

**The Characteristics of Women Diagnosed with
Breast Cancer and the Occurrence, Frequency and Severity
of Oncology Treatment-Induced Hot Flushes:
An investigation into a Relationship**

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A thesis submitted in fulfilment of the requirement for the degree of
Masters by Research (Science)

Under the supervision of Professor Deborah Marsh and Dr Sean Walsh

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Certificate of Original Authorship

I, Susan Gallagher declare that this thesis, is submitted in fulfilment of the requirements for the award of Master of Science (Research), in the Science Faculty at the University of Technology Sydney. This thesis is wholly my own work unless otherwise referenced or acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis. This document has not been submitted for qualifications at any other academic institution.

This research is supported by an Australian Government Research Training Program.

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Table of Contents

Acknowledgements	i
Table of Contents	ii
List of Tables	vi
List of Figures	vii
Abbreviations	ix
Manuscripts in preparation from this thesis	xi
Abstract	xii
Chapter 1: Introduction and Literature Review	1
1.1 Female breast cancer	1
1.1.1 Diagnosis and Pathology.....	1
1.1.2 Risk factors and outcome	2
1.1.3 Breast cancer surgery and therapy	2
1.2 Breast cancer oncology treatment-induced HF s.....	4
1.2.1 Clinical presentation of HFs.....	4
1.2.2 Pathology of HFs.....	4
1.2.3 Current treatment options for HFs	6
1.3 Acupuncture	6
1.3.1 Integrative medicine.....	9
1.3.2 Mechanisms in the treatment of HFs	9
1.4 Personalised medicine and predictors for HF s	10
1.4.1 Oncology treatment-induced HFs predictors	10
1.4.1.1 Breast cancer treatment.....	10
1.4.1.2 Demographics and lifestyle	11
1.4.1.3 Depressive symptoms and anti-depressants.....	12
1.4.2 Menopausal HFs predictors.....	12
1.4.2.1 Demographic and lifestyle	12
1.4.2.2 Anxiety, stress and depression.....	14
1.4.3 Limitations	14
1.4.4 Conclusion.....	14
1.5 Project Outline	15
1.5.1 Impact of COVID-19	15
1.6 Structure of Thesis	16
Chapter 2: Characteristics of Women with Breast Cancer: Focus on Oncology Treatment-Induced Hot Flashes	17
2.1 Anonymous Cohort Survey	17

2.1.1 Method	17
2.1.1.1 Survey content	17
2.1.1.2 Survey population and inclusion criteria	20
2.1.1.3 Survey distribution.....	20
2.1.1.4 Consent	21
2.1.1.5 Ethical considerations	21
2.1.1.6 Sample Size.....	21
2.1.2 Objective and endpoints.....	21
2.1.3 Ethics approval.....	22
2.1.4 Results	22
2.1.4.1 Survey analysis	22
2.1.4.2 Statistical methods	22
2.1.4.3 Cohort characteristics	23
2.1.4.3.1 Lifestyle.....	26
2.1.4.3.2 Menopause.....	27
2.1.4.3.3 Conventional breast cancer treatment	27
2.1.4.3.4 Emotions and QoL.....	27
2.1.4.4 HF Occurrence.....	28
2.1.4.5 HF Frequency and Severity	34
2.1.4.6 Integrative medicine	40
2.1.5 Discussion	42
2.1.5.1 Predictive factors	42
2.1.5.1.1 Conventional breast cancer treatment	42
2.1.5.1.2 Breast cancer diagnosis	43
2.1.5.1.3 Demographic and lifestyle.....	44
2.1.5.1.4 Emotions.....	45
2.1.5.2 Alleviating oncology treatment-induced HF.....	46
2.1.5.3 Observation and limitations	47
Chapter 3: Acupuncture for Treatment-induced Hot Flushes in Women with Breast Cancer: A Systematic Review.....	48
3.1 Systematic Literature review.....	48
3.1.1 Methods and eligibility criteria	48
3.1.2 RCT quality assessment	49
3.1.3 Statistical analysis	49
3.2 Results.....	49
3.2.1 Literature search.....	49
3.2.2 Risk of bias.....	50
3.2.3 Study characteristics.....	52

3.2.4 Outcome measures	52
3.2.5 Outcome: HF reduction.....	53
3.2.6 Trial duration, frequency and outcome	54
3.2.7 Intervention characteristics and outcome.....	57
3.2.8 Hormone therapy and outcome	60
3.2.9 Participant characteristics and outcome	61
3.3 Discussion	62
3.3.1 Patient characteristics.....	62
3.3.2 Acupuncture protocol.....	63
3.3.3 Patient acceptance	65
3.3.4 Limitations	66
3.5 Conclusion	66
Chapter 4: Design of a Phase II Feasibility Trial Protocol Addressing Treatment-Induced Hot Flashes in Women with Breast Cancer	67
4.1 Phase II Feasibility Trial Protocol	67
4.1.1 Study objectives and endpoints.....	67
4.1.2 Participants selection.....	68
4.1.3 Registration procedure	69
4.1.4 Study design and intervention.....	71
4.1.5 Clinical data collection.....	73
4.1.6 Statistical methods	74
4.1.7 Adverse event reporting	75
4.1.8 Data management and monitoring	76
4.1.9 Research ethics approval.....	76
Chapter 5: General Discussion and Future Direction	77
5.1 Discussion	77
5.1.1 Study findings	77
5.1.2 Construction of a feasibility trial.....	80
5.1.3 Education and communication	81
5.1.4 Strengths and limitations.....	81
5.1.4.1 Emerging therapies	81
5.1.4.2 Achieving sufficient power.....	82
5.1.5 Future direction	82
5.2 Conclusion	83
Appendices.....	84
Appendix A: Anonymous cohort survey	84
Appendix B: Survey information sheet	91
Appendix C: Survey advertising poster.....	96

Appendix D: Survey advertising flyer	97
Appendix E: Lifestyle assessment tool.....	98
Appendix F: Support information for risk of bias	99
Appendix G: Methodology and outcomes	104
Appendix H: Summary of the characteristics of trials included in this review.....	112
Appendix I: Feasibility trial information sheet and consent form.....	117
Appendix J: Sociodemographic questionnaire	124
Appendix K: Self-reported hot flush daily diary	129
Appendix L: Hot Flush-Related Daily Interference Scale.....	130
Appendix M: The Depression Anxiety Stress Scales.....	131
Appendix N: Functional Assessment of Cancer Therapy (GP).....	132
Appendix O: Acupuncture protocol for publication	133
Appendix P: HREC feasibility trial approval.....	151
References.....	152

List of Tables

Table 2.1 Factors predictive of HFs in menopausal and in women undergoing treatment for breast cancer.	17
Table 2.2 Demographic characteristics of breast cancer patients with and without oncology treatment-induced HFs.	23
Table 2.3 Univariable and multivariable models showing the association of significant variables and the occurrence of oncology treatment-induced HFs.	33
Table 2.4 Univariable models showing the associations between variables and oncology treatment-induced HF severity and frequency.	35
Table 2.5 Multivariate models showing the associations between variables and oncology treatment-induced HF severity and frequency.	40
Table 3.1 Percentage reduction in HFs at EOI and follow-up in four trials.	54
Table 3.2 Optimal acupuncture intervention characteristics.	60
Table 4.1 Acupuncture points and their location from WHO Standard Acupuncture Point Locations in the Western Pacific Region (WHO 2008).	72

List of Figures

Figure 1.1 Schematic representation of thermoregulatory interactions in the central nervous system ..	5
Figure 1.2 Local and systemic effects of acupuncture.....	8
Figure 2.1 HFRDIS: Degree in which HFs interfere with daily activities and overall QoL.	28
Figure 2.2 Proportion Plot: Estimated proportions by age with 95% CIs.....	29
Figure 2.3 Proportion Plot: Estimated proportions for level of education with 95% CIs.....	29
Figure 2.4 Proportion Plot: Estimated proportions for occupation status with 95% CIs.....	30
Figure 2.5 Proportion Plot: Estimated proportions for vegetable intake with 95% CIs.	31
Figure 2.6 Low, moderate and recommended vegetable intake compared to age.	31
Figure 2.7 Low, moderate and recommended vegetable intake compared to menopausal status at the commencement of breast cancer treatment.	32
Figure 2.8 Proportion Plot: Estimated proportions of chemotherapy and hormone therapy with 95% CIs.	33
Figure 2.9 Linear Regression: Predictive margins of menopausal status with 95% CIs.	37
Figure 2.10 Linear Regression: Menopausal status and predicted oncology treatment-induced HFs frequency.....	37
Figure 2.11 Linear Regression: Self-reported anxiety scale and predicted oncology treatment-induced HFs severity.	38
Figure 2.12 Linear Regression: Self-reported anxiety scale and predicted oncology treatment-induced HF frequency.	38
Figure 2.13 Linear Regression: Oncology treatment and predicted oncology treatment-induced HF frequency.....	39
Figure 2.14 Linear Regression: Level of education and predicted oncology treatment-induced HF frequency.....	39
Figure 2.15 Integrative medicine modalities: information received and expression of interest.	41
Figure 2.16 The source of integrative medicine information for patients.	41
Figure 3.1 PRISMA Flow Chart.	50
Figure 3.2 ROB Graph. Authors' assessments about each ROB item presented as percentages of included studies.....	51
Figure 3.3 ROB summary.	51
Figure 3.4 Reduction in mean HF frequency scores at EOI and follow-up in RCT and non-RCTs. ...	53
Figure 3.5 Reduction in HF scores at EOI compared with the number of intervention weeks.	55
Figure 3.6 Reduction in HF scores at EOI compared with the number of treatments performed.	55

Figure 3.7 Reduction in HF scores at EOI compared with frequency of weekly interventions.	56
Figure 3.8 Outcome and duration of follow-up compared with the number of intervention weeks and total number of interventions.	57
Figure 3.9 Reduction at EOI and follow-up compared with acupuncture point protocol.....	59
Figure 3.10 Acupuncture outcome at EOI and Hormone Therapy.	60
Figure 3.11 Reduction at EOI compared with mean age of participant and inferred menopausal status.	61
Figure 4.1 Data collection timeline.....	70

Abbreviations

ABS	Australian Bureau of Statistics
AI	Aromatase Inhibitor
AMED	Allied and Complementary Medicine Database
ANOVA	Analysis of Variance
ANZCTR	Australian New Zealand Clinical Trials Registry
BDI-PC	Beck Depression Inventory-Primary Care
BMI	Body Mass Index
BRCA1	Breast Cancer Type 1 Susceptibility Gene
BRCA2	Breast Cancer Type 2 Susceptibility Gene
CESD	Centre for Epidemiological Studies-Depression
CGRP	Calcitonin Gene-Related Peptide
CI	Confidence Interval
CINAHL	Cumulative Index of Nursing and Allied Health Literature.
CO	Co-Efficient
CONSORT	Consolidated Standards of Reporting Trials
DASS-21	Depression Anxiety Stress Scale 21
EMA	European Medicines Evaluation Agency
EOI	End of Intervention
ER	Oestrogen Receptor Breast Cancer
FACT-GP	Functional Assessment of Cancer Therapy General Population
FDA	Food and Drug Administration
fMRI	Functional magnetic resonance imaging
HADS	Hospital Anxiety and Depression Scale
HER	Human Epidermal Growth Factor Receptor
HF	Hot Flush
HFRDIS	Hot Flush-Related Daily Interference Scale
HREC	Human Research Ethics Committee
HRT	Hormone Replacement Therapy

MENQOL	Menopause-Specific Quality of Life Questionnaire
MetS	Metabolic Syndrome
OR	Odds Ratio
PGWB	Psychological and General Well-Being Index
PR	Progesterone Receptor Breast Cancer
QoL	Quality of Life
RCT	Randomised Controlled Trial
RNSH	Royal North Shore Hospital
ROB	Risk of Bias
SPIRIT	Standard Protocol Items Recommendations for Interventional Trials
SSRI	Selective Serotonin Reuptake Inhibitor
TCM	Traditional Chinese Medicine
UTS	University of Technology Sydney
VMS	Vasomotor Symptoms
YWBC	Young Women with Breast Cancer
YWCA	Young Women's Christian Association
WHQ	Women's Health Questionnaire

Manuscripts in preparation from this thesis

1. **Gallagher S, Livera AD, Johnstone A, Marsh DJ, Walsh S.** Oncology treatment-induced hot flushes in women treated for breast cancer: Predictors of occurrence, severity and frequency.
2. **Gallagher S, Marsh DJ, Walsh S.** Acupuncture for Oncology Treatment Induced Hot Flushes in Women diagnosed with Breast Cancer: A review of acupuncture protocols and characteristics associated with outcome

Abstract

Introduction: Since 1988 breast cancer treatment has become increasingly successful in Australia. The five-year survival rate for Australian women has increased over the last decade and in 2021 it is at 91%. With the growth in survival rate comes an increase in the number of women living with the often debilitating side effects of oncology treatment, such as hot flushes (HFs). Studies report that HFs can interfere with compliance of women prescribed lifesaving hormone medication. Women deemed at high risk of breast cancer recurrence have been reported to decline hormone therapy in part due to concerns about HFs. However, treatment options for HFs are limited. For example, commonly used hormone replacement therapy involves considerable risk of breast cancer returning, while other medications, such as the antidepressants paroxetine and venlafaxine, and the anticonvulsant gabapentin are often accompanied by side-effects. Acupuncture has been successfully trialled as a safe non-pharmacological alternative to controlling HFs and improving quality of life, however the benefits reported have been variable among individuals. This research therefore has gathered information on the characteristics of women diagnosed with breast cancer in the context of experiencing oncology treatment-induced HFs to ascertain whether specific characteristics are predictors of occurrence, frequency and/or severity. The data gathered will be combined with an investigation into the relationship between patient characteristics and response to acupuncture and will be utilised in the design and conduct of a feasibility trial.

Method: A 38 question survey covering sociodemographic, lifestyle, menopausal status, oncology interventions, HFs and emotional state was distributed on-line through Register4, a national database to fast-track cancer research, and in two leading Sydney hospitals (The Kinghorn Cancer Centre, St Vincent's Hospital and Patricia Ritchie Cancer Care Centre, Mater Hospital). The cohort studied was women who have been treated for breast cancer and either did or did not experience oncology treatment-induced HFs. Survey data was analysed using the statistical package STATA/SE 16.0 to conduct logistic and linear regression modelling to identify common characteristics associated with oncology treatment-induced HF occurrence, frequency and severity in Australian women. A literature review was performed to identify the optimal acupuncture protocol to manage these symptoms. The data from the survey and the literature review were utilised to design a feasibility trial that could investigate the effects of patient characteristics on acupuncture outcomes.

Results: Consistent with previous research, the survey results showed that in women with breast cancer, chemotherapy and hormone therapy were identified as strong predictors of HF occurrence, respectively (OR = 2.82; 95% CI = 1.18, 6.73; $p = 0.020$, OR = 7.26; 95% CI = 2.91, 18.12; $p = <0.001$). Chemotherapy was also a significant predictor of HF frequency along with the level of education reached, respectively (CO = 5.03; 95% CI = 0.96, 9.10; $p = 0.016$, CO = 3.00; 95% CI = 0.18, 5.81; $p = 0.037$). Premenopausal status was a significant predictor of HF frequency and severity,

respectively (CO = -2.20; 95% CI = -4.32, -0.08; $p = 0.042$, CO = -0.70; 95% CI = -1.27, -0.13; $p = 0.016$). Increased self-reported anxiety was also a significant predictor of HF frequency and severity, respectively (CO = 0.66; 95% CI = 0.28, 1.03; $p = 0.001$, CO = 0.42; 95% CI = 0.31, 0.52; $p = <0.001$). The feasibility trial standardised acupuncture protocol proposes acupuncture manual therapy for 20 minutes, once per week. A needle diameter of 0.30 mm and needle retention time of 20 minutes with the inclusion of the 'deqi' (dragging or aching) sensation was also specified.

Conclusion: Predictive impact is a relevant and significant question for HFs in women diagnosed with breast cancer for a number of different disciplines and reasons: the clinical implications with efficient use of finite resources; improving the success rate of reducing the impact of HFs will support ongoing treatment compliance; and finally, the humanistic perspective of improving quality of life for those women who experience discomfort and distress on a daily basis due to HFs. In summary, 45 to 54 year old women with breast cancer who may also be premenopausal, receiving chemotherapy and/or hormone therapy and may be experiencing anxiety, will require more proactive support to manage oncology treatment-induced HFs.