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Social Support as a determinant of Health Related Quality of Life in Breast Cancer survivors in California

Faiza Rab, *The University of Western Ontario*

Supervisor: Dr. Amardeep Thind, *The University of Western Ontario*

A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Epidemiology and Biostatistics

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Social Support as a determinant of Health Related Quality of Life in Breast Cancer
survivors in California

(Impact of social support on quality of life)

(Monograph)

by

Faiza Rab

Graduate Program in Epidemiology and Biostatistics

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science

The School of Graduate and Postdoctoral Studies
The University of Western Ontario
London, Ontario, Canada

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THE UNIVERSITY OF WESTERN ONTARIO
SCHOOL OF GRADUATE AND POSTDOCTORAL STUDIES

CERTIFICATE OF EXAMINATION

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entitled:

Social Support as a determinant of Health Related Quality of Life in Breast Cancer survivors in California

is accepted in Partial fulfillment of the
requirements for the degree of the
Master of Science

Date _____

Board

Chair of the Thesis Examination

Abstract and Keywords

Objective:

To evaluate the relationship between perceived social support and HRQOL (physical and emotional) in low SES breast cancer survivors.

Methods:

A cross-sectional study design was used to measure perceived social support at 18 months and HRQOL at 3 years after breast cancer diagnosis using MOS SS and MOS SF-36, respectively. Multiple regression analyses were used to evaluate the relationship.

Results:

Menopause at the time of diagnosis, adjunct chemotherapy, adjunct radiation therapy, co-morbidities, treatment side effects and depression were negatively associated with PCS scores ($p < 0.01$). Treatment side effects, anxiety and depression were negatively associated with MCS scores ($p < 0.01$).

Conclusions:

Perceived social support was not associated with HRQOL in low SES breast cancer survivors in our study. Menopause, co-morbidities, treatment side effect, adjunct chemotherapy and radiation therapy adversely affect physical HRQOL. Feelings of anxiety, depression and treatment side effects have a negative impact on emotional HRQOL.

Keywords: Breast Cancer, Social Support, Quality of Life

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Abbreviations

ASCO	American Society of Clinical Oncology
BCCTP	Breast and Cervical Cancer Treatment Program
BCEI	Breast Cancer Education Intervention
BCQ	Breast Cancer Chemotherapy Questionnaire
BDI	Beck Depression Inventory
BIBCQ	Body Image After Breast Cancer Questionnaire
BIS	Body Image Scale
BPI	Brief Pain Inventory
CaMos	Canadian Multicentre Osteoporosis Study
CES-D	Centre for Epidemiologic Studies Depression Scale
EORTC QLQ-BR 23	European Organization for Research and Treatment of Cancer Core Cancer Quality of Life Questionnaire for Breast Cancer
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer Core Cancer Quality of Life Questionnaire
FACIT – B	Functional Assessment Chronic illness Therapy Breast Cancer Questionnaire
FACIT – F	Functional Assessment Chronic illness – Fatigue Questionnaire
FACIT – G	Functional Assessment Chronic illness Therapy General Questionnaire
FACIT – SP	Functional Assessment Chronic illness Therapy Spiritual Questionnaire
FLI-C	Functional Living Index – Cancer
GHQ-28	General Health Questionnaire -28
HADS	Hospital Anxiety and Depression scale

HRQOL	Health Related Quality of Life
HFRIDS	Hot Flash Related Interference Scale
LSQ	Life Satisfaction Questionnaire
MACS	Mental Adjustment to Cancer Scale
MCS	Mental component summary
Medi-Cal	Medicaid program for the state of California
MFI	Multidimensional Fatigue Inventory
MOS SF-20	Medical Outcome Study Short form health survey with 20 questions
MOS SF-36	Medical Outcome Study Short form health survey with 36 questions
MOS SS	Medical Outcome Study Social Support
MPQ	McGill Pain Questionnaire
MSAS	Memorial Symptom Assessment Scale
PAIS	Psychological Adjustment to Illness Scale
PCS	Physical component summary
PMS	Profile Mood State
QLI	Spitzer Quality of Life Index
QLI-C	Ferrans and Powers Quality of Life Index- Cancer
RSC	Rotterdam Symptom Checklist
SDQ	Shoulder Disability Questionnaire
SIP	Sickness Impact Profile
SLDS-BC	The Satisfaction with Life Domains Scale for Breast Cancer
SSQ	Social support questionnaire
STAI	State-Trait Anxiety Inventory
SWLS	Satisfaction With Life Scale
WHO	World Health Organization

Chapter 1

Introduction and Research Objectives

Breast Cancer

Breast cancer is a chronic disease which stems from abnormal proliferation of cells in the breast tissue. Breast tissue extends from the collarbone and armpit across the ribs on both sides of the breastbone or sternum. The sternum lies in the middle of the front of chest. Breast tissue consists of skin, nipple, fat tissue, milk producing glands called lobules and ducts that carry milk from glands to the nipple.

Abnormal proliferation of cells in the breast tissue results in formation of a mass or growth known as a tumour. The abnormally proliferating cells in a tumour are known as tumour cells or malignant cells. Malignant cells can spread to the surrounding chains of lymph nodes and to other areas of the body. Breast cancer is diagnosed when a malignant tumour is present in the breast tissue with or without lymph node involvement or spread to distant areas of the body. There are two main types of breast cancers; the most common type starts in the ducts and the second type starts in the lobules within the breast tissue (1).

Breast cancer predominantly affects women; it is a rare disease among men. Factors predisposing women to breast cancer include: increasing age, genetic predisposition, family history of breast or ovarian cancer, early menarche (women getting periods before age 12 years), late menopause (after 55 years of age) and first pregnancy after 30 years of age or never being pregnant. Known risk factors for breast cancer include consuming more than 2

glasses of alcoholic drinks per day, hormone replacement therapy with estrogens, obesity and radiation to chest area for treatment of other cancers (1).

Burden of Breast Cancer

Every year ten million patients are diagnosed with cancer worldwide and women make up almost half of this patient population (2). One fifth of the 4.7 million women diagnosed with cancer each year suffer from breast cancer (3). Therefore, breast cancer is one of the most commonly diagnosed cancers among women worldwide (4). Incidence rates for breast cancer are subject to regional variations and some developed nations such as US and Canada have higher incidence rates than other developed or developing countries (3).

North America has one of the highest incidence rates for breast cancer in the world (3). It is estimated that in 2011, 230,000 new cases of breast cancer were diagnosed in US (5) and 23,000 new cases of breast cancer were diagnosed in Canada (6). Breast cancer is the most common cancer affecting Canadian women (6). Approximately 27% of Canadian women newly diagnosed with cancer have breast cancer (7) and 11.3% of Canadian women have a lifetime probability of developing breast cancer (6). Breast cancer is also the most common cancer among women in Ontario where more than 9,000 women were diagnosed with the disease in 2011 (6).

Women diagnosed with breast cancer are surviving longer due to early detection and better treatment options (8). The 5-year survival rates for breast cancer patients have improved over the last four decades from almost 60% to 90% in the US (9) and 88% in Canada (6). As a result of increased incidence and survival rates, more women are living with breast cancer today. In Canada, the number of breast cancer survivors exceeded more than 152,000 in

2007 (6). Current statistics indicate that after diagnosis with breast cancer, 82% of women survive for more than 10 years and 75% of women survive for more than 15 years in the US (9).

Chronic illnesses such as cancers result in direct as well as indirect medical costs to the health care system. Direct medical costs account for hospital stays, doctors' appointments and drug costs. Indirect medical costs include costs of private expenditures for home care, premature death and loss of productivity. In 1998, the total economic burden of illness in Canada was reported to be \$174.7 billion or 9% of the country's gross domestic product. Out of this, \$93 billion was attributed to chronic disease (10, 11). The economic burden of cancer care in Canada is estimated to be \$17.1 billion per year in direct and indirect medical costs. The direct health care or medical costs of all cancers in Canada each year are \$4.2 billion. Productivity losses due to premature death and disability as a result of all cancers, cost the Canadian economy \$12.9 billion every year (12).

In 1995, the total lifetime cost of treatment for all women with breast cancer in Canada was over \$454 million; average expenditure per breast cancer patient was estimated to be more than \$25,000 per year (12). The average costs of breast cancer care to health care systems are similar in all provinces and territories in Canada; however, additional costs for cancer care have been reported in the province of Ontario. Women with breast cancer in the province of Ontario are subjected to higher monthly out of pocket costs for patients such as costs of home health care, vitamins, alternative medicines and family care that are not covered by the provincial health plan (13).

Breast Cancer Care

Organizations such as Public Health Agency of Canada, American Society of Clinical Oncology (ASCO) and World Health Organization (WHO) have established detailed clinical practice guidelines for preventive strategies and treatment modalities for breast cancer care. To decrease the incidence and reduce global burden of breast cancer, the WHO provides a model for breast cancer care focusing on earlier detection and treatment. Early detection or screening strategies include surveillance with regular clinical breast examinations and mammography for women as well as identification of women with high risk of developing breast cancer and providing them with counselling and options for preventive care (14). In Canada breast cancer screening through biannual mammograms is recommended for women over 50 years of age (15, 16). Treatment of breast cancer may involve surgery, radiation therapy, chemotherapy, hormonal therapy, or a combination of these therapies depending on the stage of disease. The ASCO guidelines provide an update on treatment modalities available according to the stage of breast cancer (17).

In addition to preventive strategies and incorporating latest treatment modalities, clinical practice guidelines for breast cancer care in Canada focus on follow-up strategies and topics relevant to follow-up after treatment for breast cancer (18). According to the Canadian breast cancer care guidelines, it is during the follow-up period that physical and psychological issues can be identified and interventions initiated (18). Psycho-social problems are most prominent during the first year after breast cancer diagnosis and reduce considerably after 6 years in the absence of recurrence or worsening of existing illness (19).

One aspect of breast cancer care that is not adequately discussed in the Canadian breast cancer care guidelines is the role of social support in breast cancer care (19). Social support is known to improve relationships and general well-being among healthy individuals as well as those suffering from other chronic diseases (18). There is limited research on social support and its effect on quality of life in women with breast cancer; however, future research on the subject has the potential to improve considerably, the existing clinical practice guidelines (19).

Breast Cancer Research

The focus of breast cancer clinical trials and observational studies in the last four decades has mainly been on histopathology, classifying stage of breast cancer, physical symptoms, treatment modalities and psychological distress of breast cancer patients (20). These clinical trials and observational studies have improved screening and provided better treatment options for women with breast cancer. Improved screening methods and treatment modalities have led to improved survival in breast cancer patients (21).

Numbers of women living with breast cancer are increasing due to an increase in incidence as well as longer survival rates. This increase has forced researchers to adopt a multifaceted approach to breast cancer research, incorporating measures designed to improve quality of life for survivors of breast cancer (22). Cancer clinical trials consider health related quality of life (HRQOL) as an important end point in determining the efficacy of treatment modalities in breast cancer patients (23). Canadian clinical practice guidelines emphasize the need for further research on HRQOL in breast cancer patients to improve health care delivery and reduce the long term health care costs among Canadian breast cancer survivors (18).

Quality of life is a multidimensional concept which incorporates subjective evaluations of both positive and negative aspects of life (24). Several domains are measured to assess quality of life; these domains include housing, neighbourhood, job, schools and health. HRQOL encompasses those aspects of quality of life which affect physical or mental health (25). In addition to the advantages to individual breast cancer patients, assessment of HRQOL is beneficial in organizing public health prevention programs and introducing policy recommendations (24).

Individuals benefit from knowledge regarding their physical and mental well-being and impact of factors associated with their well-being during the course of their illness. Through identification of subgroups with poor perceived HRQOL, it is possible to determine factors which may be linked to the poor perception of HRQOL and thus help policy makers to allocate resources based on unmet needs of the identified subgroups. In addition, data from HRQOL surveys can be useful in strategic planning and monitoring of effects of intervention at the community level (24).

Measuring HRQOL is a challenge because experiences of individuals are different and may vary over time. Determinants of HRQOL include socio-demographic factors such as age, socio-economic status, education, marital and family demands, disease-related factors such as stage of disease, treatment modalities and side effects of medicine, access to medical care and social supports available (26).

The Merriam Webster dictionary defines “social” as ‘of or relating to human society, the interaction of the individual and the group, or the welfare of human beings as members of society’ and “support” as ‘to assist, help or advocate for’ (27, 28). Social support is a

multifaceted concept with more than 25 definitions of social support being used across various disciplines and research areas (29). Williams et al. studied the unique and shared properties of these working definitions and defined social support as ‘an amalgam of structure, type and strength of social relationships.’ In addition, social support also entails the degree of reciprocity, accessibility and reliability within the social relationships (29). Williams et al. emphasized that social support is best defined in the context of its use; in the context of HRQOL among patients suffering from chronic illness, social support is defined as *“availability of support which refers to the degree to which interpersonal relationships serve a particular function”* (30).

Social support is an important predictor for coping with difficult circumstances and adjusting to the psychological as well as social demands placed on women who have been diagnosed with breast cancer (31). Several studies indicate that perception of close supportive relationships with their spouse and family members is positively correlated with coping and adjustment by women diagnosed with breast cancer (26, 32, 33). Availability of social support such as the presence of supportive family, friends and social networks is positively associated with HRQOL (26).

Instead of counting the number of individuals available to provide support, perceived social support takes into account personal impressions of the degree of usefulness of social support rather than just presence of support (31). Thus, evaluation of perceived social support is more subjective than objective in nature.

Social support is a determinant of increased survival among women diagnosed with breast cancer (34); however, due to the subjective nature of assessment of perceived social support

there is limited literature on its impact on HRQOL in breast cancer survivors. Most studies analysing the effects of social support on HRQOL have used structural support i.e. number of individuals available to provide support rather than using perceived social support as a measure for social support (23, 26).

Despite its importance, no study to date has explored the relationship between ‘perceived social support’ and HRQOL in women with breast cancer with low socio economic status (SES). Therefore, future direction for research in breast cancer entails further exploration of the relationship between perceived social support and HRQOL among women with lower SES.

Research Objectives

Women diagnosed with breast cancer suffer from a physically and emotionally debilitating illness. These women often undergo protracted treatments and are subject to associated economic burdens in addition to the physical and psychological toll of the disease itself. Due to the economic burden of breast cancer treatment and rehabilitation, women belonging to lower economic strata face additional challenges when diagnosed with breast cancer. HRQOL is an important outcome to evaluate in order to ensure optimal quality of care for women with breast cancer; especially among women identified as being particularly vulnerable such as those belonging to lower SES.

Through our exploratory research we aim to contribute to the understanding of the relationship between perceived social support and HRQOL among low income women. Our objectives are to:

1. Determine the association between perceived availability of social support and physical HRQOL in low SES women diagnosed with breast cancer.
2. Determine the association between perceived availability of social support and emotional HRQOL in the same population of women.

Importance of our study

Our research will better inform the clinical practice guidelines for breast cancer care. At present the guidelines suggest psychosocial counselling for women diagnosed with breast cancer without specific goals for such counselling (18). While we believe that the biomedical model of breast cancer care is vital, it does not take into account all of the complex factors involved in breast cancer care. We posit that a broader, more integrative framework, which includes psycho-social factors such as social support, is necessary. Through our study, the guidelines can be improved to incorporate specific goals of psychosocial counselling.

Evidence suggests that improvements in HRQOL as a result of social support such as more visitors and support for women in labor result in decreased morbidity and as a result reduce medical costs (35). More than just diagnosis, breast cancer is costly to the Canadian health care system (10-13). Improvements in HRQOL can decrease both the direct and indirect costs by improving general health of patients diagnosed with breast cancer.

The survey for the study was conducted in California, USA. Despite many differences, the Canadian and U.S health care systems have some similarities. Universal health care in Canada covers all the costs of diagnosis and treatment for Canadian residents; although there is no universal health coverage, U.S states like California have government funded programs

which cover the cost of breast cancer treatment for low-income women diagnosed with breast or cervical cancer (36-38). Populations in California and Canada are comparable in terms of size (close to 37 and a little over 34 million respectively) and demographic characteristics such as large immigrant populations with several ethnic minorities. The burdens of breast cancer such as availability of treatment options for breast cancer and cost to the health care system for treating breast cancer patients are also similar in California and Canada. Immigrant populations in both countries face similar challenges in terms of accessing health care (41, 42). Given the similarities, the results generated from this study can have relevance to the Canadian population as well.

Chapter 2

Literature Review

Literature Review Strategy

The key words based on our research question were identified as the first step of literature review. Breast cancer, social support and quality of life were the three key words identified. The primary source of literature for our study was Pub Med; PsycINFO and EMBASE were used as secondary sources of literature.

The three key words in our study had the following MeSH (Medical Subject Heading) terms available:

1. Breast Cancer

- a. MeSH: “Breast Neoplasm”

2. Quality of Life

- a. MeSH: “Life Qualities”
- b. MeSH: “Life Quality”

3. Social Support

- a. MeSH: “Support, Social”
- b. MeSH: “Social Networks”
- c. MeSH: “Network, Social”
- d. MeSH: “Networks, Social”
- e. MeSH: “Social Network”
- f. MeSH: “Psychosocial Support Systems”
- g. MeSH: “Psychosocial Support System”
- h. MeSH: “Support System, Psychosocial”
- i. MeSH: “Support Systems, Psychosocial”
- j. MeSH: “System, Psychosocial Support”
- k. MeSH: “Systems, Psychosocial Support”

The entry terms were beneficial in searching for articles that were classified under the relevant subject headings but were given different key word designations. For each MeSH keyword all entry terms were included in the search and ‘*’ was used at the end of each term to capture key words and alternate suffixes.

The search strategy proceeded in three stages. First we narrowed our literature search by assessing the literature for quality of life in breast cancer patients.

Literature search #1: [Breast Cancer] OR [Breast Neoplasm] AND [Quality of Life] OR [Life Qualities] OR [Life Quality]

The literature in this search consisted of 320 items, most of which were not relevant to our study objectives. Through this search key articles which discussed the use of quality of life instruments to assess treatment and survival in breast cancer patients and survivors were identified.

Literature search #2: [Breast Cancer] OR [Breast Neoplasm] AND [Support, Social] OR [Social Networks] OR [Network, Social] OR [Networks, Social] OR [Social Network] OR [Psychosocial Support Systems] OR [Psychosocial Support System] OR [Support System, Psychosocial] OR [Support Systems, Psychosocial] OR [System, Psychosocial Support] OR [Systems, Psychosocial Support]

Our second search generated 202569 items; the relevancy of literature accrued through this search was extremely variable. To generate more precise literature, we included Breast Cancer as the major topic or focus of the article and Mesh terms related to ‘Social support’ in this search. This approach yielded 1000 articles. The titles and abstracts of articles were then scanned for relevant literature. Relevant literature included critiques of

existing social support models for cancer patients, assessment of psychosocial distress among breast cancer patients, support and guidance to understand and choose treatment modalities, aspect of social networks useful to breast cancer patients and usefulness of social networks during the course of treatment and recovery in breast cancer survivors.

Literature search #3: [Breast Cancer] OR [Breast Neoplasm] AND [Support, Social] OR [Social Networks] OR [Network, Social] OR [Networks, Social] OR [Social Network] OR [Psychosocial Support Systems] OR [Psychosocial Support System] OR [Support System, Psychosocial] OR [Support Systems, Psychosocial] OR [System, Psychosocial Support] OR [Systems, Psychosocial Support] AND [Quality of Life] OR [Life Qualities] OR [Life Quality]

To concisely identify literature pertaining to our study objectives, we conducted a third literature search and identified 215 items. These items were reviewed and 15 items relevant to our study objectives were identified. Out of these 15 items, 7 items were identified as key articles for our research. Relevant items consisted of articles related to quality of life and social support in breast cancer survivors. Additional literature was obtained by scanning the reference lists of key papers from the three literature searches.

Health Care System in the United States

The United States does not have a universal system of health insurance; however, approximately 84.7% of US citizens have some form of health insurance. Health insurance coverage is provided by employers (59.3%), purchased individually (8.9%), or provided by government programs (27.8%) (36). Health care facilities in the US are

mostly owned as well as operated by the private sector but health care is provided by different private and public legal entities. In the public sector, 60 – 65%, of health insurance coverage is available through government (federal and/or state) funded programs such as Medicare, Medicaid, TRICARE (Military Health System), the Children's Health Insurance Program, Veterans Health Administration, Federal Employee Health Benefits Program and the Indian Health Service (37).

Medicaid is a US government funded health program for low income individuals and families. It is funded by the state and federal governments and managed by the states (37). Each state operates its own Medicaid system which conforms to federal guidelines in order for the state to receive federal funds and grants (38). The Medicaid program is a “means-tested program.” Means-tested programs entail determination of whether an individual or family is eligible for help from the government. US citizens and permanent residents with limited assets and resources are eligible for Medicaid; however, poverty alone does not determine eligibility for Medicaid program unless they fall into certain designated eligibility groups. Various eligibility categories for Medicaid determine who gets health care coverage through the program. In addition to low-income, requirements such as assets, age and disability are considered for each category in the Medicaid program (38). The Medicaid program in the state of California is called Medi-Cal. It is administered by the California State Department of Health Care Services at the state level and the Centers for Medicare and Medicaid Services at the federal government level (37).

In the US, low-income women who are diagnosed with breast or cervical cancer and require treatment but are uninsured or under-insured, are provided health coverage

through the Breast and Cervical Cancer Treatment Program (BCCTP). BCCTP is a health coverage option in California, funded through Medicaid and legislated by the US federal government as a part of Breast and Cervical Cancer Prevention and Treatment Act of 2000. In the state of California, uninsured, low-income women are enrolled in the BCCPT program through Medi-Cal and their treatments for breast cancer are covered through the BCCPT program (39).

To be eligible for the Medi-Cal BCCPT in California, an applicant must be a resident of California, with an income that does not exceed 200% of the Federal Poverty Level (based on annual income and family size). Individuals may also be eligible if they have other health insurance coverage, as long as their premiums, co-payments and deductibles are expected to exceed \$750 annually (39).

Comparing US health system to the Canadian health system

Every Canadian citizen and permanent resident is covered by publicly funded universal health care plan governed by the Canada Health Act (40). In contrast, the US federal government does not guarantee universal health care to all its citizens; however, publicly funded health care programs help to provide for the elderly, disabled, children and the poor (38).

A 2006 study, comparing US and Canadian access to health care in 2006, found more unmet medical needs among US residents as compared to their Canadian counterparts. US residents were less likely to have a regular medical doctor and twice more likely to forgo needed medicines (41). Immigrants in both US and Canada face similar problems

accessing health care; a study comparing access to health care based on immigrant status in US and Canada concluded that immigrants in both countries have worse health care access as compared to non-immigrants (41). Another study in 2010 showed that immigrants in Canada have better access to care as compared to immigrants in US; however, most of the differences were explained by differences in socio-economic status and insurance coverage across the two countries (42).

In 2000, the World Health Organization (WHO) published a report ranking health care systems around the world based on health care outcome, funding for health care needs of the poor and health disparities due to income. Canada was ranked 30th and the US was ranked 37th in the WHO report (43). Over all, Canadians have better health outcomes as compared to the US residents; observed incidence rates for various diseases including cancer are lower in Canada than in the US (44).

According to Health Canada, the mortality rates due to cancers are similar in both US and Canada (45). Survival rates for certain cancers such as breast cancer are higher in the US as compared to Canada (46). Survival rates for cancers in both countries are similar if screening processes especially for prostate and breast cancer are not taken into consideration (47). Therefore, the Canadian and US health care systems are comparable in their delivery of cancer care based on similar mortality and survival data (46, 47). The survival rates for cancer patients in Ontario are also similar to those of cancer survivors in different parts of the US (47).

Transdisciplinary framework for breast cancer care

Health care systems and clinical practice including cancer care have advanced considerably during the last four decades (48, 49). A focus on ‘transdisciplinary’ research in breast cancer patients has the potential of yielding valuable scientific information. Hiatt and Breen presented a ‘transdisciplinary’ framework for breast cancer care, shown in **Fig 1** (50). According to Hiatt and Breen, in order to further advance cancer control research, the optimal approach would entail integration of the study of biological and physical nature of cancer and its clinical applications with the behavioural and social influences that cancer has on an individual (50).

In the framework by Hiatt and Breen, different phases of life from pre-disease to mortality in breast cancer patients are presented as a cancer continuum on the horizontal axis in **Fig 1**. Each phase is influenced by social and environmental factors. Four levels of analysis have been introduced into the framework. The introduction of each level of analysis is based on the need to highlight specific research approaches or pathways. The first level focuses on broad social conditions and policies; the second addresses the impact of healthcare systems on the cancer continuum; the third level looks at the behavioral and psychological factors; and the fourth level of analysis examines the biological mechanisms of carcinogenesis. According to Hiatt and Breen, disparities and burden of breast cancer may be reduced by introduction of interventions at any of these levels (50).

Figure 1. Hiatt and Breen's framework for cancer care (50).

Note: The framework illustrates the relationship of levels of analysis with the types of interventions along the cancer continuum for e.g. healthcare systems are less likely to influence cancer incidence than mortality and are lightly shaded in the preclinical phase of the continuum. Social determinants are represented by dark shades throughout because these are more likely to influence breast cancer survivors throughout the cancer care continuum (50).

Although the framework appears to be simple and linear, the authors recognize that the clinical, biological and social interactions are more complex and multidimensional in reality (50). Hiatt and Breen argue that social as well as behavioral and psychological determinants of breast cancer care, along with biological factors, play an important role all throughout the process of cancer care, including prevention and early detection. Health systems are mostly involved after the diagnosis. Therefore, as shown in **Fig 1**, an intervention regarding social and psychological determinants of breast cancer can have considerable impact at every level of the disease such as prevention, early detection, treatment and quality of life.

The modern perspective of clinical care and health care delivery entails improvement in quality of life as a corner stone for improving patients' experience with the health care systems (48, 49). Increased emphasis on improving patients' experiences with the health care system has brought issues related to evaluation of quality of life to the forefront. Quality of life assessments are therefore, essential in determining the quality of health care received by breast cancer patients (51).

Since the number of breast cancer survivors in North America is increasing every year (4, 5, 6) and more women are surviving breast cancer for longer durations of time, it has become necessary to turn our focus on evaluating and improving quality of life among these women. In order to understand the role of quality of life in cancer survivors, we must first understand the meaning of quality of life in the context of chronic illnesses such as breast cancer.

Quality of life in Breast Cancer Survivors

According to the World Health Organization (WHO), health is defined as *“a state of complete physical, mental, and social well-being and not merely the absence of disease.”*

The constitution of WHO puts a great deal of emphasis on the importance of measuring changes in HRQOL as well as improving HRQOL especially among chronically ill patients. The true estimate of well-being is not possible without measuring quality of life (52).

The concept of quality of life related to well-being is not new; it dates back to the ancient Egyptian civilization (53). Herodotus (450 BC) suggested that opulence of the tombs of valley of kings in Egypt and Thabes was an indication of the importance their society placed on quality of life even after death (53). The supreme chief of medicine in 2800 BC Egypt was named ‘Imhotep’ meaning *“he who gives contentment.”* Even in ancient Greece, the model of medical practice was based on a holistic approach where the patient’s wellbeing was determined by quantitative assessments of emotional reactions and interpersonal responses to their situation (53).

Quality of life is a ubiquitous notion and can be interpreted in social, political, economic, philosophical and health related contexts, sometimes described as ‘complete life’. Merriam-Webster’s dictionary defines ‘quality’ as *“degree of excellence”* and life as *“the sequence of physical and mental experiences that make up the existence of an individual.”* Scholarship on the concept of quality of life is vast and variable (54, 55). Aristotle’s (384 BC) idea of a good life consisted of ability to perform acts which led to internal and external good, resulting in individual happiness (56). Throughout history

moral philosophers, historians and scientists have quibbled over the definition of quality of life. In more recent times quality of life has become a distinct area of study especially in the fields of economics and medicine.

In the field of medicine and health care delivery, health-related quality of life (HRQOL) serves as a measurement tool for success of care provided to the sick, especially those suffering from chronic illness. Fallowfield (57) conceptualized the notion of quality of life in terms of health care and described this concept as follows: *“quality of life is not a unitary concept, but rather a complex amalgam of satisfactory functioning in essentially four core or primary domains: psychological, social, occupational and physical.”* Van Knippenberg and De Haes studied the meaning of quality of life in patients with chronic illness and especially focused on the meaning of quality of life in patients with cancer (58). According to Van Knippenberg and De Haes, for those who had experienced prolonged illness, quality of life is described as possessing a state of wellbeing, satisfaction of needs, human values and quality of survival (58).

Cella and Tulsky offer a pragmatic approach to the understanding of HRQOL; they propose that quality of life is a comparison of one's own health to an ideal state of physical and mental wellbeing (59). Cella further argues that quality of life is a combination of patient perspective as subjective information and factual knowledge of physical well-being, functional ability, emotional well-being, and social well-being (60).

Several approaches have been reviewed and subsequently used as objective assessment tools for quality of life (61, 62). Calman in 1984, presented the 'gap theory,' which describes quality of life in terms of difference between patient's ideal desires of the

standard of physical, mental and social wellbeing and the realistic expectation of what can be achieved in a given set of circumstances (61-63). The psychological theory proposed by Kleinman (61, 62, 64) suggests that quality of life can be assessed by making a distinction between the actual vs. perceptual degree, severity and duration of illness. Ware describes HRQOL in five multi-measure concepts: physical health, mental health, general health perceptions, social functioning and role functioning (65- 67). These five concepts are considered as a minimal standard for content validity of HRQOL (65 - 67).

Ware *et al.* (67 -70) standardized the approach to measurement of HRQOL in patients with chronic disease with the development of their Medical Outcome Study Short form health survey with 20 questions (MOS SF-20). The MOS short form health survey incorporates the concepts of physical health, mental health, general health perceptions, social functioning and role functioning. The Medical Outcome Study Short form health survey with 36 questions (MOS SF36) was subsequently constructed to increase the comprehensiveness and improve precision of MOS SF-20 (67). To improve the content validity of the Medical Outcome Study, Ware *et al.* included 3 more multi-measure concepts in the SF-36, which were: bodily pain, vitality and role limitations. These additional concepts were to be used to assess both physical and mental issues (67).

Over the years HRQOL instruments have evolved to include cancer specific items and in some cases items more specific to quality of life issues in breast cancer patients. European Organization for Research and Treatment of Cancer Core Cancer Quality of Life Questionnaire (EORTC QLQ-BR23) is the most commonly used instruments used to assess HRQOL among breast cancer patients (71-75). Other instruments commonly used

are the Functional Assessment Chronic Illness Therapy General Questionnaire (FACIT – G) and its module for breast cancer the Functional Assessment Chronic Illness Therapy Breast Cancer Questionnaire (FACIT – B) (76 -77). Montazeri in his review of health related HRQOL in breast cancer patients from 1974 to 2007 listed a number of validated instruments that have been used for assessment of HRQOL in breast cancer survivors in the last four decades (23). The list of instruments used to assess HRQOL was divided in the following six categories by Montazeri (23):

1. General instruments to assess HRQOL: these include the Short Form Health Survey (SF-36), Spitzer Quality of Life Index (QLI), Sickness Impact Profile (SIP), Ferrans and Powers Quality of Life Index (QLI).
2. Cancer specific instruments to assess HRQOL: these are European Organization for Research and Treatment of Cancer Core quality of Life questionnaire (EORTC QLQ-C30), Functional Assessment of Chronic Illness Therapy General Questionnaire (FACIT-G) (formerly FACT), Functional Living Index-Cancer (FLI-C) and Ferrans and Powers Quality of Life Index-Cancer (QLI-C).
3. Breast cancer specific instruments to assess HRQOL: include European Organization for Research and Treatment of Cancer Breast Cancer Quality of Life Questionnaire (EORTC QLQ-BR23), Functional Assessment of Chronic Illness Therapy-Breast (FCIT-B), Breast Cancer Chemotherapy Questionnaire (BCQ) and The Satisfaction with Life Domains Scale for Breast Cancer (SLDS-BC).
4. Psychological instruments to assess HRQOL: such as General Health Questionnaire-28 (GHQ-28), Hospital Anxiety and Depression Scale (HADS),

Beck Depression Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D), State-Trait Anxiety Inventory (STAI), Profile Mood State (PMS), Mental Adjustment to Cancer Scale (MACS) and Psychosocial Adjustment to Illness Scale (PAIS).

5. Symptom-related instruments to assess HRQOL: these measures are Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Piper Fatigue Scale (PFS), Multidimensional Fatigue Inventory (MFI), Functional Assessment of Chronic Illness Therapy-B plus Arm Morbidity Subscale (FACIT-B), Hot Flash Related Interference Scale (HFRDIS), Shoulder Disability Questionnaire (SDQ), Brief Pain Inventory (BPI), McGill Pain Questionnaire (MPQ), Memorial Symptom Assessment Scale (MSAS) and Rotterdam Symptom Checklist (RSC).
6. Other instruments to assess HRQOL: include Functional Assessment of Chronic Illness Therapy-Spiritual (FACIT-SP), Body Image Scale (BIS), Body Image After Breast Cancer Questionnaire (BIBCQ), Watts Sexual Functioning Questionnaire (WSFQ), Life Satisfaction Questionnaire (LSQ) and Satisfaction With Life Scale (SWLS).

The selection of instrument depends on the research question. For example FACIT-B would be a more suitable instrument to assess HRQOL in research related to breast cancer treatment, as compared to CES-D and BIBCQ, which may be more useful in studies related to assessment of psychological impact of breast cancer (23). Instruments such as EORTC and FACIT examine HRQOL in cancer patients with specific questions designed

for potential responses unique to breast cancer patients. Other instruments such as MOS SF-36 and QLI evaluate general HRQOL in patients with chronic illness (23, 78).

Several studies in the recent past have used breast cancer specific HRQOL instruments such as EORTC QLQ-BR23 and FACIT-B (23, 72-76). Studies suggest that HRQOL in breast cancer patients can be evaluated by using either a breast cancer specific instrument such as FACIT-B or a general instrument such as MOS SF-36 without compromising validity in both cases (76 - 78). The difference between breast cancer specific instruments and general instruments to assess HRQOL is that, in addition to HRQOL items, items specific to breast cancer care are also included in breast cancer specific instruments (67 – 74).

Breast cancer specific HRQOL instruments such as EORTC QLQ-BR23 and FACIT-B are designed to measure specific side effects of breast cancer treatment e.g. arm swelling, hormonal changes, breast oversensitivity; hence, these instruments are more useful in clinical trials comparing effects of treatment in breast cancer patients (78). Studies using breast cancer specific HRQOL instruments may be less precise in their assessment of effects of multidimensional predictors such as perceived social support on HRQOL (23). A general measure such as MOS SF-36 can be a more useful instrument in evaluating the effects of social support on HRQOL (23, 78).

Ware and Sherbourne point out that evaluation of HRQOL requires the global appraisal of several concepts encompassing physical, mental and social well-being (67). The main reasons for using general measures of HRQOL is the ability of these measures to capture individual, temporal and cross cultural variations (78).

The perception of a particular aspect of quality of life and its relative importance (i.e. weight) may vary within individuals in addition to variation across individuals. In addition, there may be temporal variations in the perception of an individual's quality of life. For example, loss of appetite in a breast cancer patient can have several causes throughout the course of treatment. A patient's loss of appetite can be attributed to toxicity due to chemotherapy, tumour activity, physical or mental co-morbidity such as diabetes or depression and may improve or get worse over time (78, 79).

The other reason for global assessment of HRQOL is that the measures to assess HRQOL in breast cancer patients ought to be cross-culturally equivalent as there may be cultural variation in perception of disease and treatment sequelae and therefore, specific aspects may be perceived differently across the multiple cultural and social class groups (78-80).

Determinants of Health Related Quality of life in Breast Cancer Patients

Through our discussion regarding the definition of HRQOL it is clear that HRQOL is a complex concept based on an individual's perception of physical, psychological and social wellbeing and satisfaction (57-58). Due to the ubiquitous nature of HRQOL, the determinants of HRQOL consist of factors that affect every aspect of an individual's life and depend on the type and duration of affliction.

The literature on HRQOL in breast cancer survivors dates back to 1974 when the first article was published discussing subjective as well as objective assessment of HRQOL after adrenalectomy and chemotherapy in breast cancer patients with metastatic disease (23, 81). Since then, more than 600 articles have been published in peer reviewed journals, establishing associations between HRQOL and its determinants in women with

breast cancer (23). A comprehensive review of the literature revealed several determinants of HRQOL in breast cancer survivors. These determinants can be broadly classified into demographic factors, treatment related factors and psycho-social factors and are listed in **Table 1**.

Some of the determinants of HRQOL in breast cancer survivors have a direct effect on HRQOL while others may have an indirect effect. For example a study in 2010 described Caucasian race, low BMI and higher education level as determinants of physical activity such as yoga in breast cancer patients (88); both BMI and physical activity also affect HRQOL in breast cancer survivors (89). Ethnicity is another determinant which alone may not have a significant effect on HRQOL, however, spiritual and social practices combined among different ethnicities can have a significant impact on HRQOL (89).

Demographic and treatment related factors that determine HRQOL have been extensively explored in the literature (23, 82-104) as shown in **Table 1**. Psycho-social factors related to HRQOL have also been researched (92-104); however, social support as a determinant of HRQOL in breast cancer patients requires further attention and exploration (92).

Table 1: List of factors that determine Health Related Quality of Life (HRQOL) in breast cancer patients (23, 82 - 104).

Demographic factors	
Age	Age at the time of diagnosis is a significant predictor of HRQOL (82 -87). Women diagnosed with breast cancer after 65 years of age showed significantly worse physical HRQOL whereas, those diagnosed between 45-65 years showed better physical HRQOL (86).
Basal Metabolic Rate (BMI)	Healthy-weight and/or overweight women with breast cancer reported significantly better physical HRQOL compared with their obese counterparts (89).
Menopause	HRQOL in Breast cancer survivors who had menopause was poor as a result of symptoms of menopause such as fatigue, pain etc. (83-85).
Income	Breast cancer survivors belonging to high-income groups have better ability to cope with disease and as a result have better physical and emotional HRQOL (23, 84, 85, 87 91).
Educational level	Breast cancer survivors with higher education level are able to understand and familiarize themselves with the disease and its possible outcome and therefore, have better emotional as well as physical HRQOL (23, 85, 91).
Marital status	Married breast cancer survivors show better HRQOL, however marriage or partnership already under stress can cause increased stress after breast cancer diagnosis. The added stress is a risk factor for deterioration in both physical and emotional HRQOL (92).
Ethnicity	African Americans and Latinas are reported to have better emotional HRQOL because of their spiritual practices (90). Most Caucasian women report better physical HRQOL because of increased engagement in physical activities (89).
Diet and exercise	Cumulative effects of physical activity, vegetable consumption and smoking cessation had a positive effect on HRQOL in women with breast cancer. (89). Yoga improved emotional and

physical HRQOL in women with breast cancer (88)	
Treatment related factors	
Stage of breast cancer	Studies suggest that stage of the disease indirectly alters quality of life. Morbidity is related to later stage of breast cancer which leads to poor physical and emotional HRQOL. Stage of disease determines the treatment modality which also has an impact on HRQOL (23).
Type of Surgery	Before breast reconstructive surgery became more common for breast cancer patients, mastectomy was related with poor emotional HRQOL due to poor body image issues related to mastectomy as compared to breast conserving surgery (23).
Chemotherapy	Breast cancer chemotherapy has evolved due to data collected on HRQOL during clinical trials for chemotherapeutic agents. The effects of chemotherapy on HRQOL are variable and depend on the stage of disease. Women with more severe disease have reported very poor physical HRQOL after receiving chemotherapy (23).
Radiation therapy	Radiation therapy is usually given in combination with surgery in breast cancer patients. Effects of radiation therapy on HRQOL are also observed in association with the surgical modality used to treat the patients. Physical side effects of radiation therapy such as arm swelling, chest pain and fatigue result in poor physical HRQOL (23).
Hormone replacement therapy	Literature on the association of hormone replacement therapy and HRQOL is limited. Some studies suggest that side effects of anti-estrogens include hot flashes, weight gain, fatigue and depression. These side effects negatively affect quality of life in breast cancer patients (23).
Co-morbidity	Physical and psychological co-morbidities have a negative effect on physical and emotional HRQOL in breast cancer patients (23).
Treatment side effects	Physical HRQOL is compromised as a result of treatment side effects. Emotional HRQOL is compromised in women

undergoing mastectomy(23).	
Psycho-social factors	
Uncertainty	Diagnosis of breast cancer can bring out feelings uncertainty in the surviving patient. Feelings of uncertainty impair emotional HRQOL in breast cancer survivors (94 -97).
Stress	A meta-analysis of psychosocial variables related to breast cancer found significant association between HRQOL in breast cancer patients and reported stressful life events (98).
Repression/ Denial	Various studies suggest that denial in women diagnosed with breast cancer deregulate the immune system and result in long term physical and psychological distress resulting in deterioration in physical and emotional HRQOL (95, 97, 101, 102).
Expression	Emotional expression is the opposite of denial. Literature demonstrates a positive association between emotional expression and emotional HRQOL in breast cancer patients (99, 100).
Spirituality	Spirituality is a determinant of HRQOL in breast cancer patients. It has been demonstrated that spirituality can enhance physical and psychological HRQOL. Levin reviewed more than 250 published empirical studies on beneficial health effects of religious or spiritual practice. Because women with breast cancer have various stressors, their spiritual awareness acts as buffer against the effects of stress (104).
Social support	Absence of social networks has been tied to decreased survival and rapid course of illness in breast cancer patients (103). Social support is a possible determinant of HRQOL; however, literature regarding the relationship between social support and HRQOL is scarce (92).
Supportive care	Efficiency of ancillary care provided by the nursing staff, paramedics and social support staff is shown to have a positive relationship with HRQOL in breast cancer patients (23).

Social Support

The term “social support” was coined in the middle of the 20th century but the concept of social support is not new. Darwin declared humans to be social animals and attributed emotions such as sympathy, pleasure, love and satisfaction to this social animal (105). Survival of the human race according to Darwin was contingent on people’s ability to ‘sympathetically’ co-exist with each other (105).

Scientists have been studying the phenomenon of social integration and interdependence for a long time and various definitions have surfaced after the term ‘social support’ was coined in the 1970s (106). Cobb in 1976 described social support as awareness by individuals that they are being cared for, loved, esteemed and valued. It is also an acknowledgement that they belong to a network of communication and shared obligation (107, 108).

According to Hupcey, the concept of social support is best defined in the context of its use; he stated (109), *“Social support is a multi-faceted concept that has been difficult to conceptualise, define or measure. Although this concept has been extensively studied, there is little agreement among theoreticians and researchers as to its theoretical and operational definition. As a result, the concept remains fuzzy and almost anything that infers a social interaction may be considered social support.”*

Although the theoretical concept of social support may be ambiguous and complex, Hupcey concluded that it was possible to operationalize it for research by categorizing it into three facets (109). The three operational facets of social support as described by

Hupcey are: 1) social network and social integration variables 2) received support and 3) perceived available support.

Lugton (1977) also conceptualized social support as a multidimensional construct. He opined that social support entailed counting and categorization of degree of individual's social ties alongside a qualitative evaluation of those social ties (107). Lugton divided social support into two categories: structural and functional support.

Based on the work by Hupcey, Lugton and others in the field, social support can be conceptualized broadly as structural or received support and functional or perceived support. Categorization of social support is presented in **Fig 2** and described below.

Hupcey opined that measuring all the facets of social support would be impossible and fruitless in a single study and it is the task of researcher to identify which aspect of social support is important to study for a given context (109). Our study was designed to analyze the relationship between perceived social support and HRQOL; therefore we measured perceived or functional support among breast cancer survivors. A discussion regarding the two categories of social support is given in the text below.

Structural/ Received Social Support:

Structural support quantifies and determines the interconnectedness of existing social relationships. For example, marital status and the dynamics of marital relationship or number of friends and relations or degree of connectedness with friends and relations would be considered in the realm of structural support (110).

Figure 2. Organizational diagram for understanding social support

Hutchison studied the concept of structural social support from three perspectives: network structure, support functions and the nature of relationships (110). Hutchison described social support in terms of quantity of one's relationships. Structural support includes the number of interpersonal relationships and the extent to which there is interconnectedness between those relationships; however, the degree or quality of interconnectedness of relationships was not described by Hutchison and is not a part of structural support (110).

Received support entails support measured in terms of numbers of individuals available to render support or in other words it is the same as structural support. Received support according to Sherbourne et al., "is confounded with need and may not accurately reflect the amount of support that is available to a person" (30).

Functional Support:

Recent literature indicates that the concept of functional component of social support addresses the issues of quality vs. the quantity of support available (110-113). This approach emphasizes the functions of interpersonal relationship, such as emotional support, instrumental support, informational support and social companionship. Functional support is a perceptual paradigm described by Sherbourne and Stewart as perceived social support which refers to: "*the degrees to which interpersonal relationships serve a particular function*" (30).

Cohen and Syme as well as Cohen and Wills concluded that an individual's perception of social support is more important than the support received (111,112). Sherbourne and Stewart argue that not having received support during a specific period of time does not

mean that there is no support available for such individual. The concept of perceived social support or functional support was examined extensively by Stewart in the field of nursing, who based this concept of degree of relationships severing a purpose on various theories including coping theory, social comparison theory, social exchange theory, attribution theory, social learning theory and social competence (69).

Role of Social support in breast cancer:

Literature suggests that greater social support is associated with longer survival in women with localized or regional breast cancer (115, 116). A prospective study looking at the effects of social context on rate of survival from breast cancer found that women with increased support, particularly outside the home, had significantly higher rates of survival at a four year follow-up (116). Furthermore, absence of a social support network has been linked to not only a higher incidence of cancer and but also a more rapid course of illness including greater severity in physical as well as psychological morbidity (117).

Measuring social support:

Translating the theoretical concept of social support into research can be challenging. McDowell categorized and described the instruments used to measure social support (118), summarized in **Table 2**. Most instruments presented in the table are self-administered.

Table 2: Comparison of instruments measuring social support

Instruments	Advantages	Disadvantages
Social Relationship Scale (119)	Used in the general population samples to measure individual's network of social relationships and their perceived helpfulness in alleviating stress.	Further testing in specific populations is required.
Social Support Questionnaire (120)	Quantifies availability of, and satisfaction with, social support.	Does not cover informational or tangible support.
RAND Social Health Battery (121)	Records resources of social support and frequency of interactions.	Does not rate the subjective experience of interactions.
MOS Social Support Survey (30)	Measures perceived social support in four categories. Main use in populations with chronic illness but can be used in general populations.	Information about validity in general population is not yet available.
Duke-UNC Functional Social Support Questionnaire (122)	Measures personal satisfaction with functional and affective aspects of social support.	Mostly used in clinical practice. Concerns about convergent validity.
Duke Social Support and Stress Scale (123)	Rates the amount of support provided and/or stress caused by family and non-family relationships.	Only used in family practice and family practice research. Low retest reliability coefficient.
Katz Adjustment Scales (124)	Measures social adjustment of Psychiatric patients following treatment.	Aspects of structural and functional support are not assessed.

Instruments	Advantages	Disadvantages
Social Functioning Schedule (125)	Assesses problems experienced in normal functioning. Was designed to evaluate treatment of neurotic patients.	Neither measures the level of social support available to patients nor assesses the level of social functioning.
Interview Schedule for Social Interaction (126)	Availability and social quality of relationships in psychiatric patients.	Administered by an expert and only for psychiatric patients.
Social Adjustment Scale (127)	Used as an outcome measure to evaluate drug treatment and psychotherapy in depressed patients. Has been used in other populations and healthy people.	Measures social adjustment rather than social support. Difficulty in scoring sicker patients as well as recovering patients.
Social Maladjustment Schedule (128)	Used to measure social maladjustment in psychiatric patients, family practice and general population.	Measures social maladjustment rather than support. Mainly used in UK and little evidence of reliability and validity has been published.
Social Dysfunction Rating Scale (129)	Assesses negative aspects of social adjustment.	Measures social adjustment rather than social support. Scoring of the instrument is unclear and there is little evidence to support validity of the instrument.
Structured & Scaled Interview to Assess Maladjustment (130)	Clinical assessment of social role performance	Assesses maladjustment and not social support. Mostly used in patients with psychiatric disorders.

Table 2 shows that most instruments measuring social support either focus on social adjustment aspect of support or social networking/ quantitative assessment of support i.e. structural support. MOS SS on the other hand only measures perceived social support.

Perceived social support as described by Sherbourne et al., entails several constructs such as ability to perceive someone who is there to help with daily chores, knowledge that someone cares about you and a realization that someone loves you (30). Sherbourne and Stewart constructed a model for perceived availability of social support (30). The model incorporated the qualitative assessment of social ties or functional aspect of perceived social support and consisted of four dimensions of social support which are (30):

1. Emotional /informational support: This means giving guidance or “appraisal support.” It involves presence of a support mechanism to provide appropriate guidance in response to any stress arising from the experience of disease.
2. Affectionate support: This dimension entails “attachment or affect”. In other words perception of someone who cares for you, loves you, takes care of you and values you as an individual.
3. Tangible support: Refers to the material, physical aid available to the individual. It involves existence of a reliable source of financial stability as well as availability of stable alliances.
4. Positive social interaction: Takes into consideration the concept of companionship and social integration.

The Medical Outcome Study Social Support survey (MOS SS) incorporates these four dimensions in a comprehensive and independent tool for assessment of perceived availability of social support (30). The MOS SS distinguishes social support measures from physical and mental health measures; it also differentiates between social support and concepts such as loneliness and family functioning and has high reliability over time (30).

Some breast cancer studies have used MOS SS due to its reliability over time and because of the instrument's ability to differentiate between the concepts of perceived social support from physical and health measures (115, 131 - 132).

Social support and HRQOL in women with breast cancer

A diagnosis with cancer is a negative event causing distress (133). Diagnosis of breast cancer causes more distress than any other diagnosis and is stressful for women regardless of prognosis (95, 134). More than one third of the women diagnosed with breast cancer experience psychological distress, most commonly depression and anxiety (135). Studies suggest that severity of distress in breast cancer patients is associated with severity of the disease itself (106 -113, 133 – 135).

Some articles on the other hand, suggest that cancer diagnosis is not a negative event (113, 135). In fact, cancer diagnosis can be considered a “psychosocial transition” which according to Andrykowski et al. is *“an event with significant negative implications that can nevertheless cause individuals to restructure their attitudes, values, and behaviours, and thus can serve to trigger positive psychosocial change”* (135).

Since breast cancer is a complex illness with a significant psychosocial and physical burden, the treatment for breast cancer has become multifaceted. In addition to surgery and systemic therapies, supportive care has become an integral part of treating breast cancer patients. Supportive care, according to Montazeri, encompasses nursing care, self-care through diet and exercise, access to care, availability of care and also social support provided to breast cancer patients (23).

Williams et al. analyzed the concept of social support in the context of HRQOL as it has evolved over the last few decades and identified two main models underpinning the concept of social support as it relates to HRQOL (133). The first model is the buffer model based on the works of Caplan and Casel and suggests that social support has a buffering or cushioning effect against life's stressors and protects the individuals from physiological and psychological harms arising from stressful situations (136- 137). The second model was termed the main-effect or direct effect model. According to the main-effect model, social support directly benefits the well-being of an individual by either fulfilling his/her basic needs or by emotionally inducing a positive effect on the immune system and thus, improve quality of life (133, 137 -139).

We found extensive literature related to HRQOL and breast cancer since 1974, when the first article on the subject was published (23); however, published literature regarding HRQOL in breast cancer patients is mostly related to the effects of treatment and surgery in breast cancer patients, followed by psychological effect of cancer diagnosis and treatment on HRQOL (23). The psychosocial factors that affect the HRQOL in breast cancer patients are listed in **Table 1** (page 30). Relationships between HRQOL and some psycho-social factors such as stress and supportive or ancillary care are already

established in literature; whereas, it is clear that more work is needed to understand the relationship between social support and HRQOL in women with breast cancer (23).

Out of more than 600 publications on factors associated with HRQOL in breast cancer patients, Montazeri identified 5 articles published between 1974 and 2006, which were related to social support and HRQOL in these patients (23, 140 – 144). Our search yielded 10 new publications related to social support and quality of life in women with breast cancer from 2007 to 2011 (145 – 154). **Table 3** lists all the articles assessing relationship between social support and quality of life in breast cancer patients from 1974 to 2011 (140 to 154).

Lee published the first article addressing the issue of support and HRQOL in patients with breast cancer in 1997. A sample of 100 women who volunteered at a community outreach program and who had undergone mastectomy for breast cancer 14 years prior to his study were mailed the Ferrans and Powers Quality of Life-Cancer Version questionnaire to assess HRQOL. Ferrans and Powers QLI measures satisfaction and quality of life in five domains: health and functioning, psychological/spiritual domain, social and economic domain, and family (140). No association between marital status and the number of type of relationships was found with HRQOL among women in the study group. Thematic analysis revealed that sharing knowledge and providing emotional support was the main motivation to volunteer at the community outreach program (140). Lee concluded that providing social support outreach programs to women with breast cancer is necessary to help women in coping with psychological stress associated with breast cancer.

Table 3: List of articles related to social support and HRQOL in breast cancer patients (1974 – 2011)

Authors (Reference)	Year	Key predictor/Intervention	Results/Conclusions
Lee (140)	1997	Social support (Reach to Recovery programme)	Social support plays a vital role in promoting overall HRQOL.
Sammarco (141)	2001	Perceived social support and uncertainty in younger breast cancer survivors	Significant positive correlation between perceived social support and HRQOL, and significant negative correlation between uncertainty and HRQOL.
Michael et al. (142)	2002	Social networks	Pre-diagnosis level of social integration was important factor in future HRQOL, and explains more of the variance than treatment or tumour characteristics.
Manning-Walsh (143)	2005	Relationships between personal and religious support and symptom distress and HRQOL	Personal support was positively related to HRQOL.
Sutton and Erlen (144)	2006	Mutual dyadic support intervention	Most dyadic relationships were supportive and improved emotional HRQOL.
Danhauer et al. (145)	2007	Collaborative, wellness-based group support for young women	No significant improvement on HRQOL , study identified areas for potential improvement in the program.
Kissane et al. (146)	2007	Supportive expressive group therapy (SEGT) for women with metastatic disease	SEGT improved HRQOL including treatment and protection against depression.
Ogce et al. (147)	2007	Social support in Turkish women	Social support improves HRQOL, family stressors have negative effects on HRQOL.

Authors (Reference)	Year	Key predictor/Intervention	Results/Conclusions
Filazoglu et al. (148)	2008	Role of social support in Turkish women	Coping and social support have a positive effect on HRQOL.
Lim et al. (149)	2008	Social support in Korean women	Direct positive effect of social support on HRQOL.
Nápoles-Springer et al. (150)	2009	Peer support counselling	Creating psychosocial programs with input from survivors and advocates who have similar self-identities to patients improve HRQOL.
Menesses et al. (151)	2009	Psycho educational support	Positive relation of Psycho educational support and HRQOL
Sammarco et al. (152)	2010	Perceived social support in Latinas and Caucasians	Perceived social support has an association with HRQOL and educational interventions should be mindful of ethnicity, cultural values and education level.
Marylin et al. (153)	2010	Social support immediately post diagnosis	Positive relation of social support and HRQOL, immediately post diagnosis.
Salonen P et al. (154)	2011	Face to face support and quality of life	Short term face to face support improves HRQOL in women with breast cancer.

Samarco analyzed the relationship between perceived social support and HRQOL and found a significant positive correlation between perceived social support and quality of life, a positive correlation between support and network size and between network size and socio-economic domain of QOL index. The study population consisted of younger women (≤ 50 years) with breast cancer. Social support questionnaire (SSQ) was used to measure social support and Ferrans and Powers Quality of Life-Cancer Version questionnaire was used to assess HRQOL for this study (141). The SSQ is a brief and easy to administer instrument which measures availability of social networks as well as some aspects of perceived social support; however, the instrument lacks the ability to comprehensively assess perceived social support as informational or tangible support are not measured using SSQ (120). No association between physical or mental HRQOL and social networks size was reported in the study.

In another study in 2010, Sammarco et al. looked at the effects of perceived social support on HRQOL using among Latinas and compared the effects with Caucasian women with breast cancer. Instruments used in the previous study (141) were used in this study as well. Caucasians had a higher perception of social support in the study (152). However, SSQ does not measure tangible and informational support (120). Cultural values and higher education showed a positive impact on HRQOL (152).

Michael et al. and Manning assessed social support as social networks and number of family members available to provide support. Both these studies evaluated the impact of structural support on HRQOL in women with breast cancer (142, 143). Michael et al. administered detailed questions related to treatment and HRQOL to 708 women diagnosed with breast cancer over a period of 4 years. Two instruments, MOS SF-36 and

Cancer Rehabilitation Evaluation System-Short Form (CARES-SF) were used to assess HRQOL. The modified Berkman–Syme Social Network Index (SNI) was used to measure frequency of involvement with social ties (which could range from intimate family and friends to extended community) (156). Michael et al. found socially isolated breast cancer patients scored lower in role functioning, vitality and physical functioning aspects of HRQOL when compared with breast cancer patients who were socially more integrated (142).

Manning looked at the effects of social support such as family members and friends available to help women with breast cancer on symptom distress as a mediator for HRQOL. Mean age of the 100 Caucasian women participating in the study was 46 years and they were administered FACIT-B questionnaire to assess HRQOL. According to Manning, having more social support reduced the negative aspects of symptom distress and positively affected HRQOL in women who had undergone surgery for breast cancer (143).

Sutton and Erlen used qualitative methodology to analyze the impact of social interactions between newly diagnosed stage I and II breast cancer patients and survivors on quality of life and interpersonal relationship of the participants in the study. Dyadic pairs consisted of 31 women newly diagnosed with breast cancer pairing with 31 survivors of breast cancer. Their biweekly interactions were logged for 8 weeks. Thematic content analysis of the log books was used to analyze the data for this study. Among the various themes emerging from the study, emotional support and focus on health and functioning were important considerations for women with newly diagnosed breast cancer. This study generated important knowledge related to HRQOL concerns

among women newly diagnosed with breast cancer and also highlighted the importance of supportive care for women with breast cancer. Because this study only used thematic analysis, no causal association could be established between dyadic support and HRQOL and the authors suggested that future quantitative studies are required to evaluate such associations (144).

Another study which evaluated the impact of having a peer based support system for women with breast cancer was published by Danhauer et al. in 2007(145). This study evaluated the effectiveness of a peer based intervention program introduced for women with breast cancer. The intervention program entailed having a group of peers diagnosed with breast cancer involved in various activities such as discussions regarding the disease process and relaxing exercises. After participating in the intervention program, women who had consented to participate in the study were sent questionnaires to assess: HRQOL (FACIT G and FACIT B), depression (Center for Epidemiologic Studies–Depression Scale), current affect (Positive and Negative Affect Schedule), satisfaction with one's life as a whole (Satisfaction with Life Scale) and program evaluation. Women diagnosed with breast cancer reported improvement by seven points on HRQOL after participating in the intervention program. This improvement according to the authors was clinically significant; however, it was not found to be statistically significant. The main purpose of the study was to assess the feasibility of collaboration between academic medical centre, regional cancer centre and community based cancer centre. Although, Danhauer et al. did not find a significant relationship between peer social support group activities and HRQOL, the women found some discussions, such as those related to coping after the news of diagnosis, to be very useful (145).

Kissane et al. used a randomized clinical trial to study the impact of supportive expressive group therapy (SEGT) in women with metastatic breast cancer. Women who had been diagnosed with metastatic breast cancer were randomized into intervention group which received SEGT and control group which did not receive SEGT, both groups received three sessions of regular relaxation therapy. Group therapy consisted 90-min sessions of SEGT every week. Women were enrolled for at least one year in the study. The aim of these sessions was to improve relationships with family, friends and physicians, create a new network of support and foster coping skills. Kissane et al. concluded that SEGT for women with metastatic breast cancer improved social functioning and reduced depression in women with metastatic breast cancer (146).

Another qualitative study evaluating the effects of peer support counselling interventions in breast cancer patients was conducted by Nàpoles-Springer et al. They identified and interviewed 89 breast cancer patients, 29 Spanish speaking breast cancer survivors and 17 culturally competent advocates for Latinos with cancer and conducted interviews. The results of the study indicated a need for supportive interventions which should begin close to diagnosis with breast cancer and psycho social programs with input from survivors. The authors believed that early psychosocial interventions are likely to improve HRQOL in diverse and underserved populations. This study provides useful information about the needs of underserved women with breast cancer and identifies steps that are required to improve HRQOL in these populations (150).

Menesses et al. evaluated the impact of psycho educational supportive intervention (breast cancer education intervention (BCEI)) on HRQOL in women with breast cancer from rural US. A convenience sample of 53 women with breast cancer were randomized

into experimental group with 27 participants and wait-control groups with 26 participants. The experimental group had more face to face educational support in the first 6 months as compared to wait-control group. In the 7th month, there was no activity for the experimental group, while the wait control group received educational support through telephone. Overall quality of life using Quality of Life Breast Cancer Survivors Tool was used as an outcome measure. Menesses et al. concluded that BCEI improved HRQOL in women with breast cancer in rural US; however, a need for better delivery system for educational sessions to women with breast cancer living in rural areas was identified (146).

More recently Salonen et al. evaluated an intervention of face to face social support in breast cancer patients. Women in the intervention group of the study were provided with face to face social support and they reported fewer arm symptoms and (clinically) better sexual functioning. Women diagnosed with breast cancer who were not provided with face to face social support intervention reported poor HRQOL. Salonen et al. argued that breast cancer patients should be offered systematic support and education tailored to their individual needs (154).

A study involving 101 women undergoing treatment for breast cancer in Turkey looked at the impact of perceived social support using Multidimensional Scale of Perceived Social Support (MSPSS) on HRQOL measured by using Rotterdam Symptom Control List (RSCL) and Karnofski Performance Status Scale (KPSS). Those who had more family support reported better psychological and global quality of life. RSCL measures the HRQOL relevant to symptoms of cancer while KPSS is limited in its capacity to appraise global HRQOL (147).

Another study from Turkey used a cross-sectional design to evaluate the impact of perceived social support on HRQOL. MPSS was used to measure perceived social support, while SF-36 was used to assess HRQOL. Multiple regression analyses indicated that social support was significantly associated with both physical and mental HRQOL (148).

A study comparing Korean-American women with breast or gynecological cancer to Korean women with breast or gynecological cancer was published in 2008. The main purpose of the study was to assess the pathways in social support that could improve HRQOL in these women. Quality of Life-Cancer Survivor (QOL-CS) was used for the assessment of QOL. MOS SS was used to assess perceived social support; in addition, structural support was measured using SNI. The researchers concluded that perceived social support directly influenced HRQOL and social networks either directly or indirectly influenced HRQOL in both Korean-American and Korean women with breast or gynecological cancer (149).

Marylin et al. used a cohort of 950 women to study the impact of perceived social support measured by MOS SS on HRQOL which was measured using the FACT-B. The researchers found a positive association between perceived social support and HRQOL immediately after diagnosis of breast cancer (153).

Gaps in the literature

Despite the significance of social support to both psychological and physical wellbeing, Peters-Golden found that only half of the women diagnosed with breast cancer feel that they have necessary social support (117). From our discussion regarding the prevalence

of breast cancer and effects of social support on quality of life in women with breast cancer, it is clear that social support as a variable deserves attention in patients with breast cancer.

Structural or received support only measures the number of individuals present in the breast cancer survivor's life. It does not measure the degree of usefulness of available support. Perceived functional support is a measure of degree of usefulness of support (30). In addition, the support structure (or received support) can vary over time for patients suffering from chronic illness such as breast cancer. Sherbourne and Stewart pointed out that not having received support during a specific period of time does not mean that there is no support available for such individual (30). Therefore, it is important to evaluate perception of social support among women with breast cancer in order to understand the presence and degree of usefulness of support available to these women.

Most studies looking at the relationship between social support and HRQOL listed in **Table 3** either evaluated the structural aspect of social support i.e. number of social networks, number of family members or friends available to provide support (142, 143, 149) or social support intervention programs (140, 144, 145, 146, 150, 151, 154). Very few studies listed in **Table 3** are evaluating the impact of 'perceived social support' on HRQOL (141, 147, 148, 149, 152).

Although, Lee's (140) conclusion supported the positive role of social support in terms of improving HQOL in women with breast cancer, these conclusions were based on a qualitative assessment of motivation to volunteer at an outreach program. The study did

not address the issue of perception of social support and its effects on HRQOL in breast cancer patients.

Similarly Sutton and Erlen as well as Nápoles-Springer et al. provided evidence that women diagnosed with breast cancer considered early psychosocial intervention to be beneficial to their HRQOL (144, 150). These studies also relied on qualitative assessment of patients' perception of social support and no association between perceived social support and HRQOL could be established in these studies.

MOS SS was used as a measure for perceived social support in only 2 of the 15 studies listed in **Table 3** (149, 153). Sammarco used SSQ (141, 152) as a measure for perceived social support. SSQ is limited in its appraisal of perceived social support as it lacks the ability to measure two (informational and tangible support) of the four domains of perceived social support measured by MOS SS. The two Turkish studies used MSPSS as measure for perceived social support (147, 148). The MSPSS is based on perceived social support in context of three sources of support which are family, friends or significant other (157). Only 2 studies listed in **Table 3**, used MOS SF-36 to assess HRQOL in women with breast cancer (142, 148). Some studies used other measures for global assessment of HRQOL such as Ferrans and Powers QLI (140, 141, 152). Other studies used breast cancer specific instruments such as FACIT-B and symptom related instruments such as RCS.

Received support only assesses amount of visible support and unlike perceived social support, it does not take into account the usefulness of that support for the affected individual. Analysing perceived social support would therefore, yield useful information

about social support from patients' perspective. MOS SS has been used as a measure of perceived social support and MOS SF-36 as a measure of HRQOL; to date, the relationship between perceived social support and HRQOL in women with breast has not been explored using both MOS SS and MOS SF-36 as predictor and outcome variables respectively in the same study.

Studies suggest that low SES is an indicator for increased mortality and morbidity in women with breast cancer (1-5). A qualitative study among breast cancer survivors in North America showed that breast cancer survivors from low SES reported poor perception of social support as well as HRQOL (150). A quantitative assessment of the effects of social support on HRQOL among low SES breast cancer survivors is the next step in further exploring this relationship.

Our literature review indicates that no quantitative study to date has reported the effects of perceived social support on HRQOL among low SES women in North America and more work is required to explore this relationship. Furthermore, this relationship has not been assessed in low SES women with breast cancer in years following their diagnosis and subsequent treatment. Our aim is to understand the relationship between perceived social support after 18 months of diagnosis and HRQOL after 3 years of diagnosis in women with breast cancer, with an objective to:

1. Determine the association between perceived social support and physical HRQOL among low SES women diagnosed with breast cancer.
2. Determine the association between perceived social support and emotional HRQOL in the same population of women.

Chapter 3

Materials and Methods

Objectives:

Few studies have looked at the association between perceived social support and HRQOL and none has examined this relationship in low SES women with breast cancer. Our study aims to fill the gap in literature by identifying the relationship between perceived social support and HRQOL among low SES women in North America over a period of 3 years.

Our research will specifically:

3. Determine the association between perceived social support and physical HRQOL among low SES women diagnosed with breast cancer.
4. Determine the association between perceived social support and emotional HRQOL in the same population of women.

Original study:

Our study uses secondary data from a previous study designed to assess determinants of breast cancer treatment in an underserved population. The aim of the original study was to obtain empirical evidence for improving health care and creating new interventions for underserved breast cancer survivors. The study followed a cohort of 921 underserved women enrolled in the BCCTP (Breast and Cervical Cancer Treatment Program) in California and individual and systems-level determinants of breast cancer treatment were analyzed.

Data were collected through patient surveys and medical chart abstraction over a period of three years. The baseline study surveyed participants at 6 months after breast cancer diagnosis, followed by surveys at 18 months and then 3 years after diagnosis (160).

The purpose of the surveys was to study the 1) Determinants of breast cancer care and 2) Determinants of survivorship in breast cancer patients. Determinants of breast cancer care were categorized as individual (e.g. stage of disease, co-morbidities, and marital status), inter-personal (e.g. relationship between patient and clinical staff) and system-level (e.g., benefits, setting of care, and access to health care). In addition, individual, inter-personal and system-level determinants of survivorship (health status, functioning, and quality of life) were also assessed in the original study. Medical records were extracted at 18 months after diagnosis to determine details of breast cancer treatment.

Study Population

The study population consisted of breast cancer patients who were newly diagnosed and spoke English or Spanish and resided in California. These women were enrolled in Medi-Cal's (California's Medicaid) BCCPT program. BCCPT is a health coverage option in California, funded through Medicaid and legislated by the U.S. federal government as a part of Breast and Cervical Cancer Prevention and Treatment Act of 2000. Women who were diagnosed with breast or cervical cancer and require treatment but are uninsured or under-insured, and have low-income are provided health coverage through BCCTP (37, 38).

The original study was approved by the UCLA Human Subjects Protection Committee and the California State Department of Health Services Human Subject Protection

Committee. The patient survey responses were anonymous and patient identities were coded, therefore, no information which could identify or report on individual participants of the study was available for this thesis. In accordance with the TCPS guidelines 3.4 and 3.5, in the absence of identifiable information, we proceeded with secondary data analysis for this thesis based on ethics approval in California (158, 159).

Eligibility criteria and selection of participants

Women who were 18 years or older and had definitively been diagnosed with breast cancer for the first time, were able to speak English or Spanish, living in California and receiving care through BCCPT were eligible to participate in the original study. Some women were newly diagnosed with breast cancer but were excluded from the original study because they: 1) could not speak either English or Spanish 2) had been diagnosed with breast cancer for more than 6 months at the time of baseline interview 3) were misdiagnosed 4) were previously diagnosed with breast cancer 5) were currently diagnosed or undergoing treatment for other cancer 6) had passed away before the baseline survey was conducted, 7) had cognitive challenges or 8) did not receive BCCPT benefits.

Data collection

Participants in the original study were identified by the California Department of Health Services as women who had been diagnosed with breast cancer for the first time in the last six months prior to their recruitment in the study. The identified participants were invited by mail to take part in a one hour telephone survey. Out of the 1869 potential participants, 239 refused, 360 were ineligible and 234 could not be contacted. Nine

hundred and twenty one of the 1508 who were eligible, scheduled an interview and completed the baseline telephone survey from March 2003 through August 2005. The response rate for the baseline survey was 61.1%. The study recruitment flow chart for our study is presented in **Fig 3**. Details of study recruitment for this data set have been published elsewhere (160) and are presented in **Appendix A**.

Data for the original study were collected 6, 18 and 36 months after diagnosis with breast cancer. The data were collected at the time of regular follow up for breast cancer patients, consistent with the American Society of Clinical Oncology (ASCO) guidelines (which recommend a physical examination by a clinician every 3-6 months for the first year after breast cancer diagnosis, then every 6-12 months for the next 2 years, and then yearly after that) (17). Stage of disease and confirmation of type of treatment received by the patient were ascertained by reviewing the medical records at 18 months after breast cancer diagnosis.

The survey interviews were conducted by trained interviewers. Data related to demographic characteristics, diagnostic options and delay, initial cancer care, barriers to cancer care, satisfaction with initial cancer care, medical decision making, co-morbidity, patients' knowledge and self-efficacy, health beliefs, acculturation and number of people available to provide support were collected at baseline.

The women were contacted for a second survey from September 2004 through October 2006, 18 months after their breast cancer diagnosis. Out of the 921 women who had completed the first survey, 798 scheduled and completed the second survey conducted again via telephone interview.

Figure 3: Our study recruitment flow chart.

At the second interview, information about follow up treatment, barriers to accessing health care, satisfaction with treatment, side effects to treatment, quality of life and perception of available social support was gathered.

The third survey, another one hour interview, was carried out from May 2005 through July 2008, 3 years after the breast cancer diagnosis and 666 women participated in this survey. Among the women who dropped out of the study, the majority were those who could not be contacted due to change of contact information, some had died and others had refused to be contacted for further studies. Questions related to recurrence, follow up questions on treatment, side effects, access to care and quality of life were asked in the third survey. A time line of data collection is given in **Appendix B**.

For our study, we used a cross-sectional study design using the cohort of low SES women 18 years and older, living in California and newly diagnosed with breast cancer who participated in the original study. Women who had been interviewed for all three surveys were selected for analyses in our study. Perceived social support and other covariates were collected at the second survey which was at 18 months after breast cancer diagnosis and HRQOL was measured 36 months after diagnosis with breast cancer. The total number of women participating in our study was 634.

Conceptual framework

The conceptual framework for our study is based on the Pearlin's stress process model (161 – 163) and derived from literature review of variables associated with HRQOL and breast cancer care (**Table 1**) as well as the contextual model for breast cancer care described by Ashing Giwa (170). Our conceptual model is presented in **Fig 4**.

The stress model evaluates the process by which stressors are able to exert their health effects over time. Pearlin's stress model is derived from social stress theory as well as literature pertaining to medical sociology (162, 163). It has been extensively used in various epidemiological studies, especially in evaluations of psychological distress and role of care givers and social networks among breast cancer patients (164 – 167). Turner and Lloyd analysed the stress processes as described by Pearlin. They concluded that through the use of the stress models, researchers can identify the interrelationship between acute or chronic stressful life experiences and social as well as personal relationships which may have an impact on health outcomes over time. This can lead to identification of targets for intervention to alleviate or reduce the negative impact of stressors and consequently improve quality of life (168).

For life events and chronic strains such as those observed in women with breast cancer, Pearlin et al. described two mechanisms through which stress is manifested. The first mechanism is the appearance of a stressful life event at a discrete point. The second mechanism is the slow and persistent presence of strain which generates either a new strain or magnifies existing strains (161).

The initial stressor is called the 'primary stressor', which in our model is being diagnosed with and living with breast cancer. The 'secondary stressors' (in our model include individual and systems-related factors) are the ones which follow the primary stressor and contribute to the duration and level of stress in breast cancer survivors. For a woman with breast cancer, the primary and secondary stressors appear in a temporal sequence as presented in **Fig 4**, which depicts a pathway between our exposure and outcome variables (169).

Figure 4: Conceptual framework for our study.

Perceived social support is known to have a buffering effect against stress in general population and those suffering with cancer in particular (104, 133, 136, 137). Therefore, in our conceptual model we propose that perception of social support in the years following diagnosis with breast cancer has an impact on the future stress outcomes such as physical and mental HRQOL.

Pearlin also described the process of ‘stress proliferation’ which explains the interconnectedness of hardships on an individual over time. The process of ‘stress proliferation’ is two fold: first, the life course itself has an impact on an individual for, e.g., those belonging to lower SES have greater hardships in life compared to those belonging to higher SES; second, the addition of burdens of life, which Pearlin terms as ‘allostatic load’. Greater the allostatic load, the more difficult it is for bodily systems to work at optimal capacity. Those already disadvantaged during their life course (e.g. belonging to lower SES), suffer from greater allostatic load which result in poor outcomes (162).

In addition to the hypothesized relationship between effects of perceived social support on HRQOL in women with breast cancer, several factors serving as secondary stressors can affect both the exposure and outcome and as a result have an impact on the exposure and outcome. In our model these factors are broadly categorized into ‘individual-related factors’ and ‘systems-related factors’.

A list of factors that affect HRQOL in women with breast cancer is given in **Table 1** (pages 28 -30). These factors serve as individual-related factors in the causal pathway between perceived social support and HRQOL in women diagnosed with breast cancer.

The systems-related factors in our conceptual model are based on contextual framework presented by Ashing-Giwa (170). Ashing-Giwa studied the socio-cultural determinants of quality of life in minorities such as Latina and Asian Americans and presented a contextual model of the relationship HRQOL and determinants of HRQOL. Ashing-Giwa's model consists of a framework to investigate areas of health disparities and risk factors for poor outcomes in HRQOL research with cancer survivors. This contextual HRQOL theoretical framework includes cultural and socio-ecological dimensions and explains that in addition to individual-related factors, factors such as relationship with hospital and staff, life stressors etc. can also have an impact on cancer care and outcomes (170). We incorporated the contextual model described by Ashing-Giwa into our model by including the systems-related factors in our causal pathway.

The stress outcomes which in our model are physical and emotional HRQOL in women with breast cancer are a consequence of combination of all the components in our model. The impact of perceived social support on HRQOL is confounded by various factors hypothesized in our conceptual model. There is ample evidence cited in the literature to support our hypothesis (23, 82-170). Thus, the model presented in **Fig 4** adequately describes the temporal causal relationship between perceived social support in women with breast cancer and their HRQOL.

Measures used in our study

Variables used in our study were collected at different time points, details of which are given in **Appendix B**. We used the conceptual framework presented in **Fig 4** to select the

variables from the original study to be used in our analysis. Details of the variables used in our study are given in the sections below.

The unit of analysis for our study was a woman who was a breast cancer survivor. A breast cancer survivor for this study was defined as ‘a woman who had been diagnosed with breast cancer 6 months prior to the baseline survey and had undergone treatment for breast cancer and is currently undergoing treatment, recurrence or convalescence.’

The central component of this study was evaluating the impact of perceived social support on HRQOL among breast cancer survivors. According to the Canadian guidelines for breast cancer care, psycho- social evaluation and interventions in breast cancer survivors are to be explored after one year of cancer diagnosis (16, 17). The time line for variables collected in the original study is given in **Appendix B**. Our key predictor variable of interest was perceived social support. Other predictor variables relevant to our study are highlighted in **Appendix B**. All predictor variables were collected at 18 months after breast cancer diagnosis except for age, menopause, ethnicity and education level, which were collected at baseline. Our outcome variables, physical and emotional HRQOL were collected at 36 months after breast cancer diagnosis.

Primary Outcome Variables:

The primary outcomes of interest in this study were physical and emotional HRQOL, measured using Medical Outcomes Study Short Form-36 (MOS SF-36). The SF-36 is a generic measure that assesses the eight most important health concepts which represent basic human values and have relevance to functional status and wellbeing (67). These eight health concepts also known as sub-scales of SF-36 and are: 1) General health 2)

Physical functioning 3) Vitality/Energy 4) Body pain 5) Role limitation due to physical functioning 6) Role limitation due to mental functioning 7) Emotional wellbeing and 8) Social functioning

The SF-36 is a reliable instrument with median reliability coefficient for each health concept sub-scale equalling or exceeding 0.8, except for the social functioning scale, which has a median reliability coefficient of 0.76 (68). The SF-36 has been validated as a tool for assessment of HRQOL in the general US population (68, 70). It has also been translated and validated in Spanish (68). The SF-36 survey is shown in **Appendix C**.

We transformed the SF-36 from survey items into component summary scores representing physical and emotional health. Thirty six questions known as items were categorized into 8 sub-scales. Thirty five items from the survey were converted into 8 sub-scales with scores between 0 and 100; 0 being the worst outcome and 100 being the best outcome for HRQOL. The 36th item in the survey measured the transition of health over a period of one year (171); the last item did not relate to our study question and was not used in our analysis.

Physical and mental component summary scores were generated from the 8 sub-scales. The physical functioning, physical role limitation and body pain scales contribute to the scoring of the Physical Component Summary (PCS) score (172) while emotional health, emotional role limitation and social functioning scales contribute to the scoring of the Mental Component Summary (MCS) score. General health, body pain and vitality/energy contribute to both PCS and MCS (172). The distribution of SF-36 items and sub-scales in relation to the physical and mental component summary scores is presented in **Fig 5**.

Fig 5: HRQOL using Medical Outcome Study Short Form-36 (65 -68).

Converting SF-36 items to sub-scales

Responses to the SF-36 survey were scored according to the standardized scoring algorithm described by Ware *et al.* (171), shown in **Appendix D**. Conversion of SF-36 items to scales was a three step process:

- 1) Item recoding: we recoded items according to pre-specified algorithm (**Appendix D**).
- 2) Items were then summed and transformed into raw scale scores.
- 3) Raw scale scores were transformed to a score of 0 -100, using the following transformation formula:

$$\textbf{Transformed Scale} = [(\textbf{Actual score} - \textbf{Lowest possible raw score}) / \textbf{Possible raw score range}] \times 100$$

Lowest possible raw score range and possible score range were pre-specified and available in literature (171). The transformed sub-scales consisted of score range from 0 – 100 for the 8 scales.

Conversion of sub-scales into component summary scores

After obtaining scores for the 8 sub-scales, we converted sub-scales' scores into physical and mental component summary scores (PCS and MCS). The conversion of SF-36 sub-scales into summary scores was based on work by Ware *et al.* (172, 173). Physical functioning and emotional functioning are considered the purest measures for PCS and MCS respectively. Body pain, general health, vitality and social functioning are

considered to be confounded sub-scales, as they contribute to a large extent to both PCS and MCS.

The PCS and MCS summary scores were obtained by multiplying z-scores for each of the eight sub-scales by a factor score coefficient and the resulting scores were summed over the eight sub-scales by using formulas given in the manual by Ware et al. (175, p51). The PCS and MCS scores were translated into T-scores by multiplying the PCS and MCS scores by 10 and adding 50 to the product (118, p671). We used previously written and verified Stata codes for PCS and MCS (177).

Both the primary outcome measures for our study i.e. PCS and MCS were continuous measures (0-100), with lower score indicating poor quality of life whereas higher score indicating better quality of life.

Key Predictor Variable

We measured perceived social support using Medical Outcome Studies Social Support (MOS SS) survey. This measure of perceived social support which was constructed by Sherbourne and Stewart and captures four dimensions of perceived social support. These dimensions are derived from qualitative assessment of social ties and the degree to which these ties are linked to serve a particular function. The dimensions include emotional/informational support, tangible support, affectionate support and positive social interaction (30); the details of 19-items for the 4 dimensions are presented in **Table 4**.

Table 4: Dimensions of perceived social support using MOS SS (30)

DIMENSION:	Emotional/ Informational Support	Tangible Support	Affectionate Support	Positive Social Interaction
ITEMS	Someone you can count on to listen to when you need to talk.	Someone to help if confined to bed.	Someone who shows love and affection.	Someone to relax with you.
	Someone to confide in for your problems.	Someone to help with daily chores.	Someone to hug you.	Someone to have a good time with.
	Someone to turn for suggestions how to deal with problems	Someone to take you to the doctor if you needed it.	Someone to love you and make you feel wanted.	Someone to do something enjoyable with.
	Someone to give you information to help you understand a situation	Someone to prepare your meals if you were unable to do it yourself.		
	Someone to give you good advice about a crisis			
	Someone whose advice you really want			
	Someone to share your most private worries and fears with			
	Someone who understands your problems			

The measure was evaluated and found to be valid and reliable to assess perceived social support (30, 178). Sherbourne et al, concluded that the 19-item scale had high convergent and discriminant validity to determine perceived social support in four dimensions.

The social support measure was also found to be empirically distinct from other measures of physical and mental health. The authors found that the reliability of the item scales was also found to be stable over a period of one year. Sherbourne and Stewart found that the MOS SS survey was easy to administer to chronically ill patients since the items were designed specifically to be short, simple and easy to understand and restricted to one idea in each stem (30).

More recently Sherbourne et al., have used a 9-item scale to assess the four dimensions of perceived social support (178). To date the 9-item scale for MOS SS survey has not been validated; however, in email correspondence, Sherbourne mentioned that she used the 9-item version as a total scale for perceived social support and not tried using sub-scales. In her experience, the domains in the sub-scale could be highly correlated, for example an individual having tangible support may have other forms of support as well. The alpha for this shorter version was 0.93 when used in a sample of the depressed population. Based on a similar discussion with Sherbourne, the investigators of the original study decided to use the 9 item scale for the patient surveys.

Please refer to **Appendix E** for the 9-item MOS SS survey. Each item in the survey had 5 corresponding answer categories and they were transformed into a 0 -100 scale for each item using a standard approach recommended by the RAND Corporation (179).

To determine scores for each item and a total score for perceived availability of social support using the RAND scoring system, the following steps were used (179):

1. Average score of each item was obtained.
2. Minimum and maximum scores in each category were 1 and 5 respectively
3. Each item was transformed to a scale of 0-100 by using the following formula:

$$\{(average\ score - minimum\ possible\ score) / (maximum\ possible\ score - minimum\ possible\ score)\} \times 100$$

4. After each item score was transformed to a scale of 0-100, average of all 9 item scores was calculated. This average score was the score for ‘perceived social support.’

The perceived social support was thus transformed into a continuous scale (0-100) and was used as the key predictor variable in our study. Lower scores showed lower perception of social support and higher scores demonstrated higher perception of available social support (30).

Other variables associated with HRQOL

Our conceptual framework shows that several variables could be associated with HRQOL in low SES women diagnosed with breast cancer. Nineteen of these variables were collected through the surveys conducted as part of the original study and analysed in our study. We categorized these variables into individual and systems-related variables to use in univariate, bivariate and multiple regression analyses in our study. All the variables were collected at 18 months after breast cancer diagnosis; except for age, ethnicity and education which were collected at 6 months after breast cancer diagnosis. Description of type as well as rationale behind coding of variables is given below.

Individual-related variables:

Individual-related variables were further categorized into demographic factors, treatment related factors and psycho-social factors.

Among the demographic factors, age was a continuous variable measured in years at the time of original diagnosis with breast cancer. Ethnicity was collapsed into three categories, White, Latina and other races. In the original study, there were 4 additional categories for ethnicity including African Americans, Asian Americans, Pacific Islanders, Native/Alaskan American. The number of respondents in the four additional categories for ethnicity was very low so we merged those four categories with the other races category in our study.

Average family income was also grouped into two categories; families with average annual income of equal to or less than 20,000 USD and families with average family income of more than 20,000 USD annually. This categorization was based on the threshold of being below poverty line, which for a family of 4 in the US was almost 20,000 USD in 2005 (70).

High school education was determined as threshold to categorize women's education level. Women were categorized into two categories of women: the first category consisted of women who had education below or up to high school level. The second category was of women who had completed some college or university degree. The women were categorized as either post-menopausal or were still pre-menopausal at the time of diagnosis with breast cancer.

Treatment related factors included stage of disease, type of surgery, received chemotherapy, received radiation therapy, number of co-morbidities and treatment side-effects. The staging of breast cancer was based on TNM (Tumor Nodes Metastasis) staging as recommended by National Cancer Institute in the US (180). Three categories were used: Stage 0 or 1, Stage II (included large number of respondents) and Stage III or IV.

Women in our study underwent two types of surgeries, mastectomy and breast-conserving surgery. The categorization of type of surgery was thus, mastectomy only, breast conserving surgery only and breast conserving surgery followed by mastectomy. Yes or no answers for those who received chemotherapy and radiation therapy were recorded.

A number of co-morbidities were listed in the original study. The co-morbidities included having history of high blood pressure, peripheral vascular disease, stroke, cerebrovascular accident, transient ischemic attack, asthma, bronchitis, chronic obstructive lung disease, stomach ulcer, peptic ulcer, diabetes, lupus, polymyalgia rheumatica, Alzheimer's, cirrhosis, leukemia, lymphoma, AIDS and cancer other than breast cancer. In our study we added up the number of co-morbidities that each patient had. Most patients did not have more than two co-morbidities, we categorized co-morbidities into three groups; none, one or two and more than two.

Possible treatment side effects were listed in the original study and included hot flashes, nausea, vomiting, difficulty with bladder control, vaginal dryness, pain with intercourse, general aches and pains, joint pains, muscle stiffness, weight gain, unhappy with body

image, forgetfulness, night sweats, difficulty in concentration, arm swelling, decreased range of motion of the arm. We categorized this variable into women who had less than or equal to 5 side effects of treatment and women who reported more than 5 side effects of breast cancer treatment.

Anxiety, depression and marital status were the three psycho-social factors included in our study. Anxiety was coded as yes or no response to the current (18 months after breast cancer diagnosis) subjective feelings of anxiety, fear or anger. Depression was coded as yes or no to the current feelings of depression, sadness or sense of loss. Marital status was categorized as married/having a partner and not married/not having a partner.

Systems-related variables:

Systems-related variables were further categorized into health systems related factors and socio-ecological factors.

Health systems related factors included regular access to health care, patient-doctor and patient-staff relationships. Women were asked if they had regular access to health care i.e. for treatment other than cancer care, their yes/no responses were recorded and used in our study.

To assess the patient-doctor/staff relationship, we assessed patient satisfaction with their clinicians. In the original study, patients were asked to rate satisfaction with their surgeon, oncologist and radiation oncologist on a likert scale which had 5 options ranging from extremely satisfied to dissatisfied. The majority of the respondents were extremely satisfied with their surgeon, oncologist and radiation oncologist; therefore, in our study we recoded the responses into extremely satisfied and not extremely satisfied.

Socio-ecological factors, according to our conceptual framework, included life burdens and neighbourhood resources. We were only able to ascertain life burdens in the form of competing life needs. Yes or no responses were recorded to the question that whether in the past year, the patient ever had to go without needed medical care because they had to spend money for food, clothing, housing or transportation.

Missing data

The outcome variables PCS and MCS each had 67 (10.5%) missing cases. There were no missing cases for the key predictor variable.

Age, ethnicity, income, education, menopause status, type of surgery, treatment with surgery and radiation, comorbidity, anxiety, depression, marital status, current access to health care, satisfaction with surgeon and oncologist and competing life needs were variables with less than 5% missing data.

A separate category of “missing” was created for those categorical variables which had more than 10% of data missing. Categorical variables with missing as an additional category included stage of disease, received chemotherapy and treatment side effects

Data Analysis

All analyses were performed using STATA Version 10 (181). The unit of analysis was a woman who was a breast cancer survivor.

Univariate analyses were performed on HRQOL summary scales (PCS and MCS), perceived social support and 19 other variables identified in the previous section. Means and confidence intervals were measured for continuous variables which included:

outcome variables (PCS and MCS), key predictor variable (perceived social support) and age at the time of diagnosis. Frequency and percentages were calculated for categorical variables which included all individual (except for age at the time of diagnosis) and systems-related variables.

Bivariate analyses were used to look at the relationship of outcome variables (PCS and MCS) with predictor variables. Simple linear regression was used to analyze relationship between outcome variables with key predictor variable and age. Comparisons of means and 95% confidence intervals were used to analyze the relationship between primary outcome variables and individual and systems-related variables.

Primary outcome variables (PCS and MCS) were included in multiple regression analyses with key predictor variable and individual as well as systems-related variables. Forward selection (entry criteria $p < 0.2$) and backward elimination (exit criteria $p < 0.2$) stepwise linear regression analyses were used to check for robustness of our main models.

Regression Diagnostics

Regression diagnostics were performed to fit the multiple regression models. Normality of residuals was tested using kernel density plots and normal probability plots. Residual versus fitted plots, imtest and hettest were used to assess homogeneity of the residuals. Variance inflation factors (VIF) was used to test for multicollinearity. Model specifications were checked using the Omitted Variables test (ovtest).

Chapter 4

Results

Sample population

Six hundred and thirty four women diagnosed with breast cancer had completed all three surveys and were therefore included in our study. The mean scores for PCS and MCS were 43.2 and 46.9 respectively. The distribution of PCS and MCS scores is presented in **Fig 6**.

Mean score for perceived social support among women in our study was 66.2. The average age of women was 51 years at the time of their diagnosis with breast cancer. A majority of women were Latina (55.0%) followed by White (28.0%). Other races made up 17% of the sample population and included: African American, Asian Americans, Pacific islanders, American Indians, Alaskan natives and women who did not specify their ethnicity.

Every woman was receiving medical care through the Medi-Cal's BCCPT program and their income was < 200% of the Federal Poverty Level; a majority of women had family income of $\leq$ 20,000 US dollars (64.1%) annually and most of them (59.4%) had education up to or less than high school. Fifty percent women were post-menopausal at the time of their diagnosis with breast cancer. Most women (46.0%) were diagnosed with stage II breast cancer, less than 13% had more severe or metastatic disease at the time of their diagnosis. Twenty two percent women were diagnosed with stage 0 or I of the breast cancer. Distribution of variables in our sample population is given in **Table 5**.

Fig 6: Distribution of PCS and MCS scores.

(Comparison of means standard deviations and range for PCS and MCS scores)

Abbreviations:

SD = Standard deviation

Max = Maximum score

Min = Minimum score

PCS = Physical Component Summary scores

MCS = Mental Component Summary scores

Table 5: Distribution of variables in our sample population; univariate analyses results

Variables	Total number of cases N = 634
Outcome variables	Mean (95% Confidence Interval)
Physical component summary scores (PCS) ^a	43.2 (42.3 to 44.1)
Mental component summary scores (MCS) ^a	46.9 (45.9 to 47.9)
Key predictor variable	
Perceived social support	66.2 (64.2 to 68.2)
Individual-related variables	
Demographic factors	
Age	50.8 (50.1 to 51.2)
	Number of cases (%)
Ethnicity	
Latina	349 (55.0%)
White	178 (28.1%)
Other races	107 (16.9 %)
Income (US dollars) ^b	
≤ 20,000	404 (64.1%)
> 20,000	226 (35.9%)
Education	
≤ High School	377 (59.5%)
> High School	257 (40.5%)
Menopause	
Premenopausal	313 (49.4 %)
Postmenopausal	321 (50.6 %)

a. Continuous variables with 67 (10.5%) missing cases; measured in units. b. Categorical variable with 4 (0.6%) missing cases; measured in 2005 US dollars.

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Treatment related factors		
Stage of breast cancer		
0 –I		140 (22.1%)
II		292 (46.1%)
III- IV		81 (12.7 %)
Missing		121 (19.1%)
Type of surgery		
Mastectomy only		212 (33.4%)
Breast conserving surgery only		329 (52.0%)
Breast conserving surgery followed by mastectomy		93 (14.7%)
Received chemotherapy		
No		190 (30.0%)
Yes		444 (70.0%)
Received radiation therapy		
No		179 (28.2%)
Yes		455 (71.8%)
Number of co-morbidities		
None		366 (57.7%)
One		179 (28.2%)
≥ 2		89 (14.1%)
Treatment side effects		
≤ 5		226 (35.6%)
> 5		231 (36.4%)
Did not report any side effects		177 (28.0%)
Psycho-social factors		
Anxiety		
No		179 (28.2%)
Yes		455 (71.8%)

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Depression		
No		332 (52.4%)
Yes		302 (47.6%)
Marital status		
Married/ having a partner		320 (50.5%)
Not married/ Not having partners		314 (49.5%)
Systems-related variables		
Health systems related factors		
Currently access to health care other than cancer care		
No		164 (25.9%)
Yes		470 (74.1%)
Satisfaction with treatment by surgeon ^a		
Extremely satisfied		464 (74.4%)
Not extremely satisfied		160 (25.6%)
Satisfaction with treatment by oncologist ^b		
Extremely satisfied		423 (71.9%)
Not extremely satisfied		165 (28.1%)
Satisfaction with treatment by radiation oncologist ^c		
Extremely satisfied		376 (59.3%)
Not extremely satisfied		82 (12.9%)
Socio-ecological factors		
Competing life needs ^d		
No		51 (81.1%)
Yes		581 (91.9%)

a. Categorical variable with 10 (1.5%) missing cases.

b. Categorical variable with 46 (7.2%) missing cases.

c. Categorical variable, 179 (28.2%) did not receive radiation therapy; however, 3 of these 179 responded to the satisfaction with treatment by radiation oncologist.

d. Categorical variable with 2 (0.003%) missing cases.

Note: The scores for outcome variables ranged from 0 to 100, 0 = worst HRQOL and 100 = best HRQOL. The scores for perceived social support ranged from 0 to 100, 0 = no support and 100 = maximum support

Our results showed that 52% women required only breast conserving surgery, mastectomy was performed in 33% women and 15% had breast conserving surgery followed by mastectomy. Seventy percent women received chemotherapy and almost 72% received radiation therapy.

According to our results 28% women had one co-morbidity and 14% had ≥ 2 co-morbidities while 57% had no co-morbidities at the time of their diagnosis with breast cancer. Thirty five percent women had ≤ 5 and 36% had > 5 treatment side effects. Twenty eight percent women did not report any treatment side effects.

Feelings of anxiety after 18 months of diagnosis with breast cancer were present in 71% women, less than 48% reported having feelings of depression at the same time. Half of the women (50.5%) were married or living with a partner.

One hundred and sixty four (24.4%) women did not have access to health care other than cancer care. More than 70% women were extremely satisfied with their surgeon and oncologist while less than 60% were extremely satisfied with their radiation oncologist (**Table 5**).

Our results showed that 91% women had competing life needs 18 months after diagnosis with breast cancer i.e. they had to go without medical care in the past year because they had to spend money for food, clothing, housing or transportation.

Bivariate analyses results

The results for bivariate analyses of physical component summary scores (PCS) and mental component summary scores (MCS) with predictor variables are presented in **Table 6** and **Table 7** respectively.

Physical component summary scores (PCS):

Table 6 shows associations between PCS and predictor variables. The association between PCS and perceived social support was found to be statistically significant ($p < 0.01$) on bivariate analysis.

Those who received chemotherapy or radiation therapy had lower PCS scores (42.0 and 42.7, respectively) as compared to women who did not receive chemotherapy or radiation therapy (46.2 and 44.4, respectively). The difference was significant for women receiving chemotherapy but, not significant for women receiving radiation therapy.

Mean PCS scores for women who had one comorbidity (41.8) or two or more comorbidities (38.3) were significantly lower than women who had no comorbidities (95% CI = 43.9 to 46.1). Women reporting > 5 treatment side effects had lower mean PCS scores (41.0) as compared to those who reported ≤ 5 treatment side effects (95% CI = 45.2 to 48.1) (**Table 6**).

Table 6: Relationship between PCS scores and predictor variables; bivariate analyses results.

Predictor variables	Outcome variable
	Physical component summary score
	N = 567
	R ^a (95% Confidence Interval)
Key predictor variable	
Perceived social support	0.06 (0.03 to 0.09)*
Individual-related variables	
Demographic factors	
Age	0.04 (-0.05 to 0.1)
	Mean (95% Confidence Interval)
Ethnicity	
Latina	42.8 (41.6 to 44.0)
White	43.4 (41.8 to 45.1)
Other races	44.1 (41.9 to 46.3)
Income (US dollars)	
≤ 20,000	43.3 (42.1 to 44.4)
> 20,000	43.0 (41.6 to 44.4)
Education	
≤ High School	42.9 (41.8 to 44.1)
> High School	43.6 (42.2 to 44.9)
Menopause	
Premenopausal	44.4 (43.4 to 44.4)
Postmenopausal	42.0 (40.7 to 43.4)

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Predictor variables	Mean (95% Confidence Interval)
Treatment related factors	
Stage of breast cancer	
0 –I	43.4 (41.4 to 45.4)
II	43.1 (41.8 to 44.3)
III- IV	41.0 (38.5 to 43.5)
Missing	44.9 (43.1 to 46.8)
Type of surgery	
Mastectomy only	42.8 (41.3 to 44.4)
Breast conserving surgery only	43.0 (41.7 to 44.3)
Breast conserving surgery followed by mastectomy	44.7 (42.7 to 46.9)
Received chemotherapy	
No	46.2 (44.7 to 47.8)
Yes	42.0 (40.9 to 43.0) *
Received radiation therapy	
No	44.4 (42.8 to 46.1)
Yes	42.7 (41.7 to 43.8)
Number of co-morbidities	
None	45.0 (43.9 to 46.1)
One	41.8 (40.1 to 43.4) *
≥ 2	38.3 (35.7 to 40.9) *
Treatment side effects	
≤ 5	46.7 (45.2 to 48.1)
> 5	41.0 (39.7 to 42.4) *
Did not report any side effects	41.5 (39.6 to 43.2) *
Psycho-social factors	
Anxiety	
No	44.5 (43.9 to 47.0)
Yes	42.3 (41.3 to 43.4) *

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Predictor variables	Mean (95% Confidence Interval)
Depression	
No	45.9 (44.9 to 47.1)
Yes	40.3 (38.9 to 41.6) *
Marital status	
Married/ having a partner	44.1 (42.9 to 45.3)
Not married/ Not having partners	42.4 (41.1 to 43.7)
Systems-related variables	
Health systems related factors	
Current access to health care other than cancer care	
No	43.1 (41.4 to 44.9)
Yes	43.3 (42.3 to 44.3)
Satisfaction with treatment by surgeon	
Extremely satisfied	43.6 (42.6 to 44.7)
Not extremely satisfied	42.1 (40.3 to 43.9)
Satisfaction with treatment by oncologist	
Extremely satisfied	43.6 (42.5 to 44.6)
Not extremely satisfied	41.5 (39.7 to 43.4)
Satisfaction with treatment by radiation oncologist	
Extremely satisfied	43.1 (41.9 to 44.2)
Not extremely satisfied	40.5 (37.9 to 42.9)
Socio-ecological factors	
Competing life needs	
No	40.4 (36.9 to 43.8)
Yes	43.5 (42.6 to 44.4)

a. R: regression co-efficient

* Mean PCS is significantly different from the reference category (p is significant at ≤ 0.05 % level)

Women having feelings of anxiety at 18 months after breast cancer diagnosis had significantly lower PCS scores (95% CI = 41.3 to 43.4) as compared to those who did not report having feelings of anxiety (95% CI = 43.9 to 47.0). Women who reported having feelings of depression at 18 months after breast cancer diagnosis had significantly lower PCS scores (95% CI = 38.9 to 41.6) as compared to those who did not report having feelings of depression (95% CI = 44.9 to 47.1).

We did not find statistically significant difference in PCS scores among any of the systems-related variables. Although women who were not extremely satisfied with their surgeon, oncologist or radiation oncologist had lower mean PCS scores (42.1, 41.4 and 40.5, respectively) as compared to women who were extremely satisfied with their surgeon, oncologist or radiation oncologist (43.1, 43.6 and 43.6, respectively) and these relationships were not statistically significant (**Table 6**).

Mental component summary scores (MCS):

Table 7 shows associations between MCS and predictor variables. The results showed statistically significant association between MCS and perceived social support ($p < 0.01$) on bivariate analysis.

We did not find statistically significant differences in mean scores for MCS among the demographic factors (**Table 7**).

Women having > 5 treatment side effects had significantly lower MCS scores (95% CI = 42.4 to 45.8) as compared to those who reported ≤ 5 treatment side effects (95% CI = 48.7 to 51.4).

Table 7: Relationship between MCS scores and predictor variables; bivariate analyses results

Predictor variables	Outcome variable
	Mental component summary score
	N = 567
	R ^a (95% Confidence Interval)
Key predictor variable	
Perceived social support	0.09 (0.05 to 0.1) *
Individual-related variables	
Demographic factors	
Age	0.02 (-0.08 to 0.1)
	Mean (95% Confidence Interval)
Ethnicity	
Latina	47.0 (45.7 to 48.3)
White	46.6 (44.4 to 48.2)
Other races	47.2 (44.6 to 49.7)
Income (US dollars)	
≤ 20,000	47.0 (45.7 to 48.2)
> 20,000	46.4 (44.8 to 48.1)
Education	
≤ High School	46.7 (45.5 to 48.0)
> High School	47.0 (45.5 to 48.6)
Menopause	
Premenopausal	46.5 (45.1 to 48.0)
Postmenopausal	47.2 (45.8 to 48.5)

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Predictor variables	Mean (95% Confidence Interval)
Treatment related factors	
Stage of breast cancer	
0 –I	47.7 (45.5 to 49.9)
II	46.6 (45.1 to 48.1)
III- IV	44.8 (41.8 to 47.9)
Missing	47.9 (45.8 to 49.9)
Type of surgery	
Mastectomy only	47.3 (45.6 to 49.1)
Breast conserving surgery only	46.9 (45.6 to 48.3)
Mastectomy and breast conserving surgery	45.4 (42.8 to 48.0)
Received chemotherapy	
No	48.0 (46.3 to 49.8)
Yes	46.4 (45.2 to 47.6)
Received radiation therapy	
No	47.4 (45.5 to 49.3)
Yes	46.7 (45.5 to 47.8)
Number of co-morbidities	
None	47.5 (46.3 to 48.7)
One	46.4 (44.4 to 48.4)
≥ 2	45.0 (42.1 to 47.9)
Treatment side effects	
≤ 5	50.0 (48.7 to 51.4)
> 5	44.1 (42.4 to 45.8) *
Did not report any side effects	46.4 (44.3 to 48.7)
Psycho-social factors	
Anxiety	
No	52.3 (50.8 to 53.7)
Yes	44.7 (43.4 to 45.9) *

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Predictor variables	Mean (95% Confidence Interval)
Depression	
No	51.1 (49.9 to 52.3)
Yes	42.2 (40.8 to 43.7) *
Marital status	
Married/ having a partner	46.9 (45.6 to 48.3)
Not married/ Not having partners	46.8 (45.3 to 48.2)
Systems-related variables	
Health systems related factors	
Current access to health care other than cancer care	
No	46.5 (44.5 to 48.5)
Yes	46.9 (45.8 to 48.1)
Satisfaction with treatment by surgeon	
Extremely satisfied	46.9 (45.8 to 48.1)
Not extremely satisfied	46.7 (44.0 to 48.6)
Satisfaction with treatment by oncologist	
Extremely satisfied	47.2 (46.0 to 48.4)
Not extremely satisfied	45.6 (43.5 to 47.7)
Satisfaction with treatment by radiation oncologist	
Extremely satisfied	46.9 (45.6 to 48.1)
Not extremely satisfied	44.9 (42.1 to 47.8)
Did not receive radiation therapy	47.6 (45.8 to 49.5)
Socio-ecological factors	
Competing life needs	
No	38.2 (34.2 to 42.3)
Yes	47.1 (46.1 to 48.1)*

a. R: regression co-efficient

* Mean MCS is significantly different from the reference category (p is significant at ≤ 0.05 % level)

Women having feelings of anxiety at 18 months after breast cancer diagnosis had significantly lower MCS scores (95% CI = 43.4 to 45.9) as compared to those who did not report having feelings of anxiety (95% CI = 50.8 to 53.7). Women who reported having feelings of depression at 18 months after breast cancer diagnosis had significantly lower MCS scores (95% CI = 40.8 to 43.7) as compared to those who did not report having feelings of depression (95% CI = 49.9 to 52.3).

Among systems-related variables, women who had competing life needs i.e. they had to go without medical care in the past year because they had to spend money for food, clothing, housing or transportation statistically, had significant higher MCS scores (95% CI = 46.1 to 48.1) as compared to those who did not have competing life needs (95% CI = 39.9 to 47.8).

Women who were not extremely satisfied with their oncologist or radiation oncologist reported lower mean MCS scores (45.6, and 44.9, respectively) as compared to women who were extremely satisfied with their oncologist or radiation oncologist, the associations were not statistically significant (**Table 7**).

Multiple regression analyses results

The results of multiple regression analyses for the variables associated with the two primary outcome variables PCS and MCS are presented in **Table 8** and **Table 9** respectively. The results were confirmed by forward selection stepwise regression models for PCS and MCS presented in **Appendix F** and **Appendix H** respectively and backward elimination stepwise regression models for PCS and MCS presented in **Appendix G** and **Appendix I** respectively.

Physical component summary scores (PCS)

Table 8 describes variables associated with physical component summary scores (PCS) from multiple regression. The model was statistically significant ($p < 0.01$). Twenty three percent of the variability in the model was accounted for by the variables in the model. Perceived social support was not significantly associated with PCS scores ($p = 0.4$) on multiple regression analysis.

Among other factors associated with PCS scores, women who were post-menopause at the time of diagnosis with breast cancer had worse PCS scores than women who were pre-menopausal at the time of their diagnosis ($\beta = -2.3$, $p = 0.01$) (**Table 8**).

Women receiving chemotherapy had significantly lower PCS scores ($\beta = -4.5$, $p < 0.01$) compared to women who did not receive chemotherapy, whereas; women who received radiation therapy had better PCS scores ($\beta = 4.4$, $p = 0.04$) than those who did not receive any radiation therapy.

Women with one co-morbidity had significantly lower PCS scores ($\beta = -2.6$, $p = 0.01$), those who had 2 or more co-morbidities also had even lower PCS scores ($\beta = -6.0$, $p < 0.01$) PCS scores when compared with women who did not have any co-morbidity. Our results also showed that women reporting > 5 treatment side effects had significantly lower PCS scores when compared to those who reported ≤ 5 treatment side effects ($\beta = -3.6$, $p < 0.01$).

Table 8: Multiple regression analysis results for PCS scores

Predictor variables	Outcome variable	
	Physical component summary score	
	N = 515	
	β^a (95% Confidence Interval)	p-value
Key predictor variable		
Perceived social support	0.01 (-0.2 to 0.05)	0.4
Individual-related variables		
Demographic factors		
Age	0.04 (-0.04 to 0.1)	0.3
Ethnicity		
Latina	<i>Reference category</i>	
White	1.3 (-0.9 to 3.6)	0.2
Other races	1.8 (-0.7 to 4.4)	0.2
Income (US dollars)		
≤ 20,000	<i>Reference category</i>	
> 20,000	-0.7 (-2.5 to 1.0)	0.4
Education		
< High School	<i>Reference category</i>	
≥ High School	-0.6 (-2.6 to 1.4)	0.5
Menopause		
Premenopausal	<i>Reference category</i>	
Postmenopausal	-2.3 (-4.1 to -0.5)	0.01*

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	β^a (95% Confidence Interval)	p-value
Treatment related factors		
Stage of breast cancer		
0 –I	<i>Reference category</i>	
II	1.8 (-0.5 to 4.3)	0.1
III- IV	-1.6 (-5.0 to 1.7)	0.3
Missing	1.1 (-1.9 to 4.1)	0.4
Type of surgery		
Mastectomy only	<i>Reference category</i>	
Breast conserving surgery only	-0.4 (-2.7 to 1.9)	0.7
Mastectomy and breast conserving surgery	1.7 (-0.9 to 4.3)	0.2
Received chemotherapy		
No	<i>Reference category</i>	
Yes	-4.2 (-6.7 to -1.8)	0.001*
Received radiation therapy		
No	<i>Reference category</i>	
Yes	5.4 (0.2 to 10.6)	0.04*
Number of co-morbidities		
None	<i>Reference category</i>	
One	-2.6 (-4.7 to -0.5)	0.01*
≥ 2	-6.3 (-9.0 to -3.7)	0.00*
Treatment side effects		
≤ 5	<i>Reference category</i>	
> 5	-3.7 (-5.7 to -1.6)	0.00*
Did not report any side effects	-2.1 (-4.5 to 0.3)	0.08
Psycho-social factors		
Anxiety		
No	<i>Reference category</i>	
Yes	-1.0 (-3.1 to 1.0)	0.3

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	β^a (95% Confidence Interval)	p-value
Depression		
No	<i>Reference category</i>	
Yes	-4.1 (-6.0 to -2.1)	0.00*
Marital status		
Married/ having a partner	<i>Reference category</i>	
Not married/ Not having partners	-0.6 (-2.5 to 1.3)	0.5
Systems-related variables		
Health systems related factors		
Current access to health care other than cancer care		
No	<i>Reference category</i>	
Yes	-0.09 (-1.9 to 2.1)	0.9
Satisfaction with treatment by surgeon		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-1.0 (-3.1 to 1.0)	0.3
Satisfaction with treatment by oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-1.0 (-3.0 to 1.1)	0.3
Satisfaction with treatment by radiation oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-2.3 (-5.0 to 0.3)	0.09
Did not receive radiation therapy	4.6 (-0.7 to 9.9)	0.09
Socio-ecological factors		
Competing life needs		
No	<i>Reference category</i>	
Yes	-0.5 (-3.3 to 3.2)	0.9

*Significant at ≤ 0.05 % level

a: regression co-efficient

Women who were feeling depressed after 18 months after diagnosis with breast cancer had lower PCS scores as compared to women who did not report feelings of depression ($\beta = -4.1, p < 0.01$). We were not able to find statistically significant association between feelings of anxiety at 18 months after diagnosis with breast cancer and PCS scores.

Mental component summary scores

Table 9 describes variables associated with mental component summary scores (MCS) from multiple regression. The model was statistically significant ($p < 0.01$). Twenty one percent of variability in the model was accounted for by the variables in the model. Perceived social support was not found to be significantly associated with MCS scores ($p = 0.1$) on multiple regression analysis.

At the individual-related, demographic factors were not found to be significantly associated with MCS scores (**Table 10**). Among treatment related factors, having 2 or more co-morbidities was associated with lower MCS scores ($\beta = -2.5, p = 0.1$). Feelings of anxiety and depression at 18 months after breast cancer diagnosis were significantly associated with lower MCS scores ($\beta = -4.2, p < 0.01$ and $\beta = -6.9, p < 0.01$, respectively). Systems-related variables were not significantly associated with MCS scores in our study (**Table 9**).

Table 9: Multiple regression analysis results for MCS scores

Predictor variables	Outcome variable	
	Mental component summary scores	
	N = 515	
	R ^a (95% Confidence Interval)	P-value
Key predictor variable		
Perceived social support	0.03 (-0.007 to 0.07)	0.1
Individual-related variables		
Demographic factors		
Age	0.05 (-0.05 to 0.1)	0.3
Ethnicity		
Latina	<i>Reference category</i>	
White	-1.8 (-4.4 to 0.7)	0.2
Other races	-0.3 (-3.2 to 2.7)	0.8
Income (US dollars)		
≤ 20,000	<i>Reference category</i>	
> 20,000	-0.3 (-2.3 to 1.8)	0.8
Education		
< High School	<i>Reference category</i>	
≥ High School	1.3 (-0.9 to 3.6)	0.3
Menopause		
Premenopausal	<i>Reference category</i>	
Postmenopausal	1.3 (-0.7 to 3.4)	0.2

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	β^a (95% Confidence Interval)	p-value
Treatment related factors		
Stage of breast cancer		
0 –I	<i>Reference category</i>	
II	0.04 (-2.7 to 2.8)	0.9
III- IV	-1.5 (-5.4 to 2.3)	0.4
Missing	2.3 (-1.2 to 2.7)	0.2
Type of surgery		
Mastectomy only	<i>Reference category</i>	
Breast conserving surgery only	0.6 (-2.1 to 3.3)	0.6
Mastectomy and breast conserving surgery	-1.2 (-4.3 to 1.7)	0.4
Received chemotherapy		
No	<i>Reference category</i>	
Yes	0.5 (-2.2 to 3.3)	0.7
Received radiation therapy		
No	<i>Reference category</i>	
Yes	3.3 (-2.8 to 9.1)	0.3
Number of co-morbidities		
None	<i>Reference category</i>	
One	-0.7 (-3.0 to 1.6)	0.5
≥ 2	-2.5 (-5.5 to 0.4)	0.1
Treatment side effects		
≤ 5	<i>Reference category</i>	
> 5	-3.1 (-5.5 to -0.7)	0.009*
Did not report any side effects	-1.0 (-3.8 to 1.7)	0.4
Psycho-social factors		
Anxiety		
No	<i>Reference category</i>	
Yes	-4.2 (-6.6 to -1.9)	0.00*

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	β^a (95% Confidence Interval)	p-value
Depression		
No	<i>Reference category</i>	
Yes	-6.7 (-8.9 to -4.5)	0.00*
Marital status		
Married/ having a partner	<i>Reference category</i>	
Not married/ Not having partners	0.6 (-1.5 to 2.8)	0.6
Systems-related variables		
Health systems related factors		
Current access to health care other than cancer care		
No	<i>Reference category</i>	
Yes	-0.5 (-2.8 to 1.8)	0.7
Satisfaction with treatment by surgeon		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	1.2 (-1.2 to 3.5)	0.3
Satisfaction with treatment by oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	0.5 (-2.9 to 1.8)	0.6
Satisfaction with treatment by radiation oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-1.6 (-4.7 to 1.4)	0.3
Did not receive radiation therapy	4.5 (-1.5 to 10.6)	0.2
Socio-ecological factors		
Competing life needs		
No	<i>Reference category</i>	
Yes	-1.2 (-4.9 to 2.5)	0.5

* Significant at $\leq 0.05\%$ level

a: regression co-efficient

Regression Diagnostics

Kernel density plots and normal probability plots for both PCS and MCS multiple regression models showed normal distributions of the residuals in both models. Residual versus fitted plots, `imtest` and `hettest` indicated that variance of residuals in PCS and MCS multiple regression models was homogenous.

We found mean variance inflation factor (VIF) of 1.9 for the PCS and mean VIF of 1.8 for MCS; indicating that multicollinearity was not observed in our multiple regression models. The omitted variable test (`ovtest`) was not significant for both models ($p = 0.2$ for PCS and $p = 0.07$ for MCS); thus, that the multiple regression models did not have specification errors.

Kernel density plots, normal probability plots and residual versus fitted plots for PCS are presented in **Appendix J** and for MCS are presented in **Appendix K**.

Chapter 5

Discussion

Sample population

Our sample population consisted of women diagnosed with breast cancer. The majority (55%) of women was Latina. Percentage of Latinas in our sample was closer to the general population in California (37.5% Latinas) but different from the US (16% Latinas) and Canadian (0.7%) general populations (196, 197).

Sixty four percent of women were living below the poverty threshold which was 20, 000 US \$ in 2005, around the time when the data were collected (198). This is very different from the general US population where 16.5% women were reported to be living below poverty threshold in 2010 (199). In Canada, almost 13% of the population (both male and female) were reported to be in low-income group in 2009 (200). Although, the percentage of women below poverty threshold was very high, it is important to remember that our sampled population consisted of women belonging to lower SES.

The incidence of breast cancer increases with increasing age. More women were diagnosed between the ages of 49 and 69 (201). The average age of women in our sample population was 51 years at the time of their diagnosis with breast cancer. The number of women who had some college or university education was 40.5% which was lower than the percentage of college or university graduates in US (56.8%) and Canadian (50%) general populations (202, 203). It is estimated that 16% of US population does not have access to health care (37). Breast cancer care was available to all the women

through BCCPT coverage; but, a high percentage (26%) of women in our sampled population did not have access to health care other than cancer care.

Univariate findings

Understanding the factors associated with physical and mental HRQOL merits a discussion on interpretation of the variables used to depict HRQOL. SF-36 physical and mental component summary scores (PCS and MCS) represent physical HRQOL and emotional HRQOL in variety of populations including breast cancer patients (67-70, 182).

To interpret the results of PCS and MCS scores, Ware et al. established norm based scoring for the physical and mental component summary scores. The summary measures have a mean of 50 and standard deviation of 10 for general US population (67). The difference from norm based mean scores determines the physical and emotional HRQOL for a specific population. Lower scores depict poor HRQOL and higher scores suggest excellent HRQOL (67, 172-176, 182).

Through general population surveys, Ware et al. also compared the norm based scores derived from US data with nine European countries including Denmark, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden and United Kingdom (182). Substantial agreement was found between the standard and country specific scoring algorithms for the two summary scores in all 10 countries which included the nine European countries and the US. The authors thus recommended that the interpretation of the summary scores based on norm based scoring is valid for international studies in general and the nine participating countries in particular (182).

Canadian normative data for SF-36 health survey comes from the Canadian Multicentre Osteoporosis Study (CaMos) (183). The study consisted of surveys designed to provide estimates of osteoporosis and osteoporosis related fractures. CaMos collected data from 9423 Canadian men and women age 25 and above, living in communities in and around 9 major Canadian cities (183). Canadians scored higher on both PCS (mean = 50.5) and MCS (mean = 51.7) as compared to their US counterparts. Scores for Canadian women were slightly lower than general Canadian population (PCS mean = 49.7, MCS mean = 50.9). The scores for Canadian women were comparable to the norm based scores presented by Ware et al. (67, 182,183).

Studies show that patients with chronic illnesses have lower scores for HRQOL as compared to general populations (67, 184-186). Physical HRQOL is generally more adversely affected in patients with chronic illness (184, 185). In some cases such as chronic kidney disease, prolonged exposure to disease can also result in lower mental HRQOL for chronically ill patients (186).

Both physical and emotional HRQOL were below average among breast cancer survivors in our study as PCS and MCS were below norm based mean scores (67). Physical HRQOL was poorer than emotional HRQOL. Lower PCS scores have been reported in other studies evaluating HRQOL in breast cancer patients (187 – 189). A population survey of women in Wisconsin (N = 2,763) used SF-36 to evaluate HRQOL among women with breast cancer. Comparisons were made between healthy women and breast cancer survivors (187). The participants were contacted four times for follow-up in 2002. Breast cancer survivors scored lower on PCS scores than control population regardless of time since diagnosis, which in some cases was up to 13 years. The MCS scores were also

lower in breast cancer patients as compared to the controls; however, two years after diagnosis with breast cancer, the MCS scores were similar in both groups (187). Ganz et al. studied HRQOL in breast cancer patients across various treatment groups; they concluded that at the end of primary treatment for breast cancer, women reported good emotional functioning but poor physical functioning (188). In a previous study, Ganz et al. reported that 6 years post-diagnosis with breast cancer both physical and mental HRQOL improved in women; however, overall breast cancer survivors reported better mental HRQOL as compared to physical HRQOL (189).

Perceived social support was our key variable of interest. During development of the scale, Sherbourne et al. concluded that mean scores for overall perceived social support in general US population for the 19-item social support scale was 70.1 ± 24 (30). Studies showed that patients with chronic illness such as chronic kidney disease and heart disease reported higher scores for perceived social support (mean ranging from 76.0 to 85.0) (190, 191). Among breast cancer patients, a study comparing the impact of cancer in non-hodgkins lymphoma and breast cancer patients concluded that perception of social support was higher (84 ± 16) in these cancer patients as compared to general population (192). We found that perception of perceived social support was lower than average among breast cancer patients in our study i.e. 66 ± 26 . The women reported lower scores despite the fact that most women in our study were Latinas and generally the Latin culture is associated with strong familial ties and social support provided by close and extended family and friends (193 – 195). Several factors could have resulted in lower perception of social support among women in our sampled population. Stress caused by the diagnosis of breast cancer, lower SES status or the fact that majority of women were

living in the US illegally could be some reasons affecting the perception of social support in these women (120, 157).

Regression findings

Factors associated with physical HRQOL

Breast cancer survivors in our study reported poor physical HRQOL and lower than average perception of social support. Studies have suggested that perceived social support has a positive correlation with physical HRQOL (141,149) in breast cancer survivors; we were not able to find an association between perceived social support and physical HRQOL.

Unlike Sammarco (141) and Lim et al. (149) who measured perceived social support and HRQOL at the same point in time, our study looked at the impact of perceived social support on HRQOL after a period of one and a half years. We evaluated the impact of perceived social support measured at 18 months after breast cancer diagnosis on physical HRQOL measured at 3 years after breast cancer diagnosis. Although our study did not show a correlation between perceived social support and physical HRQOL in low income women with breast cancer, a correlation measured at shorter interval such as 6 or 12 months cannot be ruled out. Both Sammarco and Lim et al. had fewer numbers of participants (100 in both studies). In addition, Samarco studied the relationship between perceived social support and HRQOL among younger women (only women less than 50 years of age were recruited for the study) which could have led to difference in perception of social support among Sammarco's and our study population (141).

Lim et al compared the effects of perceived social support on HRQOL between Korean and Korean American women. Socio- cultural differences among the two populations contributed to the differences in perception of social support among Korean and Korean American women. Perceived social support had an indirect impact on physical HRQOL. It was proposed by Lim et al. that perceived social support improved the general well-being of a breast cancer patient, thus, dampening the effects of medication and physical symptoms of disease, leading to improvement in physical HRQOL (149). Although, Lim et al. showed that there was an indirect relationship between perceived social support and physical HRQOL, our study shows that there is no direct relationship between these two factors.

Several individual-related factors in our study were associated with physical HRQOL. No relationship was found between systems-related factors and physical HRQOL in our study.

Women who were post-menopausal at the time of their diagnosis with breast cancer had poorer physical HRQOL after 3 years of diagnosis with breast cancer as compared to women who were pre-menopausal at the time of their diagnosis. This relationship was not significant on bivariate analysis, however, it was found to be significant on multiple regression analyses in our study. There are several physical symptoms of menopause such a fatigue, pain, hot flashes. These symptoms are responsible for poor physical HRQOL in most post-menopausal women (83-84). Some studies suggest that the effects of menopause on physical HRQOL in women diagnosed with breast cancer are not enhanced due to the cancer diagnosis (83 -84). On the other hand, there are studies similar to ours which suggest that there is a difference in physical HRQOL among pre-

menopausal and post-menopausal women and that women who had reached menopause at the time of their diagnosis had worse physical HRQOL (85-87).

Other demographic factors such as age, ethnicity, income level and education had no association with physical HRQOL.

Side effects such as nausea, vomiting and fatigue due to adjunct chemotherapy in breast cancer patients are known to decrease physical HRQOL among these women (23, 204). Our results were consistent with the findings in the literature. Almost 70% women in our study received chemotherapy and had worse physical HRQOL as compared to those who did not receive adjunct chemotherapy.

The most common side effect of radiation therapy in breast cancer is mild to moderate skin irritation. Other side effects could include arm pit discomfort, chest discomfort, fatigue and low blood counts (205). Radiation therapy in women with breast cancer is also known to adversely affect physical health (23). These affects are mostly short term because the most common side effect is skin irritation which does not have long term physical implications (205). Interestingly we found that women who received radiation therapy had better physical HRQOL. There are studies which suggest that radiation therapy does not have long term deleterious effects on physical health on women with breast cancer (205, 206). Since, more than a year had elapsed between radiation therapy for women in our study and measurement of physical HRQOL, it could account for improvements in physical HRQOL in these women.

Physical co-morbidities have a negative impact on physical HRQOL in women with breast cancer (23). Kurtz et al studied the effects of 13 co-morbidities in older breast

cancer women. According to Kurtz et al. increasing the number of co-morbidities adversely affected physical health (207). Ververs et al. studied the impact of co-morbidities resulting from axillary lymph node dissection in women with breast cancer. Physical HRQOL was found to be impaired in women having multiple co-morbidities (217). Our study also showed that multiple co-morbidities have an adverse effect on long term physical HRQOL.

In addition, having more treatment side effects also has a negative impact on physical HRQOL among low SES women with breast cancer. Studies also show that treatment side effects including those of surgery as well as chemo and radiation therapies result in short term as well as long term impairment of physical health in breast cancer patients (23, 209, 210).

Studies suggest that depression is a significant predictor of long term physical HRQOL in breast cancer survivors (98, 213-215). Christie et al. showed that lower income single Hispanic women with breast cancer have a higher risk of developing depression and suffering from the subsequent physical and mental deterioration as a result of psychosocial stress (216).

Among psycho-social factors, the feeling of depression was the only factor in our study which showed a long term negative impact on physical HRQOL in women with breast cancer. Ashing-Giwa et al. did not find depression to be a significant predictor for long term poor physical health especially among Latinas (210). In another qualitative assessment of factors associated with HRQOL in breast cancer survivors, Ashing-Giwa et al. found that psychological distress caused by fear of recurrence of breast cancer and

burden of illness resulted in deterioration of physical HRQOL in breast cancer patients. The same study showed that among Latinas social support served as a comforting factor against psychological distress (212).

Our results were similar to other studies such as a meta-analysis of effects of stress on women with breast cancer (98) and an evaluation of depression as predictor for fatigue and poor health in breast cancer survivors (211). Both studies suggested that fatigue due to depression among breast cancer survivors results in poor physical HRQOL.

Factors associated with emotional HRQOL

Among the factors associated with Mental HRQOL, perceived social support is considered as an important predictor of emotional health in breast cancer survivors (140-154). However, we were not able to find an association between perceived social support and long term emotional HRQOL.

Several studies suggest that social support both received and perceived has both direct and indirect effect on emotional HRQOL in breast cancer survivors (140 -154). Studies looking at volunteer peer groups providing face to face or telephonic support concluded that among breast cancer patients, those interventions which lead to interaction among breast cancer survivors had a positive effect on emotional HRQOL (140, 154). Other studies such Lim et al.'s analysis of effect of perceived social support on Korean and American-Korean women suggests that among the group of women living in Korea, sense of strong family ties and stronger perception of social support served as a barrier for emotional harm resulting in better emotional HRQOL (149). Similarly higher perception of social support among Turkish women (148) and Latinas (152) due to strong

family ties attributed to socio-cultural norms among these populations served as barriers to psychological distress and improved emotional HRQOL.

The only factors associated with mental HRQOL in our study were treatment side effects and psycho social factors. As discussed previously, treatment side effects including those of surgery as well as chemo and radiation therapies result in impairment of health in breast cancer patients (23, 209, 210). Literature suggests that physical health is impaired health due to treatment side effects. However, in some cases such as mastectomy, women suffer from impaired body image thus, having a long term effect on mental health (23, 209). Our study showed women who reported more treatment side effects had worse mental HRQOL.

Women with breast cancer experience higher incidence of psychological distress such as anxiety and depression as compared to general population (219). Studies suggest that stress such as anxiety and/or depression related to breast cancer diagnosis emotional well-being of breast cancer survivors (98, 220). Our study also, shows that feelings of anxiety and depression experienced 18 months after the diagnosis of breast cancer have a long term adverse effect on mental HRQOL.

Studies among Hispanic populations suggest that family support is an important stress alleviator in women with breast cancer especially among Latinas with low income (210, 216). In addition marital status is an important predictor for psycho-social stress in Latinas with breast cancer (216). A comparison between women newly diagnosed with breast cancer and those who had recurrence of the disease showed that being married was associated with better emotional well-being among women in both groups (221). The

study also showed that being single was a risk factor for long term depression in women with breast cancer. On the other hand some studies suggest that marital distress due to diagnosis of breast cancer can cause stressful events leading to increase in depression among women diagnosed with breast cancer (92, 222).

Our study did not report any association between systems-related variables and physical or emotional HRQOL. However, a study evaluating the effects of treatment and the process of care among older breast cancer survivors in the US found a positive relationship between these factors. The study concluded that satisfaction with the treatment process in addition to the therapy was a significant predictor of long term HRQOL in older breast cancer patients (218). It is important to keep in mind that systems-related variables in our study consisted of access to health care in addition to satisfaction with treating clinicians and we did not evaluate the effects of treatment process on HRQOL. In addition, in contrast to the above mentioned study which was conducted among older women, our study included younger as well as older women with breast cancer.

Limitations

Although we were able to thoroughly analyse the relationship between perceived social support and HRQOL among low SES women with breast cancer, we had a few limitations to our study.

Our study was limited by the dataset used for analysis. As a secondary dataset, it was originally designed to assess the determinants of breast cancer treatment in an underserved population. The original data set was composed of factors associated with

determinants of breast cancer treatment and breast cancer care. Evaluation of social determinants of breast cancer care was not the primary aim of the original study; therefore, the data did not contain some variables such as diet and exercise, estrogen and progesterone receptor status, uncertainty, repression/denial, expression and supportive care. These variables are presented in our conceptual framework and could have provided us with further information about the relationship between perceived social support and HRQOL.

Our sample population was unique. Data were collected from women belonging to low SES in the state of California. Latinas were the ethnic majority within the sampled population, whereas, they are a minority within general US population. It is important therefore, to cautiously interpret the results of our study.

We used a sample consisting of women participating in all three surveys. In doing so, we may have missed some women who were unavailable to participate due to any number of reasons such lack of reliable address or being too sick to participate in the study.

In addition, the results of our study may have been different if the time period between measurement of perceived social support and HRQOL was shorter such as 6 or 12 months instead of 18 months.

Implications of our study and future research

Through our research we were able to explore the long term relationship between perceived social support and HRQOL in breast cancer survivors among women belonging to low SES. Factors influencing this relationship were also explored. Our research

therefore, yielded information which will be beneficial to individual breast cancer patients as well as public health policy makers.

Our study identified multiple co-morbidities, menopause at the time of diagnosis with breast cancer, and adjunct chemotherapy as indicators for poorer long term physical HRQOL. Higher number of treatment side effects and depression in women with breast cancer resulted in poor physical and mental HRQOL. Anxiety in women with breast cancer was identified as an indicator for poorer mental HRQOL. Information regarding factors associated with HRQOL provides useful information regarding the physical and mental well-being of breast cancer survivors. The knowledge acquired through this research can help in educating survivors about their risk of impaired physical and mental health during the course of their illness.

The information gained through analysing factors affecting HRQOL is also useful for policy makers and informers of clinical practice guidelines. Resources can be allocated to earlier identification of modifiable factors such as treatment related side effects and development of stress related factors such as anxiety and depression, in order to offset the long term physical and mental impact on HRQOL. Similarly HRQOL in breast cancer survivors can be improved through introduction of clinical practice guidelines focusing on factors affecting HRQOL in breast cancers survivors.

Results from this study can be useful in better informing the clinical practice guidelines for breast cancer care. At present the guidelines suggest psychosocial counselling for women diagnosed with breast cancer without specific goals for such counselling. With the identification of vulnerable populations (such as anxious or depressed women),

clinical practice guidelines can be modified to incorporate additional surveillance options for women with breast cancer.

Additionally, our research indicates a need for further exploration of the relationship between psychological factors and perceived social support. Both anxiety and depression were strongly correlated with perceived social support in our study ($\beta = -7.2$, $p = 0.02$ and $\beta = -13.8$, $p = <0.01$, respectively). Anxiety and depression were also strongly associated with both physical and emotional HRQOL in our study. Perceived social support acts as a buffer against stressors of breast cancer. It is possible that strong negative correlations of anxiety and depression may have diluted the buffering effect of perceived social support in our population. Therefore, it is important to investigate the role of psychological factors such as anxiety and depression on the relationship between perceived social support and HRQOL in future studies.

Our study was an exploratory analysis of the relationship between perceived social support and physical as well as emotional HRQOL in low SES women with breast cancer. We were able to identify some factors related to HRQOL. There is a need to further explore the nature of this relationship between perceived social support and HRQOL among low SES.

In future, longitudinal studies evaluating the factors associated with perceived social support and their effect on HRQOL at regular time intervals will yield useful information for the patients as well as public health policy makers. We were not able to explore the systems related factors in detail. Future studies evaluating the impact of systems related factors on the relationship between perceived social support and HRQOL would provide

useful knowledge in understanding of this relationship. In addition, we would propose the use of validated scales for anxiety and depression for future studies evaluating the relationship between perceived social support and HRQOL.

Conclusions

A statistically significant association between perceived social support and long term physical or emotional HRQOL in low SES women with breast cancer was not established through our study. However, several other factors affecting HRQOL in low SES women with breast cancer were identified. Multiple co-morbidities, menopause at the time of diagnosis with breast cancer, and adjunct chemotherapy are poor prognostic factor for long term physical HRQOL. Higher number of treatment side effects and depression in women with breast cancer results in poor physical and emotional HRQOL. Anxiety in women with breast cancer was identified as poor prognostic factor for emotional HRQOL.

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Appendices

Appendix A: Original study recruitment flow chart.

Appendix B: Time line of data collection and variables collected at those points

Appendix C: Medical Outcome Study Short Form-36 (MOS SF-36) Survey

i. General Health

1. In general, would you say your health is?

Excellent (1) Very Good (2) Good (3) Fair (4) Poor (5)

How TRUE or FALSE is each of the following statements for you?

Definitely true (1) Mostly true (2) Don't know (3) Mostly false (4) Definitely false (5)

2. I seem to get sick a little easier than other people
3. I am as healthy as anybody I know
4. I expect my health to get worse
5. My health is excellent

ii. Physical Functioning

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Yes, limited a lot (1) Yes, limited a little (2) Not limited at all (3)

6. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sport
7. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf
8. Lifting or carrying groceries
9. Climbing several flights of stairs
10. Climbing one flight of stairs
11. Bending, kneeling, or stooping
12. Walking more than a mile
13. Walking several blocks
14. Walking one block
15. Bathing or dressing yourself

iii. Role – Physical

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

Yes (1) No (2)

16. Cut down on the amount of time you spent on work or other activities
17. Accomplished less than you would like
18. Were limited in the kind of work or other activities you did
19. Had difficulty performing the work or other activities (for example, it took extra time)

iv. Role - Emotional

During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

Yes (1) No (0)

- 20. Cut down on the amount of time you spent on work or other activities
- 21. Accomplished less than you would like
- 22. Didn't do work or other activities as carefully as usual

v. Bodily Pain

23. How much bodily pain have you had during the past 4 weeks?

None (1) Very mild (2) Mild (3) Moderate (4) Severe (5) Very Severe (6)

24. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Not at all (1) Slightly (2) Moderately (3) Quite a bit (4) Extremely (5)

vi. Vitality and vii Mental Health

These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the past 4 weeks

All of the time (1) Most of the time (2) A good bit of the time (3) Some of the time (4) None of the time (5)

- 25. Did you feel full of pep?
- 26. Have you been a very nervous person?
- 27. Have you felt so down in the dumps nothing could cheer you up?
- 28. Have you felt calm and peaceful?
- 29. Did you have a lot of energy?
- 30. Have you felt downhearted and blue?
- 31. Did you feel worn out?
- 32. Have you been a happy person?
- 33. Did you feel tired?

ix. Social Functioning

- 34. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with friends, neighbors or groups?
- 35. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time (1) Most of the time (2) A good bit of the time (3) Some of the time (4) None of the time (5)

36. **Compared to before your breast cancer diagnosis, how would you rate your health in general now?** Much better now (1) Somewhat better now (2) About the same (3) Somewhat worse (4) Much worse now (5)

Appendix D: Steps for conversion of MOS SF-36 into eight HRQOL sub-scales with values ranging between 0 – 100 (146).

Appendix E: Medical Outcome Study Social Support survey with 9-items

People sometimes look to others for companionship, assistance, or other types of support. How often is each of the following kinds of support available to you if you need it now?

None of the time (1) A little of the time (2) Some of the time (3) Most of the time (4) All of the time (5)

- 1 Someone to help you if you were confined to bed
- 2 Someone who shows you love and affection
- 3 Someone to take you to the doctor if you needed it
- 4 Someone to confide in or talk about yourself or your problems
- 5 Someone who hugs you
- 6 Someone to get together with for relaxation
- 7 Someone to help with daily chores if you were sick
- 8 Someone to turn to for suggestions about how to deal with a personal problem
- 9 Someone to love and make you feel wanted

Appendix F: Stepwise forward selection multiple regression for PCS scores

Outcome variable		
Physical component summary scores (PCS)		
Predictor variables	N = 515	
	β^a (95% Confidence Interval)	P-value
Individual-related variables		
Demographic factors		
Menopause		
Premenopausal	<i>Reference category</i>	
Postmenopausal	-2.1 (-3.9 to -0.3)	0.02*
Treatment related factors		
Stage of breast cancer		
0 –I	<i>Reference category</i>	
II	1.9 (-0.1 to 3.7)	0.03*
Received chemotherapy		
No	<i>Reference category</i>	
Yes	-4.5 (-6.7 to -2.5)	0.00*
Number of co-morbidities		
None	<i>Reference category</i>	
One	-3.0 (-4.9 to -1.0)	0.003*
≥ 2	-6.3 (-8.8 to -3.7)	0.00*
Treatment side effects		
≤ 5	<i>Reference category</i>	
> 5	-3.6 (-5.6 to -1.6)	0.00*
Did not report any side effects	-2.5 (-4.8 to -0.3)	0.03*
Psycho-social factors		
Depression		
No	<i>Reference category</i>	
Yes	-4.7 (-6.5 to -3.0)	0.00*

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Systems-related variables		
Health systems related factors		
Satisfaction with treatment by oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-1.4 (-3.4 to 0.5)	0.1
Satisfaction with treatment by radiation oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-2.7 (-5.4 to -0.1)	0.06

*Significant at 0.05% level

a : regression co-efficient

Appendix G: Stepwise backward elimination multiple regression for PCS scores

Predictor variables	Outcome variable	
	Physical component summary scores (PCS)	
	N = 515	
	β^a (95% Confidence Interval)	P-value
Individual-related variables		
Demographic factors		
Age	0.05 (-0.03 to 0.1)	0.2
Menopause		
Premenopausal	<i>Reference category</i>	
Postmenopausal	-2.4 (-3.9 to -0.3)	0.009*
Treatment related factors		
Stage of breast cancer		
0 – I	<i>Reference category</i>	
II	1.4 (-0.7 to 3.4)	0.1
III – IV	-2.0 (-5.0 to 0.9)	0.1
Type of surgery		
Mastectomy only	<i>Reference category</i>	
Mastectomy and breast conserving surgery	1.6 (-0.8 to 4.04)	0.2
Received chemotherapy		
No	<i>Reference category</i>	
Yes	-4.0 (-6.4 to -1.7)	0.001*
Received radiation therapy		
No	<i>Reference category</i>	
Yes	5.3 (0.2 to 10.4)	0.04*
Number of co-morbidities		
None	<i>Reference category</i>	
One	-2.8 (-4.8 to -0.8)	0.006*
≥ 2	-6.3 (-8.8 to -3.7)	0.00*

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Treatment side effects		
≤ 5	<i>Reference category</i>	
> 5	-3.7 (-5.8 to -1.7)	0.00*
Did not report any side effects	-2.5 (-4.8 to -0.2)	0.03*
Psycho-social factors		
Depression		
No	<i>Reference category</i>	
Yes	-4.8 (-6.6 to -3.0)	0.00*
Systems-related variables		
Health systems related factors		
Satisfaction with treatment by oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-1.4 (-3.4 to 0.6)	0.2
Satisfaction with treatment by radiation oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-2.7 (-5.4 to -0.1)	0.04*
Did not receive radiation therapy	4.7 (-0.5 to 9.8)	0.07 **

Significant a Significant at 0.05% level

a : regression co-efficient

Appendix H: Stepwise forward selection multiple regression for MCS scores

Outcome variable		
Mental component summary scores (MCS)		
Predictor variables	N = 515	
	β^a (95% Confidence Interval)	P-value
Key predictor variable		
Perceived social support	0.03 (-0.008 to 0.06)	0.1
Individual-related variables		
Treatment related factors		
Stage of breast cancer		
0 – I	<i>Reference category</i>	
III – IV	-1.9 (-4.7 to 0.9)	0.2
Number of co-morbidities		
None	<i>Reference category</i>	
≥ 2	-2.0 (-4.8 to 0.6)	0.1
Treatment side effects		
≤ 5	<i>Reference category</i>	
> 5	-2.7 (-4.7 to -0.7)	0.008*
Psycho-social factors		
Anxiety		
No	<i>Reference category</i>	
Yes	-4.8 (-6.6 to -3.0)	0.00*
Depression		
No	<i>Reference category</i>	
Yes	-6.7 (-8.8 to -4.6)	0.00*
Systems-related variables		
Satisfaction with treatment by radiation oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-2.0 (-4.8 to -0.8)	0.2

Significant a Significant at 0.05% level

a : regression co-efficient

Appendix I: Stepwise backward elimination multiple regression for MCS scores

Outcome variable		
Mental component summary scores (MCS)		
N = 515		
Predictor variables	β^a (95% Confidence Interval)	P-value
Key predictor variable		
Perceived social support	0.03 (-0.008 to 0.06)	0.1
Individual-related variables		
Treatment related factors		
Stage of breast cancer		
0 – I	<i>Reference category</i>	
III – IV	-1.9 (-4.8 to 0.9)	0.2
Number of co-morbidities		
None	<i>Reference category</i>	
≥ 2	-2.0 (-4.8 to 0.6)	0.1
Treatment side effects		
≤ 5	<i>Reference category</i>	
> 5	-2.7 (-4.7 to -0.7)	0.008*
Psycho-social factors		
Anxiety		
No	<i>Reference category</i>	
Yes	-4.2 (-6.6 to -1.9)	0.00*
Depression		
No	<i>Reference category</i>	
Yes	-6.7 (-8.8 to -4.6)	0.00*
Systems-related variables		
Satisfaction with treatment by radiation oncologist		
Extremely satisfied	<i>Reference category</i>	
Not extremely satisfied	-2.0 (-4.8 to -0.8)	0.2

Significant a Significant at 0.05% level

a : regression co-efficient

Appendix J: Regression diagnostic plots for PCS scores

Kernel density plot

Normal probability plot

Residual versus fitted plot

Appendix K: Regression diagnostic plots for MCS scores

Kernel density plot

Normal probability plot

Residual versus fitted plot

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