education, increasing age at first birth for parous women, being post-menopausal, ever use of oral contraceptives, current use of hormone replacement therapy and daily alcohol consumption (Table 15).

Table 15: Demographic and risk factor variables for breast cancer

Variable	Benign Disease (n=275) n^a (%)	Breast Cancer (n=239) n^a (%)	Odds Ratio 95% CI (age adjusted)
<i>Mean (SD) Age (years)</i>	57.0 (9.8)	61.3 (9.4)	1.05 (1.03-1.07)
<i>Education</i>			
Primary	14 (5.2)	7 (3.0)	1-
3-4 years secondary	109 (40.7)	86 (36.6)	1.98 (0.74-5.30)
5-6 years secondary	41 (15.3)	41 (17.4)	2.46 (0.87-7.00)
Diploma/Certificate	68 (25.3)	58 (24.7)	2.67 (0.96-7.43)
University/College	36 (13.4)	43 (18.3)	3.78 (1.31-10.91)
<i>Marital Status</i>			
Married/Defacto	189 (70.3)	156 (66.4)	1-
Single	20 (7.4)	15 (6.4)	0.74 (0.38-1.52)
Widowed	27 (10.0)	36 (15.3)	0.93 (0.51-1.70)
Divorced/Separated	33 (12.3)	28 (11.9)	0.97 (0.55-1.70)
<i>Age at birth first child</i>			
Nulliparous	44 (17.3)	31 (14.1)	1-
<20	10 (3.9)	7 (3.2)	1.40 (0.46-4.22)
20-24	84 (33.1)	47 (21.4)	0.88 (0.48-1.60)
25-29	72 (28.3)	84 (38.2)	1.77 (1.00-3.15)
30+	44 (17.3)	51 (14.1)	1.81 (0.96-3.40)
<i>Parity</i>			
Nulliparous	44 (17.1)	31 (13.8)	1-
1-2	113 (44.0)	103 (46.0)	1.55 (0.89-2.69)
3+	100 (38.9)	90 (40.2)	2.31 (0.75-2.28)
<i>Family history</i>			
No	233 (84.7)	188 (87.7)	1-
Diagnosed <50 years	11 (4.0)	22 (9.2)	2.14 (0.99-4.61)
Diagnosed 50+ years	27 (9.8)	16 (6.7)	0.64 (0.33-1.25)
Unknown	15 (5.5)	13 (5.4)	0.96 (0.44-2.11)

^aNumbers for each variable do not add up to total due to missing values.

Table 15 (continued): Demographic and risk factor variables for breast cancer

Variable	Benign Disease (n=275) n^a (%)	Breast Cancer (n=239) n^a (%)	Odds Ratio 95% CI (age adjusted)
<i>H/O Benign Breast Disease</i>			
No	223 (84.5)	188 (83.2)	1-
Yes	41 (15.5)	38 (16.8)	1.14 (0.70-1.87)
<i>Menopausal status</i>			
Premenopausal	83 (30.2)	31 (13.0)	1-
Postmenopausal	192 (69.8)	208 (87.0)	1.85 (1.05-3.25)
<i>Age at onset of menopause*</i>			
<45 years	52 (32.1)	51 (27.9)	1-
46-50 years	58 (35.8)	76 (41.5)	1.41 (0.84-2.39)
>50 years	52 (32.1)	56 (30.6)	1.16 (0.67-2.00)
<i>Ever use oral contraceptives</i>			
No	102 (42.0)	90 (42.3)	1-
Yes	141 (58.0)	123 (57.7)	1.67 (1.08-2.59)
<i>Current hormone replacement therapy</i>			
No	194 (74.6)	149 (66.2)	1-
Yes	66 (25.4)	76 (33.8)	1.51 (1.01-2.25)
<i>Alcohol consumption</i>			
None	58 (22.5)	47 (21.1)	1-
Occasional	73 (28.3)	54 (24.2)	1.03 (0.61-1.77)
Weekly	83 (32.2)	42 (18.8)	0.78 (0.45-1.36)
Daily	44 (17.1)	80 (35.9)	2.58 (1.49-4.48)
<i>Body mass index (BMI)</i>			
BMI=25	145 (59.7)	111 (52.9)	1
BMI>25	98 (40.3)	99 (47.1)	1.28 (0.87-1.87)

^aNumbers for each variable do not add up to total due to missing values.

Acute Stressors

Our first hypothesis was that there was a threshold at which acute stressors may trigger or at least promote cancer growth. This being the case we expected that significantly more women diagnosed with breast cancer would have experienced a highly threatening acute stressor compared to benign controls. One thousand, four hundred and fifty three acute stressors were recorded in the two year period prior to biopsy. The mean number of acute stressors experienced was 2.82 for the breast cancer group and 2.84 in the benign group (OR = 1.04, CI 0.94-1.16). Table 16 displays numbers of subjects reporting acute stressors according to severity ratings for long-term threat. More of the cancer group did report an acute stressor rated as extremely threatening (4.6%) in comparison to the benign group (2.9%), although after adjusting for age, the difference failed to reach statistical significance (OR = 1.06, CI 0.37-3.02). Combining stressors rated as extremely and severely threatening for long term threat, the percentage of women experiencing such was similar across groups (OR 0.89, CI 0.49-1.62). The numbers of women experiencing an acute stressor rated as of high, moderate and mild degree of threat were also similar across the groups.

Testing the hypothesis that the type rather than severity of an acute stressor was more important (for example bereavement rather than employment), we proposed that women diagnosed with breast cancer would have experienced more bereavements prior to diagnosis compared to benign controls. However, there were no significant differences between the groups for any of the ten categories of acute stressors reported and specifically the number of women widowed in the past two years was not significantly different across the two groups.

Table 16: Number of subjects reporting at least one acute stressor for each severity rating of long term threat in the two year period prior to interview

Severity Rating of Long Term Threat for Acute Stressors (rating)	Benign n (%)	Cancer n (%)	Odds Ratio (95% CI)*
<i>Extreme (5)</i>	8 (2.9)	11 (4.6)	1.06 (0.37, 3.02)
<i>Severe (4)</i>	24 (8.7)	20 (8.4)	0.95 (0.48, 1.87)
<i>High (3)</i>	61 (22.2)	47 (19.7)	0.94 (0.59, 1.50)
<i>Moderate (2)</i>	151 (54.9)	115 (48.1)	0.75 (0.51, 1.10)
<i>Mild (1)</i>	164 (59.6)	140 (58.6)	1.15 (0.77, 1.72)
<i>Extreme / Severe (4, 5)</i>	32 (11.6)	28 (11.7)	0.89 (0.49, 1.62)
<i>Extreme / Severe / High (3, 4, 5)</i>	84 (30.5)	70 (29.3)	0.92 (0.61, 1.39)

*adjusted for age

Chronic Stressors

Examining the possibility that chronic stressors were of more importance in promoting tumour growth, we hypothesised that women diagnosed with breast cancer would have more chronic stressors and more threatening stressors prior to diagnosis compared to benign controls. We recorded 852 chronic difficulties impacting on the past two years, with no group differences detected in number (OR 1.08, CI 0.94-1.24). Chronic stressors in the highest two severity ratings of long term threat were rare and similar across groups (Table 17). Women with breast cancer did report significantly more chronic stressors in the lowest (mildly threatening) severity group (OR 1.72, CI 1.19-2.49); however the benign group reported more chronic stressors in both the moderate and high severity ratings, albeit non significant. The most common chronic stressor reported related to women's own health and there were no differences in the types of chronic stressors reported between the groups.

Table 17: Number of subjects reporting at least one chronic stressor for each severity rating (long term threat) in the two year period prior to interview

Severity Ratings of Long Term Threat for Chronic Stressors	Benign n (%)	Cancer n (%)	Odds Ratio (95% CI)*
<i>Extreme (5)</i>	1 (0.4)	0 (0.0)	
<i>Severe (4)</i>	6 (2.2)	5 (2.1)	1.03 (0.30-3.50)
<i>High (3)</i>	42 (15.3)	24 (10.0)	0.70 (0.41-1.22)
<i>Moderate (2)</i>	110 (40.0)	76 (31.8)	0.77 (0.53-1.13)
<i>Mild (1)</i>	141 (51.3)	159 (66.5)	1.23 (1.04-1.44)

*adjusted for age

Cumulative Stressors

We examined a model of "stress" which proposes a cumulative impact of life stressors, hypothesising that women diagnosed with breast cancer would have experienced more cumulative stress than women with benign breast disease. To test this, we calculated scores to estimate cumulative degree of stressors, separately for acute and chronic stressors as well as combining acute and chronic. Each stressor was allocated a weight according to its severity rating, and the weighted scores were totaled. Weightings of stressors were assigned according to Brown et al.⁵⁸ Stressors rated as mild or non threatening were weighted zero. Extreme stressors were weighted 5, severe weighted 4, high weighted 3, and moderate weighted 1. No differences were seen in weighted acute, weighted chronic or weighted

combined stressors scores (Table 18).

Table 18: Weighted scores for acute and chronic stressors in the two year period prior to biopsy

Weighted Stressor Scores	Benign Mean (SD)	Cancer Mean (SD)	Odds Ratio (95% CI)*
<i>Acute Stressors</i>	5.09 (4.17)	4.85 (4.01)	1.00 (0.95, 1.05)
<i>Chronic Stressors</i>	3.29 (3.08)	3.00 (2.90)	0.97 (0.91, 1.04)
<i>Acute and Chronic Stressors</i>	8.38 (5.53)	7.85 (5.19)	0.99 (0.96, 1.03)

*adjusted for age

Vulnerability Factors

Despite finding no evidence of an independent effect for life stressors, we proceeded to examine the effect of other psychosocial factors which we hypothesised to impact on the development of breast cancer through their interaction with life stressors. The “vulnerability factors” proposed in our model were a less mature coping style, higher emotional control and poor emotional social support.

Full analysis of psychological questionnaire data is reported separately. Selected variables, namely mature defense style and emotional control, are hypothesized here as vulnerability factors, increasing or decreasing the impact of life event stress, without individual etiological significance.¹⁶⁻²⁵ These variables are summarised in Table 19. There were no significant differences detected between groups for scores of mature defense style or emotional control.

Although breast cancer subjects reported “no intimate emotional support” (29.3%) slightly more often than control subjects (24.7%), after adjusting for age the differences were not significant (OR 0.87, CI 0.57-1.34). For those who did have an intimate social support, the groups were comparable in terms of the quality of this support (Wald χ^2 (2) =0.09, p=0.96). Non-intimate support ratings were generally good, with similar percentages of adequate ratings across the groups. Interestingly, more of the benign group reported having poor or no non-intimate support, although the numbers were small in this category and overall this variable was non-significant (Wald χ^2 (2) =6.68, p=0.35). There were no differences in subjective ratings of support (Wald χ^2 (2) =4.03, p=0.13) nor in recent changes in the subjective quality of support available (Wald χ^2 (2) =1.04, p=0.59).

Table 19: Descriptives for “vulnerability factors”, Wald statistic, Odds Ratios and corresponding 95 % Confidence Interval.

	Benign (n=275) Mean (SD)	Cancer (n=239) Mean (SD)	Wald χ^2	Odds Ratio (95% CI)*
<i>Mature Defense Style</i>	6.26 (1.10)	6.44 (1.05)	$\chi^2(1)=1.82$ (p=0.18)	1.12 (0.95-1.32)
<i>Emotional Control</i>	15.72 (3.86)	15.87 (3.53)	$\chi^2(1)=0.48$ (p=0.49)	0.98 (0.94-1.03)
	Benign N (%)	Cancer N (%)	Wald χ^2	Odds Ratio (95% CI)*
<i>Intimate Emotional Support</i>			$\chi^2(3)=0.46$	
<i>Good</i>	130 (47.3)	110 (46.0)	(p=0.93)	1-
<i>Adequate</i>	45 (16.4)	35 (14.6)		0.95 (0.56-1.60)
<i>Poor</i>	32 (11.6)	24 (10.0)		0.93 (0.51-1.69)
<i>None</i>	68 (24.7)	70 (29.3)		0.86 (0.54-1.38)
<i>Non-Intimate Emotional Support</i>			$\chi^2(2)=6.68$	
<i>Good</i>	227 (82.5)	208 (87.0)	(p=0.35)	1-
<i>Adequate</i>	31 (11.3)	29 (12.1)		1.07 (0.61-1.85)
<i>Poor/None</i>	17 (6.2)	2 (0.8)		0.14 (0.03-0.63)

*adjusted for age

Interactions

For the examination of interactions between life stressors and these other psychosocial factors, acute and chronic stressors were considered together in order to increase the power of these analyses. Therefore the term "major stressor" in these analyses was used to identify subjects reporting at least one acute or chronic stressor rated as either severe or extreme for long term threat in the past two years. Experiencing a major stressor was correlated with intimate emotional support ($\chi^2(2)=10.3$, $p=0.01$), but not correlated with mature defense style ($\rho=-0.04$, $p=0.38$) or emotional control ($\rho=0.08$, $p=0.06$).

The results of interactions between vulnerability factors and a major stressor on breast cancer risk are summarized in Table 20. There was no evidence that a less mature defense style (Wald $\chi^2(1)=2.23$, $p=0.14$) or higher emotional control (Wald $\chi^2(1)=0.02$, $p=0.90$) were interacting with the impact of a major stressor on the development of breast cancer.

Table 20: Wald χ^2 statistic, Odds Ratios and corresponding 95 percent confidence intervals for interaction terms between vulnerability and major stressor variables predicting breast cancer diagnosis

Interaction terms**	Wald χ^2 (df)	Odds Ratio (95% CI)*
<i>Stressor x Mature Defense Style</i>	$\chi^2(1)=2.23$, $p=0.14$	1.57 (0.87-2.82)
<i>Stressor x Emotional Control</i>	$\chi^2(1)=0.02$, $p=0.90$	1.01 (0.87-1.17)
<i>Stressor x Intimate Social Support Rating</i>	$\chi^2(2)=10.2$, $p<0.006$	
<i>x Good Intimate Support</i>		1-
<i>x Poor/Adequate Intimate Support</i>		1.15 (0.28-4.70)
<i>x No Intimate Support</i>		7.46 (1.84-30.22)
<i>Stressor x Mature Defense Style x Social Support</i>	$\chi^2(2)=0.18$, $p=0.91$	
<i>Stressor x Emotional Control x Social Support</i>	$\chi^2(2)=0.49$, $p=0.78$	

*age adjusted

**each interaction term tested by adding to the main effects only model

However, there was a significant interaction between a major stressor and intimate emotional support (Wald $\chi^2(2) = 10.19, p = 0.006$). For subjects who had a major stressor in the past two years, those rated as having "no intimate emotional support" had an age adjusted odds ratio for breast cancer of 7.46 (CI 1.84-30.22), compared to those rated as having "good" intimate emotional support. Of note, only 26 subjects (5.1 percent of sample) were in this category, 19 (73.1 percent) of whom were diagnosed with breast cancer. Of subjects who had a major stressor, those rated as having "poor or adequate" intimate emotional support were not significantly different from those rated with good intimate emotional support in the odds ratio for breast cancer (OR 1.15, CI 0.28-4.70).

We hypothesized that mature defense style and/or emotional control may be important in the face of a major stressor when no social support was available. However, we found no evidence to support these higher order interactions (Table 20).

Potential Confounders

A number of variables were considered as potential confounders for inclusion in the multivariate model for psychosocial predictors of breast cancer. Among sociodemographic and medical variables, age and education were treated as confounding variables, being associated with both stressor variables and with breast cancer. Also included were family history of breast cancer, history of benign breast disease, age at onset of menopause, age at birth of first child, parity, oral contraceptive use, current use of hormone replacement therapy, body mass index, and alcohol consumption. These were chosen on statistical and empirical grounds.⁵³

Although age was included as a potential confounder, there was still some concern that the impact of age was not adequately controlled.⁷ We hypothesized that age may have affected the likelihood of experiencing certain types or severity of stressors. Analyses were repeated separately on 271 women aged less than 60 years and on 243 women aged 60 years and over. No differences were seen between the breast cancer group and benign controls in each age group, in severity of events and difficulties reported, nor in the cumulative stressor scores.

Of trait personality variables examined (locus of control, emotional expression and control, defense style, self esteem, trait anxiety) and their sub-factors, none were independently associated with breast cancer, or with life event variables and therefore these were excluded as confounders. Higher state anxiety was associated with the number of chronic stressors

reported ($\rho=0.16$, $p<0.001$) but not the number of acute stressors ($p=0.26$) or severity of stressors ($p=0.16$) suggesting that anxiety was due to ongoing stressors, rather than anxiety influencing the reporting of stressors generally. With no group differences in levels of state anxiety, it was excluded as a confounder.

State depression scores, although not associated with the number of acute or chronic stressors, were associated with stressors in the highest two categories of threat ($\rho=0.14$, $p=0.002$); therefore state depression was treated as a potential confounder, despite not being associated with breast cancer. Non-intimate social support was also considered as a likely confounder, given the significance of intimate emotional support, and the trend for the control group to have poorer levels of non-intimate support, albeit non-significant.

The results of the multiple logistic regression model of psychosocial predictors of breast cancer including as potential confounders age, education, age at onset of menopause, family history of breast cancer, history of benign breast disease, age at birth of first child, parity, body mass index, alcohol consumption, oral contraceptive use, hormone replacement therapy, state depression and non-intimate social support are displayed in Table 21. The odds ratio for breast cancer for subjects reporting both a major stressor in the past two years and no intimate emotional support was 9.39 (CI 1.90-46.42). Thus considering the main effect variables, the odds of developing breast cancer for those reporting a major stressor in the past two years and no intimate emotional support is 3.5 times that of women reporting neither a major stressor in the past two years nor an absence of an intimate emotional support.

Table 21: Final Multiple Logistic Regression Model for Predictors of Breast Cancer

Term	β (SE)	Wald χ^2 (df), p	Odds Ratio (95% CI)*
<i>Stressor</i>	-0.66 (0.58)	$\chi^2(1)=1.31$	0.52 (0.17-1.60)
<i>Intimate Emotional Support</i>		$\chi^2(2)=1.52$	
<i>Good</i>			1-
<i>Poor/Adequate</i>	-0.04 (0.27)		0.96 (0.57-1.64)
<i>None</i>	-0.35 (0.29)		0.70 (0.39-1.25)
<i>Stressor*Intimate Emotional Support</i>		$\chi^2(2)=11.27,$ p=0.004	
+ <i>Stressor * Good Support</i>			1-
+ <i>Stressor * Poor/Adequate</i>	-0.21 (0.81)		1.03 (0.22-4.67)
+ <i>Stressor * No Intimate Support</i>	2.24 (0.82)		9.39 (1.90-46.42)

* includes main effects of age, education, age at menopause, family history of breast cancer, h/o benign breast disease, age at birth of first child, parity, body mass index, frequency of alcohol consumption, oral contraceptive use, hormone replacement therapy, state depression and non-intimate emotional support.

Discussion

The results of the current study revealed a significant increase in the development of breast cancer for women reporting a recent stressor independently rated at the highest levels of threat, but only for those without any intimate emotional support. (An intimate support refers to a partner in life, as opposed to close friend or family). The effect size for this specific group increased somewhat after adjustment for potential confounders including age, education, menopausal status, family history, history of benign breast disease, body mass index, reproductive history, alcohol consumption, oral contraceptive use, hormone replacement therapy and depression, and was 3.5 times those with neither of these features.

In contrast to past findings, we found no evidence for an independent association between recent life stressors and the development of breast cancer. Using the same method of assessing life event stress, both Geyer¹⁵⁻¹⁶ and Chen et al.¹ have reported a significant increase in risk of breast cancer following severely threatening life event stressors. The LEDS interview employed in these studies is a well established, reliable and comprehensive instrument, enabling independent rating of stressors according to precise definitions and encompassing contextual information.

Despite similarities in designs, the current study does vary from the earlier studies in a number of ways. The population from which our sample was drawn is more homogeneous being community based, asymptomatic and recalled for assessment purely on radiological grounds. Other studies have used symptomatic women, assessed by their primary physician, referred for biopsy from multiple sources and for varied reasons. The possibility that "awareness" of their diagnosis affected the reporting of psychosocial variables in our study is minimal.

As a consequence of targeting a mammography screened population, our sample was "older"; our breast cancer group an average of 61 years of age and our controls 57 years of age. The Geyer¹⁶ breast cancer group had a mean age of 49 years and controls 43 years and the Chen et al.¹ breast cancer group were an average of 57 years and controls had a mean age of 50 years. Although our two groups were significantly different in age, in real terms the difference was small and considerably less than the six to seven years age difference in the smaller studies, enabling us to better control for the influence of age.

These differences in age of study participants may be important in reconciling differences in reported outcome. Age is an independent risk factor for breast cancer, and is also associated

with the type and number of life events experienced, as well as social support. Although often included in analyses, McGee⁷ suggests the effects of age may not be adequately controlled by simple statistical means. This difficulty is most marked in smaller studies with larger ranges in age and it is possible that the independent effects of severely threatening events on the development of breast cancer reported by Geyer¹⁶ and Chen et al.¹ may in fact have been confounded by age. It is also possible that different psychosocial factors are influential with increasing age. Thus, age differences in samples may explain inconsistent findings, particularly as it is clearly possible that psychoendocrine factors may be the link between stress and breast cancer.

A potential limitation of the present study is the relatively short time period covered in assessing life stressors. This time frame was influenced by a desire to obtain an optimal balance between reliability of recall and the presumed time period of tumour growth. Geyer examined the influence of the time period in which severely threatening events were assessed on breast cancer risk and found that both those occurring in the three year period prior to interview as well as more distant events were similarly predictive of breast cancer risk.¹⁵ Likewise, Chen et al.¹ noted that average annual rate of severely threatening life events did not vary significantly over the five year period examined or differ between the groups. Notwithstanding this, all studies to date in fact probably assess the effect of stressors on tumour growth.

One strength of the current study is the sample size, which includes the largest series of breast cancer cases examined prior to diagnosis in this area of research. We believe the power of our study ensures that the likelihood of missing even a modest association between severely threatening stressors and the development of breast cancer, is minimal. Our sample size has also enabled multiple variables to be assessed simultaneously (life events, coping style, affect, personality, and social support) and more importantly, for their interactions to be examined.

The progression to exploring the interaction between distinct but interrelating variables is important in this field of research. Although there was no evidence from our data for a direct association between social support, coping style or emotional control and breast cancer, the usefulness of examining these without consideration of external stressors an individual is coping with is questionable. Our findings concur with the Brown and Harris theory that "vulnerability factors", (here social support, coping style and emotional control), may have no independent significant effect, but impact largely through their interaction with provoking agents such as life stressors.²⁵ This theoretical model is also consistent with Temoshok's

model of the cancer prone individual, where the Type C coping style interacts with stressors. Under conditions of severe stress, the effectiveness of this coping style breaks down, producing a greater level of strain.³¹

The importance of coping in moderating the impact of stressors is well established,⁵⁹ although few studies have examined coping style in conjunction with life event stress and the development of breast cancer. Chen et al.,¹ reported that confronting stress increased the risk of developing breast cancer, independently of life events. However, there was no mention of this interaction being tested or removed from their final model. The only other study to examine the interaction between life event stress and coping style reported no significant differences in the development of breast cancer for either of these variables or their interaction.¹⁹ We found no evidence that coping style interacted with the impact of life stress in the development of breast cancer. It is possible that our measure of coping was not tapping the appropriate concept.

Although there is some evidence for the tendency to control or suppress negative emotions being associated with the development of breast cancer,⁶⁰⁻⁶² some studies have failed to support this notion.^{42, 63} With one exception,⁶⁰ emotional control has not previously been considered in conjunction with life event stress, and none have explored the relationship between these two variables. Again we found no evidence for a role for emotional control in the development of breast cancer, nor did we find evidence of an interaction between emotional control and life event stress.

Our finding of an interaction between severely threatening life events and the absence of social support was somewhat unexpected given the absence of independent effects. However, this is not without some precedence.¹⁷ Much of the focus on social support and breast cancer has been in relation to its role after diagnosis. The only previous study to consider their interaction in the development of breast cancer, reported no significant differences between breast cancer cases and controls in number or severity of life events, coping style or social support or their interactions.¹⁹ The results of our study provides support for the model described by Hilakivi-Clarke et al.³² that emphasizes the interaction between life events and stress related variables such as social support in mediating breast cancer risk. Adding credence to our significant interaction between highly threatening stressors and the absence of intimate emotional support is that these two variables, although not totally independent, were assessed and rated quite independently.⁴³

The current study found no evidence of an independent relationship between recent life event stress and the development of breast cancer. However, examining the interactions between life event stress and a number of vulnerability factors, we identified a small group of women who were at significantly greater risk of breast cancer: those experiencing a highly threatening stressor within the previous two years and without any intimate emotional support. This group includes, but is not exclusively, those women recently widowed or divorced. We found no evidence that other vulnerability factors such as coping style and emotional control interacted with life stressors in the development of breast cancer. The current study demonstrates the importance of social support, or the lack thereof, as a specific vulnerability factor for the impact of life event stress in the development of breast cancer. Although the results support a multifactorial view of breast cancer development, they also suggest that the role of psychosocial factors in the etiology of breast cancer in general is small and specific. Women should be reassured that stress per se does not cause breast cancer; however, in the absence of intimate emotional support, situations of severe stress may increase vulnerability to this disease. Health professionals should be encouraged to identify individuals in circumstances of severe stress, if feasible explore avenues for reducing stress and promote the use of available support systems, and encourage the utilization of counseling and other supportive services.

References

1. Chen CC, David AS, Nunnerley H, Michell M, Dawson JL, Berry H, et al. Adverse life events and breast cancer: case-control study. *BMJ* 1995; 311(7019):1527-30.
2. Roberts FD, Newcomb PA, Trentham-Dietz A, Storer BE. Self-reported stress and risk of breast cancer. *Cancer* 1996; 77(6):1089-93.
3. Ginsberg A, Price S, Ingram D, Nottage E. Life events and the risk of breast cancer: a case-control study. *Eur J Cancer* 1996; 32A(12):2049-52.
4. Cassileth BR. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1996; 77(6):1015-6.
5. Barraclough J. Adverse life events and breast cancer. Other studies have found no association. *BMJ* 1996; 312(7034):845.
6. Faragher MG, Cooper CL. 'Are life events related to the onset of breast cancer?'. *Psychol Med* 1997; 27(2):497-8.
7. McGee R, Williams S, Elwood M. Are life events related to the onset of breast cancer? *Psychol Med* 1996; 26:441-7.

8. Burke MA, Goodkin, K. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1997; 79(5):1055-9.
9. Baghurst KI, Baghurst PA, Record SJ. Public perceptions of the role of dietary and other environmental factors in cancer causation or prevention. *J Epidemiol Community Health* 1992; 46:120-6.
10. Brinton LA, Malone KE, Liff J, Schoenberg JB. Re: "Should we consider a subject's knowledge of the etiologic hypothesis in the analysis of case-control studies?". *Am J Epidemiol* 1994; 140:1054-6.
11. Ewertz M. Bereavement and breast cancer. *Br J Cancer* 1986; 53:701-3.
12. Kvikstad A, Vatten LJ, Tretli S, Kvinnsland S. Death of a husband or marital divorce related to risk of breast cancer in middle-aged women. A nested case-control study among Norwegian women born 1935-1954. *Eur J Cancer* 1994; 30A(4):473-7.
13. Muslin HL, Gyarfás K, Pieper WJ. Separation experience and cancer of the breast. *Ann N-Y Acad Sci* 1966; 125(3):802-6.
14. Scherg H, Blohmke M. Associations between selected life events and cancer. *Behav Med* 1988; 14(3):119-24.
15. Geyer S. Life events prior to manifestation of breast cancer: a limited prospective study covering eight years before diagnosis. *J Psychosom Res* 1991; 35(2-3):355-63.
16. Geyer S. Life events, chronic difficulties and vulnerability factors preceding breast cancer. *Soc Sci Med* 1993; 37(12):1545-55.
17. Brown GW, Harris TO. Life Events and Illness. New York: The Guilford Press, 1989.
18. Priestman TJ, Priestman SG, Bradshaw C. Stress and breast cancer. *Br J Cancer* 1985; 51(4):493-8.
19. Edwards JR, Cooper CL, Pearl SG, de Paredes ESO, Leary T, Wilhelm MC. The relationship between psychosocial factors and breast cancer: some unexpected results. *Behav Med* 1990; 16(1):5-14.
20. Fox CM, Harper AP, Hyner GC, Lyle RM. Loneliness, emotional repression, marital quality, and major life events in women who develop breast cancer. *J Community Health* 1994; 19(6):467-82.
21. Cheang A, Cooper CL. Psychosocial factors in breast cancer. *Stress Med* 1985; 1:61-6.
22. Forsen A. Psychosocial stress as a risk for breast cancer. *Psychother Psychosom* 1991; 55(2-4):176-85.

23. Schonfield J. Psychological and life-experience differences between Israeli women with benign and cancerous breast lesions. *J Psychosom Res* 1975; 19(4):229-34.
24. Cooper CL, Cooper R, Faragher EB. Incidence and perception of psychosocial stress: the relationship with breast cancer. *Psychol Med* 1989; 19(2):415-22.
25. Brown GW, Harris TO. Social origins of depression: a study of psychiatric disorder in women. London: Tavistock, 1978.
26. Protheroe D, Turvey K, Horgan K, Benson E, Bowers D, House A. Stressful life events and difficulties and onset of breast cancer: case-control study. *BMJ* 1999; 319:1027-30.
27. George LK. Stress, Social Support, and Depression over the Life-Course. In: Markides KS, Cooper CL, eds. *Aging Stress and Health*. Chichester, England: John Wiley and Sons, 1989; 241-67.
28. Cooper CL, Faragher EB. Psychosocial stress and breast cancer: the inter-relationship between stress events, coping strategies and personality. *Psychol Med* 1993; 23(3):653-62.
29. Butow PN, Hiller JE, Price MA, Thackway SV, Krickler A, Tennant CC. Epidemiological evidence for a relationship between life events, coping style and personality factors in the development of breast cancer. *J Psychosom Res* 2000; *In Press*.
30. Greer S, Watson M. Towards a psychobiological model of cancer: psychological considerations. *Soc Sci Med* 1985; 20(8):773-7.
31. Temoshok L. Personality, coping style, emotion and cancer: toward an integrative model. *Cancer Surveys* 1987; 6:545-67.
32. Hilakivi-Clarke L, Rowland J, Clarke R, Lippman ME. Psychosocial factors in the development and progression of breast cancer. *Breast Cancer Res Treat* 1993; 29(2):141-60.
33. Levy S, Herberman R, Lippman M, d'Angelo T. Correlation of stress factors with sustained depression of natural killer cell activity and predicted prognosis in patients with breast cancer. *J Clin Oncol* 1987; 5(3):348-53.
34. Achat H, Kawachi I, Levine S, Berkey C, Coakley E, Colditz G. Social networks, stress and health-related quality of life. *Quality of Life Research* 1998; 7(8):735-50.
35. Stansfeld SA, Bosma H, Hemingway H, Marmot MG. Psychosocial work characteristics and social support as predictors of SF-36 health functioning: the Whitehall II study.

Psychosom Med 1998; 60(3):247-55.

36. Neuling SJ, Winefield HR. Social support and recovery after surgery for breast cancer: frequency and correlates of supportive behaviours by family, friends and surgeon. *Soc Sci Med* 1988; 27(4):385-92.
37. Waxler-Morrison N, Hislop TG, Mears B, Kan L. Effects of social relationships on survival for women with breast cancer: A prospective study. *Soc Sci Med* 1991; 33(2):177-83.
38. Ell K, Nishimoto R, Mediansky L, Mantell J, Hamovitch M. Social relations, social support and survival among patients with cancer. *J Psychosom Res* 1992; 36(6):531-41.
39. Spiegel D. Effects of Psychosocial Support on Patients with Metastatic Breast Cancer. *J Psychosoc Oncol* 1992; 10(2):113-20.
40. Roberts CS, Cox CE, Shannon VJ, Wells NL. A closer look at social support as a moderator of stress in breast cancer. *Health Social Work* 1994; 19(3):157-64.
41. Koopman C, Hermanson K, Diamond S, Angell K, Spiegel D. Social support, life stress, pain and emotional adjustment to advanced breast cancer. *Psychooncology* 1998; 7:101-11.
42. Bleiker EM, van der Ploeg HM, Hendriks JH, Ader HJ. Personality factors and breast cancer development: a prospective longitudinal study. *J Natl Cancer Instit* 1996; 88(20):1478-82.
43. Tennant C, Langeluddecke P, Byrne D. The concept of stress. *Aust NZ J Psychiat* 1985; 19(2):113-8.
44. Andrews G, Singh M, Bond M. The Defense Style Questionnaire. *J Nerv Mental Diseases* 1993; 181(4):246-56.
45. Craig A, Franklin J, Andrews G. A scale to measure locus of control of behaviour. *Br J Med Psychol* 1984; 57:173-80.
46. Bleiker EM, van der Ploeg HM, Hendriks JH, Leer JW, Kleijn WC. Rationality, emotional expression and control: psychometric characteristics of a questionnaire for research in psycho-oncology. *J Psychosom Res* 1993; 37(8):861-72.
47. Rosenberg M. Society and the adolescent self-image. Princeton, New Jersey: Princeton University Press, 1965.
48. Spielberger CD, Jacobs GA, Crane RS, Russell SF, Westberry L, Barker L, et al. Preliminary manual for the State-Trait Personality Inventory (STPI). Tampa,

University of South Florida: Human Resources Institute, 1979.

49. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67:361-70.
50. Henderson S, Duncan-Jones P, Byrne DG, Scott R. Measuring social relationships: The Interview Schedule for Social Interaction. *Psychol Med* 1980; 10:723-34.
51. Friberg S, Mattson S. On the growth rates of human malignant tumours: implications for medical decision making. *J Surg Oncol* 1997; 65(4):284-97.
52. Funch DP, Marshall JR. Measuring Life Stress: Factors Affecting Fall-Off in the Reporting of Life Events. *J Health Soc Behaviour* 1984; 25:453-64.
53. Price MA, Tennant CC, Smith RC, Butow PN, Kennedy SJ, Kossoff MB, et al. Predictors of breast cancer in women recalled following screening. *Aust N Z J Surg* 1999; 69:639-46.
54. The Essendon Breast X-ray Program Collaborative Group. A mammographic screening pilot project in Victoria 1988-1990. *Med J Aust* 1992; 157(10):670-3.
55. Daures JP, Peray P, Bousquet J, Stoebner A, Gouzes C, Lamarque JL, et al. Mass screening for breast cancer in Hérault county. First results in women between 40 and 70 years old. *J Gynecol Obstet Biol Reprod* 1992; 21(2):173-8.
56. Thurfjell E. Population-based mammography screening in clinical practice. Results from the prevalence round in Uppsala county. *Acta Radiol* 1994; 35(5):487-91.
57. Dean PB, Pamilo M. Screening mammography in Finland--1.5 million examinations with 97 percent specificity. Mammography Working Group, Radiological Society of Finland. *Acta Oncol* 1999; 38(Suppl 13):47-54.
58. Brown GW, Adler Z, Bifulco A. Life events, difficulties and recovery from chronic depression. *Br J Psychiat* 1988; 152:487-98.
59. Folkman S, Lazarus RS. An analysis of coping in a middle-aged community sample. *J Health Soc Behav* 1980; 21:219-39.
60. Greer S, Morris, T. Psychological attributes of women who develop breast cancer: a controlled study. *J Psychosom Res* 1975; 19(2):147-53.
61. Scherg H, Cramer I, Blohmke M. Psychosocial factors and breast cancer: a critical reevaluation of established hypotheses. *Cancer Detect Prev* 1981; 4:165-71.
62. Grassi L, Cappellari L. State and trait psychological characteristics of breast cancer patients. *New Trends Experimental Clin Psychiatry* 1988; IV-N.2:99-109.

63. Kreitler S, Chaitchik S, Kreitler H. Repressiveness: cause or result of cancer?
Psychooncology 1993; 2:43-54.

CHAPTER 6: SUMMARY AND CONCLUSIONS

The aim of the study presented in this thesis was to examine the role of psychosocial variables as risk factors in the development of breast cancer. A semi-prospective study design was employed using a sample of women attending routine breast screening who were recalled for further testing. All women completed a self-report questionnaire containing items related to established risk factors and a number of psychosocial questionnaires examining features of the cancer prone personality, coping style, emotion expression and control, and affect. Specific features of Temoshok's (1987) Cancer Prone Personality were hypothesized to increase the risk of being diagnosed with breast cancer. The women were divided into four groups according to the final diagnosis as well as the medical procedures required to obtain the diagnosis of breast disease. The result was that women diagnosed with breast cancer were compared with three control groups: those with normal breast tissue, those with benign or cystic breast disease diagnosed without a fine needle biopsy and those diagnosed with benign breast disease via fine needle biopsy. Women undergoing fine needle biopsy were interviewed for a history of recent life events and social support. Hypotheses were based on empirical findings and Hilakivi-Clarke et al.'s (1993) model of psychosocial variables in the development of breast cancer, namely that it is the interaction between life event stress, social support, personality, and an individual's ability to cope that is important in increasing women's vulnerability to developing breast cancer. Specific features of the Cancer Prone Personality were included as vulnerability factors in testing this model. For the life event stress variables and interactions with other psychosocial variables, women subsequently diagnosed with breast cancer were compared with benign biopsy controls. The results of this study are summarized below.

Established Risk Factors for Breast Cancer

The primary objective of examining established risk factors for developing breast cancer in the present cohort was to control for these variables in the analyses of psychosocial variables, ensuring that any differences between the groups on psychosocial variables were independent of established risk factors. The second reason was to identify and control for potential confounding effects of established risk factors in the examination of psychosocial variables, in particular age. The main findings are summarized below.

Sociodemographic Variables

The breast cancer group was significantly older than all three non-cancer control groups. Age differences between the breast cancer subjects and controls accounted for the higher proportion of widowed and retirees in the cancer group. There was a non-significant trend for higher level of education to be associated with the cancer group and no significant differences between the groups in type of employment. Most non-Australian born women were born in countries with similar incidences of breast cancer to Australian born women.

Family History of Breast Cancer

A family history of breast cancer was similar across the groups and most probably characteristic of the present cohort rather than representative of breast cancer risk. In general, a family history is very important in the small proportion of women who have familial breast cancer. However, in the current study the cohort was a community-based population of women over the age of forty years and excluded women who had already developed breast cancer. Data from the United Kingdom breast screening program showed similar frequencies of family history (12 to 17 percent) to the present sample (14 to 17.5 percent) and showed no independent impact of family history on breast cancer risk in women aged over 55 years (Thomas, Cade, & Vail, 1996). The lack of an association between family history and breast cancer may be partly due to a greater propensity for women with a family history to attend screening, even if their particular family history is not associated with a greater risk of breast cancer.

Benign Breast Disease

There were no significant differences between breast cancer cases and non-cancer controls in history of benign breast disease. However, the normal tissue control group was less likely to have ever been diagnosed with benign breast disease than both the benign breast disease control groups and the breast cancer group.

Reproductive factors

There was a non-significant trend towards an older age at first birth in the breast cancer group. There were no differences between the groups in parity or history of lactation. Breast cancer was more common in post-menopausal women, but there were no group differences in the age at onset of menopause.

Exogenous Hormonal Factors

There were significant differences between the breast cancer cases and non-cancer controls in history of oral contraceptive (OC) use. Women who had ever used OC's were 50 percent more likely to have developed breast cancer than women who had never used. There was a trend of increasing risk of breast cancer with duration of OC use, reaching significance in women who had used OC's for over ten years.

No differences were detected between breast cancer cases and non-cancer controls in current use of Hormone Replacement Therapy (HRT). However, the benign biopsy control group was less likely to be currently using HRT than the normal tissue control group, the non-biopsy benign/cystic breast disease control group and the breast cancer group.

Lifestyle Factors

The breast cancer group was more likely to have a Body Mass Index (BMI) above 25 than the three non-cancer control groups. There was a modest but significant difference between the cancer and non-cancer groups for alcohol consumption, with the breast cancer group more likely to consume alcohol daily. There were no significant group differences in lifetime consumption of cigarettes.

Summary

In the present cohort of women recalled for further testing following mammography screening increasing age, being post-menopausal, obesity, having ever used oral contraceptives and daily alcohol consumption were significantly more common in breast cancer cases than non-cancer controls. These variables were included in multivariate analyses of psychosocial variables ensuring that the results for psychosocial variables were independent of these risk factor variables. A history of benign breast disease and current use of hormone replacement therapy, although not related to breast cancer in this sample, were treated as potential confounders in multivariate analyses. A number of other variables were treated as potential confounders in multivariate analyses because of their status as well-established risk factors, despite no significant group differences being detected in the present sample. These included a family history of breast cancer, age at birth of first child, parity, and age at onset of menopause. As a potential covariate of psychosocial variables, level of education in addition to age, was included in all multivariate analyses.

Psychosocial Risk Factors

Two distinct but clearly interrelated lines of enquiry have dominated the examination of psychosocial variables in relation to the development of breast cancer: personality and stress. Features of a Cancer Prone Personality described by Greer and Watson (1985) and Temoshok (Temoshok, 1987) portray this personality profile as stress related, being maladaptive under conditions of severe or prolonged stress, increasing rather than reducing the impact of life event stress. Highly threatening life events have themselves independently been associated with an increase risk of developing breast cancer (Geyer, 1991, 1993; Chen et al., 1995). Rarely, however, have these related lines of enquiry been examined together, or their interactions explored. The present study was designed to unite these areas of research, and by teasing apart the components of stress, examine the interactive effects of these variables in relation to their role in the development of breast cancer.

The Cancer Prone Personality

The first step was to examine the features of the Cancer Prone Personality, namely a distinctive coping style, difficulty in expressing emotions or suppression of emotions, and a tendency towards helplessness and hopelessness. With a lack of consensus as to the features of an appropriate control group with which to compare breast cancer subjects for these variables, the present breast cancer group was compared with three non-cancer control groups as described above. In summary, the present study found no evidence to support the proposal that specific personality features, as defined in Temoshok's (1987) Cancer Prone Personality, were associated with the development of breast cancer.

There was no evidence to support the proposal that women who develop breast cancer have a distinctive style of coping. There were no significant differences between breast cancer subjects and the three non-cancer control groups on measures of emotion-focused coping or problem-focused coping. This finding is consistent with results reported by a number of studies (Greer & Morris, 1975; Schwarz, 1984; Edwards et al., 1990; Cooper & Faragher, 1992), but contrasts with others (Watson et al., 1984; Chen et al., 1995).

Watson et al. (1984) reported that breast cancer subjects scored significantly higher on repressive coping style under conditions of experimental stress than non-cancer controls, reinforcing the importance of examining coping style in conjunction with stress. Chen et al. (1995) examined coping style in conjunction with life event stress, reporting that women who confronted stress by focusing on the problem were at greater risk of breast cancer, independent of life events and other risk factors. The finding was contrary to expectation,

without any explanation offered by the authors and, being inconsistent with the theory that this coping style ameliorates the negative impact of life event stress, difficult to reconcile.

The present data has not replicated the Chen et al. (1995) finding for an independent effect of coping style on breast cancer risk, nor of an interactive effect with life event stress. The interaction between life events and coping style will be discussed further in conjunction with the results of the life event stress data.

Perhaps more surprising was the absence of any association between the emotional expression and control variables and breast cancer development in the current data. The suppression or control of negative emotions, particularly of anger, is central to Temoshok's (1987) Cancer Prone Personality and Greer and Watson's (1985) Type C behaviour, theorized on the basis of existing research. However, closer examination of existing data suggests that these variables may be of greatest importance in younger women.

Greer and Morris (1975) found women with breast cancer under age 50 were more likely to be extreme suppressors or extreme expressors of emotion when compared with benign controls. Similarly, Morris et al. (1981) reported less expression of anger in breast cancer patients than controls, although only the 40 to 49 year age group approached significance ($p=0.08$). It is possible that emotional expression and control may be less important in older women, such as the present sample, who were on average 56 years of age. However, the negative result for emotional expression and control variables is consistent with the findings of Bleiker et al's (1996) large prospective study of a Dutch screening population.

The third feature of the proposed Cancer Prone Personality, helplessness and hopelessness, was not supported by data from the present study. Neither state nor trait measures of depression and anxiety varied significantly between the control groups and the breast cancer group. This result is consistent with the majority of studies examining these features (Greer & Morris, 1975; Schonfield, 1975; Morris et al., 1981; Hahn & Petitti, 1988; Jasmin et al., 1990; Chen et al., 1995; Bleiker et al., 1996). Higher state depression scores, but not clinical depression, were significantly correlated with severely threatening life events and may be a proxy measure of the severity of recent life event stress.

The helplessness and hopelessness dimension of the Cancer Prone Personality is least well elucidated in Temoshok's (1987) theory or data that it has originated. It appears to have been derived from studies examining various aspects of depression and anxiety. However, it may be that specific measures of particular dimensions of depression, such as Beck's

Hopelessness scale, may be more useful measures than depression or self esteem. As a result the negative result in this study may not be a robust finding.

In summary, the present study provides no evidence to support a direct role for the features of Temoshok's Cancer Prone Personality in the development of breast cancer. It is possible that repression or emotional control is a response to cancer rather than a risk of cancer. However, it is also possible that while personality variables such as emotional suppression or control and coping style have no direct impact on the development of breast cancer, they are vulnerability factors which moderate the impact of life event stress on the development of breast cancer.

Life Event Stress

The second step was to examine the evidence for life event stress as an independent risk factor for developing breast cancer. Due to time constraints with conducting interviews within a semi-prospective design, life event stress and social support variables were examined in a subgroup of the study cohort, those women undergoing fine needle biopsy. There was no evidence to support the hypothesis that life event stress, above a critical threshold for severity, was related to the development of breast cancer. The benign and breast cancer groups reported a similar number, type and severity of life event stress within the past two years. In contrast to the findings of Geyer (1991, 1993) and Chen et al. (1995), there was no independent association between severely threatening life event stressors, and the development of breast cancer. This result, however, is consistent with more recent results in a larger sample reported by Protheroe et al. (1999).

One particular feature of the present study sample that differs from others in this area of research is an older mean age and this may be important in reconciling differences in findings. In addition to age being an independent risk factor for breast cancer as addressed earlier in this thesis, age is associated with psychosocial variables, and in particular with the number, type and severity of life events experienced and social support. The difficulty of statistically controlling for age differences between groups is particularly marked in smaller studies with larger ranges in age and introduces the possibility that the independent effects of severely threatening events on the development of breast cancer reported by Geyer (1991, 1993) and Chen et al. (1995) may in fact be confounded by age. However, equally important to consider is the possibility that there may be variation in the importance of specific psychosocial variables or sets of psychosocial variables within different age groups in the development of breast cancer. It is possible that in younger women, highly threatening life

events may be an independent risk factor for developing breast cancer, similar to the possibility already highlighted suggesting emotional suppression may be more important in younger women. Thus, age differences in samples may assist in reconciling inconsistent findings, particularly as it is clearly possible that psycho-endocrine factors may be the link between life event stress and breast cancer.

Life Event Stress and Vulnerability Factor Interactions

The third step in the process of examining psychosocial factors in the development of breast cancer was to examine the interactions between the variables, as proposed by Hilakivi-Clarke et al. (1993). Consequently, a number of specific vulnerability factors proposed to mediate the impact of life event stress on the development of breast cancer and these interactions were tested. Two were specific features of the Cancer Prone Personality, a specific style of coping and a tendency to control negative emotions.

The importance of coping in moderating the impact of life event stress is well established, although to date few studies have examined coping style in conjunction with life event stress and the development of breast cancer. It was hypothesized that a less mature style of coping, under conditions of severe life event stress, would increase the level of strain, and thus increase the impact of severely threatening life event stress on the risk of developing breast cancer. However, the results of the present study found no evidence to support this hypothesis. As noted earlier, this finding contrasts with Chen et al. (1995) who reported that women who confronted stress were at increased risk of developing breast cancer, independently of life events, as well as increasing the impact of life event stress on breast cancer risk. However, the present finding is consistent with the only other study to examine the interaction between life event stress and coping style in the development of breast cancer. That study reported no differences in breast cancer and controls in recent life event stress, coping style or their interaction (Edwards et al., 1990).

The second proposed vulnerability factor was the suppression or control of negative emotions. There was no evidence to support the hypothesis that the control of emotions interacted with life event stress to alter the risk of developing breast cancer. While some previous studies report a tendency to control or suppress negative emotions being associated with the development of breast cancer, no other study has explored the relationship between these two variables.

The third proposed vulnerability factor was social support. It was hypothesized that poor or

absent social support would increase the impact of life event stress on breast cancer development, while good quality support would reduce the impact of life event stress on breast cancer development. Somewhat surprisingly, the absence of an intimate support or partner in life was the vulnerability factor, which in combination with experiencing a severely threatening life event within the previous two years, was associated with a diagnosis of breast cancer. This is regardless of the quality of the intimate support (poor, adequate or good), suggesting that it is the presence of a partner in life that is important. The presence of non-intimate (other sources) emotional and practical support, even of good quality, did not significantly moderate this result.

This result provides support for the model described by Hilakivi-Clarke et al. (1993). The model proposes that the presence of stress itself is not the crucial factor in cancer development, rather the interaction between stressors, personality and social support that alters an individual's ability to cope that in turn mediates breast cancer risk via alteration in neuroendocrine and immune functioning. While the present study found no evidence that personality or coping style are related to breast cancer risk (as currently assessed), it does confirm Hilakivi-Clarke et al.'s (1993) theory that life event stress alone is not related to breast cancer development. Rather it is the interaction between the severity of life event stress and the absence of an intimate relationship that is important in moderating breast cancer risk.

Adding credence to the significant interaction between highly threatening stressors and the absence of intimate emotional support in the present study is that these two variables, although not totally independent, were assessed and rated quite independently (Tennant et al., 1985). However, the result that it is the presence of an intimate relationship, rather than the quality of the emotional support within the relationship, that is important, suggests that the focus of future research should consider closely the way in which social support is defined and measured.

A large literature focuses on the role of social support in reducing psychological distress in response to life event stressors (Roberts et al., 1994; Thoits, 1982, 1995) and to a less degree the beneficial influence of social support on physical health (Spiegel, 1992). The buffering theory of social support proposes that support is a coping resource in times of stress that acts as a buffer against the harmful effects of stress. The pathway by which this mechanism may operate is uncertain, possibly directly by biological, possibly indirectly via behavioural or cognitive influences, or both. There is some evidence to suggest that social contact and support mitigate the effect of stress on immune function (Spiegel & Sephton, 2001). There

also evidence that support reduces depression, and increases the use of more active coping strategies (Fawzy, Kemeny, Fawzy, Elashoff, Morton, Cousins & Fahey, 1990). Further investigation of these possible pathways by which social support buffers the impact of life event stress merits attention.

The interaction between severely threatening life events and the absence of an intimate social support may go some way to explain some of the conflicting results regarding the relationship between life event stress and breast cancer development. Indeed, Geyer (1991, 1993) attempted to examine social support in addition to life event stress. However, the high correlation between the two measures necessitated the social support variable to be discarded. Of note, it was these highly threatening events, highly correlated with social support in this study, that were significantly associated with an increased risk of breast cancer development.

Summary

The present study found no evidence for an independent relationship between recent life event stress, coping style, emotional control or affect and the development of breast cancer. However, following examination of the interactions between life event stress and a number of vulnerability factors, a small group of women who were at significantly greater risk of breast cancer were identified - those experiencing a life event or ongoing difficulty independently rated at the highest levels of threat within the previous two years and who were without an intimate emotional support. In this analysis, an intimate support refers to a partner in life, as opposed to close friend or family. While this group includes women recently widowed or divorced, it is not exclusively comprised of these women. After adjusting for potential confounders including age, education, menopausal status, family history, history of benign breast disease, body mass index, reproductive history, alcohol consumption, oral contraceptive use, hormone replacement therapy, state depression, and quality of non-intimate social support, the increase in the odds of being diagnosed with breast cancer for these women was 9.39 (CI 1.90-46.42).

There is no evidence to suggest that other vulnerability factors such as coping style and emotional control moderate the impact of life event stress in the development of breast cancer. This study demonstrates the importance of social support, or the lack thereof, as a specific vulnerability factor for the impact of life event stress in the development of breast cancer and supports Hilakivi-Clarke's et al. (1993) proposal that it is the interactions between psychosocial variables that mediate the risk of developing breast cancer. However,

given the unexpectedness of this significant result, and the lack of significant main effects, this finding requires corroboration before being accepted.

Strengths

A major strength of this study lies in the homogenous nature of the sample. Women were recruited via a community based screening program recalled for assessment purely on radiological grounds. Other studies have used women presenting with breast symptoms, some having already been assessed by their primary physician, being referred for biopsy from multiple sources and for varied reasons. The possibility of guessing or knowing their diagnosis ahead of time and influencing the reporting of psychosocial variables in the present study is minimal.

The semi-prospective design employed minimizes biases associated with retrospective data collection, particularly important with self-report measures. As a further control against any bias associated with varied testing conditions, non-cancer control subjects were separated into three control groups based on medical investigative procedures required for a definitive diagnosis of their breast disease (fine needle biopsy versus no biopsy) as well as distinguishing between those with "normal" breast tissue and those with benign breast disease.

Another strength lies in the power of this study, provided by the large sample size and the number of breast cancer cases, to test the proposed hypotheses, as well as to control extensively for potential confounding variables. This ensured that the likelihood of missing even a modest association between severely threatening stressors and the development of breast cancer was minimal, and enabled multiple variables to be assessed simultaneously (life events, coping style, affect, personality, and social support) and more importantly, for their interactions to be examined.

The measures used were reliable, well validated, psychometrically sound and specifically selected to independently assess the characteristics outlined by Temoshok's (1987) Cancer Prone Personality and Hilakivi-Clarke's et al.'s (1993) model of the interaction between life event stress, personality, social support and coping. Of particular advantage was the use of the Life Events and Difficulties Schedule (Brown & Harris, 1978), a methodologically superior approach, independently rating the severity of an event according to the meaning of an event to that individual and the context in which it occurred.

Limitations

A limitation of the present study is the relatively short time period covered in assessing life events stress. The choice of a two-year time frame was influenced by a desire to obtain an optimal balance between reliability of recall and the presumed time period of tumour growth. Most previous studies have examined life events for between two and five years prior to symptomatic presentation. Both Geyer (1991, 1993) and Chen et al. (1995) reported that severely threatening events were similarly predictive of breast cancer risk across the eight and five years respectively in symptomatic samples. The unanswered questions include the length of time in which psychosocial variables impact on tumour growth and whether there is a critical period in which their influence is more prominent.

A second limitation is that the analysis of life event stress and social support variables, and the testing of interactions, was conducted only in women undergoing biopsy. Ideally the whole sample would be included in these analyses. The decision to employ the methodological superior LEDS interview to assess life event stress and to maintain a semi-prospective design required a compromise, as the time available at the assessment clinics prior to results being available meant that only a sub-sample of women could be interviewed. The result was to focus on the biopsy sub-sample, who were available for longer periods and underwent the same medical procedures. Although there were no differences between the groups on personality variables examined in the larger sample, it is possible that the pathways via which life event stress and social support and their interactions influence tumour growth may also influence benign tumour growth, potentially masking their impact or their mode of influence.

A third potential limitation of this study is that the measures selected to assess coping style and emotional expression and control varied from other studies and it is possible that they were not adequately tapping the hypothesized features. Although the Emotional Expression and Control scale (van der Ploeg, 1989) used in this study was developed from the more widely used Courtauld Emotional Control Scale (Watson & Greer, 1983) and shares many of the items, the resulting measure may not be measuring the same concept.

Future Direction

The findings of the present study direct future research towards large scale well-designed empirical studies enabling examination of the interactions of psychosocial factors in the development of breast cancer. Ideally, a prospective study design should be used in a sample from a homogeneous source with a clearly defined control group. Subjects with a previous history of breast cancer should be excluded, and well established risk factor variables and other potential confounding variables should be considered. Particular attention should be paid to the confounding effect of age, and age should be controlled for statistically even when groups are age-matched. Sample size calculations should be employed to ensure adequate power to simultaneously examine multiple psychosocial variables and their interactions.

The present results also reinforces the importance of future studies utilizing a measure such as the LEDS to enable the severity of life events to be examined, as it appears that there is a critical threshold for severity of life event stress that is important, rather than the number and type or the cumulative effect of minor stressors. Similarly, the quality and intimacy of available social support should be assessed, rather than the number of social contacts. While coping style, emotional control and other personality features were not found to be important in the present sample, future research should seek to test their importance as mediators of life event stress in other groups of women vulnerable to developing breast cancer. Many of the methodological limitations in the present study would be overcome with the progression to prospective studies, targeted at specific groups of women, such as those at increased risk of developing breast cancer due to high familial or genetic risk.

A significant weakness in this area of research is the essentially atheoretical approach to examining clearly interrelated psychosocial concepts in a multi-factorial disease such as breast cancer. Progression in the understanding of the role of psychosocial variables in breast cancer development and the mechanisms by which they exert their effects, requires the guidance of a model which acknowledges links with the endocrine, nervous and immune systems such as the model proposed by Hilakivi-Clarke et al. (1993) and tested in this thesis.

Finally, a key unanswered question is whether there is a critical time period during which psychosocial factors have a greater impact. Future studies should explore psychosocial variables, in particular life event stress and social support, over different time periods to test for differential impact.

REFERENCES

- Achat, H., Kawachi, I., Byrne, C., Hankinson, S., & Colditz, G. (2000). A prospective study of job strain and risk of breast cancer. *International Journal of Epidemiology*, 29(4), 622-628.
- Achat, H., Kawachi, I., Levine, S., Berkey, C., Coakley, E., & Colditz, G. (1998). Social networks, stress and health-related quality of life. *Quality of Life Research*, 7(8), 735-750.
- Alyard, P.R., Goodling, J.H., McKenna, P.J., & Snaith, R.P. (1987). A validation study of three anxiety and depression self-assessment scales. *Journal of Psychosomatic Research*, 31(2), 261-268.
- American Psychiatric Association (Ed.). (1987). *Diagnostic and Statistical Manual of Mental Disorders III Revised (DSM-III-R)*. Washington DC.
- Anagnostopoulos, F., Vaslamatzis, G., Markidis, M., Katsouyanni, K., Vassilaros, S., & Stefanis, C. (1993). An investigation of hostile and alexithymic characteristics in breast cancer patients. *Psychotherapy and Psychosomatics*, 59(3-4), 179-189.
- Anderson, C.D. (1981). Expression of affect and physiological response in psychosomatic patients. *Journal of Psychosomatic Research*, 25(3), 143-149.
- Andrews, G., Singh, M., & Bond, M. (1993). The Defense Style Questionnaire. *Journal of Nervous and Mental Disease*, 181(4), 246-256.
- Andrews, G., Stewart, G., Morris-Yates, A., Holt, P., Henderson, S. (1990). Evidence for a General Neurotic Syndrome. *British Journal of Psychiatry*, 157, 6-12.
- Andrieu, N., Clavel, F., Auquier, A., Le, M. G., Gairard, B., Piana, L., Bremond, A., Lansac, J., Flamant, R., & Renaud, R. (1993). Variations in the risk of breast cancer associated with a family history of breast cancer according to age at onset and reproductive factors. *Journal of Clinical Epidemiology*, 46(9), 973-980.
- Anton-Culver, H., Kurosaki, T., Taylor, T. H., Gildea, M., Brunner, D., & Bringman, D. (1996). Validation of Family History of Breast Cancer and Identification of the BRCA1 and Other Syndromes Using a Population-Based Cancer Registry. *Genetic Epidemiology*, 13, 193-205.
- Aragona, M., Muscatello, M. R. A., & Mesiti, M. (1997). Depressive Mood Disorders in Patients with Operable Breast Cancer. *Journal of Experimental and Clinical Cancer Research*, 16(1), 111-118.

- Bacon, C. L., Renneker, R., Cutler, M. (1952). A Psychosomatic Survey of Cancer of the Breast. *Psychosomatic Medicine*, XIV, 453-460.
- Bageley, C. (1979). Control of the emotions, remote stress, and the emergence of breast cancer. *Indian Journal of Clinical Psychology*, 6, 213-220.
- Baghurst, K. I., Baghurst, P. A., & Record, S. J. (1992). Public perceptions of the role of dietary and other environmental factors in cancer causation or prevention. *Journal of Epidemiology and Community Health*, 46, 120-126.
- Bahnson, C. B. (1980). Stress and cancer: The state of the art (part 1). *Psychosomatics*, 21(12), 975-981.
- Bahnson, C. B. (1981). Stress and cancer: The state of the art (part 2). *Psychosomatics*, 22, 207-220.
- Bahnson, C. B., & Bahnson, M.B. (1966). Role of the ego defenses: denial and repression in the etiology of malignant neoplasm. *Annals of the New York Academy of Sciences*, 125(3), 827-845.
- Bahnson, M. B., & Bahnson, C. B. (1979). Development of a psychosocial screening questionnaire for cancer. *Cancer Detection and Prevention*, 2, 295-305.
- Ballard-Barbash, R., & Swanson, C. A. (1996). Body weight: estimation of risk for breast and endometrial cancers. *American Journal of Clinical Nutrition*, 63(suppl), 437S-441S.
- Baltrusch, H. J. F., Stangel, W., & Titze, I. (1991). Stress, Cancer and Immunity: New developments in biopsychosocial and psychoneuroimmunologic research. *Acta Neurologica*, 13(4), 315-327.
- Baltrusch, H. J. F., Stangel, W., & Waltz, W.E. (1988). Cancer from the biobehavioral perspective: the type C pattern. *Activitas Nervosa Superior (Praha)*, 30(1), 18-21.
- Barraclough J. (1996). Adverse life events and breast cancer. Other studies have found no association. *British Medical Journal*, 312(7034): 845.
- Barraclough, J. (1994). Life events and the outcome of breast cancer. In C. E. Lewis & C. O'Sullivan & J. Barraclough (Eds.), *The Psychoimmunology of Cancer: Mind and Body in the Fight for Survival?* (pp. 213-227). Oxford: Oxford University Press.
- Barraclough, J., Pinder, P., Cruddas, M., Osmond, C., Taylor, I., & Perry, M. (1992). Life events and breast cancer prognosis. *British Medical Journal*, 304, 1078-1081.
- Baum, A., & Posluszny, D. M. (1999). Health Psychology: Mapping Biobehavioral Contributions to Health and Illness. *Annual Review of Psychology*, 50, 137-163.

- Becher, H., & Chang-Claude, J. (1996). Estimating Disease Risks for Individuals With a Given Family History in Different Populations With an Application to Breast Cancer. *Genetic Epidemiology*, 13, 229-242.
- Bedford, A. (1978). *Personality Deviance Scale (Manual)*. Windsor: NFER-Nelson.
- Bennett, E. J., Piesse, C., Palmer, K., Badcock, C-A., Tennant, C. C., & Kellow, J. E. (1998a). Functional gastrointestinal disorders: psychological, social, and somatic features. *Gut*, 42, 414-420.
- Bennett, E. J., Tennant, C. C., Piesse, C., Badcock, C-A., & Kellow, J. E. (1998b). Level of chronic life stress predicts clinical outcome in irritable bowel syndrome. *Gut*, 43, 256-261.
- Bennett, E., Beaufrepaire, J., Langeluddecke, P., Kellow, J., & Tennant, C. (1991). Life stress and non-ulcer dyspepsia: a case-control study. *Journal of Psychosomatic Research*, 35(4/5), 579-590.
- Biondi, M., Costantini, A., & Parisi, A. (1996). Can loss and grief activate latent neoplasia? A clinical case of possible interaction between genetic risk and stress in breast cancer. *Psychotherapy and Psychosomatics*, 65(2), 102-105.
- Bleiker, E. M., van der Ploeg, H. M., Ader, H. J., van Daal, W. A., & Hendriks, J. H. (1995). Personality traits of women with breast cancer: before and after diagnosis. *Psychological Reports*, 76(3 Pt 2), 1139-1146.
- Bleiker, E. M., van der Ploeg, H. M., Hendriks, J. H., & Ader, H. J. (1996). Personality factors and breast cancer development: a prospective longitudinal study. *Journal of the National Cancer Institute*, 88(20), 1478-1482.
- Bleiker, E. M., van der Ploeg, H. M., Hendriks, J. H., Leer, J. W., & Kleijn, W. C. (1993). Rationality, emotional expression and control: psychometric characteristics of a questionnaire for research in psycho-oncology. *Journal of Psychosomatic Research*, 37(8), 861-872.
- Bloom, J. R. (1982). Social support, accommodation to stress and adjustment to breast cancer. *Social Science and Medicine*, 16, 1329-1338.
- Bloom, J. R., Kang, S. H., & Romano, P. (1991). Cancer and Stress: The Effect of Social Support as a Resource. In C. L. Cooper & M. Watson (Eds.), *Cancer and Stress: Psychological, Biological and Coping Studies* (pp. 95-124). Chichester: John Wiley and Sons.
- Bodian, C. A. (1993). Benign Breast Diseases, Carcinoma In Situ, and Breast Cancer Risk.

Epidemiologic Reviews, 15(1), 177-187.

- Bondy, M. L., Lustbader, E. D., Halabi, S., Ross, E., & Vogel, V. G. (1994). Validation of a Breast Cancer Risk Assessment Model in Women With a Positive Family History. *Journal of the National Cancer Institute*, 86(8), 620-625.
- Bortner, R. W. (1969). A short rating scale as a potential measure of pattern A behavior. *Journal of Chronic Diseases*, 22(2), 87-91.
- Brémond, A., Kune, G. A., & Bahnson, C. B. (1986). Psychosomatic Factors in Breast Cancer Patients. Results of a Case Control Study. *Journal of Psychosomatic Obstetrics and Gynaecology*, 5, 127-136.
- Brinton, L. A., Malone, K. E., Liff, J., & Schoenberg, J. B. (1994). Re: "Should we consider a subject's knowledge of the etiologic hypothesis in the analysis of case-control studies?". *American Journal of Epidemiology*, 140, 1054-1056.
- Brinton, L. A., Potischman, N. A., Swanson, C. A., Schoenberg, J. B., Coates, R. J., Gammon, M. D., Malone, K. E., Stanford, J. L., & Daling, J. R. (1995). Breastfeeding and breast cancer risk. *Cancer Causes and Control*, 6, 199-208.
- Brown, G. W. (1981). Life events, psychiatric disorder and physical illness. *Journal of Psychosomatic Research*, 25(5), 461-473.
- Brown, G. W., & Harris, T. O. (1978). *Social origins of depression: a study of psychiatric disorder in women*. London: Tavistock.
- Brown, G. W., & Harris, T. O. (1989). *Life Events and Illness*. New York: The Guilford Press.
- Brown, G. W., Adler, Z., & Bifulco, A. (1988). Life events, difficulties and recovery from chronic depression. *British Journal of Psychiatry*, 152, 487-498.
- Brown, G. W., Harris, T. (1982). Fall-Off in the Reporting of Life Events. *Social Psychiatry*, 17, 23-28.
- Bryla, C. M. (1996). The relationship between stress and the development of breast cancer: a literature review. *Oncology Nursing Forum*, 23(3), 441-448.
- Burke, M. A., Goodkin, K. (1997). Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer*, 79(5), 1055-1059.
- Butow, P. N., Hiller, J. E., Price, M. A., Thackway, S. V., Kricker, A., & Tennant, C. C. (2000). Epidemiological evidence for a relationship between life events, coping style and personality factors in the development of breast cancer. *Journal of Psychosomatic Research*, 49, 169-181.

- Cassileth, B. R. (1996). Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer*, 77(6), 1015-1016.
- Cella, D. F., & Holland, J. C. (1988). Methodological considerations in studying the stress-illness connection in women with breast cancer. In C. L. Cooper (Ed.), *Stress and Breast Cancer* (pp. 197-214). Chichester: John Wiley and Sons.
- Cheang, A., & Cooper, C. L. (1985). Psychosocial factors in breast cancer. *Stress Medicine*, 1, 61-66.
- Chen, C. C., David, A. S., Nunnerley, H., Michell, M., Dawson, J. L., Berry, H., Dobbs, J., & Fahy, T. (1995). Adverse life events and breast cancer: case-control study. *British Medical Journal*, 311(7019), 1527-1530.
- Chorot, P., & Sandin, B. (1994). Life events and stress reactivity as predictors of cancer, coronary heart disease and anxiety disorders. *International Journal of Psychosomatics*, 41(1-4), 34-40.
- Coakes, S. J., Steed, L. G. (1997). SPSS: Analysis without anguish. Version 6.1 for IBM and Machintosh users. Brisbane: John Wiley and Sons.
- Colditz, G. A. (1993). Epidemiology of Breast Cancer. Findings from the Nurses' Health Study. *Cancer*, 71(4), 1480-1489.
- Colditz, G. A., Willett, W. C., Hunter, D. J., Stampfer, M. J., Manson, J. E., Hennekens, C. H., Rosner, B. A., & Speizer, F. E. (1993). Family History, Age, and Risk of Breast Cancer. Prospective Data From the Nurses' Health Study. *Journal of the American Medical Association*, 270(3), 338-343.
- Collaborative Group on Hormonal Factors in Breast Cancer. (1996). Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet*, 347, 1713-1727.
- Collaborative Group on Hormonal Factors in Breast Cancer. (1997). Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. *Lancet*, 350, 1047-1059.
- Cooper, C. L., & Faragher, E. B. (1992). Coping strategies and breast disorders/cancer. *Psychological Medicine*, 22(2), 447-455.
- Cooper, C. L., & Faragher, E. B. (1993). Psychosocial stress and breast cancer: the inter-relationship between stress events, coping strategies and personality. *Psychological*

Medicine, 23(3), 653-662.

- Cooper, C. L., Cooper, R., & Faragher, E. B. (1989). Incidence and perception of psychosocial stress: the relationship with breast cancer. *Psychological Medicine*, 19(2), 415-422.
- Cooper, C. L., Davies Cooper, R. F., & Faragher, E. B. (1986). A prospective study of the relationship between breast cancer and life events, type A behaviour, social support and coping skills. *Stress Medicine*, 2, 271-277.
- Craig, A., Franklin, J., & Andrews, G. (1984). A scale to measure locus of control of behaviour. *British Journal of Medical Psychology*, 57, 173-180.
- Crowne, D. P., & Marlowe, D. (1960). A new scale of social desirability independent of psychopathology. *Journal of Consulting Psychology*, 24, 349-354.
- Curbow, B., & Somerfield, M. (1991). Use of the Rosenberg Self-Esteem Scale with Adult Cancer Patients. *Journal of Psychosocial Oncology*, 9(2), 113-131.
- Datta, M. (1993). You cannot exclude the explanation you have not considered. *Lancet*, 342, 345-347.
- Daures, J. P., Peray, P., Bousquet, J., Stoebner, A., Gouzes, C., Lamarque, J. L., Laurent, J. C., Cherif Cheikh, J., Boulet, P., & Pujol, J. (1992). Mass screening for breast cancer in Herault county. First results in women between 40 and 70 years old. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction*, 21(2), 173-178.
- Dean, P. B., & Pamilo, M. (1999). Screening mammography in Finland - 1.5 million examinations with 97 percent specificity. Mammography Working Group, Radiological Society of Finland. *Acta Oncologica*, 38(Suppl 13), 47-54.
- Deslypere, J. P. (1995). Obesity and Cancer. *Metabolism: Clinical and Experimental*, 44(9 (suppl 3)), 24-27.
- Dorgan, J. F., Reichman, M. E., Judd, J. T., Brown, C., Longcope, C., Schatzkin, A., Campbell, W. S., Franz, C., Kahle, L., & Taylor, P. R. (1994). The relation of reported alcohol ingestion to plasma levels of estrogens and androgens in premenopausal women. *Cancer Causes and Control*, 5, 53-60.
- Edwards, J. R., Cooper, C. L., Pearl, S. G., de Paredes, E. S. O., Leary, T., & Wilhelm, M. C. (1990). The relationship between psychosocial factors and breast cancer: some unexpected results. *Behavioral Medicine*, 16(1), 5-14.
- Ell, K., Nishimoto, R., Mediansky, L., Mantell, J., & Hamovitch, M. (1992). Social relations, social support and survival among patients with cancer. *Journal of Psychosomatic*

Research, 36(6), 531-541.

- Ellman, R., & Thomas, B. A. (1995). Is psychological wellbeing impaired in long-term survivors of breast cancer? *Journal of Medical Screening*, 2(1), 5-9.
- Ewertz, M. (1986). Bereavement and breast cancer. *British Journal of Cancer*, 53, 701-703.
- Eysenck, H. J. (1988). Personality, stress and cancer: Prediction and prophylaxis. *British Journal of Medical Psychology*, 61, 57-75.
- Eysenck, H. J. (1991). Cancer and Personality. In C. L. Cooper, Watson, M. (Ed.), *Cancer and Stress: Psychological, Biological and Coping Studies* (pp. 73-94). Chichester: John Wiley and Sons.
- Eysenck, H. J., & Eysenck, S. B. G. (1964). *The Eysenck Personality Inventory*. London: London University Press.
- Eysenck, H. J., & Eysenck, S. B. G. (1975). *Manual of the Eysenck Personality Questionnaire*. London: Hodder and Stoughton.
- Faragher, E. B., & Cooper, C. L. (1990). Type A stress prone behaviour and breast cancer. *Psychological Medicine*, 20(3), 663-670.
- Faragher, M. G., & Cooper, C. L. (1997). 'Are life events related to the onset of breast cancer?' *Psychological Medicine*, 27(2), 497-498.
- Fawzy, F. I., Kemeny, M. E., Fawzy, N. W., Elashoff, R., Morton, D., Cousins, N., & Fahey, J. L. (1990). A structured psychiatric intervention for cancer patients. *Archives of General Psychiatry*, 47, 729-735.
- Floderus, B., Barlow, L., & Mack, T. M. (1990). Recall Bias in Subjective Reports of Familial Cancer. *Epidemiology*, 1, 318-321.
- Folkman, S., & Lazarus, R. S. (1980). An analysis of coping in a middle-aged community sample. *Journal of Health Social Behavior*, 21, 219-239.
- Forbes, J. F. (1997). The Incidence of Breast Cancer: The Global Burden, Public Health Considerations. *Seminars in Oncology*, 24(suppl1), S1-20-S21-35.
- Forsén, A. (1991). Psychosocial stress as a risk for breast cancer. *Psychotherapy and Psychosomatics*, 55(2-4), 176-185.
- Fox, B. H. (1978). Premorbid Psychological factors as Related to Cancer Incidence. *Journal of Behavioral Medicine*, 1(1), 45-133.
- Fox, B. H. (1995). The role of psychological factors in cancer incidence and progression. *Oncology*, 9(3), 245-253.

- Fox, C. M., Harper, A. P., Hyner, G. C., & Lyle, R. M. (1994). Loneliness, emotional repression, marital quality, and major life events in women who develop breast cancer. *Journal of Community Health, 19*(6), 467-482.
- Franceschi, S., Favero, A., La Vecchia, C., Baron, A. E., Negri, E., Dal Maso, L., Giacosa, A., Montella, M., Conti, E., & Amadori, D. (1996). Body size indices and breast cancer risk before and after menopause. *International Journal of Cancer, 67*, 181-186.
- Friberg, S., & Mattson, S. (1997). On the growth rates of human malignant tumours: implications for medical decision making. *Journal of Surgical Oncology, 65*(4), 284-297.
- Funch, D. P., & Marshall, J. R. (1984). Measuring Life Stress: Factors Affecting Fall-Off in the Reporting of Life Events. *Journal of Health and Social Behavior, 25*, 453-464.
- Funch, D. P., & Marshall, J. (1983). The role of stress, social support and age in survival from breast cancer. *Journal of Psychosomatic Research, 27*, 77-83.
- Gapstur, S. M., Potter, J. D., Sellers, T. A., & Folsom, A. R. (1992). Increased Risk of Breast Cancer with Alcohol Consumption in Postmenopausal Women. *American Journal of Epidemiology, 136*(10), 1221-1231.
- George, L. K. (1989). Stress, Social Support, and Depression over the Life-Course. In K. S. Markides & C. L. Cooper (Eds.). *Aging Stress and Health* (pp. 241-267). Chichester: John Wiley and Sons.
- Geyer, S. (1991). Life events prior to manifestation of breast cancer: a limited prospective study covering eight years before diagnosis. *Journal of Psychosomatic Research, 35*(2-3), 355-363.
- Geyer, S. (1992). Artifacts in "limited prospective" designs? Testing confounding effects of response behaviour of women prior to breast surgery. *Journal of Psychosomatic Research, 36*(2), 107-116.
- Geyer, S. (1993). Life events, chronic difficulties and vulnerability factors preceding breast cancer. *Social Science and Medicine, 37*(12), 1545-55.
- Ginsberg, A., Price, S., Ingram, D., & Nottage, E. (1996). Life events and the risk of breast cancer: a case-control study. *European Journal of Cancer, 32A*(12), 2049-52.
- Goodkin, K., Antoni, M. H., & Blaney, P. H. (1986). Stress and hopelessness in the promotion of cervical intraepithelial neoplasia to invasive squamous cell carcinoma of the cervix. *Journal of Psychosomatic Research, 30*(1), 67-76.
- Grassi, L., & Cappellari, L. (1988). State and trait psychological characteristics of breast

- cancer patients. *New Trends in Experimental Clinical Psychiatry*, IV-N.2, 99-109.
- Greer, S. (1979). Psychological enquiry: a contribution to cancer research. *Psychological Medicine*, 9(1), 81-9.
- Greer, S., & Morris, T. (1975). Psychological attributes of women who develop breast cancer: a controlled study. *Journal of Psychosomatic Research*, 19(2), 147-153.
- Greer, S., & Morris, T. (1978). The study of psychological factors in breast cancer: problems of method. *Social Science and Medicine*, 12(3A), 129-34.
- Greer, S., & Watson, M. (1985). Towards a psychobiological model of cancer: psychological considerations. *Social Science and Medicine*, 20(8), 773-7.
- Gross, J. (1989). Emotional Expression in Cancer Onset and Progression. *Social Science and Medicine*, 28(12), 1239-48.
- Grossarth-Maticek, R., Kanazir, D. T., Schmidt, P., & Vetter, H. (1982). Psychosomatic Factors in the Process of Cancerogenesis: Theoretical Models and Empirical Results. *Psychotherapy and Psychosomatics*, 38, 284-302.
- Hahn, R. C., & Petitti, D. B. (1988). Minnesota Multiphasic Personality Inventory-Rated Depression and the Incidence of Breast Cancer. *Cancer*, 61, 845-8.
- Hall, M., Baum, A., Buysse, D. J., Prigerson, H. G., Kupfer, D. J., Reynolds, C. F. (1998). Sleep as a Mediator of the Stress-Immune Relationship. *Psychosomatic Medicine*, 60(1), 48-51.
- Hamilton, M. (1967). Development of a scale for primary depressive illness. *British Journal of Social and Clinical Psychology*, 6(4), 278-96.
- Hancock, K., Craig, A., Tennant, C., & Chang, E. (1993). The influence of spinal cord injury on coping styles and self-perceptions: a controlled study. *Australian and New Zealand Journal of Psychiatry*, 27(3), 450-6.
- Hankinson, S. E., Colditz, G. A., Hunter, D. J., Manson, J. E., Willett, W. C., Stampfer, M. J., Longcope, C., & Speizer, F. E. (1995). Reproductive factors and family history of breast cancer in relation to plasma estrogen and prolactin levels in postmenopausal women in the Nurses' Health Study. *Cancer Causes and Control*, 6, 217-224.
- Hankinson, S. E., Colditz, G. A., Manson, J. E., Willett, W. C., Hunter, D. J., Stampfer, M. J., & Speizer, F. E. (1997). A prospective study of oral contraceptive use and risk of breast cancer. *Cancer Causes and Control*, 8, 65-72.
- Harris, J. R., Lippman, M. E., Veronesi, U., & Willett, W. (1992). Breast Cancer (First of Three Parts). *New England Journal of Medicine*, 327(5), 319-328.

- Hathaway, S. R., & McKinley, J. C. (1951). *Minnesota Multiphasic Personality Inventory*. New York: Psychological Corporation.
- Heck, K. E., & Pamuk, E. R. (1997). Explaining the Relation Between Education and Postmenopausal Breast Cancer. *American Journal of Epidemiology*, 145(4), 366-372.
- Henderson, I. C. (1993). Risk Factors for Breast Cancer Development. *Cancer*, 71(6), 2127-2140.
- Henderson, S., Duncan-Jones, P., Byrne, D. G., & Scott, R. (1980). Measuring social relationships: The Interview Schedule for Social Interaction. *Psychological Medicine*, 10, 723-734.
- Hilakivi-Clarke, L., Rowland, J., Clarke, R., & Lippman, M. E. (1993). Psychosocial factors in the development and progression of breast cancer. *Breast Cancer Research and Treatment*, 29(2), 141-160.
- Holmes, T. H., & Rahe, R. H. (1967). The Social Readjustment Rating Scale. *Psychosomatic Medicine*, 11, 213-218.
- Hosmer, D. W., & Lemeshow, S. (1989). *Applied Logistic Regression*. New York: Wiley & Sons.
- Hunter, D. J., Spiegelman, D., Adami, H.-O., van den Brandt, P. A., Folsom, A. R., Goldbohm, R. A., Graham, S., Howe, G. R., Kushi, L. H., Marshall, J. R., Miller, A. B., Speizer, F. E., Willett, W., Wolk, A., & Yaun, S.-S. (1997). Non-dietary factors as risk factors for breast cancer, and as effect modifiers of the association of fat intake and risk of breast cancer. *Cancer Causes and Control*, 8, 49-56.
- Hunyor, S. N., Bartrop, R., Craig, A., Cejnar, M., Liggins, G., Henderson, R., & Jones, M. (1991). Voluntary blood pressure control by biofeedback: relationship to psychological characteristics. *Clinical and Experimental Pharmacology and Physiology*, 18(1), 55-59.
- Jacobs, G. A., Latham, L.E., & Brown M.S. (1988). Test-retest reliability of the state-trait personality inventory and the anger expression scale. *Anxiety Research*, 1, 263-265.
- Jacobs, J., & Bovasso, G. (2000). Early and chronic stress and their relation to breast cancer. *Psychological Medicine*, 30(3), 669-678.
- Jansen, M. A., & Muenz, L. R. (1984). A retrospective study of personality variables associated with fibrocystic disease and breast cancer. *Journal of Psychosomatic Research*, 28(1), 35-42.
- Jasmin, C., Le, M. G., Marty, P., Herzberg, R., & Psycho-Oncology Group. (1990).

- Evidence for a link between certain psychological factors and the risk of breast cancer in a case-control study. *Annal Oncologica*, 1(1), 22-9.
- Jelicic, M., Bonke, B., & Millar, K. (1993). Clinical note on the use of denial in patients undergoing surgery for breast cancer. *Psychological Reports*, 72(3 pt 1), 952-954.
- Jones, D. R., Goldblatt, P. O., & Leon, D. A. (1984). Bereavement and cancer: some data on deaths of spouses from the longitudinal study of Office of Population Censuses and Surveys. *British Medical Journal*, 289, 461-464.
- Karasek, R., & Theorell, T. (1990). *Healthy Work: Stress, Productivity, and the Reconstruction of Working Life*. New York: Basic Books.
- Katsouyanni, K., Trichopoulou, A., Stuver, S., Vassilaros, S., Papadiamantis, Y., Bournas, N., Skarpou, N., Mueller, N., & Trichopoulos, D. (1994). Ethanol and breast cancer: an association that may be both confounded and causal. *International Journal of Cancer*, 58, 356-361.
- Kellner, R. (1976). *Abridged Manual of the Symptom Questionnaire*. Albuquerque: University of New Mexico.
- Kelsey, J. L. (1993). Breast Cancer Epidemiology: Summary and Future Directions. *Epidemiologic Reviews*, 15(1), 256-263.
- Kelsey, J. L., & Berkowitz, G., S. (1988). Breast Cancer Epidemiology. *Cancer Research*, 48, 5615-5623.
- Kelsey, J. L., Gammon, M. D., & John, E. M. (1993). Reproductive Factors and Breast Cancer. *Epidemiologic Reviews*, 15(1), 36-47.
- Kissen, D. M. (1966). The significance of personality in lung cancer in men. *Annals of the New York Academy of Sciences*, 125(3), 820-6.
- Kissen, D. M., & Eysenck, H. J. (1962). Personality in Male Lung Cancer Patients. *Journal of Psychosomatic Research*, 6, 123-7.
- Koopman, C., Hermanson, K., Diamond, S., Angell, K., & Spiegel, D. (1998). Social support, life stress, pain and emotional adjustment to advanced breast cancer. *Psycho-Oncology*, 7, 101-11.
- Kornblith, A. B., Herndon II, J. E., Zuckerman, E., Viscoli, C. M., Horwitz, R. I., Cooper, M. R., Harris, L., Tkaczuk, K. H., Perry, M. C., Budman, D., Norton, L. C., Holland, J., & Cancer and Leukemia Group B. (2001). Social support as a buffer to the psychological impact of stressful life events in women with breast cancer. *Cancer*, 91(2), 443-454.

- Kowal, S. J. (1955). Emotions as a cause of cancer: 18th and 19th century contributions. *Psychoanalytic Review*, 42(3), 217-27.
- Kreitler, S., Chaitchik, S., & Kreitler, H. (1993). Repressiveness: cause or result of cancer? *Psycho-Oncology*, 2, 43-54.
- Kricker, A., & Jelfs, P. (1996). *Breast cancer in Australian women 1921-1994* (Cancer Series No.6). Canberra: Australian Institute of Health and Welfare.
- Kvikstad, A., Vatten, L. J., Tretli, S., & Kvinnsland, S. (1994). Death of a husband or marital divorce related to risk of breast cancer in middle-aged women. A nested case-control study among Norwegian women born 1935-1954. *European Journal of Cancer*, 30A(4), 473-477.
- La Vecchia, C., Negri, E., Franceschi, S., Favero, A., Nanni, O., Filiberti, R., Conti, E., Montella, M., Veronesi, A., Ferraroni, M., & Decarli, A. (1995). Hormone replacement treatment and breast cancer risk: a cooperative Italian study. *British Journal of Cancer*, 72, 244-248.
- La Vecchia, C., Negri, E., Franceschi, S., Talamini, R., Amadori, D., Filiberti, R., Conti, E., Montella, M., Veronesi, A., Parazzini, F., Ferraroni, M., & Decarli, A. (1995). Oral contraceptives and breast cancer: a cooperative Italian study. *International Journal of Cancer*, 60, 163-167.
- La Vecchia, C., Negri, E., Franceschi, S., Talamini, R., Palli, D., & Decarli, A. (1997). Body mass index and post-menopausal breast cancer: an age-specific analysis. *British Journal of Cancer*, 75(3), 441-444.
- LeShan, L. (1959). Psychological States as Factors in the Development of Malignant Diseases: A Critical Review. *Journal of the National Cancer Institute*, 22(1), 1-18.
- LeShan, L., & Worthington, R. E. (1956). Some recurrent life history patterns observed in patients with malignant disease. *Journal of Nervous and Mental Diseases*, 124, 460-465.
- Levenson, J. L., & Bemis, C. (1991). The Role of Psychological Factors in Cancer Onset and Progression. *Psychosomatics*, 32(2), 124-132.
- Levi, F., Pasche, C., Lucchini, F., & La Vecchia, C. (1996). Alcohol and Breast Cancer in the Swiss Canton of Vaud. *European Journal of Cancer*, 32A(12), 2108-13.
- Levy, S., Herberman, R., Lippman, M., & d'Angelo, T. (1987). Correlation of stress factors with sustained depression of natural killer cell activity and predicted prognosis in patients with breast cancer. *Journal of Clinical Oncology*, 5(3), 348-353.

- Lewin, T. J., Carr, V. J., & Webster, R. A. (1998). Recovery from post-earthquake psychological morbidity: who suffers and who recovers? *Australian and New Zealand Journal of Psychiatry*, 32(1), 15-20.
- Lillberg, K., Verkasalo, J., Teppo, L., Helenius, H., & Loskenvuo, M. (2001). Stress of daily activities and risk of breast cancer: a prospective cohort study in Finland. *International Journal of Cancer*, 91, 888-893.
- Litherland, J. C., Evans, A. J., & Wilson, A. R. M. (1997). The Effect of Hormone Replacement Therapy on Recall Rate in the National Health Service Breast Screening Programme. *Clinical Radiology*, 52, 276-279.
- London, S. J., Colditz, G. A., Stampfer, M. J., Willett, W. C., Rosner, B. A., Corsano, K., & Speizer, F. E. (1990). Lactation and risk of breast cancer in a cohort of US women. *American Journal of Epidemiology*, 132(1), 17-26.
- Longnecker, M. P. (1993). Do Hormones Link Alcohol With Breast Cancer? *Journal of the National Cancer Institute*, 85(9), 692-693.
- Longnecker, M. P. (1994). Alcoholic beverage consumption in relation to risk of breast cancer: meta-analysis and review. *Cancer Causes and Control*, 5, 73-82.
- Longnecker, M. P., Newcomb, P. A., Mittendorf, R., Greenberg, E. R., Clapp, R. W., Bogdan, G. F., Baron, J., MacMahon, B., & Willett, W. C. (1995). Risk of Breast Cancer in Relation to Lifetime Alcohol Consumption. *Journal of the National Cancer Institute*, 87(12), 923-929.
- Longnecker, M. P., Paganini-Hill, A., & Ross, R. K. (1995). Lifetime Alcohol Consumption and Breast Cancer Risk among Postmenopausal Women in Los Angeles. *Cancer Epidemiology, Biomarkers and Prevention*, 4, 721-725.
- Madigan, M. P., Ziegler, R. G., Benichou, J., Byrne, C., & Hoover, R. N. (1995). Proportion of Breast Cancer Cases in the United States Explained by Well-Established Risk Factors. *Journal of the National Cancer Institute*, 87(22), 1681-1685.
- Malone, K. E., Daling, J. R., & Weiss, N. S. (1993). Oral Contraceptives in Relation to Breast Cancer. *Epidemiologic Reviews*, 15(1), 80-97.
- Maraste, R., Brandt, L., Olsson, H., & Ryde-Brandt, B. (1992). Anxiety and depression in breast cancer patients at the start of adjuvant radiotherapy. Relations to age and type of surgery. *Acta Oncologica*, 31(6), 641-643.
- Martin-Moreno, J. M., Boyle, P., Gorgojo, L., Willett, W. C., Gonzalez, J., Villar, F., & Maisonneuve, P. (1993). Alcoholic beverage consumption and risk of breast cancer in

- Spain. *Cancer Causes and Control*, 4, 345-353.
- McGee, R., Williams, S., & Elwood, M. (1994). Depression and the development of cancer: a meta-analysis. *Social Science and Medicine*, 38(1), 187-192.
- McGee, R., Williams, S., & Elwood, M. (1996). Are life events related to the onset of breast cancer? *Psychological Medicine*, 26, 441-447.
- Mettlin, C., Croghan, I., Natarajan, N., & Lane, W. (1990). The association of age and familial risk in a case-control study of breast cancer. *American Journal of Epidemiology*, 131(6), 973-983.
- Michels, K. B., Willett, W. C., Rosner, B. A., Manson, J. E., Hunter, D. J., Colditz, G. A., Hankinson, S. E., & Speizer, F. E. (1996). Prospective assessment of breastfeeding and breast cancer incidence among 89 887 women. *Lancet*, 347, 431-436.
- Millar, K., Jelcic, M., Bonke, B., & Asbury, A. J. (1995). Assessment of preoperative anxiety: comparison of measures in patients awaiting surgery for breast cancer. *British Journal of Anaesthesia*, 74(2), 180-183.
- Monroe, S. M., & Roberts, J. E. (1990). Conceptualizing and measuring life stress: problems, principles, procedures, progress. *Stress Medicine*, 6, 209-216.
- Moorey, S., Greer, S., Watson, M., Gorman, C., Rowden, L., Tunmore, R., Robertson, B., & Bliss, J. (1991). The Factor Structure Stability of the Hospital Anxiety and Depression Scale in Patients with Cancer. *British Journal of Psychiatry*, 158, 255-259.
- Morley, J. E., Benton, D., & Solomon, G. F. (1991). The role of stress and opioids as regulators of the immune system. In McCubbin, J. A., Kaufman, P. G., & Nemeroff, C. B. (Eds.), *Stress, neuropeptides and systemic disease* (pp. 233-260). San Diego: Academic Press.
- Morris, T., & Greer, S. (1982). Psychological characteristics of women electing to attend a breast screening clinic. *Clinical Oncology*, 8(2), 113-119.
- Morris, T., Greer, S., Pettingale, K. W., & Watson, M. (1981). Patterns of expression of anger and their psychological correlates in women with breast cancer. *Journal of Psychosomatic Research*, 25(2), 111-117.
- Muslin, H. L., Gyarfás, K., & Pieper, W. J. (1966). Separation experience and cancer of the breast. *Annals of the New York Academy of Science*, 125(3), 802-806.
- Neuhaus, W., Zok, C., Gohring, U. J., & Scharl, A. (1994). A prospective study concerning psychological characteristics of patients with breast cancer. *Archives of Gynecology and Obstetrics*, 255(4), 201-209.

- Neuling, S. J., & Winefield, H. R. (1988). Social support and recovery after surgery for breast cancer: frequency and correlates of supportive behaviours by family, friends and surgeon. *Social Science and Medicine*, 27(4), 385-392.
- Newcomb, P. A., Longnecker, M. P., Storer, B. E., Mittendorf, R., Baron, J., Clapp, R. W., Bogdan, G., & Willett, W. C. (1995). Long-term Hormone Replacement Therapy and Risk of Breast Cancer in Postmenopausal Women. *American Journal of Epidemiology*, 142(8), 788-795.
- Newcomb, P. A., Longnecker, M. P., Storer, B. E., Mittendorf, R., Baron, J., Clapp, R. W., Trentham-Dietz, A., & Willett, W. C. (1996). Recent oral contraceptive use and risk of breast cancer (United States). *Cancer Causes and Control*, 7, 525-532.
- Olf, M. (1999). Stress, depression and immunity: the role of defense and coping styles. *Psychiatric Research*, 85(1), 7-15.
- Parent, M.-E., Ghadirian, P., Lacroix, A., & Perret, C. (1997). The Reliability of Recollections of Family History: Implications for the Medical Provider. *Journal of Cancer Education*, 12(2), 114-120.
- Pathak, D. R., & Whittemore, A. S. (1992). Combined Effects of Body Size, Parity, and Menstrual Events on Breast Cancer Incidence in Seven Countries. *American Journal of Epidemiology*, 135(2), 153-168.
- Pettingale, K. W., Watson, M., & Greer, S. (1984). The Validity of Emotional Control as a Trait in Breast Cancer Patients. *Journal of Psychosocial Oncology*, 2 (3/4), 21-30.
- Pharoah, P. D. P., Day, N. E., Duffy, S., Easton, D. F., & Ponder, B. A. J. (1997). Family history and the risk of breast cancer: a systematic review and meta-analysis. *International Journal of Cancer*, 71, 800-809.
- Potischman, N., Swanson, C. A., Siiteri, P., & Hoover, R. N. (1996). Reversal of Relation Between Body Mass and Endogenous Estrogen Concentrations With Menopausal Status. *Journal of the National Cancer Institute*, 88(11), 756-758.
- Price, M. A., Tennant, C. C., Smith, R. C., Butow, P. N., Kennedy, S. J., Kossoff, M. B., & Dunn, S. M. (1999). Predictors of breast cancer in women recalled following screening. *Australian and New Zealand Journal of Surgery*, 69, 639-646.
- Priestman, T. J., Priestman, S. G., & Bradshaw, C. (1985). Stress and breast cancer. *British Journal of Cancer*, 51(4), 493-498.
- Protheroe, D., Turvey, K., Horgan, K., Benson, E., Bowers, D., & House, A. (1999). Stressful life events and difficulties and onset of breast cancer: case-control study.

- British Medical Journal*, 319, 1027-1030.
- Rabin, B. S., Cohen, S., Ganguli, R., Lysle, D. T., & Cunnick, J. E. (1989). Bidirectional interaction between the central nervous system and the immune system. *Critical Reviews in Immunology*, 9, 279-312.
- Reichman, M. E., Judd, J. T., Longcope, C., Schatzin, A., Clevidence, B. A., Nair, P. P., Campbell, W. S., & Taylor, P. R. (1993). Effects of Alcohol Consumption on Plasma and Urinary Hormone Concentrations in Premenopausal Women. *Journal of the National Cancer Institute*, 85(9), 722-727.
- Roberts, C. S., Cox, C. E., Shannon, V. J., & Wells, N. L. (1994). A closer look at social support as a moderator of stress in breast cancer. *Health Social Work*, 19(3), 157-164.
- Roberts, F. D., Newcomb, P. A., Trentham-Dietz, A., & Storer, B. E. (1996). Self-reported stress and risk of breast cancer. *Cancer*, 77(6), 1089-1093.
- Rosch, P. J. (1993). Is cancer another "disease of adaptation"? Some insights into the role of stress and civilization. *Comprehensive Therapy*, 19(5), 183-187.
- Roseman, D. L., Straus, A. K., & Shorey, W. (1990). A Positive Family History of Breast Cancer: Does Its Effect Diminish With Age? *Archives of Internal Medicine*, 150, 191-194.
- Rosenberg, L., Metzger, L. S., & Palmer, J. (1993). Alcohol Consumption and Risk of Breast Cancer: A Review of the Epidemiologic Evidence. *Epidemiologic Reviews*, 15(1), 133-144.
- Rosenberg, M. (1965). *Society and the adolescent self-image*. Princeton, New Jersey: Princeton University Press.
- Sarason, I. G., Levine, H. M., Basham, R. B., & Sarason, B. R. (1983). Assessing social support: the Social Support Questionnaire. *Journal of Personality and Social Psychology*, 44, 127-139.
- Scherg, H. (1987). Psychosocial factors and disease bias in breast cancer patients. *Psychosomatic Medicine*, 49(3), 302-312.
- Scherg, H., & Blohmke, M. (1988). Associations between selected life events and cancer. *Behavioral Medicine*, 14(3), 119-124.
- Scherg, H., Cramer, I., & Blohmke, M. (1981). Psychosocial factors and breast cancer: a critical reevaluation of established hypotheses. *Cancer Detection and Prevention*, 4, 165-171.
- Schonfield, J. (1975). Psychological and life-experience differences between Israeli women

- with benign and cancerous breast lesions. *Journal of Psychosomatic Research*, 19(4), 229-234.
- Schwarz, R., & Geyer, S. (1984). Social and psychological differences between cancer and noncancer patients: cause or consequence of the disease? *Psychotherapy and Psychosomatics*, 41(4), 195-199.
- Scott, D. W. (1983). Anxiety, critical thinking and information processing during and after breast biopsy. *Nursing Research*, 32(1), 24-28.
- Seidman, H., Stellman, S. D., & Mushinski, M. H. (1982). A Different Perspective on Breast Cancer Risk Factors: Some Implications of the Nonattributable Risk. *Ca: A Cancer Journal for Clinicians*, 32(5), 301-313.
- Sellers, T. A., Kushi, L. H., Potter, J. D., Kaye, S. A., Nelson, C. L., McGovern, P. G., & Folsom, A. R. (1992). Effect of family history, body-fat distribution, and reproductive factors on the risk of postmenopausal breast cancer. *The New England Journal of Medicine*, 326, 1323-1329.
- Shevlin, M. E., Bunting, B. P., & Lewis, C. A. (1995). Confirmatory factor analysis of the Rosenberg Self-Esteem scale. *Psychological Reports*, 76, 707-710.
- Slattery, M. L., & Kerber, R. A. (1993). A Comprehensive Evaluation of Family History and Breast Cancer Risk. The Utah Population Database. *Journal of the American Medical Association*, 270(13), 1563-1568.
- Snell, L., & Graham, S. (1971). Social trauma as related to cancer of the breast. *British Journal of Cancer*, 25(4), 721-734.
- Spiegel, D. (1992). Effects of Psychosocial Support on Patients with Metastatic Breast Cancer. *Journal of Psychosocial Oncology*, 10(2), 113-120.
- Spiegel, D., & Sephton, S. E. (2001). Psychoneuroimmune and Endocrine Pathways in Cancer: Effects of Stress and Support. *Seminars in Clinical Neuropsychiatry*, 6(4), 252-265.
- Spielberger, C. D. (1988). *State-Trait Anger Expression Inventory*, STAXI. Odesa, FL: PAR.
- Spielberger, C. D., Gorsuch, R. C., & Lushene, R. E. (1970). *The State-Trait Anxiety Inventory*. Palo Alto: Consulting Psychologists Press.
- Spielberger, C. D., Jacobs, G. A., Crane, R. S., Russell, S. F., Westberry, L., Barker, L., Johnson, E., Knight, J., & Marks, E. (1979). *Preliminary manual for the State-Trait Personality Inventory (STPI)*. Tampa, University of South Florida: Human Resources Institute.

- Stanford, J. L., Brinton, L. A., & Hoover, R. N. (1989). Oral contraceptives and breast cancer: results from an expanded case-control study. *British Journal of Cancer*, 60, 375-381.
- Stansfeld, S. A., Bosma, H., Hemingway, H., & Marmot, M. G. (1998). Psychosocial work characteristics and social support as predictors of SF-36 health functioning: the Whitehall II study. *Psychosomatic Medicine*, 60(3), 247-255.
- Stevens, J. (1996). *Applied Multivariate Statistics for the Social Sciences* (3rd ed.). Mahwah, New Jersey: Lawrence Erlbaum Associates.
- Swanson, C. A., Coates, R. J., Malone, K. E., Gammon, M. D., Schoenberg, J. B., Brogan, D. J., McAdams, M., Potischman, N., Hoover, R. N., & Brinton, L. A. (1997). Alcohol Consumption and Breast Cancer Risk among Women under Age 45 Years. *Epidemiology*, 8(3), 231-237.
- Tabachnick, B. G., Fidell, L. S. (2001). *Using Multivariate Statistics* (4th ed.). Boston: Allyn & Bacon.
- Taioli, E., Barone, J., & Wynder, E. L. (1995). A Case-Control Study on Breast Cancer and Body Mass. *European Journal of Cancer*, 31A(5), 723-728.
- Talamini, R., Franceschi, S., La Vecchia, C., Negri, E., Borsa, L., Montella, M., Falcini, F., Conti, E., & Rossi, C. (1996). The Role of Reproductive and Menstrual Factors in Cancer of the Breast Before and After Menopause. *European Journal of Cancer*, 32A(2), 303-310.
- Tavani, A., Braga, C., La Vecchia, C., Negri, E., Russo, A., & Franceschi, S. (1997). Attributable risks for breast cancer in Italy: education, family history and reproductive and hormonal factors. *International Journal of Cancer*, 70, 159-163.
- Taylor, G. J., Ryan, D., & Bagby, R. M. (1985). Towards the development of a new self-report alexithymia scale. *Psychotherapy and Psychosomatics*, 44, 191-199.
- Taylor, R., & Boyages, J. (2000). Absolute risk of breast cancer for Australian women with a family history. *Australian and New Zealand Journal of Surgery*, 70(10), 725-731.
- Taylor, R., & Boyages, J. (2001). Estimating risk of breast cancer from population incidence affected by widespread mammographic screening. *Journal of Medical Screening*, 8(2), 73-76.
- Temoshok, L. (1987). Personality, coping style, emotion and cancer: toward an integrative model. *Cancer Surveys*, 6, 545-567.
- Tennant, C. (1994). Life-event stress and psychiatric illness. *Current Opinion in Psychiatry*,

- Tennant, C. C., Langeluddecke, P. M., Fulcher, G., & Wilby, J. (1988). Acute and chronic life event stress in coronary atherosclerosis. *Journal of Psychosomatic Research*, 32(1), 13-20.
- Tennant, C. C., Palmer, K. J., Langeluddecke, P. M., Jones, M. P., & Nelson, G. (1994). Life event stress and myocardial reinfarction: a prospective study. *European Heart Journal*, 15, 472-478.
- Tennant, C., & Andrews, G. (1976). A scale to measure the stress of life events. *Australian and New Zealand Journal of Psychiatry*, 10, 27-32.
- Tennant, C., Langeluddecke, P., & Byrne, D. (1985). The concept of stress. *Australian and New Zealand Journal of Psychiatry*, 19(2), 113-118.
- Tennant, C., Mihailidou, A., Scott, A., Smith, R., Kellow, J., Jones, M., Hunyor, S., Lorang, M., & Hoschl, R. (1994). Psychological symptom profiles in patients with chest pain. *Journal of Psychosomatic Research*, 38(4), 365-371.
- Tennant, C., Smith, P., Bebbington, P., & Hurry, J. (1979). The contextual threat of life events: the concept and its reliability. *Psychological Medicine*, 9, 525-528.
- The Essendon Breast X-ray Program Collaborative Group. (1992). A mammographic screening pilot project in Victoria 1988-1990. *Medical Journal of Australia*, 157(10): 670-673.
- Thoits, P. A. (1982). Conceptual, methodological, and theoretical problems in studying social support as a buffer against life stress. *Journal of Health & Social Behavior*, 23(2), 145-159.
- Thoits, P. A. (1995). Stress, coping, and social support processes: where are we? What next? *Journal of Health & Social Behavior, Spec*, 53-79.
- Thomas, E., Cade, J., & Vail, A. (1996). Risk factor analysis of data from assessment clinics in the UK breast screening programme: a case-control study in Portsmouth and Southampton. *Journal of Epidemiology and Community Health*, 50, 144-148.
- Thurfjell E. (1994). Population-based mammography screening in clinical practice. Results from the prevalence round in Uppsala county. *Acta Radiologica*, 35(5): 487-491.
- Tobin, D. L., Holroyd, K. A., & Reynolds, V. C. (1984). *User's manual for the coping strategies inventory*. Ohio: Department of Psychology, University of Ohio.
- Todarello, O., La Pesa, M.W., Zaka, S., Martino, V., & Lattanzio, E. (1989). Alexithymia and Breast Cancer: Survey of 200 Women Undergoing Mammography.

Psychotherapy and Psychosomatics, 51(51-55).

- United Kingdom National Case-Control Study Group. (1993). Breast feeding and risk of breast cancer in young women. *British Medical Journal*, 307:17-20.
- Ursin, H., & Olf, M. (1993). Psychobiology of coping and defense strategies. *Neuropsychobiology*, 28(1-2), 66-71.
- van den Brandt, P. A., Goldbohm, R. A., & van' t Veer, P. (1995). Alcohol and Breast Cancer: Results from the Netherlands Cohort Study. *American Journal of Epidemiology*, 141(10), 907-915.
- van der Ploeg, H. M. (1989). *Self-Assessment Questionnaire-Nijmegen*. Lisse, The Netherlands: Swets en Zeitlinger.
- Vogel, V. G. (1996). Assessing Women's Potential Risk of Developing Breast Cancer. *Oncology*, 10(10), 1451-1463.
- Watson, M., & Greer, S. (1983). Development of a questionnaire measure of emotional control. *Journal of Psychosomatic Research*, 27(4), 299-305.
- Watson, M., Pettingale, K. W., & Greer, S. (1984). Emotional control and autonomic arousal in breast cancer patients. *Journal of Psychosomatic Research*, 28(6), 467-474.
- Waxler-Morrison, N., Hislop, T. G., Mears, B., & Kan, L. (1991). Effects of social relationships on survival for women with breast cancer: A prospective study. *Social Science and Medicine*, 33(2), 177-183.
- Weinberger, D. A., Schwartz, G. E., & Davidson, R. J. (1979). Low anxious, high anxious, and repressive coping styles: psychometric patterns and behavioral and physiological responses to stress. *Journal of Abnormal Psychology*, 88, 369-380.
- Weinstein, A. L., Mahoney, M. C., Nasca, P. C., Hanson, R. L., Leske, M. C., & Varma, A. O. (1993). Oestrogen Replacement Therapy and Breast Cancer Risk: A Case-Control Study. *International Journal of Epidemiology*, 22(5), 781-789.
- Wethington, E., Brown, G. W., & Kessler, R. C. (1997). Interview Measures of Stressful Life Events. In S. Cohen & R. C. Kessler (Eds.), *Measuring stress: A guide for health and social scientists* (pp. 59-79). New York: Oxford University Press.
- Wirsching, M., Hoffmann, F., Stierlin, H., Weber, G., & Wirsching, B. (1985). Prebiotic psychological characteristics of breast cancer patients. *Psychotherapy and Psychosomatics*, 43(2), 69-76.
- Yoo, K.-Y., Tajima, K., Kuroishi, T., Hirose, K., Yoshida, M., Miura, S., & Murai, H. (1992). Independent Protective Effect of Lactation against Breast Cancer: A Case-

- Control Study in Japan. *American Journal of Epidemiology*, 135(7), 726-733.
- Zemore, R., & Shepel, L. F. (1989). Effects of breast cancer and mastectomy on emotional support and adjustment. *Social Science and Medicine*, 28(1), 19-27.
- Zigmond, A. S., & Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, 67, 361-370.

Appendix I: Research Information Letter

LIFESTYLE AND BREAST HEALTH

An important issue in women's health today is breast care. Many factors have been implicated in contributing to breast problems, but to date the exact role of these variables is not clearly understood. In recent years there has been increasing recognition of the importance of psychological as well as physical factors in health and illness. This is equally relevant in promoting good health and in the prevention or early detection of health problems.

From 1994 to 1997 a team of researchers from the Royal North Shore Hospital and the University of Sydney will be studying the role of some lifestyle issues including stress, emotional reactions to stress and ways of coping in breast health and disease. The most effective way to achieve this is through the breast screening program. For this, however, your help is also needed.

Firstly, let us assure you that we recognise that this can be a difficult day for some women. At the same time, the importance of research in this vital area of women's health cannot be underestimated.

Your participation in this study will be greatly appreciated; however it must be purely voluntary. You can withdraw from the study at any time and no ongoing commitment is required. The research project has been designed around the normal assessment procedure; thus agreeing to participate will not interfere with your schedule of investigations in any way.

You may be asked by one of two researchers, Melanie Price or Susan Kennedy, to complete a questionnaire. This should take about 25 minutes to complete and can be done while you are here.

Some women may also be asked for a brief interview. Completing the questionnaire will not obligate you to an interview and you will only be approached for this interview if there is time while you are waiting.

The information obtained in this study will remain in the confidence of the researchers. The contribution of your time by participating in this study will prove invaluable in addressing

the particular needs of this area of women's health in the future.

Thank you for taking the time to consider.

Melanie Price and Susan Kennedy

Researchers. Contact phone no.: 9926-7746

Mr Tony Kimber

Patient representative for RNSH. Contact phone no.: 9926-7612

This research is funded by the National Health and Medical Research Council of Australia

Appendix II: Consent Form

ROYAL NORTH SHORE HOSPITAL

CONSENT FORM TO PARTICIPATE IN A RESEARCH PROJECT

I, (Full Name).....
of (Address).....
have been invited to participate in a research project entitled:

LIFESTYLE AND BREAST HEALTH

I am aware that:

1. This project has the approval of the Medical Research Ethics Committee of Royal North Shore Hospital.
2. This project aims to assess the role of lifestyle factors in breast health and disease.
3. The results of my involvement may not be of direct benefit to myself or my management.
4. My participation in the study will involve completing a questionnaire and possibly an interview.
5. The researchers will have access to my test results.
6. The only adverse effect or risk related to the project is the donation of time to fill in questionnaires and possibly participate in an interview.
7. I can cease my involvement any time I wish.
8. Should I develop any problem which may be related to this area of research, I am aware that I can contact the researchers for reassurance, Melanie Price or Susan Kennedy, phone 9926-7746.
9. Should I have any queries about the way this study is conducted, I am aware I can contact an independent person, Mr Tony Kimber, who is the patient representative within the hospital, phone 9926-7612.
10. I can refuse to take part in the project and it will have no effect on my assessment procedure.
11. The participation in this project involves no financial cost to me.
12. The information I disclose in this research will be kept confidential so as in no way reveal my identity.

After considering the above, I agree to participate in this project.

SIGNATURE.....

WITNESS.....

Date.....

Date

Appendix III: Demographic and Somatic Risk Factor Questionnaire

1. Age: _____

1a. Date of Birth: ___/___/19___

2. Country of Birth: _____

3. Marital Status (tick one of the following)

- married
- living as married
- single / never married
- widowed
- divorced
- divorced / remarried
- separated

4. Present Occupational Status (please tick one of the following)

- Home employment: Full time
- Full time income earning employment
- Part time income earning employment
- Seeking income earning employment
- Retired

If employed, what is your present occupation? _____

If retired or unemployed, what was your usual occupation? _____

5. Education (please tick one of the following)

- Completed primary school
- Completed 3 or 4 years of secondary school
- Completed 5 or 6 years of secondary school
- Completed Diploma or Professional Certificate
- Completed Degree at College or University

6. Husbands'/Partners' Occupational Status

- Not applicable
- Home employment: Full time
- Full time income earning employment
- Part time income earning employment
- Seeking income earning employment
- Retired

If employed, what is his present occupation? _____

If retired or unemployed, what was his usual occupation? _____

7. Have you ever been told by a doctor that you have: (circle yes or no)

- Asthma, eczema or hay fever? Yes / No
- Diabetes? Yes / No
- Heart Disease? Yes / No
- Arthritis? Yes / No
- Cancer, tumour or leukaemia? Yes / No

Please answer the following questions by CIRCLING yes or no or circling the correct age group.

1. Have you had a hysterectomy? Yes / No

IF YES, what age were you? (circle one of the following age groups)

under 25 / 25-30 / 31-35 / 36-40 / 41-45 / 46-50 / over 50

2. Have you had an ovary surgically removed? Yes / No / Unsure

IF YES, what age were you?

under 25 / 25-30 / 31-35 / 36-40 / 41-45 / 46-50 / over 50

3. Are you currently taking Hormone Replacement Therapy? Yes / No

IF YES, what age were you when you started?

under 35 / 36-40 / 41-45 / 46-50 / over 50

3b. What age did you stop menstruating?

Still menstruating / under 35 / 36-40 / 41-45 / 46-50 / over 50

4. Have you ever been pregnant? Yes / No

IF YES: (a) How many full term pregnancies have you had? _____

(b) How old were you when your first child was born? _____

(c) How many incomplete pregnancies have you had? (include miscarriages, ectopic pregnancies, induced terminations) _____

5. Have you ever breastfed? Yes / No

IF YES, please state approximately how long for each child

(e.g. 1st-3mths, 2nd-No, 3rd-9mths)

6. Have you ever taken drugs for infertility? Yes / No

IF YES, what age were you when you started?

under 25 / 25-30 / 31-35 / 36-40 / over 41

How many years in total did you take drugs for infertility?

under 1 / 1-3 / 4-6 / 7-10 / over 10

7. Have you ever taken birth control pills? Yes / No

IF YES, what age did you start?

under 25 / 25-30 / 31-35 / 36-40 / 41-45 / over 46

How many years in total did you take birth control pills?

under 1 / 1-3 / 4-6 / 7-10 / over 10

8. Have you ever had a lump removed from your breast that was not breast cancer?

Yes / No

IF YES, in which breast? Right / Left / Both

How long ago was this? _____

In your own words, what was the diagnosis? _____

9. Have you ever smoked cigarettes? Yes / No

IF YES, have you ever smoked regularly? Yes / No

IF YES,

how many years have you/did you smoke regularly? _____

how many cigarettes on average do you/did you smoke per day? _____

10. Do you drink alcohol? Yes / No

IF YES, do you drink alcohol: every day / every week / less than once a week

How many glasses of alcohol would you regularly have a week?

under 5 / 5-10 / 11-15 / 16-20 / 21-25 / over 25

11. How tall are you? _____ (feet and inches are fine)

12. What is your weight? _____ (stone and pounds are also fine)

13. Is there a family history of breast cancer among your first degree relatives (i.e. your mother, sister, daughter)? Yes / No / Unknown

IF YES, please tick who: Mother ___ Sister ___ Daughter ___

Were any of them diagnosed before age 50? Yes / No / Unknown

Did any relative have cancer in both breasts? Yes / No / Unknown

Appendix IV: Defense Style Questionnaire

Below are a number of statements about PERSONAL ATTITUDES. Please read each of these statements and circle a number on the 9 point scale to indicate how much you agree or disagree with them. For example, 5 indicates that you neither agree nor disagree, 3 indicates that you moderately disagree and 9 indicates that you strongly agree.

- | | Strongly
Disagree | Strongly
Agree |
|--|----------------------|-------------------|
| I get satisfaction from helping others and if this were taken away from me I would get depressed | 1 | 2 3 4 5 6 7 8 9 |
| I'm able to keep a problem out of my mind until I have time to deal with it | 1 | 2 3 4 5 6 7 8 9 |
| 3. I work out my anxiety through doing something constructive like painting | 1 | 2 3 4 5 6 7 8 9 |
| 4. I am able to find good reasons for everything I do | 1 | 2 3 4 5 6 7 8 9 |
| 5. I'm able to laugh at myself pretty easily | 1 | 2 3 4 5 6 7 8 9 |
| 6. People tend to mistreat me | 1 | 2 3 4 5 6 7 8 9 |
| 7. If someone mugged me and stole my money, I'd rather he be helped than punished | 1 | 2 3 4 5 6 7 8 9 |
| 8. People say I tend to ignore unpleasant facts as if they didn't exist | 1 | 2 3 4 5 6 7 8 9 |
| 9. I ignore danger as if I was Superman | 1 | 2 3 4 5 6 7 8 9 |
| 10. I pride myself on my ability to cut people down to size | 1 | 2 3 4 5 6 7 8 9 |
| 11. I often act impulsively when something is bothering me | 1 | 2 3 4 5 6 7 8 9 |
| 12. I get physically ill when things aren't going well | 1 | 2 3 4 5 6 7 8 9 |
| 13. I'm a very inhibited person | 1 | 2 3 4 5 6 7 8 9 |

- | | Strongly
Disagree | Strongly
Agree |
|---|----------------------|-------------------|
| 14. I get more satisfaction from my fantasies than from my real life | 1 | 9 |
| 15. I've special talents that allow me to go through life with no problems | 1 | 9 |
| 16. There are always good reasons when things don't work out for me | 1 | 9 |
| 17. I work more things out in my daydreams than in my real life | 1 | 9 |
| 18. I fear nothing | 1 | 9 |
| 19. Sometimes I think I'm an angel and other times I think I'm the devil | 1 | 9 |
| 20. I get openly aggressive when I feel hurt | 1 | 9 |
| 21. I always feel that someone I know is like a guardian angel | 1 | 9 |
| 22. As far as I'm concerned, people are either good or bad | 1 | 9 |
| 23. If my boss bugged me, I might make a mistake in my work, or work more slowly to get back at him | 1 | 9 |
| 24. There is someone I know who can do anything and is absolutely fair and just | 1 | 9 |
| 25. I can keep a lid on my feelings if letting them out would interfere with what I am doing | 1 | 9 |
| 26. I'm usually able to see the funny side of an other wise painful predicament | 1 | 9 |
| 27. I get a headache when I have to do something I don't like | 1 | 9 |
| 28. I often find myself being very nice to people who by all rights I should be angry at | 1 | 9 |

	Strongly Disagree	Strongly Agree
29. I am sure I get a raw deal from life	1_2_3_4_5_6_7_8_9	
30. When I have to face a difficult situation I try to imagine what it will be like and plan ways to cope with it	1_2_3_4_5_6_7_8_9	
31. Doctors never really understand what is wrong with me	1_2_3_4_5_6_7_8_9	
32. After I fight for my rights, I tend to apologise for my assertiveness	1_2_3_4_5_6_7_8_9	
33. When I'm depressed or anxious, eating makes me feel better	1_2_3_4_5_6_7_8_9	
34. I'm often told that I don't show my feelings	1_2_3_4_5_6_7_8_9	
35. If I can predict that I'm going to be sad ahead of time, I can cope better	1_2_3_4_5_6_7_8_9	
36. No matter how much I complain, I never get a satisfactory response	1_2_3_4_5_6_7_8_9	
37. Often I find that I don't feel anything when the situation would seem to warrant strong emotions	1_2_3_4_5_6_7_8_9	
38. Sticking to the task at hand keeps me from feeling depressed or anxious	1_2_3_4_5_6_7_8_9	
39. If I were in a crisis, I would seek out another person who had the same problem	1_2_3_4_5_6_7_8_9	
40. If I have an aggressive thought, I feel the need to do something to compensate for it	1_2_3_4_5_6_7_8_9	

Appendix V: Locus of Control of Behaviour

Below are a number of statements about how various topics affect your PERSONAL BELIEFS. There are no right or wrong answers. Using the scale shown below, please indicate how much you agree or disagree by circling the scale beside each statement.

Strongly Disagree	Generally Disagree	Somewhat Disagree	Somewhat Agree	Generally Agree	Strongly Agree
0	1	2	3	4	5

- | | |
|--|------------------|
| 1. I can anticipate difficulties and take action to avoid them | 0__1__2__3__4__5 |
| 2. A great deal of what happens to me is probably just a matter of luck | 0__1__2__3__4__5 |
| 3. Everyone knows that luck or chance determines one's future | 0__1__2__3__4__5 |
| 4. I can control my problems only if I have outside support | 0__1__2__3__4__5 |
| 5. When I make plans, I am almost certain I can make them work | 0__1__2__3__4__5 |
| 6. My problem(s) will dominate me all my life | 0__1__2__3__4__5 |
| 7. My mistakes and problems are my responsibility to deal with | 0__1__2__3__4__5 |
| 8. Becoming a success is a matter of hard work, luck has little or nothing to do with it | 0__1__2__3__4__5 |
| 9. My life is controlled by outside actions and events | 0__1__2__3__4__5 |
| 10. People are victims of circumstances beyond their control | 0__1__2__3__4__5 |
| 11. To continually manage my problems I need professional help | 0__1__2__3__4__5 |
| 12. I believe a person can truly be the master of their fate | 0__1__2__3__4__5 |
| 13. I am confident of being able to deal successfully with future problems | 0__1__2__3__4__5 |
| 14. Maintaining control over my problem(s) is due mostly to luck | 0__1__2__3__4__5 |

Appendix VI: Self Esteem

Please circle the number corresponding to the statement best fitting how the following statements relate to you.

	Strongly Agree 1	Agree 2	Disagree 3	Strongly Disagree 4
1. I feel that I'm a person of worth, at least on an equal basis with others	1	2	3	4
2. I feel that I have a number of good qualities			1	2 3 4
3. All in all, I'm inclined to feel that I am a failure			1	2 3 4
4. I am able to do things as well as other people			1	2 3 4
5. I feel I do not have much to be proud of.			1	2 3 4
6. I take a positive attitude toward myself			1	2 3 4
7. On the whole, I am satisfied with myself			1	2 3 4
8. I wish I could have more respect for myself			1	2 3 4
9. I certainly feel useless at times			1	2 3 4
10. At times I think I am no good at all			1	2 3 4

Appendix VII: Emotional Expression and Control

The following statements describe the reactions people have to certain feelings and emotions. Read through each one and indicate how far it describes the way you generally react by circling a number on the scale.

	Almost Never 1	Sometimes 2	Often 3	Almost Always 4
1. When I feel unhappy or miserable, I keep quiet.	1	2	3	4
2. When I feel angry or very annoyed, I control my behaviour.	1	2	3	4
3. When afraid or worried, I keep quiet.	1	2	3	4
4. When I feel unhappy or miserable, I control my behaviour.	1	2	3	4
5. When I feel angry or annoyed, I keep quiet.	1	2	3	4
6. When I feel afraid or worried, I control my behaviour.	1	2	3	4
7. When I feel unhappy or miserable, I say what I feel.	1	2	3	4
8. When I feel, afraid or worried, I let others see how I feel.	1	2	3	4
9. When afraid or worried, I say what I feel.	1	2	3	4
10. When I feel angry or very annoyed, I let others see how I feel.	1	2	3	4
11. When I feel unhappy or miserable, I let others see how I feel.	1	2	3	4
12. When I feel angry or very annoyed, I say what I feel.	1	2	3	4
13. When I feel afraid or worried, I hide my worries.	1	2	3	4
14. When I feel unhappy or miserable, I hide my unhappiness.	1	2	3	4
15. When I feel angry or very annoyed, I hide my annoyance.	1	2	3	4
16. When I feel unhappy or miserable, I smother my feelings.	1	2	3	4
17. When I feel afraid or worried, I smother my feelings.	1	2	3	4
18. When I feel angry or very annoyed, I smother my feelings.	1	2	3	4

Appendix VIII: Trait Anxiety

Below are a number of statements people have used to describe themselves. Please read each of the statements and circle the number which corresponds to how you **GENERALLY FEEL**. Do not spend too much time on each question. Your first response will be the most accurate.

Almost Never	Sometimes	Often	Almost Always
1	2	3	4
1. I am a steady person			1__2__3__4
2. I feel satisfied with myself			1__2__3__4
3. I feel nervous and restless			1__2__3__4
4. I wish I could be as happy as others seem to be			1__2__3__4
5. I feel like a failure			1__2__3__4
6. I get in a state of tension or turmoil as I think over my recent concerns and interests			1__2__3__4
7. I feel secure			1__2__3__4
8. I lack self-confidence			1__2__3__4
9. I feel inadequate			1__2__3__4
10. I worry too much over something that really does not matter			1__2__3__4

Appendix IX: Hospital Anxiety and Depression

Please read each of the following items and circle the ONE reply that closest resembles how you have been feeling IN THE LAST WEEK. Work quickly and do not spend too much time on each item.

1. I feel tense or 'wound up':

- (1) Most of the time
- (2) A lot of the time
- (3) Time to time, Occasionally
- (4) Not at all

2. I still enjoy the things I used to enjoy:

- (1) Definitely as much
- (2) Not quite so much
- (3) Only a little
- (4) Hardly at all

3. I get a sort of frightened feeling as if something awful is about to happen:

- (1) Very definitely and quite badly
- (2) Yes, but not too badly
- (3) A little, but it doesn't worry me
- (4) Not at all

4. I can laugh and see the funny side of move:

- (1) As much as I always could
- (2) Not quite so much now
- (3) Definitely not so much now
- (4) Not at all

8. I feel as if I am slowed down:

- (1) Nearly all the time
- (2) Very often
- (3) Sometimes
- (4) Not at all

9. I get a sort of frightened feeling like 'butterflies' in the stomach:

- (1) Not at all
- (2) Occasionally
- (3) Quite often
- (4) Very often

10. I have lost interest in my appearance:

- (1) Definitely
- (2) I don't take so much care as I should
- (3) I may not take quite s much care
- (4) I take just as much as ever

11. I feel restless as if I have to be on the things:

- (1) Very much indeed
- (2) Quite a lot
- (3) Not very much
- (4) Not at all

5. Worrying thoughts go through my mind:

- (1) A great deal of the time
- (2) A lot of the time
- (3) From time to time but not too often
- (4) Only occasionally

6. I feel cheerful:

- (1) Not at all
- (2) Not often
- (3) Sometimes
- (4) Most of the time

7. I can sit at ease and feel relaxed:

- (1) Definitely
- (2) Usually
- (3) Not often
- (4) Not at all

12. I look forward with enjoyment to things:

- (1) As much as I ever did
- (2) Rather less than I used to
- (3) Definitely less than I used to
- (4) Hardly at all

13. I get sudden feelings of panic:

- (1) Very often indeed
- (2) Quite often
- (3) Not very often
- (4) Not at all

14. I can enjoy a good book or radio or TV programme:

- (1) Often
- (2) Sometimes
- (3) Not often
- (4) Very seldom

Appendix X: Life Events and Difficulties Schedule

DEMOGRAPHY

Age, marriage, past divorce or widowhood, children, stepchildren, grandchildren, who lives in the same house, do you work, retired, unemployed?

A. HEALTH AND ILLNESS

Have you had any serious illnesses or operations in your life?

What were these?

When was this?

Any ongoing problems or treatment?

Has anyone in your family been ill or hurt recently?

Spouse?

Children?

Parents or grandchildren?

How serious was this?

Was anyone out of work because of this?

What happened?

Has anyone (family or close friend) been admitted to hospital in the last two years?

For what reason? Routine or emergency?

How long in hospital?

What changes did this involve for you?

How are they now?

Does anyone in the family have any long-standing health problems?

Anything that interfere with their daily activities?

How does this affect you?

Is any relative or close friend a worry to you?

Because of: old age/incapacity

physical/mental handicap

behaviour problems

Has there been any accidents? e.g. road accidents, accidents to children etc

Has there been any pregnancies or births in the family?

Was it planned?

Anyone lost a baby? (miscarriage, stillbirth, abortion)

B. DEATHS

Are your mother and father still alive?

How long ago?

How did this affect you?

Did you ever have any children who died?

When was this?

How did this affect you?

Have any relatives or other people you were involved with die in the two years?

Were you present?

Did you expect it?

How did you find out?

What led up to the death?

Were you involved in any way?

C. ROLE CHANGES, INTERACTION CHANGES/FRIENDS

Has anyone in the family been married in the last 2 years?

Children, brothers or sisters, close friend?

How were you involved?

Has anyone become engaged?

When was it decided?

How involved were you?

Has anyone separated or divorced?

When?

Were you involved?

Did you expect it?

Has anyone started school, college or university?

How did you feel about this?

Has anyone taken important exams or tests or received exam results?

Have you made any new friendships?

Have you lost contact with someone close?

Has anyone left home?

Have any close friends moved away?

D. CRISES, NEWS, FORECASTS

Have there been any crises or emergencies?

Self, family, friends?

Any particular worries with the children?

What about burglaries or fires?

Any pets lost unexpectedly?

Any relative had an emergency you helped with?

Have you had any particularly good or bad news at all?

Have you had to break bad news to someone else?

Have you had any news about something which is going to happen in the future?

Have you learnt anything unexpected about someone you thought you knew well - something that has changed your ideas about them?

Do you feel you have had any other kind of disappointment in the last 2 years?

Have other pleasant things happened to you?

E. HOUSING

What type of accommodation do you have?

(house, unit etc.)

How long have you lived in your present housing?

(if moved was this positive, negative or neutral)

Do you like living where you are?

Why? Why not?

What about the area?

Are there any structural problems with yours housing?

Any big building/renovation costs?

Do you have any problems with the rent, landlord or neighbours?

F. FINANCES

Have you had any money worries in the last 2 years?

Difficulties in meeting commitments, rent, low wages, lack of work?

Over the last 2 years have you received any social benefits at all?

Family allowance, dole, sickness benefits, pension benefits?

How did you feel about this?

G. EMPLOYMENT

You said you worked as a

What jobs did you have before?

Have there been any periods of unemployment in the last 2 years?

What happened? Why were you unemployed?

How long were you off work?

Do you enjoy your job?

What are the conditions like (hours, demands etc.)

What are your work-mates like?

Is the job interesting?

Do you think you will stay in your job?

Have you had any promotion/demotion in the last 2 years? A change in hours or responsibilities?

Have you ever had any major difficulties with work?

such as redundancy, dismissal

Tell me about this?

Have you ever been employed?

How did you go with that?

Does your spouse work? Has he ever had time off through sickness or lack of work?

Has he any troubles with work?

H. MARITAL/RELATIONSHIPS

Have you ever been separated or divorced?

When was that? For how long?

how did that affect you?

IF NOT MARRIED

Do you have a steady relationship at present? When did you meet?

IF YES

Have there been any changes in the relationship in the last 2 years?

Increase in arguments? How severe?

Any affairs - self or partner?

Reconciliation?

How did your family/friends react?

IF NO

Have you broken off a relationship in the last 2 years?

How long had it been going on?

Did the break upset you?

I. MISCELLANEOUS

Have you had any especially nice things happen?

a holiday? a child returning home? good news?

Has anything turned out better than you expected?

At work?

A child doing well at school?

Financial windfall?

Has anything else given you pleasure?

New furniture/clothes/car?

Someone thanking you or praising you for something?

Looking over your life, would you say there is anything you wish had turned out differently?

Do you have any regrets or disappointment?

Has anything given you special fulfillment or satisfaction?

Is there anything of importance that we may have overlooked or you wish to include about your life events or things that have happened in the last 2 years?

Appendix XI: Examples of Life Events

Examples of events rated as extremely threatening

Death of a spouse or child

Marital breakdown

Life threatening illness, such as heart attack or injuries from an accident for self, spouse or child.

Examples of events rated as severely threatening

Death of an elderly parent living in the same house

Diagnosis of a life threatening illness, or injury, to a friend, or family member not living with the subject (this may vary according to the closeness of the relationship).

Examples of events rated as highly threatening

Death of a parent-in-law with whom the subject has regular contact but lives separately

Diagnosis of a major illness or injury that is not immediately life threatening but has ongoing implications occurring to a friend or family member not living with the subject (again this may vary according to the closeness of the relationship).

Appendix XII: Interview Schedule for Social Interaction

1. Intimate Support. What is your partner like as a support in times of stress?

Can you talk about things that upset you?

Is s/he a good listener?

Can you give me an example?

What about the more practical things?

Example? (if can't think of one, ask about an event for the interview)

What if anything interferes with them being a good support person for you?

2. Non-Intimate Support.

Who else can you turn to in times of need for emotional and more practical support?

Is s/he a good listener?

Can you give me any example?

3. How would you rate your overall support system? (good, adequate or poor?)

4. Has this changed in the past two years? (better, worse, no change?)

Why?

Appendix XIII: Predictors of breast cancer in women recalled following screening

Aust. N.Z. J. Surg. (1999) 69, 639-646

ORIGINAL ARTICLE

PREDICTORS OF BREAST CANCER IN WOMEN RECALLED FOLLOWING SCREENING

MELANIE A. PRICE,* CHRISTOPHER C. TENNANT,* ROSS C. SMITH,† SUSAN J. KENNEDY,* PHYLLIS N. BUTOW,* MARJORIE B. KOSSOFF‡ AND STEWART M. DUNN*

*Departments of *Psychological Medicine and †Surgery, University of Sydney at Royal North Shore Hospital and ‡Northern Sydney and Lower Central Coast BreastScreen, New South Wales, Australia*

Background: Established risk factors are associated with between 25 and 56% of breast cancer cases, but the relative importance and relevance to different age groups is unclear.

Methods: This case-control study examines established risk factors in 298 women with breast cancer and 1926 women without breast cancer aged 40-87 who were recalled for assessment following routine mammography.

Results: The cancer group were significantly older than the non-cancer group ($F_{1,227} = 107.6$; $P < 0.0001$). Postmenopausal obesity increased the odds of developing breast cancer (OR: 2.35; CI: 1.33-4.16). The breast cancer group were more likely to have used oral contraceptives (OR: 1.50; CI: 1.09-2.05), and women who used contraceptives for more than 10 years in total were at the highest risk (OR: 1.73; CI: 1.13-2.65). Daily consumption of alcohol was also associated with increased risk of developing breast cancer (OR: 1.62; CI: 1.13-2.33). Reproductive factors and a family history of breast cancer did not affect the odds of developing breast cancer and the reasons for these findings are explored.

Conclusions: Results suggest that the effects of weight reduction in reducing postmenopausal breast cancer risk should be assessed.

Key words: alcohol consumption, breast neoplasms, obesity, oral contraceptive, risk factors.

INTRODUCTION

Breast cancer is the most common cancer in women in developed countries, with an estimated 790 000 cases worldwide in 1990 and approximately 1 million new cases currently diagnosed each year.¹ Hormonal factors are generally considered to play an aetiological role in breast cancer because of consistent association between reproductive factors and breast cancer.² Established risk factors for breast cancer include increasing age, older age at first birth, older age at menopause, nulliparity and high parity, family history and history of benign breast disease.²⁻⁵ Exogenous hormone therapy such as oral contraceptives and hormone replacement therapy (HRT) increase breast cancer risk, although the risk diminishes with time.^{6,7} Evidence is increasing for a modest positive association between alcohol intake and breast cancer, although a causal relationship has not been established.⁸⁻¹² Obesity is considered to be a risk factor for breast cancer in postmenopausal women, but it is protective in pre-menopausal women, although results are not universally consistent.¹³⁻¹⁷ Long periods of lactation have been reported as being protective against breast cancer, especially in pre-menopausal women.^{18,19}

Consensus on the relative importance of individual risk factors, the magnitude of each, and their relevance to different age groups, is rare. Opinion also varies as to how well-established risk factors explain the incidence of breast cancer. Madigan *et al.* estimate that 41% of US breast cancer cases can be explained by

later first birth, nulliparity, family history and higher socioeconomic status.⁵ Tavani *et al.* estimate that higher education, older age at first birth, nulliparity, older age at menopause, HRT and family history can account for 56% of cases in Italy.²⁰ However, the American Cancer Society claims that recognized risk factors can account for as little as 25% of breast cancer cases.³

Routine breast screening provides a unique opportunity to prospectively examine risk factors for the development of breast cancer in asymptomatic women at risk of breast cancer primarily because of their age. The present case-control study investigates 'established' risk factors for breast cancer in a cohort of older Australian women recalled for assessment following routine mammography.

METHODS

The National Breast Screening Programme commenced in Australia in 1993, actively recruiting women aged 50-69 for screening mammography from electoral rolls. Free mammograms, however, are available to all women over age 40. Women recalled for assessment to Northern Sydney and Lower Central Coast BreastScreen from April 1994 to April 1997 were invited to participate in research examining the role of psychosocial, demographic and somatic factors in breast cancer. Ethical approval was granted by the Royal North Shore Hospital Medical Research Ethics Committee. Screening rounds one and two were in progress during the period of the present study. On arrival at the clinic, informed consent was sought, and consenting women completed a self-administered questionnaire while waiting for assessment. The questionnaire included items on demographics, reproductive history, hormonal variables, and several psychological questionnaires (psychosocial data will be reported separately).

Correspondence: M. Price, Psychological Medicine, Level 5/Block 4, Royal North Shore Hospital, St Leonards, NSW 2065, Australia.
Email: <melaniep@mail.med.usyd.edu.au>

Accepted for publication 8 April 1999.

Logistic regression analysis was used to distinguish between women with and without breast cancer for individual risk factors. Age was included as a confounder in all analyses. Where indicated, other confounders were also included in analysis, all variables being entered simultaneously. Analyses were performed using SPSS for windows (SPSS Inc., version 6.1.3).

RESULTS

A total of 2989 women were invited to participate in the present study. The exclusion criteria were: prior personal history of breast cancer ($n = 39$); non-English speaking ($n = 93$); and physical or psychiatric impairment preventing completion of the questionnaire ($n = 34$). One woman diagnosed with lymphoma and one woman whose final diagnosis was outstanding were excluded from analysis. A total of 13% declined participation and 8% had incomplete questionnaires, resulting in a total of 2224 (79%) questionnaires used in the final analysis. The final sample consisted of 298 (13%) breast cancer cases and 1926 (87%) controls, including those who had no abnormality detected and those diagnosed with cysts or benign breast disease.

Demographic variables are summarized in Table 1. The age of the present cohort ranged from 40 to 87 years, with a mean age of 56.1 years. The cancer group was significantly older than the non-cancer group, having a mean age of 61.2 years (standard error (SE) ± 0.55) and 55.3 years (SE ± 0.21), respectively ($F_{1,222} = 107.6$; $P < 0.0001$). A total of 15% of the cancer group were widowed compared to 8% of the non-cancer group; the difference was non-significant after controlling for age. We found a trend of increasing level of education and increasing risk of breast cancer, albeit non-significant. The cancer group were more likely to be retired than in current employment, an effect attenuating with age, and there were no differences in type of work undertaken, past or present.

Seventy-two per cent of our cohort were Australian born. Women born outside of Australia were born in 62 different countries, making individual comparison impossible. Instead, non-Australian-born women were allocated to an incidence group based on the relative incidence of breast cancer in women born in their country compared to that of Australian-born women (lower, equivalent, higher, unknown). The relative incidence for each country was estimated from a tabulation of breast cancer cases by country of birth undertaken in New South

Table 1. Distribution of demographic variables for cancer and non-cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

	Cancer ($n = 298$) ^a n (%)	Non-cancer ($n = 1926$) ^a n (%)	Odds ratio (95% CI) age adjusted
Current marital status			$P = 0.92$
Married/de facto	202 (68.9)	1426 (74.5)	1.00
Single/never married	17 (5.8)	112 (5.9)	0.87 (0.50, 1.50)
Widowed	44 (15.0)	149 (7.8)	1.07 (0.71, 1.60)
Divorced	30 (10.2)	226 (11.8)	0.95 (0.63, 1.44)
Level of education			$P = 0.24$
Primary	10 (3.4)	70 (3.7)	1.00
3-4 years secondary	112 (38.1)	717 (37.6)	1.60 (0.78, 3.25)
5-6 years secondary	51 (17.3)	293 (15.4)	1.83 (0.87, 3.88)
Diploma/certificate	72 (24.5)	460 (24.1)	2.07 (0.99, 4.31)
University/college	49 (16.7)	368 (19.3)	2.02 (0.94, 4.31)
Current occupational status			$P = 0.48$
Home employment	64 (21.8)	384 (20.1)	1.00
Full time work	69 (23.5)	567 (29.7)	1.14 (0.77, 1.69)
Part time work	50 (17.0)	489 (25.6)	0.92 (0.61, 1.39)
Seeking work/pension	3 (1.0)	44 (2.3)	0.45 (0.13, 1.54)
Retired	108 (36.7)	428 (22.4)	0.89 (0.62, 1.28)
Type of work (past/present) ^b			$P = 0.89$
Professional	5 (2.2)	41 (2.7)	1.00
Manager/small business	17 (7.6)	151 (10.1)	0.98 (0.34, 2.88)
Trade	81 (36.2)	538 (36.1)	1.21 (0.46, 3.23)
Clerical	78 (34.8)	461 (30.9)	1.17 (0.44, 3.12)
Semi-skilled/unskilled	43 (19.2)	300 (20.1)	1.02 (0.37, 2.78)
Country of birth ^c			$P = 0.19$
Australia	222 (74.7)	1372 (71.3)	1.00
Incidence < Australia ^d	2 (0.7)	34 (1.8)	0.44 (0.10, 1.85)
Incidence ~ Australia ^e	57 (19.2)	427 (22.2)	0.89 (0.64, 1.22)
Incidence > Australia ^f	9 (3.0)	65 (3.4)	1.05 (0.50, 2.17)
Incidence unknown cf. Australia ^g	7 (2.4)	27 (1.4)	2.44 (1.03, 5.82)

^aNumbers for each variable do not add up to total due to missing values. ^bPaid employment only. ^cIncidence rates by country of birth estimated from breast cancer cases in NSW during 1987-1992. ^dIncidence rates for breast cancer lower than Australian-born women in women born in China, Estonia, Greece, Italy, Malta, Taiwan, Ukraine, Vietnam, Wales, Yugoslavia. ^eIncidence rates for breast cancer equivalent to Australian-born women in women born in Austria, Bulgaria, Canada, Cyprus, Czechoslovakia, Denmark, Egypt, England, Finland, France, Germany, Hong Kong, Hungary, India, Indonesia, Iran, Iraq, Ireland, Israel, Lebanon, Netherlands, Norway, Philippines, Poland, Portugal, Romania, Scotland, South Africa, Spain, Sri Lanka, Sweden, Switzerland, Syria, Turkey, USA. ^fIncidence rates for breast cancer higher than Australian-born women in women born in Malaysia, New Zealand, Singapore, USSR. ^gIncidence rates for breast cancer unknown compared to Australian-born women in women born in Bolivia, Chile, Fiji, Japan, Kenya, Macau, Mauritius, Namibia, Papua New Guinea, Peru, Tanzania, Thailand, Tonga, Zimbabwe.

Wales during 1987-92.²¹ Most non-Australian-born women were born in countries with a similar incidence of breast cancer to Australia. No differences in risk of breast cancer were seen in non-Australian-born women compared to Australian-born women (Table 1).

Maintaining consistency with the screening programme, our definition of family history was restricted to women who had a mother, sister or daughter with breast cancer (Table 2). A total of 18% of the cancer group and 14% of the non-cancer group reported a positive family history. The odds ratio (OR) for developing breast cancer with a positive maternal history was 1.18 (95% confidence interval (CI): 0.73-1.92) and 1.03 (CI: 0.62-1.77) for a sister with breast cancer. Sixteen women reported both mother and a sister with breast cancer and the odds ratio for breast cancer with this family history was non-significant (OR: 1.51; CI: 0.41-5.57). Only nine women

reported a daughter with breast cancer; the odds for developing breast cancer in this instance were 3.76 (CI: 0.86-16.4).

There was a non-significant but increasing trend between age at first birth and risk of breast cancer (Table 2). Compared to nulliparous women, those with their first birth under age 20 were less at risk of breast cancer while those with a first birth at ≥ 30 years were at increased breast cancer risk. There were no group differences in parity, incomplete pregnancies, history of lactation or history of benign breast disease.

Women currently menstruating were classified as pre-menopausal. Women with a history of a hysterectomy were considered pre-menopausal if currently aged < 50 years (3%) and postmenopausal if currently aged ≥ 50 years (21.5%). Women with missing responses were also classified as pre-menopausal if they were < 50 years (1.3%) and postmenopausal if aged ≥ 50 years (3.6%). The cancer group were more likely to be

Table 2. Distribution of family history of breast cancer and reproductive variables for cancer and non-cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n = 298) ^a n (%)	Non-cancer (n = 1926) ^a n (%)	Odds ratio (95% CI) adjusted for age	Odds ratio 95% CI multivariate adjusted
Family history of breast cancer				
None	231 (77.5)	1579 (82.0)	1.00	1.00
Mother (father)	25 (8.4)	158 (8.2)	1.25 (0.79, 1.97)	1.18 (0.73, 1.92)
Sister	19 (6.4)	93 (4.8)	1.03 (0.61, 1.75)	1.03 (0.62, 1.77)
Daughter	5 (1.7)	4 (0.2)	3.97 (1.00, 15.7)	3.76 (0.86, 16.40)
Mother and sister	3 (1.0)	13 (0.7)	1.55 (0.42, 5.70)	1.51 (0.41, 5.57)
Unknown	15 (5.0)	78 (4.1)	1.11 (0.62, 2.00)	1.29 (0.71, 2.34)
History of benign breast disease				
No	231 (81.1)	1581 (83.8)	1.00	1.00
Yes	54 (18.9)	305 (16.2)	1.11 (0.80, 1.53)	1.12 (0.80, 1.57)
Age at first child				
Nulliparous	36 (12.9)	260 (14.0)	1.00	1.00
< 20 years	8 (2.9)	88 (4.7)	0.81 (0.36, 1.85)	0.95 (0.41, 2.18)
20-24 years	75 (27.0)	540 (29.0)	1.00 (0.65, 1.56)	1.06 (0.67, 1.67)
25-29 years	101 (36.3)	632 (34.0)	1.20 (0.67, 1.55)	1.25 (0.80, 1.95)
≥ 30 years	58 (20.9)	340 (18.3)	1.35 (0.65, 1.63)	1.45 (0.87, 2.42)
No. full pregnancies				
None	36 (12.8)	264 (14.1)	1.00	1.00
1-2	132 (46.8)	913 (48.6)	1.20 (0.80, 1.80)	1.40 (0.87, 2.23)
≥ 3	114 (40.4)	701 (37.3)	1.16 (0.77, 1.76)	1.45 (0.87, 2.42)
No. incomplete pregnancies				
None	161 (57.9)	1074 (57.7)	1.00	1.00
1	76 (27.3)	453 (24.3)	1.22 (0.90, 1.65)	1.25 (0.92, 1.71)
2	23 (8.3)	194 (10.4)	0.94 (0.58, 1.51)	0.95 (0.59, 1.54)
≥ 3	18 (6.5)	140 (7.5)	1.02 (0.60, 1.74)	1.03 (0.60, 1.76)
Lifetime lactation				
None	69 (25.7)	492 (27.0)	1.00	1.00
1-6 months	63 (23.5)	442 (24.3)	1.12 (0.77, 1.64)	1.09 (0.67, 1.75)
7-36 months	129 (48.1)	839 (46.0)	1.06 (0.77, 1.46)	1.03 (0.66, 1.61)
> 36 months	7 (2.6)	49 (2.7)	1.48 (0.63, 3.49)	1.39 (0.55, 3.51)
Menopausal status				
Pre-menopausal	37 (12.4)	631 (32.8)	1.00	1.00
Postmenopausal	261 (87.6)	1395 (67.2)	1.59 (1.03, 2.44)	1.61 (1.00, 2.59)
Age at menopause^b				
< 35 years	1 (0.6)	8 (1.0)	0.41 (0.05, 3.40)	—
36-40 years	9 (5.2)	30 (3.6)	1.30 (0.57, 2.95)	—
41-45 years	22 (12.8)	132 (16.0)	0.73 (0.43, 1.25)	—
46-50 years	75 (43.6)	340 (41.2)	1.11 (0.77, 1.61)	—
> 50 years	65 (38.2)	315 (38.2)	1.00	—

^aNumbers do not add up to total due to missing values. ^bKnown age of menopause only. ^cAge, age at first birth, parity, menopausal status. ^dAge, age at first birth, parity, family history, menopausal status. ^eAge, age at first child, parity, menopausal status, family history, education. ^fAge, age at first child, parity, body mass index.

postmenopausal than the non-cancer group, with an odds ratio of 1.61 (CI: 1.00–2.59) adjusted for age, age at first child, parity and body mass index (Table 2). In women who had a known age at menopause, we found no differences between women with

cancer and the non-cancer controls. Both groups were also similar in the current use of HRT (Table 3).

A total of 66% of the cancer group and 73% of the non-cancer group had ever used oral contraceptives (OC). Use of OC sig-

Table 3. Distribution of exogenous hormonal variables for cancer and non-cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n = 298) ^a n (%)	Non-cancer (n = 1926) ^a n (%)	Odds ratio (95% CI) adjusted for age	Odds ratio (95% CI) adjusted multivariate
<i>P</i> = 0.68				
Current use of hormone replacement therapy				
No	181 (64.0)	1245 (65.8)	1.00	1.00
Yes	102 (36.0)	646 (34.2)	1.06 (0.81, 1.38)	0.93 (0.70, 1.25)
<i>P</i> = 0.01				
Ever used oral contraceptive pill				
No	96 (34.2)	508 (26.9)	1.00	1.00
Yes	185 (65.8)	1378 (73.1)	1.50 (1.09, 2.05)	1.44 (1.04, 2.00)
<i>P</i> = 0.02				
Age when started oral contraceptives				
Never used	96 (35.3)	508 (27.9)	1.00	1.00
< 25 years	57 (21.0)	693 (38.0)	1.44 (0.89, 2.35)	1.44 (0.88, 2.37)
25–29 years	54 (19.9)	333 (18.3)	1.85 (1.20, 2.83)	1.78 (1.15, 2.75)
30–34 years	26 (9.6)	169 (9.3)	1.10 (0.68, 1.79)	1.12 (0.69, 1.84)
35+ years	39 (14.3)	119 (6.5)	1.68 (1.09, 2.60)	1.54 (0.98, 2.41)
<i>P</i> = 0.12				
Total years oral contraceptives				
Never used	96 (35.8)	508 (28.2)	1.00	1.00
< 1 year	18 (6.7)	161 (8.9)	1.08 (0.62, 1.90)	1.11 (0.63, 1.96)
1–3 years	37 (13.8)	294 (16.3)	1.47 (0.94, 2.30)	1.32 (0.83, 2.09)
4–6 years	38 (14.2)	287 (15.9)	1.55 (0.99, 2.43)	1.53 (0.97, 2.42)
7–10 years	30 (11.2)	238 (13.2)	1.42 (0.88, 2.28)	1.36 (0.83, 2.22)
10+ years	49 (18.3)	315 (17.5)	1.77 (1.17, 2.68)	1.73 (1.13, 2.65)

^aNumbers for each variable do not add up to total due to missing values. ^bControlled for age, menopausal status, oral contraceptive use, family history and education. ^cControlled for age, age first child, parity, family history and education.

Table 4. Distribution of alcohol and cigarette consumption, body mass index and body mass index by menopausal status for cancer and non-cancer groups, odds ratios and corresponding 95% confidence intervals (CI)

Variables	Cancer (n = 298) ^a n (%)	Non-cancer (n = 1926) ^a n (%)	Odds ratio (95% CI) adjusted for age
<i>P</i> = 0.17			
Amount of alcohol consumption			
None	62 (22.5)	400 (21.7)	1.00
< 5 drinks/week	99 (35.9)	765 (41.4)	1.00 (0.71, 1.42)
5–10 drinks/week	72 (26.1)	413 (22.4)	1.30 (0.89, 1.89)
11–15 drinks/week	31 (11.2)	151 (8.2)	1.55 (0.95, 2.51)
> 15 drinks/week	12 (4.3)	117 (6.3)	0.84 (0.43, 1.63)
<i>P</i> = 0.009			
Frequency of alcohol consumption			
None	62 (22.1)	400 (21.5)	1.00
Occasional	64 (22.8)	498 (27.0)	0.98 (0.67, 1.44)
Weekly	65 (23.1)	549 (29.8)	1.01 (0.69, 1.48)
Daily	90 (32.0)	401 (21.7)	1.62 (1.13, 2.33)
<i>P</i> = 0.25			
Total cigarettes ever smoked			
0–1 (thousand)	180 (65.0)	1188 (64.8)	1.00
1–100 (thousand)	38 (13.7)	319 (17.4)	0.90 (0.62, 1.32)
> 100 (thousand)	59 (21.3)	325 (17.7)	1.27 (0.91, 1.75)
<i>P</i> = 0.004			
Body mass index			
≤ 25	137 (51.9)	1122 (62.9)	1.00
> 25	127 (48.1)	663 (37.1)	1.48 (1.13, 1.93)
<i>P</i> = 0.006			
Interaction			
Body mass index by menopausal status			
Pre-menopausal and BMI ≤ 25	19 (7.2)	389 (21.8)	1.00
Pre-menopausal and BMI > 25	16 (6.1)	204 (11.4)	1.50 (0.75, 2.98)
Postmenopausal and BMI ≤ 25	118 (44.7)	733 (41.1)	1.60 (0.91, 2.81)
Postmenopausal and BMI > 25	111 (42.0)	459 (25.7)	2.35 (1.33, 4.16)

^aNumbers for each variable do not add up to total due to missing values. BMI, body mass index.

nificantly increased the odds of breast cancer to 1.44 (CI: 1.04–2.00; $P = 0.03$), independent of age at first birth, parity, family history and level of education (Table 3). There was an inconsistent pattern of risk with age at first use; the only age range that significantly increased the risk of breast cancer was the age 25–29 years (OR 1.78, CI 1.15–2.75; $P = 0.01$). We found an increasing trend of breast cancer with length of OC use, significantly higher in women using OC for more than 10 years in total (OR 1.73, CI 1.13–2.65; $P = 0.01$).

A body mass index (BMI) > 25 was more common in the cancer group, independent of age (Table 4). Controlling for age, the odds of breast cancer in women with a BMI > 25 were significantly increased in postmenopausal women (OR: 2.03; CI: 1.13–3.66), but not in pre-menopausal women (OR: 1.52; CI: 0.74–3.11).

Alcohol consumption was examined by considering both the frequency of intake and the average weekly consumption. The proportion of alcohol abstainers was similar in both groups, with a non-significant trend for increased alcohol consumption associated with breast cancer (Table 4). Compared to non-drinkers, daily alcohol consumption increased the odds of breast cancer to 1.62 (CI: 1.13–2.33).

DISCUSSION

In our cohort of women recalled for further assessment following routine breast screening, the single most important risk factor identified for breast cancer was increasing age.¹⁶ Although the cancer group were more likely to be widowed, the older age of this group accounted for the difference. Age also accounted for the higher proportion of retirees in the cancer group. Type of employment was similar across the present sample, but we found a non-significant trend of higher level of education associated with increasing risk of breast cancer, consistent with previous reports.^{20,22} Our cohort was drawn from one geographical area of Sydney, which may explain the relative uniformity of socio-demographics. Most non-Australian-born women were born in countries with similar incidences of breast cancer to Australia, and no group difference was detected.

A consistent finding in the literature is a two-to-three-fold increase in risk of breast cancer associated with a first-degree family history.^{5,14,23–27} This risk appears to be independent of reproductive factors.^{25,28} In the present cohort, the small number of women who had a daughter with breast cancer, or a sister and mother with breast cancer, were more likely to have developed breast cancer, although the trend was non-significant. We did not detect any difference in the risk of breast cancer in women reporting a mother or a sister with breast cancer. There are a number of possible explanations for family history not being a factor in our sample. First, reliability of the data should be considered. With a participation rate of 79%, response bias is unlikely. As in most epidemiological studies, we relied on self-reported information, and the accuracy of this information depends on both memory and knowledge. The few studies examining the accuracy of self-reported family history data confirm that information about breast cancer history in first-degree relatives is usually reliable.^{29,30} Floderus *et al.* found a slight underreporting by unaffected twins in a discordant twin study, even for first-degree relatives.³¹ Our information was collected before diagnoses were available, avoiding the possibility of recall bias, and any tendency to underreport would be similar in both groups.

A second possible explanation, and perhaps more likely, lies

within our sample. Genetic breast cancers account for a small percentage of breast cancers and are usually associated with early onset.^{24,25} These women, once diagnosed, would not be included in our screening population. Our cohort was drawn from women over 40 years of age who attended screening because of the risk of breast cancer associated with age, and who were recalled for further assessment. Roseman *et al.* found that after age 45, the increased risk associated with a positive family history declined, and for women over 60, those with a family history were not at greater risk of breast cancer than women with no family history.³² Both Mettlin *et al.* and Sellers *et al.* report a reduced influence of family history on breast cancer risk in women over age 55 years compared to younger women.^{33,34} In the present cohort, 73% were over age 50 and this may account for the lower than expected impact of family history. Our finding is consistent with a recent UK screening study that reported similar levels of family history (12–17%) to our cohort (14–17.5%), and found no independent impact of family history on breast cancer risk in women aged > 55 years.¹⁶ Of interest to note were differences in family history within age groups in the present cohort. Women in their 70s had a higher incidence of family history, as would be expected with concurrently ageing sisters and daughters. The incidence of family history for women in their 40s was similar to the older age groups, but the 40–49-years age group were more likely to report a mother than a sister with breast cancer. With women in their 40s self-referring for screening, it is not surprising that a high proportion of these women have a mother with breast cancer. The unanswered question is whether those women with a family history of breast cancer are more likely to be recalled for further testing, and are therefore perhaps creating a bias in our sample for this variable.

There was also a general uniformity in reproductive history across our sample. Many studies indicate that a younger age at first birth reduces the risk of breast cancer independently of parity and other risk factors.^{11,20,35} We found a trend for increased risk of breast cancer with an older age at first birth and, although not significant, the direction of the trend is consistent with previous findings. There were no differences between groups in parity, despite both nulliparity and high parity being previously reported as independent risks factors for breast cancer.³⁶ In our cohort 13.8% of women had no children and 37.7% of women had at least three children, therefore insufficient power is an unlikely explanation of these findings.

We found no evidence to support the idea that lactation protects against breast cancer, a finding consistent with most Western studies.^{37–39} Most evidence for a protective role of lactation comes from Asian countries, where breastfeeding for a number of years is common practice.³⁹ A total of 75% of our cohort breastfed, with an average duration of 10 months. This is similar to figures from the United States but well below China, Japan and Taiwan where the average duration of lactation is more than 3 years.³⁹ Less than 3% of our cohort breastfed for more than 3 years, making any protective effect of breastfeeding for long periods unlikely to be detected.

Seventy per cent of our cohort were postmenopausal and breast cancer was more common in postmenopausal women; the difference was attributable to the older age of our cohort and to the increasing risk of breast cancer with age. We found no difference in the age at onset of menopause between groups. However, ~25% of the present sample had a hysterectomy prior to or around the time of menopause, therefore the age at onset of menopause was

unknown for these women, resulting in incomplete and potentially biased data that were difficult to interpret with certainty.

A second potential confounder in assessing the onset of menopause and an independent risk factor, is HRT. Individual studies provide mixed evidence that suggests that hormone replacement therapy affects breast cancer risk.⁴⁰⁻⁴² However, a recent re-analysis of worldwide data on hormonal replacement therapy and breast cancer risk reports an increased risk of 1.023 with each year of use, restricted to time of use and persisting up to 5 years after ceasing.⁷ Thirty-four per cent of our cohort were currently using HRT, and we found no differences between the groups. Two limitations are important to note regarding our examination of HRT. The first is that we examined current use only, rather than also including past use. The second limitation is inherent in the sample population and concerns both users and diagnosis rate. Women using HRT have been reported to have a slightly higher rate of recall following mammography, particularly after the first screening round, and a lower cancer detection rate at screening, due to the effect of HRT on breast density.⁴³

Where we did detect a significant difference was in history of OC use. Women who had used OC currently or in the past were 50% more likely to have developed breast cancer than women who had never used OC. There was a trend of increasing risk of breast cancer with duration of use, reaching significance in women who had used OC for more than 10 years. In contrast, there was no linear pattern of risk associated with age at first use of OC. We found that women who first used OC between the ages of 25 and 29 years were at significantly higher risk of breast cancer compared to those who never used OC; and women who started using OC either under 25 or over 29 years showed a non-significant increase in risk compared to women who never used OC.

Previous individual studies report a slight or no increase in risk with early use, and no association between length of use and breast cancer risk. In 1996 the Collaborative Group on Hormonal Factors in Breast Cancer re-analysed some 90% of worldwide data on OC and breast cancer risk, reporting a small but significant increase in risk of breast cancer with OC use.⁶ This increase in risk was most evident in current users, and was detectable up to 10 years after ceasing contraceptive use. The Collaborative Group also report that recent use, rather than age at first use or duration of use, was the best predictor of risk associated with OC.

There are, however, a number of differences both in the nature of our cohort and our results that suggests we should not assume consistency with the Collaborative Group. First, the average age of the present cohort is 56 years, an average of 7 years older than the Collaborative Cohort, and equally it is 7 years more since their OC use. Second, 72% of our cohort reported ever using OC, substantially higher than recent studies in Italy, where use was reported in 14-18% of women;²⁶ in the US (38-46%);^{44,45} and of past studies worldwide (an average of 40%).⁶ Third, the older age of our cohort has impacted on use, age at first use and duration of use, primarily due to the time when OC were introduced for widespread use. For example, a woman now in her 70s would have been aged in her 30s when OC were first available for general use, and therefore would be less likely to have ever used, have been unable to start in early reproductive years and consequentially be less likely to have used for a long duration. In contrast, a woman now in her 40s potentially would have had access to OC from her teen years. This is reflected in the rate of use, with 90% of women in their 40s compared to 25% of women in their 70s having ever used OC.

This being the case, it is likely that the inconsistent trend of risk that we found for age at first use and breast cancer risk is an artefact of our cohort. The number of women commencing OC use after the age of 30 years was small, and they were more likely to be older women and therefore less likely to use OC for long periods. Despite this, our data provide strong evidence that use of OC significantly increases breast cancer risk, that it is highest with a long duration of use, regardless of age, age at first birth, parity, family history of breast cancer, and education. This is highlighted by the fact that older women most at risk of cancer and least likely to have used OC demonstrated a significant OC effect similar to the younger women, who were least at risk of cancer but who used OC for long periods, demonstrating a significant OC effect. In contrast to the findings from the Collaborative Group, our results suggest that the increase in risk of breast cancer associated with using OC may persist in the long term after ceasing.

Our finding of a modest association between alcohol consumption and breast cancer is consistent with the growing body of evidence which suggests that the two are related, although a causal relationship has yet to be established. Alcohol is thought to increase endogenous oestrogen levels, demonstrated by Reichman *et al.* in pre-menopausal women,⁴¹ although these findings are not universal⁴⁶ and the effect on hormonal levels in post-menopausal women is unclear.⁴⁷ A number of epidemiological studies provide support for a small positive association between alcohol intake and breast cancer,^{9-12,48-50} with as little as one glass a day increasing risk.^{4,50} Some studies have found a dose-response relationship,⁵¹ while others report a threshold effect.^{9,46} Our findings suggest that frequency rather than amount is the important indicator of risk, and are consistent with Katsouyanni *et al.* who reported that frequency of alcohol intake was more important than length of intake or early consumption.⁹

Obesity and weight gain have been reported as risk factors for breast cancer, particularly in postmenopausal women.¹²⁻¹⁷ Oestradiol levels are higher in obese women than in lean women,^{52,53} and may be responsible for the increased risk for breast cancer.⁵⁴ Our findings add to the growing body of evidence for an increase in risk of breast cancer in overweight postmenopausal women. In our relatively small sample of pre-menopausal women, obesity did not affect breast cancer risk.

CONCLUSION

Increasing age, postmenopausal obesity and use of OC increase the odds of breast cancer in a population of women recalled for further testing following mammography screening. Daily alcohol consumption provided a modest increase in risk of breast cancer, consistent with previous findings. These results should provide some reassurance for women over 40 years of age that the unalterable variables of family history and reproductive factors do not substantially affect their risk of breast cancer, and suggest that the effects of weight reduction should be assessed.

ACKNOWLEDGEMENTS

This research was funded by the National Health and Medical Research Council of Australia and was supported by the staff of Northern Sydney and Lower Central Coast BreastScreen New South Wales.

REFERENCES

- Forbes JF. The incidence of breast cancer: The global burden, public health considerations. *Semin. Oncol.* 1997; 24 (Suppl. 1): S1-20-S1-35.
- Hankinson SE, Colditz GA, Hunter DJ *et al.* Reproductive factors and family history of breast cancer in relation to plasma estrogen and prolactin levels in postmenopausal women in the Nurses' Health Study (United States). *Cancer Causes Control* 1995; 6: 217-24.
- Seidman H, Stellman SD, Mushinski MH. A different perspective on breast cancer risk factors: Some implications of the nonattributable risk. *CA Cancer J. Clin.* 1982; 32: 301-13.
- La Vecchia C, Negri E, Franceschi S *et al.* Hormone replacement treatment and breast cancer risk: A cooperative Italian study. *Br. J. Cancer* 1995; 72: 244-8.
- Madigan MP, Ziegler RG, Benichou J, Byrne C, Hoover RN. Proportion of breast cancer cases in the United States explained by well-established risk factors. *J. Natl Cancer Inst.* 1995; 87: 1681-5.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: Collaborative reanalysis of individual data on 53 297 women with breast cancer and 100 239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996; 347: 1713-27.
- Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: Collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. *Lancet* 1997; 350: 1047-59.
- Martin-Moreno JM, Boyle P, Gorgojo L *et al.* Alcoholic beverage consumption and risk of breast cancer in Spain. *Cancer Causes Control* 1993; 4: 345-53.
- Katsouyanni K, Trichopoulos A, Stuver S *et al.* Ethanol and breast cancer: An association that may be both confounded and causal. *Int. J. Cancer* 1994; 58: 356-61.
- Longnecker MP, Paganini-Hill A, Ross RK. Lifetime alcohol consumption and breast cancer risk among postmenopausal women in Los Angeles. *Cancer Epidemiol. Biomarkers Prev.* 1995; 4: 721-5.
- Levi F, Pasche C, Lucchini F, La Vecchia C. Alcohol and breast cancer in the Swiss Canton of Vaud. *Eur. J. Cancer* 1996; 32A: 2108-13.
- Swanson CA, Coates RJ, Malone KE *et al.* Alcohol consumption and breast cancer risk among women under age 45 years. *Epidemiology* 1997; 8: 231-7.
- Pathak DR, Whittemore AS. Combined effects of body size, parity, and menstrual events on breast cancer incidence in seven countries. *Am. J. Epidemiol.* 1992; 135: 153-68.
- Taioli E, Barone J, Wynder EL. A case-control study on breast cancer and body mass. *Eur. J. Cancer* 1995; 31A: 723-8.
- Franceschi S, Favero A, La Vecchia C *et al.* Body size indices and breast cancer risk before and after menopause. *Int. J. Cancer* 1996; 67: 181-6.
- Thomas E, Cade J, Vail A. Risk factor analysis of data from assessment clinics in the UK breast screening programme: A case-control study in Portsmouth and Southampton. *J. Epidemiol. Community Health* 1996; 50: 144-8.
- La Vecchia C, Negri E, Franceschi S, Talamini R, Palli D, Decarli A. Body mass index and post-menopausal breast cancer: An age-specific analysis. *Br. J. Cancer* 1997; 75: 441-4.
- Yoo K-Y, Tajima K, Kuroishi T *et al.* Independent protective effect of lactation against breast cancer: A case-control study in Japan. *Am. J. Epidemiol.* 1992; 135: 726-33.
- United Kingdom National Case-Control Study Group. Breast feeding and risk of breast cancer in young women. *BMJ* 1993; 307: 17-20.
- Tavani A, Braga C, La Vecchia C, Negri E, Russo A, Francheschi S. Attributable risks for breast cancer in Italy: Education, family history and reproductive and hormonal factors. *Int. J. Cancer* 1997; 70: 159-63.
- Kricker A, Jelfs P. *Breast Cancer in Australian Women 1921-94: Cancer Series no. 6.* Canberra: Australian Institute of Health and Welfare, 1996.
- Heck KE, Pamuk ER. Explaining the relation between education and postmenopausal breast cancer. *Am. J. Epidemiol.* 1997; 145: 366-72.
- Gapstur SM, Potter JD, Sellers TA, Folsom AR. Increased risk of breast cancer with alcohol consumption in postmenopausal women. *Am. J. Epidemiol.* 1992; 136: 1221-31.
- Slattery ML, Kerber RAA. Comprehensive evaluation of family history and breast cancer risk: The Utah population database. *JAMA* 1993; 270: 1563-8.
- Colditz GA, Willett WC, Hunter DJ *et al.* Family history, age, and risk of breast cancer: Prospective data from the Nurses' Health Study. *JAMA* 1993; 270: 338-43.
- La Vecchia C, Negri E, Franceschi S *et al.* Oral contraceptives and breast cancer: A cooperative Italian study. *Int. J. Cancer* 1995; 60: 163-7.
- Hunter DJ, Spiegelman D, Adami H-O *et al.* Non-dietary factors as risk factors for breast cancer, and as effect modifiers of the association of fat intake and risk of breast cancer. *Cancer Causes Control* 1997; 8: 49-56.
- Andrieu N, Clavel F, Auquier A *et al.* Variations in the risk of breast cancer associated with a family history of breast cancer according to age at onset and reproductive factors. *J. Clin. Epidemiol.* 1993; 46: 973-80.
- Anton-Culver H, Kurosaki T, Taylor TH, Gildea M, Brunner D, Bringman D. Validation of family history of breast cancer and identification of the BRCA1 and other syndromes using a population-based cancer registry. *Genet. Epidemiol.* 1996; 13: 193-205.
- Parent M-E, Ghadirian P, Lacroix A, Perret C. The reliability of recollections of family history: implications for the medical provider. *J. Cancer Educ.* 1997; 12: 114-20.
- Floderus B, Barlow L, Mack TM. Recall bias in subjective reports of familial cancer. *Epidemiology* 1990; 1: 318-21.
- Roseman DL, Straus AK, Shorey WA. Positive family history of breast cancer: Does its effect diminish with age? *Arch. Intern. Med.* 1990; 150: 191-4.
- Metlin C, Croghan I, Natarajan N, Lane W. The association of age and familial risk in a case-control study of breast cancer. *Am. J. Epidemiol.* 1990; 131: 973-83.
- Sellers TA, Kushi LH, Potter JD *et al.* Effect of family history, body-fat distribution, and reproductive factors on the risk of postmenopausal breast cancer. *N. Engl. J. Med.* 1992; 326: 1323-9.
- Talamini R, Franceschi S, La Vecchia C *et al.* The role of reproductive and menstrual factors in cancer of the breast before and after menopause. *Eur. J. Cancer* 1996; 32A: 303-10.
- Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol. Rev.* 1993; 15: 36-47.
- London SJ, Colditz GA, Stampfer MJ *et al.* Lactation and risk of breast cancer in a cohort of US women. *Am. J. Epidemiol.* 1990; 132: 17-26.
- Brinton LA, Potischman NA, Swanson CA *et al.* Breastfeeding and breast cancer risk. *Cancer Causes Control* 1995; 6: 199-208.
- Michels KB, Willett WC, Rosner BA *et al.* Prospective assessment of breastfeeding and breast cancer incidence among 89 887 women. *Lancet* 1996; 347: 431-6.
- Weinstein AL, Mahoney MC, Nasca PC, Hanson RL, Leske MC, Varma AO. Oestrogen replacement therapy and breast cancer risk: A case-control study. *Int. J. Epidemiol.* 1993; 22: 781-9.

41. Reichman ME, Judd JT, Longcope C *et al.* Effects of alcohol consumption on plasma and urinary hormone concentrations in premenopausal women. *J. Natl Cancer Inst.* 1993; 85: 722-7.
42. Newcomb PA, Longnecker MP, Storer BE *et al.* Long-term hormone replacement therapy and risk of breast cancer in postmenopausal women. *Am. J. Epidemiol.* 1995; 142: 788-95.
43. Litherland JC, Evans AJ, Wilson ARM. The effect of hormone replacement therapy on recall rate in the National Health Service Breast Screening Programme. *Clin. Radiol.* 1997; 52: 276-9.
44. Newcomb PA, Longnecker MP, Storer BE *et al.* Recent oral contraceptive use and risk of breast cancer (United States). *Cancer Causes Control* 1996; 7: 525-32.
45. Hankinson SE, Colditz GA, Manson JE *et al.* A prospective study of oral contraceptive use and risk of breast cancer (Nurses' Health Study, United States). *Cancer Causes Control* 1997; 8: 65-72.
46. Dorgan JF, Reichman ME, Judd JT *et al.* The relation of reported alcohol ingestion to plasma levels of estrogens and androgens in premenopausal women (Maryland, United States). *Cancer Causes Control* 1994; 5: 53-60.
47. Longnecker MP. Do hormones link alcohol with breast cancer? *J. Natl Cancer Inst.* 1993; 85: 692-3.
48. Rosenberg L, Metzger LS, Palmer JR. Alcohol consumption and risk of breast cancer: A review of the epidemiologic evidence. *Epidemiol. Rev.* 1993; 15: 133-44.
49. van den Brandt PA, Goldbohm RA, van't Veer P. Alcohol and breast cancer: Results from the Netherlands Cohort Study. *Am. J. Epidemiol.* 1995; 141: 907-15.
50. Longnecker MP, Newcomb PA, Mittendorf R *et al.* Risk of breast cancer in relation to lifetime alcohol consumption. *J. Natl Cancer Inst.* 1995; 87: 923-9.
51. Longnecker MP. Alcoholic beverage consumption in relation to risk of breast cancer: Meta-analysis and review. *Cancer Causes Control* 1994; 5: 73-82.
52. Deslypere JP. Obesity and cancer. *Metabolism* 1995; 44 (Suppl. 3): 24-7.
53. Potischman N, Swanson CA, Siiteri P, Hoover RN. Reversal of relation between body mass and endogenous estrogen concentrations with menopausal status. *J. Natl Cancer Inst.* 1996; 88: 756-8.
54. Kelsey JL. Breast cancer epidemiology: Summary and future directions. *Epidemiol. Rev.* 1993; 15: 256-63.

The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part I

The Cancer Prone Personality

Melanie A. Price, B.Sc. (Hons)¹
Christopher C. Tennant, M.D.¹
Ross C. Smith, M.D.²
Phyllis N. Butow, Ph.D.¹
Susan J. Kennedy, M.A.¹
Marjorie B. Kossoff, M.D.³
Stewart M. Dunn, Ph.D.¹

¹ Department of Psychological Medicine, University of Sydney, Royal North Shore Hospital, St. Leonards, New South Wales, Australia.

² Department of Surgery, University of Sydney, Royal North Shore Hospital, St. Leonards, New South Wales, Australia.

³ BreastScreen NSW, Royal North Shore Hospital, St. Leonards, New South Wales, Australia.

See also accompanying article on pages 686–97, this issue.

Supported by the National Health and Medical Research Council of Australia.

Address for reprints: Melanie Price, B.Sc. (Hons), Department of Psychological Medicine, University of Sydney, Royal North Shore Hospital, St. Leonards, New South Wales, Australia; Fax: (011) +61 2 9926-7730; E-mail: melaniep@mail.med.usyd.edu.au

Received October 13, 2000; accepted October 13, 2000.

© 2001 American Cancer Society

BACKGROUND. The authors conducted the current study to determine whether personality predisposes some individuals to develop cancer.

METHODS. The current study examined the role of personality variables in 2224 older women recalled for assessment after routine mammography in a breast screening program. Using a semipropective design, subjects completed self-report measures of defense style, locus of control, emotional expression and control, self-esteem, trait anxiety, and state anxiety and depression while waiting for medical examination. Multivariate analysis of variance was used to control for known risk factor variables and to examine differences between 3 control groups (normal tissue controls, benign/cystic controls not requiring biopsy, and benign biopsy controls) and 298 breast carcinoma subjects.

RESULTS. No differences were detected between breast carcinoma subjects and controls based on measures of mature, immature, and neurotic defense style; locus of control of behavior; emotional expression-in, emotional expression-out, and emotional control; self-esteem; anxiety; or depression.

CONCLUSIONS. The results of the current study found no evidence to support an independent association between these personality measures and the development of breast carcinoma. [See accompanying article on pages 686–97, this issue.] *Cancer* 2001;91:679–85. © 2001 American Cancer Society.

KEYWORDS: breast neoplasms, personality, defense mechanisms, emotions, psychology.

Despite limited empiric evidence of a role for psychosocial factors in the development of breast carcinoma, there is widespread belief to the contrary.^{1,2} Although some researchers are satisfied the role of psychosocial variables in the development of breast carcinoma is negligible,^{3,4} others believe that the evidence to date has not been of sufficient quality to constitute a “fair test” of this hypothesis.^{5–7}

One of the main factors studied and the focus of the current report is personality. The “Cancer Prone Personality” theoretically predisposes some individuals to develop cancer and experience a more rapid disease progression.⁸ The three components of this personality type are: 1) a distinctive coping style characterized by abrogating one’s needs in favor of the needs of others; 2) difficulty in expressing emotions; and 3) an attitude of helplessness or hopelessness.⁸ The empiric evidence to support this theory in the case of breast carcinoma is equivocal. To our knowledge much of the research focuses on emotional suppression or emotional control. Six of 13 studies in this area reported negative results.^{9–14} Of the seven studies reporting positive results,^{15–21} only two were adjusted for age;

one of these had a very poor response rate¹⁹ (perhaps introducing significant sample bias), whereas the other found anger repression to be associated with the development of breast carcinoma only in patients age < 50 years.¹⁶

The current study examined the role of several personality variables including defense style and emotional expression and control, as well as recent life events and social support. The goal was to tease apart the components of "stress" and personality in a large sample, thus offering a fair test of the role for psychosocial variables in the development of breast carcinoma. The current study reports our findings concerning three domains of the type C personality style in relation to the development of breast carcinoma. Results of the accompanying data regarding life event stress and social support in a subset of this sample will be reported separately.

MATERIALS AND METHODS

National breast screening was initiated in Australia in 1993, and actively recruited women ages 50–69 years for screening from electoral rolls. However, free screening is available to all women age > 40 years. Women attending the Northern Sydney and Lower Central Coast Breast Screening Program between April 1994 and April 1997 and who were recalled for assessment based on radiologic grounds (i.e., an abnormal screening mammogram) were invited to participate in research examining psychosocial factors in breast carcinoma development. Screening Rounds 1 and 2 were in progress during the period of the current study. The study was approved by the Royal North Shore Hospital Medical Research Ethics Committee.

On arrival at the clinic, consenting women completed a self-administered questionnaire while waiting for assessment. The assessment procedure could include mammography, physical examination, ultrasound, and biopsy when indicated. The questionnaire included items regarding demographics and biologic risk factors including reproductive history and hormonal variables, as well as several psychologic questionnaires. These data are the focus of the current study. A subset of this sample, those women requiring fine-needle biopsy for a definitive diagnosis, was interviewed for a history of recent life events, bereavement, and social support prior to their test results being available; these data are reported separately. Results of the assessment procedure subsequently were established through the clinic records.

The inclusion criteria were: 1) attendance for assessment after routine breast screening; 2) age \geq 40 years; and 3) adequate command of English. The exclusion criteria were: 1) a prior history of breast car-

cinoma; 2) breast symptoms prompting screening; 3) knowledge of final assessment diagnosis; and 4) physical or psychiatric impairment inhibiting completion of the questionnaire and/or interview.

Demographic and somatic risk factor variables were collected by self-report and included age, marital status, education, employment, family history of breast carcinoma, history of benign breast disease, parity, age at birth of the first child, lactation, menopausal status, age at the onset of menopause, oral contraceptive use, use of hormone replacement therapy, height, weight, and alcohol and cigarette consumption.

Self-report questionnaires were used to examine the three domains of the Temoshok's "cancer prone personality."⁸ Each questionnaire has accepted validity and reliability and has been used in similar populations.

Coping Style

Emotion-focused coping was assessed by the Defense Style Questionnaire (DSQ-40).²² Defense style reflects a stable pattern of feelings, thoughts, or behaviors used to alleviate the conflict or stressors that give rise to anxiety.²³ Based on DSM-111-R definitions,²³ the 40-item measure yields scores for three defense styles: mature, neurotic, and immature. Higher scores reflect greater use of a defense style. Problem-focused coping was measured by the Locus of Control of Behavior (LCB) scale.²⁴ Designed to assess perceived control over behavior, this 14-item measure yields a single factor reflecting an internal/external locus of control of behavior. A higher score indicates an external locus of control and a lower score indicates an internal locus of control.

Emotional Expression and Control

The Emotional Expression and Control (EEC) scale was used to assess the expression and control of negative emotions.²⁵ Developed from the Watson and Greer²⁶ measure of emotional control and Spielberger et al.'s concept of anger expression,²⁷ the focus is on self-reported expression and control of anger, anxiety, and depression. The 18-item measure yields scores concerning three factors: emotional expression-in, reflecting the expression of emotions to one's self; emotional expression-out, reflecting the expression of emotions toward others; and emotional control, reflecting the extent of control over one's emotions.²⁵ Higher scores reflect more emotional expression-in, more emotional expression-out, and more emotional control, respectively.

Helplessness and Hopelessness

Rosenberg's 10-item self-esteem scale measures the self-acceptance aspect of self-esteem and was used as a measure of trait depression.²⁸ Lower scores on this scale reflect higher self-esteem. Trait anxiety was assessed using the subscale from the State-Trait Personality Inventory (STPI) by Spielberger et al.²⁹ The 10 items refer to how a person generally feels and a higher total score reflects higher trait anxiety. The Hospital Anxiety and Depression (HAD) scale³⁰ assesses state anxiety and state depression. Excluding any reference to somatic symptoms, the 14 items refer to how the respondent has been feeling in the last week. Anxiety and depression in this measure are distinguished clearly, with scores > 10 on either subscale reflecting clinically significant mood disturbance and scores between 8 and 10 representing borderline mood disturbance.

Multivariate analysis of covariance was performed using SPSS for Windows 6.1.3 software (SPSS, Inc., Chicago, IL). The psychologic variables included in analysis were continuous and included mature, immature, and neurotic defense style; locus of control of behavior; emotional expression-in, emotional expression-out, and emotional control; self-esteem; and trait anxiety, state anxiety, and state depression. Eleven variables were included as covariates: age, level of education, age at onset of menopause, first birth after age 29 years, parity, family history of breast carcinoma, history of benign breast disease, oral contraceptive use, current use of hormone replacement therapy, alcohol consumption, and body mass index.

RESULTS

A total of 2821 women were eligible to participate in this study. Approximately 13% of eligible women declined participation and a further 8% had incomplete questionnaires, resulting in a total of 2224 questionnaires (79%) available for the final analysis. Subjects were classified into four groups according to diagnosis and testing conditions. There were 3 control groups: normal tissue controls ($n = 947$), benign or cystic lesions not requiring biopsy confirmation ($n = 644$), and benign lesions requiring biopsy confirmation ($n = 335$). These 3 groups were compared with a group of breast carcinoma subjects ($n = 298$).

No direct information was available for women declining to participate in the study. However, comparing our sample with the available statistics from the screening program assessment clinic, data concerning age, the percentage of women requiring biopsy, and the percentage of women diagnosed with breast carcinoma during the years 1994-1996 inclu-

sive suggests minimal participation bias with respect to these variables. The mean age of the women recalled for assessment was 56.7 years and the mean age of the current study sample was 56.1 years. The percentage of women recalled for assessment requiring needle biopsy was 23.3% compared with 28.5% of the current study sample. Approximately 11% of the women recalled were diagnosed with breast carcinoma compared with 13.4% of the current study sample. Our higher percentage of subjects undergoing biopsy in comparison with assessment clinic attendees is consistent with those women not requiring biopsy having less time to complete their questionnaire prior to the completion of medical assessment.

Demographic and somatic risk factor variables are summarized in Table 1. The current study sample was ages 40-87 years with a mean age of 56.1 years. The breast carcinoma group, with a mean age of 61.2 years, was significantly older than each of the 3 control groups ($P < 0.0001$). After controlling for age, there were no group differences with regard to marital status, education, or employment.

Family history was defined as having a first-degree relative diagnosed with breast carcinoma, distinguishing between a diagnosis before age 50 years and one after age 50 years; group differences were not significant ($P > 0.053$). No significant differences were detected with regard to age at birth of the first child, parity, age at the onset of menopause, length of lactation, or cigarette consumption. Normal tissue controls were less likely than the other groups to previously have undergone surgical removal of benign breast tissue ($P < 0.01$). Significant differences were detected between groups with regard to menopausal status, oral contraceptive use, current use of hormone replacement therapy, daily alcohol consumption, and body mass index (Table 1). Further details regarding these data are published elsewhere.³¹

Age, surgical removal of benign breast tissue, oral contraceptive use, current use of hormone replacement therapy, daily alcohol consumption, and body mass index were selected as confounders on the basis of significant group differences. Age at the onset of menopause (premenopausal/postmenopausal, age < 40 years, ages 41-45 years, ages 46-50 years, age 50+ years, and unknown), family history of breast carcinoma (none, diagnosed age 50+ years, diagnosed age < 50 years, and unknown), first birth after age 29 years, and parity (0, 1-2, and 3+) were included as well documented correlates of breast carcinoma. The woman's level of education was found to be highly correlated with the majority of psychologic variables and was included as a covariate.

Table 2 displays group means for the 11 psycho-

TABLE 1
Demographic and Somatic Risk Variables for the Breast Carcinoma Group and Noncancer Control Groups

Variable	Groups				Statistic
	Nonbiopsy		Biopsy		
	Normal tissue (n = 947) No. (%)	Benign/cystic (n = 644) No. (%)	Benign disease (n = 335) No. (%)	Breast carcinoma (n = 298) No. (%)	
Mean age (SD) (yrs)	54.67 (9.16)	55.30 (8.54)	57.08 (9.91)	61.22 (9.43)	F = 41.87, P < 0.0001
Current marital status					$\chi^2(6) = 23.60$ (P = 0.005)
Married/defacto	723 (76.7)	472 (73.6)	231 (70.2)	202 (68.9)	
Single/never married	50 (5.3)	39 (6.1)	23 (7.0)	17 (5.8)	
Widowed	65 (6.9)	50 (7.8)	34 (10.3)	44 (15.0)	
Divorced	105 (11.1)	80 (12.5)	41 (12.5)	30 (10.2)	
Level of education					$\chi^2(12) = 11.9$ (P = 0.45)
Primary	34 (3.6)	19 (3.0)	17 (5.2)	10 (3.4)	
3-4 years secondary	357 (37.9)	230 (36.0)	130 (39.6)	112 (38.1)	
5-6 years secondary	147 (15.6)	93 (14.6)	53 (16.2)	51 (17.3)	
Diploma/certificate	212 (22.5)	170 (26.6)	78 (23.8)	72 (24.5)	
University/college	191 (20.3)	127 (19.9)	50 (15.2)	49 (16.7)	
Family history of breast carcinoma					$\chi^2(9) = 16.71$ (P = 0.053)
None	765 (80.8)	544 (84.5)	270 (80.6)	231 (77.5)	
Diagnosed after age 50 yrs	79 (8.3)	43 (6.7)	16 (4.8)	29 (9.7)	
Diagnosed before age 50 yrs	58 (6.1)	31 (4.8)	31 (9.3)	22 (7.4)	
Unknown family history	45 (4.8)	26 (4.0)	18 (5.4)	16 (5.4)	
History of benign breast disease					$\chi^2(3) = 13.18$ P = 0.004
No	802 (86.6)	510 (80.1)	269 (83.3)	231 (81.1)	
Yes	124 (13.4)	127 (19.9)	54 (16.7)	54 (18.9)	
Age at birth of the first child					$\chi^2(12) = 11.3$ P = 0.50
Nulliparous	136 (14.7)	77 (12.3)	47 (15.1)	36 (12.9)	
< 20 yrs	48 (5.2)	28 (4.5)	12 (3.9)	8 (2.9)	
20-24 yrs	261 (28.3)	179 (28.6)	100 (32.2)	75 (27.0)	
25-29 yrs	308 (33.4)	231 (36.9)	93 (29.9)	101 (36.3)	
≥ 30 yrs	170 (18.4)	111 (17.7)	59 (19.0)	58 (20.9)	
Parity					$\chi^2(6) = 5.24$ P = 0.51
Nulliparous	136 (14.6)	77 (12.2)	47 (15.1)	36 (12.8)	
1-2	463 (49.7)	302 (47.9)	148 (47.0)	132 (46.8)	
≥ 3	333 (35.7)	252 (39.9)	119 (37.8)	114 (40.4)	
Menopausal status					$\chi^2(3) = 55.8$ P < 0.0001
Premenopausal	332 (35.1)	200 (31.1)	99 (29.6)	37 (12.4)	
Postmenopausal	615 (64.9)	444 (68.9)	236 (70.4)	261 (88.6)	
Age at menopause ^a					$\chi^2(6) = 3.96$ P = 0.68
< 45 yrs	214 (35.7)	141 (32.5)	71 (34.8)	68 (28.9)	
46-50 yrs	215 (35.8)	160 (36.9)	74 (36.3)	94 (40.0)	
> 50 yrs	171 (28.5)	133 (30.6)	59 (28.9)	73 (31.1)	
Oral contraceptives					$\chi^2(3) = 9.26$ P = 0.026
< 1 yr in total ever	319 (35.8)	219 (35.8)	131 (43.5)	114 (42.5)	
≥ 1 yr total ever	571 (64.2)	393 (64.2)	170 (56.5)	154 (57.5)	
Hormone replacement therapy					$\chi^2(3) = 10.81$ P = 0.01
No current use	613 (65.6)	389 (62.5)	233 (73.0)	181 (64.0)	
Current use	321 (34.4)	239 (37.5)	86 (27.0)	102 (36.0)	
Alcohol consumption					$\chi^2(9) = 28.7$ P = 0.0007
None	181 (19.9)	147 (23.7)	69 (21.9)	61 (21.8)	
Occasional	227 (25.0)	178 (28.7)	93 (29.5)	64 (22.9)	
Weekly	278 (30.6)	176 (28.3)	95 (30.2)	65 (23.2)	
Daily	223 (24.5)	120 (19.3)	58 (18.4)	90 (32.1)	
(BMI)					$\chi^2(3) = 16.9$ P = 0.0007
< 25	555 (62.8)	394 (65.6)	173 (57.7)	137 (51.9)	
≥ 25	329 (37.2)	207 (34.4)	127 (42.3)	127 (48.1)	

SD: standard deviation.

Numbers for each variable may not add up to total due to missing values.

^a Known age at menopause only.

TABLE 2
Mean Scores (SD) and Univariate F Tests for Group Differences Based on Psychologic Variables Between the Breast Carcinoma Group and Noncancer Control Groups

	Groups				Statistic
	Nonbiopsy		Biopsy		
	Normal tissue (n = 947)	Benign/cystic (n = 644)	Benign disease (n = 335)	Breast carcinoma (n = 298)	
Defense style					
Mature	6.24 (1.09)	6.28 (1.13)	6.27 (1.14)	6.37 (1.07)	$F_{(3,2209)} = 0.05$, $P = 0.99$
Neurotic	5.08 (1.13)	5.02 (1.13)	5.18 (1.20)	5.21 (1.14)	$F_{(3,2209)} = 0.73$, $P = 0.54$
Immature	3.63 (0.87)	3.60 (0.88)	3.69 (0.95)	3.69 (0.96)	$F_{(3,2209)} = 2.08$, $P = 0.10$
Locus of control of behaviour	21.48 (8.11)	20.61 (7.89)	21.76 (8.34)	21.96 (7.97)	$F_{(3,2209)} = 1.62$, $P = 0.18$
Emotional expression and control					
EE-in	15.10 (4.08)	15.05 (4.06)	15.28 (4.49)	15.44 (3.88)	$F_{(3,2209)} = 0.29$, $P = 0.83$
EE-out	12.88 (3.43)	12.81 (3.12)	12.73 (3.52)	12.26 (3.01)	$F_{(3,2209)} = 0.55$, $P = 0.65$
Emotional control	15.53 (3.79)	15.49 (3.77)	15.56 (4.16)	15.76 (3.62)	$F_{(3,2209)} = 0.77$, $P = 0.51$
Self-esteem	18.06 (4.60)	17.54 (4.65)	18.29 (4.74)	17.83 (4.29)	$F_{(3,2209)} = 1.44$, $P = 0.23$
Trait anxiety	17.72 (4.85)	17.17 (4.68)	17.74 (5.17)	17.22 (4.60)	$F_{(3,2209)} = 1.39$, $P = 0.25$
State anxiety	7.66 (3.99)	7.13 (3.78)	7.52 (4.14)	7.54 (3.76)	$F_{(3,2209)} = 2.88$, $P = 0.04$
State depression	3.23 (2.90)	2.98 (2.65)	3.16 (2.97)	2.83 (2.44)	$F_{(3,2209)} = 0.93$, $P = 0.43$

SD: standard deviation; df: degree of freedom; EE: emotional expression.

* Analysis controlled for age, education, age at onset of menopause (premenopausal, age < 45 years, ages 46-50 years, age 50+ years, and unknown), family history of breast carcinoma (none, developing at age 50+ years, developing at age < 50 years, and unknown), first birth at age > 29 years, parity (none, 1-2, and 3+), body mass index (< 25 and 25+), oral contraceptive use (< 1 year total or > 1 year total), daily alcohol consumption, removal of benign breast disease, and current use of hormone replacement therapy.

logic variables. Using Wilk's criterion, these variables were not found to be significantly different across the 4 groups ($F_{(33, 6479.36)} = 1.13$; $P = 0.28$). Results of univariate F tests for individual variables controlling for covariates and confounders and other psychologic variables also are shown in Table 2. To increase power, the three control groups were combined into one "noncancer" control group for comparison with the breast carcinoma group; this did not appear to change the findings substantially.

DISCUSSION

The current study employed a semiprospective design to examine the three domains of Temoshok's⁸ "cancer prone personality" in relation to the diagnosis of breast carcinoma in a community sample of older women recalled after routine breast screening. This method minimized biases associated with the hospi-

tal-based sampling of symptomatic women and enabled a standardization in the assessment process and reporting. Women attending for similar breast screening have scores similar to community normative data for the Eysenck Personality Questionnaire (EPQ) and State-Trait Anxiety Inventory (STAI).³²

With disagreement remaining regarding the appropriate comparison group for breast carcinoma,^{4,33} we distinguished between "normal" breast tissue controls and those individuals with benign breast disease. As an added precaution against a potential impact of ongoing testing procedures during participation, we made a further distinction between those who did and those who did not undergo needle biopsy.

Controlling extensively for established risk factors for breast carcinoma, we found no evidence of an association between defense style, locus of control of behavior, self-esteem, trait or state anxiety or state

depression, and breast carcinoma in this large sample. Of particular note was the absence of an association between breast carcinoma and emotional expression and control variables.

There are some findings from previous research offering evidence of emotional suppression, repression, or control being associated with breast carcinoma. Both Grassi and Cappellari¹⁵ and Fox et al.¹⁹ reported significantly higher emotional control in breast carcinoma patients. However, Greer and Morris¹⁶ found women with breast carcinoma diagnosed before age 50 years were more likely to be extreme suppressors or extreme expressors of emotion compared with benign controls. Morris et al.¹³ reported less expression of anger in breast carcinoma patients than controls, although only those in the 40–49 years age group approached statistical significance ($P = 0.08$). Similarly, Scherg et al.¹⁷ found breast carcinoma patients showed significantly more suppression of anger, but only in the group of patients ages 20–50 years.

It could be argued that our somewhat "older" sample (mean age of 56 years) may mask the importance of emotional control or suppression that may have an effect in younger women. However, in reanalyzing our data for the 726 women ages 40–50 years, we found no evidence of an association between emotional expression and control variables, or the other psychologic variables, and breast carcinoma. Although in the current study the number of breast carcinoma subjects for comparison was small ($n = 39$), the numbers are not dissimilar to other studies reporting a positive association between emotional control or suppression and breast carcinoma.

However, the findings of the current study are consistent with those of Bleiker et al. in a large prospective study of a Dutch screening population that found no association between emotional expression and control and subsequent breast carcinoma diagnosis.¹⁰ With what to our knowledge is the largest series of breast carcinoma subjects in this area of research, we believe our study has sufficient power to detect small differences between groups.

To our knowledge the importance of controlling for established risk factor variables in the examination of potential psychologic risk factors in patients with breast carcinoma is undisputed, although the process of selecting adequate and appropriate combinations of confounding variables is not precise. Although we considered a large number of risk factor variables, some limitations should be noted. Age at menarche was not included, primarily because the accuracy in recalling this information in older women has been queried and there is some evidence this variable is

more important in younger women.³⁴ We considered the history of benign breast disease in terms of surgical confirmation rather than prior breast biopsy, which currently is a more common method of diagnosing benign breast disease. In addition, the use of hormone replacement therapy was limited to current use, rather than including recent use, which recently has been identified as increasing breast carcinoma risk.³⁵

Although we employed a quasiprospective design to examine a large asymptomatic community-based sample, the inherent limitations of this design can be overcome only with a truly prospective design. It is possible that the measures we have employed, although reliable and valid, may not be adequate to assess the concept of the type C personality. However, it may be more likely that the contribution of psychologic factors in the incidence of breast carcinoma is small.^{36,37} If there is a premorbid cancer personality, the usefulness of examining personality alone (rather than in conjunction with stress) is questionable, given that the two are linked fundamentally.³⁶

The findings of the current study do not support a direct role for personality in the development of breast carcinoma in older asymptomatic women attending a free community-based mammography screening program. It is possible that personality variables such as emotional control and defense style have no direct impact on the development of breast carcinoma, but are vulnerability factors that moderate the impact of life event stress on the development of breast carcinoma. We currently are exploring the latter hypothesis in our analysis of stressful life events.

REFERENCES

1. Baghurst KI, Baghurst PA, Record SJ. Public perceptions of the role of dietary and other environmental factors in cancer causation or prevention. *J Epidemiol Community Health* 1992;46:120–6.
2. Brinton LA, Malone KE, Liff J, Schoenberg JB. Re: "Should we consider a subject's knowledge of the etiologic hypothesis in the analysis of case-control studies?" *Am J Epidemiol* 1994; 140:1054–6.
3. Cassileth BR. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1996;77(6):1015–6.
4. Barraclough J. Adverse life events and breast cancer. Other studies have found no association. *BMJ* 1996;312(7034):845.
5. McGee R, Williams S, Elwood M. Are life events related to the onset of breast cancer? *Psychol Med* 1996;26:441–7.
6. Burke MA, Goodkin K. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1997;79(5):1055–9.
7. Faragher MG, Cooper CL. "Are life events related to the onset of breast cancer?" *Psychol Med* 1997;27(2):497–8.
8. Temoshok L. Personality, coping style, emotion and cancer: toward an integrative model. *Cancer Surv* 1987;6:545–67.

9. Hahn RC, Petitti DB. Minnesota Multiphasic Personality Inventory-Rated Depression and the incidence of breast cancer. *Cancer* 1988;61:845-8.
10. Bleiker EM, van der Ploeg HM, Hendriks JH, Ader HJ. Personality factors and breast cancer development: a prospective longitudinal study. *J Natl Cancer Inst* 1996;88(20):1478-82.
11. Kreitler S, Chaitchik S, Kreitler H. Repressiveness: cause or result of cancer? *Psychooncology* 1993;2:43-54.
12. Edwards JR, Cooper CL, Pearl SG, de Paredes ESO, Leary T, Wilhelm MC. The relationship between psychosocial factors and breast cancer: some unexpected results. *Behav Med* 1990;16(1):5-14.
13. Morris T, Greer S, Pettingale KW, Watson M. Patterns of expression of anger and their psychological correlates in women with breast cancer. *J Psychosom Res* 1981;25(2):111-7.
14. Anagnostopoulos F, Vaslamatzis G, Markidis M, Katsouyanni K, Vassilaros S, Stefanis C. An investigation of hostile and alexithymic characteristics in breast cancer patients. *Psychother Psychosom* 1993;59(3-4):179-89.
15. Grassi L, Cappellari L. State and trait psychological characteristics of breast cancer patients. *New Trends Exp Clin Psychiatry* 1988;IV-N:2:99-109.
16. Greer S, Morris T. Psychological attributes of women who develop breast cancer: a controlled study. *J Psychosom Res* 1975;19(2):147-53.
17. Scherg H, Cramer I, Blohrnk M. Psychosocial factors and breast cancer: a critical reevaluation of established hypotheses. *Cancer Detect Prev* 1981;4:165-71.
18. Faragher EB, Cooper CL. Type A stress prone behaviour and breast cancer. *Psychol Med* 1990;20(3):663-70.
19. Fox CM, Harper AP, Hyner GC, Lyle RM. Loneliness, emotional repression, marital quality, and major life events in women who develop breast cancer. *J Community Health* 1994;19(6):467-82.
20. Cheang A, Cooper CL. Psychosocial factors in breast cancer. *Stress Med* 1985;1:61-6.
21. Watson M, Pettingale KW, Greer S. Emotional control and autonomic arousal in breast cancer patients. *J Psychosom Res* 1984;28(6):467-74.
22. Andrews G, Singh M, Bond M. The Defense Style Questionnaire. *J Nerv Ment Dis* 1993;181(4):246-56.
23. American Psychiatric Association. Diagnostic and statistical manual of mental disorders III. Revised (DSM-III-R). Washington, DC: American Psychiatric Association, 1987.
24. Craig A, Franklin J, Andrews G. A scale to measure locus of control of behaviour. *Br J Med Psychol* 1984;57:173-80.
25. Bleiker EM, van der Ploeg HM, Hendriks JH, Leer JW, Kleijn WC. Rationality, emotional expression and control: psychometric characteristics of a questionnaire for research in psycho-oncology. *J Psychosom Res* 1993;37(8):861-72.
26. Watson M, Greer S. Development of a questionnaire measure of emotional control. *J Psychosom Res* 1983;27(4):299-305.
27. Spielberger CD. State-Trait Anger Expression Inventory, STAXI. Professional manual. Odesa, FL: PAR, 1988.
28. Rosenberg M. Society and the adolescent self-image. Princeton, NJ: Princeton University Press, 1965.
29. Spielberger CD, Jacobs GA, Crane RS, Russell SF, Westberry L, Barker L, et al. Preliminary manual for the State-Trait Personality Inventory (STPI). University of South Florida, Tampa, FL: Human Resources Institute, 1979.
30. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;67:361-70.
31. Price MA, Tennant CC, Smith RC, Butow PN, Kennedy SJ, Kossoff MB, et al. Predictors of breast cancer in women recalled following screening. *Aust N Z J Surg* 1999;69:639-46.
32. Morris T, Greer S. Psychological characteristics of women electing to attend a breast screening clinic. *Clin Oncol (R Coll Radiol)* 1982;8(2):113-9.
33. Barraclough J. Life events and the outcome of breast cancer. In: Lewis CE, O'Sullivan C, Barraclough J, editors. The psychoneuroimmunology of cancer: mind and body in the fight for survival? Oxford: Oxford University Press, 1994:213-27.
34. Kelsey JL, Gammon MD, John EM. Reproductive factors and breast cancer. *Epidemiol Rev* 1993;15(1):36-47.
35. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data from 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. *Lancet* 1997;350:1047-59.
36. Fox BH. Premorbid psychological factors as related to cancer incidence. *J Behav Med* 1978;1(1):45-133.
37. Fox BH. The role of psychological factors in cancer incidence and progression. *Oncology* 1995;9(3):245-53.

The Role of Psychosocial Factors in the Development of Breast Carcinoma: Part II

Life Event Stressors, Social Support, Defense Style, and Emotional Control and Their Interactions

Melanie A. Price, B.Sc. (Hons)¹
Christopher C. Tennant, M.D.¹
Phyllis N. Butow, Ph.D.¹
Ross C. Smith, M.D.²
Susan J. Kennedy, M.A.¹
Marjorie B. Kossoff, M.D.³
Stewart M. Dunn, Ph.D.¹

¹ Department of Psychological Medicine, University of Sydney, Royal North Shore Hospital, St. Leonards, New South Wales, Australia.

² Department of Surgery, University of Sydney, Royal North Shore Hospital, St. Leonards, New South Wales, Australia.

³ BreastScreen NSW, Royal North Shore Hospital, St. Leonards, New South Wales, Australia.

See also accompanying article on pages 679–85, this issue.

Data were presented in abstract form at the 5th World Congress in Psycho-Oncology, Melbourne, Australia, September 3–7, 2000.

Supported by the National Health and Medical Research Council of Australia.

Address for reprints: Melanie Price, B.Sc. (Hons), Department of Psychological Medicine, University of Sydney, Royal North Shore Hospital, St. Leonards, New South Wales, Australia; Fax: (011) +61 2 9926-7730; E-mail: melaniep@mail.med.usyd.edu.au

Received October 13, 2000; accepted October 13, 2000.

© 2001 American Cancer Society

BACKGROUND. The evidence supporting an association between life event stress and breast carcinoma development is inconsistent.

METHODS. Five hundred fourteen women requiring biopsy after routine mammographic breast screening were interviewed using the Brown and Harris Life Event and Difficulties Schedule. Other psychosocial variables assessed included social support, emotional control, and defense style. Biopsy results identified 239 women with breast carcinoma and 275 women with benign breast disease. Multiple logistic regression analysis was used to distinguish between breast carcinoma subjects and benign breast disease controls based on these psychosocial variables and their interactions.

RESULTS. The findings of the current study revealed a significant interaction between highly threatening life stressors and social support. Women experiencing a stressor objectively rated as highly threatening and who were without intimate emotional social support had a ninefold increase in risk of developing breast carcinoma.

CONCLUSIONS. Although there was no evidence of an independent association between life event stress and breast carcinoma, the findings of the current study provided strong evidence that social support interacts with highly threatening life stressors to increase the risk of breast carcinoma significantly. [See also accompanying article on pages 679–85, this issue.] *Cancer* 2001;91:686–97.

© 2001 American Cancer Society.

KEYWORDS: breast neoplasms, emotions, life change events, personality, social support, stress, psychologic.

Renewed debate regarding the association between stress and the development of breast carcinoma has coincided with the recent publication of three studies, two of which report a significant association between antecedent life events and breast carcinoma and a third that found no association.^{1–3} The series of commentaries concerning the topic of stress and the development of breast carcinoma also reflect the inconsistency of research findings.^{4–8} Assessments of existing findings include the opinion that stress or other emotional factors play a “relatively minor” role in the etiology of breast carcinoma,⁴ that the question is clinically insignificant,⁵ that major life events in the presence of other psychosocial factors increase the risk of breast carcinoma,⁶ and that an adequate test of the hypothesis has yet to be performed.^{7,8} Despite this, there is widespread belief in the community that stress is a risk factor for cancer,⁹ in particular breast carcinoma.^{9,10}

Population-based studies examining widowhood and divorce have found no association with breast carcinoma.^{11,12} Early childhood losses or separation from parents also have been studied, with some studies reporting no increased risk of breast carcinoma¹³ whereas others report a significantly higher risk of cancer (including breast carcinoma) in individuals who have experienced such events.¹⁴

The majority of life event studies have used event checklists, an approach prone to underreporting of events, bias by mood state,^{15,16} and "insensitivity" due to lack of specificity and contextual details.¹⁷ It therefore is not surprising that studies using this approach have yielded mixed results: four negative findings,^{2,18-20} three positive findings,^{3,21,22} and two cases in which the breast carcinoma group experienced significantly less stress than the control group.^{23,24}

Use of the Life Events and Difficulties Schedule (LEDS)²⁵ to assess life event stress objectively has produced somewhat more consistent results. This interview enables precise event definition and encompasses contextual information in independent ratings of event severity. Two studies have reported that recent events rated as the highest category of severity of threat were reported to occur two to three times more often in women diagnosed with breast carcinoma than in those women with benign breast disease.^{1,16} However, a recent study using this approach failed to replicate these findings.²⁶

However, the study of life events alone may be a somewhat incomplete approach. It may be that life event stressors, when examined in conjunction with vulnerability factors such as coping style, emotional and behavioral patterns, and social support, will enable the relative impact of components of psychosocial "stress" to be teased apart.^{8,27} To our knowledge only a few studies reported to date have assessed these multiple factors;^{1,16,19,28} this perhaps is due to the large samples required for sufficient power with which to assess the interaction of these psychosocial variables adequately.

A significant weakness in this area of research is the essentially atheoretic approach to examining clearly interrelated psychosocial concepts in a multifactorial disease such as breast carcinoma, despite models being available.²⁹ Both Greer and Watson³⁰ and Temoshok³¹ described a cancer prone personality that is believed to predispose an individual to developing cancer. This personality is related to stress, and purported to be maladaptive under conditions of prolonged or severe stress, increasing rather than reducing the impact of stressors^{30,31}; however, life event stress and personality rarely are considered together.

Based on existing evidence, Hilakivi-Clarke et al. outlined a comprehensive model in which life event stress, personality, and social support influenced an individual's ability to cope, which in turn mediated breast carcinoma risk via alterations in neuroendocrine and immune functioning.³² The crucial factor in this model is not the stressor, but the complex interaction between stressors, personality, and social support that affect an individual's ability to cope. This model is compatible with more general models of stress and illness.¹⁷ In the Brown and Harris model,¹⁷ life events are conceptualized as provoking agents for illness, are influenced by specific vulnerability factors such as social support, and are proposed to increase the impact of life events and consequently the resulting stress and strain.

Although the potential benefits of social support on health, quality of life, and immunity are well established,³³⁻³⁵ consideration of the role of social support in breast carcinoma generally has focused on its ability to mitigate the impact of diagnosis, adjustment to illness, and prognosis.³⁶⁻⁴¹

To our knowledge, only a few studies to date have considered social support in relation to the development of breast carcinoma. Using an unspecified self-report measure of social support, Bleiker et al. reported no association with breast carcinoma.⁴² Cooper et al.²⁸ and Edwards et al.¹⁹ reported no differences in the number of social supports available in a crisis between breast carcinoma cases and controls. In what to our knowledge is one of the few studies in this research area with a theoretic basis, the Brown and Harris model was used to examine the modifying effect of social support on stressful life events in the development of breast carcinoma.^{15,16} However, a high correlation between "lack of social support" and "life events" precluded the inclusion of support in the model. To overcome the difficulty of assessing the components of stress, Tennant et al. suggested that stress-related variables such as life events, social support, personality, and coping should be assessed as distinct concepts.⁴³

The aim of the current study was to examine the role of antecedent life stressors, together with psychosocial "vulnerability" factors including social support, coping style, and emotional control, in the diagnosis of breast carcinoma in asymptomatic women attending a community-based mammographic breast carcinoma screening program. This study design was chosen to minimize selection bias and enabled assessment to be performed with both subjects and researchers blind to disease status.

MATERIALS AND METHODS

Subjects

Eligible subjects were asymptomatic women requiring fine-needle biopsy for the diagnosis of breast disease after routine breast screening. Women attending the Northern Sydney and Lower Central Coast Breast Screening Program between April 1994 and April 1997 and who were recalled on radiologic grounds were invited to participate in research examining the psychosocial factors in the development of breast carcinoma. Participation involved completing a self-report questionnaire. Life event stress and social support details were collected by personal interview. The ideal of interviewing all subjects was not feasible; instead, a subset of the sample, those women undergoing breast biopsy, were selected for interview. This group shared similar conditions of testing and were expected to experience similar apprehension prior to diagnosis. The current study focuses on interview and questionnaire data from women undergoing biopsy.

The inclusion criteria were: 1) undergoing breast biopsy after routine breast screening; 2) age \geq 40 years; and 3) adequate command of English. The exclusion criteria were: 1) prior history of breast carcinoma; 2) breast symptoms prompting screening; 3) knowledge of results of biopsy; and 4) physical or psychiatric impairment inhibiting completion of the questionnaire and/or the interview.

Procedure

The complete assessment procedure, from mammography to ultrasound, physical examination, and biopsy, usually occurred on the same day. On arrival at the clinic, consenting women completed a self-administered questionnaire while waiting for assessment. After consenting to the biopsy procedure, subjects were interviewed prior to their test results being available. Approval for the study was granted by the Royal North Shore Hospital Medical Research Ethics Committee.

Measures

Demographic and somatic risk factor variables were collected by self-report and included age, marital status, education, employment, family history of breast carcinoma, history of benign breast disease, parity, age at the birth of the first child, lactation, menopausal status, age at the onset of menopause, oral contraceptive use, use of hormone replacement therapy, height, weight, and alcohol and cigarette consumption.

Self-report psychologic questionnaires assessed features of Temoshok's "cancer prone personality."³¹ Emotion-focused coping was assessed using the DSQ-

40, yielding scores for mature, immature, and neurotic defense styles.⁴⁴ Problem-focused coping was assessed by the Locus of Control of Behaviour (LCB) scale yielding a single factor reflecting internal/external locus of control.⁴⁵ The Emotional Expression and Control (EEC) scale measured the expression and control of anger, anxiety, and depression resulting in three factor scores: emotional expression-in, emotional expression-out, and emotional control.⁴⁶ Rosenberg's Self-Esteem scale measured the self-acceptance aspect of self-esteem.⁴⁷ Trait anxiety was assessed using the State-Trait Personality Inventory (STPI).⁴⁸ State anxiety and state depression was assessed using the Hospital Anxiety and Depression (HAD) scale.⁴⁹ Detailed analysis of these data were reported separately.

An abbreviated version of the Henderson Social Support Interview Schedule was administered to assess social support.⁵⁰ Independent ratings of intimate and nonintimate support for both emotional and instrumental support were made to reflect availability and quality. Ratings were made on a three-point scale (poor, adequate, and good), in which a "good" rating reflected support generally available and comforting, an "adequate" rating reflected support available but with some form of restriction, and a "poor" rating reflected limited availability and/or uncertainty in the quality of support. Subjective appraisal of support also was recorded using this three-point scale and subjective evaluation of change in support during the past 2 years was recorded (better, worse, and no change).

The Bedford College LEDS²⁵ was used to collect details regarding life stressors occurring during the previous 2 years. This semistructured interview allows details of life stressors and the context in which they occurred to be recorded. A vignette of each subject's personal circumstances and stressors was presented to independent raters, without reference to the subject's emotional responses or diagnosis. Of prime interest in this study was the ongoing impact of stressors reflected in the ratings of long-term "threat."

Long-term threat defines the degree of impact of a stressor 1 week after the occurrence. The severity of long-term threat was rated for each stressor on a five-point scale. Ratings were based on the criteria described and detailed examples provided by the authors of the schedule, with the addition of categories (none and extreme) to allow further distinction of stressors at the extremes. For example, the death of a spouse or child would be rated at the highest level of threat (extreme) and the death of an elderly parent living in the same home would be rated a degree lower (severe), whereas the death of a parent-in-law not living in the same home but with regular contact

would be rated another degree lower (highly threatening).

A distinction was made according to the duration of the stressor. Stressors were regarded as acute if < 6 months in duration and chronic if they continued for ≥ 6 months. Both acute and chronic stressors were categorized according to type (health of self, health of others, death, role/interaction, crisis/news, employment, financial, marital, and miscellaneous).

Training of the interviewers and raters for this study was conducted by an expert in the field (C.T.). Interviews were conducted prior to results being available to either the subject or interviewer. The content of the interviews were rated independently with both the interviewer and rater blind to the disease status of the women. Interrater reliability for this study was 0.92.

The choice of time frame for the assessment of stressors involved a difficult balance between the time period during which the impact of stressors is believed to influence tumor development and that of optimizing reliability in recalling life event stressors. The time from etiology to the early detection of breast carcinoma is difficult to determine, but has been approximated at 18 years.⁵¹ The majority of reports suggesting a relation between life event stressors and the diagnosis of breast carcinoma refer to a relatively short time frame, most commonly between 2–5 years, suggesting that any impact of stressors would be related to promoting tumor growth. Accuracy of recall using the checklist approach to examining life events rapidly decreases over 6 months, particularly for less severe events, although the most severe events are least affected.⁵² However, using the LEDS approach, the decrease in the reporting of events is approximately 5% per year and is similar for severe and nonsevere events.¹⁷ Given these data, a 2-year time frame for life events in our asymptomatic sample approximates the longer recall period of symptomatic women in previous studies, and ensures a high degree of reliability in recall.

Diagnosis of Breast Carcinoma

The diagnosis of breast carcinoma was confirmed by histopathologic results of breast tissue biopsy. Those women without malignancy were classified as benign controls.

Statistical Analysis

Data were analyzed using logistic regression to distinguish between subjects with breast carcinoma and control subjects with benign breast disease. Age was included as a confounder in all analyses. The final model included other confounders selected on both

statistical and theoretic grounds.⁵³ All variables were entered simultaneously. Results were reported in terms of the Wald statistic, odds ratio (OR), and 95% confidence intervals (95% CI). Variables initially were examined as "main effects." Interaction between the main effect variables were examined regardless of the individual significance of each main effect. All analyses were performed using SPSS for Windows (SPSS Inc., Chicago, IL). Correlations are reported as Pearson's r (two-tailed) for continuous variables and Spearman's ρ (two-tailed) for categorical variables.

RESULTS

Sample Characteristics

Of 2821 women recalled for assessment on radiologic grounds after routine breast screening, 848 underwent needle biopsy and were invited to participate in this part of the study. One hundred eight women (12.7%) declined to participate and an additional 48 women who initially agreed to participate later declined to be interviewed (6%), representing a response rate of 81.6%. Of the 692 women participating, 176 (25.4%) were unable to be interviewed for logistical reasons including the preliminary biopsy results being given to the subject prior to the interview, the subject leaving the clinic while the other subjects were being interviewed, and no private space being available for the interview to be conducted. Five hundred sixteen women were interviewed prior to biopsy results being available. One woman who was diagnosed with lymphoma and one woman whose final diagnosis was outstanding were excluded from analyses. Interview data were available for 239 women who later were confirmed to have breast carcinoma (46.5%) and 275 women who were diagnosed with benign breast disease (53.5%). Of all the women requiring biopsy after breast screening during 1994–1996 inclusive, 47.2% were diagnosed with breast carcinoma, suggesting our sample is representative of our region. The benign to malignant biopsy ratio was consistent with other screening programs.^{54–57}

The mean age of the breast carcinoma group was 61.3 years (standard deviation [SD] of 9.4), which was significantly older than benign controls, who had a mean age of 57.0 years (SD of 9.8), giving an OR of 1.05 (95% CI, 1.03–1.07). No differences were detected based on marital status, occupational status, family history of breast carcinoma, history of benign breast disease, parity, age at menopause, or obesity. There were increased odds of breast carcinoma with increasing level of education, increasing age at first birth for parous women, being postmenopausal, ever use of oral contraceptives, current use of hormone replace-

ment therapy, and daily alcohol consumption (Table 1).

Acute Stressors

Our first hypothesis was that there was a threshold at which acute stressors may trigger or at least promote tumor growth. This being the case, we expected that significantly more women diagnosed with breast carcinoma would have experienced a highly threatening acute stressor compared with benign controls. One thousand four hundred fifty-three acute stressors were recorded in the 2-year period prior to biopsy. The mean number of acute stressors experienced was 2.82 for the breast carcinoma group and 2.84 for the benign group (OR = 1.04; 95% CI, 0.94–1.16). Table 2 shows the numbers of subjects reporting acute stressors according to severity ratings for long-term threat. More of the women in the breast carcinoma group did report an acute stressor that was rated as extremely threatening (4.6%) compared with the benign group (2.9%), although, after adjusting for age, the difference failed to reach statistical significance (OR = 1.06; 95% CI, 0.37–3.02). Combining stressors rated as extremely and severely threatening for long-term threat, the percentage of women experiencing such stressors was similar across groups (OR = 0.89; 95% CI, 0.49–1.62). The numbers of women experiencing an acute stressor rated as being of high, moderate, and mild degree of threat also were similar across the groups.

Testing the hypothesis that the type rather than the severity of an acute stressor was more important (for example bereavement rather than employment), we proposed that women diagnosed with breast carcinoma would have experienced more bereavements prior to diagnosis compared with benign controls. However, there were no significant differences between the groups with regard to any of the 10 categories of acute stressors reported and, specifically, the number of women widowed in the previous 2 years was not significantly different across the 2 groups.

Chronic Stressors

Examining the possibility that chronic stressors were more important in promoting tumor growth, we hypothesized that women diagnosed with breast carcinoma would have more chronic stressors and more threatening stressors prior to diagnosis compared with benign controls. We recorded 852 chronic difficulties impacting on the past 2 years, with no group differences detected in number (OR = 1.08; 95% CI, 0.94–1.24). Chronic stressors in the highest two severity ratings of long-term threat were rare and similar across groups (Table 3). Women with breast carcinoma did report significantly more chronic stressors

in the lowest (mildly threatening) severity group (OR = 1.72; 95% CI, 1.19–2.49); however, the benign group reported more chronic stressors in both the moderate and high severity ratings, albeit a nonsignificant difference. The most common chronic stressor reported were related to the women's own health and there were no differences in the types of chronic stressors reported between the groups.

Cumulative Stressors

We examined a model of stress that proposed a cumulative impact of life stressors, hypothesizing that women diagnosed with breast carcinoma would have experienced more cumulative stress than women with benign breast disease. To test this theory, we calculated scores to estimate cumulative degree of stressors, separately for acute and chronic stressors as well as a combination of acute and chronic stressors. Each stressor was allocated a weight according to its severity rating, and the weighted scores were totaled. Weightings of stressors were assigned according to Brown et al.⁵⁸ Stressors rated as mild or nonthreatening were weighted zero. Extreme stressors were weighted 5, severe stressors were weighted 4, high stressors were weighted 3, and moderate stressors were weighted 1. No differences were noted with regard to weighted acute, weighted chronic, or weighted combined stressors scores (Table 4).

Vulnerability Factors

Despite finding no evidence of an independent effect for life stressors, we proceeded to examine the effect of other psychosocial factors that we hypothesized would impact on the development of breast carcinoma through their interaction with life stressors. The "vulnerability factors" proposed in our model were a less mature coping style, higher emotional control, and poor emotional social support.

Full analysis of psychologic questionnaire data is reported separately. Selected variables, namely mature defense style and emotional control, are hypothesized in the current study as vulnerability factors, increasing or decreasing the impact of life event stress, without individual etiologic significance.^{16–25} These variables are summarized in Table 5. There were no significant differences detected between groups based on scores of mature defense style or emotional control.

Although breast carcinoma subjects reported "no intimate emotional support" (29.3%) slightly more often than control subjects (24.7%), after adjusting for age the differences were not found to be significant (OR = 0.87; 95% CI, 0.57–1.34). For those who did have an intimate social support system, the groups were

TABLE 1
Demographic and Risk Factor Variables for Breast Carcinoma

Variable	Benign disease (n = 275) No. (%)	Breast carcinoma (n = 239) No. (%)	Odds ratio 95% CI (age-adjusted)
Mean (SD) age (yrs)	57.0 (9.8)	61.3 (9.4)	1.05 (1.03-1.07)
Education			
Primary	14 (5.2)	7 (3.0)	1-
3-4 years secondary	109 (40.7)	86 (36.6)	1.98 (0.74-5.30)
5-6 years secondary	41 (15.3)	41 (17.4)	2.46 (0.87-7.00)
Diploma/certificate	68 (25.3)	58 (24.7)	2.67 (0.96-7.43)
University/college	36 (13.4)	43 (18.3)	3.78 (1.31-10.91)
Marital status			
Married/defacto	189 (70.3)	156 (66.4)	1-
Single	20 (7.4)	15 (6.4)	0.74 (0.38-1.52)
Widowed	27 (10.0)	36 (15.3)	0.93 (0.51-1.70)
Divorced/separated	33 (12.3)	28 (11.9)	0.97 (0.55-1.70)
Age at birth of first child			
Nulliparous	44 (17.3)	31 (14.1)	1-
< 20 yrs	10 (3.9)	7 (3.2)	1.40 (0.46-4.22)
20-24 yrs	84 (33.1)	47 (21.4)	0.88 (0.48-1.60)
25-29 yrs	72 (28.3)	84 (38.2)	1.77 (1.00-3.15)
30+ yrs	44 (17.3)	51 (14.1)	1.81 (0.96-3.40)
Parity			
Nulliparous	44 (17.1)	31 (13.8)	1-
1-2	113 (44.0)	103 (46.0)	1.55 (0.89-2.69)
3+	100 (38.9)	90 (40.2)	2.31 (0.75-2.28)
Family history			
No	222 (80.7)	188 (78.7)	1-
Diagnosed at age < 50 yrs	11 (4.0)	22 (9.2)	2.14 (0.99-4.61)
Diagnosed at age 50+ yrs	27 (9.8)	16 (6.7)	0.64 (0.33-1.25)
Unknown	15 (5.5)	13 (5.4)	0.96 (0.44-2.11)
H/O benign breast disease			
No	223 (84.5)	188 (83.2)	1-
Yes	41 (15.5)	38 (16.8)	1.14 (0.70-1.87)
Menopausal status			
Premenopausal	83 (30.2)	31 (13.0)	1-
Postmenopausal	192 (69.8)	208 (87.0)	1.85 (1.05-3.25)
Age at onset of menopause*			
< 45 yrs	52 (32.1)	51 (27.9)	1-
46-50 yrs	58 (35.8)	76 (41.5)	1.41 (0.84-2.39)
> 50 yrs	52 (32.1)	56 (30.6)	1.16 (0.67-2.00)
Ever use of oral contraceptives			
No	102 (42.0)	90 (42.3)	1-
Yes	141 (58.0)	123 (57.7)	1.67 (1.08-2.59)
Current use of hormone replacement therapy			
No	194 (74.6)	149 (66.2)	1-
Yes	66 (25.4)	76 (33.8)	1.51 (1.01-2.25)
Alcohol consumption			
None	58 (22.5)	47 (21.1)	1-
Occasional	73 (28.3)	54 (24.2)	1.03 (0.61-1.77)
Weekly	83 (32.2)	42 (18.8)	0.78 (0.45-1.36)
Daily	44 (17.1)	80 (35.9)	2.58 (1.49-4.48)
(BMI)			
< 25	145 (59.7)	111 (52.9)	1
≥ 25	98 (40.3)	99 (47.1)	1.28 (0.87-1.87)

95% CI: 95% confidence interval; SD: standard deviation; H/O: history of; BMI: body mass index.

* Numbers for each variable do not add up to total due to missing values.

TABLE 2
Number of Subjects Reporting at Least 1 Acute Stressor for Each Severity Rating of Long Term Threat in the 2-Year Period Prior to Interview

Severity rating of long term threat for acute stressors (rating)	Benign No. (%)	Breast carcinoma No. (%)	Odds ratio (95% CI)*
Extreme (5)	8 (2.9)	11 (4.6)	1.06 (0.37-3.02)
Severe (4)	24 (8.7)	20 (8.4)	0.95 (0.48-1.87)
High (3)	61 (22.2)	47 (19.7)	0.94 (0.59-1.50)
Moderate (2)	151 (54.9)	115 (48.1)	0.75 (0.51-1.10)
Mild (1)	164 (59.6)	140 (58.6)	1.15 (0.77-1.72)
Extreme/severe (4, 5)	32 (11.6)	28 (11.7)	0.89 (0.49-1.62)
Extreme/severe/high (3, 4, 5)	84 (30.5)	70 (29.3)	0.92 (0.61-1.39)

95% CI: 95% confidence interval.

* Adjusted for age.

TABLE 3
Number of Subjects Reporting at Least 1 Chronic Stressor for Each Severity Rating (Long Term Threat) in the 2-Year Period Prior to Interview

Severity ratings of long term threat for chronic stressors	Benign No. (%)	Breast carcinoma No. (%)	Odds ratio (95% CI)*
Extreme (5)	1 (0.4)	0 (0.0)	
Severe (4)	6 (2.2)	5 (2.1)	1.03 (0.30-3.50)
High (3)	42 (15.3)	24 (10.0)	0.70 (0.41-1.22)
Moderate (2)	110 (40.0)	76 (31.8)	0.77 (0.53-1.13)
Mild (1)	141 (51.3)	159 (66.5)	1.23 (1.04-1.44)

95% CI: 95% confidence interval.

* Adjusted for age.

TABLE 4
Weighted Scores for Acute and Chronic Stressors in the 2-Year Period Prior to Biopsy

Weighted stressor scores	Benign Mean (SD)	Breast carcinoma Mean (SD)	Odds ratio (95% CI)*
Acute stressors	5.09 (4.17)	4.85 (4.01)	1.00 (0.95-1.05)
Chronic stressors	3.29 (3.08)	3.00 (2.90)	0.97 (0.91-1.04)
Acute and chronic stressors	4.38 (5.53)	4.85 (5.19)	0.99 (0.96-1.03)

SD: standard deviation; 95% CI: 95% confidence interval.

* Adjusted for age.

comparable in terms of the quality of this support (Wald chi-square (2) = 0.09, $P = 0.96$). Nonintimate support ratings generally were good, with similar percentages of adequate ratings across the groups. It is interesting to note that more of the benign group reported having poor or no nonintimate support, al-

though the numbers were small in this category and overall this variable was found to be nonsignificant (Wald chi-square (2) = 6.68; $P = 0.35$). There were no differences in subjective ratings of support (Wald chi-square (2) = 4.03; $P = 0.13$) or in recent changes in the subjective quality of support available (Wald chi-square (2) = 1.04; $P = 0.59$).

Interactions

For the examination of interactions between life stressors and these other psychosocial factors, acute and chronic stressors were considered together to increase the power of these analyses. Therefore the term "major stressor" in these analyses was used to identify subjects reporting at least one acute or chronic stressor rated as either severe or extreme for long-term threat in the previous 2 years. Experiencing a major stressor was correlated with intimate emotional support (chi-square (2) = 10.3; $P = 0.01$), but was not correlated with mature defense style ($\rho = -0.04$; $P = 0.38$) or emotional control ($\rho = 0.08$; $P = 0.06$).

The results of interactions between vulnerability factors and a major stressor on breast carcinoma risk are summarized in Table 6. There was no evidence that a less mature defense style (Wald chi-square(1) = 2.23; $P = 0.14$) or higher emotional control (Wald chi-square(1) = 0.02; $P = 0.90$) were interacting with the impact of a major stressor on the development of breast carcinoma.

However, there was a significant interaction between a major stressor and intimate emotional support (Wald chi-square (2) = 10.19; $P = 0.006$). For subjects who had experienced a major stressor within the past 2 years, those rated as having "no intimate emotional support" had an age-adjusted OR for breast carcinoma of 7.46 (95% CI, 1.84-30.22) compared with those rated as having "good" intimate emotional support. Of note, only 26 subjects (5.1% of sample) were in this category, 19 (73.1%) of whom were diagnosed with breast carcinoma. Of the subjects who had experienced a major stressor, those rated as having "poor or adequate" intimate emotional support were not found to be significantly different from those rated as having good intimate emotional support in the OR for breast carcinoma (OR = 1.15; 95%CI, 0.28-4.70).

We hypothesized that mature defense style and/or emotional control may be important in the face of a major stressor when no social support was available. However, we found no evidence to support these higher order interactions (Table 6).

Potential Confounders

A number of variables were considered to be potential confounders for inclusion in the multivariate model

TABLE 5
Descriptives for Vulnerability Factors, Wald Statistic, Odds Ratios, and Corresponding 95% CI

	Benign Mean (SD)	Breast carcinoma Mean (SD)	Wald chi-square (χ^2)	Odds ratio (95% CI) ^a
Mature defense style	6.26 (1.10)	6.44 (1.05)	$\chi^2(1) = 1.82$ (<i>P</i> = 0.18)	1.12 (0.95-1.32)
Emotional control	15.72 (3.86)	15.87 (3.53)	$\chi^2(1) = 0.48$ (<i>P</i> = 0.49)	0.98 (0.94-1.03)

	Benign No. (%)	Breast carcinoma No. (%)	Wald chi-square (χ^2)	Odds ratio (95% CI) ^a
Intimate emotional support			$\chi^2(3) = 0.46$ (<i>P</i> = 0.93)	
Good	130 (47.3)	110 (46.0)		1-
Adequate	45 (16.4)	35 (14.6)		0.95 (0.56-1.60)
Poor	32 (11.6)	24 (10.0)		0.93 (0.51-1.69)
None	68 (24.7)	70 (29.3)		0.86 (0.54-1.38)
Nonintimate emotional support			$\chi^2(2) = 6.68$ (<i>P</i> = 0.35)	
Good	227 (82.5)	208 (87.0)		1-
Adequate	31 (11.3)	29 (12.1)		1.07 (0.61-1.85)
Poor/none	17 (6.2)	2 (0.8)		0.14 (0.03-0.63)

95% CI: 95% confidence interval; SD: standard deviation.
^a Adjusted for age.

TABLE 6
Wald Chi-Square Statistic, Odds Ratios, and Corresponding 95% CI for Interaction Terms between Vulnerability and Major Stressor Variables Predicting Breast Carcinoma Diagnosis

Interaction terms ^a	Wald chi-square (χ^2) (df)	Odds ratio (95% CI) ^b
Stressor X, mature defense style	$\chi^2(1) = 2.23, P = 0.14$	1.57 (0.87-2.82)
Stressor X, emotional control	$\chi^2(1) = 0.02, P = 0.90$	1.01 (0.87-1.17)
Stressor X, intimate social support rating	$\chi^2(2) = 10.2, P < 0.006$	
X Good intimate support		1-
X Poor/adequate intimate support		1.15 (0.28-4.70)
X No intimate support		7.46 (1.84-30.22)
Stressor X, mature defense style X social support	$\chi^2(2) = 0.18, P = 0.91$	
Stressor X, emotional control X social support	$\chi^2(2) = 0.49, P = 0.78$	

95% CI: 95% confidence interval; df: degree of freedom.
^a Each interaction term tested by adding to the main effects only model.
^b Age adjusted.

for psychosocial predictors of breast carcinoma. Among sociodemographic and medical variables, age and education were treated as confounding variables, being associated with both stressor variables and with breast carcinoma. Also included were a family history of breast carcinoma, a history of benign breast dis-

ease, age at the onset of menopause, age at birth of the first child, parity, oral contraceptive use, current use of hormone replacement therapy, body mass index, and alcohol consumption. These were chosen based on statistical and empiric grounds.⁵³

Although age was included as a potential confounder, there still was some concern that the impact of age was not controlled adequately.⁷ We hypothesized that age may have affected the likelihood of experiencing certain types or severity of stressors. Analyses were repeated separately on 271 women age < 60 years and on 243 women age ≥ 60 years. No differences were noted between the breast carcinoma group and benign controls in each age group, in severity of events and difficulties reported, or in the cumulative stressor scores.

Of trait personality variables examined (locus of control, emotional expression and control, defense style, self-esteem, and trait anxiety) and their subfactors, none were found to be associated independently with breast carcinoma or with life event variables and therefore these were excluded as confounders. Higher state anxiety was associated with the number of chronic stressors reported ($\rho = 0.16; P < 0.001$) but not the number of acute stressors (*P* = 0.26) or severity of stressors (*P* = 0.16), suggesting that anxiety was due to ongoing stressors rather than anxiety influencing the reporting of stressors generally. With no group

TABLE 7
Final Multiple Logistic Regression Model for Predictors of Breast Carcinoma

Term	β (SE)	Wald chi-square (χ^2) (df), P value	Odds ratio (95% CI)*
Stressor	-0.66 (0.50)	$\chi^2(1) = 1.31$	0.52 (0.17-1.60)
Intimate emotional support		$\chi^2(2) = 1.52$	
Good			1-
Poor/adequate	-0.04 (0.27)		0.96 (0.57-1.64)
None	-0.35 (0.29)		0.70 (0.39-1.25)
Stressor X, intimate emotional support		$\chi^2(2) = 11.27$, P = 0.004	
+ Stressor X, good support			1-
+ Stressor X, poor/adequate support	-0.21 (0.81)		1.03 (0.22-4.67)
+ Stressor X, no intimate support	2.24 (0.82)		9.39 (1.90-46.42)

SE: standard error; df: degrees of freedom; 95% CI: 95% confidence interval.

* Includes main effects of age, education, age at menopause, family history of breast carcinoma, history of benign breast disease, age at birth of first child, parity, body mass index, frequency of alcohol consumption, oral contraceptive use, use of hormone replacement therapy, state depression, and nonintimate emotional support.

differences in levels of state anxiety, it was excluded as a confounder.

State depression scores, although not associated with the number of acute or chronic stressors, were associated with stressors in the highest 2 categories of threat ($\rho = 0.14$; $P = 0.002$); therefore state depression was treated as a potential confounder, despite not being associated with breast carcinoma. Nonintimate social support also was considered as a likely confounder, given the significance of intimate emotional support and the trend toward the control group to have poorer levels of nonintimate support, albeit a nonsignificant difference.

The results of the multiple logistic regression model of psychosocial predictors of breast carcinoma, including as potential confounders age, education, age at the onset of menopause, family history of breast carcinoma, history of benign breast disease, age at birth of the first child, parity, body mass index, alcohol consumption, oral contraceptive use, use of hormone replacement therapy, state depression, and nonintimate social support, are presented in Table 7. The OR for breast carcinoma for subjects reporting a major stressor in the past 2 years with no intimate emotional support was 9.39 (95%CI, 1.90-46.42).

DISCUSSION

The results of the current study revealed a significant increase in the development of breast carcinoma for

women reporting a recent stressor independently rated at the highest levels of threat, but only for those without any intimate emotional support. (An intimate support refers to a partner in life, as opposed to close friend or family). The effect size for this specific group increased somewhat after adjustment for potential confounders including age, education, menopausal status, family history, history of benign breast disease, body mass index, reproductive history, alcohol consumption, oral contraceptive use, use of hormone replacement therapy, and depression, and was in the order of a ninefold increase in risk.

In contrast to past findings, we found no evidence of an independent association between recent life stressors and the development of breast carcinoma. Using the same method of assessing life event stress, both Geyer^{15,16} and Chen et al.¹ reported a significant increase in the risk of breast carcinoma after severely threatening life event stressors. The LEDS interview employed in these studies is a well established, reliable, and comprehensive instrument, enabling independent rating of stressors according to precise definitions and encompassing contextual information.

Despite similarities in designs, the current study does vary from the earlier studies in a number of ways. The population from which our sample was drawn is more homogeneous, being community-based, asymptomatic, and recalled for assessment purely on radiologic grounds. Other studies have used symptomatic women who were assessed by their primary physician and referred for biopsy from multiple sources and for varied reasons. The possibility that "awareness" of their diagnosis affected the reporting of psychosocial variables in the current study is minimal.

As a consequence of targeting a population screened by mammography, our sample were "older"; our breast carcinoma group had an average age of 61 years and the current study controls had an average age of 57 years. The Geyer¹⁶ breast carcinoma group had a mean age of 49 years and the controls had a mean age of 43 years; in the study by Chen et al.¹ the breast carcinoma group had an average age 57 years and the controls had a mean age of 50 years. Although our 2 groups were significantly different with regard to age, in real terms the difference was small and considerably less than the 6-7-year age difference in the smaller studies, enabling us to better control for the influence of age.

These differences in the ages of the study participants may be important in reconciling differences in reported outcome. Age is an independent risk factor for breast carcinoma and also is associated with the type and number of life events experienced, as well as social support. Although often included in analyses,

McGee et al.⁷ suggest the effects of age may not be controlled adequately by simple statistical means. This difficulty is most marked in smaller studies with larger ranges in age and it is possible that the independent effects of severely threatening events on the development of breast carcinoma reported by Geyer¹⁶ and Chen et al.¹ may in fact have been confounded by age. It also is possible that different psychosocial factors are influential with increasing age. Thus, age differences in samples may explain inconsistent findings, particularly because it is clearly possible that psychoendocrine factors may be the link between stress and breast carcinoma.

A potential limitation of the current study is the relatively short time period covered in assessing life stressors. This time frame was influenced by a desire to obtain an optimal balance between reliability of recall and the presumed time period of tumor growth. Geyer examined the influence of the time period in which severely threatening events were assessed with regard to breast carcinoma risk and found that both those occurring in the 3-year period prior to interview as well as more distant events were similarly predictive of breast carcinoma risk.¹⁵ Likewise, Chen et al.¹ noted that the average annual rate of severely threatening life events did not vary significantly over the 5-year period examined or differ between the groups. This finding notwithstanding, to our knowledge all studies reported to date in fact most likely assess the effect of stressors on tumor growth.

One strength of the current study is the sample size, which includes what we believe to be the largest series of breast carcinoma cases examined prior to diagnosis in this area of research. We believe the power of our study ensures that the likelihood of missing even a modest association between severely threatening stressors and the development of breast carcinoma is minimal. Our sample size also has enabled multiple variables to be assessed simultaneously (life events, coping style, affect, personality, and social support) and more important, for their interactions to be examined.

The progression to exploring the interaction between distinct but interrelating variables is important in this field of research. Although there was no evidence from the current study data of a direct association between social support, coping style, or emotional control and breast carcinoma, the usefulness of examining these variables without consideration of the external stressors with which an individual is coping is questionable. The current study findings concur with the theory of Brown and Harris that "vulnerability factors" (in the current study, social support, coping style, and emotional control) may have no inde-

pendent significant effect, but impact largely through their interaction with provoking agents such as life stressors.²⁵ This theoretic model also is consistent with Temoshok's model of the cancer prone individual, in which the type C coping style interacts with stressors. Under conditions of severe stress, the effectiveness of this coping style breaks down, producing a greater level of strain.³¹

The importance of coping in moderating the impact of stressors is well established,⁵⁹ although to our knowledge few studies to date have examined coping style in conjunction with life event stress and the development of breast carcinoma. Chen et al.¹ reported that confronting stress increased the risk of developing breast carcinoma, independent of life events. However, to our knowledge there was no mention of this interaction being tested or removed from their final model. In what to our knowledge is the only other study to examine the interaction between life event stress and coping style, no significant differences in the development of breast carcinoma were reported for either of these variables or their interaction.¹⁹ We found no evidence that coping style interacted with the impact of life stress in the development of breast carcinoma. It is possible that our measure of coping was not tapping the appropriate concept.

Although there is some evidence of the tendency to control or suppress negative emotions being associated with the development of breast carcinoma,⁶⁰⁻⁶² some studies have failed to support this notion.^{42,63} With one exception,⁶⁰ to our knowledge emotional control has not been considered previously in conjunction with life event stress, and no studies have explored the relation between these two variables. Again, we found no evidence of a role for emotional control in the development of breast carcinoma, nor did we find evidence of an interaction between emotional control and life event stress.

Our finding of an interaction between severely threatening life events and the absence of social support was somewhat unexpected given the absence of independent effects. However, this finding is not without some precedence.¹⁷ Much of the focus on social support and breast carcinoma has been in relation to its role after diagnosis. To our knowledge the only previous study to consider their interaction in the development of breast carcinoma reported no significant differences between breast carcinoma cases and controls in the number or severity of life events, coping style, or social support or their interactions.¹⁹ The results of the current study provide support for the model described by Hilakivi-Clarke et al.³² that emphasizes the interaction between life events and stress-related variables such as social support in me-

diating breast carcinoma risk. Adding credence to our significant interaction between highly threatening stressors and the absence of intimate emotional support is that these two variables, although not totally independent, were assessed and rated quite independently.⁴³

The current study found no evidence of an independent relation between recent life event stress and the development of breast carcinoma. However, examining the interactions between life event stress and a number of vulnerability factors, we identified a small group of women who were at significantly greater risk of breast carcinoma: those experiencing a highly threatening stressor within the previous 2 years and without any intimate emotional support. This group includes, but is not exclusively comprised of, those women recently widowed or divorced. We found no evidence that other vulnerability factors such as coping style and emotional control interacted with life stressors in the development of breast carcinoma. The current study demonstrates the importance of social support, or the lack thereof, as a specific vulnerability factor for the impact of life event stress in the development of breast carcinoma. Although the results of the current study support a multifactorial view of breast carcinoma development, they also suggest that the role of psychosocial factors in the etiology of breast carcinoma in general is small and specific. Women should be reassured that stress per se does not cause breast carcinoma; however, in the absence of intimate emotional support, situations of severe stress may increase a woman's vulnerability to this disease. Health professionals should be encouraged to identify individuals in circumstances of severe stress and if feasible explore avenues for reducing the stress and promoting the use of available support systems, and encourage the utilization of counseling and other supportive services.

REFERENCES

- Chen CC, David AS, Nunnerley H, Michell M, Dawson JL, Berry H, et al. Adverse life events and breast cancer: case-control study. *BMJ* 1995;311(7019):1527-30.
- Roberts FD, Newcomb PA, Trentham-Dietz A, Storer BE. Self-reported stress and risk of breast cancer. *Cancer* 1996;77(6):1089-93.
- Ginsberg A, Price S, Ingram D, Nottage E. Life events and the risk of breast cancer: a case-control study. *Eur J Cancer* 1996;32A(12):2049-52.
- Cassileth BR. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1996;77(6):1015-6.
- Barraclough J. Adverse life events and breast cancer. Other studies have found no association. *BMJ* 1996;312(7034):845.
- Faragher MG, Cooper CL. "Are life events related to the onset of breast cancer?". *Psychol Med* 1997;27(2):497-8.
- McGee R, Williams S, Elwood M. Are life events related to the onset of breast cancer? *Psychol Med* 1996;26:441-7.
- Burke MA, Goodkin, K. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1997;79(5):1055-9.
- Baghurst KI, Baghurst PA, Record SJ. Public perceptions of the role of dietary and other environmental factors in cancer causation or prevention. *J Epidemiol Community Health* 1992;46:120-6.
- Brinton LA, Malone KE, Liff J, Schoenberg JB. Re: "Should we consider a subject's knowledge of the etiologic hypothesis in the analysis of case-control studies?". *Am J Epidemiol* 1994;140:1054-6.
- Ewertz M. Bereavement and breast cancer. *Br J Cancer* 1986;53:701-3.
- Kvikstad A, Vatten LJ, Tretli S, Kvinnsland S. Death of a husband or marital divorce related to risk of breast cancer in middle-aged women. A nested case-control study among Norwegian women born 1935-1954. *Eur J Cancer* 1994;30A(4):473-7.
- Muslin HL, Gyarfás K, Pieper WJ. Separation experience and cancer of the breast. *Ann N Y Acad Sci* 1966;125(3):802-6.
- Scherg H, Blohmke M. Associations between selected life events and cancer. *Behav Med* 1988;14(3):119-24.
- Geyer S. Life events prior to manifestation of breast cancer: a limited prospective study covering eight years before diagnosis. *J Psychosom Res* 1991;35(2-3):355-63.
- Geyer S. Life events, chronic difficulties and vulnerability factors preceding breast cancer. *Soc Sci Med* 1993;37(12):1545-55.
- Brown GW, Harris TO. Life events and illness. New York: The Guilford Press, 1989.
- Priestman TJ, Priestman SG, Bradshaw C. Stress and breast cancer. *Br J Cancer* 1985;51(4):493-8.
- Edwards JR, Cooper CL, Pearl SG, de Paredes ESO, Leary T, Wilhelm MC. The relationship between psychosocial factors and breast cancer: some unexpected results. *Behav Med* 1990;16(1):5-14.
- Fox CM, Harper AP, Hyner GC, Lyle RM. Loneliness, emotional repression, marital quality, and major life events in women who develop breast cancer. *J Community Health* 1994;19(6):467-82.
- Cheang A, Cooper CL. Psychosocial factors in breast cancer. *Stress Med* 1985;1:61-6.
- Forsen A. Psychosocial stress as a risk for breast cancer. *Psychother Psychosom* 1991;55(2-4):176-85.
- Schonfield J. Psychological and life-experience differences between Israeli women with benign and cancerous breast lesions. *J Psychosom Res* 1975;19(4):229-34.
- Cooper CL, Cooper R, Faragher EB. Incidence and perception of psychosocial stress: the relationship with breast cancer. *Psychol Med* 1989;19(2):415-22.
- Brown GW, Harris TO. Social origins of depression: a study of psychiatric disorder in women. London: Tavistock, 1978.
- Protheroe D, Turvey K, Horgan K, Benson E, Bowers D, House A. Stressful life events and difficulties and onset of breast cancer: case-control study. *BMJ* 1999;319:1027-30.
- George LK. Stress, social support, and depression over the life-course. In: Markides KS, Cooper CL, editors. Aging stress and health. Chichester, England: John Wiley and Sons, 1989: 241-67.
- Cooper CL, Faragher EB. Psychosocial stress and breast cancer: the inter-relationship between stress events, coping strategies and personality. *Psychol Med* 1993;23(3):653-62.

29. Butow PN, Hiller JE, Price MA, Thackway SV, Krickler A, Tennant CC. Epidemiological evidence for a relationship between life events, coping style and personality factors in the development of breast cancer. *J Psychosom Res* 2000;49:169-81.
30. Greer S, Watson M. Towards a psychobiological model of cancer: psychological considerations. *Soc Sci Med* 1985;20(8):773-7.
31. Temoshok L. Personality, coping style, emotion and cancer: toward an integrative model. *Cancer Surv* 1987;6:545-67.
32. Hilakivi-Clarke L, Rowland J, Clarke R, Lippman ME. Psychosocial factors in the development and progression of breast cancer. *Breast Cancer Res Treat* 1993;29(2):141-60.
33. Levy S, Herberman R, Lippman M, d'Angelo T. Correlation of stress factors with sustained depression of natural killer cell activity and predicted prognosis in patients with breast cancer. *J Clin Oncol* 1987;5(3):348-53.
34. Achat H, Kawachi I, Levine S, Berkey C, Coakley E, Colditz G. Social networks, stress and health-related quality of life. *Qual Life Res* 1998;7(8):735-50.
35. Stansfeld SA, Bosma H, Hemingway H, Marmot MG. Psychosocial work characteristics and social support as predictors of SF-36 health functioning: the Whitehall II study. *Psychosom Med* 1998;60(3):247-55.
36. Neuling SJ, Winefield HR. Social support and recovery after surgery for breast cancer: frequency and correlates of supportive behaviours by family, friends and surgeon. *Soc Sci Med* 1988;27(4):385-92.
37. Waxler-Morrison N, Hislop TG, Mears B, Kan L. Effects of social relationships on survival for women with breast cancer: a prospective study. *Soc Sci Med* 1991;33(2):177-83.
38. Ell K, Nishimoto R, Mediansky L, Mantell J, Hamovitch M. Social relations, social support and survival among patients with cancer. *J Psychosom Res* 1992;36(6):531-41.
39. Spiegel D. Effects of psychosocial support on patients with metastatic breast cancer. *J Psychosoc Oncol* 1992;10(2):113-20.
40. Roberts CS, Cox CE, Shannon VJ, Wells NL. A closer look at social support as a moderator of stress in breast cancer. *Health Soc Work* 1994;19(3):157-64.
41. Koopman C, Hermanson K, Diamond S, Angell K, Spiegel D. Social support, life stress, pain and emotional adjustment to advanced breast cancer. *Psychooncology* 1998;7:101-11.
42. Bleiker EM, van der Ploeg HM, Hendriks JH, Ader HJ. Personality factors and breast cancer development: a prospective longitudinal study. *J Natl Cancer Inst* 1996;88(20):1478-82.
43. Tennant C, Langelluddecke P, Byrne D. The concept of stress. *Aust N Z J Psychiatry* 1985;19(2):113-8.
44. Andrews G, Singh M, Bond M. The Defense Style Questionnaire. *J Nerv Ment Dis* 1993;181(4):246-56.
45. Craig A, Franklin J, Andrews G. A scale to measure locus of control of behaviour. *Br J Med Psychol* 1984;57:173-80.
46. Bleiker EM, van der Ploeg HM, Hendriks JH, Leer JW, Kleijn WC. Rationality, emotional expression and control: psychometric characteristics of a questionnaire for research in psycho-oncology. *J Psychosom Res* 1993;37(8):861-72.
47. Rosenberg M. Society and the adolescent self-image. Princeton, NJ: Princeton University Press, 1965.
48. Spielberger CD, Jacobs GA, Crane RS, Russell SF, Westberry L, Barker L, et al. Preliminary manual for the State-Trait Personality Inventory (STPI). University of South Florida, Tampa, FL: Human Resources Institute, 1979.
49. Zigmund AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983;67:361-70.
50. Henderson S, Duncan-Jones P, Byrne DG, Scott R. Measuring social relationships: the Interview Schedule for Social Interaction. *Psychol Med* 1980;10:723-34.
51. Friberg S, Mattson S. On the growth rates of human malignant tumours: implications for medical decision making. *J Surg Oncol* 1997;65(4):284-97.
52. Funch DP, Marshall JR. Measuring life stress: factors affecting fall-off in the reporting of life events. *J Health Soc Behav* 1984;25:453-64.
53. Price MA, Tennant CC, Smith RC, Butow PN, Kennedy SJ, Kossoff MB, et al. Predictors of breast cancer in women recalled following screening. *Aust N Z J Surg* 1999;69:639-46.
54. The Essendon Breast X-ray Program Collaborative Group. A mammographic screening pilot project in Victoria 1988-1990. *Med J Aust* 1992;157(10):670-3.
55. Daures JP, Peray P, Bousquet J, Stoebner A, Gouzes C, Lamarque JL, et al. Mass screening for breast cancer in Herault county. First results in women between 40 and 70 years old. *J Gynecol Obstet Biol Reprod* 1992;21(2):173-8.
56. Thurjell E. Population-based mammography screening in clinical practice. Results from the prevalence round in Uppsala county. *Acta Radiol* 1994;35(5):487-91.
57. Dean PB, Pamilo M. Screening mammography in Finland—1.5 million examinations with 97 percent specificity. Mammography Working Group, Radiological Society of Finland. *Acta Oncol* 1999;38(Suppl 13):47-54.
58. Brown GW, Adler Z, Bifulco A. Life events, difficulties and recovery from chronic depression. *Br J Psychiatr* 1988;152:487-98.
59. Folkman S, Lazarus RS. An analysis of coping in a middle-aged community sample. *J Health Soc Behav* 1980;21:219-39.
60. Greer S, Morris T. Psychological attributes of women who develop breast cancer: a controlled study. *J Psychosom Res* 1975;19(2):147-53.
61. Scherg H, Cramer I, Blohmke M. Psychosocial factors and breast cancer: a critical reevaluation of established hypotheses. *Cancer Detect Prev* 1981;4:165-71.
62. Grassi L, Cappellari L. State and trait psychological characteristics of breast cancer patients. *New Trends Exp Clin Psychiatry* 1988;IV-N.2:99-109.
63. Kretler S, Chaitchik S, Kretler H. Repressiveness: cause or result of cancer? *Psychooncology* 1993;2:43-54.

Appendix XVI: Epidemiological evidence for a relationship between life events, coping style, and personality factors in the development of breast cancer



ELSEVIER

Journal of Psychosomatic Research 49 (2000) 169–181

Journal of
Psychosomatic
Research

Epidemiological evidence for a relationship between life events, coping style, and personality factors in the development of breast cancer

Phyllis N. Butow^{a,*}, Janet E. Hiller^b, Melanie A. Price^a, Sarah V. Thackway^c, Anne Krickler^c, Christopher C. Tennant^a

^aDepartment of Psychological Medicine, Royal North Shore Hospital, and University of Sydney, NWS 2065, Australia

^bDepartment of Public Health, University of Adelaide, Adelaide, Australia

^cNational Breast Cancer Centre of Australia, Sydney, Australia

Received 8 September 1999; accepted 25 April 2000

Abstract

Objective: Review empirical evidence for a relationship between psychosocial factors and breast cancer development. **Methods:** Standardised quality assessment criteria were utilised to assess the evidence of psychosocial predictors of breast cancer development in the following domains: (a) stressful life events, (b) coping style, (c) social support, and (d) emotional and personality factors. **Results:** Few well-designed studies report any association between life events and breast cancer, the exception being two small studies using the Life Events and Difficulties Schedule (LEDS) reporting an association between severely threatening events and breast cancer risk. Seven studies show anger repression

or alexithymia are predictors, the strongest evidence suggesting younger women are at increased risk. There is no evidence that social support, chronic anxiety, or depression affects breast cancer development. With the exception of rationality/anti-emotionality, personality factors do not predict breast cancer risk. **Conclusion:** The evidence for a relationship between psychosocial factors and breast cancer is weak. The strongest predictors are emotional repression and severe life events. Future research would benefit from theoretical grounding and greater methodological rigour. Recommendations are given. © 2000 Elsevier Science Inc. All rights reserved.

Keywords: Breast neoplasms; Emotions; Life change events; Personality; Social support; Stress

Introduction

The notion that cancer might be related to stress or emotional factors can be traced back to around 200 AD when Galen noted that melancholic women were much more susceptible to cancer than other females [1]. In 1759, Guy, a surgeon, emphasised “such disasters in life, as occasion much trouble and grief” in the causation of cancer [2]. In the first half of this century the search focused on external explanations for illness, influenced by Descartes, who viewed the mind as distinctly separate and an unrelated entity from the mechanistic body.

Renewed interest in the mind–body relationship over the past three decades parallels our increasing understanding of the complex interrelationships between the immunological, endocrine, and nervous systems. There is mounting evidence that stress can disturb many areas of the immune system and that impaired immune system function predisposes to malignant growth [3,4]. The impact of life event stress is related not only to the type and severity of the event itself, but may be modified by the availability of resources to deal with the demands. It is unclear whether psychosocial factors impact directly on endocrine, immune, and nervous systems or indirectly by affecting behaviours such as diet, exercise, sleep, etc., which themselves have links to endocrine and immune functioning [5–7]. Hilakivi-Clarke et al. [8] have developed a model in which life event stress, personality, and social support influence an individual’s ability to cope, which in turn mediates breast cancer risk via alterations in neuroendocrine and immune functioning. These data and

* Corresponding author. Department of Psychological Medicine, Royal North Shore Hospital, St. Leonards, NSW 2065, Australia. Tel.: +61-2-9515-6580; fax: +61-2-9515-5697.

E-mail address: phyllisb@med.usyd.edu.au (P.N. Butow).

model provide an avenue for explaining clinical and epidemiological observations in this area, as well as the anecdotal reports of women who believe that “stress” or “depression” was a factor in the development of their cancer [9,10].

There have been many review articles published in this area, some focusing on life events, others on the cancer prone personality, some covering psychosocial factors in disease onset, and some in outcome, while others are more theoretical in nature [5,8,11–20]. However, none of these reviews have attempted to integrate the literature in these disparate areas in a systematic manner. Furthermore, many have focused on cancer in general which may cloud the picture. Because cancer is a biologically diverse disease, it is unlikely that any single psychosocial factor, or set of factors, will be related in the same fashion to the onset of all cancers.

We have chosen to focus on breast cancer, being hormonally sensitive. Since “stress” is involved in activation of the endocrine system, it seems likely that psychosocial factors may potentially play a greater role in cancer of the breast than at other sites. This review focuses on the psychosocial factors thought to be related to the development of breast cancer; namely life events, coping style, affect, personality, and social support. These areas are clearly interrelated. Although they are at times measured together, rarely are their interactive effects examined. Therefore, each domain is considered separately and where possible their interrelationships are discussed. We have chosen to focus only on predictors of breast cancer development, rather than outcome, as the literature on the latter issue is as vast, with differing predictors and theoretical pathways.

Method

Studies were identified from MedLine, PsychInfo, NEJM, Cinahl, and Cancerlit databases. The inclusion criteria were: an outcome diagnosis of breast cancer; assessment of one or more psychosocial risk factors; prospective, limited prospective or case-control design; at least one comparison group of healthy women, or women with benign breast disease; peer review publication in English. The exclusion criteria were: case reports; unpublished conference abstracts; conference proceedings; letters, news items or commentaries; focus on cancer in general rather than specifically breast cancer; or psychosocial factors in coping with treatment, prognosis, or relapse.

Each study was assessed using a standardised quality assessment form (see Appendix A), developed for this review based on previously published scales and checklists [21–23]. The key features of quality assessment were: definition of case status and representativeness of cases and controls or cohort; data collection procedures and response rates. Articles were independently reviewed by

two experts in the area. Disagreements between reviewers were noted and were discussed until consensus was reached. This occurred rarely. Where a consensus agreement could not be achieved, the more conservative (negative) rating was used.

Studies were excluded if they had a serious design flaw such as: low response rate with differential refusal rates between cases and non-cases; subjective ratings by an interviewer not blind to case status; breast cancer data not separated from other cancer data; inappropriate control groups such as hospital staff or relatives. An exception was made for the Cooper series, a substantial body of work that used an inappropriate control group, but covered aspects not covered elsewhere in the literature [24–27].

Studies were also excluded if they had several less serious design flaws that reviewers felt compromised the study such as: statistical analysis not described or could not be inferred; failure to minimise recall bias in case-control studies; warning of diagnosis in limited prospective studies; unvalidated psychological measures; failure to adjust data for potential confounders, especially age. In cases where the same data were presented in multiple publications, the most comprehensive presentation was included.

During the review process, a weighted quality assessment score (0–100) was calculated for each study. Firstly, each question in the quality assessment was given a response score ranging from 1 to 6. The highest score was given when the paper provided adequate details of the measures taken by the investigators to reduce systematic errors and the lowest score when no information was provided or the study did not sufficiently account for the relevant variable.

Each question was also weighted (range 1 to 3) according to the relative importance of each variable to the study outcome and effect measures. The greatest weight was given for the representativeness of the study population and compatibility in data collection. The final quality score was a weighted response score (response score multiplied by the weight).

Holman et al. [28] 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; rather the score was used as a way of weighting studies included in the review.

High scores reflect clear evidence of steps taken to reduce systematic errors and improve generalisability. Each design type was judged by its own relevant criteria. Thus, while a prospective and case-control study could receive equal scores, the prospective study would still be regarded as superior due to the inherent methodological superiority of the design. Results are discussed in general and with reference to the higher quality studies.

Methodological issues

Most studies have a limited prospective or case-control design. A limited prospective study is one in which the number of subjects required for analysis is limited by selecting those known to be at risk, such as women undergoing biopsy. These studies are usually hospital-based, with attendant sampling bias. Their strength, however, is in their capacity to evaluate psychological variables in subjects prior to confirmation of benign, malignant or no breast disease under similar conditions. Nevertheless, the a priori probability of being diagnosed with breast cancer may not be the same for all participants and this may introduce bias. Geyer [29] reported that women correctly suspecting their cancer diagnosis were more depressed prior to diagnosis; depression was not, however, associated with the reporting of life events, refuting the notion of recall bias. However, consistent with the claimed influence of “awareness” of diagnosis is the finding that post-diagnosis repression and defensiveness increases [30].

The choice of a comparison group is also of importance. Subjects with benign disease share the same apprehensiveness prior to diagnosis as those found to have cancer, but the former are also at greater ultimate risk of developing breast cancer. A normal control sample lacks any “investigation-related” concerns, and so, group differences in this regard may be inappropriately excessive. The source of cases and controls needs to be clearly identified and when collected from varying sources their data separately reported.

The choice of time frame for examining life events most frequently has been between 2 and 5 years. With the time from initiation to detection of breast cancer estimated as up to 18 years [31], the proposed relationship between life event stress and breast cancer appears to be associated with tumour growth, rather than initiation. Unless there is a critical time in tumour development at which the impact of stress is greater, presumably the longer the time frame studied, the stronger the association between life events and breast cancer. One complication in examining extended time frames for life event stress is the reliability of recalling long past events. The fall-off in reporting of events using the checklist approach rapidly decreases for periods greater than 6 months [32]. Recall of events via interview, such as the Life Events and Difficulties Schedule (LEDS), however, has been reported as reliable for up to 10 years [33].

Potential confounders in the form of well-established risk factors ideally need to be considered in design and/or analyses. These include age, age at menarche, age at first full-term pregnancy, age at menopause, family history, and body mass index (BMI) [34]. In most studies, age is a confounder and not always adequately controlled. As well as being an independent risk factor for breast cancer, age is an important consideration in psychosocial research as life events and psychological variables may also be influenced by age.

Life events

Life events are discrete occurrences of daily life, either physical and/or psychological in nature, that disrupt (or threaten to disrupt) normal life activities [35]. Events may be positive (birth of a child) or negative (illness). The impact of such events or the resulting “stress” is dependent upon the intensity of the event and an individual’s resources to adapt to the event, such as coping style and social support [36].

The assessment of stressful life events is generally based on either standardised checklists or structured interview [35,37]. The most commonly utilised checklist is the Social Readjustment Rating Scale (SRRS) [37], containing 43 events. Each event is assigned a weighting, which reflects the amount of adjustment resulting from that event. The checklist approach has been criticised for the potentially limited range of experiences covered, and the lack of both specificity and sensitivity of event definition. There are also significant problems of reliability and of ensuring events are independent of the disease in question. Furthermore, the events are based solely on subjects self-report and thus may be influenced by mood or personality [38]. The semi-structured interview approach, the LEDS by Brown and Harris [35], largely excludes these biases [39].

We review 17 studies addressing life events and the development of breast cancer that met our inclusion criteria. Variation in measures and data presentation precluded meta-analysis. Major findings are summarised in Table 1.

Population-based case-control studies

Two population-based record linkage studies provide an unbiased assessment of two life events, namely widowhood and divorce. Ewertz [40] used Danish cancer incidence records and population registry data to match marital status in 1792 breast cancer cases and 1739 randomly selected age-stratified controls. Neither widowhood nor divorce was associated with developing breast cancer. Kvikstad et al. [41], using similar population registry data from Norway, included 4491 incident cases of breast cancer and 44,910 age-matched cancer-free controls. Adjusting for age at first birth and parity, widowhood was not associated with increased risk, while the odds ratio (OR) for divorce indicated a negative association with breast cancer (OR = 0.83, CI 0.75–0.92).

Life Events and Difficulties Schedule (LEDS)

Two limited prospective studies have used the Brown and Harris LEDS [35]. While both studies have methodological limitations, their use of the interview-based LEDS assessment is a strength, as is their sampling frame and statistical analyses which controlled for a number of appropriate confounders. Geyer [42,43] examined women aged 25–60 with a breast lump prior to surgical diagnosis. Of

Table 1
Summary of studies examining life events and the development of breast cancer

Study type/author	Quality score	Life event measure	Time frame	Association between life events and breast cancer development
<i>Record linkage studies</i>				
Ewertz [40]	86	widowhood divorce	life time	ns ^a (marital status)
Kvikstad et al. [41]	83	widowhood divorce	up to 5 years pre-diagnosis	widowhood ns ^a divorce OR 0.83, CI 0.75-0.92 ^a
<i>Limited prospective studies</i>				
Geyer [42,43]	93	LEDS ^d	8 years	Severe life event ($r = 0.28$) ^a
Greer and Morris [56]	92	structured psychiatric interview	5 years	ns (events resulting in severe and prolonged emotional distress)
Chen et al. [44]	91	LEDS	5 years	severe life event (OR 15.0; CI 3.7-60.4) ^a
Edwards et al. [46]	90	Cheang and Cooper LEI ^f	2 years	ns ^a
Schonfield [45]	85	SRRS ^a (modified)	3 years	controls higher SRRS scores ($p < 0.05$) ^a
Schwarz and Geyer [57]	79	non-standardised interview	not given	ns ^a
Fox et al. [48]	78	SRRS	2 years	ns ^a death of spouse/family member
<i>Case-control studies</i>				
Roberts et al. [55]	87	SRRS (modified)	5 years	ns ^a
Priestman et al. [50]	83	Cochrane and Robertson LEI	3 years	ns
Cooper et al. [25,27]	73	Cheang and Cooper LEI	2 years	different type of events less events but perceived severity of events higher in cancer group
Bremond et al. [58]	68	non-standardised interview	5 years	ns (total sample) ^a
Forsen [52]	49	SRRS	1 year	<45 years OR = 4.33; CI 1.2-16.0 SRRS 1 year RR = 2.67; CI 1.13-6.30 ^a
		SRRS (modified)	6 years	Emotional loss 6 years RR = 5.02; CI ^a 1.7-14.7 ^a
Cheang and Cooper [47]	47	Cheang and Cooper LEI	2 years	Life event scores ($p < 0.01$) Loss/illness event ($p = 0.002$)
Ginsberg et al. [53]	78	Tennant and Andrews LEI	2 years 10 years	ns (2 years) ^a 10 year RR = 4.67; 1.33-16.4 ^a

OR, odds ratio; CI, 95% confidence interval; LEDS, Life Events and Difficulties Schedule; r , regression coefficient; LEI, Life Event Inventory; SRRS, Social Readjustment Rating Scale; RR, relative risk.

^a Age adjusted.

these, 33 had malignant disease and 59 had benign disease. Using regression techniques to adjust for age and family history of breast cancer, Geyer reports that the most severe life events, those associated with loss, were more common in the cancer group. Although there was no group difference in family history, severe life events, and family history were highly correlated in the cancer group, but uncorrelated in the benign group. The adjusted regression coefficients, presented without standard errors or tests of significance, demonstrated a stronger association between life events in the past 8 years and breast cancer ($r = 0.28$) than between age and breast cancer ($r = 0.19$).

Chen et al. [44] report on 72 women referred for examination of breast lesions following mammographic screening and 47 symptomatic women undergoing biopsies; 41 were diagnosed with cancer and 78 with benign disease. Age, marital status, menopausal status, age at menarche, age at first birth, alcohol use, and family history were included in analyses as confounders. The adjusted OR for severely threatening events during the past 5 years was 15.00 although the confidence interval (CI) was wide (3.74-60.44), possibly reflecting the inappropriately high number of variables in the analysis, given the relatively small sample size. "Important moderately threatening" events

were also associated with increased risk of breast cancer (OR = 9.70, CI 2.45–38.17). Although not presented, the authors state these associations were seen in both the screened and symptomatic samples.

Checklist approach

Limited prospective studies

The three limited prospective studies were based on very different populations and report quite different results. Schonfield [45] examined 112 women undergoing a breast biopsy, 27 subsequently diagnosed with cancer and 85 with benign disease. Confounders were dealt with by stratifying by median age and place of birth. Contrary to their expectations, analysis of variance revealed women with benign tumours had significantly higher life change unit scores on the SRRS than women with breast cancer for the 3 years prior to diagnosis.

Edwards et al. [46] report on a mixed sample of symptomatic and asymptomatic women undergoing breast examination and mammography. A total of 79 had breast cancer, 71 had pre-cancerous growths, 505 had benign breast disease, and 397 normal breast tissue. The only important distinguishing factor was a prior history of cancer, subsequently controlled for in analyses. Factor analysis of the Cheang and Cooper Life Event Checklist [47] yielded eight life event factors, none of which predicted a cancer diagnosis.

Fox et al. [48] reports on 826 women (response rate 41%), presenting for mammograms, of whom 20 were newly diagnosed cases, 52 had previous breast cancer, 488 had fibrocystic disease, and 266 had normal results. After adjusting for age and other confounders, no significant differences were detected between new cases and the three control groups on SRRS scores. Individual item analysis revealed 60% of the newly diagnosed cancer group had experienced the death of a spouse or close family member within the past 2 years compared to only 27% of normal controls. However, because individual item analyses were not adjusted for age or other confounders, the findings are difficult to interpret.

Case-control studies

These six case-control studies vary in quality. Cheang and Cooper [47] compared 121 breast biopsy patients and 42 healthy controls. Assessment of stressful life events was based on interview recall of events that had occurred 2 years before the discovery of the breast lump, or before interview for controls. The 46 women subsequently diagnosed with breast cancer reported more life events and more stressful life events than the cancer-free women ($p < 0.01$). Ninety eight percent of cases reported at least one loss or illness event compared with 71% of the benign group ($p = 0.002$). However, only unadjusted data were presented, despite "minor" age differences between groups (mean age cases: 50.5 years; benign group 48 years; healthy controls 42

years), and other potential confounders were not considered. These results should be interpreted cautiously.

A second study by this group used the same 48-item checklist [47] in a sample of 1324 women attending a surgical outpatient clinic for breast symptoms, 272 women attending a breast clinic for breast symptoms, and 567 asymptomatic women attending a primary health care facility [25–27,49]. Potential confounders were not considered in analyses. Despite claiming age-adjusted analyses for item frequency and severity, group differences were consistent with unadjusted or incompletely adjusted data. The younger control group reported more events relating to work, children, and mortgages; the cancer group reported more events related to retirement, grandchildren, and the death of friends. There were few differences in the incidence of individual events, although reported severity of some events was greater in the cancer group. The choice of comparison groups and approach to analysis limits the validity of this work, with the authors highlighting individual item differences rather than examining overall patterns.

Priestman et al. [50] compared 100 women with breast cancer, 100 women with benign disease (both from surgical clinics) and a convenience sample of 100 normal women. No differences were reported in the mean number of life events or the severity of these events during the previous 3 years between any of these groups using the Cochrane and Robertson Life Events Inventory (LEI) [51].

Forsen [52] examined 87 women newly diagnosed with breast cancer and 87 controls matched on age and parity. Other potential confounders were not considered and no details were provided on the source of controls. The cancer group had significantly higher weighted life events scores for both 12 months (SRRS) and 6 years (modified SRRS) prior to diagnosis. Multivariate analysis adjusting for anxiety, depression, marital status, education, and social class confirmed that life event scores for the 12 months preceding diagnosis, and sustaining an important emotional loss, were significant predictors of breast cancer risk.

Ginsberg et al. [53] report a case-control study of 98 cases and 98 controls randomly selected from the electoral roll, matched for age and place of residence. Adjusting for age at menarche, nulliparity, breast cancer history, exercise, body weight, BMI, smoking, alcohol, and other dietary factors, women who scored in the highest quartile of life change scores for the past 10 years (Tennant and Andrews LEI) [54] were 4.67 (CI 1.33–16.41) times more likely to have developed cancer. Life "change" scores for the most recent 2-year period, and life event "distress" scores for both the 2- and 10-year periods showed non-significant trends of increased breast cancer risk.

These positive findings are in contrast to the findings of Roberts et al. [55]. In a well-designed population-based, case-control study they examined 258 newly diagnosed breast cancer cases and 614 randomly selected controls (50–79 years). An abbreviated, age relevant version of the SRRS was used. Reported ORs were adjusted for age, age at

first birth, parity, family history of breast cancer, BMI, and age at menarche. No differences were seen in the number of events or experience of loss generally.

Interviews and other scales

Two limited prospective studies and one case-control study used non-standardised structured interviews. Greer and Morris [56] interviewed 69 women with breast cancer and 91 women with benign breast disease prior to diagnosis. Any event causing "severe or prolonged emotional distress" in the previous 5 years was recorded. Benign controls were significantly younger than cases, but no adjustment or stratification for age was reported. No differences were recorded in either the number of stressful life events or loss events. Schwarz and Geyer [57] briefly described the use of a non-standardised, structured interview to assess stress among women undergoing a biopsy. Among the 76 women included in a path analysis, the experience of loss was not associated with breast cancer risk.

Bremond et al. [58] examined 50 women with breast cancer and 100 age-matched controls from the same clinic. Women under age 45 with breast cancer reported having a "serious psychological shock during the past 5 years" more often than their age-matched controls (OR 4.33, CI 1.2–16.0); there was no such relation for the total sample or for women over 45 years. No rationale was given for age stratification and it may well have been opportunistic.

In summary, the evidence for an association between life event stress and breast cancer risk is inconsistent and far from convincing. Two population-based record linkage studies found no evidence of a link between widowhood or divorce and breast cancer incidence. The nine studies using checklists vary in quality and provide mixed results with five positive results, three negative results, and one reporting, paradoxically, more events in the control group. This suggests that additive measure of life events is not a useful approach. Of four studies using non-standardised interviews, only one found an association between life events and breast cancer and only in younger women. However, two studies using the LEDS interview, a comprehensive method of estimating the degree of severity of stressor exposure and far superior to the checklist approach, reported positive results. Despite small sample sizes, this method has produced the most consistent results, suggesting that severely threatening life events should not be yet discounted as influencing the development of breast cancer. Further studies using the Brown and Harris LEDS interview should be replicated in other settings, with careful consideration given to the choice of comparison populations and analyses adjusting for age and other known risk factors.

Coping with life events

Folkman and Lazarus [59] defined coping as "the cognitive and behavioural efforts made to master, tolerate, or

reduce external and internal demands and conflicts among them." Their Coping Strategies Inventory (or Ways of Coping Checklist), distinguishes between problem-focused coping which deals with the source of the stress and emotion-focused coping which regulates stressful emotion. We found only five studies with adequate design, directly addressing coping strategies in relation to breast cancer risk.

Coping Strategies Inventory and variants

Chen et al. [44] used the Coping Strategies Inventory [60] in 119 women undergoing biopsy. Contrary to their hypothesis, women who confronted stress by working out a plan to deal with the problem were at higher risk of breast cancer (OR = 5.12; CI 1.46–17.89), independent of life events, and adjusted for age, family history, menopausal status, personality, tobacco, and alcohol use. This group report a significant increase in breast cancer risk for women experiencing a severely threatening life event and confronting stress by focusing on the problem at hand (OR = 3.1; CI 1.18–8.19). However, it is unclear if this interaction was tested on the whole sample and/or in their multivariate model.

Cooper and Faragher [26] asked an undefined sample to describe methods used to cope with stressful events, creating a checklist of the 36 most commonly reported items based on the Ways of Coping Checklist. Few differences were detected in their large case-control study (described above) after adjusting for age, despite some 130 tests of significance.

Edwards et al. [46] (described above), using a 38-item version of the Ways of Coping Checklist, found no association between breast cancer risk and either individual items or the four coping scales produced via factor analysis. Testing for an interaction effect, additional analysis revealed that coping did not modify the effect of life event stress on breast cancer risk, after adjusting for age and history of breast cancer.

Other approaches to the assessment of coping strategies

Schwarz and Geyer [57] used a German psychological instrument [61] designed to measure "action control" as an indicator of reactions to stress, in a limited prospective study of women undergoing biopsy, and found no association with cancer. Scherg [62] used a questionnaire developed by Bahnson and Bahnson [63] to examine the association between a number of psychosocial scales and breast cancer risk in 75 matched cases and controls. Conditional logistic regression analysis found 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.

In summary, the evidence for an association between breast cancer and short-term coping styles is scant, inconsistent, and thus, insufficient to conclude that coping strategies contribute to breast cancer. The highest quality

study, contrary to expectation, reported that confronting stress significantly increased the risk of breast cancer. Only two studies have considered the interaction of coping style and life events on breast cancer risk, one non-significant, and the other reporting a significant interaction between severely threatening events and dealing with stress by confronting it, although this interaction does not appear in the final multivariate model.

Social support

Social support is generally defined either structurally in terms of the number of individuals within one's social network, or functionally in terms of the availability of trusted individuals [64,65]. Most research examining the relationship between social support and breast cancer focuses on the role of support after diagnosis. Only three studies have considered social support in relation to the development of breast cancer. Both Cooper et al. [24] and Edwards et al. [46] used an unspecified inventory to assess the number of people an individual could turn to in a crisis and their relationship to that person. Cooper et al. [24] found no differences in the number of supports available; differences in who was available for support were consistent with a confounding effect of age. Edwards et al. [46] reported no differences in the number or relationship of social supports, and support did not interact with life event scores in predicting diagnosis. Based on work by Brown and Harris, Geyer [42,43] proposed social support as modifying the effect of stressful life events. In his study, social support was rated for individual events, although the details are not clearly described. However, high correlation of "lack of social support" with "life events" precluded the inclusion of support in the model.

Long-term emotional and personality factors

We identified 18 papers exploring the impact of long-term emotional and personality factors on the develop-

ment of breast cancer, with adequate design and analysis characteristics. Most of these papers explored the impact of (a) emotional repression/emotional control/alexithymia, (b) chronic anxiety/depression, and/or (c) various related personality features (see Table 2 for definitions). Variability in study design, range of measurement tools used, and statistics reported precluded meta-analysis. Findings are summarised in Table 3.

Emotional repression/alexithymia/type A behaviour

Prospective studies

Two prospective studies have been reported in this area. Hahn and Petitti [66] report on MMPI data collected from 8932 women involved in a prospective contraceptive drug study commenced in 1969. Follow-up via computer-stored hospital discharge records in 1982 identified 117 biopsy confirmed breast cancers developed after study entry. Univariate and multivariate analyses failed to detect significant group differences on the depression and repression/sensitisation sub-scales.

Bleiker et al. [67] invited all women over 43 years of age in the Dutch city of Nijmegen to attend breast screening. Of the 9705 volunteers (34% response rate), 131 were later diagnosed with breast cancer. Six age-matched normal controls per case were also selected. Logistic regression analyses, controlling for somatic factors such as family history, early menarche, late menopause, obesity, and parity, were used to predict case versus control status. Expression or suppression of emotion, as assessed by well-validated personality scales (SAQ-N) [68], was not related to breast cancer risk.

Limited prospective studies

Greer and Morris [56,69] developed a structured interview schedule for measuring expression of anger and other feelings, and reported results from 160 women undergoing breast biopsy. In an age-adjusted non-parametric analysis, breast cancer cases under age 50 were more likely to be extreme suppressors or extreme expressors of emotion (especially anger) ($p < 0.001$) than benign controls. Re-

Table 2
Definitions of psychological terms

Terminology	Definition
Alexithymia	difficulty in identifying and describing feelings [90]
Type A	competitive, ambitious, and hard driving [30]
Emotional repression	tendency to minimise emotional upset [30]
Emotional control	controlling or suppressing emotional responses when angry, anxious or depressed [72]
Anti-emotionality or emotional defensiveness	avoidance of emotion in interpersonal situations [91]
Rationality	logical and rational behaviour [92]
Action control	degree to which intended actions are actually performed [93]
Extroversion	sociable, impulsive, easy-going, feelings not tightly controlled [89]
Neuroticism	anxious worrying individual, moody, overly emotional [89]

Table 3
Summary of studies examining personality variables and the development of breast cancer

Study type/author	Quality score	Repression/alexithymia	Anxiety/depression	General personality
<i>Prospective studies</i>				
Bleiker et al. [67]	74	ns ^a	ns ^a	anti-emotionality RR 1.19 ^a ; trait anger, rationality, understanding, optimism ns ^a .
Hahn and Pettiti [66]	57	ns ^a	ns ^a	-
<i>Limited prospective studies</i>				
Grassi and Cappellari [73]	93	$p < 0.05$	ns	-
Kreidler et al. [30]	93	ns	-	-
Greer and Morris [56,69]	92	< 50 years ($p < 0.001$) ^a	ns	extroversion, neuroticism, hostility, adjustment ns
Chen et al. [44]	91	-	ns ^a	extroversion, neuroticism ns ^a
Edwards et al. [46]	90	ns	-	-
Scherg et al. [81]	90	< 50 years ($p < 0.05$) ^a	ns ^a	social desirability, authoritarianism, dependence, external control, religiosity, commitment ns ^a
Schonfield [45]	85	-	ns ^a	-
Morris et al. [71]	83	ns ^a	ns ^a	-
Anagnostopoulos et al. [77]	80	ns ^a	-	low denigratory attitudes ($p < 0.05$) ^a ; hostility, self- confidence, dependence, ns ^a
Faragher and Cooper [49]	80	$p < 0.05$	-	-
Fox et al. [48]	78	$p < 0.0001$ ^a	-	-
Jasmin et al. [86]	71	-	ns ^a	excessive self-esteem (RR = 10) ^a ; hysterical disposition (RR = 8.2) ^a
Cheang and Cooper [47]	47	$p < 0.05$	-	-
<i>Case-control studies</i>				
Priestman et al. [50]	83	-	-	neuroticism, extroversion, ns ^a
Watson et al. [74]	66	$p < 0.05$	trait anxiety ns	trait anger ns curiosity ($p < 0.02$), social desirability ($p < 0.001$)

^a Age adjusted.

analysing a sub-sample of these women, controlling for menopausal status and age, Bageley [70] found women with cancer were more likely to repress feelings ($p < 0.01$).

Refining the above procedure, interviews with 50 women (17 cases, 33 benign controls) were independently rated by three raters blind to diagnosis [71]. Inter-rater reliability was 0.91. The mean expression of anger rating for cancer cases was significantly lower than controls ($p < 0.01$). However, after age-stratification, only the 40-49 age group approached significance ($p = 0.08$); and with small numbers in the remaining cells, these data are difficult to interpret.

The Courtauld Emotional Control Scale (CECS)

Two limited prospective studies and one case-control study used the CECS [73], developed to measure the extent individuals control their reactions when angry, anxious, and depressed. Grassi and Cappellari [73] report results from 76 women who completed the CECS prior to breast lump biopsy; 41 subjects had cancer and 35 had benign disease. Groups were comparable except that the cancer patients were significantly older. Cancer patients reported a non-

significant trend of greater control on all three sub-scales of the CECS ($p < 0.055$), but reaching significance for the total emotional control score ($p < 0.044$). Furthermore, cancer patients reported significantly less hostility ($p < 0.02$). However, the analysis did not control for age or other known predictors of breast cancer.

Fox et al. [48] report on 826 women at a mammography clinic. After adjustment for age and other known risk factors, 20 women newly diagnosed with breast cancer reported significantly greater control over emotions (CECS) than the 52 with previous breast cancer, 488 with benign disease and 266 normal controls ($p < 0.0001$). This result needs to be viewed in the light of possible selection bias due to the poor response rate (41%).

Watson et al. [74] compared psychological and autonomic responses in 30 breast cancer patients and 27 controls who had recently undergone breast screening, matched for social class, and marital status. Subjects completed the CECS [72], STPI [75], and the Marlowe Crowne Scale [76], before being exposed to one neutral and two stressful videotapes. Subjects rated anger, anxiety, and sadness induced by each video, and the extent to which they tried to hide these feelings. The cancer

group reported a tendency to control anger ($p < 0.05$) and to respond to stress with a repressive coping style ($p < 0.001$). The cancer group also reported experiencing more anxiety and disturbance during one stress video ($p < 0.05$), and were also more likely to inhibit their reactions ($p < 0.01$). Autonomic arousal (heart rate and skin resistance) was not significantly different between groups. The authors acknowledged differences in reactions to stressors might be influenced by having cancer; however the cancer group were on average 27 months post-diagnosis reducing the likelihood of their responses being influenced by the stress of a cancer diagnosis.

Type A

Cheang and Cooper [47] found no differences in type A scores between 121 breast biopsy patients and 42 healthy patients from a well women's clinic. Items addressing emotional repression distinguished the cancer group from one of the control groups (not stated) in analyses unadjusted for confounders. The validity of individual item analyses is questionable. Faragher and Cooper [49] (described above), factor analysing the Bortner type A scale, found cancer patients ($n = 171$) tended to suppress feelings, and have few personal relationships outside of home and work, compared to 1110 women with benign disease. In contrast, Edwards et al. [46] (described above), found no differences on the Bortner type A scale in 1052 women attending for breast examination and mammography.

Other scales

Anagnostopoulos et al. [77] report on 448 women attending breast screening, with 180 later diagnosed with breast cancer, 112 with benign disease, and 156 with healthy breast tissue. All women completed a measure of hostility (PDS) [78], and a random subset of 100 women (breakdown of diagnosis unclear) completed the Toronto Alexithymia Scale (TAS) [79]. After adjusting for most potential confounders, denigratory attitudes were significantly lower in cases ($p < 0.05$), but there were no group differences in expression of hostility or other feelings.

Kreidler et al. [30] employed the repression questionnaire [80] in a pre-post-study of 72 women undergoing biopsy and 26 women awaiting non-cancer surgery. Repressors are defined as scoring low on anxiety and high on defensiveness and non-repressors are all other score combinations. The women completed the questionnaire before and after surgery. There were no pre-surgery group differences; however, repression increased significantly post-surgery in the cancer group. The authors suggest that repression is a response to, not a cause of, cancer. However, this small study had limited power to detect differences between the groups.

Scherg et al. [81] present results on 100 cases and age-matched healthy controls, and 69 cases and age-matched benign controls, from a sample of 3036 women attending a gynaecological clinic. Prior to diagnosis, each subject completed a modified version of the Bahnson and Bahn-

son psychosocial questionnaire [63] that included scales for suppression of anger, external control, pattern A behaviour, and social desirability. Cancer patients showed significantly more suppression of anger in the 20–50 age group only, supporting findings of Greer and Morris [56,69], although overall the psychosocial questionnaire discriminated poorly between the groups.

Emotional repression summary

The evidence for the impact of emotional repression, in particular anger, on the development of breast cancer, is equivocal, but intriguing. Six out of thirteen studies reported negative results, although some of these studies were not directly measuring repression of anger, but related issues such as self-awareness or the absence of type A personality. Included in these studies reporting negative results are two prospective studies. However, one used sub-scales of the MMPI, which has a theory-base not in wide current use and which did not directly measure emotional repression; the other had a 34% response rate, suggesting that systematic sampling bias may be distorting the results.

Of the seven studies reporting positive results, three were adjusted for age; one of these had a very poor response rate, perhaps introducing significant sample bias. Among the highest quality studies are three positive findings, including the two reporting a positive association with repression of anger in women under age 50 years. These findings not only highlight the necessity to adjust for age and other confounders, but also suggest that repression is a more important variable for younger women (possibly linked to the pre-menopausal hormonal profile). Confirmatory evidence exploring subsets of cancer patients with standardised measures specifically targeting emotional repression are needed. Scales directly measuring repression of emotions, particularly anger (such as the CECS) appear to be more 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.

Chronic anxiety and depression

Hahn and Petitti [66] using data from a prospective drug study (described above) found no significant differences between breast cancer patients and healthy women using the MMPI depression sub-scale. Non-significant differences between patients and controls in limited prospective studies assessing anxiety and depression have been reported by: Greer and Morris [56,69]; (Hamilton Rating Scale of Depression) [82]; Schonfield [45] (MMPI depression sub-scale [83]; IPAT covert and overt anxiety) [84]; Grassi and Cappellari [73] (Symptom Questionnaire) [85]; Jasmin et al. [86] (psychosomatic interview); Chen et al. [44] (GHQ) [87]; Bleiker et al. [67] (SAQ-N) [68].

Scherg et al. [81] using the psychosocial scale (described above) found non-significant differences in anxiety in the

direction opposite to that hypothesised: benign patients had slightly higher anxiety scores than cancer patients; while Morris et al. [71] found that benign patients scored significantly higher on trait anxiety, as measured on the STAI [88].

Other personality features

Investigations of general personality factors related to breast cancer have not produced promising results. Two limited prospective studies [44,56], and one case-control study [50] reported non-significant results for extroversion and neuroticism using the EPI [89]. Scherg et al. [81] report no differences between groups in social desirability, authoritarianism, dependence, external control, religiosity, and commitment, although their questionnaire is non-validated. Greer and Morris [56,69] found no differences between groups in hostility and general adjustment, based on a combination of psychiatric interview and questionnaires.

Two studies have reported significant findings. In a large prospective case-control study, Bleiker et al. [67] 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. Jasmin et al. [86] classified 77 women awaiting breast biopsy (18 cancers, 59 benign disease) as psychotic, poorly organised neurotic or well-organised neurotic. These classifications were not well defined and no inter-rater reliability data were presented. Multivariate analysis adjusted for age, family history, age at first delivery, and parity found women with a poorly organised neurosis or psychosis were at increased risk of breast cancer (Relative Risk (RR) = 17.8, $p < 0.009$). 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. These results are intriguing, but require replication in a larger study with better reporting of inter- and intra-reliability of ratings.

Summary and conclusions

There is a paucity of large scale, well-designed empirical studies examining the role of psychosocial factors in the development of breast cancer. Many studies have reported on small sample sizes and convenience samples with indeterminate bias. Cases and controls from different sources were sometimes combined. Comparison groups were frequently selected from different source populations than the cases, making accurate data interpretation impossible. Response rates were at times low or not reported. Data were rarely adequately adjusted for potential confounders, in particular age and few studies consider other well-established risk factors. Multivariate analysis estimating the independent effect of psychosocial factors on breast cancer risk is rare, although more recent studies have improved

methodology. It is therefore not surprising that this field of research has yielded inconsistent findings.

Few well-designed studies report an association between life events and breast cancer. The exception is two small studies using the Brown and Harris LEDS that found that severe events predict breast cancer risk suggesting that there may be some threshold for severity of stressors that is critical rather than the number and type or the cumulative effect of minor stressors. Seven out of thirteen studies reported that anger repression is predictive, especially in younger women; however many of these had design flaws and no attempt has been made to integrate repression with life event data. There is no evidence that social support, chronic anxiety or depression affects breast cancer development. Similarly, personality factors have not been found to be related to breast cancer risk, with the exception of one study showing rationality/anti-emotionality slightly increasing breast cancer risk. In general, the evidence for a relationship between psychosocial factors and breast cancer is weak. The strongest predictors are emotional repression (especially of anger) and severely threatening life events that would include the loss of a significant other. Although the available evidence does not support a major role for psychosocial factors in breast cancer development, few studies have been of sufficient quality to state definitively that such a role does not exist. Our methodological recommendations for future research are summarised in Table 4.

A significant weakness in this area of research is the essentially atheoretical approach to examining clearly inter-related psychosocial concepts in a multifactorial disease such as breast cancer. Progression in the understanding of the role of psychosocial variables in breast cancer development and the mechanisms by which they exert their effects, requires the guidance of a model which acknowledges links with the endocrine, nervous, and immune systems. One such model has been proposed by Hilakivi-Clarke et al. [8], briefly described earlier in this article, and interested readers

Table 4
Methodological recommendations for future research

Methodological recommendations

- Articulate the model that forms the basis of the research.
- Develop distinct hypotheses to be tested.
- A prospective study design is the ideal.
- Choose a clearly defined control group from a homogenous source.
- Exclude subjects with a previous history of breast cancer.
- Conduct sample size calculations to ensure adequate power.
- Consider at least some confounders.
- Control statistically for the confounding effects of age (even when groups are age-matched).
- Examine multiple psychosocial variables simultaneously.
- Concentration on the severity of life events rather than the number or cumulative effect.
- Use objective rather than subjective assessment of life events (serious consideration should be given to using the LEDS).

are referred to the referenced article. Sufficient power to test such a model requires sample sizes considerably larger than most studies to date, essential for the interaction between variables to be explored, rather than simply measured concurrently. With little data available on the way in which the various independent but clearly interrelated psychosocial variables of life event stress, coping style, social support, affect, and personality interact in relation to breast cancer development, examining these interactions would be a useful starting point.

Acknowledgments

This review was financially supported by the National Breast Cancer Centre of Australia.

References

- [1] Rosch PJ. Is cancer another "disease of adaptation?" Some insights into the role of stress and civilization. *Compr Ther* 1993;19(5):183–7.
- [2] Kowal SJ. Emotions as a cause of cancer: 18th and 19th century contributions. *Psychoanal Rev* 1955;42(3):217–27.
- [3] Morley JE, Benton D, Solomon GF. The role of stress and opioids as regulators of the immune system. In: McCubbin JA, Kaufman PG, Nemeroff CB, editors. *Stress, Neuropeptides, and Systemic Disease*. San Diego: Academic Press, 1991. pp. 233–60.
- [4] Rabin BS, Cohen S, Ganguli R, Lysle DT, Cunnick JE. Bidirectional interaction between the central nervous system and the immune system. *Crit Rev Immunol* 1989;9:279–312.
- [5] Baltrusch HJF, Stangel W, Titze I. Stress, cancer and immunity: new developments in biopsychosocial and psychoneuroimmunologic research. *Acta Neurol* 1991;13(4):315–27.
- [6] Baum A, Posluszny DM. Health psychology: mapping biobehavioral contributions to health and illness. *Annu Rev Psychol* 1999;50:137–63.
- [7] Hall M, Baum A, Buysse DJ, Prigerson HG, Kupfer DJ, Reynolds CF. Sleep as a mediator of the stress-immune relationship. *Psychosom Med* 1998;60(1):48–51.
- [8] Hilakivi-Clarke L, Rowland J, Clarke R, Lippman ME. Psychosocial factors in the development and progression of breast cancer. *Breast Cancer Res Treat* 1993;29(2):141–60.
- [9] Baghurst KI, Baghurst PA, Record SJ. Public perceptions of the role of dietary and other environmental factors in cancer causation or prevention. *J Epidemiol Community Health* 1992;46:120–6.
- [10] Brinton LA, Malone KE, Liff J, Schoenberg JB. Re: "Should we consider a subject's knowledge of the etiologic hypothesis in the analysis of case-control studies?" *Am J Epidemiol* 1994;140:1054–6.
- [11] Gross J. Emotional expression in cancer onset and progression. *Soc Sci Med* 1989;28(12):1239–48.
- [12] Levenson JL, Bemis C. The role of psychological factors in cancer onset and progression. *Psychosomatics* 1991;32(2):124–32.
- [13] McGee R, Williams S, Elwood M. Are life events related to the onset of breast cancer? *Psychol Med* 1996;26:441–7.
- [14] Bryla CM. The relationship between stress and the development of breast cancer: a literature review. *Oncol Nurs Forum* 1996;23(3):441–8.
- [15] Temoshok L. Personality, coping style, emotion, and cancer: toward an integrative model. *Cancer Surv* 1987;6:545–67.
- [16] Baltrusch HJF, Stangel W, Waltz WE. Cancer from the biobehavioral perspective: the type C pattern. *Act Nerv Super (Praha)* 1988;30(1):18–21.
- [17] Burke MA, Goodkin K. Stress and the development of breast cancer: a persistent and popular link despite contrary evidence. *Cancer* 1997;79(5):1055–9.
- [18] Eysenck HJ. Cancer and personality. In: Cooper CL, Watson M, editors. *Cancer and Stress: Psychological, Biological, and Coping Studies*. Chichester: Wiley, 1991. pp. 73–94.
- [19] Greer S, Watson M. Towards a psychobiological model of cancer: psychological considerations. *Soc Sci Med* 1985;20(8):773–7.
- [20] Grossarth-Maticke R, Kanazir DT, Schmidt P, Vetter H. Psychosomatic factors in the process of carcinogenesis: theoretical models and empirical results. *Psychother Psychosom* 1982;38:284–302.
- [21] Longnecker MP. Alcoholic beverage consumption in relation to risk of breast cancer: a meta-analysis and review. *Cancer Causes Control* 1994;5:73–82.
- [22] Oxman AD. Checklists for review articles. *BMJ* 1994;309:648–51.
- [23] English DR, Holman CDJ, Milne E. The Quantification of Drug Caused Morbidity and Mortality in Australia. Canberra: AGPS, 1995.
- [24] Cooper CL, Davies Cooper RF, Faragher EB. A prospective study of the relationship between breast cancer and life events, type A behaviour, social support, and coping skills. *Stress Med* 1986;2:271–7.
- [25] Cooper CL, Cooper R, Faragher EB. Incidence and perception of psychosocial stress: the relationship with breast cancer. *Psychol Med* 1989;19(2):415–22.
- [26] Cooper CL, Faragher EB. Coping strategies and breast disorders/cancer. *Psychol Med* 1992;22(2):447–55.
- [27] Cooper CL, Faragher EB. Psychosocial stress and breast cancer: the inter-relationship between stress events, coping strategies, and personality. *Psychol Med* 1993;23(3):653–62.
- [28] Holman CD, English DR, Milne E, Winter MG. Meta-analysis of alcohol and all-cause mortality: a validation of NHMRC recommendations. *Med J Aust* 1996;164:141–5.
- [29] Geyer S. Artifacts in "limited prospective" designs? Testing confounding effects of response behaviour of women prior to breast surgery. *J Psychosom Res* 1992;36(2):107–16.
- [30] Kreitler S, Chaitchik S, Kreitler H. Repressiveness: cause or result of cancer? *Psychooncology* 1993;2:43–54.
- [31] Friberg S, Mattson S. On the growth rates of human malignant tumours: implications for medical decision making. *J Surg Oncol* 1997;65(4):284–97.
- [32] Funch DP, Marshall JR. Measuring life stress: factors affecting fall-off in the reporting of life events. *J Health Soc Behav* 1984;25:453–64.
- [33] Brown GW, Harris TO. *Life Events and Illness*. New York: Guilford Press, 1989.
- [34] Kelsey JL. Breast cancer epidemiology: summary and future directions. *Epidemiol Rev* 1993;15(1):256–63.
- [35] Brown GW, Harris TO. *Social Origins of Depression: A Study of Psychiatric Disorder in Women*. London: Tavistock, 1978.
- [36] Tennant C, Langelluddecke P, Byrne D. The concept of stress. *Aust NZJ Psychiat* 1985;19(2):113–8.
- [37] Holmes TH, Rahe RH. The Social Readjustment Rating Scale. *Psychosom Med* 1967;11:213–8.
- [38] Monroe SM, Roberts JE. Conceptualizing and measuring life stress: problems, principles, procedures, progress. *Stress Med* 1990;6:209–16.
- [39] Tennant C, Smith P, Bebbington P, Hurry J. The contextual threat of life events: the concept and its reliability. *Psychol Med* 1979;9:525–8.
- [40] Ewertz M. Bereavement and breast cancer. *Br J Cancer* 1986;53:701–3.
- [41] Kvikstad A, Vatten LJ, Trelli S, Kvinnsland S. Death of a husband or marital divorce related to risk of breast cancer in middle-aged women. A nested case-control study among Norwegian women born 1935–1954. *Eur J Cancer* 1994;30A(4):473–7.
- [42] Geyer S. Life events prior to manifestation of breast cancer: a limited prospective study covering eight years before diagnosis. *J Psychosom Res* 1991;35(2–3):355–63.
- [43] Geyer S. Life events, chronic difficulties, and vulnerability factors preceding breast cancer. *Soc Sci Med* 1993;37(12):1545–55.
- [44] Chen CC, David AS, Nunnerley H, Michell M, Dawson JL, Berry H, Dobbs J, Fahy T. Adverse life events and breast cancer: case-control study. *BMJ* 1995;311(7019):1527–30.

- [45] Schonfield J. Psychological and life-experience differences between Israeli women with benign and cancerous breast lesions. *J Psychosom Res* 1975;19(4):229-34.
- [46] Edwards JR, Cooper CL, Pearl SG, De Paredes ESO, Leary T, Wilhelm MC. The relationship between psychosocial factors and breast cancer: some unexpected results. *Behav Med* 1990;16(1):5-14.
- [47] Cheang A, Cooper CL. Psychosocial factors in breast cancer. *Stress Med* 1985;1:61-6.
- [48] Fox CM, Harper AP, Hyner GC, Lyle RM. Loneliness, emotional repression, marital quality, and major life events in women who develop breast cancer. *J Community Health* 1994;19(6):467-82.
- [49] Faragher EB, Cooper CL. Type A stress prone behaviour and breast cancer. *Psychol Med* 1990;20(3):663-70.
- [50] Priestman TJ, Priestman SG, Bradshaw C. Stress and breast cancer. *Br J Cancer* 1985;51(4):493-8.
- [51] Cochrane R, Robertson A. The Life Events Inventory: a measure of the relative severity of psycho-social stressors. *J Psychosom Res* 1973;17:135-9.
- [52] Forsen A. Psychosocial stress as a risk for breast cancer. *Psychother Psychosom* 1991;55(2-4):176-85.
- [53] Ginsberg A, Price S, Ingram D, Nottage E. Life events and the risk of breast cancer: a case-control study. *Eur J Cancer* 1996;32A(12):2049-52.
- [54] Tennant C, Andrews G. A scale to measure the stress of life events. *Aust NZJ Psychiat* 1976;10:27-32.
- [55] Roberts FD, Newcomb PA, Trentham-Dietz AESB. Self-reported stress and risk of breast cancer. *Cancer* 1996;77(6):1089-93.
- [56] Greer S, Morris T. Psychological attributes of women who develop breast cancer: a controlled study. *J Psychosom Res* 1975;19(2):147-53.
- [57] Schwarz R, Geyer S. Social and psychological differences between cancer and noncancer patients: cause or consequence of the disease? *Psychother Psychosom* 1984;41(4):195-9.
- [58] Bremond A, Kune GA, Bahnson CB. Psychosomatic factors in breast cancer patients. Results of a case control study. *J Psychosom Obstet Gynaecol* 1986;5:127-36.
- [59] Folkman S, Lazarus RS. An analysis of coping in a middle-aged community sample. *J Health Soc Behav* 1980;21:219-39.
- [60] Tobin DL, Holroyd KA, Reynolds VC. User's Manual for the Coping Strategies Inventory. Ohio: Department of Psychology, University of Ohio, 1984.
- [61] Kuhl J. Handlungs- und Lageorientierung als Vermittler zwischen Intention und Handeln. 22 Int Kongr Psychol, Leipzig.
- [62] Scherg H. Psychosocial factors and disease bias in breast cancer patients. *Psychosom Med* 1987;49(3):302-12.
- [63] Bahnson MB, Bahnson CB. Development of a psychosocial screening questionnaire for cancer. *Cancer Detect Prev* 1979;2:295-305.
- [64] Henderson S, Duncan-Jones P, Byrne DG, Scott R. Measuring social relationships: the interview schedule for social interaction. *Psychol Med* 1980;10:723-34.
- [65] Bloom JR, Kang SH, Romano P. Cancer and stress: the effect of social support as a resource. In: Cooper CL, Watson M, editors. *Cancer and Stress: Psychological, Biological, and Coping Studies*. Chichester: Wiley, 1991. pp. 95-124.
- [66] Hahn RC, Pettiti DB. Minnesota Multiphasic Personality Inventory-rated depression and the incidence of breast cancer. *Cancer* 1988;61:845-8.
- [67] Bleiker EM, van der Ploeg HM, Hendriks JH, Ader HJ. Personality factors and breast cancer development: a prospective longitudinal study. *J Natl Cancer Inst* 20 1996;88:1478-82.
- [68] van der Ploeg HM. Self-Assessment Questionnaire-Nijmegen. Lisse, The Netherlands: Swets en Zeitlinger, 1989.
- [69] Greer S, Morris T. The study of psychological factors in breast cancer: problems of method. *Soc Sci Med* 1978;12(3A):129-34.
- [70] Bageley C. Control of the emotions, remote stress, and the emergence of breast cancer. *Indian J Clin Psychol* 1979;6:213-20.
- [71] Morris T, Greer S, Pettingale KW, Watson M. Patterns of expression of anger and their psychological correlates in women with breast cancer. *J Psychosom Res* 1981;25(2):111-7.
- [72] Watson M, Greer S. Development of a questionnaire measure of emotional control. *J Psychosom Res* 1983;27(4):299-305.
- [73] Grassi L, Cappellari L. State and trait psychological characteristics of breast cancer patients. *New Trends Exp Clin Psychiatry* 1988;IV(2):99-109.
- [74] Watson M, Pettingale KW, Greer S. Emotional control and autonomic arousal in breast cancer patients. *J Psychosom Res* 1984;28(6):467-74.
- [75] Spielberger CD, Jacobs GA, Crane RS, Russel SF, Westberry L, Barker L, Johnson E, Knight J, Marks E. Preliminary Manual for the State-Trait Personality Inventory (STPI). Tampa: Human Resources Institute, University of South Florida, 1979.
- [76] Crowne DP, Marlowe D. A new scale of social desirability independent of psychopathology. *J Consult Psychiatry* 1960;24:349-54.
- [77] Anagnostopoulos F, Vaslamatzis G, Markidis M, Katsouyanni K, Vasilaras F, Stepanis C. An investigation of hostile and alexithymic characteristics in breast cancer patients. *Psychother Psychosom* 1993;59(3-4):179-89.
- [78] Bedford A. Personality Deviance Scale (Manual). Windsor: NFER-Nelson, 1978.
- [79] Taylor GI, Ryan D, Bagby RM. Towards the development of a new self-report alexithymia scale. *Psychother Psychosom* 1985;44:191-9.
- [80] Weinberger DA, Schwartz GE, Davidson RJ. Low anxious, high anxious, and repressive coping styles: psychometric patterns and behavioral and physiological responses to stress. *J Abnorm Psychol* 1979;88:369-80.
- [81] Scherg H, Cramer I, Blohmke M. Psychosocial factors and breast cancer: a critical reevaluation of established hypotheses. *Cancer Detect Prev* 1981;4:165-71.
- [82] Hamilton M. Development of a scale for primary depressive illness. *Br J Soc Clin Psychol* 1967;6(4):278-96.
- [83] Hathaway SR, McKinley JC. Minnesota Multiphasic Personality Inventory. New York: Psychological Corporation, 1951.
- [84] Cattell RB, Scheir IH. Handbook for the IPAT Anxiety Scale (Self Analysis Form). Champaign, IL: Institute Personality Ability Testing, 1963.
- [85] Kellner R. Abridged Manual of the Symptom Questionnaire. Albuquerque: University of New Mexico, 1976.
- [86] Jasmin C, Le MG, Marty P, Herzberg R. Psycho-Oncology G. Evidence for a link between certain psychological factors and the risk of breast cancer in a case-control study. *Ann Oncol* 1990;1(1):22-9.
- [87] Goldberg DP, Williams P. A User's Guide to the General Health Questionnaire. London: NFER-Nelson, 1988.
- [88] Spielberger CD, Gorsuch RC, Lushene RE. The State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologists Press, 1970.
- [89] Eysenck HJ, Eysenck SBG. The Eysenck Personality Inventory. London: London Univ. Press, 1964.
- [90] Bagby RM, Parker JDA, Taylor GI. The twenty-item Toronto Alexithymia Scale - I. Item selection and cross-validation of the factor structure. *J Psychosom Res* 1994;38(1):23-32.
- [91] Bleiker EM, van der Ploeg HM, Hendriks JH, Leer JW, Kleijn WC. Rationality, emotional expression and control: psychometric characteristics of a questionnaire for research in psycho-oncology. *J Psychosom Res* 1993;37(8):861-72.
- [92] Bleiker EM, van der Ploeg HM, Ader HJ, van Daal WA, Hendriks JH. Personality traits of women with breast cancer: before and after diagnosis. *Psychol Rep* 1995;76(3 Pt 2):1139-46.
- [93] Kuhl J. Motivation and information processing: a new look at decision making, dynamic change, and action control. In: Sorrento RM, editor. *Handbook of Motivation and Cognition: Foundations of Social Behavior*. New York: Guilford Press, 1986. pp. 404-34.

Appendix A. Quality assessment form

✓ where appropriate

Yes Probably Possibly Unlikely No Don't know

Case definition

Was the breast cancer confirmed histologically?

Choice of study population

Were the cases truly representative of women with breast cancer?

Case-control and limited prospective studies

Would the controls fit the case definition if they had breast cancer?

Were the data collected in the same way for cases and controls

If the study was matched did the authors do any of the following?

- a. Use the same interviewer?
- b. Conduct matched analysis?
- c. Compare unmatched to matched analyses?
- d. Adequately account for matching factors in unmatched analyses?

To eliminate recall bias did the authors do any of the following?

- a. Use a structured interview sheet?
- b. Interviews were blinded to case status?
- c. Attempt to eliminate recall bias not stated?

Was the same exposure period used for cases and controls?

Was the response rate among cases at least 70%?

Was the response rate among controls at least 70%?

Cohort studies

Were the women in the cohort truly representative of the general community?

Was the follow-up rate at least 80%?

Was exposure information updated during follow-up?