Stress Reactivity Patterns in Breast Cancer Survivors and the Implications of Various Psychosocial Factors

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Abstract

The stress system comprises the hypothalamic-pituitary-adrenal (HPA) and the sympathetic-adrenal-medullary (SAM) axes. The two operate synergistically to regulate metabolic and biological processes, maintain homeostasis, and manage physiological responses towards various environmental challenges, known as stressors. Numerous studies have observed impaired HPA response among White breast cancer survivors followed by an eventual normalization of the HPA axis, but little is known about SAM functioning, the complementary relationship between physiological and psychological stress, and the influence of culturally related factors. This dissertation aims to address these gaps in the literature via three studies.

In Study 1, we examined the diurnal and reactive patterns of salivary alpha-amylase, a SAM biomarker, in a sample of predominantly White women with and without a prior diagnosis of breast cancer. The purpose was to establish an initial understanding of SAM functioning in relation to the participants' HPA activity as measured by cortisol responses (complementary to a previously published study in the laboratory). Results of Study 1 revealed no abnormal response to stress. Virtually identical alpha-amylase slopes were observed between breast cancer survivors and control participants, except that breast cancer survivors had elevated basal levels of alpha-amylase, thus suggesting a "heightened sympathetic tone".

In Study 2 acute and diurnal cortisol profiles and their accompanying psychological stress responses were examined in a sample of Chinese and White women with and without a prior diagnosis of breast cancer. In the same participants, we also examined chronic stress levels via hair cortisol concentrations which was the subject of Study 3. In both studies 2 and 3, we assessed the potential influences of cultural orientation and ethnocultural group membership on physiological and psychological stress patterns.

For the most part, Study 2 supported previous findings from the literature and our laboratory: Breast cancer survivors displayed a blunted cortisol response and their diurnal profile was comparable to that of control participants. But contrary to our hypotheses, ethnocultural membership and cultural orientation did not influence physiological patterns of stress. However, an interaction between ethnocultural group, health status, and time (i.e., from baseline to one hour after stress induction) was observed in the subjective appraisal of an acute stressor. Specifically, White breast cancer survivors reported significantly lower levels of perceived stress than the other three groups. These results suggest that health-related stress may supersede the effects of culturally related stress and indicate the potential presence of posttraumatic growth among our sample of White breast cancer survivors only.

Study 3 revealed no differences in hair cortisol concentrations between breast cancer survivors and control participants, nor between Chinese and White breast cancer survivors. However, it was observed that healthy Chinese women exhibited significantly higher levels of hair cortisol concentrations than their Western counterpart. Further analyses revealed that health status and cultural orientation did not significantly predict the observed patterns of physiological or psychological stress. Although non-significant, Study 3 results offered preliminary evidence that higher orientation towards both the dominant and non-dominant cultures is associated with higher levels of chronic physiological and psychological stress.

Collectively, our studies may provide support for the long-term recovery of the HPA axis via the examination of acute, diurnal, and chronic patterns of cortisol, but further research will be required. The dissertation also highlights several important key points regarding culturally related factors, health, and stress: (1) The perception of stress is influenced by one's degree of cultural orientation and (2) effects of health-related stress may supersede those of culturally

related stress, but (3) among healthy women, ethnocultural minorities may have more stressful encounters than their Western counterpart, thus having important clinical implications for ethnocultural minorities who are newly diagnosed with a chronic condition. Together, results of the studies highlight the importance of further investigating the enduring and acute implications of psychosocial variables – particularly the influence of cultural orientation – on the experience and perception of stress.

Statement of Candidate Contribution

The candidate, Cynthia Wan, solely wrote the text of the dissertation. The dissertation comprises three studies. For Study 1, the candidate analyzed data from a pre-existing dataset. In an effort to replicate previous findings and to add to the current literature, Wan and Bielajew proceeded to design and recruit participants for two additional studies (Study 2 and 3), which entailed a cross-cultural examination of salivary and hair cortisol concentration. Wan collected, analyzed, and disseminated the data for Study 2 and 3. Bielajew provided feedback and assistance in a supervisory manner, and oversaw the process of the research.

Study 1 has been published as part of a special issue in the *International Journal of Environmental Research and Public Health.* Study 2 has been published by *Breast Cancer Management.* Study 3 has been revised and submitted for publication, and it is currently consideration for publication. Author contributions for each manuscript will be described accordingly, prior to its presentation in the dissertation. The manuscripts are appended as part of the dissertation, but minor formatting changes have been made to ensure consistency throughout the document.

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General Introduction

Stress Reactivity Patterns in Breast Cancer Survivors and the Implications of Various Psychosocial Factors

Organization of the Dissertation

The overarching goal of the dissertation was to determine whether there were differences in physiological and/or psychological patterns of stress between women with and without a prior diagnosis of breast cancer via the assessments of stress biomarkers (i.e., alpha-amylase and cortisol) and subjective measures of stress. The potential implications of various psychosocial factors on the stress reactivity of our sample of women were also explored; of particular interest was whether cultural orientation and ethnocultural membership played a role in their stress profiles.

In Study 1, we examined acute and diurnal profiles of salivary alpha-amylase, a sympathetic stress biomarker, of White women with and without a prior diagnosis of breast cancer. This study was an extension of previous research conducted in the laboratory (i.e., salivary cortisol patterns among White women with and without a prior diagnosis of breast cancer). The purpose of this study was to establish an initial understanding of salivary alpha-amylase profiles among White breast cancer survivors to complement our existing knowledge of cortisol reactivity among breast cancer survivors, which, together, would provide an overview of the functioning of the stress system (i.e., sympathetic adrenal medullary and hypothalamic pituitary adrenal systems).

With an understanding of acute and diurnal profiles of salivary cortisol and alpha-amylase among White breast cancer survivors, we proceeded with Study 2 — an examination of salivary cortisol patterns in Chinese women with and without a prior diagnosis of breast cancer,

in comparison with a new cohort of White participants. The purpose of Study 2 was two-fold: First, we intended to replicate previous findings from the laboratory (see Couture-Lalande, Lebel, & Bielajew, 2014). Second, we aimed to examine whether physiological and psychological stress profiles showed further differences due to ethnocultural membership.

In the last study, Study 3, we explored the chronic physiological and psychological stress profiles of the same set of participants as in Study 2. Chronic stress was evaluated via hair cortisol concentrations and subjective measures of chronic stress (i.e., Life Experiences Survey and Perceived Stress Scale – Modified). Further, we investigated whether an individual's degree of orientation towards the dominant and non-dominant cultures influenced her chronic stress profiles.

The dissertation is organized into five main sections: General Introduction, Study 1, Study 2, Study 3, and General Discussion. It is then followed by General References, Dissertation Figures, Dissertation Tables, and Dissertation Appendices. The General Introduction includes the following parts: 1) An overview of terms; 2) the prevalence of breast cancer in Canada and China; 3) a review of the literature pertaining to stress and culturally related factors; 4) a review of the empirical studies assessing stress reactivity in healthy and clinical samples; and lastly 5) an overview of the psychosocial stressors along the breast cancer survivorship trajectory.

In the first two subsections of the General Introduction, breast cancer survivorship and other common terms used throughout the dissertation such as "caretaker" and "cancer free" are reviewed and operationally defined. The dissertation then outlines the prevalence of breast cancer in Canada and China, highlighting the importance in conducting a cross-cultural investigation regarding the experience of breast cancer survivors. The third subsection focuses

on the theoretical understanding of stress and culturally related factors, such as how stress is related to one's acculturative experience and how we define stress. The last portion of the General Introduction discusses how stress is assessed in a laboratory setting and reviews the biomarkers used to index stress reactions. After establishing the relationship between physiological stress and breast cancer, we discuss the various psychosocial stressors related to the breast cancer trajectory, such as cancer-related fatigue and fear of recurrence. Finally, the General Introduction finishes with an outline of the objectives and hypotheses of the dissertation.

The next three sections of the dissertation describe Study 1, 2, and 3 (manuscripts appended). For the purposes of this dissertation, the referencing format, tables, and figures in each of the manuscripts have been collated, reformatted, and/or re-numbered to ensure consistency throughout the text. Tables and figures of each study (e.g., Study 1 Figure 1) may be found after the main text of its corresponding manuscript. Individual reference lists were omitted and will be presented as part of the General References.

The last section of the dissertation is the General Discussion, which summarizes the findings of the presented studies, and discusses a few of the limitations in further detail. Clinical and future research implications are also discussed. Following the General Discussion is the General References, as well as the Dissertation Tables, Figures, and Appendices.

Terms and Definitions

Survivorship may be defined as the moment of diagnosis until the time that the individual is considered "cancer free", "in remission", or "NED" (no evidence of disease) (Ganz et al., 2004), or the process and experience of living with cancer and beyond — the moment of diagnosis until death (Vickberg, 2003). The term *survivor* may also be used to refer to anyone affected by a cancer diagnosis — the diagnosed individual or his/her loved ones and family

(National Coalition for Cancer Survivorship, 2014). While we acknowledge the many uses and definitions of the terms, we decided to adopt the colloquial term, “cancer free”, in order to avoid the use of medical terms and to develop a personal and relaxed rapport with the participants. Further, because breast cancer is understood as a chronic and lifelong disease within the dissertation, we have adopted Vickberg’s (2003) definition of *survivorship* (i.e., moment of diagnosis until death). For ease of communication, the term *survivor* will be used to solely refer to the diagnosed individual.

Prevalence of Breast Cancer

With the exception of non-melanoma skin cancers, breast cancer is the most commonly diagnosed cancer among Canadian women. In recent years, it has been noted that the prevalence of breast cancer among men and women are on the rise. In 2017 the incidence of breast cancer in men was 1.2 per 100,000 people and 130.3 per 100,000 people for women (Canadian Cancer Society, 2018), vis-à-vis an incidence rate of 0.9 and 100 in men and women, respectively, in 2015 (Canadian Cancer Society, 2015). Approximately 26,300 women were diagnosed in 2017 (25% of all new cases; (Canadian Cancer Society, 2018), and it accounted for roughly 13% of all cancer deaths in Canadian women in 2017 (Canadian Cancer Society, 2018). Mortality rates have decreased considerably since the mid-1980s, however, due to improvements in screening programs and treatments. In fact, the survival rate for breast cancer is now estimated to be 87% for Canadian women (Canadian Cancer Society, 2018).

Breast cancer has been traditionally viewed as a “White woman’s disease”. That is to say, a disease that predominantly affects White women in developed countries such as Canada and the United States (Brown et al., 2017; Ford, 2018; Queen Mary University of London, 2018). But recent studies have shown that the prevalence of breast cancer is increasing among ethnocultural

minority groups within Canada and the United States, as well as countries in Eastern Asia such as China.

Cancer has been named the leading cause of death in China since 2010 (Chen et al., 2016). Breast cancer, in particular, was the most commonly diagnosed cancer among women in China (Linos et al., 2008). Ferlay et al. (2015) estimated that in 2012, there were 277,100 new breast cancer cases and 68,500 deaths due to breast cancer in Eastern Asia. When they examined age-standardized rates (100,000 persons-years) using the population-weighted average of the incidence and mortality rates, Ferlay et al. (2015) estimated that in 2012 the age-standardized rate for breast cancer in more developed regions was 74.1 per 100,000 whereas in less developed regions, 31.3 (27 in Eastern Asia). These statistics are particularly alarming, considering that over 1.4 billion people live in China alone (Worldometers, 2018).

Researchers have also noted that the incidence of breast cancer in China increased at an annual rate of approximately 3.5% between 2000 to 2013 (Chen et al., 2013; Ferlay et al., 2015; Jemal et al., 2011; Linos et al., 2008; Luo, 2017; Wang, Wei, Liu, Li, & Wang, 2012). In fact, based on an analysis of 72 local, population-based cancer registries from 2009 to 2011, Chen et al. (2016) reported that breast cancer likely accounted for 15% of all new cancers in women in China in 2015. Ferlay et al. (2015), in particular, estimated that approximately 794,000 new breast cancer cases occurred in women in more developed regions of China in 2012, while approximately 883,000 cases occurred in women in less developed regions (with an estimated 25% and 37%, respectively, resulting in death). Furthermore, based on a modeling analysis involving approximately 130 million Chinese women between the ages of 35 to 49 in 2001, it has been suggested that by 2021, 2.5 million Chinese women would be diagnosed with breast cancer with more than 100 new breast cancer cases per 100,000 Chinese women between the

ages of 55 and 69 (Linos et al., 2008).

It is worthwhile to note that breast cancer incidence has not only been on the rise in China, but also among Asian-American women (Deapen, Liu, Perkins, Bernstein, & Ross, 2002). Although there appears to be a difference in prevalence rates among women of different ethnocultural groups in Canada and the United States, as detailed in Dissertation Table 1, the only ethnoculturally bound risk factor that has been identified is having Ashkenazi Jewish ancestry (Canadian Cancer Society, 2018). There are otherwise no known ethnoculturally bound risk factors (Canadian Cancer Society, 2018; Colditz & Rosner, 2000; Pathak & Whittemore, 1992). In fact, it was reported that the molecular composition of breast tumors of Asian women are similar to those of White women (Yu, Lee, Tan, & Tan, 2004). Therefore, the increasing prevalence of breast cancer among Asian women may be in fact due to socio-cultural-economic factors.

Some researchers have postulated that the increase in breast cancer incidence may be due to a shift in risk factor profiles of younger women (i.e., a cohort effect), use of hormonal contraceptives, and a westernized lifestyle (Chia et al., 2005; Minami et al., 2004). Other suggested factors – typically pertaining to women in China – include the one-child policy and various socioeconomic and lifestyle factors such as education, socioeconomic status, disease awareness, use of screening and detection services, and hormonal changes due to stress (Chen et al., 2016; Luo, 2017). In order to provide appropriate care and support, it is necessary to understand the breast cancer survivorship experience among ethnocultural minority groups and to become culturally sensitive and aware of this phenomenon.

Defining Stress

Regardless of socioeconomic status, ethnocultural membership, sex, or age, we all

experience stress to a certain degree. *Stress* is an elusive construct that has been defined and used various ways, depending on context and culture. It is a vague term used to describe a variety of situations that *caused* stress or emotions as a *result* of stress (e.g., burnout, frustration, anxiety, tension). Stressors can come in a variety of forms and intensities such as extreme temperatures, deadlines, minor arguments, recent death of a loved one, major or minor changes in workplace, or the diagnosis of a chronic illness; and in the event of a stressor, both physiological and psychological responses are elicited. The following sections will focus on the different definitions of stress and how it is operationalized in this dissertation.

Stress as a physiological response to adversity. Selye (1946), one of the pioneers of stress research, proposed that *stress* is a physiological response towards any (good or bad) environmental demand (i.e., stressor). Each stressful encounter will cause wear and tear on the body and affect health outcomes. Based on his animal research, Selye (1946) developed a paradigm called the General Adaptation Syndrome (GAS). He proposed that every stress response progresses in three stages (i.e., Alarm, Resistance, and Exhaustion), and the main goal is to maintain stability and homeostasis. During the first two stages, the sympathetic and parasympathetic nervous systems are activated in order to prepare the body for the stressor (*Alarm*) and to return physiological functions to homeostasis (*Resistance*). Often, the third stage, *Exhaustion*, is prevented if homeostasis occurs. However, individuals enter the third stage if homeostasis has not been achieved, and the stressor is prolonged and/or beyond the body's capacity to handle (i.e., adaptive energy). Based on the GAS model, individuals have a finite amount of adaptive energy and every stressful encounter would deplete it (i.e., physiological wear and tear). The exhaustion of adaptive energy may induce "diseases of adaptation", such as arthritis, hypertension, and cancer, and ultimately, it is followed by death upon full depletion

(Selye, 1946).

Since then, many investigators have contested Selye's concept and noted a few inherent shortcomings such as not accounting for psychological stress, the positive effects of coping behaviour (Cox & Ferguson, 1991; Eisenberg, Fabes, & Guthrie, 1997; Roth & Cohen, 1986; Scheier, Weintraub, & Carver, 1986), and the different outcomes associated with one's appraisal of the situation (Seaward, 2015). Nonetheless, Selye was a pioneer in stress research and numerous other physiological models were proposed since then.

Like Selye, McEwen (1998a) viewed stress as a physiological response towards an adversity (implied or real) that induces biological wear and tear on the body. However, McEwen's (1998a) approach is a more cohesive framework that considers the cascading and intertwining relationships between environmental factors and one's experiences, genetic propensity, and behaviour. As shown in Dissertation Figure 1, McEwen (1998b) also took into account two factors that can affect an individual's response to potentially stressful situations: 1) appraisal; and 2) general state of health at the time, which is determined by genetic factors as well as lifestyle and behavioural choices.

Allostasis is an essential component of McEwen's homeostasis theory (McEwen, 1998a; 1998b). McEwen and Wingfield (2003) defined *allostasis* as "achieving stability through change … a process that supports homeostasis, i.e., those physiological parameters essential for life … as environments and/or life history change" (pp. 3). Homeostasis and allostasis are different in the sense that the former refers to the stability and balance of essential bodily systems, while the latter refers to the mediators (e.g., the HPA axis, the autonomic nervous system, and metabolic systems) that work to maintain the balance of the systems whilst responding to the demands of the environment (McEwen & Wingfield, 2003).

The systems that are implicated in allostasis are also indirectly involved in coping and adaptation, and closely linked to the individual's behaviour and psychological state (McEwen, 1998a)**.** For example, an individual's lifestyle and behavioural choices (e.g., smoking, diet, physical activity, and coping strategies) may exacerbate or reduce the consequences of stress. Reactive responses are also highly dependent on the state and coping capabilities of the individual at the time of the event (McEwen, 1998a).

During allostasis, there is usually an imbalance of the mediators (i.e., over- or underproduction) and the individual will likely experience physiological setbacks such as high blood pressure, disrupted cortisol rhythms, and elevation of inflammatory cytokines (McEwen & Wingfield, 2003). If the imbalance persists beyond the body's capacity to maintain homeostasis, it will result in an allostatic (over)load. While allostatic loads are a normal part of allostasis as an adaptive response, *allostatic (over)load* refers to "the wear and tear on the body and brain resulting from chronic overactivity or inactivity of physiological systems that are normally involved in adaptation to environmental challenge" (McEwen, 1998a, p. 37). Allostatic (over)loads may lead to health problems such as hypertension, stroke, inflammatory and autoimmune disorders, and neuronal atrophy (McEwen, 1998a).

Stress as a product of life events. In the late 1960s, *stress* was viewed as the product of life changes, events, or hassles and it was measured in terms of adaptation and readjustment (Holmes & Rahe, 1967; Kanner, Coyne, Schaefer, & Lazarus, 1981; Sarason, Johnson, & Siegel, 1978). It was reasoned that too many life changes or events in a short period of time would likely increase one's vulnerability to illness (Holmes & Rahe, 1967). Based on this perspective, the individual is a passive recipient of stress (Lyon, 2012). However, an integral problem to this belief is the assumption that all life changes are stressful and have the same magnitude of

demand on each individual. Related to this problem is the homogeneous view that the stressor will affect all individuals the same way — disregarding individual differences in terms of appraisal, coping abilities, resilience, hardiness, and the effects of external or internal locus of control (Antonovsky, 1987; Kobasa, 1979; Southwick, Vythilingam, & Charney, 2005).

Stress as the product of the interaction between the self and environment. As stress research matured, a transactional theory of stress and coping was eventually developed. Lazarus (1966) suggested that stress is a result of a transaction, or interaction, between the individual and the environment. In this view, *stress* is a multifaceted construct that involves cognitive, affective, and coping factors, and may be defined as any occurrence that we perceive as beyond our coping abilities and therefore inducing a negative emotional state (Lazarus, 1966). But if the individual has a sense of controllability of the situation and the ability to overcome the obstacle, the stressor may also elicit positive emotions such as happiness, pride, and relief (Lazarus, 1966).

Stress as defined in the dissertation. McEwen's (1998a, 1998b) and Lazarus'(1966) models are very similar and are complementary to each other: The former focuses on physiological input whereas the latter centers on psychological input. In this dissertation, stress is evaluated as both a physiological and psychological phenomenon with the aim to explore the relationship between subjective feelings of stress and physiological response towards a "stressor".

Inspired by McEwen's (1998a, 1998b) and Lazarus's (1966) approach, *stress* in this context is defined as a product of an interaction between an individual and the environment; and unless otherwise noted, it will refer to *negative stress* (or distress). That is to say, when an individual no longer has the capacity or resources to cope with a stressor, whether real or imagined, that is perceived as threatening to one's mental, physical, or psychological well-being.

As a result, a *stress response* – a series of physiological, psychological, and behavioural responses and adaptations – is elicited. Due to the processes and resources involved, prolonged exposure or chronic stress may therefore pose a physiological and/or psychological toll on the individual.

Acculturative Stress, Cultural Orientation, and Health

Acculturation is a catch all term that refers to the process of adjusting and adapting to a new cultural context (Berry, 1980; Tsai, Chentsova-Dutton, & Wong, 2002), and it encompasses a variety of domains of research including acculturative stress (Berry, 1970). The notion of *acculturative stress* is largely inspired by Lazarus's transactional theory of stress (see Lazarus & Folkman, 1984), and it refers to "a response by people to life events that are rooted in intercultural contact. Frequently, these reactions include heightened levels of depression … and of anxiety" (Berry, 2006a, p. 43). Berry's (2006a) model takes into account moderating group-level (e.g., political context) and individual-level factors that may affect one's acculturative experience. For individual-level factors, in particular, he distinguishes between moderating factors *prior* to acculturation, such as age, gender, education, economic status, migration expectations and motivations, and *during* acculturation (e.g., acculturation attitudes, cultural distance). These variables affect every step of the acculturation process and experience.

Acculturative stress, in particular, is one of three approaches conceptualizing the potential psychological difficulties that immigrants may face (Berry, 2006b). Like Lazarus's (1966) model, the perception of control is a vital component of the appraisal of the event, which will dictate the behaviours and reactions that follow. Conceptually, immigrants experience acculturative stress when they encounter stressors upon intercultural contact that they appraise as beyond what they can *manage* and *control* (Berry, 2006b).

Berry, Kim, Minde, and Mok (1987) also identified five broad categories of acculturative stressors: physical environment (climate, housing, safety), biological (food security, health), social (isolation, homesickness), cultural (norms and behaviours of a new cultural society, discrimination), and psychological (psychological state of the individual, resistance to acculturating). Later, Ying (2005) proposed *functional stressors* as a sixth category, which encompasses the learning of a new language, finding employment and/or schools.

As one may expect, depending on the acculturative stressors experienced and coping strategies used, one's level of stress may vary, and the long-term outcomes may be adaptive or non-adaptive. Adaptation in this sense refers to *psychological adaptation*, one's psychological well-being and satisfaction (Schmitz, 1992; Ward & Rana-Deuba, 1999); and *sociocultural adaptation*, the ability to manage daily activities in a new cultural setting (Ward & Rana-Deuba, 1999), including differences in socioeconomic status (Aycan & Berry, 1996) and/or new familial roles or expectations (Ataca & Berry, 2002). Although adaptation to acculturation and handling of acculturative stressors may influence well-being, cultural orientation is another aspect that cannot be ignored.

Berry (1980) suggested that the acculturation experience is not homogenous and that there are a variety of acculturation strategies that individuals may use throughout the acculturation process to deal with acculturative stressors. Berry (1980; 2006b) suggested four acculturation strategies: 1) *Assimilation*, "when individuals do not wish to maintain their cultural identity and seek daily interaction with other cultures" (Berry, 2006b, p. 290); 2) *Separation*, "when individuals place a value on holding on to their original culture, and at the same time wish to avoid interaction with others" (Berry, 2006b, p. 290); 3) *Integration,* "an interest to maintaining one's original culture, while in daily interaction with other groups" (Berry, 2006b, p.

290); and 4) *Marginalization*, "little possibility or interest in cultural maintenance … and little interest in having relations with others" (Berry, 2006b, p. 291). Each strategy may lead to different consequences and outcomes, however (e.g., distress, adaptation and adjustment; Berry, 2006b).

Empirical research supports the notion that acculturative stress can negatively impact health and well-being (Berry et al., 1987; Williams, 2000). For example, various studies have suggested that stress is associated with increased levels of inflammatory markers (Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Kiecolt-Glaser, Robles, Heffner, Loving, & Glaser, 2002; Steptoe, Hamer, & Chida, 2007), which in turn, may disrupt the stress system (Rohleder, 2011) and increase the likelihood of developing hypertension and cardiovascular diseases (Kaplan & Nunes, 2003; Steffen, Smith, Larson, & Butler, 2006), diabetes (Chun & Chesla, 2004; Chun, Chesla, & Kwan, 2011), psychiatric disorders (Dantzer, O'Connor, Freund, Johnson, & Kelley, 2008; Spitzer et al., 2010), and cancers (Rakoff-Nahoum, 2006; Silva, Dillon, Verdejo, Sanchez, & De La Rosa, 2017).

Fang, Ross, Pathak, Godwin, and Tseng (2014), for example, demonstrated that acculturative stress is associated with the inflammatory markers, C-reactive protein (CRP) and soluble tumor necrosis factor receptor 2 (sTNFR2), in a Chinese immigrant population. CRP is now considered a reliable marker of systemic inflammation (Gabay & Kushner, 1999) and sTNFR2 has been suggested as an inflammatory marker for diabetes and breast cancer risk (Gross, Newschaffer, Hoffman-Bolton, Rifai, & Visvanathan, 2013; Rose, Komninou, & Stephenson, 2004; Tilg & Moschen, 2006). In Fang et al.'s (2014) study, they measured acculturative stress using the Migration-Acculturation Scale, the impact of major life events via the Life Experiences Survey, and acculturation in terms of degree of cultural orientation via the

General Ethnicity Questionnaire, in a sample of 407 foreign-born Chinese American women. They reported that life events were not associated with CRP or sTNFR2 levels; however, higher levels of CRP and sTNFR2 levels were significantly associated with higher levels of acculturative stress but not when accounting for degree of cultural orientation.

Cultural orientation is the degree that one is influenced by and engages in activities of a specific culture (Tsai & Chentsova-Dutton, 2002; Tsai et al., 2002; Ying, 1995). Whereas the acculturation strategy framework may be useful in explaining outcomes related to various behaviours, cultural orientation is more relevant to one's cultural identity. There are four main domains of cultural orientation (Tsai & Chentsova-Dutton, 2002): Social affiliation, participation in cultural practices and activities, language proficiency and preference, and attitudes towards host and native cultures. Researchers have also proposed unidimensional and bidimensional models of cultural orientation (Tsai et al., 2002), both of which were incorporated in Berry's (1980) acculturation framework, which was previously discussed.

Although empirical support exists for both models, recent studies have suggested that to fully understand an ethnocultural group and which cultural orientation model may be the best fit, one of the variables to consider is place of birth. Tsai et al. (2002) noted that one's place of birth is a determinant of cultural exposure and experience, which in turn, influences cultural orientation. Some research groups report that American-born Asians exhibit a bidimensional model of cultural orientation, whereas immigrated Asians typically exhibit a unidimensional mode of cultural orientation (Ryder, Alden, & Paulhus, 2000; Tsai, 2000; Tsai, Ying, & Lee, 2000). Despite mixed findings in the literature, there is a general consensus that integrated acculturation, or being oriented to both cultures, is associated with higher levels of psychological adjustment (Berry, 2006b), greater life satisfaction, more positive affect, and lower levels of

depression (Tsai et al., 2003).

Moreover, with the growth of visible minority groups in Western countries, increasingly more researchers have been examining the implications of culturally related stressors on psychological and physiological health (Choi, 1997; Fang et al., 2014; Logan, Barksdale, Carlson, Carlson, & Rowsey, 2012). In general, researchers have acknowledged that acculturative stress is associated with negative psychological and physiological health outcomes. For instance, Choi (1997) reported that high levels of acculturative stress were associated with depressive symptomology among Korean Americans. Logan et al. (2012) have also recently reported that acculturative stress may indirectly increase the risk of arterial stiffness. They based this finding on the significant relationship between systolic blood pressure and acculturative stress, as well as significant associations between perceived stress, acculturative stress, state and trait anxiety (collectively referred to as "psychological stress"), and arterial stiffness.

Beyond the health implications, understanding an individual's cultural orientation also has significant impact on the communication of illness, treatment or intervention, and post-treatment services. For example, in a study contrasting the perspectives that unacculturated Chinese Americans and White Americans had on depression, it was reported that unacculturated Chinese Americans had a collectivistic view of depression that was consistent with traditional Chinese culture and views of medicine and illness — that there was no separation between the mind and the body (Ying, 1988). However, a similar study conducted years later yielded different results: Ying, Lee, Tsai, Yeh, and Huang (2000) reported that Chinese Americans exhibited very similar views of depression to that of White Americans, which may be due to the increased cultural exposure in the 2000s versus the late 1980s. Taken together, it highlights the importance of understanding cultural orientation and its influence on chronic illness whilst taking

into account the environmental context. It may be especially pertinent for healthcare providers to be sensitive to the cultural orientation of patients and other cultural factors, such as cultural distance and exposure, in order to better address health concerns, treatments, and post-treatment care.

Current Literature on Chinese Breast Cancer Survivors

The majority of the existing research on Chinese breast cancer survivors are typically qualitative investigations of their quality of life (QOL), overall breast cancer experience, symptomology, or difference in treatment or screening decisions. Although there are some empirical studies on stress biomarkers, most of the studies were completed in the United States or Asia. Given that location plays a big part in the acculturation process and affects cultural orientation in terms of the degree of exposure to different cultural values, it is important to remain cautious when interpreting results concerning studies conducted elsewhere. That is to say, while the survivorship experience of Chinese breast cancer survivors may be considerably different than those in United States, it is possible that Chinese-American breast cancer survivors may also have a different survivorship experience than Chinese-Canadian breast cancer survivors due to the different cultural climates and the heterogeneity of Asian culture.

In spite of this, empirical studies have generally agreed that higher acculturation is associated with better health-related quality of life (HRQOL) during the breast cancer trajectory (Kim, Ashing-Giwa, Singer, & Tejero, 2006; Lim, Yi, & Zebrack, 2008; Tsai, Morisky, Kagawa-Singer, & Ashing-Giwa, 2011). In fact, higher levels of acculturation have been found to be related to more positive health beliefs, social support (with larger and more diverse network), and positive coping and adjustment strategies (Lim, 2014; Lim et al., 2008; Tsai et al., 2011). But due to the heterogeneity of Asian culture, there may be group differences in levels of stress

between different Asian subgroups (Williams, 2000). Indeed, Williams (2000) reported that different levels of perceived stress were reported between Chinese, Vietnamese, and Koreans. Chinese participants reported the highest levels of stress across several domains (e.g., global, occupational, relationship, financial, and violence stress), whereas Korean participants reported lower levels of stress in comparison to the other two subgroups.

But before quantifying QOL, it is important to understand the components that constitute QOL for the ethnocultural groups in question. Using a qualitative approach, Wong-Kim, Sun, Merighi, and Chow (2005) explored the meaning of having a positive QOL and identity beliefs between 15 American-born and 15 foreign-born Chinese breast cancer survivors. Wong-Kim et al. (2005) noted that both groups reported family relationships and family support to be two central factors towards having a positive QOL. American-born Chinese breast cancer survivors, in particular, highlighted the importance of friendship; whereas foreign-born Chinese breast cancer survivors emphasized the importance of wealth (Wong-Kim et al., 2005). This finding, however, may reflect the sociodemographic difference between American-born and immigrants and the additional hardships that immigrants may face such as learning a new language, finding a comparable or better career after immigration, and building relationships in an unfamiliar environment. There were some observed similarities in both groups despite their difference in degrees of acculturation, however. Specifically, both groups expressed feelings of shame and stigma associated with their breast cancer diagnosis and had harbored fatalistic views (Wong-Kim et al., 2005). *Fatalistic views* or *fatalism* (Greer & Watson, 1987) refers to the acknowledgement of the diagnosis, a feeling of loss of control over the course of the illness, and the perception that the diagnosis is incurable and will ultimately lead to death. But despite the fatalistic views, while foreign-born breast cancer survivors described their experience as ‘fate’, it

also encouraged them to engage in more self-care and prioritize their own health over family demands (Wong-Kim et al., 2005).

The perception of the diagnosis and mental adjustment styles have been found to be associated with QOL and affect (Yeung & Lu, 2014). Mental adjustment styles refer to the cognitive and behavioural response to a cancer diagnosis (Greer, Moorey, & Watson, 1989). It has been shown that positive QOL is associated with positive affect and a "fighting spirit" (i.e., optimistic attitude with a realistic appraisal of the illness (Greer & Watson, 1987) and negatively associated with fatalism in Chinese cancer survivors (Yeung & Lu, 2014). These results highlight the importance of culturally sensitive psychosocial interventions and the role that appraisal and affect may play in the breast cancer trajectory. While acculturation level may affect the breast cancer experience to a certain degree, there are still similar issues underlying the cultural group as a whole (Yeung & Lu, 2014).

A Synthesis of the Stress System and Different Measures of Stress

Stress is an influential factor in psychological and physical well-being that affects native citizens and usually, to a greater degree, immigrants. We postulate that while the perception and coping strategies one may use in the face of a stressor varies between individuals, the experience of (chronic) stress will have a psychological and physiological toll, such as feelings of distress and anxiety, fatigue, or compromised immune responses.

As shown in Dissertation Figure 2, there are two main components of the stress system: The hypothalamic-pituitary-adrenal (HPA) and the sympathetic-adrenal-medullary (SAM) axes, which operate in tandem to maintain homeostasis and prepare the organism to deal with environmental challenges (Thiel & Dretsch, 2011). One way to assess their functioning is via the examination of the secretion patterns of stress-related biomarkers in response to such

challenges.

Salivary cortisol in health and breast cancer research. Cortisol is a glucocorticoid hormone and a stress biomarker of the HPA axis. Cortisol is an essential hormone for regulating bodily functions (e.g., homeostasis, metabolism, immune response) and it plays an important role in responding to environmental challenges and stress (Fulford & Harbuz, 2005). Briefly, when individuals perceive a stressor, the hypothalamus releases CRH (corticotropin releasing hormone), which triggers the pituitary gland to release ACTH (adrenocorticotropic hormones). The production of ACTH then prompts the adrenal glands to produce glucocorticoids (GC) such as cortisol in humans and corticosterone in animals. Cortisol then initiates a series of metabolic processes to prepare the body to handle the stressor, such as raising blood sugar levels, suppressing immune function or other bodily responses that are less pressing at the time (e.g., fatigue and hunger). After a certain level of hormones is reached, the HPA axis enters a negative feedback loop — the production of GCs inhibits the pituitary glands and the hypothalamus from further production of ACTH and CRH, respectively (Gunnar & Quevedo, 2007).

Cortisol is one of the most commonly studied stress biomarkers (Hellhammer, Wüst, & Kudielka, 2009) because there are multiple ways to collect and assess acute and diurnal cortisol levels (e.g., serum, plasma, urinary, salivary; Dorn, Lucke, Loucks, & Berga, 2007; Kirschbaum & Hellhammer, 1994). In fact, salivary cortisol is commonly collected in laboratory settings in response to acute stress due to its ease of collection, non-invasiveness, amenability to serial sampling, and reasonable correlation with serum cortisol (Dorn et al., 2007; Kirschbaum & Hellhammer, 1994). In addition to its ease of collection and assessment, cortisol also has a relatively stable diurnal pattern in healthy individuals (Foley & Kirschbaum, 2010; Stone et al., 2001), with its peak typically occurring within 30 to 60 minutes after waking and thereafter

steadily declining throughout the day (Foley & Kirschbaum, 2010). In an acute stress situation, the HPA axis temporarily increases cortisol secretion to allow for optimal performance, and it usually returns to basal levels within one or two hours following the stressor (Armario, Vallès, Dal-Zotto, Márquez, & Belda, 2004).

But cortisol secretion can be affected by numerous factors such as physical fitness (Traustadóttir, Bosch, & Matt, 2005), age and gender (Kudielka, Hellhammer, & Wüst, 2009; Larsson, Gullberg, Rastam, & Lindblad, 2009), hormonal status (Childs & Wit, 2009), circadian rhythm (Buckley & Schatzberg, 2015; van Eekelen, Kerkhof, & van Amsterdam, 2003), the consumption of certain foods and nicotine (Childs & Wit, 2009; Kudielka, Broderick, & Kirschbaum, 2003; Kudielka et al., 2009; Larsson et al., 2009; Weibel, 2003), illnesses such as cancer (Couture-Lalande et al., 2014; Lundstrom & Furst, 2003), burnout syndrome (Melamed et al., 1999), and various sleep disorders (Buckley & Schatzberg, 2015). Studies have also shown that menstrual cycle, pregnancy, and menopausal transition may affect circadian and reactive cortisol (Foley & Kirschbaum, 2010; Nierop et al., 2006). In addition, Torres, Mata-Greve, and Harkins (2018) have also recently shown that acculturative stress also influences circadian cortisol patterns. In particular, they found that Latina women who reported higher levels of acculturative stress typically exhibited a lower cortisol awakening concentration and flatter diurnal cortisol responses (Torres et al., 2018), which may be indicative of cortisol dysregulation.

Some studies have also suggested that metastatic breast cancer survivors (typically stage 4) are much more likely to show abnormal diurnal cortisol patterns in comparison to that of healthy individuals (Abercrombie et al., 2004; Porter et al., 2003; Spiegel, Giese-Davis, Taylor, & Kraemer, 2006; Touitou, Bogdan, Levi, Benavides, & Auzeby, 1996). Abercrombie et al.

(2004), for example, noted that metastatic breast cancer survivors with a more severe metastatic spread often displayed higher mean cortisol levels and flatter slopes in their diurnal profiles. Sephton, Sapolsky, Kraemer, & Spiegel (2000) also reported that over a 7-year period, there were higher mortality rates for metastatic breast cancer survivors who had a blunted diurnal cortisol response, which has been speculated to be associated with more rapid cancer progression (Spiegel et al., 2006). Despite these findings among metastatic breast cancer survivors, numerous groups have observed normal diurnal patterns in breast cancer survivors (diagnosed up to Stage 3), and a positive relationship between reactive salivary cortisol levels and time since diagnosis in breast cancer survivors (Couture-Lalande et al., 2014). Specifically, Couture-Lalande et al. (2014) have previously reported that women diagnosed over five years post-diagnosis showed cortisol reactivity levels approaching that of control participants without a history of cancer.

Although the HPA axis is an important component of the neuroendocrine system that regulates various body processes and stress responses, it is only one part of the human stress system. To fully appreciate the complexity of stress mechanisms, one needs to understand its synergistic relationship with its counterpart, the SAM axis. In this vein, investigators have become interested in exploring alpha-amylase, a biomarker that reflects sympathetic nervous system (SNS) activity (Nater & Rohleder, 2009).

Salivary alpha-amylase in health and breast cancer research. Alpha-amylase is a salivary enzyme that is modulated by the autonomic nervous system (ANS), which controls various visceral functions, such as salivation. Research exploring the involvement of the ANS (sympathetic and parasympathetic branches) in the secretion of alpha-amylase began in the early 1970s, and several important discoveries were made via animal studies. It was observed that beta-adrenergic receptors in the parotid gland were involved in alpha-amylase production among

rats (Batzri & Selinger, 1973; Batzri, Selinger, Schramm, & Robinovitch, 1973). Researchers also examined the individual roles of sympathetic and parasympathetic branches of the ANS, and it was observed that independent sympathetic and parasympathetic stimulations of the parotid gland produced different concentrations of amylase among rats (Anderson et al., 1984; Asking, 1985). However, the combination of the two stimulations produced a synergistic effect, which was reasoned to be the result of greater alpha-amylase concentrations to beta-1-adrenoceptors Asking (1985).

In addition to the numerous animal studies investigating the involvement of ANS in alpha-amylase production at the time, Speirs, Herring, Cooper, Hardy, & Hind (1974) tested the relationship between norepinephrine and alpha-amylase production in humans. In particular, Speirs et al. (1974) paired a stressor (i.e., immersion of participants' lower body into cold water) with the ingestion of isoprenaline or propranolol, and assessed the participants' alpha-amylase production level. Speirs et al. (1974) reported that propranolol alone reduced alpha-amylase levels, while increased alpha-amylase levels were observed when the challenges were combined.

By the late 1970s, numerous researchers started to examine the relationship between alpha-amylase and stress, and they have concluded that it is a reliable biomarker of the SNS and that it can index both physical and psychological stress in humans (Bosch, Veerman, Geus, & Proctor, 2011; Chatterton, Vogelsong, Lu, Ellman, & Hudgens, 1996; Gilman, Thornton, Miller, & Biersner, 1979; Granger, Kivlighan, El-Shiekh, Gordis, & Stroud, 2007; Nater & Rohleder, 2009). It has also been suggested that alpha-amylase exhibits a relatively stable diurnal pattern albeit distinctly different from that of cortisol (Rohleder & Nater, 2009). Unlike cortisol, Rohleder & Nater (2009) noted that alpha-amylase concentrations reduced significantly within 60 minutes after waking, followed by a gradual increase, with peak levels occurring in the late

afternoon.

Alpha-amylase has been measured in response to a variety of acute stressors such as examinations and various physical and leisure activities (e.g., Bosch et al., 1998; Chatterton, Vogelsong, Lu, & Hudgens, 1996; Skosnik, Chatterton, Swisher, & Park, 2000). In addition to the cold stress immersion test, the Trier Social Stress Test (TSST; Kirschbaum, Pirke, & Hellhammer, 1993) is a commonly used standardized laboratory procedure to induce acute stress (Allen, Kennedy, Cryan, Dinan, & Clarke, 2014). In fact, numerous researchers have observed a notable increase in alpha-amylase reactivity among participants of varying ages in response to the TSST (Gordis, Granger, Susman, & Trickett, 2008; Granger et al., 2007; Grillon, Duncko, Covington, Kopperman, & Kling, 2007; Nater et al., 2005).

Although there may be some variations in the TSST from study to study, it typically has two components: (1) a mock job interview in front of a committee panel made up of confederates; and (2) an arithmetic task (Kirschbaum et al., 1993). Indeed, the TSST has been shown to be very effective in producing stress-related physiological responses. In fact, a two- to threefold increase in salivary cortisol levels has been observed in the majority of participants (70 to 80%), with peak levels occurring around 10 to 20 minutes after TSST cessation (Kudielka, Hellhammer, & Kirschbaum, 2007).

Many researchers have also concurrently examined alpha-amylase and cortisol profiles. In fact, a simple search in PSYCInfo with the terms “cortisol”, “alpha-amylase” and “stress”, yielded over 1,600 results. However, the number of hits dramatically reduced as the search was narrowed to cancer or breast cancer. To our knowledge, Ariza-García et al. (2013) were one of the first research groups, if not the first, to publish a study examining both cortisol and alpha-amylase levels in breast cancer survivors. They investigated the effects that physical inactivity

would have on the psychophysiological state of 108 breast cancer survivors (diagnosed with stage 1, 2, or 3 breast cancer). Ariza-Garcìa et al. (2013) concluded that physically inactive breast cancer survivors exhibited a worse psychoneurobiological state than active breast cancer survivors. Further, they reported that physical activity was associated with overall better mood (i.e., lower levels of depression, anger, and confusion, lower levels of fatigue), lower diastolic blood pressure, and lower alpha-amylase activity, regardless of age, tumour stage, treatment, time since diagnosis, educational level, and marital status. Indeed, numerous studies in the literature have also noted that physical activity can partially mediate the relationship between pain, distress, and cancer-related fatigue among breast cancer survivors (Courneya & Friedenreich, 2011; Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; Lambert, Brunet, Couture-Lalande, & Bielajew, 2019; Mock et al., 2001).

Current stress research development: An examination of hair cortisol. While the collection and analysis of saliva, serum, urinary, or plasma samples are viable methods to assess acute and diurnal stress responses, they are not appropriate for the evaluation of chronic stress. Hair cortisol, however, may be the most practical option towards the investigation of chronic physiological stress. The analysis of hair biomarkers dates back to the 1970s as a means to evaluate an individual's exposure to exogenous compounds (Kintz, Villain, & Cirimele, 2006; Pragst & Balikova, 2006). But in the early 2000s, Cirimele, Kintz, Dumestre, Gouillé, and Ludes (2000) began investigating whether glucocorticoids could be detected in human hair. Cirimele et al. (2000) collected hair samples from individuals receiving different drugs for medical issues (e.g., prednisone, beclomethasone), and they were able to detect cortisol, cortisone, and eight other glucocorticoids.

Following this discovery, Koren et al. (2002) used methanol and a modified salivary

enzyme-linked immunosorbent assay (ELISA) method to extract and analyze cortisol concentrations in hair samples obtained from hyraxes. Approximately 7 to 20 mg of hair was extracted for analysis. Results indicated a significant positive correlation between hair cortisol concentration, social ranking, and dominance (Koren, Mokady, & Geffen, 2008; Koren et al., 2002). Other animal studies, which involved the collection of regrown hair sample (i.e., hair at the particular sampling area was shaved off at the beginning of the study and regrown hair was collected at the end of the sampling period), typically reported strong positive associations between hair cortisol concentrations and mean salivary cortisol levels (e.g., Accorsi et al., 2008; Bennett & Hayssen, 2010; Davenport, Tiefenbacher, Lutz, Novak, & Meyer, 2006).

After numerous animal studies, researchers began investigating whether hair constituents could be used as a marker of chronic stress in humans. As shown in Dissertation Figure 3, the rate of hair growth is approximately one centimeter per month (Russell, Koren, Rieder, & Van Uum, 2012; Wennig, 2000), with each centimeter representing one month of cortisol accumulation. The analysis of hair cortisol concentration would therefore be a better alternative than other modes of collection for the assessment of chronic stress because it would remove the burden of multiple sample collection from participants, and allow researchers to easily assess cortisol concentrations over a longer period of time — at least one month, and reliably up to a period of three months (Russell et al., 2012; Wennig, 2000).

Using a similar methodology as Koren et al. (2002), Sauvé, Koren, Walsh, Tokmakejian, and Uum (2007) collected, analyzed, and compared 39 human hair samples to saliva, blood, and urine collections from the same participants. They reported a positive correlation between cortisol concentrations in hair and urine samples (r = .33), but unlike previous animal studies, there were no significant correlations between hair, salivary, or serum cortisol (*cf.* Accorsi et al.,

2008; Bennett & Hayssen, 2010; Davenport et al., 2006). However, these results may be due to methodological differences: Sauvé et al. (2007) did not collect regrown hair as per the methodology used in previous animal studies, and the hair segments that were collected did not correspond to the collection period of the saliva, serum, and urinary cortisol samples. Hence, although they analyzed approximately 2 cm of hair (equivalent to two months of accumulated cortisol), the comparison samples typically reflected cortisol levels within the last 24 hours at most. Other researchers also contended that the lack of concordance between human and non-human validation studies were due to differences in the regions from which the hair samples were collected (Sauvé et al., 2007; Stalder & Kirschbaum, 2012). Based on these observations, Sauvé et al. (2007) suggested that human hair samples should be collected from the vertex posterior region of the scalp because it has the lowest intra-individual coefficient of variation for cortisol concentration.

Following a similar methodology of earlier animal studies, D'Anna-Hernandez, Ross, Natvig, and Laudenslager (2011) published the first human study involving regrown hair samples and reported findings that were comparable to the results based on animal models. They sought to validate hair cortisol as a measure of extended cortisol activity by comparing hair cortisol levels of 21 pregnant women at each trimester and 3 months postpartum with diurnal salivary cortisol levels. Saliva samples were collected three times per day for three days; samples were obtained five times during pregnancy and six weeks postpartum. D'Anna-Hernandez et al. (2011) reported an increase in hair and salivary cortisol levels during pregnancy and indicated that the area under the curve of hair cortisol and diurnal salivary cortisol were correlated.

More recently, researchers began investigating the hair cortisol patterns of individuals suffering from various ailments and comparing it with other types of cortisol (e.g., salivary,

plasma, urinary), but these studies have typically yielded mixed results (Luo et al., 2012; Staufenbiel, Penninx, Spijker, Elzinga, & Rossum, 2013; Steudte et al., 2013; Steudte-Schmiedgen, Kirschbaum, Alexander, & Stalder, 2016). For instance, while Luo et al. (2012) found that individuals with PTSD had an overall higher hair cortisol concentration than that of control participants; Steudte et al. (2013) reported that PTSD patients and traumatized control patients exhibited lower hair cortisol concentrations than that of non-traumatized control participants (59% and 51% lower, respectively). Furthermore, contrary to the general belief that individuals with GAD suffer from hypercortisolism, Steudte et al. (2011) reported that diurnal salivary cortisol profiles did not differ between groups, but GAD patients had significantly lower hair cortisol concentrations than control participants.

Taken together, these studies highlight the importance of further research in order to understand the relationship and nuances between short-term and long-term stress measures. Despite the prevalence of breast cancer diagnoses among women and the advances in stress research, to the best of our knowledge there are no published studies examining chronic stress patterns via hair cortisol assessments among breast cancer survivors.

Psychosocial Stressors During the Breast Cancer Trajectory

Although it is important to investigate physiological responses to stress, psychosocial stressors and their psychological consequences should also be considered. While acute stressors may negatively affect one's well-being in the short-term, persistent stressors (e.g., chronic illnesses) are pervasive and a lifetime battle. Breast cancer survivors, for example, may experience various physiological and psychosocial stressors throughout the cancer trajectory. Despite the positive survival and treatment statistics associated with diagnoses, the long-term emotional distress and physical stressors associated with being a cancer survivor can lead to

other health problems (Lundberg, 2005; McEwen, 1998a; Mehnert & Koch, 2007).

Psychosocial stressors may be punctual, that is, associated with the diagnosis, anxiety over the reactions of loved ones, the treatment itself (Kedde, Wiel, Schultz, & Wijsen, 2013; Knobf, 2007); or chronic and persisting following treatment, such as fear of death or recurrence, persistent fatigue, or concerns in regards to managing lifestyle changes, returning to work, and reentering everyday life (Bower et al., 2006; Hauken, Larsen, & Holsen, 2013; Schmidt et al., 2015, 2016; Tiedtke, Rijk, Casterlé, Christiaens, & Donceel, 2010). Depending on the intensity, frequency, and chronicity of the stressor, it may implicate the physiological stress response differently.

For example, Wan, Couture-Lalande, Lebel, and Bielajew (2017) recently examined the relationship between the perceived impact of stressful life events within the past year and the overall peak cortisol response after an acute stressor (i.e., TSST). Wan et al. (2017) reported that although there were no differences between overall frequency and perceived impact of stressful life events between women with or without a previous diagnosis of breast cancer, the total number of stressful life events and the perceived impact correlated negatively with peak cortisol responses among breast cancer survivors only. Thus indicating that the experience of (positive or negative) stressful life events may significantly affect the endocrine system of breast cancer survivors, but not women without a prior diagnosis (Wan et al., 2017).

Alongside non-cancer related life events, breast cancer survivors must also manage a unique set of stressors that relates to their diagnosis. Lebel, Rosberger, Edgar, and Devins (2007) compared four common stressors experienced throughout the breast cancer trajectory in 72 women diagnosed with breast cancer. They compared four fears (fear of the future, physical limitations, pain, and the occurrence of interpersonal problems due to cancer) at five different

time points (3, 7, 11, 15 months, and 6 years). As expected, the intensity of each stressor was different for each participant and decreased over time, but two findings were consistent: First, fear and uncertainty of the future was the most pressing stressor for participants at all time points (Lebel et al., 2007). Second, higher levels of stress were reported after a cancer recurrence or metastasis. According to Lebel, Rosberger, Edgar, & Devins (2009) even if the extent of fear or uncertainty of the future decreases over time, it will not lead to a reduction in emotional distress. Rather, emotional distress influences one's feelings of fear (Lebel et al., 2009).

Fear of recurrence, in particular, is a well-studied pervasive stressor that affects all cancer survivors. *Fear of recurrence*, the "fear or worry that cancer will return or progress in the same organ or in another part of the body" (Vickberg, 2003, p. 18), can be an intrusive and debilitating stressor. It has been ranked as an area of great concern for breast cancer survivors and is one of the most prevalent long-term psychological consequences of breast cancer survivorship (van den Beuken-van Everdingen et al., 2008). Studies report that approximately 33% to 56% of survivors are considered to have moderate to high-risk fears, which are associated with lower quality of life and higher levels of psychological distress (Arès, Lebel, & Bielajew, 2014; Lebel, Beattie, Arès, & Bielajew, 2013; van den Beuken-van Everdingen et al., 2008; Vickberg, 2003; Wan et al., 2018; Wan, Silverstein, Arès, & Bielajew, 2016). Sometimes the fears can be so overwhelming that the survivor has difficulty performing daily and social activities, thus causing impairment that is disproportionate to the actual risk of recurrence (Koch et al., 2014).

But various sociodemographic and medical factors may influence one's degree of fear of recurrence. For instance, some studies have shown that fear of recurrence remains an issue for some long-term breast cancer survivors (i.e., five or more years since diagnosis; Koch et al., 2014). While other studies have observed a significant decrease in worries about the future,

especially among survivors who did not experience a recurrence or metastasis (Bloom, Steward, Chang, & Banks, 2004). In fact, Bloom et al. (2004) reported that 92% of the survivors in their study rated their health as good or excellent five years post-diagnosis, thus suggesting fears and worries about the future may decrease over time. In addition to time since diagnosis, age may also influence the degree of fears and worries. Kornblith et al. (2007), for example, reported that younger survivors (18 to 55 years old) scored significantly worse than older survivors (65 years old or older) on a range of QOL measures, including fear of recurrence. It was reasoned that younger survivors might experience more distress due to the various responsibilities they may have, such as providing care to younger children (Kornblith et al., 2007).

Indeed, in various studies conducted by our research group, we found that age and motherhood were related to fear of breast cancer recurrence (Arès et al., 2014; Lebel et al., 2013; Wan et al., 2018; Wan, Silverstein et al., 2016). In particular, our results indicated that a more recent diagnosis, younger age at diagnosis, and higher stage of diagnosis were associated with greater overall fears (Lebel et al., 2013; Wan, Silverstein et al., 2016). Wan, Silverstein et al. (2016) reasoned that a larger proponent of the fears may be related to one's ability to cope with health conditions whilst balancing demands of motherhood and parenting responsibilities. These findings were also later corroborated in a study examining models of well-being between young breast cancer survivors with and without children (Wan et al., 2018). Specifically, Wan et al. (2018) noted that although models of well-being were similar between young breast cancer survivors with and without children, psychological distress, illness intrusiveness, and fear of recurrence co-occurred more frequently among young breast cancer survivors with children. Combined, these results suggest that the demands of motherhood may be associated with higher levels of fear among young breast cancer survivors in both the short- and long-term survivorship

periods (Arès et al., 2014; Lebel et al., 2013; Wan et al., 2018; Wan, Silverstein et al., 2016).

In addition to fear of recurrence, cancer-related fatigue is another stressor that is commonly experienced by breast cancer patients and survivors. Cancer-related fatigue is a chronic stressor that affects not only the QOL of breast cancer patients, but researchers have purported that it may have an underlying physiological cause (Bower et al., 2006). In a longitudinal study comprising 763 breast cancer survivors, Bower et al. (2006) reported that a similar proportion of participants at both time points (1 to 5 years post-diagnosis and 5 to 10 years post-diagnosis) were experiencing significant symptoms of fatigue (35% and 34%, respectively). They also observed that approximately 21% of their participants reported symptoms of severe fatigue at both time points (i.e., persistent fatigue; Bower et al., 2006). Furthermore, Bower et al. (2006) noted three factors that influenced the severity and persistence of fatigue: cardiovascular problems, presence of depressive symptoms, and type of cancer treatment. It was reported that breast cancer survivors had an increased risk of experiencing fatigue 5 to 10 years post-diagnosis, if they had high blood pressure or heart disease or if they were in a depressed mood prior to treatment (Bower et al., 2006). Although Bower et al. (2006) observed that women who underwent either chemotherapy or radiation alone showed a small improvement in fatigue 5 to 10 years after diagnosis (vs. women who had both treatments), mixed results have been reported in the literature (*cf.* Bardwell & Ancoli-Israel, 2008).

In later studies, it was suggested that persistent fatigue may also be associated with pre-existing psychological conditions such as depressive symptoms or physical conditions such as migraine and arthritis (Schmidt et al., 2015). Numerous researchers have suggested that this cluster of symptoms (pain, depression, and fatigue) is a result of an inflammatory reaction that triggers a disruption in the HPA axis and SNS and that the dysregulated systems promote further

inflammation (Cleeland et al., 2003; Dantzer et al., 2008; Miller, Ancoli-Israel, Bower, Capuron, & Irwin, 2008).

Dissertation Objectives and Hypotheses

As discussed, numerous health and behavioural factors are associated with irregular physiological stress responses and differences in one's psychological health. But the focus of this literature, particularly in the area of physiological stress, centers primarily on the experiences of White healthy participants. Therefore, the goal of this dissertation was to examine whether health status, ethnocultural membership, and/or cultural orientation influences physiological and psychological stress patterns. To achieve this goal, three studies were conducted with the intention to broaden our knowledge of the stress and breast cancer survivorship literature and to extend the research boundaries to be inclusive of cross-cultural comparisons.

The purpose of Study 1 (published; Wan, Couture-Lalande, Narain, Lebel, & Bielajew, 2016) was to complement an earlier study published by our group on the cortisol reactivity of breast cancer survivors (see Couture-Lalande et al., 2014). Study 1 examined the reactivity patterns of alpha-amylase in the same set of breast cancer survivors and healthy women as in the Couture-Lalande et al. (2014) study. Earlier we found that breast cancer survivors and healthy women exhibited differences in cortisol reactivity due to a dysregulation of the HPA axis in breast cancer survivors (Couture-Lalande et al., 2014). Based on these results, we reasoned that the SAM axis of breast cancer survivors may also be dysregulated, and consequently, display atypical alpha-amylase patterns. Despite the growing number of studies examining alpha-amylase as an index of stress in clinical and non-clinical populations (e.g., Bosch et al., 2011; Nater & Rohleder, 2009; Thoma et al., 2012; Wolf et al., 2008), to the best of our knowledge, this was the first empirical assessment of alpha-amylase as a stress biomarker among breast

cancer survivors at the time. To date, this area of research in the breast cancer population remains relatively new. In fact, a recent review of the literature revealed only one other study published during the last five years (see Sultan, Pati, Chaudhary & Parganiha, 2018)

Research on stress reactivity is largely based on healthy ethnocultural majority samples, and the role of cultural orientation and ethnocultural membership has been neglected. After establishing a general idea of the stress reactivity profiles of a sample of predominantly White breast cancer survivors, Study 2 investigated the diurnal and reactivity profiles of cortisol in a sample of Chinese and White women with and without a prior diagnosis of breast cancer. The goals of Study 2 (published; Wan et al., 2019) were (1) to determine whether the findings reported by Couture-Lalande et al. (2014) could be replicated in a new cohort of White breast cancer survivors; and (2) to evaluate whether ethnocultural membership and/or degree of cultural orientation impacted their physiological and psychological stress profiles. We expected differences in stress appraisals, regardless of health status, with accompanying differences in physiological stress when accounting for health status and cultural orientation. We anticipated breast cancer survivors (regardless of ethnocultural membership) to exhibit a blunted cortisol pattern in response to an acute stress, as already documented by Couture-Lalande et al. (2014). Further, we expected Chinese women, irrespective of health status, to exhibit different stress patterns from those of White women.

Finally, in Study 3 we examined the hair cortisol concentrations of Chinese and White women with and without a prior diagnosis (same participant pool as in Study 2). To our knowledge, Study 3 is the first study to examine chronic (via hair cortisol) physiological and psychological stress patterns among a cross-cultural sample of women with and without a previous diagnosis of breast cancer. Although numerous studies have shown that chronic stress

impacts the breast cancer survivorship trajectory (Arès et al., 2014; Cormanique et al., 2015; Lam & Fielding, 2003; Wan et al., 2018; Wan et al., 2017; Wong-Kim et al., 2005; Yusuf, Hadi, Mahamood, Ahmad, & Keng, 2013), minimal attention has been paid to physiological patterns of chronic stress and the implications of other psychosocial factors (e.g., cultural orientation). Therefore, the goal of Study 3 was to provide an overview of hair cortisol patterns between Chinese and White women with and without a diagnosis of breast cancer, and to determine whether cultural orientation and/or health status would predict their chronic stress levels. Regardless of health status, we expected Chinese women to exhibit higher hair cortisol concentrations in comparison to White women. We also predicted that breast cancer survivors (regardless of ethnocultural membership) would have higher levels of hair cortisol concentrations than that of healthy women. Finally, we expected Chinese women who were more culturally oriented to the dominant (Canadian) culture to experience lower levels of chronic stress (based on physiological and psychological indices).

Recruitment of participants for Study 2 and 3 was conducted in Toronto and Ottawa. For these studies, we recruited a sample of East Asian (Chinese) breast cancer survivors. We focused our recruitment efforts on Chinese breast cancer survivors for practical reasons. In the most recent 2016 census, it was reported that there were approximately 7.5 million immigrants in Canada (including people who have obtained Canadian citizenship by naturalization), and nearly half of them (48%) were from Asia (Statistics Canada, 2017a). In fact, it was reported that approximately 2.6 million immigrants lived in Toronto, accounting for 48% of Toronto's total population and rendering Toronto as the metropolitan city in Canada with the highest number immigrants (Statistics Canada, 2017a, 2017b). Ottawa-Gatineau was shown to have the fifth highest population of immigrants, home to 213,875 immigrants, which represented roughly 22%

of the region's total population. The Chinese community was also noted as one of the largest visible minority groups in both Toronto and Ottawa (Statistics Canada, 2017a, 2017b). Thus, coupled with an increasing incidence rate of breast cancer among Eastern Asians, it was deemed most practical to focus our research efforts on the breast cancer survivorship experience of Chinese women.

Study 1: Salivary Alpha-Amylase Reactivity in Breast Cancer Survivors

Wan, C., Couture-Lalande, M-È., Narain, T. A., Lebel, S., & Bielajew, C.

Study 1 was completed and published in a special issue on Stress Biomarkers in 2016 in the International Journal of Environmental Research and Public Health. Study 1 investigated the reactivity (both diurnal and acute profiles) of alpha-amylase in White women with and without a prior diagnosis of breast cancer. Analyses in this study were contrasted to an earlier study on the reactivity of cortisol in the same group of participants (see Couture-Lalande et al., 2014).

Author contributions: Wan performed the final statistical analyses and prepared the manuscript. Couture-Lalande and Narain coordinated the study, recruited participants, and performed preliminary statistical analyses. Couture-Lalande and Bielajew designed the study and consulted with Lebel throughout the process. Bielajew supervised the entire process and revised the manuscript.

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Salivary Alpha-Amylase Reactivity in Breast Cancer Survivors

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Abstract

The two main components of the stress system are the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal-medullary (SAM) axes. While cortisol has been commonly used as a biomarker of HPA functioning, much less attention has been paid to the role of the SAM in this context. Studies have shown that long-term breast cancer survivors display abnormal reactive cortisol patterns, suggesting a dysregulation of their HPA axis. To fully understand the integrity of the stress response in this population, this paper explored the diurnal and acute alpha-amylase profiles of 22 breast cancer survivors and 26 women with no history of cancer. Results revealed that breast cancer survivors displayed identical but elevated patterns of alpha-amylase concentrations in both diurnal and acute profiles relative to that of healthy women, $F(1, 39) = 17.95$, $p < 0.001$ and $F(1, 37) = 7.29$, $p = 0.010$, respectively. The average area under the curve for the diurnal and reactive profiles was 631.54 ± 66.94 SEM and 1238.78 ± 111.84 SEM, respectively. This is in sharp contrast to their cortisol results, which showed normal diurnal and blunted acute patterns. The complexity of the stress system necessitates further investigation to understand the synergistic relationship of the HPA and SAM axes.

Keywords: alpha-amylase; stress; breast cancer survivorship

Introduction

It has been estimated that one in nine women will develop breast cancer during her lifetime (Canadian Cancer Society, 2015). In 2013, breast cancer accounted for 14% of all cancer deaths in Canadian women and it has been estimated that 24,400 women will be diagnosed with breast cancer in 2014 (approximately 26% of cancer cases in women; Canadian Cancer Society, 2015). Now, due to improved screening and treatment procedures, the five-year survival rate of breast cancer in Canadian women has been steadily increasing and is now roughly 88%. Despite these positive numbers, the long-term emotional and physical stressors associated with being a cancer survivor can lead to serious health problems (Lundberg, 2005; McEwen, 1998a; Mehnert & Koch, 2007).

Stress is an influential factor in psychological and physical well-being. Breast cancer survivors, defined in this study as individuals with a diagnosis of breast cancer and currently in remission, may experience various stressors throughout the cancer trajectory. Stressors may be punctual—associated with the diagnosis, anxiety over the reactions of loved ones, or the treatment itself (Kedde et al., 2013; Knobf, 2011); or chronic—persisting following treatment, due to fear of death or recurrence, or concerns with managing lifestyle changes, returning to work, and coping with the minutiae of everyday life (Hauken et al., 2013; Tiedtke et al., 2010).

The two main components of the stress system, the hypothalamic-pituitary-adrenal (HPA) and sympathetic-adrenal-medullary (SAM) axes, operate in tandem to maintain homeostasis and prepare the organism to deal with environmental challenges (Thiel & Dretsch, 2011). One way to assess their functioning is via the examination of the secretion patterns of specific stress-related biomarkers. The focus of this paper is the enzyme alpha-amylase, a stress biomarker of the sympathetic nervous system (Nater & Rohleder, 2009; Strahler, Mueller, Rosenloecher,

Kirschbaum, & Rohleder, 2010), and one that has received much less attention than the omnipresent cortisol in research on stress physiology. Cortisol, a steroid hormone secreted in response to stress, has a long history as a stress endocrine marker (Couture-Lalande et al., 2014; McEwen, 2008; Stone et al., 2001). For that reason and comparison purposes, we first review background and data on cortisol.

Salivary cortisol as a stress biomarker. Cortisol, one of a class of glucocorticoid hormones, is associated with the HPA axis and is an essential steroid hormone for regulating bodily functions (Hellhammer et al., 2009). Cortisol is released from the adrenal glands through a cascade of events initiated by a stressful stimulus, which includes interaction with a host of anatomical structures related to the sympathetic nervous system (SNS). Studies have shown that it has a relatively stable diurnal pattern in healthy individuals (Foley & Kirschbaum, 2010; Stone et al., 2001), with its peak typically occurring within 30 min to 60 min after waking and thereafter steadily declining throughout the day (Foley & Kirschbaum, 2010). In the face of an acute stressor, cortisol secretion is briefly increased and usually returns to basal levels within one or two hours following stressor cessation (Armario et al., 2004).

It has been demonstrated that approximately 10% of the healthy population exhibits abnormal diurnal cortisol, also referred to as dysregulated cortisol patterns (Stone et al., 2001). Such patterns are characterized by a significantly blunted diurnal cortisol response in comparison to that of healthy individuals (Abercrombie et al., 2004; Porter et al., 2003; Spiegel et al., 2006). In clinical populations, metastatic breast cancer survivors (stage 4), in particular, are much more likely to show abnormal diurnal cortisol rhythms (Touitou et al., 1996).

Abercrombie et al. (2004) noted that breast cancer survivors with greater metastatic severity showed higher mean cortisol levels and flatter diurnal cortisol rhythms. Moreover, Sephton

et al. (2000) showed that a blunted diurnal cortisol response, which they speculated to be associated with more rapid cancer progression, predicted higher mortality rates for metastatic breast cancer survivors (Spiegel et al., 2006). In our laboratory, we have observed normal diurnal patterns in breast cancer survivors (mostly diagnosed with stage 2 or less), but a positive relationship between reactive salivary cortisol levels and time since diagnosis in breast cancer survivors; women diagnosed more than five years earlier show cortisol levels approaching that of control participants without a history of cancer (Couture-Lalande et al., 2014).

Salivary alpha-amylase as a stress biomarker. Recently, investigators have become interested in exploring biomarkers that reflect SNS activity as a way of understanding the synergistic relationship between the HPA and SAM systems as adaptive stress mechanisms. Alpha-amylase, a salivary enzyme that is modulated by the autonomic nervous system (ANS), controls various visceral functions, such as salivation. Studies exploring the involvement of the ANS in the secretion of alpha-amylase first began in the early 1970s. In a series of studies examining the parotid gland in rats (Batzri & Selinger, 1973; Batzri et al., 1973), Batzri's group (1973; 1973) noted that beta-adrenergic receptors were involved in the secretion of alpha-amylase. Subsequently, Anderson et al. (1984) and Asking (1985) evaluated the contributions of the parasympathetic and sympathetic branches of the ANS to alpha-amylase secretion in rats. They found that sympathetic stimulation of the parotid gland produced a low salivary flow rate with high concentrations of amylase, whereas the reverse was observed in response to parasympathetic stimulation (Anderson et al., 1984; Asking, 1985). Moreover, Asking (1985) found that the effects of combined sympathetic and parasympathetic stimulation produced a synergistic effect and attributed the cause of greater alpha-amylase concentrations to beta-1-adrenoceptors.

While animal studies provided evidence for ANS involvement in alpha-amylase production, Speirs et al. (1974) published one of the first studies to demonstrate the role of SNS in alpha-amylase production in humans and its connection to norepinephrine. In their study, participants were either immersed in cold water (4 °C to 5 °C) up to their waist or given isoprenaline (a beta-adrenergic agonist) or propranolol (a beta-adrenergic blocker) and found that the combined challenges increased alpha-amylase concentrations in the parotid gland while propranolol alone reduced it.

By the late 1970s, numerous researchers had begun to investigate the relationship between alpha-amylase and stress; the evidence generated since then suggests that alpha-amylase is a SNS biomarker and a reliable measure of both physical and psychological stress in humans (Bosch et al., 2011; Chatterton et al., 1996; Gilman et al., 1979; Granger et al., 2007; Nater & Rohleder, 2009). Like cortisol, alpha-amylase exhibits a relatively stable diurnal pattern albeit distinctly different from that of cortisol (Rohleder & Nater, 2009). Alpha-amylase concentrations are reduced significantly within 60 min after waking, followed by a gradual increase, with peak levels occurring in the late afternoon (Rohleder & Nater, 2009).

Alpha-amylase has been measured in response to a variety of acute stressors including writing a test (Bosch et al., 1998), skydiving (Chatterton et al., 1997), and playing video games (Skosnik et al., 2000). However, some studies have used a standardized psychosocial stress test such as the Trier Social Stress Test (TSST) to examine the reactivity of alpha-amylase and other biomarkers in response to psychologically induced stress.

The TSST is now considered the gold standard for inducing an acute stress response in the laboratory (Allen et al., 2014). Although there may be some variations in the TSST from study to study, it typically has two components—a mock job interview followed by an arithmetic

task (Kirschbaum et al., 1993). The TSST has been shown to be very effective in producing stress-related physiological responses, including a two to threefold increase in salivary cortisol levels in 70% to 80% of participants, with peak levels occurring around 10 min to 20 min after TSST cessation (Kudielka et al., 2007). Studies have reported significant alpha-amylase reactivity to the TSST in healthy children (Granger et al., 2007), youths (Gordis et al., 2008), and adults (Grillon et al., 2007).

The aim of the current study was to compare the circadian and reactive profiles of alpha-amylase in the same breast cancer survivors and in women with no history of breast cancer. Although researchers have begun examining alpha-amylase profiles in individuals with chronic illnesses (Rohleder & Nater, 2009), to our knowledge there is no study to date examining circadian and reactive profiles of alpha-amylase in breast cancer survivors. We reasoned that the stress associated with the breast cancer trajectory would be reflected by a dysregulation of the SNS, as indexed by salivary alpha amylase concentrations.

Method

Participants

A community sample of 22 female breast cancer survivors was recruited through printed advertisements and various cancer support groups. For complete participant demographics and medical characteristics, see Study 1 Tables 1 and 2.

Eligible participants were between the ages of 29 and 80 who understood English. Inclusion criteria for the breast cancer survivor group were as follows: A prior diagnosis of breast cancer (more than one year earlier) and completion of all local and/or systemic adjuvant therapy at least six months earlier. Individuals were ineligible if they had a previous history of other cancers (with the exception of non-invasive skin cancer and cervical cancer), substance

abuse, or any major disabling conditions that would interfere with their quality of life. Women who were breast feeding or pregnant were also excluded from the current study. All eligible participants received $50 to compensate for any travel costs incurred and were entered into a draw for one of four $250 prizes. The study received ethical approval from the University of Ottawa Research Ethics Board (file number 04-09-04). All participants gave their written informed consent prior to inclusion in the study.

Measures of stress

Salivary alpha-amylase. Commercially available kinetic reaction assay kits were used to assay saliva samples for alpha-amylase, using protocols designed by Salimetrics, State College, PA, USA (Salimetrics, 2015).

Trier Social Stress Test (TSST). The TSST (Kirschbaum et al., 1993) protocol we used consisted of two components—a mock job interview and an arithmetic task. Participants were given five minutes to prepare a five-minute free speech to a panel of three confederates acting as members of a hiring committee. This was followed by a five-minute arithmetic task that entailed the serial subtraction of 13 from 1022. In the event of an error, the participant was asked to start the task from the beginning. Committee members were instructed to provide no feedback to the participant.

Visual Analog Scale (VAS). A visual analog scale (VAS; Aitken, 1969) was used to measure subjective stress responses. It consisted of a 100 mm bipolar line on which participants were asked to estimate their stress level on a continuum from 0 equaling *not at all* to 100 equaling *very much* based on the statement “I feel stressed”. Scores were determined by measuring the distance from the left end to the appraisal mark.

Questionnaires. Participants completed a series of questionnaires designed to provide

socio-demographic information, and to assess their perception of stress. These included the Daily Stress Inventory (Brantley, Waggoner, Jones, & Rappaport, 1987), the Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983), and the Life Experiences Survey (Sarason et al., 1978). Each measures a different aspect of stress and its impact on the individual. The Perceived Stress Scale is a 14-item questionnaire that measures subjective appraisals of situations as stressful in the past month, the Daily Stress Inventory of 58-items inquires about recent (past 24 h) stressful events and their intensity, and the Life Experiences Survey is a 57-item self-report questionnaire that measures the frequency and impact of positive and negative events that occurred in the past year.

Finally we also assessed the breast cancer survivors' fear of recurrence using the Concerns About Recurrence Scale (Vickberg, 2003), a 30-item questionnaire. It evaluates five different domains related to fear of recurrence—worries pertaining to womanhood, role, health, death, and overall fear.

Procedure

Once participants were deemed eligible by telephone, they were scheduled at their convenience for two laboratory visits at the University of Ottawa. The first visit, approximately 30 min in length, served to obtain informed consent, and provide specific instructions on the correct method of collecting saliva samples at home. Afterwards, participants were given pre-labeled salivettes (synthetic swabs) to use at home at each time point—waking, 30 min after waking, 12:00 p.m., 4:00 p.m., and 9:00 p.m. They were instructed to rinse their mouths with water 10 min prior to collection (to avoid sample dilution), to place the salivette directly under their tongues for three minutes, and to store the salivettes in the refrigerator until delivery to the laboratory. Participants were also provided an insulated lunch bag with freezable ice packs to

keep the samples cool in the event that they did not have access to a refrigerator and/or during their commute to the laboratory. They were also asked to avoid smoking and alcohol consumption 24 h before sample collection and eating or drinking caffeinated products and exercising one hour prior to sample collection. As a test of compliance, they entered the collection time in a recording book. Saliva samples were collected for two consecutive days. A second laboratory visit was scheduled within seven days following the home-based saliva collection.

On the day of the visit, participants were asked to collect three saliva samples at home at waking, 30 min after waking, and at noon. The laboratory component lasted approximately two hours during which a total of seven saliva samples were collected; at each of the seven time points, participants were also asked to indicate their subjective stress level on the VAS. Study 1 Figure 1 is a schematic illustration of the procedure of the laboratory session.

The first saliva sample, labeled “arrival”, was retrieved upon arrival to the laboratory. The participant was then escorted to a testing room and introduced to a mock panel of committee members and in their presence, explained the task instructions. These were to prepare a five-minute speech about her suitability for a mock job position and deliver it to the panel. No aids, such as notes, were permitted during the speech delivery. The arithmetic task immediately followed the speech presentation. Saliva samples were collected after the speech preparation (labeled “anticipation”) and, upon completion of the arithmetic task (labeled “arithmetic”).

Afterwards, the participant was asked to relax in the room for one hour and to complete a series of questionnaires assessing perceived stress, feelings of anxiety, and fear of recurrence. During this phase, four additional saliva samples were collected at 10 min, 20 min, 40 min, and 60 min. The participant was then debriefed and explained the purpose of the TSST. All saliva

samples were transferred to Eppendorf tubes and stored in a freezer at −80 °C until assayed for alpha-amylase.

Results

Participant characteristics

Details of the participant demographics and characteristics were reported in Couture-Lalande et al. (2014). Briefly, 22 breast cancer survivors and 26 women without a prior diagnosis of breast cancer completed the study. Participants were not matched, but both groups had a similar age distribution (average in late 50s, t-test group difference $p = 0.488$), the number of women with postmenopausal status was similar (χ^2 group difference $p = 0.147$), and roughly 90% self-identified as White. See Study 1 Table 1 for details. Participants in the control group ranged from 29 years to 73 years of age, and participants in the breast cancer survivor group ranged from 39 years to 80 years of age (Study 1 Table 1).

To our knowledge, there were no serious or untreated medical conditions in participants in either group. There were, however, a few cases of hypertension, diabetes (one or two per group), and osteoarthritis (in breast cancer survivors only); please refer to Couture-Lalande et al. (2014) for more details. While studies suggest that the sympathetic nervous system may be implicated in the medical conditions mentioned, we chose to retain the participants' data in order to avoid further reducing our sample sizes.

Study 1 Table 2 provides the medical characteristics of the breast cancer survivors. The mean age at diagnosis was 54 ± 9 years (SD). On average participants were recruited about five years after diagnosis with the majority identified with stage 1 breast cancer. Most underwent surgical procedure for lumpectomy (approximately 45%). Two of the participants experienced a recurrence of breast cancer. Moreover, breast cancer survivors in the current study may have

experienced one or a combination of the following treatments: chemotherapy, radiation, hormone therapy, and/or surgery. Please refer to Couture-Lalande et al. (2014), for additional detail regarding the analysis of demographic and medical characteristics.

Data analysis

Missing values were imputed using the EM algorithm in SPSS V22 (IBM Corporation, Armonk, USA) for participants with up to two missing saliva samples of a total of 10 (usually due to inadequate saliva amounts) for their home-based saliva collection, and for participants with up to three missing samples out of the seven samples collected during the laboratory session. We imputed 4.6% of the diurnal and 5.7% of the TSST data related to alpha-amylase. For comparison to salivary cortisol, 3.8% and 5.7% were imputed for the same participants (Couture-Lalande et al., 2014).

A series of mixed-design Analysis of Variance (ANOVA) were conducted to assess the diurnal and acute reactive profiles of alpha-amylase. In the event that Mauchly's Test of Sphericity was significant, the Huynh–Feldt correction was applied, which adjusts the degrees of freedom (Tabachnick & Fidell, 2013).

Diurnal alpha-amylase

A 2 × 5 mixed-design Analysis of Variance (ANOVA) was used to assess differences in mean alpha-amylase concentrations over two consecutive days. The between-subject factor was *group* (breast cancer survivor or control) and the repeated factor was *time* (waking, 30 min after waking, 12:00 p.m., 4:00 p.m., and 9:00 p.m.).

Study 1 Figure 2 shows the plot of the diurnal data. The inset graph on the upper right side contains the cortisol data from the same subjects for comparison purposes (Couture-Lalande et al., 2014). The statistical results revealed a significant main effect of time ($F(3.39, 132.21) =$

14.32, $p < 0.001$, $\eta_p^2 = 0.269$) and group (F (1, 39) = 17.95, $p < 0.001$, $\eta_p^2 = 0.315$) and no significant interaction between the two factors ($p = 0.094$). Across all time points, Bonferroni corrected main comparisons revealed that the mean alpha-amylase level at 30 min after waking was significantly lower than that associated with all other time points (p ranged from <0.001 to 0.038). Moreover, mean sAA levels were significantly lower at waking or shortly afterwards compared to that at the end of the day at 9:00 p.m. ($p = 0.021$).

As shown in Study 1 Figure 2, although the group basal levels of alpha-amylase markedly different, the slopes of both patterns are similar; in contrast, the diurnal cortisol profiles that represent the two groups, shown in the inset graph, are virtually superimposable.

An additional analysis was performed to assess the relationship between time since diagnosis (in years) and diurnal alpha-amylase concentrations; no significant correlations were found at any of the five time points.

Alpha-amylase in response to acute stress

Study 1 Figure 3 depicts the salivary alpha-amylase profile in response to an acute stressor—the TSST. The inset graph shows the salivary cortisol data for the same subjects for comparison purposes (Couture-Lalande et al., 2014). A 2 × 7 mixed-design ANOVA was used to assess salivary alpha-amylase levels in this phase of the study. The between-group factor was *group* (breast cancer survivor or control participants) and the repeated factor was *time* (arrival, anticipation, arithmetic, and 10 min, 20 min, 40 min, and 60 min following the TSST).

The analysis revealed a significant main effect of time, F (4.75, 175.79) = 16.85, $p < 0.001$, $\eta_p^2 = 0.313$, and group, F (1, 37) = 7.29, $p = 0.010$, $\eta_p^2 = 0.165$, but no interaction ($p = 0.563$). Bonferroni corrected follow-up analysis revealed that sAA levels at Time 3 (“Arithmetic”) differed significantly from all other time points (p varied from <0.001 to 0.002). Furthermore,

alpha-amylase concentrations did not differ significantly between Time 1 (Arrival) and Time 7 (60 min following the TSST), suggesting that all participants returned to baseline within one hour following the TSST ($p = 1.00$).

Similar to their sAA diurnal profile, breast cancer survivors had a higher basal level of alpha-amylase in comparison to the control group and a parallel time course, despite the difference in concentrations. This pattern contrasts with their acute cortisol patterns, shown in the inset graph of Study 1 Figure 3; these were markedly different between the two groups with breast cancer survivors exhibiting a blunted cortisol response relative to that of the control group (Couture-Lalande et al., 2014).

We also examined the correlation between time since diagnosis (in years) with alpha-amylase concentrations at all seven time points to assess whether sAA responses to an acute stressor were associated with the passage of time since diagnosis and found no significant relationships.

Area under the curve: Alpha-amylase

Finally, we determined the area under the curve (auc) using trapezoidal integration for mean diurnal and reactive sAA levels in both groups. The auc for both groups was calculated with respect to the ground. The average auc for the diurnal and reactive sAA levels for breast cancer survivors was 631.54 ± 66.94 SEM and 1238.78 ± 111.84 SEM respectively. For diurnal and reactive sAA profiles in control participants, the values were 306.42 ± 39.23 SEM and 813.67 ± 107.02 SEM respectively. T-test results revealed significant group differences in both the diurnal t (29.5) = −4.19, $p < 0.001$, $d = 1.356$, and reactive stress profiles t (37) = −2.74, $p = 0.009$, $d = 0.88$, due to consistently higher values in breast cancer survivors *versus* those of the control participants. Note that the group difference, averaged across all time points, was similar

overall for both diurnal (36%) and reactive patterns (34%).

Subjective measures in relation to alpha-amylase

Results regarding subjective levels of stress were reported in a previously published study based on the same subjects; please see Couture-Lalande et al. (2014) for an in-depth discussion of these analyses and results. Briefly, to document subjective levels of stress during the different phases of the TSST, participants were asked to indicate their overall stress at each time point, based on a visual analog scale. A mixed-design ANOVA was used to analyze these subjective responses; we found a significant main effect of time, $p < 0.001$, due to increased subjective stress during the anticipation, arithmetic, and 20 min time points, but there were no group or interaction effects. Indeed, the group patterns were virtually identical.

We also correlated each group's scores from the three stress scales (Perceived Stress Scale, Daily Stress Inventory, and Life Experiences Survey; (Brantley et al., 1987; Cohen et al., 1983; Sarason et al., 1978) with their average auc (area under the curve) for diurnal and reactive sAA levels and found no significant relationship.

Finally, for breast cancer survivors, we correlated their scores from the Concerns About Recurrence Scale (CARS; Vickberg, 2003) with their average auc for diurnal and reactive sAA levels. Analyses revealed weak correlations between the various domains and average auc for diurnal and reactive sAA levels; diurnal data (r values ranged from 0.024 to 0.324 and p values ranged from 0.238 to 0.931); reactive data (r values ranged from 0.100 to 0.255 and p values ranged from 0.360 to 0.724).

Discussion

In a previous paper, we explored the diurnal and reactive patterns of cortisol in breast cancer survivors and women without a diagnosis of breast cancer (Couture-Lalande et al., 2014).

Those data revealed almost identical group diurnal cortisol profiles and subjective appraisals of stress, but their cortisol levels in response to an acute stressor were considerably different. Breast cancer survivors exhibited a blunted cortisol response that showed some degree of normalization, that is, reactive cortisol patterns that approached that of the control group as a function of time since diagnosis (Couture-Lalande et al., 2014).

The goal of the current study was to complement the cortisol findings by exploring diurnal stress and reactivity profiles based on sAA concentrations in the same participants. The breast cancer survivors varied from one to 11 years since diagnosis ($M = 4.6 \pm 3$ years), but we did not find a correlation between "time since diagnosis" and cortisol or alpha-amylase concentrations at any of the collected time points. We reasoned that the apparent HPA dysregulation to an acute stressor in breast cancer survivors, as interpreted from cortisol patterns, would be accompanied by SNS impairments. To better understand the synergistic relationship between the HPA axis and SNS, it was therefore important to explore the diurnal and acute sAA profiles in the same individuals.

Based on our current sample, we found significant time and group differences in the diurnal and reactive alpha-amylase profiles of women with and without a prior diagnosis of cancer. These patterns are consistent with the literature, corroborating the findings of Nater et al. (2005; 2007). sAA concentrations decreased significantly immediately after waking, followed by a steady increase (see Study 1 Figure 2). The reactive sAA patterns peaked at the arithmetic collection phase (see Study 1 Figure 3). While both diurnal and reactive sAA patterns were elevated in breast cancer survivors, compared to that of women with no history of cancer, they increased to the same degree—36% increase in diurnal and 34% increase in reactive profiles. Thus the sAA difference in acute stress responses reflected a heightened basal level and was not

related to a specific acute stress response. This is in contrast to cortisol group patterns, which showed a blunted response to the acute stressor in breast cancer survivors but otherwise diurnal rhythms identical to control participants.

Taken together, our data suggest that the experience of breast cancer is associated with dysregulated HPA and SAM functioning, possibly due to the various stressors that accompany a breast cancer diagnosis and its aftermath. The long-term state of chronic stress may have led to an allostatic overload (McEwen, 1998a; McEwen, 2008). *Allostasis* refers to the body's active process of responding and adapting to external adverse events, in order to maintain homeostasis (Sterling & Eyer, 1988). However, in the process of constant adaptation, problems such as allostatic overload may occur, which refers to the consequential biological wear and tear due to chronic stress. An allostatic overload may result in either an inadequate or overactive response or of the failure to adapt to repeated exposure to the same type of stressor (McEwen, 1998b; McEwen, 2008).

To assess stress in the short and long term, we administered questionnaires that assessed levels of perceived stress in the past day, month, and over the last year, and found no significant relationship. For breast cancer survivors, we also added a questionnaire assessing their extent of fear of recurrence, a common chronic stressor experienced by most, if not all, cancer survivors, and likewise, found no association between particular worries and overall alpha-amylase values. While chronic stress may negatively impact the sympathetic nervous system, the levels observed in our sample did not appear to have any particular relationship to participants' stress-related biomarker values.

Chronic stress has previously been documented to produce atypical cortisol levels (e.g., (Couture-Lalande et al., 2014; Miller, Chen, & Zhou, 2007). In a study investigating the

functioning of HPA and SAM in response to repeated stress, Schommer et al. (2003) exposed healthy participants to the TSST three times and found a mean decrease of 37% to 46% from TSST 1 to TSST 3 in HPA responses, whereas SNS responses remained unchanged. They concluded that the two systems respond to repeated psychosocial stress differently, and the HPA system, in particular, appears to habituate more quickly. They also noted that participants exhibited increased basal epinephrine levels at the third TSST, possibly due to the anticipation of stress.

Anticipation is an important aspect of allostasis (McEwen, 1998a). Anticipation in this context refers to the psychological state of worry, anxiety, and cognitive preparation for an event (McEwen, 1998a). By that definition, breast cancer survivors are in a constant state of anticipation. While the diagnosis and treatment of breast cancer is a stressful experience, anxiety, fears, and worries persist years after remission (Lebel et al., 2007; Lebel, Rosberger, Edgar, & Devins, 2008; Wan, Silverstein et al., 2016). This state of chronic anxiety and stress may contribute to dysregulated HPA and SAM stress systems, but manifested differently in each case depending on its allostatic mechanism. Since breast cancer survivors are often distressed and anticipate adversity in the form of a recurrence or other cancer, it is plausible that this aspect disrupts stress-related SNS functioning by increasing alpha-amylase basal levels, representing an overactive response to adverse external events. In contrast, the HPA system via cortisol may signify an underactive response to chronic stress.

Associated with the notion of the accumulation of biological wear and tear is “age”, a determinant of alpha-amylase reactivity that has been shown to be associated with different sAA basal levels. It has been documented that basal levels of alpha-amylase reach that of adults’ values within the first three years and are then relatively stable across the life span (Rohleder &

Nater, 2009). However, some researchers suggest otherwise and have attributed attenuated sympathetic responses due to a chronic accumulation of sympathetic activation—the older the individual, the greater the SNS activation (Seals & Dinenno, 2004; Strahler, Berndt, Kirschbaum, & Rohleder, 2010; Strahler, Mueller et al., 2010).

In a recent study investigating age differences in alpha-amylase reactivity, Almela et al. (2011) had older adults (ages 54 to 71) and younger adults (ages 18 to 35) perform the TSST task or a control condition. In the latter, participants read aloud for five minutes followed by five minutes of counting. Almela et al. (2011) did not find any group differences in sAA reactivity, but reported that overall sAA levels were higher in older adults. Moreover, they reported that in the stress condition, the total amount of cortisol secretion was positively related to the total amount of sAA secretion and heart rate increase was positively related to sAA increase. On that basis, they suggested that rather than an attenuated autonomic nervous system, a "heightened sympathetic tone" was a better explanation.

While it is possible that chronic stress and its consequent cumulative sympathetic activation with age may eventually lead to dysregulated stress systems in healthy individuals, chronic illnesses, such as a breast cancer diagnosis, may pose additional stress and exacerbate the effects. But these conclusions must be interpreted with caution; alpha-amylase has only recently been purported to be a surrogate SNS stress biomarker, and our understanding of its role in stress response and regulation is still expanding.

Only a scarce number of studies have explored diurnal sAA rhythms in sufferers of somatic or psychiatric diseases, or physical ailments, such as periodontitis (Rohleder & Nater, 2009), asthma (Wolf et al., 2008), and posttraumatic stress disorder (Thoma et al., 2012). Several researchers have found lower sAA levels in pediatric patients suffering from a variety of chronic

illnesses such as asthma and juvenile arthritis (Rohleder & Nater, 2009), but generally elevated sAA levels in different adult samples. For example, higher sAA concentrations were observed in adult patients with obstructive pulmonary disease, whereas lower sAA levels were found in adult patients who self-identified as habitual smokers (Yigla, Berkovich, & Nagler, 2007). Higher sAA levels were also recorded in individuals suffering from Parkinson's disease (Tumilasci et al., 2006) and type-2 diabetes (Aydin, 2007).

Thoma et al. (2012) recently published a study exploring the relationship between posttraumatic stress disorder and diurnal sAA patterns, and reported that the awakening response, in particular, was altered in comparison to that of healthy control participants. They found that sAA levels of patients suffering from posttraumatic stress disorder increased after waking, whereas sAA levels associated with the control group showed a sharp decrease in sAA levels after waking. Although limited, these findings point to the importance of evaluating other factors that appear to influence sAA profiles such as type of illness and age, and the individual's role—for example, patient *versus* caregiver (Rohleder, Marin, Ma, & Miller, 2009).

Briefly, Rohleder et al. (2009) assessed the inflammatory and neurohormonal processes in caregivers over a one-year period. They noted that half the caregivers in the study showed a substantial linear increase in systemic inflammation, which if prolonged, may lead to low-grade chronic inflammation. Their endocrine results indicated that over time, caregivers' diurnal secretion of sAA declined—that is, displaying a flattening of slope. However, their diurnal cortisol patterns were not affected.

Research concerning alpha-amylase's role in stress reactivity in cancer patients and caregivers is still in its infancy. The complexity of the stress system and its interaction with chronic illness required further investigation to understand the synergistic relationship of the

HPA and SAM axes in this context.

Limitations and Future Directions

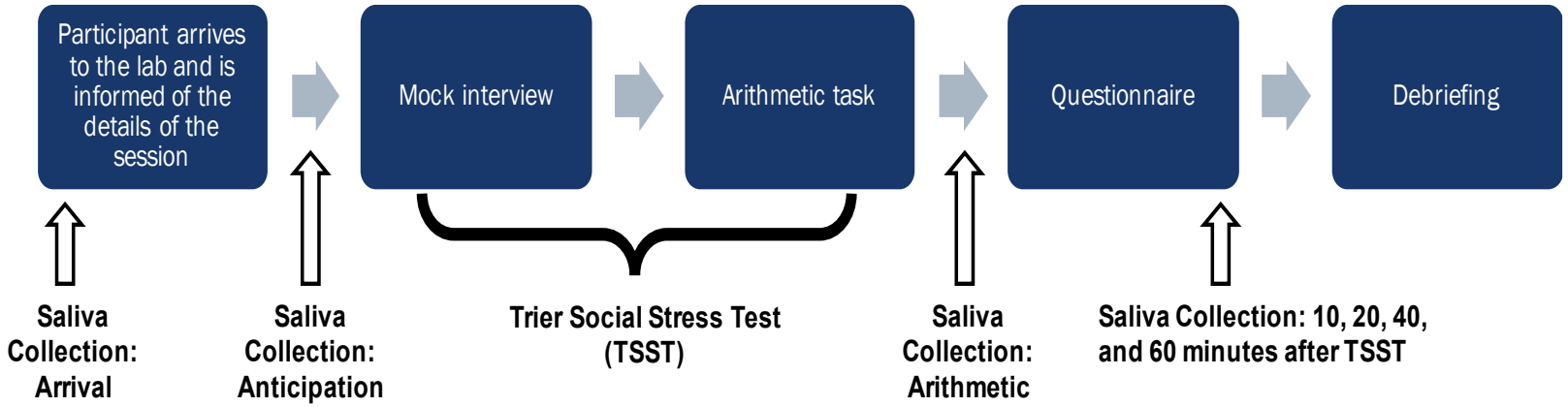
The current study relied on convenience sampling and thus, may not be representative of all breast cancer survivors. Although the sample size is relatively small, it rivals the very few studies that have assessed sAA levels in breast cancer survivors—from about 20 per treatment group in an exploratory study (Lipschitz, Kuhn, Kinney, Donaldson, & Nakamura, 2013) to over 100 in cross-sectional studies of breast cancer survivors (Ariza-García et al., 2013).

Alpha-amylase levels can be affected by behavioural and life-style factors such as smoking, drinking, and physical exercise. Hormonal fluctuations due to menstrual cycle, the use of hormonal contraceptives, or hormonal replacement therapy also may impact alpha-amylase concentrations. In addition, the type of treatment received, such as chemotherapy and/or, radiation, certain chronic health conditions such as hypertension and diabetes, may be critical factors. Although we accounted for smoking and drinking habits in the study, we did not control for exercise habits or the use of hormonal contraception or hormonal replacement therapy. Future studies should investigate the influence of particular treatments and strive to include participants without other chronic pre-existing medical conditions. Our sample size was insufficient to perform a sub-group analysis based on treatment and menstrual status, but accounting for the nuances caused by hormonal fluctuations will be an important aspect to investigate.

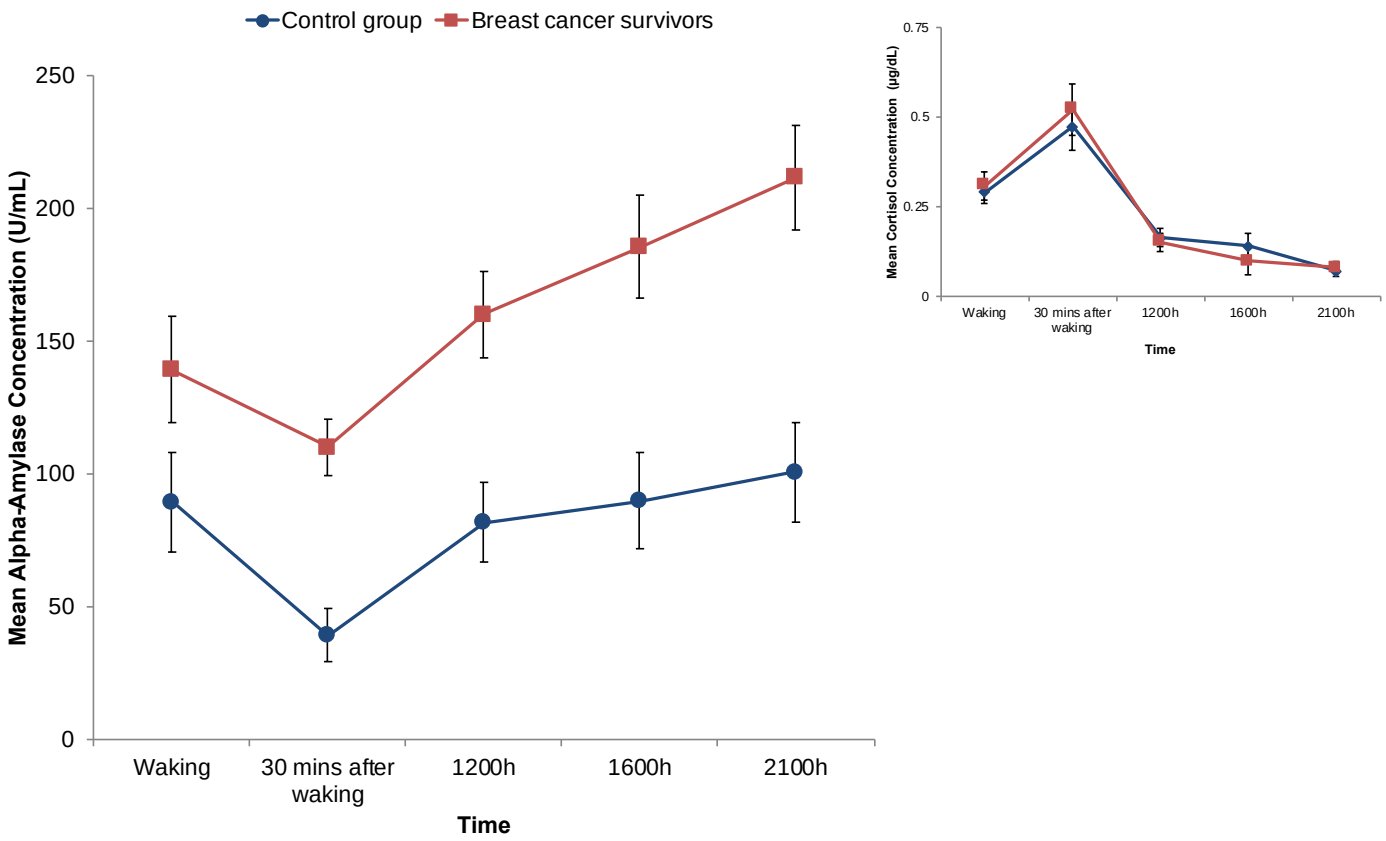
Finally, the stress measures used in the current study evaluated primarily acute or short-term stress (within the last month, for example). The Life Experiences Survey only addressed the frequency and impact of perceived major stressful events that occurred in the past year; most participants did not indicate having such experiences. It would be important to explore in this context the influences of experiences over the lifetime and not limited to a particular time frame.

Conclusions

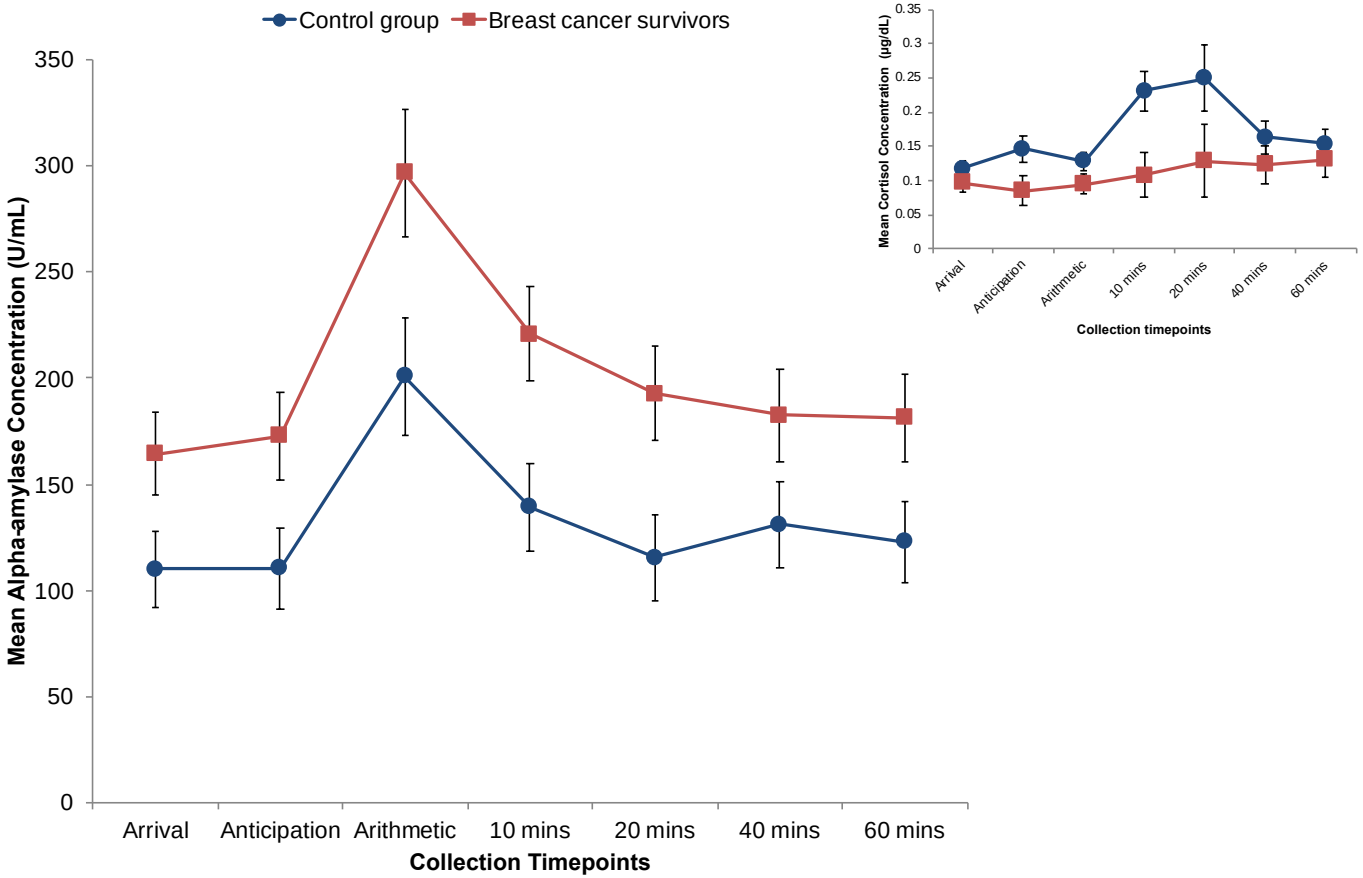
In the current study, we did not find atypical sAA profiles in breast cancer survivors. Rather, we found that breast cancer survivors exhibited elevated basal sAA levels, but the patterns paralleled the alpha-amylase reactivity of healthy women. The patterns were not related to the occurrence of stressful events in either group. More research is needed to determine the factors that influence the relationship between disease and stress biomarker patterns. Other routes could include the moderating effects of coping and social seeking behavior, fear of recurrence, and lifestyle habits. The relationship between HPA and SAM axes in maintaining homeostasis and managing stress is an important area of investigation, in order to understand their synergistic mechanisms and the consequences of their functioning in chronic disease.



Study 1 Figure 1. Schematic representation of the laboratory session procedure.



Study 1 Figure 2. Mean diurnal alpha-amylase concentrations (U/mL) over two consecutive days. Inset graph includes published diurnal cortisol responses (ug/dL) for the same sample (Couture-Lalande et al., 2014). Error bars represent standard error of the mean.



Study 1 Figure 3. Mean acute alpha-amylase concentrations (U/mL). Inset graph includes published acute cortisol concentrations (ug/dL) for the same sample (Couture-Lalande et al., 2014). Error bars represent standard error of the mean.

Study 1 Table 1. Demographic characteristics of participants.

Demographic Characteristics	**Breast Cancer Survivors (*N* = 22)**	**Control Group (*N* = 26)**
Age (years) mean ± SD	58.9 ± 10.1	57.4 ± 11
	No. of Participants (%)	**No. of Participants (%)**
Ethnicity		
White	20 (90.9)	23 (88.5)
Black		1 (3.8)
Asian		2 (7.7)
First Nations	2 (9.1)	
Highest level of education		
High School	6 (27.3)	9 (34.6)
College	4 (18.2)	4 (15.4)
Bachelor's degree	11 (50)	7 (26.9)
Master's degree	1 (4.5)	5 (19.2)
Doctoral degree		1 (3.8)
Family income (CDN) *		
Under $40,000	3 (15)	5 (20.8)
$40,000 to $79,999	10 (50)	10 (41.7)
$80,000 to $ 119,999	5 (25)	5 (20.8)
$120,000 and over	2 (10)	4 (16.7)

*Breast cancer survivor group (*N* = 20); Control group (*N* = 24)

Study 1 Table 2. Medical characteristics of breast cancer survivors.

Medical Characteristics	Breast Cancer Survivors (*N* = 22)
Mean age of diagnosis ± SD (years)	54.1 ± 8.7
Mean time (years) since diagnosis ± SD (years)	4.6 ± 3
	No. of Participants (%)
Breast cancer stage	
0	4 (18.2)
1	10 (45.5)
2	5 (22.7)
3	2 (13.6)
Type of surgery	
Unilateral mastectomy	6 (27.3)
Bilateral mastectomy	7 (31.8)
Lumpectomy	9 (40.9)
Treatment *	
Chemotherapy	10 (45.5)
Hormone therapy	14 (63.6)
Radiation therapy	14 (63.6)
Breast cancer recurrence	
None	20 (83.3)
One recurrence	1 (4.2)
Two recurrences	1 (4.2)

*Almost all participants received a combination of treatments.

Study 2: A Cross-Cultural Analysis of Salivary Cortisol Patterns in Breast Cancer Survivors

Wan, C., Boileau, K., D'Amico, D., Huang, V., Fiocco, A. J., Clément, R., & Bielajew, C

The aim of Study 2 was to replicate previous findings (see Couture-Lalande et al., 2014) and to extend the current literature by comparing the cortisol and psychological stress profiles of breast cancer survivors of different ethnocultural memberships. The methodology and procedure for Study 2 is very similar to Study 1, but minor changes were made to accommodate this particular research question and sample. Study 2 has been published by the journal of Breast Cancer Management in 2019.

Author contributions: Wan and Bielajew designed the study. Wan performed the final analyses and drafted the manuscript. Boileau assisted in the data collection process and preliminary data analysis. D'Amico, Huang, and Fiocco assisted in recruitment and data collection. Clément provided support and consultation throughout the process. Bielajew supervised the entire process and revised the manuscript.

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A Cross-Cultural Analysis of Salivary Cortisol Patterns in Breast Cancer

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Abstract

Aims: In this study, we examined whether Chinese and White women with and without a history of breast cancer exhibit differences in physiological and psychological stress profiles.

Methods: Diurnal and reactive salivary cortisol profiles and psychological stress patterns of 41 breast cancer survivors and 58 healthy women were assessed.

Results: Breast cancer survivors displayed a blunted acute cortisol response, but there was no main effect of ethnocultural membership. Subjective appraisals of stress during the acute stressor revealed a significant interaction between ethnocultural group, health status, and time ($p = .032$).

Conclusion: Our results support the existing literature but suggest group differences in the appraisal of stress; thus, underscoring the importance of cultural sensitivity and awareness among clinicians and existing programs.

Keywords: salivary cortisol; diurnal cortisol; acute cortisol; reactivity; physiological stress; psychological stress; breast cancer survivorship; cultural orientation

Introduction

Breast cancer is increasingly diagnosed in Asian American women (Deapen et al., 2002). Researchers have suggested several factors that account for this, such as shifts in risk factor profiles (Minami et al., 2004), westernized lifestyles (Chia et al., 2005), and acculturative stress (Silva et al., 2017). To better understand the breast cancer survivorship experience in Asian women, more and more studies are investigating the physiological and psychological effects of breast cancer in this group as a means of understanding ethnocultural differences in survivorship trajectory (Wan et al., 2017, 2018; Wan, Couture-Lalande et al., 2016; Wan, Silverstein et al., 2016; Wen, Fang, & Ma, 2014).

Stress and Health

Stress is a universal experience, the product of an interaction between an individual and the environment, namely the individual's appraisal of the environment and coping capabilities (Lazarus & Folkman, 1987). Thus, stress can be viewed as positive, negative, or neutral and beneficial towards promoting one's survival (Nesse, Bhatnagar, & Ellis, 2016). In response to a stressor, the hypothalamic-pituitary-adrenal (HPA) axis is activated to prepare the organism to deal with environmental challenges (Thiel & Dretsch, 2011), which initiates the production of glucocorticoids, such as cortisol. Cortisol is a hormone that regulates bodily functions, such as homeostasis and immune response (Fulford & Harbuz, 2005), and is commonly measured via plasma, serum, urine, or saliva (Hellhammer et al., 2009).

Cortisol has a relatively stable diurnal pattern in healthy individuals (Foley & Kirschbaum, 2010; Stone et al., 2001). It reaches its peak approximately 30 to 60 minutes after waking, thereafter steadily declining throughout the day (Foley & Kirschbaum, 2010). Cortisol secretion and basal levels can be affected by numerous factors, such as hormonal status (Huang,

Zhou, Wu, Wang, & Zhao, 2015), age and sex (Kudielka et al., 2009), circadian rhythm (Buckley & Schatzberg, 2015), and illnesses such as cancer (Lundstrom & Furst, 2003).

While there are many studies assessing cortisol profiles of women with breast cancer during treatment (e.g., Dedert et al., 2012; Ho, Fong, Chan, & Chan, 2013), very few have focused on post-treatment biomarker patterns (Alexander, Minton, Andrews, & Stone, 2009; Couture-Lalande, et al., 2014; Wan et al., 2017). Based on the limited findings, most studies report no significant differences in diurnal cortisol patterns between breast cancer survivors and healthy women (Alexander et al., 2009; Couture-Lalande et al., 2014). However, in metastatic breast cancer survivors, a flattened profile and/or differences in peaks and troughs in the diurnal rhythm (see Touitou et al., 1996; Touitou et al., 1995) have been observed.

In contrast, cortisol patterns are markedly different in acute stress situations compared to that of daily patterns. In response to an acute stressor, cortisol secretion typically increases and returns to basal levels within one to two hours after cessation (Kirschbaum et al., 1993); however, breast cancer survivors exhibit a blunted cortisol response to an acute stressor, which has been interpreted as a consequence of chronic inflammation and chronic stress – the continuous and prolonged activation of the HPA axis — resulting in a hyporeactive HPA axis (Couture-Lalande et al., 2014; Miller et al., 2007).

Acculturative Stress and Cortisol Rhythms

Acculturative stress is defined as a stress response to various acculturation-related stressors (e.g., learning a new language, set of values, or behaviours) and life events (Berry, 2006a; Silva et al., 2017) and may be experienced by first-, second- and third generation immigrants (Phinney, Ong, & Madden, 2000; Stroink & Lalonde, 2009).

Many studies acknowledge the impact that acculturative stress has on an individual's psychological and physiological health (Choi, 1997; Fang et al., 2014; Logan et al., 2012). For instance, Choi (1997) noted that high levels of acculturative stress were associated with depressive symptomology among Korean Americans. Furthermore, Logan et al. (2012) found that acculturative stress was related to arterial stiffness, demonstrating a marginally significant relationship between acculturative stress and diastolic blood pressure.

Based on existing stress literature, which predominantly examines the stress responses of White breast cancer survivors, it is often assumed that breast cancer in Chinese women also leads to a dysregulated HPA axis. Thus, the focus of studies is often on the efficacy of various interventions on the stress system and/or their qualitative survivorship experience. Recently, Ho et al. (2013) noted that Chinese breast cancer survivors exhibited a flatter diurnal cortisol slope. Further, they observed an association between the slope of the diurnal cortisol rhythm with higher negative social support and poorer perceived health. Despite these findings, to our knowledge, there are no empirical studies investigating the differences in HPA axis reactivity between Chinese and White women with and without a prior breast cancer diagnosis, whilst considering the effects of various psychosocial variables, such as cultural orientation.

To address the gaps in the literature, our study investigated whether ethnocultural membership and health status influences one's physiological and psychological stress patterns. To do so, we examined differences in diurnal and acute cortisol patterns, as well as psychological patterns of stress between Chinese and White women with and without a prior diagnosis of breast cancer. Following a similar study design as the one in Couture-Lalande et al. (2014), we expected to see a replication of results: Breast cancer survivors, irrespective of ethnocultural group membership, would exhibit a blunted acute cortisol response and display

diurnal patterns of cortisol reactivity comparable to that of healthy control participants. With the added complexity of acculturative stress, we further hypothesized that the dysregulation in acute stress response in Chinese breast cancer survivors would be more pronounced than that of White breast cancer survivors.

Methods

Participants

Chinese and White women with and without a prior diagnosis of breast cancer were recruited from Ottawa and Toronto via online classifieds (e.g., Kijiji, comefromchina.com) and through various community and cancer support groups (e.g., Babes4Breast, Breast Cancer Action Ottawa, Ottawa Regional Cancer Foundation). A total of 69 healthy women (31 Chinese, 38 White) and 50 breast cancer survivors (20 Chinese, 30 White) were recruited for the study. Due to missing data, our analyses included a final sample of 58 healthy women (27 Chinese, 31 White) and 41 breast cancer survivors (17 Chinese, 24 White). Sample sizes were based on prior power analyses of similar studies conducted in the laboratory (e.g., Couture-Lalande et al., 2014; Wan, Couture-Lalande et al., 2016), which revealed that a sample size of between 22 and 25 was sufficient to detect significant group differences in stress profiles.

Individuals were included in the study if they met the following eligibility criteria: (1) A woman of Chinese or White descent; (2) between the ages of 30 and 80; (3) currently residing in either Ottawa or Toronto, Ontario; and (4) able to read and understand English. In addition to these criteria, to be eligible for the breast cancer survivor group, individuals must also (5) have had a prior diagnosis of breast cancer; (6) have completed all systemic treatment at least six months prior to the study start date (hormonal treatment excepted); and (7) be currently considered cancer free. Individuals were excluded if they (1) had a previous diagnosis of other

cancers (non-invasive skin cancer and cervical cancer excepted); (2) have or have had a debilitating psychiatric or medical illness (other than breast cancer); and (3) were pregnant at the time of the study. Participants were compensated $50 for their involvement in the study.

Measures

Sociodemographic Questionnaire (SDQ). We developed the SDQ for other studies in our laboratory (e.g., Couture-Lalande et al., 2014; Wan, Couture-Lalande et al., 2016; Wan, Silverstein et al., 2016; Wan et al., 2017, 2018) it includes questions relating to age, marital status, education, and income. We added questions regarding participants' place of birth, their age of immigration (if applicable), and number of years spent in Canada. The SDQ also has items pertaining to medical characteristics and habits known to influence cortisol concentrations (e.g., smoking, teeth brushing). Breast cancer survivors were asked to complete additional items related to their breast cancer history (e.g., age of diagnosis, stage, treatment).

General Ethnicity Questionnaire – Abridged (GEQ). The GEQ (Tsai et al., 2000) is a 77-item questionnaire that measures cultural orientation, that is, the degree to which an individual identifies with a dominant and non-dominant culture by assessing the extent to which they participate in the activities, traditions, and lifestyle of the two cultures. Questions pertaining to orientation towards Canadian (GEQCA, dominant culture) and Chinese (GEQCH, non-dominant culture) cultures were identical in wording with the exception of the culture being referenced. The scale measures six domains of acculturation: language use and proficiency, social affiliation, cultural participation, cultural pride, cultural exposure, and preference for cultural food and media. Participants rated the items on a 5-point Likert-type scale, ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). Higher scores reflect higher orientation towards that particular culture. Tsai et al. (2000) assessed cultural orientation towards Chinese (GEQCH) and

American (GEQA) cultures, and they reported that the GEQ had high internal reliability (α = .92 for both scales). Test-retest reliability was .62 (*SD* = .22; GEQCH) and .57 (*SD* = .16; GEQA). In the present study, the GEQ demonstrated high internal reliability for all groups (α = .88 to .93, GEQCA; and .86 to .93, GEQCH).

Bidimensional Fatigue Scale (BFS). The BFS (Chalder et al., 1993) is a 14-item questionnaire that assesses the degree of physical and mental fatigue experienced within the past two weeks. Participants rate items such as "[d]o you feel sleepy or drowsy?" on a 4-point scale ranging from 1 (*better than usual*) to 4 (*much worse than usual*). Scores are summed, with higher scores indicating higher severity of fatigue. The BFS demonstrates high internal reliability and reasonable discriminant validity. We used the revised 11-item version, which was shown to have a Cronbach's alpha of 0.89 (Chalder et al., 1993), high sensitivity (92%), and negative predictive value (94%) towards detecting severely high fatigue among cancer patients (i.e., scores of 11 or above; Alexander, Minton, & Stone, 2009). The reliability of the BFS for the current sample ranged from .85 to .92.

Concerns About Recurrence Scale (CARS). Breast cancer survivors completed CARS (Vickberg, 2003), which measures one's fear of disease recurrence. CARS is a 30-item inventory divided into five types of worries related to a potential cancer recurrence: (1) Death worries; (2) Health worries; (3) Role worries; (4) Womanhood worries; and (5) Overall Fear of Recurrence. With the exception of the four items assessing Overall Fear of Recurrence (on a scale of 1 to 6), participants rated the remaining 26 items on a scale of 1 (*not at all*) to 4 (*extremely*). Higher scores indicate more concerns and fears. The four subscales and overall fear index are reported to have high internal consistency (α = .87 to .94). For the present study, CARS was shown to be

highly reliable (α = .95 for Chinese breast cancer survivors and .96 for White breast cancer survivors).

Perceived Stress Scale (PSS). The PSS (Cohen et al., 1983) is a 14-item questionnaire that measures stress-related frequency occurrence over the past month (e.g., "[i]n the last month, how often have you been upset because of something that happened unexpectedly?"). Participants rated each item on a scale ranging from 0 (*never*) to 4 (*very often*). Scores are summed, with higher scores indicating a higher degree of stress experienced during the past month. The reliability of the PSS ranges between α = .84 to .86. For the current sample, Cronbach's alpha ranged from .77 to .84, depending on group.

Daily Stress Inventory (DSI). The DSI (Brantley et al., 1987) is a 58-item inventory that describes events that participants may have experienced within the past 24 hours. If relevant, they are asked to rate the degree of stress they experienced on a scale ranging from 1 (*Occurred but was not stressful*) to 7 (*caused to panic*). The Average Impact Rating scores (AIR; sum of total impact scores divided by number of events) were used for our analyses. Brantley et al. (1987) reported that the DSI has a Cronbach's alpha above .80, and AIR scores demonstrated adequate concurrent validity with a global rating of stress (r = .49, p < .01). For the current sample, the DSI had a Cronbach's alpha ranging from .85 to .98.

Visual Analog Scale (VAS). The VAS is a 100mm bipolar line that can be used to measure the intensity of any given characteristic on a continuum ranging from 0 to 100. Participants indicated their level of subjective feelings of stress (Aitken, 1969) through the statement "I feel stressed". Scores were determined by measuring the distance from 0 (*not at all*) to the appraisal mark, up to 100 (*very much*).

Trier Social Stress Test (TSST). The TSST is a commonly used procedure to induce moderate psychological stress in a laboratory setting (Kirschbaum et al., 1993). The TSST consists of two tasks: (1) A 5-minute mock job interview in front of a panel of three confederates, which in our case included at least one male and one female and at least one White and one Chinese individual; and (2) a 5-minute arithmetic task that required participants to count backwards sequentially by 13 from 1022. Throughout the TSST, confederates were instructed to remain neutral and to provide no verbal or nonverbal feedback to the participant.

Salivary cortisol. To measure diurnal and acute cortisol reactivity, a total of 17 saliva samples were collected from participants. Participants were instructed to collect 10 samples at home over two consecutive days to serve as a diurnal assessment. Seven additional saliva samples were collected during the laboratory session to measure acute cortisol reactivity. Saliva samples were aliquoted into Eppendorf tubes and stored in a freezer at -80ºC until processed. Saliva samples were assayed for cortisol using enzyme-linked immunosorbent assay (ELISA) kits following a protocol developed by Salimetrics, State College, PA (2014). Samples were assayed in duplicate and the average cortisol concentration was used for the analyses.

Procedure

Preliminary consultation and diurnal saliva collection. Eligible participants were invited to a preliminary consultation to provide more information on the study and instructions for at-home (diurnal) saliva collection. Participants received a kit, which included an insulated lunch bag, an ice pack, 10 pre-labeled salivettes to use at each timepoint (Waking, 30 minutes after waking, 12 PM, 4 PM, and 9 PM each of the two days), reminder instructions, and a compliance recording booklet.

In preparation for the diurnal collection, participants were instructed to not ingest any alcohol 24 hours prior to sample collection. They were also asked to refrain from exercising, brushing their teeth, ingesting caffeinated products, and/or having a large meal one hour prior to sample collection. The collection procedure involved (1) participants rinsing their mouths with water 10 minutes prior to sampling; (2) placing the swab underneath their tongues for three minutes; and (3) after three minutes, to expectorate the swab back into the salivette and refrigerate it immediately, or keep it cool by using the provided insulated lunch bag and ice pack. Participants also completed a set of compliance questions paired with each collection timepoint. To document their perceived stress level at the time of saliva collection, participants indicated on a VAS their stress level based on the statement "I feel stressed" after each collection.

Laboratory session. The laboratory session was typically two hours in length and was scheduled within a month of the first meeting, between 3:30 PM and 6:30 PM. As shown in Study 2 Figure 1, the laboratory session comprised two parts: the TSST and the questionnaire component. Upon arrival, each participant indicated on the VAS how stressed she felt, in order to determine whether a stressor was experienced prior to the laboratory session, which may have biased later results. Participants were offered a cup of water to drink, followed by a 10-minute acclimatization period. After 10 minutes, the first of the seven additional saliva samples were collected: Arrival, Anticipation, Arithmetic, 10-, 20-, 40-, and 60-minutes after TSST. The "Arrival" sample served as a baseline cortisol measurement and subjective stress prior to the acute stressor. After, the participant was introduced to the TSST tasks and a second saliva collection, "Anticipation", was collected immediately before they began the first task of the TSST, to serve as a measure of anticipatory stress. Immediately after the TSST, "Arithmetic" was collected to assess stress patterns after the acute stressor, followed by the remaining four

saliva collections at the pre-determined time points of the recovery period. The questionnaires were also completed during the recovery period (i.e., 10 to 60-minutes following the TSST), and participants were instructed to complete the questionnaires based on their general stress, *not* in relation to the TSST. After the last sample collection, the participant was debriefed of the study and compensated $50 for her involvement in the study.

Data preparation and covariate considerations

Missing data were imputed using EM algorithm on SPSS V23. Biomarker data were imputed for participants with up to two missing diurnal cortisol data points and up to three missing acute cortisol data points, inclusive of removed univariate outliers. Of the total number of data points collected across participants, 2.1% of diurnal cortisol values and 4.8% of acute cortisol values were imputed. Eight participants were removed due to significant missing diurnal and acute cortisol data.

Participants were excluded from analyses if they had 15% or more missing responses on any of the questionnaires, inclusive of removed univariate outliers (no bivariate outliers were identified). Twelve participants were excluded from the analyses for this reason. Approximately 2% of the total questionnaire data were imputed (less than 1% for each group). The majority of the scales were normally distributed, with the exception of the responses on the Bidimensional Fatigue Scale for the White control group. We opted to not transform any of the scales because they were normally distributed for the other groups. The final sample included 27 Chinese control participants, 31 White control participants, 17 Chinese breast cancer survivors, and 24 White breast cancer survivors.

Based on the literature, we selected the following eight variables to test as possible covariates for an analysis of covariance (ANCOVA): age, number of years in Canada, cultural

orientation, mental and physical fatigue, time since diagnosis, stage of diagnosis, fear of recurrence, and perceived stress (i.e., PSS score). None of the selected variables met the assumptions of covariates for either diurnal or acute salivary cortisol data (Tabachnick & Fidell, 2013); therefore, no covariates were incorporated in the analyses.

Data analysis plan

Sociodemographic, medical, and cultural orientation variables

Following data preparation, a series of 2 X 2 multivariate analysis of variance (MANOVA) and chi-squares were conducted to determine whether there were group differences (ethnocultural and health statuses) in various sociodemographic and medical characteristics. Variables entered in the two-way MANOVA included “age” and “number of years in Canada”. We also computed a chi-square analysis to detect significant differences in the following sociodemographic variables between groups: whether one was born in Canada, relationship status, level of education, employment status, annual family income, average of alcohol and caffeine consumed per day, and smoking (yes/no).

Similar analyses were conducted to determine group differences in medical characteristics between Chinese and White breast cancer survivors. Specifically, an ANOVA was computed to assess whether there were group differences in age at diagnosis. A chi-square analysis was also used to determine whether there were group differences in stage of diagnosis, type of surgery, types of therapy and surgery (radiation, chemotherapy, hormone, breast reconstruction), and whether one had a breast cancer recurrence.

A one-way MANOVA was also computed to assess whether there were differences in medical characteristics between Chinese and White breast cancer survivors. An additional 2 X 2 MANOVA was performed to determine whether there were significant differences in degree of

cultural orientation towards the dominant (Canadian) and non-dominant (Chinese) cultures between Chinese and White participants.

Physiological stress

The physiological data were analyzed via a mixed-design 2 X 2 X 5 and 2 X 2 X 7 ANOVA to assess whether there were ethnocultural group and health status differences in average cortisol concentrations across (1) an average of five diurnal collection timepoints collected over a two-day period (at Waking, 30 minutes after waking, 12 PM, 4 PM, and 9 PM); and (2) seven acute stress collection timepoints (Arrival, Anticipation, Arithmetic, 10-, 20-, 40-, and 60-minutes). In addition, we also performed a series of 2 X 2 ANOVAs to assess whether there were significant differences between ethnocultural group and health status in diurnal and acute cortisol concentrations as determined by area under the curve from increase (AUC_i).

Psychosocial variables in relation to physiological stress

Mixed-design 2 X 2 X 5 and 2 X 2 X 7 ANOVAs were performed to assess whether participants' perception of stress, as measured via the VAS, differed significantly during the diurnal and acute stress periods. Additional post-hoc two-way ANOVAs were performed to further explore significant interactions. In addition to the main VAS analyses, we also computed a 2 X 2 ANOVA to examine whether there were ethnocultural group or health status differences in the perception of stress (as determined by the VAS) at the onset of the acute stressor in comparison to their baseline response (i.e., *Arithmetic* minus *Arrival*).

For the other psychological stress measures, namely the Perceived Stress Scale (PSS) and Daily Stress Inventory (DSI), two separate 2 (ethnocultural group) X 2 (health status) ANOVAs were performed. Specifically, the analyses were computed to detect group differences in total

perceived stress within the past month as measured via the PSS, and the calculated average impact rating of daily stressors as determined by the DSI.

Finally, a series of 2 X 2 mixed-design MANOVAs were conducted to evaluate whether there were ethnocultural group or health status differences in reported levels of fatigue (physical, mental, and total) and fear of recurrence (overall fears, health worries, womanhood worries, role worries, and death worries).

Results

Sociodemographic and medical characteristics

Participants' sociodemographic characteristics are displayed in Study 2 Supplementary Table 1. Results revealed a significant difference among ethnocultural groups, $F(2,31) = 5.78$, Pillai's Trace = .27, $\eta_p^2 = .271$, and health status, $F(2, 31) = 5.56$, $p = .009$, Pillai's Trace = .26, $\eta_p^2 = .264$, but no interaction between the sociodemographic variables. Specifically, White participants had been in Canada longer than Chinese participants ($M = 36.97$ years, $SE = 4.53$ *vs.* $M = 19.94$ years, $SD = 2.69$, $p = .003$) and breast cancer survivors were significantly older than control participants ($M = 58.85$, $SE = 2.86$ vs. $M = 45.33$ years, $SE = 2.82$, $p = .002$). Significantly more White participants were born in Canada than Chinese participants ($p < .001$) and the majority of Chinese and White participants reported being in a civil union or married relationship ($p = .014$). White participants also reported higher caffeinated consumption per day than Chinese participants ($p < .001$). On average, participants typically reported white collar occupations, with a higher proportion of control participants in white collar occupations than breast cancer survivors (65% vs. 35%, $p = .002$). As shown in Study 2 Supplementary Table 2, Chinese and White breast cancer survivors exhibited similar medical characteristics with no significant differences found.

Degree of cultural orientation

Study 2 Figure 2 shows participants' degree of cultural orientation towards the dominant (Canadian) and non-dominant (Chinese) cultures. Significant differences were found between ethnocultural groups, $F(2, 94) = 113.38$, $p < .001$, Pillai's Trace = .71, $\eta_p^2 = .71$, and health status, $F(2, 94) = 3.22$, $p = .044$, Pillai's Trace = .06, $\eta_p^2 = .06$, but no significant interaction. Although participants were typically more oriented towards their own respective culture, results revealed that breast cancer survivors (irrespective of ethnocultural group) were significantly more oriented towards the dominant culture than was observed in control participants ($M = 3.84$, $SE = .06$ vs. $M = 4.06$, $SE = .07$).

Compliance

Participants were deemed non-compliant if they ingested alcohol within 24 hours of saliva collection, or if they ingested a large meal, exercised, or brushed their teeth within one hour of saliva collection. Further, participants were marked as non-compliant if samples were not collected within 30 minutes of the collection time. The majority of participants complied for the earlier sample collection times (88.9% to 92.9%; $M = 2.92$ to 11.03 minutes late, $SD = 13.24$ to 20.07), but their compliance declined for the 9 PM collections (Day 1: 80.8%, $M = 18.42$ minutes late, $SD = 30.60$; Day 2: 78.8%, $M = 11.36$ minutes late, $SD = 21.93$).

Specifically, on both days, participants generally collected the Waking samples between 6:39AM and 7:08AM (median time: 6:30AM to 7:15AM; *SD*: 49 to 86 minutes), and they were typically on time for the second collection (30 minutes after waking; average time: 7:14AM to 7:44AM; median time: 7:01AM to 7:45AM; *SD*: 49 to 72 minutes). Compliance reports also indicated that participants typically collected the 12 PM and 4 PM collections on time (average times: 12:02 PM to 12:10PM, and 4:01PM to 4:14PM; median time: 12:00PM to 12:07PM, and

4:00PM to 4:10PM; *SD*: 7 to 23 minutes, and 5 to 30 minutes, respectively). Compliance for 9 PM collections declined, however, and on average, they were collected between 8:32PM and 9:23PM (median time: 9:00PM to 9:05PM, *SD*: 14 to 247 minutes).

Physiological stress profiles

Diurnal cortisol patterns. Average cortisol concentrations of Day 1 and Day 2 can be found in Study 2 Supplementary Table 3 (raw data presented); collapsed mean cortisol concentrations across both days are graphed in Study 2 Figure 3A (cleaned data as used in analyses). As shown in Study 2 Figure 3A, regardless of ethnocultural membership, breast cancer survivors and control participants displayed similar diurnal cortisol patterns. Results revealed no group differences or interactions between ethnocultural group and health status, Time, and ethnocultural membership, or Time and health status (*ps* = .509 to .994). The three-way interaction was not significant ($p = .547$). Note that there were also no significant group differences in the cortisol secretion at awakening (usually referred to as the cortisol awakening response or CAR) based on the first two data time points (*ps* = .267 to .663).

Acute cortisol patterns. As depicted in Study 2 Supplementary Table 3 and Study 2 Figure 3B, a significant quadratic trend was revealed in the acute cortisol patterns, $F(1,90) = 47.79$, $p < .001$, $\eta_p^2 = .35$. Although the main effect of ethnocultural membership was not significant ($p = .344$), there was a significant main effect of health status, $F = 6.50$, $p = .012$, $\eta_p^2 = .067$. Specifically, breast cancer survivors displayed lower cortisol concentration values than that of control participants. There were no significant two- or three-way interactions between Time, ethnocultural group, or health status (*ps* ranged from .161 to .951).

Although Chinese breast cancer survivors displayed a lower *Arrival* cortisol concentration level than that of White breast cancer survivors, the slope of increase in cortisol

reactivity of Chinese breast cancer survivors was greater than that of White breast cancer survivors, resulting in a higher peak at 20-minutes post-TSST for Chinese breast cancer survivors. This pattern suggests that Chinese breast cancer survivors exhibited similar cortisol reactivity to that of Chinese health control participants.

Area under the curve (AUCi). Results for AUCi analyses of both diurnal and acute cortisol patterns revealed no significant group main effects or interactions (*ps* = .331 to .867 and .166 to .407, respectively).

Psychosocial variables in relation to physiological stress.

Visual Analog Scale (VAS). Participants' typical subjective perceptions of stress during the acute stressor (i.e., TSST; Time VAS) are shown in Study 2 Figure 3C; breakdown of reports (by Day) are shown in Study 2 Supplementary Table 3. Results revealed a significant main effect of *Time VAS*, $F(3.61, 310.52) = 77.21$, $p < .001$, $\eta_p^2 = .47$, but not of ethnocultural group ($p = .868$) or health status ($p = .203$). Results also indicated a significant two-way interaction between ethnocultural group and health status, $F(1,86) = 8.35$, $p = .005$, $\eta_p^2 = .09$, and a significant three-way interaction between ethnocultural group, health status, and Time VAS, $F(3.61,310.52) = 2.77$, $p = .032$, $\eta_p^2 = .03$.

To further examine the significant three-way interaction, we assessed whether (1) there was an interaction between health status and Time VAS on both levels of ethnocultural group, and (2) whether there was an interaction between ethnocultural group and Time VAS on both levels of health status. Results of the first follow-up analysis indicated that there was a main effect of *Time VAS* on both levels of ethnocultural group (*ps* < .001), but no significant interactions (*ps* = .199 to .250). However, in a test of between-subjects effects White control participants reported significantly higher average levels of perceived stress on the VAS than

White breast cancer survivors ($p < .001$). No such differences were found among Chinese control participants and breast cancer survivors.

The second follow-up analysis revealed a significant main effect of Time VAS on both levels of health status, and an interaction between ethnocultural group and Time VAS in control participants, $F(3.74,198) = 5.55$, $p < .001$, $\eta_p^2 = .095$. No such interactions were observed among breast cancer survivors ($p = .624$). Results suggest that White control participants reported significantly higher average levels of perceived stress than did Chinese control participants, $F(1,53) = 4.08$, $p = .049$, $\eta_p^2 = ,071$, whereas White breast cancer survivors reported significantly lower levels of perceived stress than Chinese breast cancer survivors, $F(1,33) = 5.27$, $p = .028$, $\eta_p^2 = .138$. Simple main effects analyses revealed that Chinese control participants reported significantly lower levels of perceived stress than White control participants at timepoints 2, 3, and 4 (i.e., Anticipation, Arithmetic, and 10 minutes after TSST cessation; *ps* = .001 to .01).

Taken together, results revealed no significant difference in levels of perceived stress as reported by Chinese breast cancer survivors and Chinese control participants. Further, while White control participants reported markedly higher levels of stress than White breast cancer survivors at all timepoints, there was only a difference in reported levels between White and Chinese control participants for the duration of the acute stressor.

We also examined whether there were ethnocultural group or health status differences in the perception of stress at the onset of the acute stressor in comparison to their baseline response (i.e., VAS scores at *Arithmetic* minus *Arrival*). Results did not reveal significant main effects, but a significant interaction between the two factors was found, $F(1,89) = 3.97$, $p = .049$, $\eta_p^2 = .043$. Simple main effects analyses indicated that there were no significant differences in ethnocultural group on either level of health status, and vice versa (*ps* = .053 to .344). These

results were corroborated by follow-up independent t-tests (White control participants vs. White breast cancer survivors, $p = .376$; and Chinese control participants vs. Chinese breast cancer survivors, $p = .053$). Therefore, despite the interaction, there appears to be no significant statistical difference between subjective levels of stress at the onset of the acute stressor and baseline.

Other psychological measures of stress. Results revealed a significant main effect of ethnocultural group, $F(1, 95) = 4.14$, $p = .045$, $\eta_p^2 = .04$. Specifically, Chinese participants, regardless of health status, reported experiencing significantly more perceived stress than did White participants (*Ms* = 25.04 vs. 22.26). There was neither a significant main effect of health status ($p = .810$) nor a significant interaction between the two factors ($p = .112$).

Results of participants' Average Impact Rating (AIR) of daily stress (as determined by the DSI) revealed no significant main effects of ethnocultural group or health status (*ps* = .326 and .339, respectively), as depicted in Study 2 Figure 4, there was a significant interaction between the two factors, $F(1,95) = 6.06$, $p = .016$, $\eta_p^2 = .06$. While three of the four groups reported similar AIR, markedly lower AIR values were ($M = 2.67$) disclosed by White breast cancer survivors.

Fatigue and concerns about cancer recurrence. Analyses did not reveal any significant group differences or interactions between ethnocultural groups and health status for physical, mental, or total fatigue (*ps* ranged from .079 to .511) or for fear of recurrence (*p*s ranged from .069 to .988).

Discussion

The present study investigated whether Chinese breast cancer survivors exhibit different diurnal and acute cortisol patterns in comparison to that of healthy Chinese women and White

women with and without a prior diagnosis of breast cancer. In line with previous findings, diurnal profiles did not differ between groups (Couture-Lalande et al., 2014; Hsiao et al., 2012). But atypical acute cortisol patterns were found, suggesting changes in the HPA stress mechanisms of breast cancer survivors, possibly due to the chronic activation of the HPA axis throughout the disease trajectory (Alexander et al., 2009; Couture-Lalande et al., 2014).

All groups indicated similar patterns of subjective stress appraisal during the TSST protocol (i.e., VAS stress ratings). They showed increasingly higher levels of psychological stress during the *Anticipation* and *Arithmetic* phases of the protocol and a gradual decrease in psychological stress levels during the recovery period (10 to 60 minutes after) with some minor differences across the groups (see Study 2 Figure 3C). Although our VAS results were inconsistent with previous findings (*cf.* Couture-Lalande et al., 2014), the differences in psychological profiles of stress observed in our study may be explained by cultural factors or posttraumatic growth).

The added burden of acculturative stress may have enhanced the acute stress reactivity of Chinese participants, such that Chinese participants exhibited augmented acute stress responses irrespective of health status. Indeed, our findings indicated that Chinese women may respond to acute stress differently than that of White women. In the event of an acute stressor, while the cortisol reactivity slopes among Chinese breast cancer survivors and Chinese control participants were similar, their reactivity slopes were steeper than that of their western counterparts. Thus, indicating that there may be an association between acculturation, ethnocultural membership status, and cortisol reactivity slopes, but this relationship needs to be further explored.

An individual's understanding and perception of the illness is central to improving her well-being and subjective feelings of stress; to do this, the role of culture-bound values, beliefs,

and perceptions of illness need to be considered (Cordova et al., 2007). Cultural values often influence individuals' understanding of their illness and disease trajectory (Ashing-Giwa et al., 2004; Cordova et al., 2007). Our study indicated that there was a significant interaction between ethnocultural membership, health status, and perceived stress. However, despite the differences in the perception of stress, upon closer investigation, it was revealed that Chinese women with and without a prior diagnosis of breast cancer exhibited similar patterns of acute cortisol reactivity, while White control participants exhibited higher levels of cortisol at all timepoints than that of White breast cancer survivors and only higher levels than that of Chinese control participants during the acute stressor. Thus, our results may be indicative of posttraumatic growth, particularly among White breast cancer survivors.

It has often been reported that survivors of trauma, including medical illnesses such as breast cancer, experience posttraumatic growth, a positive psychological change due to an adverse experience (Jim & Jacobsen, 2008). The relationship between posttraumatic growth, stress appraisal, and overall well-being is convoluted, however. In addition to posttraumatic growth, many studies have noted that survivors of trauma also often report a re-evaluation of their core beliefs and values, the adoption and use of various coping mechanisms, and the availability and use of social support – all factors that contribute towards improving their well-being and promoting resilience towards future challenges (Diaz, Aldridge-Gerry, & Spiegel, 2014; Jim & Jacobsen, 2008). Supporting this literature, many breast cancer survivors in the present study anecdotally expressed changes in their perception and appraisal of stressors after their breast cancer diagnosis and treatment, such as accepting the illness as part of their new identity, adoption of new beliefs, and reappraisal of their values.

The similarity in reactive cortisol profiles among Chinese breast cancer survivors and control participants may be indicative of the influences of differences in cultural values and culture-related stress. Studies have suggested that values associated with eastern or collectivistic cultures, such as greater social constraints towards discussing one's illness, hesitation towards seeking social support, and fatalism, negatively affect survivorship outcomes and promote stress-related symptoms (Ashing-Giwa et al., 2004). In addition to cultural differences in illness management and perception, Chinese women also endure various acculturative stressors, regardless of their degree of acculturation. Although Chinese control participants in the present study typically demonstrated bicultural orientation, or in the case of Chinese breast cancer survivors, a higher degree of orientation towards the Canadian culture, they may still experience various acculturative stressors, such as the reconciliation of different cultural beliefs and values, discrimination and/or rejection from in-groups and out-groups, and intergenerational conflicts (Phinney et al., 2000; Stroink & Lalonde, 2009). Acculturative stress, in addition to health-related stress, may therefore contribute to the observed higher subjective stress appraisals among Chinese breast cancer survivors than that indicated by White breast cancer survivors. This notion is supported by the results of two other subjective measures of stress used in this study – the Perceived Stress Scale and the Daily Stress Inventory – both of which showed that Chinese participants, regardless of health status, typically reported feeling upset, stressed, angry, or nervous more often than did White participants within the past month.

Limitations

Although our results replicated previous findings regarding physiological stress responses towards an acute stressor, unlike earlier studies (e.g., Couture-Lalande et al., 2014), our findings also suggested a blunting effect in psychological patterns of stress. We offered potential

interpretations of the discrepant findings on psychological and physiological stress profiles; however, further research is required as the findings may be spurious or due to cohort effects. In particular, breast cancer survivors in the present study were on average 10 to 12 years older than their healthy counterparts, and as noted by the literature, age may affect one's HPA functioning and stress appraisal. However, our results are consistent with other similar studies (e.g., Alexander et al., 2009; Couture-Lalande et al., 2014; Dedert at al., 2012; Ho et al., 2013; Touitou et al., 1995, 1996), which included breast cancer survivors of varying ages; thus, it is unlikely that observed differences in cortisol response were due to the age difference. Another potential cohort effect is geographical location: Our participants were recruited from large Canadian urban centers (Ottawa and Toronto, Ontario) where different cultures are shared and respected. Therefore, Chinese participants in the present study may have different experiences than that of Chinese women in rural Canadian towns or cities in China, where individuals may not be immersed in a multicultural environment.

We also acknowledge that there are several other limitations to our study, such as its cross-sectional design, small sample size, and stringent eligibility criteria; therefore, our results should be interpreted with caution. One important methodological consideration may be the order in which questionnaires are presented in relation to the acute stressor. In the present study, questionnaires were administered after the TSST, which may potentially introduce bias in subjective measurements of stress even though participants were explicitly instructed to not account for the TSST experience during the completion of the questionnaires. However, the administration of questionnaires prior to the acute stressor may also introduce other limitations, such as the priming of participants to be more emotionally agitated or distressed, thus biasing the

results of the TSST. Hence, it is recommended that future studies explore and control for possible order effects of the administration of subjective measures of stress on cortisol release.

In addition, acculturative effects may also have been obscured due to the inclusion requirement of English comprehension, which may have prevented our study from capturing the full spectrum of acculturative stress. Participants in the present study were also mostly older adults who were well-educated, married, and employed with mid- to high-income, thus precluding them from stressors that may be associated with members of other socioeconomic and demographic characteristics (e.g., inability to pay bills, child rearing, lack of job security). Therefore, our findings may not be generalizable and representative of the population, especially within the Chinese community.

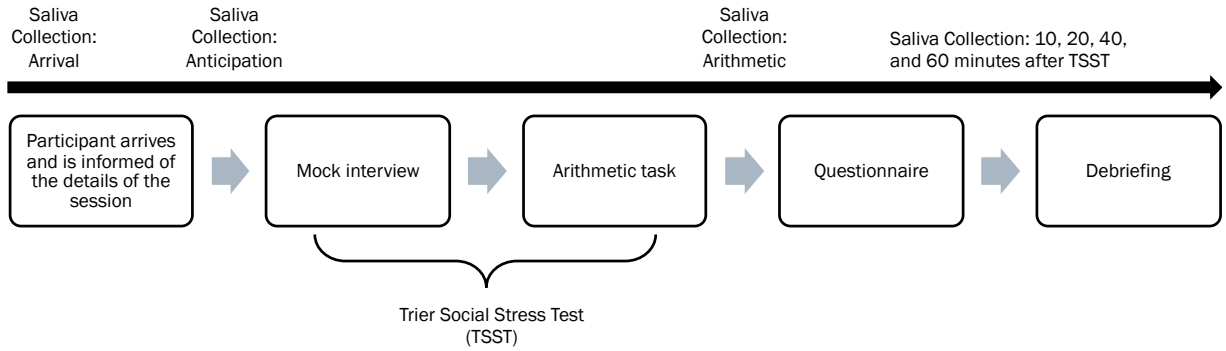
Future perspective

Future studies pursuing this avenue of research should recruit a larger sample that is more diverse in their sociodemographic characteristics and degree of acculturation (i.e., number of years in Canada and at various points of the acculturative process). It would also be useful to include more measures to examine other aspects of acculturation, such as perceived discrimination, family functioning, and perception of illness, as well as appraisal of stressors as it relates to one's culture. Indeed, discrimination and family conflict have often been reported to negatively affect the psychological and physiological well-being of second generation adolescents (Busse, Yim, Campos, & Marshburn, 2017; Crane, Ngai, Larson, & Hafen, 2005). Considering the extent of multiculturalism and ethnic diversity within Canada, it is important to increase health providers' awareness of the implications of cultural beliefs and values, which will likely improve and promote a positive survivorship experience for patients of varying ethnicities. Recent developments in symptom management services and programs allow survivors to access

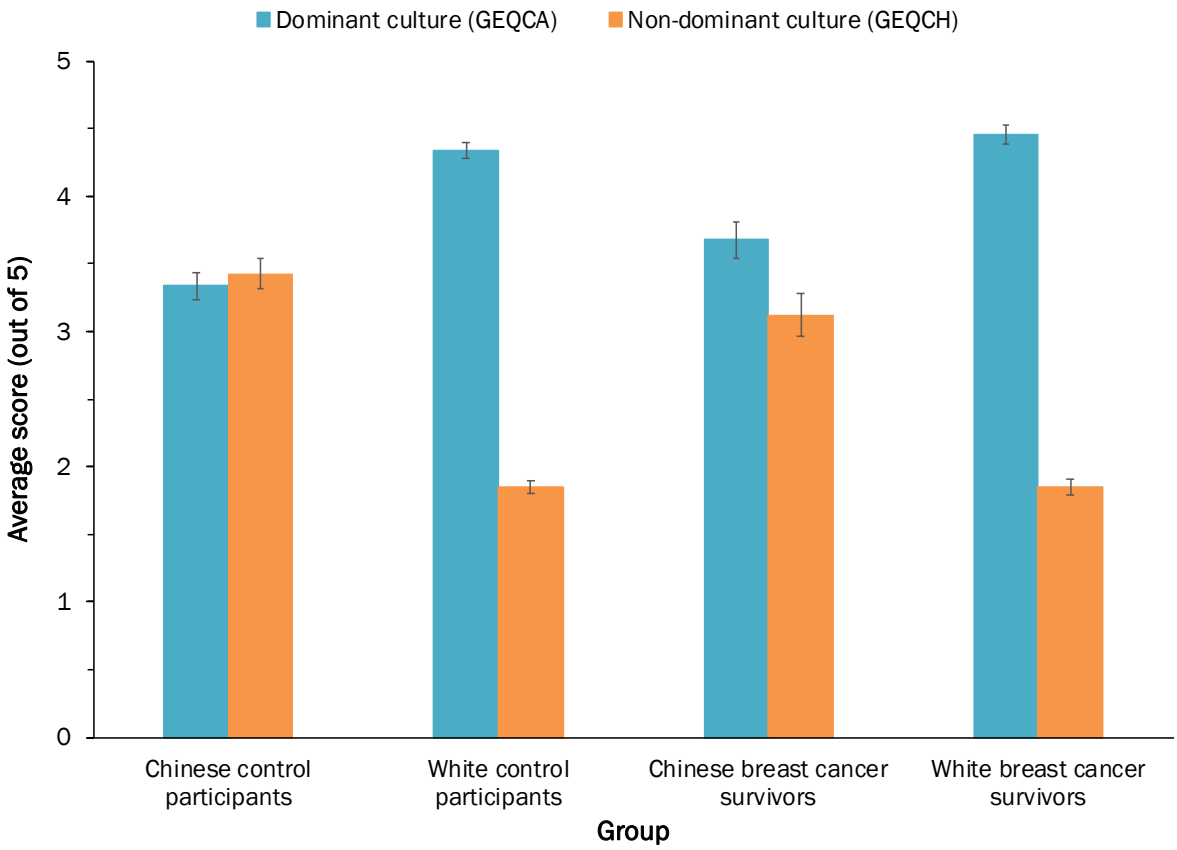
support services more readily; however, the existing programs and services are still heavily influenced by western beliefs. Given the influence of cultural beliefs and values on perception of illness, appraisal of stressors, and survivorship outcomes (Ashing-Giwa et al., 2004), future studies are encouraged to further investigate and develop culturally appropriate treatment plans and post-treatment services.

Conclusion

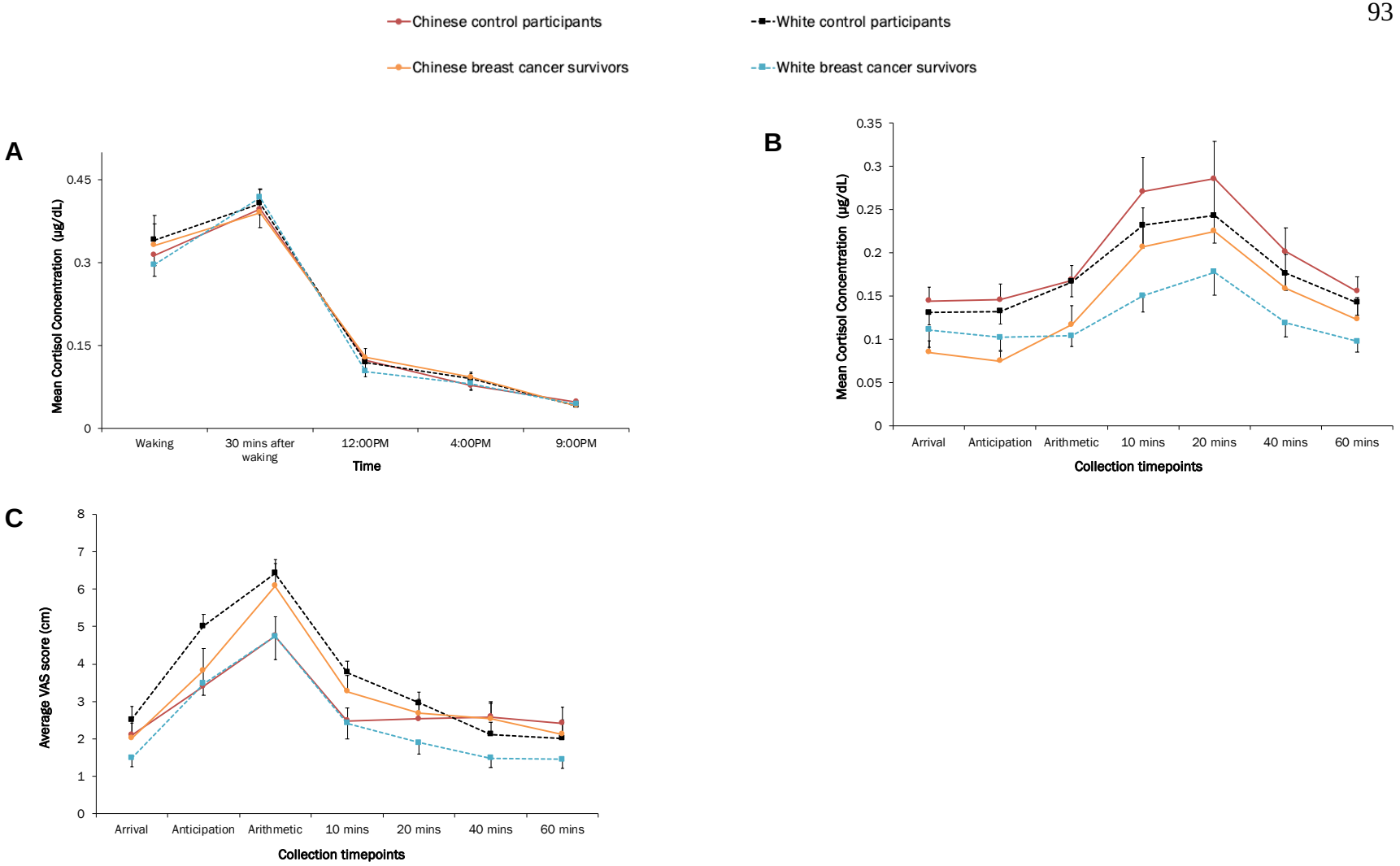
To our knowledge, this is the first study to provide a physiological and psychological account of stress between Chinese and White women with and without a prior diagnosis of breast cancer. Our results replicated previous findings in physiological patterns of stress: Regardless of ethnocultural membership, when compared to control participants, breast cancer survivors exhibited a blunted acute cortisol response despite no differences in diurnal cortisol profiles. But contrary to previous studies, we also found group differences in psychological profiles of stress. Although further investigation is warranted, our study provides preliminary evidence that ethnocultural membership and cultural orientation may influence individuals' appraisal and perception of stress, thus affecting their immediate physiological (i.e., slope of cortisol reactivity) and psychological responses towards a stressor. Our study therefore highlights the impact of acculturative stress on physiological and psychological stress profiles and underscores the need for more research and greater understanding of the effects of culture on well-being and health.



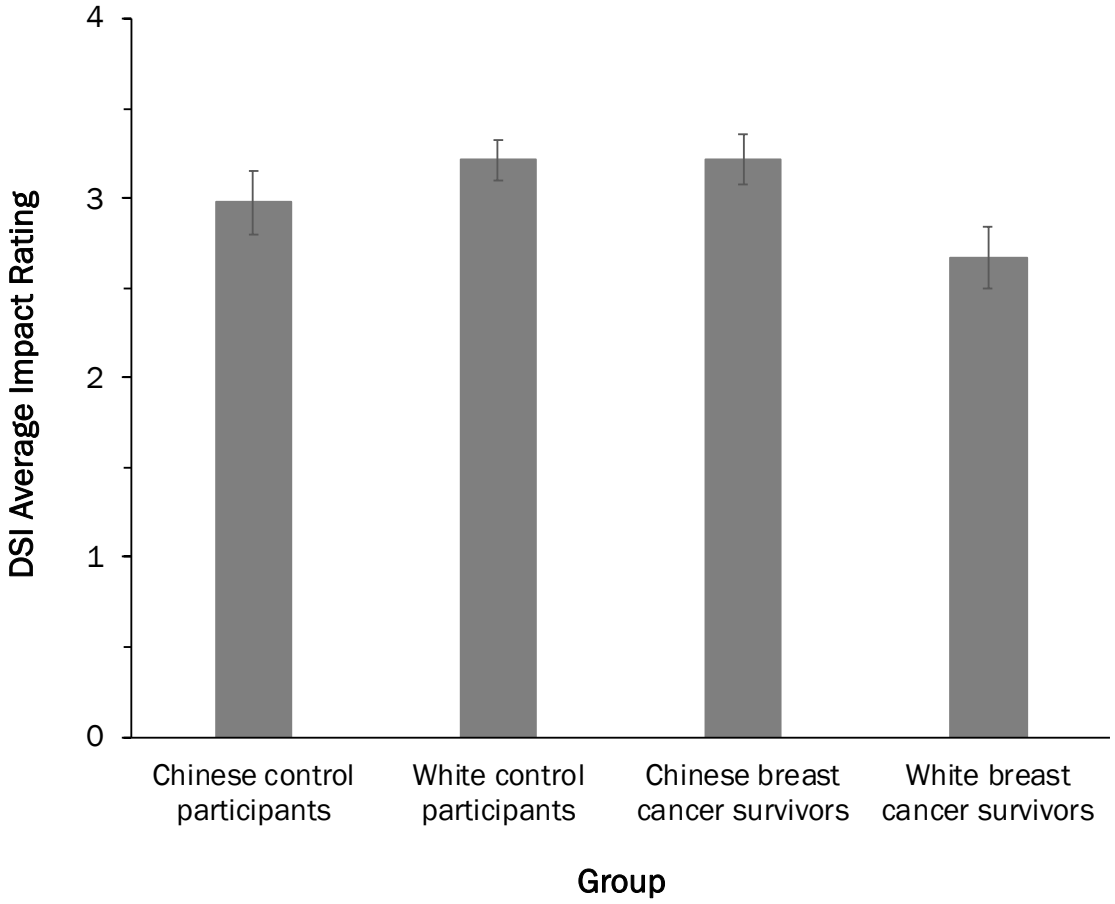
Study 2 Figure 1. Schematic diagram of laboratory timeline. Laboratory sessions were approximately 1.5 to 2 hours in length, and seven saliva samples were collected throughout the session. At each saliva collection, participants were required to indicate their level of subjective stress on a visual analog scale.



Study 2 Figure 2. Degree of orientation towards dominant (Canadian, GEQCA) and non-dominant (Chinese, GEQCH) cultures. Error bars represent standard error of the mean.



Study 2 Figure 3. (A) Mean diurnal cortisol concentration; **(B)** Mean acute cortisol concentration; and **(C)** Participants' average score on the statement "I feel stressed" as indicated on the visual analog scale (0 to 10 cm) at each saliva collection time point of the laboratory session. Error bars represent standard error of the mean.



Study 2 Figure 4. Participants' mean Average Impact Rating (AIR) on the Daily Stress Inventory. Error bars represent standard error of the mean.

Study 2 Supplementary Table 1. Participant demographics.

	Breast cancer survivors		**Control participants**	
	White (n = 24)	Chinese (n = 17)	White (n = 31)	Chinese (n = 27)
Mean age in years (± SD)	65.60±4.62	53.75±7.81	43.75±10.40	47.63±12.43
Mean years in Canada (± SD)	44.94±20.06	24.38±9.12	29.00±17.64	17.80±13.22
Born in Canada				
Yes	19 (79.2%)	4 (23.5%)	27 (87.1%)	4 (14.8%)
No	5 (20.8%)	13 (76.5%)	4 (12.9%)	23 (85.2%)
Relationship status				
Single	3 (12.5%)	3 (17.6%)	7 (22.6%)	3 (11.5%)
Dating	2 (8.3%)	0 (0.0%)	7 (22.6%)	2 (7.7%)
Common law	3 (12.5%)	0 (0.0%)	8 (25.8%)	1 (3.8%)
Married or civil union	12 (50.0%)	13 (76.5%)	7 (22.6%)	15 (57.7%)
Separated or divorced	2 (8.3%)	0 (0.0%)	2 (6.5%)	4 (15.4%)
Widowed	2 (8.3%)	1 (5.9%)	0 (0.0%)	1 (3.8%)
Highest level of education				
High school	6 (25.0%)	1 (6.3%)	5 (16.1%)	0 (0.0%)
College diploma	4 (16.7%)	4 (25.0%)	2 (6.5%)	2 (7.4%)
Bachelor's degree	7 (29.2%)	7 (43.8%)	15 (48.4%)	13 (48.1%)
Master's degree	6 (25.0%)	4 (25.0%)	8 (25.8%)	8 (29.6%)
Doctoral degree	1 (4.2%)	0 (0.0%)	1 (3.2%)	4 (14.8%)
Employment status				
Blue collar	0 (0.0%)	0 (0.0%)	4 (12.9%)	1 (3.8%)
White collar	8 (33.3%)	8 (47.1%)	16 (51.6%)	14 (53.8%)
Self-employed	1 (4.2%)	3 (17.6%)	2 (6.5%)	3 (11.5%)
Unemployed or retired	10 (41.7%)	3 (17.6%)	5 (16.1%)	5 (19.2%)
Student	0 (0.0%)	0 (0.0%)	3 (9.7%)	3 (11.5%)
Homemaker	0 (0.0%)	1 (5.9%)	1 (3.2%)	0 (0.0%)
Medical leave of absence	5 (20.8%)	2 (11.8%)	0 (0.0%)	0 (0.0%)
Annual family income (CDN)				
Under $40,000	2 (9.1%)	5 (31.3%)	10 (32.3%)	6 (23.1%)
$40,000-79,999	4 (18.2%)	4 (25.0%)	9 (29.0%)	9 (34.6%)
$80,000-119,999	4 (18.2%)	2 (12.5%)	8 (25.8%)	10 (38.5%)
$120,000-159,999	8 (36.4%)	3 (18.8%)	3 (9.7%)	0 (0.0%)
$160,000 and over	4 (18.2%)	2 (12.5%)	1 (3.2%)	1 (3.8%)
Average number of alcoholic beverages consumed per day				
0-1	20 (83.3%)	16 (100.0%)	30 (96.8%)	25 (96.2%)
2-3	4 (16.7%)	0 (0.0%)	1 (3.2%)	1 (3.8%)
4 and greater	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Average number of caffeinated beverages consumed per day				
0-1	6 (25.0%)	12 (70.6%)	13 (41.9%)	23 (85.2%)
2-3	12 (50.0%)	5 (29.4%)	17 (54.8%)	4 (14.8%)
4 and greater	6 (25.0%)	0 (0.0%)	1 (3.2%)	0 (0.0%)
Smoker				
Yes	1 (4.2%)	0 (0.0%)	2 (6.5%)	0 (0.0%)
No	23 (95.8%)	17 (100.0%)	29 (93.5%)	27 (100.0%)

Note. [a] Sample size differs per variable; percentage reflects number of respondents

Study 2 Supplementary Table 2. Medical and treatment history of breast cancer survivors.

	White (n = 24)	Chinese (n = 17)
Mean age of diagnosis in years (± SD)	50.67±11.35	46.65±5.99
Time since diagnosis in years (± SD)	6.48±7.82	6.06±5.23
Stage of diagnosis		
0	2 (8.3%)	3 (17.6%)
1	6 (25.0%)	6 (35.3%)
2	10 (41.7%)	2 (11.8%)
3	6 (25.0%)	6 (35.3%)
Type of surgery		
Unilateral mastectomy	8 (33.3%)	5 (29.4%)
Bilateral mastectomy	3 (12.5%)	2 (11.8%)
Lumpectomy on one breast	13 (54.2%)	10 (58.8%)
Lumpectomy on two breasts	0 (0.0%)	0 (0.0%)
No surgery	0 (0.0%)	0 (0.0%)
Received chemotherapy?		
Yes	16 (66.7%)	10 (58.8%)
No, but will	3 (12.5%)	0 (0.0%)
No and will not	5 (20.8%)	7 (41.2%)
Received hormone therapy?		
Yes	16 (66.7%)	10 (58.8%)
No, but will	0 (0.0%)	0 (0.0%)
No and will not	8 (33.3%)	7 (41.2%)
Received radiation therapy?		
Yes	22 (91.7%)	14 (82.4%)
No, but will	0 (0.0%)	0 (0.0%)
No and will not	2 (8.3%)	3 (17.6%)
Breast cancer recurrence		
Yes	1 (4.2%)	3 (17.6%)
No	23 (95.8%)	14 (82.4%)
Diagnosis of other cancers		
Yes	0 (0.0%)	0 (0.0%)
No	23 (100.0%)	17 (100.0%)
Chronic medical condition		
Yes	6 (25.0%)	3 (17.6%)
No	18 (75.0%)	14 (82.4%)

[a] Sample size differs per variable; percentage reflects number of respondents

Study 2 Supplementary Table 3. Descriptive characteristics of diurnal and acute cortisol concentrations (μg/dL) and subjective stress appraisals (via VAS, in centimetres) during collection time. Raw data presented.

	Breast cancer survivors		**Control participants**	
	White	Chinese	White	Chinese
Mean diurnal cortisol concentration (± SD)				
Waking				
Day 1	.29 ± .15	.30 ± .19	.33 ± .19	.37 ± .20
Day 2	.29 ± .11	.33 ± .21	.35 ± .15	.32 ± .13
30 minutes after waking				
Day 1	.40 ± .17	.42 ± .23	.40 ± .19	.45 ± .31
Day 2	.43 ± .16	.39 ± .15	.43 ± .16	.41 ± .21
12:00 PM				
Day 1	.11 ± .09	.12 ± .08	.12 ± .05	.12 ± .06
Day 2	.10 ± .04	.13 ± .09	.16 ± .25	.18 ± .26
4:00 PM				
Day 1	.09 ± .09	.10 ± .05	.09 ± .08	.11 ± .15
Day 2	.07 ± .07	.08 ± .05	.09 ± .04	.07 ± .04
9:00 PM				
Day 1	.05 ± .05	.04 ± .02	.05 ± .06	.12 ± .36
Day 2	.07 ± .17	.04 ± .04	.05 ± .04	.07 ± .10
Mean acute cortisol concentration (± SD)				
Arrival	.11 ± .09	.09 ± .05	.13 ± .08	.14 ± .08
Anticipation	.10 ± .07	.08 ± .05	.13 ± .08	.15 ± .10
Arithmetic	.10 ± .06	.12 ± .08	.17 ± .10	.17 ± .09
10 minutes post TSST	.15 ± .09	.21 ± .18	.23 ± .15	.27 ± .20
20 minutes post TSST	.18 ± .12	.22 ± .23	.24 ± .17	.29 ± .22
40 minutes post TSST	.12 ± .07	.16 ± .15	.18 ± .11	.20 ± .14
60 minutes post TSST	.10 ± .06	.12 ± .10	.14 ± .08	.16 ± .09
Mean diurnal subjective stress appraisal (± SD)				
Waking				
Day 1	1.86 ± 2.11	3.09 ± 3.18	2.15 ± 2.13	2.10 ± 2.23
Day 2	1.16 ± 1.69	3.21 ± 3.04	2.16 ± 2.22	1.84 ± 2.32
30 minutes after waking				
Day 1	1.58 ± 1.99	2.77 ± 2.71	2.20 ± 1.80	2.06 ± 2.10
Day 2	1.07 ± 1.30	3.52 ± 2.59	2.31 ± 2.28	1.95 ± 2.13
12:00 PM				
Day 1	2.04 ± 1.92	2.90 ± 1.84	2.68 ± 2.25	2.58 ± 2.65
Day 2	1.51 ± 1.93	2.74 ± 1.53	3.20 ± 2.59	2.85 ± 2.76
4:00 PM				
Day 1	2.29 ± 2.34	2.24 ± 1.64	3.21 ± 2.29	2.96 ± 2.81
Day 2	1.74 ± 1.93	2.03 ± 1.47	3.01 ± 2.13	2.58 ± 2.25
9:00 PM				
Day 1	1.11 ± 1.06	2.58 ± 1.34	2.15 ± 1.77	2.21 ± 2.36
Day 2	1.31 ± 1.34	2.67 ± 1.69	1.58 ± 1.28	1.91 ± 2.03

Mean acute subjective stress appraisal (± SD)				
Arrival	1.48 ± 1.03	2.01 ± 1.56	2.52 ± 1.95	2.10 ± 2.17
Anticipation	3.48 ± 1.40	3.83 ± 2.24	5.01 ± 1.73	3.40 ± 2.37
Arithmetic	4.74 ± 2.80	6.08 ± 2.31	6.42 ± 1.96	4.75 ± 2.60
10 minutes post TSST	2.42 ± 1.91	3.27 ± 1.63	3.78 ± 1.70	2.48 ± 1.77
20 minutes post TSST	1.90 ± 1.41	2.69 ± 1.40	2.96 ± 1.68	2.54 ± 2.21
40 minutes post TSST	1.48 ± 1.11	2.54 ± 1.58	2.12 ± 1.78	2.59 ± 2.11
60 minutes post TSST	1.46 ± 1.12	2.12 ± 1.48	2.02 ± 2.07	2.42 ± 2.16

Note. Descriptive statistics based on valid cases: White breast cancer survivors (N=19 to 24), Chinese breast cancer survivors (N=14 to 17 White control participants (N=25 to 31), and Chinese control participants (N=23 to 27).

Study 3: Physiological and Psychological Patterns of Chronic Stress in a Cross-Cultural Sample of Women With and Without a Prior Diagnosis of Breast Cancer

Wan, C., Zuchowski, M., Moyes, C., Huang, V., Fiocco, A. J., Clément, R., & Bielajew, C.

In Study 3, we aimed to explore the chronic physiological and psychological stress profiles of Chinese and White women with and without a prior diagnosis of breast cancer. Chronic physiological and psychological stress were assessed via the examination of hair cortisol concentration based on a three-centimeter collection of hair sample (i.e., 3-month period assessment) and a battery of questionnaires. The study has been revised and submitted to the Journal of Cross-Cultural Psychology for publication considerations. The most up-to-date version was appended to this dissertation (last updated: June 2019).

Author contributions: Wan and Bielajew designed the study and methodology. Wan was responsible for participant recruitment, data collection and preparation, data analysis, and the preparation of the manuscript. Zuchowski and Moyes assisted in the data collection and sample preparation process. Huang and Fiocco assisted in recruitment and data collection. Clément provided statistical support and was consulted throughout the process. Bielajew supervised the entire process and revised the manuscript.

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Physiological and Psychological Patterns of Chronic Stress in a Cross-Cultural Sample of Women With and Without a Prior Diagnosis of Breast Cancer

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Abstract

The current literature on cross-cultural cancer survivorship is largely based on qualitative accounts rather than objective investigations of breast cancer survivors' health as it relates to stress, often overlooking psychosocial and acculturative factors. To address this gap, we examined the physiological and psychological chronic stress patterns of Chinese and White breast cancer survivors, while considering other factors such as cultural orientation. Chronic stress profiles of 45 breast cancer survivors (27 White, 18 Chinese; average six years post diagnosis) and 65 healthy women (35 White, 30 Chinese) were evaluated via hair cortisol concentrations and questionnaires. Cortisol was extracted from a 3-cm hair sample collected from the vertex posterior region of the scalp (i.e., three months of exposure to stressors). Our results revealed that healthy Chinese women exhibited significantly higher levels of hair cortisol concentration than healthy White women (p = .048); no other significant group differences in cortisol levels and in psychological patterns of stress were observed. Among Chinese women in particular, hierarchical regression analyses revealed that health status and degree of orientation towards Canadian and/or Chinese cultures did not significantly predict physiological or psychological patterns of stress. Notwithstanding the results, regression analyses suggest that cultural orientation may influence physiological and psychological experiences of stress differently. Interpretation of the results and the implications of cultural orientation are discussed.

Introduction

In comparison to their Western counterpart, ethnocultural minority group members may endure higher levels of stress due to the additional challenges they may encounter as a result of their interactions with the dominant culture. The degree to which these stressors influence long-term psychological and physiological health depends on a host of factors, such as their degree of adaptation (sociocultural, marital, economic) to the dominant culture and coping behaviours (Ataca & Berry, 2002; Aycan & Berry, 1996; Ward & Rana-Deuba, 1999). In this study, we investigated the relationship between cultural orientation and psychological and physiological indices of stress in Chinese and White women with and without a prior diagnosis of breast

Defining Stress

Stress is defined here as a physiological and psychological response towards an event or experience that is perceived as beyond our coping abilities and prolonged exposure to such experiences leads to *chronic stress* (Hammen, Kim, Eberhart, & Brennan, 2009; Miller et al., 2007). This definition is inspired by Lazarus' (Lazarus, 1966; Lazarus & Folkman, 1987) and McEwen's (1998a, 1998b) theories of stress. Lazarus' transactional theory of stress, on the one hand, postulates that stress is a negative emotional state that is the result of an interaction between the individual and the environment (Lazarus, 1966). According to Lazarus, stress can be viewed as a multifaceted construct that is dependent on the individual's cognitive and affective appraisal. McEwen's allostatic load theory, on the other hand, focuses on the physiological impact of stress. He argues that the prolonged over- or under-activity of the physiological systems that are involved in the acclimatization to environmental challenges and stressors can result in various health consequences such as inflammatory and autoimmune disorders (McEwen, 1998a, 1998b). Despite the heavy emphasis on physiological consequences,

McEwen's theory acknowledges that the systems involved in the maintenance of homeostasis are also closely linked to the individual's behaviour and psychological state. Considering the relationship between stress and physiological and psychological well-being, our interest was to explore the effects of pervasive stressors such as chronic illness and culturally related stress, namely, ethnocultural membership, cultural identity and intercultural interaction.

Culturally related Stress as a Chronic Stressor

Culturally related stress has been associated with a host of health problems such as an increase in the likelihood of developing hypertension and cardiovascular diseases (Rohleder, 2011), diabetes (Chun et al., 2011), psychiatric disorders (Dantzer et al., 2008), as well as an increased risk for systemic inflammation (Fang et al., 2014) and various cancers (Gross et al., 2013; Rakoff-Nahoum, 2006). In a recent systematic review of the breast cancer survivorship of Asian-American women, Wen, Fang, and Ma (2014) noted that qualitative studies collectively reported that Asian-American breast cancer survivors typically experienced unmet physical and emotional challenges that negatively affect and impede on their ability to improve their health quality of life such as fear of recurrence, anxiety, and various other negative emotions (e.g., lack of peacefulness, unhappiness, reluctance to recall their breast cancer experience). Further, it was reported that the reviewed quantitative studies consistently noted that cultural health beliefs, culturally related stress, acculturation level, English proficiency, spirituality, availability of social support, and socioeconomic status to affect Asian-American breast cancer patients' health behaviours and their health-related quality of life (Wen et al., 2014). Thus, there are no known ethnically or culturally bound risk factors to breast cancer. The increasing incidence of breast cancer among Asian-American women and the chronic and pervasive nature of culturally related stress, however, justifies closer scrutiny (Deapen et al., 2002; Wen et al., 2014).

Ethnocultural membership, as well as the traditions and beliefs that individuals endorse may contribute to their culturally related stress, which in turn, have been found to affect an individual's health-related quality of life and breast cancer survivorship experience. The way in which one deals with culturally related stressors can be influenced by one's *cultural orientation*, which refers to the degree to which one is influenced by, identifies and engages in activities of a specific culture, as well as the extent of proficiency in that culture's language (Tsai & Chentsova-Dutton, 2002; Ying, 2005). Berry (e.g., 2005) introduced a four-fold model representing minorities' attitudes towards the combinations of desired affiliations to the original and dominant group, which he terms acculturative strategies. Following Clément and Noels (1992), we contend that cultural orientation can be likened to and understood via that acculturative strategies framework, such that certain patterns of identification may facilitate coping with culturally related stressors more effectively. Thus, individuals may demonstrate a *marginalized acculturative identity* (low orientation towards dominant [host] and non-dominant [home] cultures, *separated acculturative identity* (low orientation towards dominant culture and high orientation towards non-dominant culture), *assimilated acculturative identity* (high orientation towards dominant culture and low orientation towards non-dominant culture), or *integrated acculturative identity* (high orientation towards both dominant and non-dominant cultures). As such, individuals who demonstrate an *assimilated acculturative identity* and have fully adopted the norms and behaviours of the dominant culture may be able to avoid or reduce cultural conflict. Applying the acculturative strategies framework to the above identity patterns, it is believed that those with an *integrated acculturative identity*, that is a balanced endorsement of norms and behaviours of both cultures, would yield the best well-being outcomes (Berry, 2006; Berry, 2005; Ying, 2005). Indeed, studies have reported that individuals with a balanced

cultural orientation experienced greater life satisfaction, more positive affect, and better health outcomes (Berry, 1980; Ying, 1988; Ying, Lee, & Tsai, 2000).

Hair Cortisol as a Physiological Assessment of Stress and Health

Stress does not affect every individual to the same extent and its consequences may vary. Various factors, such as availability of psychosocial resources, cognitive appraisal, stress management abilities, and coping strategies, may buffer the impact of stress on the individual (Creswell et al., 2005; Nierop, Wirtz, Bratsikas, Zimmermann, & Ehlert, 2008). Regardless, physiological assessments of stress are important in understanding the relationship between stress, health, well-being, and immune response (Dantzer et al., 2008; Segerstrom & Miller, 2004; Smoller, 2016).

The stress system comprises two components that operate synergistically to maintain homeostasis in the organism whilst dealing with various environmental challenges and stressors (Thiel & Dretsch, 2011): the hypothalamic-pituitary-adrenal (HPA) and the sympathetic-adrenal-medullary (SAM) axes. The functioning of these axes is typically assessed via the measurement of cortisol and alpha-amylase, respectively. Cortisol, the focus of this paper, has been shown to have relatively stable diurnal and reactive patterns in healthy individuals (Foley & Kirschbaum, 2010). While traditional cortisol collection methods, via saliva, blood, and urine samples, may provide a reliable index of acute stress, they are not the best methods for the evaluation of chronic stress due to the logistics required – extent of effort and commitment on the part of the participants in insuring recurring daily sample collections for an extended period of time.

Recognizing that the analysis of hair samples may be the most practical option for assessing the physiological consequences of stress, researchers began investigating the possibility of detecting glucocorticoids in human hair in the early 2000s. Investigators found that

10 different glucocorticoids, including cortisol and cortisone, could be detected in hair samples (Cirimele et al., 2000). Numerous studies ensued and hair cortisol concentrations were found to be positively correlated with urinary and salivary cortisol (Accorsi et al., 2008; Bennett & Hayssen, 2010; Koren et al., 2002; Sauvé et al., 2007), thus rendering hair analysis a viable and reliable option for evaluating chronic stress. The accumulation of stress-related hormones over a one month period can be analyzed from one centimetre of hair (Sauvé et al., 2007), providing a retrospective measure of cortisol levels associated with chronic stress. In contrast, cortisol extracted from saliva, urine, and blood sources of cortisol (saliva, urine, blood) indexes immediate stress reactions.

More recently, researchers have begun investigating chronic stress via hair cortisol in individuals suffering from various ailments, somatic disorders, and psychiatric conditions (e.g., Staufenbiel et al., 2013). Based on these studies, it was suggested that normal hair cortisol concentrations range from 5.9 to 22.6 pg/mg (Rocky Mountain Analytical, 2014). It is important to note that individuals at the extreme ends of the range are not necessarily at an increased risk for illness, but those suffering from various ailments, psychiatric conditions, or chronic stress tend to exhibit elevated levels of hair cortisol levels, or have levels outside the expected range (Manenschijn et al., 2013; Pereg et al., 2013; Stalder et al., 2017; Steudte-Schmiedgen et al., 2017).

To the best of our knowledge, there are currently no studies investigating the relationship between culturally related stress, specifically cultural orientation, and hair cortisol profiles among breast cancer survivors. But Torres et al. (2018) recently published a study examining acculturative stress, cultural orientation, and its relationship with diurnal salivary cortisol patterns among 18 healthy Latina women. Torres et al. (2018) reported that acculturative stress

was significantly and negatively associated with orientation towards the dominant culture (i.e., American culture). Specifically, they reported that women in the high acculturative stress category, as determined via a median-split division in the acculturative stress measure, were associated with a blunted cortisol awakening response and flatter diurnal cortisol response. However, they based their interpretation on three time points collected over a single day (i.e., Waking, 30 minutes after waking, and bedtime), whereas most protocols recommend that at least five time points be collected on each of two or even three days and their average used to represent the diurnal rhythm (e.g., Couture-Lalande et al., 2014; Wan, Couture-Lalande et al., 2016). Despite these limitations, Torres et al.'s (2018) preliminary findings highlights the importance in further investigating the relationship between culturally related factors and the stress system.

The Current Study

The aim of our study was to examine whether cultural orientation, ethnocultural membership, and/or health status would influence the physiological and psychological profiles of chronic stress, based on the following three hypotheses: (1) Regardless of health status, we expected Chinese women to show higher levels of accumulated cortisol concentration in comparison to that of their Western counterpart; (2) Breast cancer survivors, irrespective of ethnocultural membership, would exhibit higher levels of accumulated cortisol concentration than that of women without a prior diagnosis; and (3) Chinese women (irrespective of health status) with higher orientation towards the Canadian culture would exhibit lower levels of accumulated hair cortisol concentrations and psychological distress.

Method

Participants

Participants were recruited via online classifieds and forums (e.g., Kijiji, comefromchina.com, centralhealthline.ca), as well as through the assistance of program facilitators at local cancer support groups and community centres (e.g., Ottawa Regional Cancer Foundation, Breast Cancer Action Ottawa, Ottawa Integrative Cancer Centre). The study was also advertised through support group listservs (e.g., Babes4Breast) and advertisements posted at various University Health Network facilities (e.g., ELLICSR Health, Wellness & Cancer Survivorship Centre).

To be eligible for the study, potential participants had to be (1) women of Chinese or White descent; (2) between the ages of 30 and 80; (3) residing in Ottawa or Toronto regions; (4) proficient in reading and understanding English; and (5) have completed all local and/or systemic adjuvant therapy at least six months ago, with the exception of hormonal therapy. For practical reasons, we did not control for place of birth and citizenship status. This decision was based on the assumption that regardless of whether the participants were Canadian-born or immigrant Chinese, they would experience culturally related stress and cultural orientation to some degree. Individuals were considered ineligible for the study if they had a history of psychiatric or physical conditions that could interfere with their overall quality of life or if they were breastfeeding and/or pregnant at the time of the study.

As detailed in Study 3 Supplementary Table 1, the final sample comprised 35 healthy White women (M_{age} = 38.56, SD = 10.03 years), 30 healthy Chinese women (M_{age} = 45.38, SD_{age} = 11.69 years), 27 White breast cancer survivors (M_{age} = 56.04, SD_{age} = 11.98 years), and 18 Chinese breast cancer survivors (M_{age} = 53.94, SD_{age} = 6.95 years). Not all the White participants were native Canadians – five breast cancer survivors and four control participants immigrated to Canada from United States of America or Europe (e.g., England, France) – and their average

number of years in Canada ranged from 29 to 45 years. Furthermore, 38 Chinese participants (13 breast cancer survivors, 25 control participants) indicated that they were not born in Canada. Chinese participants predominantly emigrated from China (n = 24), including People's Republic of China, Hong Kong, and Macau, as well as from other countries such as Malaysia.

The medical characteristics and treatment history of breast cancer survivors are summarized in Study 3 Supplementary Table 2. The majority of the White breast cancer survivors were diagnosed with Stage 2 breast cancer (37%), whereas Chinese breast cancer survivors were typically diagnosed with Stage 1 (33.3%) or Stage 3 (38.9%). Both Chinese and White breast cancer survivors reported that they were diagnosed between 40 to 50 years of age. The average number of years since diagnosis was approximately 6.5 years (*range* = 1 to 17 years, *SD* = 5.03 years; *median* = 5 years, *IQR* = 6 years) for Chinese breast cancer survivors, and about 6 years for White breast cancer survivors (*range* = 0 to 34 years, *SD* = 7.30 years; *median* = 3 years, *IQR* = 6.5 years).

Hair care and treatment history of the current sample are detailed in Study 3 Supplementary Table 3. In the present sample, the majority of the Chinese participants reported having black or brown hair, whereas the majority of the White participants reported having brown or blonde hair. Nearly half of our participants from each group reported washing their hair 1 to 3 times per week, and between 60 to 89% reported at least chemically treating their hair once within the last 12 months. We also asked participants to report how many hours it has been since the last hair wash at the time of the hair collection. Although the distribution differed depending on group, a large proportion of the participants reported that they washed their hair 11 to 30 hours prior to the hair collection.

Measures

Physiological measure of stress. For our purposes, we opted to confine our examination of chronic stress to the past three months because it has been shown that cortisol remains stable in hair for up to three months (Russell et al., 2012). The hair sample was approximately 2 to 3 mm in diameter and it was collected from the vertex posterior region of the skull. After the collection, samples were stored in an aluminium foil envelope at room temperature until further analysis. The preparation process for cortisol extraction was completed over a six day period (see Meyer, Novak, Hamel, & Rosenberg, 2014 for protocol), followed by an assay designed by Salimetrics, State College, PA (Salimetrics, 2014).

Psychological measures of stress and related variables. Participants completed two questionnaires in order to assess subjective levels of chronic stress – a modified version of the Perceived Stress Scale (PSS; Cohen et al., 1983) and the Life Experience Survey (LES; Sarason et al., 1978). Participants also completed the General Ethnicity Questionnaire – Abridged (GEQ; Tsai et al., 2000), which assessed their degree of orientation towards the dominant (Canadian) and non-dominant culture (Chinese) and completed two in-house developed questionnaires: the Hair Care and Treatment History (HCTH) and the Sociodemographic Questionnaire (SDQ); these results are reported above and in the appendices.

The PSS is a 14-item questionnaire that assesses the degree to which individuals find a situation stressful and/or their ability to handle stressful situations within the past month. Participants rated items such as "in the last month, how often have you dealt successfully with life hassles?" on a scale from *0* (never) to *4* (very often). The reliability of the PSS ranges between $\alpha = .84$ to .86. Test-retest reliability, however, differs depending on the interval of days ($\alpha = .85$ after a 2-day interval vs. $\alpha = .55$ after a 6-week interval). For the current study, we modified the timeframe of the questionnaire to within the past three months (PSS-3M). The

purpose of this modification was to complement the physiological measure of chronic stress, which assessed three months' accumulation of hair cortisol concentration. For our sample, the Cronbach-based reliability of the PSS-3M ranged from α = .74 to .91.

The LES is a 57-item self-report measure that requires individuals to rate a variety of major life events on a 7-point scale ranging from *-3* (extremely negative impact) to *0* (no impact) to *+3* (extremely positive impact). Based on a 5-6 week test-retest interval, the LES has been shown to have a moderate test-retest reliability with coefficients of positive, negative, and total scores ranging from .19 to .88 based on an undergraduate sample. Reliability testing for the current sample was not conducted because too few participants within each group reported experiencing a major life event within the past year.

The GEQ assesses participants' degree of identification with their dominant (American culture) and non-dominant culture (Chinese culture). The American subscale comprised 38 items, whereas the Chinese subscale had 39 items. The items on both subscales were almost identical, with the exception of cultural reference (e.g., "I was raised in a way that was American" vs. "I was raised in a way that was Chinese"). In comparison to the American version, the Chinese subscale had one extra item: "Are you bilingual?" (yes/no. If yes, which languages). The items measure the following domains of acculturation: language use and proficiency, social affiliation, cultural participation, cultural pride, cultural exposure, and preference for food and media. Participants rated the items on a 5-point Likert-type scale, ranging from *1* (strongly disagree) to *5* (strongly agree). Tsai et al. (2000) reported that although both subscales (American and Chinese) showed high internal reliability (α = .92 for both scales), test-retest reliability for the scales were .62 (SD = .22) and .57 (SD = .16), respectively. For the present study, the GEQ was revised to replace "American" with "Canadian". For Chinese

participants, scores on both Canadian and Chinese subscales were taken into account in our analyses. Only scores on the Canadian subscale were examined for White participants. Reliability testing for our sample indicated that the Canadian cultural orientation subscale had a high internal reliability for all groups in our study (α = .886 to .933). The Chinese cultural orientation subscale also displayed high internal reliability among Chinese breast cancer survivors and control participants (α = .936 and .933, respectively)

Procedure

Eligible participants were invited to attend a 30- to 45-minute laboratory session during which they completed the questionnaire package and provided a hair sample. The procedure consisted of securing a bundle of hair, approximately 2 to 3 mm in diameter, using a clear rubber band. The hair was cut as close to the scalp as possible and was taken from the back of the scalp in order to be less noticeable. The hair sample was then wrapped in aluminum foil and stored at room temperature for later analysis. After completion of the questionnaire and hair sample collection, the participant was compensated $25.

Results

Data Preparation

Physiological data. Two participants were excluded from analyses due to missing hair cortisol concentration values and/or hair concentration levels that were deemed as outliers (z = 3.29, p < .001). No data were imputed yielding a total sample of 110 (45 breast cancer survivors and 65 healthy control participants). A square root transformation was applied to normalize the distribution of hair cortisol concentration data.

Psychological data. Participants with more than 15% missing data in the administered battery of questionnaires, inclusive of univariate outliers (z = 3.29, p < .001), were removed from

the analyses. The missing data from participants with an admissible amount of data after the removal of the univariate outliers were imputed using the expectation-maximization algorithm imputation analysis. No multivariate outliers were identified, and except for the LES, all composite scores were normally distributed in all groups. A square root transformation was applied to the LES *Positive Impact*, *Negative Impact*, and *Total Impact* composite scores to reduce their significant skew and kurtosis characteristics. After the transformation, the *Negative Impact* composite score remained skewed but acceptable for the Chinese breast cancer group (z = 4.77). *Positive Impact* and *Total Impact* composite scores were normally distributed in all groups after the transformation. Transformed physiological and psychological data were used when applicable. The data used for the various analyses complied with the associated statistical assumptions and no multivariate outliers were identified (Field, 2009; Tabachnick & Fidell, 2013).

Preliminary Analyses

Participant characteristics. We performed a series of 2 X 2 MANOVAs and chi-square analyses to determine whether there were significant group differences on participants' sociodemographic, medical, and hair care/treatment characteristics. Our analyses revealed significant ethnocultural group differences *Years in Canada* and *Caffeine consumption per day* (*ps* < .001); and differences between breast cancer survivors and the control group in *Years in Canada*, *Age*, *Caffeine*, and *Frequency of cardiovascular exercise* (*ps* < .001 to .042). There were no significant group interactions between health status and ethnocultural membership for any of the examined sociodemographic characteristics. Furthermore, our analyses indicated no significant differences in the medical characteristics of Chinese and White breast cancer survivors. Finally, with hair care and treatment history, significant differences were found in *hair*

colour, *natural hair quality*, and *hours since last hair wash* between Chinese and White participants (*ps* < .001 to .045), but there were no significant interactions.

Testing for potential covariates. Based on the literature, we selected 16 variables to test as potential covariates because they were identified as most likely to affect hair cortisol concentrations (Dettenborn, Tietze, Kirschbaum, & Stalder, 2012; Hoffman, Karban, Benitez, Goodteacher, & Laudenslager, 2014). The variables were as follows: Age, number of years in Canada, born in Canada, average number of caffeinated beverages consumed per day, smoker (yes/no), frequency of hair washing in a typical week, chemical treatment of hair (lifetime), time since most recent chemical treatment, hours since hair last washed, total cultural orientation score (Canadian and Chinese combined), impact scores for major life events (negative, positive, total), and the total score for perceived stress within the last three months. None of the selected variables met the assumptions for an analysis of covariance (ANCOVA; Field, 2009; Tabachnick & Fidell, 2013) and therefore were not included in the analyses.

Correlations of the examined variables. Although none of the selected variables met the assumptions for an ANCOVA, we recognize that certain variables, such as *Number of years in Canada* and whether one was *born in Canada*, may play an essential role in one's degree of cultural orientation. Therefore, we examined the correlation of the two mentioned variables with the participants' degree of orientation towards the Canadian and Chinese cultures. In addition, we also examined whether there was a correlation between the various chronic stress measures (i.e., hair cortisol concentration, perceived stress within the last three months, and impact of major life events) and cultural orientation measures.

Number of years in Canada was not significantly correlated with one's degree of Canadian or Chinese cultural orientation for any of the groups, with the exception of Chinese

control participants. Specifically, it showed a moderate positive correlation with Chinese control participants' degree of orientation towards Canadian culture (r = .58, p = .011), and a moderate negative correlation with their degree of orientation towards Chinese culture (r = -.58, p = .011). Whether one was *born in Canada* was found to be significantly associated with one's degree of orientation to the Canadian and/or Chinese cultures for White breast cancer survivors (Canadian cultural orientation: r = .50, p = .008), Chinese breast cancer survivors (Canadian cultural orientation: r = .67, p = .002; and Chinese cultural orientation: r = -.64, p = .004) and Chinese control participants (Canadian cultural orientation: r = .70, p < .001; and Chinese cultural orientation: r = -.65, p < .001). Hence, although the number of years one has resided in Canada and whether one is a native Canadian did not have a covarying effect with cultural orientation, these factors are associated with higher orientation towards Canadian culture and lower orientation towards Chinese culture for Chinese participants. The mean scores for the perceived stress within the last three months, impact of major life events, and hair cortisol concentrations were not significantly correlated with degree of orientation towards the Canadian or Chinese cultures for any of the groups.

Hypotheses 1 & 2: Comparison of chronic physiological stress profiles of Chinese and White women. We hypothesized that (1) Chinese women, overall, would show higher levels of accumulated cortisol concentrations than White women; and (2) breast cancer survivors, in particular, would exhibit higher levels of accumulated cortisol concentration than healthy women. To address these hypotheses, we computed an omnibus 2 X 2 ANOVA to determine whether mean hair cortisol concentrations differed based on health status and/or ethnocultural membership. Omnibus test results did not reveal any significant main effects of health status or ethnocultural membership, nor interaction (p = .102 to .287). But although there

were virtually no differences in mean hair cortisol concentrations between Chinese and White women (health status collapsed; $p = .131$); results showed that breast cancer survivors, irrespective of ethnocultural membership, exhibited marginally higher hair cortisol concentrations than healthy women ($M = 2.91$, $SD = .81$ vs. $M = 2.64$, $SD = .78$; $F[1,108] = 2.97$, $p = .088$, $\eta_p^2 = .027$).

Notwithstanding, we proceeded to perform a series of focused analyses to investigate whether there were differences in mean hair cortisol concentrations among broader grouping categories. In particular, we performed a series of planned comparisons using one-way ANOVAs between (1) Chinese and White breast cancer survivors; (2) Chinese and White control participants; (3) White breast cancer survivors and White control participants; and (4) Chinese breast cancer survivors and Chinese control participants.

As shown in Study 3 Figure 1 (untransformed values plotted), the planned comparison analyses revealed that significantly higher levels of mean hair cortisol concentration were found among the Chinese control participants versus White control participants, $F(1,64) = 4.08$, $p = .048$, $\eta_p^2 = .061$. No differences were found among Chinese and White breast cancer survivors ($p = .839$) and Chinese breast cancer survivors and Chinese control participants ($p = .652$). However, a marginally significant difference in hair cortisol concentrations were observed among White breast cancer survivors and White control participants ($p = .064$).

Hypothesis 3: Examination of differences in chronic stress patterns as determined by cultural orientation. We postulated that Chinese women, irrespective of health status, who are more culturally oriented towards the Canadian culture, would exhibit lower levels of physiological and psychological chronic stress. To determine whether cultural orientation has an incremental effect in predicting chronic stress among Chinese women (N = 48), we computed a

hierarchical regression analysis for each of the following output variables: Mean hair cortisol concentration, total perceived stress within the last three months, and impact (negative, positive, total) from major life events. For each of the regression analyses, health status (breast cancer survivor or control participant) was entered in Step 1, followed by the Canadian cultural orientation and Chinese cultural orientation total scores in Step 2, and the cultural orientation interaction term in Step 3. We also repeated these analyses without controlling for health status (i.e., omitting Step 1), which yielded similar results and thus are not included in this report. The results of the three-step hierarchical regression analyses are summarized in Study 3 Table 1.

Hair cortisol concentration. Model 1 results indicated that health status alone accounted for 0.40% of the variance (F[1,46] = .206, p = .652, R^2 = .004, R^2_{adj} = -.017) and did not significantly predict hair cortisol concentrations. However, with the addition of the new predictors — cultural orientation towards Canadian and Chinese cultures – Model 2 accounted for an additional 19.7% of the variance (F[3,44] = 3.60, p = .021, R^2 = .197, R^2_{adj} = .142). The amount of variance accounted for by the addition of the interaction term was, however, virtually the same as Model 2 (F[4,43] = 2.68, p = .044, R^2 = .200, R^2_{adj} = .125).

Upon closer examination, Model 3 results revealed that Chinese breast cancer survivors did not have significantly different hair cortisol concentrations than that of Chinese control participants (p = .993). Further, results suggest that with every standard deviation increase of orientation towards the Canadian culture (SD = .58), there was a significant increase in Chinese participants' mean hair cortisol concentrations (t = 3.20, p = .003, ß = .646). Similar results were observed for orientation towards the Chinese culture (SD = .62; t = 2.41, p = .02, ß = .491). The interaction between Canadian and Chinese cultural orientations did not significantly predict hair cortisol concentration levels (p = .707).

In spite of these findings, the unique contributions of the terms towards the model variance may offer useful insight on the roles that cultural orientation and health status may play in the physiological response to stress. Details regarding zero-order and semipartial correlations of the predictors can be found on Study 3 Table 1. Briefly, semipartial correlations of the terms in Model 3 revealed that Canadian cultural orientation uniquely contributed to approximately 19% of the model variance (r = .303, sr = .436, sr^2 = .19). Furthermore, despite the lack of zero-order correlation between Chinese cultural orientation and mean hair cortisol concentrations, the semipartial correlation between Chinese cultural orientation and mean hair cortisol concentration were comparatively high (r = -.0004, sr = .328, sr^2 = .107), which may indicate possible suppression effects (e.g., Pandey & Elliott, 2010). This was subsequently tested in a hierarchical regression model with and without Chinese cultural orientation as a predictor in Step 2, and results revealed a R^2 change of .278 (R^2 = .444 and .166, with and without Chinese cultural orientation as predictor, respectively).

Subjective measures of stress. Model summary results revealed that health status, one's orientation towards the Canadian or Chinese cultures, and/or the interaction of the two cultural orientations, did not significantly predict Chinese women's perceived stress within the last three months (R^2 = .046, R^2_{adj} = -.043, p = .722), the positive impact of major life events (R^2 = .096, R^2_{adj} = .012, p = .352), or the total impact of major life events (R^2 = .069, R^2_{adj} = -.018, p = .537). For all subjective stress outcome variables, the interaction between Canadian and Chinese cultural orientation were not significant (r = -.114 to -.013, sr = -.025 to .021, p = .864 to .889). But despite these results, several observations should be noted.

Perceived stress within the last three months. Although non-significant, Model 3 results suggested that every one standard deviation increase of orientation towards the Canadian culture,

levels of perceived stress within the last three months decreased (t = -0.96, p = .341, ß = -.212), whereas the opposite effect was observed with degree of Chinese cultural orientation (t = 0.02, p = .986, ß = .004).

Impact of major life events. Model 3 results revealed that one standard deviation increase of orientation towards the Canadian culture significantly predicted an increase in the positive impact of major life events (t = 2.04, p = .048, ß = .438). By contrast, orientation towards the Chinese culture marginally predicted the positive impact of major life events (t = 1.86, p = .07, ß = .403).

In comparison to the results pertaining to the reported positive impact of major life events, results revealed that health status was a marginally significant predictor for the reported negative impact of life events (Model 1: t = 1.92, p = .061, ß = .273, R^2 = .074, R^2_{adj} = .054). This effect was lost after other predictors were entered into subsequent models (p = .110 and .114 for Model 2 and 3, respectively), however. Cultural orientation towards either culture did not significantly predict the negative impact of major life events in Model 2 and 3 (p = .936 and .615, Chinese and Canadian cultural orientations, respectively). Finally, none of the entered predictors predicted the total impact of major life events (ps = .182 to .888).

Discussion

In this study, we used physiological and psychological measures to assess the chronic stress profiles of breast cancer survivors from two different ethnocultural groups, while taking their acculturative identity, as determined by their degree of cultural orientation towards both cultures, into consideration. We tested three hypotheses: (1) Chinese women, overall, would show higher levels of accumulated cortisol concentration in comparison to that of White women; (2) Breast cancer survivors, irrespective of ethnocultural membership, would have higher levels

of mean hair cortisol concentration than that of women without a prior diagnosis; and (3) Chinese women, irrespective of health status, endorsing an assimilated or integrative acculturative identity (i.e., high orientation towards the Canadian culture, and either high or low orientation towards the Chinese culture), would experience lower levels of physiological and psychological stress. Although not all of our hypotheses were fully supported, important implications could be drawn from our findings.

The Normalization of a Dysregulated Stress System

Contrary to our expectations, regardless of ethnocultural group, breast cancer survivors did not have higher mean hair cortisol concentrations in comparison to the control group. Many past physiological studies, including our own assessments, have suggested that breast cancer survivors suffer from a dysregulated stress system (e.g., Couture-Lalande et al., 2014), as determined from acute stress exposure (for example, the Trier test). But using a cross-sectional design to examine diurnal and acute patterns of salivary cortisol, Couture-Lalande et al. (2014) reported that although an atypical stress response towards an acute stressor was observed among breast cancer survivors, they purported that with time, the stress system returns to normal functioning. Our study offers a different approach than that of Couture-Lalande et al. (2014), such that we examined hair cortisol concentrations which provide a three-month index of physiological stress. However, our results corroborated with Couture-Lalande et al.'s (2014) conclusion: Although stressors may compromise the stress system of breast cancer survivors for a finite period of time, our findings suggest that they may not translate into a chronic dysregulation, but further research would be required to investigate this relationship. In fact, both breast cancer survivor groups and control groups exhibited average hair cortisol concentrations that were within the normal range (5.9 to 22.6 pg/mg; Rocky Mountain Analytical, 2014); and

upon closer inspection, Chinese and White breast cancer survivors displayed virtually the same levels of hair cortisol concentrations. The similarity in hair cortisol concentrations between Chinese and White breast cancer survivors may not be all that surprising, however.

A breast cancer diagnosis and its ensuing trajectory represents a major and potentially life-threatening event that typically has consequences beyond that of typical daily stressors. That is to say, the distress accompanying a breast cancer trajectory may surpass the extent of distress that one would experience with typical environmental and psychosocial stressors, and therefore there may not be any detectable incremental effects of culturally related stress on their biological stress system. For breast cancer survivors, in particular, their diagnosis and treatments can be viewed as an event or stressor that was once beyond their ability to cope (albeit pervasive), but they have now overcome. Thus although it may have introduced considerable load to their physiological system at the time, it may have also fostered resilience and growth. This interpretation is supported by two observations in the study.

First, breast cancer survivors in this study expressed changes in their psychological experience of stress – namely, events that they may have perceived as stressful before their diagnosis – as having much less impact after surviving breast cancer. In support of our anecdotal evidence, numerous qualitative studies have also reported similar findings (e.g., Hefferon, Grealy, & Mutrie, 2009). Second, results revealed that while Chinese cultural orientation appeared to have no correlation with mean hair cortisol concentrations, after partialling out other predictors, the unique contribution of Chinese cultural orientation was comparatively large (10.5%; see Study 3 Table 1 for zero-order and semipartial correlations). Further, Canadian cultural orientation uniquely accounted for approximately 19%, after controlling for the effects of health status and Chinese cultural orientation. Taken together, our findings indicate that health

status (i.e., breast cancer diagnosis) does not predict levels of physiological stress among Chinese women, but rather, the orientation towards the Canadian culture may play a larger role in determining the extent of physiological stress experienced. Further, one's degree of orientation towards the Chinese culture may further enhances the relationship between Canadian cultural orientation and physiological stress, and influence the degree of physiological stress experienced.

Chronic Stress Patterns between Chinese and White Health Women

The main finding of this study was a significant difference in mean hair cortisol concentrations between Chinese and White healthy women, with higher values observed in the Chinese group. Paradoxically, White women in our sample also reported experiencing significantly more major life events, both positively and negatively appraised, within the past year compared to that of healthy Chinese women. There are a few reasons that may contribute to why the Chinese group exhibited higher hair cortisol concentrations despite reporting fewer major life events.

First, it is possible that the occurrences of major life events were not fully or accurately captured in our study due to the difference in timeframes. To assess the relationship between major life events and physiological stress via hair cortisol concentrations, we opted to use the Life Experiences Survey (LES), which covers events experienced within the past year. Although the timeframe assessed in the LES encompasses the 3-month assessment period used in the study, it is difficult to know the exact timing of stressful events – particularly, whether an event occurred during the assessment period or at any other time point during the 12-month timeframe that the LES evaluates. Therefore, it is possible that while our sample of healthy White participants experienced more life events, fewer of them occurred during the assessment period, thus resulting in lower hair cortisol concentration.

Second, differences in chronic stress levels could be due to individual differences in the subjective appraisal of life events, personality, use of coping strategies, access to (and use of) social support, as well as cultural differences in help-seeking behaviour, which were not assessed in the present study. Tsai et al. (2011), for example, showed that Chinese women with stronger Chinese cultural beliefs, were more likely to believe that their breast cancer were due to external forces, such as karma, the will of God, or an imbalance of energy. It may therefore be due to their strong traditional cultural beliefs that they were also less likely to access functional social support and less likely to undergo adjuvant therapy. Tsai et al.'s (2011) findings underscore the alarming inter-group differences in acknowledging the gravity of mental states and consequences of chronic stress, and the importance of culturally-sensitive treatment plans and intervention.

Lastly, differences in mean hair cortisol concentrations between the Chinese and White control groups may be associated with culturally related stressors related to a bicultural orientation (or identity), but not necessarily cultural orientation itself. In our study, we examined not only the physiological and psychological profiles of chronic stress, but also the role that cultural orientation plays in chronic stress. It is believed that a higher degree of orientation towards the dominant culture would lead to better well-being and health outcomes (Tsai et al., 2002). However, our analyses indicated that while Chinese control participants had higher hair cortisol concentrations than White control participants, the degree of orientation towards the dominant and/or the non-dominant cultures did not significantly predict average hair cortisol concentrations among Chinese participants (with and without controlling for health status). Thus, indicating that other processes may implicate the physiological patterns of stress.

Generally, our data showed that birth place (Canada) and number of years living in Canada were significantly and positively correlated with Chinese participants' degree of

orientation towards the Canadian culture, thus suggesting a bicultural orientation with exposure and time. However, when examining the relationship between Canadian and Chinese cultural orientation and stress, our results suggested that as participants' orientation towards the Canadian or the Chinese culture increased, they also exhibited a significant increase in their levels of physiological stress. Although cultural orientation did not significantly predict psychological distress, our analyses suggested that subjective appraisals of stress may follow a similar pattern: Higher orientation towards either culture was typically associated with greater psychological distress (i.e., perceived stress and the reported negative impact of major life events).

Due to the lack of interactive effects, we are unable to draw conclusions regarding the interrelationships of Canadian and Chinese cultural orientations, and whether stress outcomes differ depending on the endorsement of different acculturative identities; thus we caution readers when interpreting our results. But despite the exploratory nature of our study, we offer a possible interpretation of the results. Our findings suggest that individuals with bicultural identities (i.e,. assimilated or integrated) may in fact have a greater experience of physiological and psychological distress due to the addition of culturally related stressors (Chen & Sheldon, 2012; Stroink & Lalonde, 2009). Bicultural orientations, by virtue, require individuals to learn and endorse the values and beliefs of the dominant culture, and in some cases, to balance the demands and expectations of both dominant and non-dominant cultures. It is therefore likely that the demands of a bicultural orientation would present individuals with additional challenges and stressors. Indeed, numerous studies have found that bicultural individuals may experience a plethora of additional stressors such as discrimination and/or rejection from in-groups and out-groups (Berry, 2006; Romero, Martinez, & Carvajal, 2007), language and communication barriers (Choi, 1997), and intergenerational conflicts (Phinney et al., 2000). It may therefore be

due to these reasons that higher levels of physiological chronic stress were observed among our sample of Chinese women.

Limitations and Future Directions

The intersection between cultural orientation, chronic stress, and health, is still a relatively new area of research, and our findings should be considered as exploratory and preliminary evidence for future studies. We acknowledge that our study has limitations that may affect the generalizability and representativeness of our results such as (1) its small sample size – due to the stringent eligibility criteria, relatively lower incidence rate of breast cancer in Chinese women in Canada, and willingness of participation (Kwok & White, 2011; Lebel & Devins, 2008; Wu, West, Chen, & Hergert, 2006); (2) the region-specific recruitment; and (3) the short assessment period. In particular, we recognize that although it is recommended to limit the assessment of hair cortisol concentrations to a maximum of three months (Russell et al., 2012), stress profiles can easily be skewed by the presence of a single negative life event during that timeframe.

In addition, although there is a large body of literature on acculturative stress, the concept of cultural orientation has not been studied as thoroughly and there is no precise and objective method of measuring it. While our study provided preliminary findings towards the investigation of acculturative identities (or orientation patterns) on chronic stress, due to the small cell sizes and the limited acculturative diversity in our sample, our findings should be interpreted with caution. Although we have observed possible suppression effects and noted the unique contributions of cultural orientation towards predicting physiological stress, it is possible that we did not capture the full extent and the various nuances of cultural orientation and its potential

influences on the stress system and one's health. Thus we urge future studies to further examine the relationship and incremental value of cultural orientation on stress patterns.

In addition to the mentioned limitations, our study focused solely on the stress profiles of Chinese women, thus our results may not be representative of all Asian communities. As noted by Wen et al. (2014), existing studies have observed significant differences and variations in health behaviours, survivorship experience, and health-related quality of life among different Asian-American sub-groups; therefore we encourage future studies to examine stress profiles of breast cancer survivors of varying ethnocultural minority groups and sub-groups.

In addition to focusing our recruitment efforts on Chinese breast cancer survivors only, due to the measures used in the study and the requirement to read and comprehend English, it is likely that our participants were already fairly adapted to the Canadian culture, which may have contributed to the truncated range for *Number of Years in Canada* and the significant differences in *Age* between groups. However, we do not expect egregious confounding effects stemming from these differences among our groups.

Differences in *Years in Canada* as well as *Age* were expected because we did not control for immigration status and it is reasonable to detect differences in number of years in Canada between Chinese and White participants. Moreover, since we aimed to recruit breast cancer survivors who have fully completed their treatment regimen, it is also likely that it would set the groups of participants apart in terms of age. But we acknowledge that the number of years an individual has spent in a host country is an important determinant of acculturation and cultural orientation, and should be thoroughly investigated. Therefore, we recommend future studies to recruit with the aim of having a variable range of residency in the host country, to employ various acculturative measures to assess the role of cultural orientation and biculturalism, and to

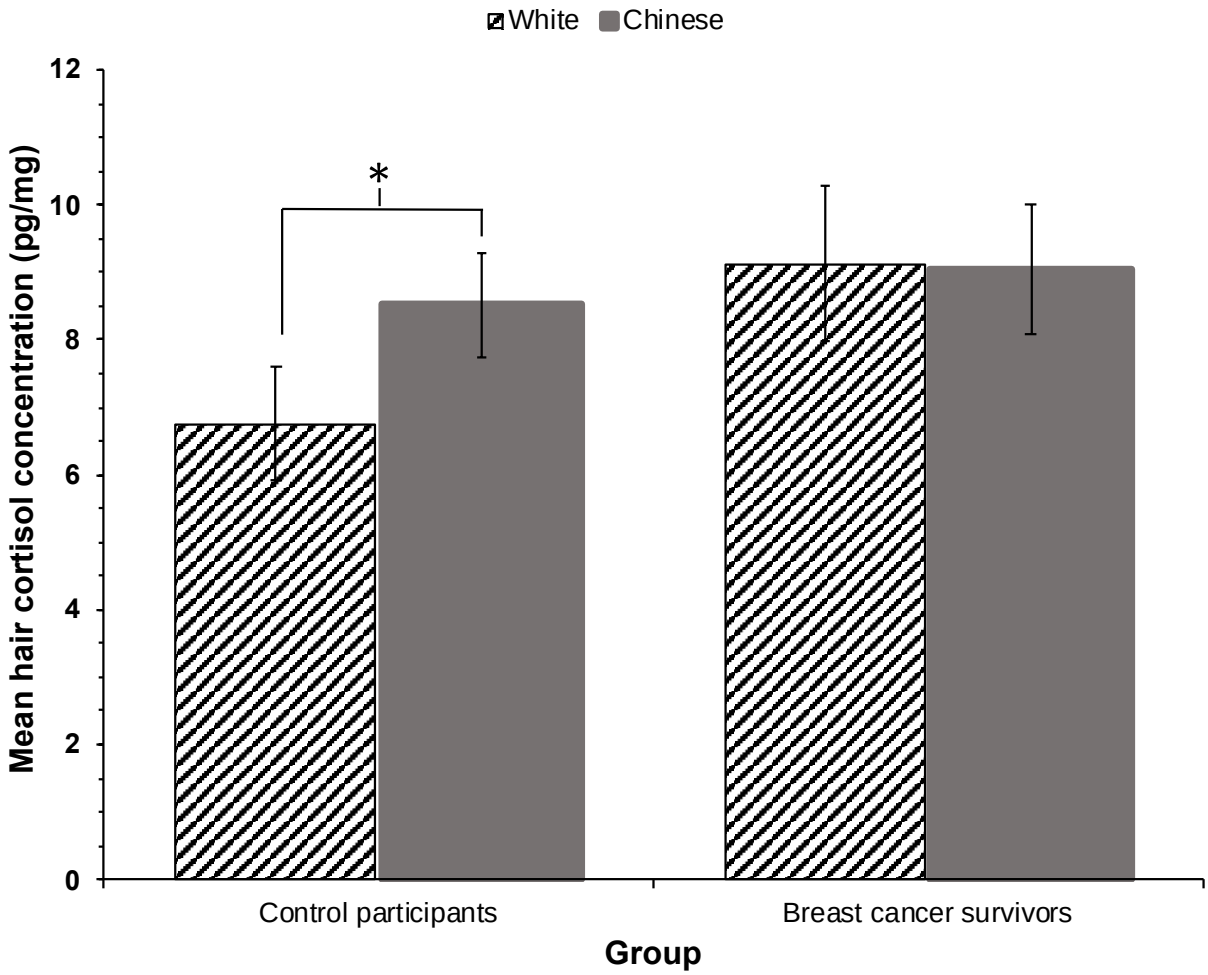
further investigate the health outcomes of varying generations of immigrants and acculturative identities.

Finally, although our study has shown that the functioning of the stress system of breast cancer survivors was not significantly different than that of our control participants, it is important to remember that the survivors were on average six years post-diagnosis and treatment and therefore any earlier dysregulations had normalized. Further, we acknowledge that chronic stress levels may be affected by each survivor's unique medical history (e.g., stage of diagnosis, metastasis, other medical conditions), however, due to small sample and cell sizes, we opted to not examine the impact of the varying medical variables. Indeed, with a large enough cell size, it may be possible to detect differences in stress patterns after taking medical variables (e.g., stage of diagnosis) into consideration. Thus, we recommend future studies to examine stress patterns of breast cancer survivors at varying stages of breast cancer diagnosis in order to inform clinical and intervention practices. Despite the limitations, our analyses demonstrated significant differences in physiological chronic stress among Chinese and White control participants, which underscores the importance of investigating the role of culture, stress, and health among newly diagnosed women and women who are currently undergoing treatment. Specifically, at the beginning of the disease trajectory, women belong to minority ethnocultural groups may display an exponential increase in physiological levels of stress, possibly at a concerning degree for a prolonged period of time, which may ultimately affect prognosis and survivorship outcome. Therefore, we strongly recommend future studies in investigating the role of acculturation and culture in women of varying ethnocultural memberships and varying stages of disease because it may inform us on the need of implementing early stress management and support interventions for these marginalized groups.

Conclusion

Our findings highlight the importance of taking cultural orientation and ethnocultural membership into account when evaluating physiological and psychological profiles of stress. Our study had three key findings: First, breast cancer survivors were not more chronically stressed than their healthy counterparts and there were no differences in chronic stress patterns between Chinese and White breast cancer survivors. Second, in the healthy control groups, Chinese women displayed significantly higher hair cortisol levels than that of White women, despite encountering fewer major life events during the assessment period. Finally, although an interactive effect of cultural orientation was not observed, our findings suggested that a higher orientation towards the dominant and non-dominant cultures significantly predicted higher levels of physiological distress. Our findings underscore the pervasive nature of culturally related stress and points to the need for more research and greater understanding in the relationship between culturally related factors and health.

Finally, with the increasing number of individuals immigrating to Canada (Government of Canada, 2017), this avenue of research is of particular relevance. Being cognisant of individuals' cultural beliefs, variability in their process of acculturation, and the relationship between acculturation and psychological and physiological well-being and health will promote a smoother integration into Canadian society and further the development of culturally sensitive and appropriate healthcare and support programs.



Study 3 Figure 1. Comparison of mean hair cortisol concentrations (pg/mg; untransformed values, indicated on top of bars) over a three-month time period in control participants (35 White and 30 Chinese) and breast cancer survivors (27 White and 18 Chinese). The only observed significant group difference was between Chinese and White control participants, $F(1,64) = 4.08$, $p = .048$. Error bars represent standard error of the mean.

Study 3 Table 1. Summary of hierarchical regression results: Health status, Canadian cultural orientation (GEQCA), Chinese cultural orientation (GEQCH), and the cultural orientation interaction term (GEQCA X GEQCH) in predicting mean hair cortisol concentrations, perceived stress (last 3 months; PSS-3M), and the negative, positive, and total impact of major life events (LES) among Chinese women (N=48).

	Model 1						**Model 2**						**Model 3**					
	F	$\triangle R^2$	ß	*t*	*r*	*sr*	F	$\triangle R^2$	ß	*t*	*r*	*sr*	F	$\triangle R^2$	ß	*t*	*r*	*sr*
Mean hair cortisol	.21	.004					3.60*	.192**					2.68*	.003				
Health status			.067	.45	.067	.067			.010	.07	.067	.010			.001	.01	.067	.001
GEQCA									.649	3.25**	.303	.438			.646	3.20**	.303	.436
GEQCH									.477	2.40*	-.0004	.324			.491	2.41*	-.0004	.328
GEQ Interaction															-.055	-.38	-.073	-.052
PSS-3M	.20	.004					.70	.041					.52	.0004				
Health status			.066	.45	.066	.066			.118	.78	.066	.114			.115	.74	.066	.109
GEQCA									-.211	-.97	-.180	-.143			-.212	-.96	-.180	-.143
GEQCH									-.002	-.10	.126	-.001			.004	.02	.126	.003
GEQ Interaction															-.023	-.14	.012	-.021
LES-Negative	3.70^{+}	$.074^{+}$					1.37	.011					1.10	.001				
Health status			.273	1.92^{+}	.273	.273			.251	1.68	.273	.242			.247	1.61	.273	.235
GEQCA									-.016	-.08	.133	-.011			-.017	-.08	.133	-.012
GEQCH									-.117	-.55	-.161	-.080			-.110	-.51	-.161	-.074
GEQ Interaction															-.027	-.17	-.114	-.025
LES-Positive	.02	.0003					1.54	.095					1.14	.001				
Health status			.018	.12	.018	.018			-.004	-.03	.018	-.004			-.008	-.05	.018	-.008
GEQCA									.439	2.07*	.148	.297			.438	2.04*	.148	.296
GEQCH									.396	1.88^{+}	.076	.270			.403	1.86^{+}	.076	.270
GEQ Interaction															-.026	-.17	-.013	-.024
LES-Total	1.27	.027					1.07	.041					.79	.0004				
Health status			.164	1.13	.164	.164			.126	.84	.164	.122			.130	.84	.164	.124
GEQCA									.294	1.37	.205	.199			.295	1.36	.205	.199
GEQCH									.165	.77	-.078	.112			.159	.72	-.078	.106
GEQ Interaction															.022	.14	-.036	.021

Note. Model 1: Health status; Model 2: Health status, GEQCA, GEQCH; Model 3: Health status, GEQCA, GEQCH, and GEQCA X GEQCH interaction.
$^{+}p < .10$; *p < .05; **p < .01

Study 3 Supplementary Table 1. Participant demographics.

	Breast Cancer Survivors		Control Participants	
	White (n=27)	Chinese (n=18)	White (n = 35)	Chinese (n = 30)
Mean age in years (±SD)	56.04 ± 11.98	53.94 ± 6.95	38.56 ± 10.03	45.38 ± 11.69
Mean years in Canada (±SD)[a]	44.94 ± 20.06	23.00 ± 9.94	29.00 ± 17.64	16.50 ± 12.64
Born in Canada				
Yes	22 (81.5%)	5 (27.8%)	31 (88.6%)	5 (16.7%)
No	5 (18.5%)	13 (72.2%)	4 (11.4%)	25 (83.3%)
Relationship status				
Single	3 (11.1%)	3 (16.7%)	8 (22.9%)	3 (10.3%)
Dating	2 (7.4%)	0 (0.0%)	8 (22.9%)	2 (6.9%)
Common Law	3 (11.1%)	0 (0.0%)	9 (25.7%)	1 (3.4%)
Married or Civil Union	14 (51.9%)	13 (72.2%)	7 (20.0%)	18 (62.1%)
Separated or Divorced	2 (7.4%)	1 (5.6%)	3 (8.6%)	4 (13.8%)
Widowed	3 (11.1%)	1 (5.6%)	0 (0.0%)	1 (3.4%)
Highest level of education				
High School	7 (25.9%)	1 (5.6%)	5 (14.3%)	0 (0.0%)
College Diploma	5 (18.5%)	4 (22.2%)	4 (11.4%)	2 (6.7%)
Bachelor's Degree	8 (29.6%)	9 (50.0%)	15 (42.9%)	15 (50.0%)
Master's Degree	5 (18.5%)	4 (22.2%)	10 (28.6%)	9 (30.0%)
Doctoral Degree	2 (7.4%)	0 (0.0%)	1 (2.9%)	4 (13.3%)
Employment status				
Blue Collar	0 (0.0%)	0 (0.0%)	5 (14.3%)	2 (6.9%)
White Collar	10 (37.0%)	7 (38.9%)	18 (51.4%)	15 (51.7%)
Self-Employed	1 (3.7%)	4 (22.2%)	2 (5.7%)	3 (10.3%)
Unemployed or Retired	10 (37.0%)	4 (22.2%)	5 (14.3%)	5 (17.2%)
Student	0 (0.0%)	0 (0.0%)	4 (11.4%)	4 (13.8%)
Homemaker	0 (0.0%)	1 (5.6%)	1 (2.9%)	0 (0.0%)
Medical Leave of Absence	6 (22.2%)	2 (11.1%)	0 (0.0%)	0 (0.0%)
Annual family income ($)				
Under 39,999	2 (8.0%)	6 (35.3%)	11 (31.4%)	6 (20.7%)
40,000 – 79,999	6 (24.0%)	5 (29.4%)	11 (31.4%)	12 (41.4%)
80,000 – 119,999	4 (16.0%)	2 (11.8%)	9 (25.7%)	9 (31.0%)
120,000 – 159,999	9 (36.0%)	2 (11.8%)	3 (8.6%)	1 (3.4%)
160,000 and above	4 (16.0%)	2 (11.8%)	1 (2.9%)	1 (3.4%)
Average number of alcoholic beverages consumed per day				
0 – 1	23 (85.2%)	17 (100.0%)	34 (97.1%)	28 (96.6%)
2 – 3	4 (14.8%)	0 (0.0%)	1 (2.9%)	1 (3.4%)
Greater than 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Average number of caffeinated drinks consumed per day				
0 -1	6 (22.2%)	14 (77.8%)	13 (38.2%)	26 (86.7%)
2 – 3	15 (55.6%)	4 (22.2%)	19 (55.9%)	4 (13.3%)
Greater than 4	6 (22.2%)	0 (0.0%)	2 (5.9%)	0 (0.0%)
Smoker				
Yes	1 (3.7%)	0 (0.0%)	3 (8.6%)	0 (0.0%)
No	26 (96.3%)	18 (100.0%)	32 (91.4%)	30 (100.0%)

Frequency of cardiovascular exercise				
Once a week or less	6 (22.2%)	6 (33.3%)	9 (25.7%)	17 (58.6%)
2 – 3 times a week	8 (29.6%)	9 (50.0%)	17 (48.6%)	9 (31.0%)
4 – 5 times a week	10 (37.0%)	1 (5.6%)	5 (14.3%)	2 (6.9%)
6 – 7 times a week	2 (7.4%)	2 (11.1%)	3 (8.6%)	1 (3.4%)
More than 7 times a week	1 (3.7%)	0 (0.0%)	1 (2.9%)	0 (0.0%)

Study 3 Supplementary Table 2. Medical and treatment history of breast cancer survivors.

	White (*n*=27)	**Chinese** (*n*=18)
Age of Diagnosis in Years (Mean ± SD)	50.81± 11.09	47.44 ± 5.97
Time since Diagnosis in Years (Mean ±SD)	5.88 ± 7.34	6.47 ± 5.04
Stage of Diagnosis		
0	2 (7.4%)	2 (11.1%)
1	7 (25.9%)	6 (33.3%)
2	10 (37.0%)	3 (16.7%)
3	8 (29.6%)	7 (38.9%)
Type of Surgery		
Unilateral Mastectomy	10 (37.0%)	5 (27.8%)
Bilateral Mastectomy	5 (18.5%)	3 (16.7%)
Lumpectomy on one breast	12 (44.4%)	10 (55.6%)
Lumpectomy on both breasts	0 (0.0%)	0 (0.0%)
No surgery	0 (0.0%)	0 (0.0%)
Received Chemotherapy?		
Yes	18 (66.7%)	12 (66.7%)
No, but will	3 (11.1%)	0 (0.0%)
No and will not	6 (22.2%)	6 (33.3%)
Received Hormone Therapy?		
Yes	18 (66.7%)	11 (61.1%)
No, but will	0 (0.0%)	0 (0.0%)
No and will not	9 (33.3%)	7 (38.9%)
Received Radiation Therapy?		
Yes	24 (88.9%)	14 (77.8%)
No, but will	0 (0.0%)	0 (0.0%)
No and will not	3 (11.1%)	4 (22.2%)
Breast Cancer Recurrence		
Yes	1 (3.7%)	3 (16.7%)
No	26 (96.3%)	15 (83.3%)
Diagnosis of other cancers		
Yes	1 (3.8%)	0 (0.0%)
No	25 (96.2%)	18 (100.0%)
Chronic Medical Condition		
Yes	8 (29.6%)	5 (27.8%)
No	19 (70.4%)	13 (72.2%)

Study 3 Supplementary Table 3. Hair care and treatment history of participants.

	Breast Cancer Survivors		**Control Participants**	
	White (*n*=27)	Chinese (*n*=18)	White (*n* = 35)	Chinese (*n* = 30)
Hair colour				
Black	1 (3.7%)	14 (77.8%)	0 (0.0%)	24 (80.0%)
Brown	18 (66.7%)	3 (16.7%)	27 (77.1%)	5 (16.7%)
Blonde	4 (14.8%)	0 (0.0%)	6 (17.1%)	0 (0.0%)
Red	0 (0.0%)	0 (0.0%)	1 (2.9%)	0 (0.0%)
Other	4 (14.8%)	1 (5.6%)	1 (2.9%)	1 (3.3%)
Natural hair quality				
Straight	11 (40.7%)	15 (83.3%)	14 (40.0%)	25 (83.3%)
Curly	1 (3.7%)	1 (5.6%)	6 (17.1%)	3 (10.0%)
Wavy	13 (48.1%)	2 (11.1%)	15 (42.9%)	2 (6.7%)
Other	2 (7.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Frequency of washing in a typical week				
1 – 3 times	14 (51.9%)	9 (50.0%)	16 (45.7%)	18 (60.0%)
4 – 6 times	8 (29.6%)	5 (27.8%)	13 (37.1%)	8 (26.7%)
Daily	5 (18.5%)	4 (22.2%)	6 (17.1%)	4 (13.3%)
Chemical treatment of hair (lifetime)				
Yes	19 (70.4%)	13 (72.2%)	31 (88.6%)	18 (60.0%)
No	8 (29.6%)	5 (27.8%)	4 (11.4%)	12 (40.0%)
Most recent chemical treatment				
0 to 12 months ago	11 (73.3%)	8 (88.9%)	25 (89.3%)	9 (64.3%)
13 to 24 months ago	2 (13.3%)	0 (0.0%)	1 (3.6%)	2 (14.3%)
25 or more months ago	2 (13.3%)	1 (11.1%)	2 (7.1%)	3 (21.4%)
Hours since last hair wash				
0 - 10	7 (25.9%)	2 (12.5%)	16 (45.7%)	5 (16.7%)
11 - 30	9 (33.3%)	8 (50.0%)	9 (25.7%)	9 (30.0%)
31 - 50	8 (29.6%)	4 (25.0%)	7 (20.0%)	12 (40.0%)
51 +	3 (11.1%)	2 (12.5%)	3 (8.6%)	4 (13.3%)

General Discussion

The aim of this dissertation was to investigate whether chronic disease – specifically breast cancer – influences an individual's physiological and psychological stress reactivity. It is in that vein that we examined the functioning of the sympathetic adrenal medullary (SAM) and hypothalamic pituitary adrenal (HPA) axes of women with and without a prior diagnosis of breast cancer based on salivary alpha-amylase, salivary cortisol, and hair cortisol concentrations. We assessed stress biomarker profiles vis-à-vis subjective stress appraisals to evaluate the consistency between the physiological and psychological experience of stress; we also examined the influences of cultural orientation on the objective and subjective experience of stress.

Although many studies have examined stress reactivity of breast cancer survivors, most of the existing literature focuses on cortisol stress-related patterns in White participants (Couture-Lalande et al., 2014; Cantarero-Villanueva et al., 2011; Dedert et al., 2012; Dettenborn et al., 2012; Fernández-Lao et al., 2012; Foley & Kirschbaum, 2010; Lambert et al., 2019; Lipschitz et al., 2013; Stalder et al., 2017; Sultan et al., 2018). Much less effort has been paid to the role of alpha-amylase in stress studies or the role of culturally related stress factors on stress patterns overall. This dissertation sought to address these gaps in the literature via the completion of three experimental studies.

The purpose of Study 1 was to establish a general understanding of SAM functioning as indexed by alpha amylase activity among a group of breast cancer survivors and to complement our findings from a prior study examining cortisol reactivity in the same group (see Couture-Lalande et al., 2014). Given the paucity of alpha-amylase studies in the breast cancer survivorship literature, in order to understand the synergistic relationship between the HPA and SAM axes, it was deemed appropriate to investigate the alpha-amylase profiles of the same set of

participants in the Couture-Lalande et al. (2014) study. In the case of Study 2 and 3, a new sample of breast cancer survivors and healthy control participants were recruited.

The purpose of Study 2 was to replicate the findings of Couture-Lalande et al. (2014) and to explore the implications of ethnocultural membership and cultural orientation on the diurnal and reactive profiles of cortisol. Finally, in Study 3, we aimed to expand the existing stress literature by evaluating the predictive roles of cultural orientation on chronic stress profiles of breast cancer survivors via the examination of hair cortisol.

Physiological Stress Patterns in Breast Cancer Survivors

Based on earlier observations of cortisol dysregulation in breast cancer survivors (Bower, Ganz, & Aziz, 2005; Bower, Ganz, Dickerson, et al., 2005; Couture-Lalande et al., 2014), we theorized that impairments might also be observed in stress-related alpha-amylase profiles. Despite the synergistic relationship between the two systems, different allostatic responses were observed in the SAM axis as compared to the HPA axis (*cf.* Couture-Lalande et al., 2014). Study 1 results revealed that breast cancer survivors exhibited higher basal levels of alpha-amylase, but their responses were of the same magnitude as those of women without a diagnosis. In fact, the slopes of diurnal and acute alpha-amylase levels were virtually identical to those of healthy women.

Although both the SAM and HPA axes are activated in the event of a stressor, they are responsible for difference processes within the body. The SAM axis or the sympathetic nervous system, on the one hand, primarily responds to acute stressors, initiates the “fight-or-flight” response, and regulates biological processes such as blood pressure, heart rate, and respiration (Piazza, Almeida, Dmitrieva, & Klein, 2010). The HPA axis, on the other hand, governs various metabolic processes, maintains homeostasis, and typically exhibits a slower and longer response

towards a stressor (Dickerson & Kemeny, 2004; Fulford & Harbuz, 2005). While the SAM and HPA responses may be adaptive during punctual events, the frequent activation of the stress systems may lead to an allostatic overload and impairment of stress mechanisms (McEwen, 1998b; Piazza et al., 2010; Selye, 1946). It is also comprehensible that the quality or type of impairments may be unique to each system due to the differences in their activation and roles in the stress response.

In addition to the frequency of activation and quantity of stressors, one's appraisal of the stressor – the extent of perceived control, the associated emotions (e.g., fear, anger), as well as uncertainty (or the anticipation of the stressor) – would also determine the severity of the stressful experience, and have important implications on the extent of allostatic overload (Dickerson & Kemeny, 2004; Lazarus, 1966, 1974; Lazarus & Folkman, 1987; McEwen, 1998a, 1998b; Piazza et al., 2010; Wan, Couture-Lalande et al., 2016). The anticipation of cancer recurrence (i.e., fear of a cancer recurrence or metastasis), for example, may subject breast cancer survivors to a chronic state of intense distress (Wan, Silverstein, et al., 2016), thus leading to frequent and lengthy sympathetic activation. In turn, the experience of adversity and/or the cumulative sympathetic activation across a long period of time may lead to various biological changes and/or impairments, including elevated sAA basal levels as observed in Study 1 (Wan, Couture-Lalande et al., 2016), higher sAA reactivity (Bosch et al., 1998; Kuras et al., 2017), and increased sympathetic-related responses (e.g., higher diastolic and systolic blood pressure (Inagaki & Eisenberger, 2016; Piazza et al., 2010). Due to the synergistic relationship of the two systems and possible differences in allostatic mechanisms, the HPA axis may therefore deliver an underactive response (Bower, Ganz, & Aziz, 2005; Bower, Ganz, Dickerson et al., 2005; Couture-Lalande et al., 2014; Wan et al., 2019 [Study 2]) to account for the "heightened

sympathetic tone" (Wan, Couture-Lalande et al., 2016). But it is important to note that this relationship may be bidirectional and would require further experimental testing to determine its association.

Whereas Study 1 provided a general idea of the SAM response among breast cancer survivors, Study 2 offered insight on whether the HPA dysregulation may be influenced by other psychosocial factors, such as cultural orientation and ethnocultural group membership. Study 2 revealed that (1) Chinese participants exhibited a more reactive response towards an acute stressor than White participants, as indicated by the slopes of their cortisol increase, and (2) the impact of health-related stressors may supersede the effects of culturally related stressors and factors. These results were further corroborated in Study 3, which revealed that the short-term consequences of frequent HPA activation do not lead to long-term deficits in HPA functioning among breast cancer survivors, regardless of ethnocultural membership. Further, Study 3 also provided preliminary evidence that although health-related stressors may eclipse the effects of culturally related factors (i.e., cultural orientation), the incremental effects of cultural orientation can still be detected upon close examination.

In fact, one of the pertinent findings of Study 3 is that similar hair cortisol concentrations were observed between breast cancer survivors and healthy women. Comparable levels were also observed within the breast cancer survivors group (i.e., Chinese vs. White breast cancer survivors). This finding is important because it suggests a normalization of the HPA axis among breast cancer survivors over a long period of time (versus two or three days. See Bower, Ganz, & Aziz, 2005; Bower, Ganz, Dickerson et al., 2005; Couture-Lalande et al., 2014; Wan et al., 2019 [Study 2]). However, this speculation would require further testing with either an additional control group (i.e., breast cancer control) or longitudinal design to fully explore this relationship.

Another pertinent finding from Study 3 was the observed difference in hair cortisol concentrations between Chinese and White healthy women. Consistent with our expectations, Chinese healthy women exhibited higher levels of hair cortisol concentrations than that of White healthy women, which we attributed to culturally related factors such as bicultural orientation, which may entail other stressors such as intergenerational and intercultural conflicts (Berry, 2006a, 2006b; Choi, 1997; Phinney et al., 2000; Romero et al., 2007). Albeit non-significant, Study 3 findings suggested that a high orientation towards both Canadian and Chinese cultures predicted higher levels of average hair cortisol concentrations among Chinese participants than other patterns of orientations (i.e., acculturative identities). Thus, in the absence of health-related stressors such as breast cancer, the physiological consequences of culturally related stressors are more conspicuous.

Although it is beyond the scope of this dissertation, this particular finding in Study 3 has important clinical implications for newly diagnosed women. As mentioned, the chronic activation of the HPA axis may lead to dysregulation and aversive health outcomes or the exacerbation of negative health conditions (Dickerson & Kemeny, 2004; McEwen, 1998b; Piazza et al., 2010). Coupled with the observation in Study 2, newly diagnosed women of ethnocultural minority groups may be at higher risk of experiencing severe HPA impairments in comparison to newly diagnosed White women due to the reactivity of their stress system and higher levels of chronic stress. Although further research will be required to have a better understanding of the intersection of health, stress, and culture, our speculation highlights the importance of having screening procedures and support programs targeted at newly diagnosed women of ethnocultural minority groups. Culturally informed screening procedures and support programs may also alleviate the allostatic overload and prevent a deterioration of their stress

systems, which may ultimately have implications on their disease trajectory and other biological processes.

Psychological Stress and Psychosocial Factors Influencing Physiological Stress

Cultural orientation is pertinent towards understanding stress appraisal, especially in the context of a chronic illness. Previous research supports the notion that cultural attitudes and values are likely to affect emotional regulation (Butler, Lee, & Gross, 2007), screening practices (Parsa, Kandiah, Abdul Rahman, & Mohd Zulkefi, 2006), health beliefs, and adaptation strategies such as seeking social support (Simpson, 2003; Uskul, 2010; Wu et al., 2006; Ye, 2006) — all of which may affect the perception of stress. Thus, in addition to physiological patterns of stress, we also examined the complementary psychological stress responses in Study 2 and 3. These findings must be interpreted with caution, however, because of the various study limitations that are later discussed (e.g., small sample size, lack of acculturative identity).

Nonetheless, the pattern of results in Study 2 and 3 suggest that one's perceptions of acute and chronic stress is more strongly associated with one's degree of orientation towards the dominant (vs. non-dominant) culture. Specifically, Study 2 revealed that Chinese participants (regardless of health status) reported significantly higher levels of day-to-day stress than both White breast cancer survivors and White healthy participants; and Study 3 results, albeit non-significant, suggests that higher orientation towards the Canadian culture was associated with lower levels of perceived stress within the last three months.

Regarding the perceived *impact* of daily stress and major life events, it was found that White breast cancer survivors reported markedly lower average daily stress impact than that of the other three groups. Furthermore, Study 3 showed that a higher orientation towards Canadian culture significantly predicted higher reports of positive impact of major life events, while higher

orientation towards Chinese culture only marginally predicted higher reports of positive impact of major life events. Taken together, for Chinese women (regardless of health status), we contend that a greater orientation towards Canadian culture would consequently lead to a shift in their cultural values and beliefs, thus affecting their illness management, health behaviours, and psychological adjustment. For White breast cancer survivors, we reasoned that their breast cancer experience had led to posttraumatic growth, which contributed towards reducing their perceived impact of daily stressors.

Indeed, prior studies have shown that traditional Eastern beliefs and values tend to associate chronic illnesses with stigmatism and fatalism, which have been reported to negatively affect individuals' well-being, survivorship trajectory, and willingness to seek additional help and social support. (Ashing, Padilla, Tejero, & Kagawa-Singer, 2003; Ashing-Giwa et al., 2004; Kwok & White, 2011; Lam & Fielding, 2003; Wang et al., 2012; Yusuf et al., 2013). In comparison to women holding traditional Eastern beliefs and values, those with stronger Western beliefs may therefore endorse more help-seeking behaviours and coping strategies, thus positively influencing their illness management and overall levels of chronic psychological stress (Abdullah & Brown, 2011; Ashing et al., 2003; Ashing-Giwa & Lim, 2010; Ashing-Giwa et al., 2004; Simpson, 2003; Wang et al., 2012). This interpretation is in support of the existing literature, which posits that biculturally oriented (or integrated) individuals typically have better well-being and psychological outcomes than those who do not demonstrate integration (Berry, 1980; Berry, 2005).

However, unlike White breast cancer survivors, Chinese breast cancer survivors in the present studies did not provide anecdotal evidence, nor did the results suggest, that they displayed signs of posttraumatic growth. Posttraumatic growth involves a change and re-

evaluation of core beliefs and values, use of various help-seeking and coping behaviours, as well as social support to improve resiliency and well-being (Jim & Jacobsen, 2008). Considering that posttraumatic growth requires an inherent change in cognitions, values, and beliefs, it is possible that we did not observe this phenomenon among our sample of Chinese breast cancer survivors due to the competing intercultural conflicts with Eastern and Western values, beliefs, and perception of chronic illness (Ashing-Giwa et al., 2004; Cordova et al., 2007). However, further investigations will be required to fully explore this avenue of research and the validity of our speculation.

Our studies also underscored the apparent incongruence between participants' physiological and psychological experiences of stress. One plausible explanation is that culturally related factors may in fact play different roles in physiological and psychological patterns of stress. Although bicultural orientation has been shown to predict better psychological well-being and adjustment (e.g., Ashing et al., 2003; Berry, 1980; Berry, 2005), it could also impose more long-term physiological stress and load. Indeed, an inherent requirement towards maintaining a bicultural (or integrated) orientation is the ability to balance the demands, values, and beliefs of both the dominant and non-dominant cultures (Chen & Sheldon, 2012; Stroink & Lalonde, 2009). As such, individuals with a bicultural orientation may experience intercultural conflicts and/or challenges that would tax their stress systems, in addition to other daily stressors.

Beyond culturally related stressors, other psychosocial factors, such as fatigue (physical, mental, and total fatigue) and fear of cancer recurrence, were also examined. Fatigue is one of the most distressing symptoms reported by breast cancer patients (Berger, Gerber, & Mayer, 2012). Due to the role that the HPA axis plays in the regulation of bodily processes, including immune responses and energy metabolism, it has been postulated that atypical cortisol patterns

are associated with cancer-related fatigue and chronic fatigue syndrome (Adam et al., 2017; Ho et al., 2013; Hsiao et al., 2012; Roerink et al., 2018; Schmidt et al., 2015, 2016; Strahler, Skoluda, Rohleder, & Nater, 2016; Tell, Mathews, & Janusek, 2014). In a recent examination of diurnal cortisol patterns and levels of physical, affective, and cognitive fatigue of 265 breast cancer patients undergoing adjuvant therapy, Schmidt et al. (2016) reported that only physical fatigue was associated with diurnal cortisol dysregulations. Specifically, Schmidt et al. (2016) reported that breast cancer patients exhibiting physical fatigue displayed a flatter cortisol slope near the evening (from 5pm to 10pm or bedtime) and an overall higher diurnal cortisol secretion. These results were similar to those of Bower, Ganz, Dickerson et al.'s (2005) study, which examined the relationship between diurnal cortisol rhythms and fatigue among breast cancer survivors. But contrary to these studies, levels of mental, physical, and total fatigue did not significantly differ between our groups.

Cancer-related fatigue is a debilitating symptom, and individuals experiencing significant fatigue typically report lower quality of life, higher levels of distress, and is comorbid with other conditions such as depression (Alexander et al., 2009; Berger et al., 2012; Jones et al., 2016). But it is a symptom that is typically more commonly experienced by cancer patients in treatment than those in remission (Berger et al., 2012; Jones et al., 2016). In fact, it was reported that only between 35 to 45% breast cancer survivors report experiencing significant levels of fatigue between one to 10 years post-diagnosis (Bower et al., 2006; Jones et al., 2016). Due to our inclusion criteria (i.e., absence of major disabling medical or psychiatric condition that could interfere with one's quality of life) and the extent of time since diagnosis (on average five to six years), it would be unlikely for our sample of breast cancer survivors to suffer from cancer-related fatigue. Furthermore, as presented in Study 2, comparable diurnal cortisol profiles were

observed between breast cancer survivors and healthy women. Taken together, it is therefore probable that our samples were more representative of the remaining 55% to 65% of breast cancer survivors who do not suffer from severe levels of fatigue. Although our participants did not display significant levels of fatigue, further research should be pursued in order to determine the role that cancer-related fatigue may play in breast cancer survivors' physiological and psychological stress reactivity.

Limitations and Future Research Directions

To our knowledge, the studies presented in this dissertation were among the first to explore the roles of cultural orientation and ethnocultural membership on acute, diurnal, and chronic physiological stress patterns of female breast cancer survivors with the accompaniment of corresponding subjective stress measures. But these studies were not without limitations, and although detailed accounts of limitations were discussed in each study, there are three that merit additional review: (1) The compliance of participants in saliva collection procedures; (2) the lack of heterogeneity of acculturative experience within our sample; and (3) the sample size as well as the characteristics of our participants.

The reliance on participants to comply with saliva collection instructions is a limitation that was unique to Study 1 and 2. Although saliva collection is the most cost effective and non-invasive methodology, participants were required to follow very specific instructions in order to not compromise the quality of the samples (e.g., no alcohol consumption, no teeth brushing, and collections at precise times for two consecutive days). To account for extraneous factors, we asked all participants in all the studies to fill out compliance reporting books during the two-day collection period. As expected, a small subset of participants did not comply with the saliva collection instructions (e.g., late or non-collection, consumption of alcohol or caffeine).

A related issue was the usability of samples. Occasionally due to non-compliance (e.g., forgetting to rinse their mouth prior to sample collection, consumption of certain foods) and/or individual characteristics (e.g., dry mouth), the quantity and quality of the samples were compromised (e.g., insufficient sample, sediments in sample). But nonetheless, the overall compliance rate of participants was comparable to that reported by others in the literature (*cf.* Broderick, Arnold, Kudielka, & Kirschbaum, 2004; Jacobs et al., 2005; Kudielka et al., 2003).

There are mixed findings regarding the extent of distortion that non-compliance may have on overall diurnal cortisol profiles (see Jacobs et al., 2005; Kudeilka et al., 2003). Kudielka et al., (2003) and Broderick et al. (2004) both indicated that diurnal cortisol patters differed significantly between those who complied and who did not. In particular, they observed a larger cortisol awakening response among compliant than non-compliant participants (Broderick et al., 2004; Kudielka et al., 2003). But in a later study, Jacobs et al. (2005) reported that the inclusion of non-compliant samples did not distort the overall diurnal cortisol profile despite using a narrower time window to determine compliance than was used in the previous two studies.

Despite these limitations, saliva collection is still commonly used in biomarker research due to ease of collection and its non-invasive nature. But more recently, researchers began developing and exploring other collection methods and equipment to ensure compliance. One of which is the experience sampling method, which employs a device that signals participants when to collect a sample (e.g., a watch with preset alarms; see Jacobs et al., 2005; Peeters et al., 2005). Other researchers have also used electronic monitoring caps (e.g., MEMS, eDEM; Aardex Ltd., Switzerland), which records the opening times of the cap (within 60 seconds accuracy) and thus may mitigate the issue of non-compliance and/or dishonest self-reports of compliance (see Broderick et al., 2004; Eatough, Shockley, & Yu, 2016; Jacobs et al., 2005; Kudielka et al.,

2003). Despite these advances in sampling methods, they have their own limitations: Electronic monitoring caps are markedly more expensive than traditional collection methods and they are designed to record *each* time the cap is opened and closed (Eatough et al., 2016). Thus, it is possible for participants to accidentally overwrite the recorded time by a simple gesture of closing and re-opening the salivette.

Some researchers have also started to explore the possibility of developing wearable devices to offer real-time detection and measurement of cortisol (Anastasova et al., 2017; Kaushik, Vasudev, Arya, Pasha, & Bhansali, 2014; Lillehoj, Huang, Truong, & Ho, 2013; Loncaric, Tang, Ho, Parameswaran, & Yu, 2012; Perry, 2018). One such development is a wearable adhesive patch for detecting cortisol concentrations in perspiration (Anastasova et al., 2017; Perry, 2018). The general purpose of these patches is to collect perspiration via perforations or channels on the patch into a guided biosensor area, thus offering real-time analysis (Anastasova et al., 2017; Perry, 2018). Based on its design, researchers contend large volumes of perspiration would not be required for cortisol detection (vs. saliva) due to the sensitive analytic procedure and biosensors present in the patch (Anastasova et al., 2017; Kaushik et al., 2014).

Although perspiration has been shown to be a viable source of cortisol collection and strong associations between perspiration and hair cortisol levels have been noted (see Russell, Koren, Rieder, & Van Uum, 2014), there are a few drawbacks. Namely, perspiration levels are largely dependent on weather conditions, physical activity levels, as well as individual characteristics of participants (Kaushik et al., 2014). Large variability of cortisol concentrations across participants have also been reported in various validation studies; thus the use of these devices must be further investigated (Anastasova et al., 2017). Therefore, while wearable sensors

may be a viable method for future biomarker studies, to this date, immunoassays and collection via saliva, urine, serum, or blood still remain as the gold standards (Kaushik et al., 2014). In that regard, salivary collection coupled with the use of a compliance reporting book and/or an electronic monitoring cap (accompanied by clear user instructions) and the encouragement of honest dialogue between participants and researchers may still be the most effective strategy to conduct such studies and to manage non-compliance.

Another limitation, which is unique to Study 2 and 3, is the lack of heterogeneity of acculturative experience within our sample. For practical reasons, we did not control for the extent of acculturation, nor the immigration status of our Chinese participants. Combined with the inclusion criteria used for the studies, it is likely that our samples of Chinese participants in were already fairly acculturated. Indeed, upon closer examination, Chinese participants in our studies have, on average, resided in Canada for 16 to 29 years. Thus implications on physiological and psychological stress profiles that could be observed at earlier stages of acculturation may have been overlooked. In particular, our studies can only offer speculation regarding the implications of stressors and life events on the perception and experience of stress among acculturated individuals of ethnocultural minority membership, rather than the acculturative experience itself.

The final major limitation of the three studies is the employment of a cross-sectional design and the recruitment of participants via convenience sampling, which may affect the generalizability and representativeness of our results. In particular, for Study 2 and 3, Chinese participants were recruited from two major urban cities (Toronto and Ottawa); thus our results may not represent the survivorship experience of Chinese participants living in rural Canadian cities nor Chinese participants living in Asia. Moreover, Study 1, 2, and 3 were also limited by

small sample sizes, which prevented further stratification of data (e.g., stage of diagnosis, treatment) and more complex analyses. Ideally, future studies would recruit a larger sample of breast cancer survivors with varying stages of diagnoses and treatments, in order to elucidate the implications of treatment and other psychosocial factors on cortisol and alpha-amylase patterns. It would also be beneficial towards the advancement of the literature to investigate the roles of environment, acculturation, and other culturally related factors on health and well-being outcomes by recruiting breast cancer survivors of ethnocultural minority groups with varying exposure to Western and Eastern cultures, residing in both urban and rural cities.

Clinical Implications

Despite the limitations, the current studies represent a novel step towards understanding and bridging the gap between health and cross-cultural psychology. They hold clinical significance by providing insight on the differences in stress response patterns and the potential moderating effects of various psychosocial and culturally related factors. Although our studies did not demonstrate any significant differences in physiological stress levels between Chinese and White breast cancer survivors, such differences were observed among Chinese and White healthy women.

The participants were on average five to six years post-diagnosis and therefore they may have adjusted to their new lifestyle and "new normal" (Cordova et al., 2007; Costanzo et al., 2007; Hefferon et al., 2009; Jim & Jacobsen, 2008; Trusson, Pilnick, & Roy, 2016). The differences in physiological stress levels among healthy Chinese and White healthy women may point to the need to pay particular attention to newly diagnosed breast cancer patients of ethnocultural minority groups. A recent diagnosis as well as the treatment trajectory may significantly impact their stress system, and thus it is possible that a pronounced dysregulation

may be observed among recently diagnosed Chinese breast cancer patients. Although the physiological and psychological stress patterns of recently diagnosed breast cancer patients are outside the scope of the present dissertation, we urge researchers to replicate these studies with this particular population in order to better inform existing support programs and interventions for newly diagnosed minority patients.

Conclusion

Cross-cultural research in the health domain is a fairly recent advancement, and given the significant population of immigrants in Canada, is a critical area to explore. As shown in the literature, non-native breast cancer survivors experience numerous culturally related challenges that ultimately affect their quality of life and survivorship experience. Differences in cultural values and beliefs would also undoubtedly affect each survivor's course of illness. Cultural orientation may be one of the few persisting factors that influence an individual's experience during diagnosis, treatment, and post-treatment. Studies presented in this dissertation offered insights on the long-term functioning of the stress systems and the nuanced effects of cultural orientation on the psychological well-being of breast cancer survivors. Further investigations of various intermediary and culturally related factors are recommended in order to facilitate a better understanding for clinicians and caretakers when diagnosing, treating, or providing post-treatment care to non-native patients.

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Dissertation Figures

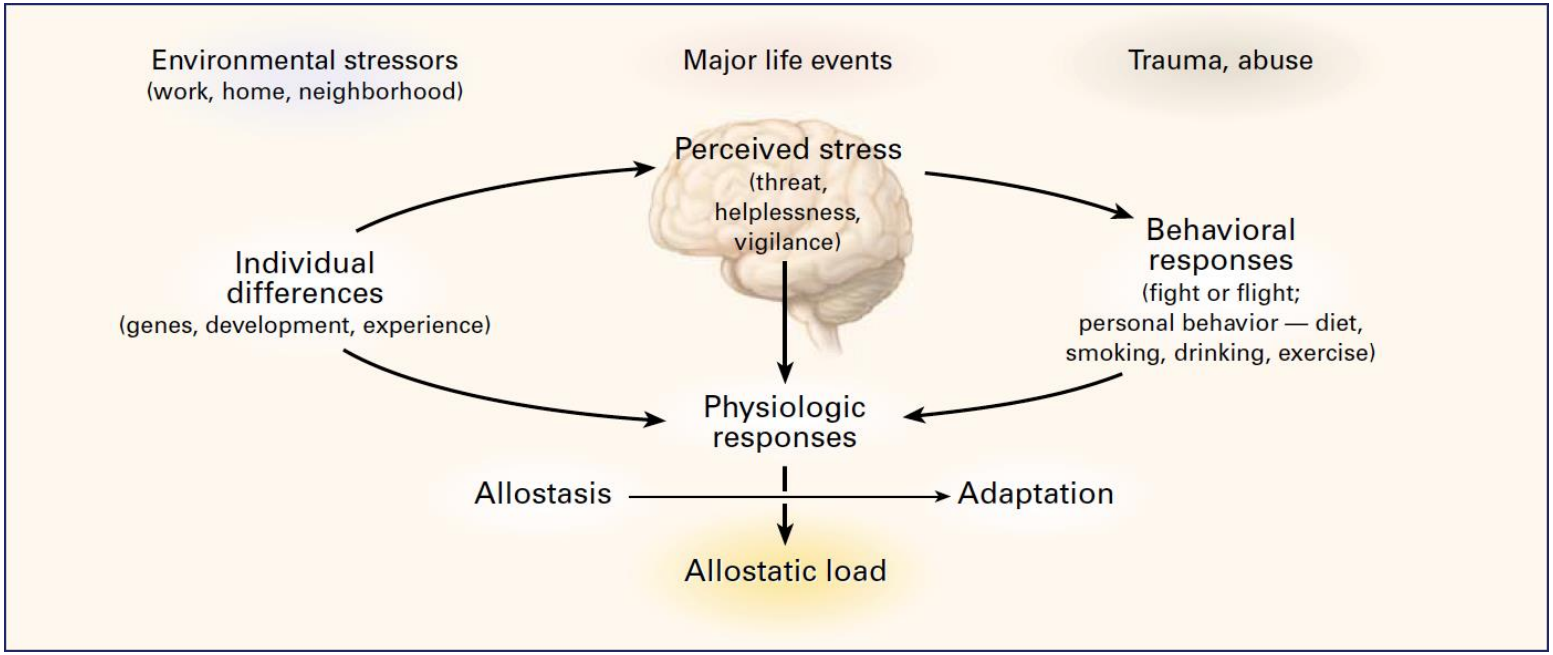


Figure 1. Allostatic load framework (reprinted with permission from McEwen, 1998b). When an individual perceives an event as stressful and a threat, physiologic responses are initiated, leading to allostasis and adaptation. Personal behavioural choices also play a role in allostasis and adaptation. Chronic activation of the involved mediating systems will result in the accumulation of allostatic load, leading to health consequences and disease.

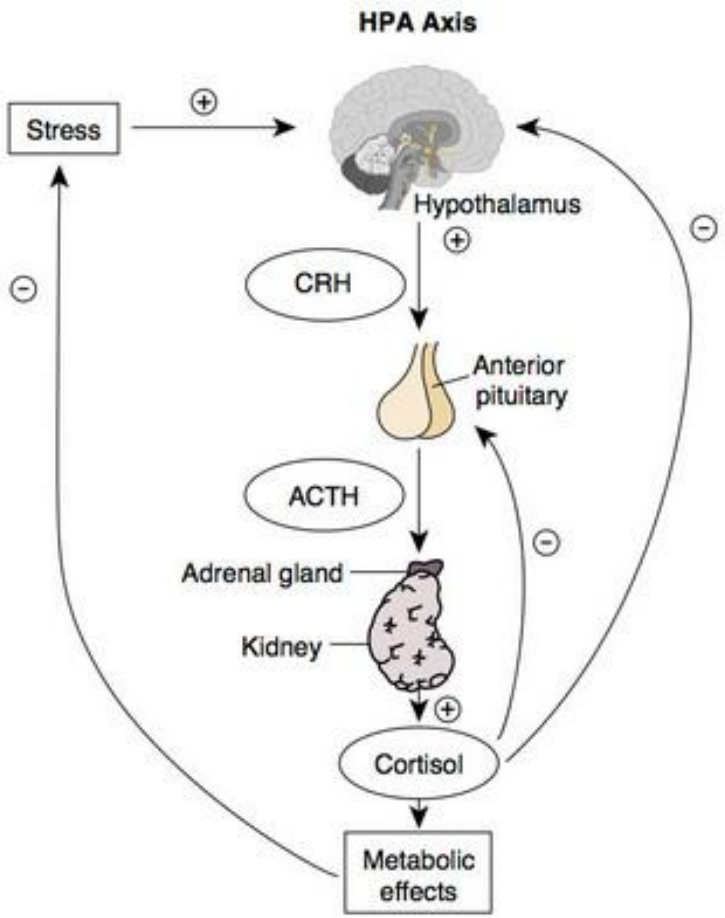


Figure 2. Main components of the HPA axis.

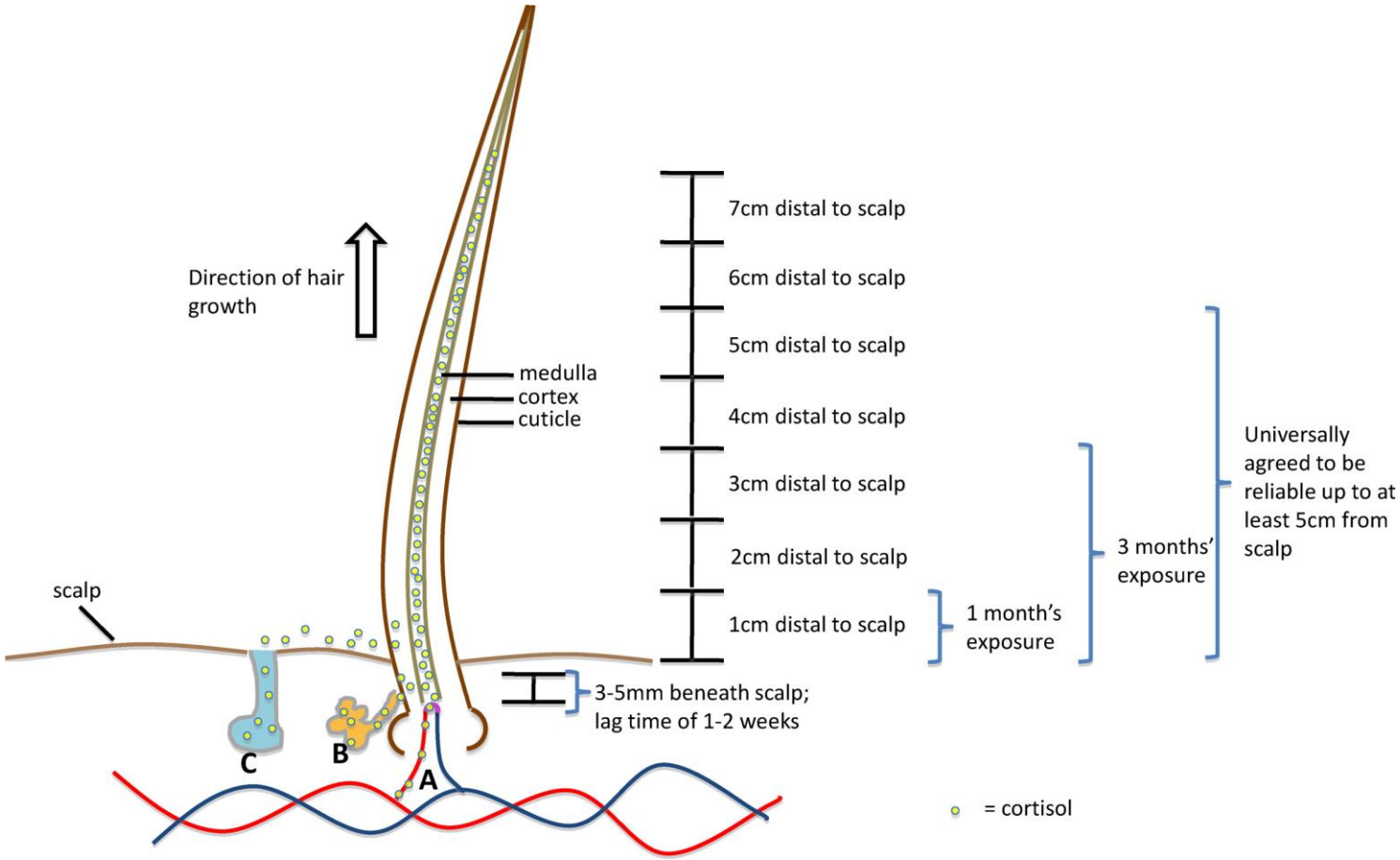


Figure 3. Illustration of the accumulation of cortisol in hair samples (Russell et al., 2012).

Dissertation Tables

Table 1. Risk factors for breast cancer.

Known risk factors	Possible risk factors
• Older age • Ashkenazi Jewish ancestry* • Previous diagnosis of breast cancer • Family history of breast cancer and other cancers • Reproductive history (e.g., early menarche, late or no pregnancy, less breast feeding, lower parity or nulliparity, longer interval between births) • High socio-economic status • Taller adult height** • Physical inactivity • Obesity and higher BMI^{+} • High mammographic density • Alcohol intake • Use of oral contraceptives • Postmenopausal hormone use • Hormone replacement therapy • Exposure to ionizing radiation • Genetic conditions (e.g., Li-Fraumenai syndrome, Ataxia telangiectasia, Cowden syndrome, Peutz-Jeghers syndrome) • Gene mutations (e.g., BRCA1, BRCA2, CHEK2, PALB2) • Atypical hyperplasia	• Adult weight gain • Night shift work • Smoking and second-hand smoke • High birth weight (in association with in utero estrogen exposure) • Some benign breast conditions (e.g., hyperplasia, fibrocystic breast changes, radial scar, complex fibroadenoma, sclerosing adenosis, papillomatosis)

Sources: *Canadian Cancer Society, 2018; Colditz & Rosner, 2000*

**The only identified ethnoculturally-bound risk factor reported by Canadian Cancer Society (2018). Women of Ashkenazi Jewish descent were reported to have a higher risk of developing breast cancer because of a higher likelihood of having a BRCA1 and BRCA2 gene mutation (1 in 40 Ashkenazi women vs. 1 in 500 women in the general population).*

***Tall women are at a greater risk of developing breast cancer after menopause. Rather than height itself, it was suggested that the energy intake and diet, which affect adult height, to be the factors increasing the risk (Canadian Cancer Society, 2018).*

$^{+}$Colditz & Rosner (2000) found that higher BMI was associated with reduced risk of breast cancer in premenopausal women, but an increased risk in post-menopausal women. Canadian Cancer Society (2018) reported that women who have never taken hormone replacement therapy and have a BMI ≥ 31.1 is at 2.5 times greater risk of developing breast cancer than those with a BMI ≤ 22.6

Appendices

Appendix A: TSST protocol and script (for confederates)

Before the participant arrives

Room preparation:

- *There will be three confederates acting as committee members. Each committee member will have a seat behind a table, a pen, and a notepad.*
- *A video camera will be set up and plugged in, but it will not be recording.*
- *A stopwatch for Confederate A to time the tasks*

Confederates

During the experimental procedure, ***confederates will be asked to not give any emotional or verbal feedback to the participant. Respond in a neutral manner, polite (but stern) manner. Do not harass or anger the participant.*** *Only one confederate (A) will be asking questions, and will be introduced as the interviewer sent on behalf of the Hudson's Bay Company to conduct the interviews. The second and third confederates (B & C) will be introduced as individuals who have been trained to monitor nonverbal behaviour during the task. Confederates will be encouraged to take notes on the participant's performance as if were a real interview.*

Experimenter will bring the participant into the room and introduce the participant to the confederates approximately 15 minutes after the participant's arrival. After the introduction and brief explanation, experimenter will bring participant back to the other room to prepare her speech (5 minutes).

What to do if…

- The participant tries to shake the committee members hands → Please stay where you are.
- The participant asks if we have any questions (and used up 5 minutes) → No, we will be moving onto the next task.
- The participant says that they do not want to continue → **Do not force them to continue**. Ask if they would like to try the second task (arithmetic), if so introduce the second task as you normally would: "For your second task,…" If they say no say: "that is ok (with no emotion). That will be all."

First task: Mock Job Interview

After the participant re-enters the experimental room, one of the confederates will pretend to turn on the video camera. Confederate A will let the participant know that she may begin her speech.

If participant's speech is less than 5 minutes:
Confederate A: You still have some time left. Please continue!

If participant finishes before 5 minutes a second time:
Pause briefly (~20 seconds) and proceed with asking prepared questions to fill up the 5 minutes:

- What are your personal strengths and weaknesses?
- Have you had any conflicts with a previous team member or colleague? How did you handle it?
- Where do you see yourself in 5 years?
- What is the most difficult task that you have had to deal with at a previous job?
- What are three traits that you consider to be important in the position you are applying for?
- What makes you better than other applicants for the same position?

Once 5 minutes is over: Confederate A will give the instructions to the second task.

Second task: Arithmetic task

Confederate A: That's fine, thank you. For the second task please serially subtract 13 from 1022, as fast and accurately as possible. If you make a mistake, you will need to restart the task from the beginning. Do you have any questions?

If participant says yes: Confederate A will answer the question.

If the participant does not know what it is meant by a serial subtraction, Confederate A, please define it as counting down by a certain number. For example, to serially subtract 2 from 12, means to start at 12 and to continuously subtract 2 from the answer, so 12, 10, 8, 6, and so on.

(If participant says "no") Confederate A: You may begin.

(If participant makes a mistake) That is incorrect, please start again from 1022.

After 5 minutes: Confederate A: That will be all. We're done, please return to the other room.

1022	476	-70
1009	463	-83
996	450	-96
983	437	-109
970	424	-122
957	411	-135
944	398	-148
931	385	-161
918	372	-174
905	359	-187
892	346	-200
879	333	-213
866	320	-226
853	307	-239
840	294	-252
827	281	-265
814	268	
801	255	
788	242	
775	229	
762	216	
749	203	
736	190	
723	177	
710	164	
697	151	
684	138	
671	125	
658	112	
645	99	
632	86	
619	73	
606	60	
593	47	
580	34	
567	21	
554	8	
541	-5	
528	-18	
515	-31	
502	-44	
489	-57	

Appendix B: Visual Analog Scales: Home-based saliva collection

Day 2 – 12:00PM DATE: _____

Day 2 – 30 MINS AFTER WAKING DATE: _____

Day 2 – WAKING DATE: _____

Day 1 – 9:00PM DATE: _____

Day 1 – 4:00PM DATE: _____

Day 1 – 12:00PM DATE: _____

Day 1 – 30 MINS AFTER WAKING DATE: _____

Day 1 – WAKING DATE: _____

Breast Cancer Study: Recording Book KIT #: _____

If you have any questions please contact Cynthia at uobreastcancerstudy@gmail.com or 613-562-5800, ext. 3892.

Please rinse your mouth at least 10 minutes BEFORE the afternoon sample collections*. Thank you.

DAY 1	DAY 2	LAB DAY
1) Waking	1) Waking	1) Waking
2) 30 minutes after waking	2) 30 minutes after waking	2) 30 minutes after waking
3) 12:00pm*	3) 12:00pm*	3) 12:00pm*
4) 4:00pm*	4) 4:00pm*	
5) 9:00pm*	5) 9:00pm*	**Second laboratory visit**

My second laboratory visit is on: _____ at _____ pm.

Day 2 – 4:00PM DATE: _____

Day 2 – 9:00PM DATE: _____

Instructions for the day of the second laboratory visit

LAB DAY – WAKING DATE: _____

LAB DAY – 30 MINS AFTER WAKING DATE: _____

LAB DAY – 12:00PM DATE: _____

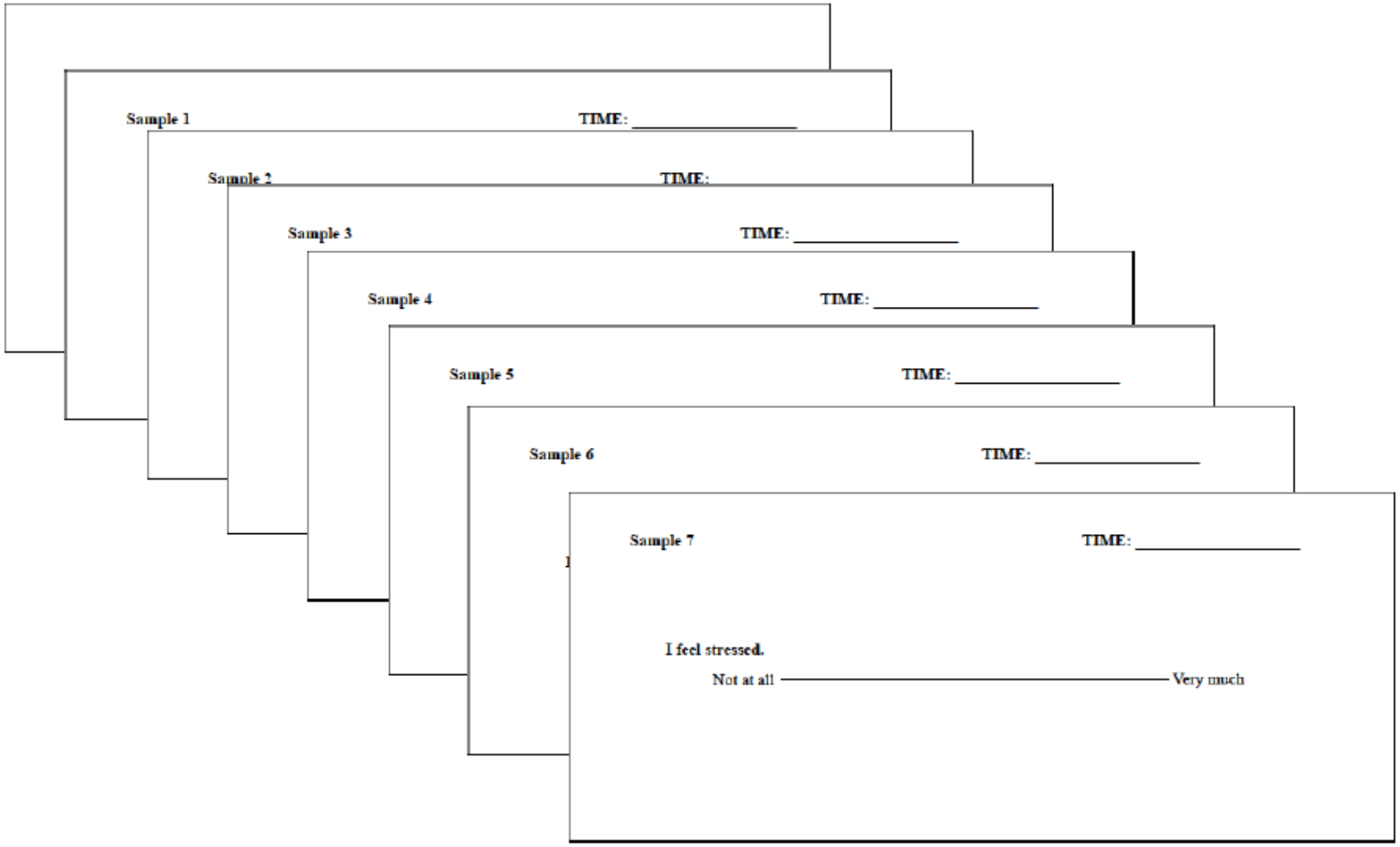
1. What time did you take the sample? _____
2. Have you had a cigarette (or tobacco) in the last hour? _____
3. Have you had any form of caffeine in the last hour (e.g., coffee, soda, energy drinks, etc.)? _____
4. Have you had alcohol in the last 12 hours? _____
5. Have you brushed your teeth in the last hour? _____
6. Have you eaten a big meal in the last hour? _____
7. Have you done any exercise in the last hour? _____

I feel stressed.

Not at all ——————————————— Very much

What were you doing right before you took your sample? _____

Appendix C: Visual Analog Scale: Laboratory Session (TSST)



Appendix D: Home-based saliva collection instructions

The Do's and Don'ts of Saliva Sample Collection

LIST OF THINGS TO AVOID

1. Avoid alcohol consumption **24 hours before** sample collection.

2. Do not eat a major meal **within 60 minutes** of sample collection.

3. Avoid dairy products, foods high in sugar and/or acidity (e.g., candy, soda, oranges, etc.), caffeinated products (e.g., chocolate, coffee, tea, energy drinks), and non-prescription medication **1 hour before** sample collection.

4. Avoid exercising/workingout/training and brushing your teeth 1 hour before sample collection.

LIST OF THINGS TO DO

1. **Rinse your mouth** with water to remove food residue before sample collection (**for afternoon samples only**) and to swallow to increase saliva production.

2. **Wait at least 10 minutes** after rinsing before you collect saliva samples.

3. Put the swab directly under your tongue and leave it there for **three minutes**. When the time is up put the swab back into its appropriate tube, **avoid using your fingers**.

Detailed instructions for saliva sample collection

*****Please DO NOT drink alcohol on the day/night before or on your second lab visit*****

1. On each night before the collection (2 consecutive nights and lab day), please place the collection tubes by your bedside.

2. Please avoid alcohol consumption the day/night before the collection days because alcohol interferes with the stress hormones found in saliva.

3. On each day, please avoid eating, drinking, and brushing your teeth until **both** morning samples are collected (i.e., waking and 30 minutes after waking), as well as one hour before afternoon samples (i.e., 12:00pm, 4:00pm, and 9:00pm).

4. Please keep the saliva samples **refrigerated** until your second lab visit.

5. Fill out the corresponding page in the recording book after each saliva collection.

Specific instructions

MORNING SAMPLES: Waking, 30 minutes after waking

1. Immediately after you wake up, take the tube labeled as *waking* and put the synthetic swab in that tube under your tongue for 3 minutes. **Please stay in bed during the 3 minutes**.
2. Do not eat, drink, smoke, or brush your teeth **until** you have collected the *30 minutes after waking* sample.
3. Refrigerate all saliva samples after collection and fill out recording book.

AFTERNOON SAMPLES: 12:00pm, 4:00pm, 9:00pm

1. Avoid eating and drinking **1 hour** before the scheduled collection time. Please especially avoid the following foods/drinks 1 hour before the collection: non-prescription medication, caffeine (e.g., coffee, tea, chocolate, energy drinks), dairy products, chips, and chewing gum.
2. Avoid exercise and brushing your teeth 1 hour before the scheduled collection time.
3. Rinse your mouth 10 minutes before the scheduled collection time.
4. Place the swab under your tongue for 3 minutes, then place it back into the appropriate tube without touching the swab with your fingers.
5. Refrigerate all saliva samples immediately after collection and fill out recording book.

Appendix E: Sociodemographic Questionnaire (Study 1)

SOCIO-DEMOGRAPHIC QUESTIONNAIRE
The following question involves gathering information with respect to your socio-demographic background. For each question, please circle the appropriate answer.

General history

sd1. What is your ethnic background?
a. White/Caucasian
b. Black (e.g. Haitian, African, Jamaican, Somali)
c. Asian (e.g. Chinese, East Indian, Japanese, Vietnamese)
d. Latino or Hispanic
e. Pacific Islander
f. Middle Eastern
g. Native Canadian/First Nations/Métis
h. Other. Specify: _____

sd2. How old are you? _____

sd3. What is your relationship status?
a. Single
b. Dating
c. Common Law
d. Married/Civil Union
e. Separated/Divorced
f. Widowed

sd4. If you are in a relationship, how long have you been with your partner (months and/or years)? _____

sd5. What level of education have you completed?
a. Elementary School
b. High School
c. College
d. Bachelor's Degree
e. Masters Degree
f. Doctoral Degree

sd6. What is your current work status?
a. Blue collar (construction, factory worker, manual work, etc.)
b. White collar (administrator, lawyer, director, office work, sales, etc.)
c. Business owner or self-worker
d. Unemployed
e. Student
f. Stay at home

g. Medical leave of absence
   If so, what was your employment before? _____
   How long have you been on a medical leave of absence? _____
h. Retired
   If so, what was your employment before? _____
i. Other
   please specify: _____

sd7. What is your current annual family income?
Under $20, 000
a. $20, 000 – $39, 999
b. $40, 000 - $59, 999
c. $60, 000 – $79, 999
d. $80, 000 – $99, 999
e. $100, 000 – $119, 999
f. $120, 000 – $139, 999
g. $140, 000 – $159, 999
h. $160, 000 – $179, 999
i. $180, 000 – $199, 999
j. $200, 000 and above

Breast cancer history
The breast cancer history section is divided in two sections. The first one pertains to an initial breast cancer diagnosis and its treatment, the second section pertains to a recurrence in breast cancer (if this applies) and its treatment.
Initial breast cancer:

sd8. When were you diagnosed with your initial breast cancer? _____/_____
Month Year

sd9. How old were you when you were diagnosed? _____

sd10. What stage of breast cancer were you diagnosed with?
a. Stage 0 (very early or "in situ")
b. Stage I (localized, no spreading)
c. Stage II (some localized spreading into lymph nodes)
d. Stage III (some localized spreading into lymph nodes)
e. Stage IV (metastases, where the cancer has spread to other parts of the body)
f. Not sure

We would like to know more about the treatment you received for your initial breast cancer diagnosis.

sd11. What type of surgery did you have?
a. Unilateral mastectomy
b. Bilateral mastectomy
c. Lumpectomy on one breast

d. Lumpectomy on both breasts
e. No Surgery

sd12. Did you receive chemotherapy?
a. Yes
b. No, but I will (please go directly to question no. 13)
c. No, and I will not (please go directly to question no. 13)

What type of chemotherapy did you receive?
sd12a. I received neoadjuvant chemotherapy only (given before surgery to shrink the size of a tumor)
a. Yes
b. No

sd12b. I received adjuvant chemotherapy only (given after surgery to reduce the risk of recurrence)
a. Yes
b. No

sd12c. I received palliative chemotherapy (used to control the cancer in settings in which the cancer has spread beyond the breast and localized lymph nodes)
a. Yes
b. No

What chemotherapy regimen did you receive?
sd12d. Frequency (e.g. once every three weeks): _____

sd12e. Duration (e.g. 5 months): _____

sd13. Did you receive hormone therapy (or are you still receiving hormone therapy)?
a. Yes
b. No, but I will (please go directly to question no. 14)
c. No, and I will not (please go directly to question no. 14)

Sd13a. What type of hormone therapy did you receive (i.e. Tamoxifen)? _____

Sd13b. How long did you receive hormone therapy for (or how long have you been receiving hormone therapy)? _____

sd14. Did you receive radiation therapy?
a. Yes
b. No, but I will (please go directly to question no. 15)
c. No, and I will not (please go directly to question no. 15)

sd14a. If yes, how many sessions in total did you have? _____
sd15. Have you had breast reconstruction surgery or are you planning on having this surgery?

a. Yes, I have had breast reconstruction surgery
b. Yes, I plan on having breast reconstruction surgery
c. No, I have not, and do not plan on having breast reconstruction surgery

sd16. Have you experienced a recurrence in breast cancer?
a. Yes
b. No (Please go directly to question no. 26)

Recurrence in breast cancer

sd17. When did your recurrence occur? _____/_____
Month Year

sd18. How old were you when you were diagnosed with your recurrence? _____

sd19. What stage of breast cancer were you diagnosed with for this cancer?
a. Stage 0 (very early or "in situ")
b. Stage I (localized, no spreading)
c. Stage II (some localized spreading into lymph nodes)
d. Stage III (some localized spreading into lymph nodes)
e. Stage IV (metastases, where the cancer has spread to other parts of the body)
f. Not sure

sd20. What type of surgery did you have?
a. Unilateral mastectomy
b. Bilateral mastectomy
c. Lumpectomy on one breast
d. Lumpectomy on both breasts
e. No Surgery

sd21. Did you receive chemotherapy?
a. Yes
b. No (please go directly to question no. 22)
c. No, and I will not (please go directly to question no. 22)

What type of chemotherapy did you receive? (Please select all the ones that apply)
sd21a. I received neoadjuvant chemotherapy only (given before surgery to shrink the size of a tumor)
a. Yes
b. No

sd21b. I received adjuvant chemotherapy only (given after surgery to reduce the risk of recurrence)
a. Yes
b. No

sd21c. I received palliative chemotherapy (used to control the cancer in settings in which the

cancer has spread beyond the breast and localized lymph nodes)

a. Yes
b. No

sd22. Did you receive hormone therapy (or are you still receiving hormone therapy)?

a. Yes
b. No, but I will (please go directly to question no. 23)
c. No, and I will not (please go directly to question no. 23)

sd22a. What type of hormone therapy did you receive (i.e. Tamoxifen)? _____

sd22b. How long did you receive hormone therapy for (or how long have you been receiving hormone therapy)? _____

sd23. Did you receive radiation therapy?

a. Yes
b. No, but I will (please go directly to question no. 24)
c. No, and I will not (please go directly to question no. 24)

sd23a. If yes, how many sessions in total did you have? _____

sd24. Have you had breast reconstruction surgery or are you planning on having this surgery?

a. Yes, I have had breast reconstruction surgery
b. Yes, I plan on having breast reconstruction surgery
c. No, I have not, and do not plan on having breast reconstruction surgery

sd25. Have you experienced a recurrence in breast cancer?

a. Yes (Please complete the "recurrence in breast cancer" section)
b. No (Please skip to the "other health history" section)

Other health history

sd26. Have you been diagnosed with another cancer (of any type) after being diagnosed with breast cancer (apart from breast cancer recurrence)?

a. Yes
b. No (if no, please go directly to question no. 27)

sd26a. What kind of cancer were you diagnosed with? _____

sd26b. When were you diagnosed? _____

sd26c. How was it treated? Please indicate whether you had surgery, chemotherapy, hormone therapy, radiation therapy, or another treatment:

_____

sd27. Have you ever had a chronic medical condition other than breast cancer (e.g. diabetes, high blood pressure, multiple sclerosis, etc.)?

a. Yes. Please specify: _____
b. No (if no, please go to question no. 28)

sd27a. How much do you worry about this (these) medical condition(s)?

a. Not at all
b. A little bit
c. A lot
d. All the time

sd27b. Does (Do) this (these) medical condition(s) interfere with your daily activities?

a. Not at all
b. A little bit
c. A lot
d. All the time

Habits

sd28. Do you take any prescribed medication? If so, please list the name(s) and dose(s):
_____
_____

sd29. Please indicate the average amount of alcoholic beverages you consume per day.

a. 0-1
b. 2-3
c. 4-5
d. 6-7
e. 8 +

sd30. Please indicate the average amount of caffeinated beverages you consume per day.

a. 0-1
b. 2-3
c. 4-5
d. 6-7
e. 8 +

sd31. Do you smoke cigarettes? _____

a. Yes
b. No (if no, please go directly to question no. 33)

sd32. If so, please indicate the average amount of cigarettes you smoke per day?

a. Half a pack or less
b. 1 pack
c. 1 . pack
d. 2 packs or more

sd33. How often do you brush your teeth?

a. Two times or more per day
b. One time per day
c. One time every two days
d. Less than one time every two days

sd34. When you brush your teeth, is there blood in your saliva?

a. Always
b. Often
c. Sometimes
d. Never

sd35. When was your last visit to the dentist?

a. Within the last 6 months
b. Within the last year
c. Within the last 18 months
d. Within the last 24 months
e. More than 24 months ago

sd36. How often do you do cardiovascular exercise?

a. Once a week or less
b. Two to three times a week
c. Four to five times a week
d. Six to seven times a week
e. More than seven times a week

Appendix F: Questionnaire package – Visit 1 (Study 2 and 3**)**

BREAST CANCER STUDY

Cultural Differences in
Breast Cancer Survivorship

Visit #1

PLEASE DO NOT WRITE IN THIS AREA

Participant ID #: _____

Date Completed: _____

Initials of Experimenter: _____

Date Data Entered: _____

uOttawa

In collaboration with Ryerson University, Department of Psychology, 350 Victoria Street, Toronto, ON, M5B 2K3.

RYERSON UNIVERSITY

This questionnaire asks various general questions such as the extent of fatigue you feel, perception of stress, and amount of physical activity you engage in.

Each section has directions, in bold type, on how to answer the questions. If a question does not apply to you, please write NA (not applicable) in the space provided. If you do not feel comfortable answering a question, please draw a slash through it and go to the next question.

When you have finished answering the questionnaire, please notify the experimenter. All of your answers are completely confidential and anonymous, please answer as honestly as possible.

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BFS

Read each item carefully and indicate which comes closest to how you have been feeling in the past two weeks, do not take too long over your replies.

	Better than usual	**No more than usual**	**Worse than usual**	**Much worse than usual**	
	1	**2**	**3**	**4**	
1. Do you have problems with tiredness?	1	2	3	4	
2. Do you need to rest more?	1	2	3	4	
3. Do you feel sleepy or drowsy?	1	2	3	4	
4. Do you have problems starting things?	1	2	3	4	
5. Are you lacking in energy?	1	2	3	4	
6. Do you have less strength in your muscles?	1	2	3	4	
7. Do you feel weak?	1	2	3	4	
8. Do you have difficulty concentrating?	1	2	3	4	
9. Do you have problems thinking clearly?	1	2	3	4	
10.Do you make slips of the tongue when speaking?	1	2	3	4	
11. How is your memory?	1	2	3	4	

PSQI

The following questions relate to your usual sleep habits during the past month *only*. Your answers should indicate the most accurate reply for the *majority* of days an nights in the past month. Please answer all questions.

1. During the past month, when have you usually gone to bed? **Usual bed time: _____**
2. During the past month, how long (in minutes) has it usually take you to fall asleep each night? **Number of minutes: _____**
3. During the past month, when have you usually gotten up in the morning? **Usual getting up time: _____**
4. During the past month, how many hours of *actual sleep* did you get at night? (This may be different than the number of hours you spend in bed). **Hours of sleep per night: _____**

For each of the remaining questions, check the one best response. Please answer *all* questions.

5. During the past month, how often have you had trouble sleeping because you…

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a) Cannot get to sleep within 30 minutes	☐	☐	☐	☐
b) Wake up in the middle of the night or early morning	☐	☐	☐	☐
c) Have to get up to use the bathroom	☐	☐	☐	☐
d) Cannot breathe comfortably	☐	☐	☐	☐
e) Cough or snore loudly	☐	☐	☐	☐
f) Feel too cold	☐	☐	☐	☐
g) Feel too hot	☐	☐	☐	☐

PSQI

For each of the remaining questions, check the one best response. Please answer *all* questions.

5. During the past month, how often have you had trouble sleeping because you…

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
h) Had bad dreams	☐	☐	☐	☐
i) Have pain	☐	☐	☐	☐
Other reason(s), please describe in the space provided below:				
j)	☐	☐	☐	☐
k)	☐	☐	☐	☐
l)	☐	☐	☐	☐

PSQI

For each of the remaining questions, check the one best response. Please answer *all* questions.

6. During the past month, how would your rate your sleep quality overall?

☐ Very good ☐ Fairly good ☐ Fairly bad ☐ Very bad

7. During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?

☐ Not during the past month ☐ Less than once a week
☐ Once or twice a week ☐ Three or more times a week

8. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?

☐ Not during the past month ☐ Less than once a week
☐ Once or twice a week ☐ Three or more times a week

9. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?

☐ No problem at all ☐ Only a very slight problem
☐ Somewhat of a problem ☐ A very big problem

10. Do you have a bed partner or roommate?

☐ No bed partner or roommate ☐ Partner/roommate in other room
☐ Partner in same room, but not same bed ☐ Partner in same bed

If you have a roommate or bed partner, ask him/her how often in the past month you have had…

	Not during the past month	**Less than once a week**	**Once or twice a week**	**Three or more times a week**
a) Loud snoring	☐	☐	☐	☐
b) Long pauses between breaths while asleep	☐	☐	☐	☐

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PSQI

For each of the remaining questions, check the one best response. Please answer *all* questions.

If you have a roommate or bed partner, ask him/her how often in the past month you have had…

	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
c) Legs twitching or jerking while you sleep	☐	☐	☐	☐
d) Episodes of disorientation or confusion during sleep	☐	☐	☐	☐
Other restlessness while you sleep; please describe in the space provided below:				
e)	☐	☐	☐	☐
f)	☐	☐	☐	☐
g)	☐	☐	☐	☐

PSS-M

The questions in this scale ask you about your feelings and thoughts during the last month and during the past three months (in general). In each case, you will be asked to indicate *how often* you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

For each question, choose among the following alternatives:

Never	Almost never	Sometimes	Fairly often	Very often
0	1	2	3	4

	In the last month	In general, during the last three months
1. How often have you been upset because of something that happened unexpectedly?	_____	_____
2. How often have you felt that you were unable to control the important things in your life?	_____	_____
3. How often have you felt nervous and "stressed"?	_____	_____
4. How often have you dealt successfully with irritating life hassles?	_____	_____
5. How often have you felt that you were effectively coping with important changes that were occurring in your life?	_____	_____
6. How often have you felt confident about your ability to handle your personal problems?	_____	_____
7. How often have you felt that things were going your way?	_____	_____

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PSS-M

For each question, choose among the following alternatives:

Never	Almost never	Sometimes	Fairly often	Very often
0	1	2	3	4

	During the past month	In general, during the past three months
8. How often have you found that you could not cope with all the things that you had to do?	_____	_____
9. How often have you been able to control irritations in your life?	_____	_____
10. How often have you felt that you were on top of things?	_____	_____
11. How often have you been angered because of things that happened that were outside of your control?	_____	_____
12. How often have you found yourself thinking about things that you have to accomplish?	_____	_____
13. How often have you been able to control the way you spend your time?	_____	_____
14. How often have you felt difficulties were piling up so high that you could not overcome them?	_____	_____

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GSQ

1. **Considering a <u>7-day period</u> (a week), how many times on the average do you do the following kinds of exercise <u>for more than 15 minutes</u> during your free time?**

   Write on each line the appropriate number.

	Times per week
A. Strenuous exercise (heart beats rapidly) I.e., running, jogging, hockey, football, soccer, squash, basketball, cross country skiing, judo, roller skating, vigorous swimming, vigorous long distance bicycling. Other: _____	_____
B. Moderate exercise (not exhausting) I.e., fast walking, baseball, tennis, easy bicycling, volleyball, badminton, easy swimming, alpine skiing, popular and folk dancing. Other: _____	_____
C. Mild exercise (minimal effort) I.e., yoga, archery, fishing, bowling, horseshoes, golf, snow-mobiling, easy walking. Other: _____	_____

2. **Considering a <u>7-day period</u> (a week), during your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?**

   ☐ Often ☐ Sometimes ☐ Never/Rarely

CERQ

How do you cope with events? Everyone gets confronted with negative or unpleasant events now and then and everyone responds to them in his or her own way. By the following questions you are asked to indicate what you generally think, when you experience negative or unpleasant events.

(Almost) Never	Sometimes	Regularly	Often	(Almost) Always
1	2	3	4	5

1. I feel that I am the one to blame for it.	1	2	3	4	5
2. I think that I have to accept that this has happened.	1	2	3	4	5
3. I often think about how I feel about what I have experienced.	1	2	3	4	5
4. I think of nicer things than what I have experienced.	1	2	3	4	5
5. I think of what I can do best.	1	2	3	4	5
6. I think I can learn something from the situation.	1	2	3	4	5
7. I think that it all could have been much worse.	1	2	3	4	5
8. I often think that what I have experienced is much worse than what others have experienced.	1	2	3	4	5
9. I feel that others are to blame for it.	1	2	3	4	5
10. I feel that I am the one who is responsible for what has happened.	1	2	3	4	5
11. I think that I have to accept the situation.	1	2	3	4	5
12. I am preoccupied with what I think and feel about what I have experienced.	1	2	3	4	5
13. I think of pleasant things that have nothing to do with it.	1	2	3	4	5

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CERQ

How do you cope with events? Everyone gets confronted with negative or unpleasant events now and then and everyone responds to them in his or her own way. By the following questions you are asked to indicate what you generally think, when you experience negative or unpleasant events.

(Almost) Never	Sometimes	Regularly	Often	(Almost) Always
1	2	3	4	5

14. I think about how I can best cope with the situation.	1	2	3	4	5
15. I think that I can become a stronger person as a result of what has happened.	1	2	3	4	5
16. I think that other people go through much worse experiences.	1	2	3	4	5
17. I keep thinking about how terrible it is what I have experienced.	1	2	3	4	5
18. I feel that others are responsible for what has happened.	1	2	3	4	5
19. I think about the mistakes I have made in this matter.	1	2	3	4	5
20. I think that I cannot change anything about it.	1	2	3	4	5
21. I want to understand why I feel the way I do about what I have experienced.	1	2	3	4	5
22. I think of something nice instead of what has happened.	1	2	3	4	5
23. I think about how to change the situation.	1	2	3	4	5
24. I think that the situation also has its positive sides.	1	2	3	4	5
25. I think that it hasn't been too bad compared to other things.	1	2	3	4	5
26. I often think that what I have experienced is the worst that can happen to a person.	1	2	3	4	5

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CERQ

How do you cope with events? Everyone gets confronted with negative or unpleasant events now and then and everyone responds to them in his or her own way. By the following questions you are asked to indicate what you generally think, when you experience negative or unpleasant events.

(Almost) Never	Sometimes	Regularly	Often	(Almost) Always
1	2	3	4	5

27. I think about the mistakes others have made in this matter.	1	2	3	4	5
28. I think that basically the cause must lie within myself.	1	2	3	4	5
29. I think that I must learn to live with it.	1	2	3	4	5
30. I dwell upon the feelings the situation has evoked in me.	1	2	3	4	5
31. I think about pleasant experiences.	1	2	3	4	5
32. I think about a plan of what I can do best.	1	2	3	4	5
33. I look for the positive sides to the matter.	1	2	3	4	5
34. I tell myself that there are worse things in life.	1	2	3	4	5
35. I continually think how horrible the situation has been.	1	2	3	4	5
36. I feel that basically the cause lies with others.	1	2	3	4	5

HCTH

The following questions involve gathering information specific to the history of your hair care. For each question, please check the appropriate answer.

1. What is your natural hair colour?

   ☐ Black ☐ Brown ☐ Blonde ☐ Red ☐ Other: _____

2. My hair is naturally…

   ☐ Straight ☐ Curly ☐ Wavy ☐ Other: _____

3. On a typical week (7 days), how often do you wash (i.e., shampoo and/or condition) your hair?

   ☐ Once ☐ Twice ☐ Three times
   ☐ Four times ☐ Five times ☐ Six times
   ☐ I wash my hair everyday

4. Have you ever chemically treated your hair (e.g., perm, straightening, semi-permanent colour, highlights/lowlights, bleach etc.)?

   ☐ Yes ☐ No (please skip to question 5)

   a. If yes, what chemical treatment(s) did you have in the past year and what were the effects? E.g., Dyed my hair (brown), permed my hair, added highlights (blonde)

   _____

   _____

   b. What is your most recent treatment? _____

   c. When was your most recent treatment? _____ _____
   Month Year

5. How many hours has it been since you last washed (i.e., shampoo and/or condition) your hair? _____

If you wish to make any comments about your answers for this questionnaire, please feel free to write as much or as little as you in the space below.

Thank you for your comments. Please let the experimenter know that you are done.

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Appendix G: Questionnaire package – Visit 2 (Study 2 and 3)

BREAST CANCER STUDY

Cultural Differences in Breast Cancer Survivorship

Visit #2

PLEASE DO NOT WRITE IN THIS AREA

Participant ID #: _____

Date Completed: _____

Initials of Experimenter: _____

Date Data Entered: _____

uOttawa

In collaboration with Ryerson University, Department of Psychology, 350 Victoria Street, Toronto, ON, M5B 2K3.

RYERSON UNIVERSITY

This questionnaire asks about your sociodemographic information, medical history, perception of stress, and emotional health.

Each section has directions, in bold type, on how to answer the questions. If a question does not apply to you, please write NA (not applicable) in the space provided. If you do not feel comfortable answering a question, please draw a slash through it and go to the next question.

When you have finished answering the questionnaire, please notify the experimenter. All of your answers are completely confidential and anonymous, please answer as honestly as possible.

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SDQ-BC

The following questions involve gathering information with respect to your socio-demographic background. For each question, please check the appropriate answer.

1. What is your ethnic background?
   - ☐ White/Caucasian
   - ☐ Black (e.g., Haitian, African, Jamaican, Somali)
   - ☐ Asian (e.g., Chinese, East Indian, Japanese, Vietnamese)
   - ☐ Latino or Hispanic
   - ☐ Pacific Islander
   - ☐ Middle Eastern
   - ☐ Native Canadian/First Nations/Métis
   - ☐ Other. Please specify: _____

2. Were you born in Canada? ☐ No ☐ Yes (please skip to question 3)
   a. If no, what country were you born in? _____
   b. If no, at what age did you move to Canada? _____
   c. If no, when did you move to Canada (e.g., 1999)? _____

3. How old are you? _____

4. What is your current relationship status?
   - ☐ Single
   - ☐ Married/Civil union
   - ☐ Dating
   - ☐ Separated/Divorced
   - ☐ Common law
   - ☐ Widowed

5. If you are currently in a relationship, how long you been with your partner (months and/or years)? _____

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6. What level of education have you completed?

- ☐ Elementary school
- ☐ High school
- ☐ College
- ☐ Bachelor's degree
- ☐ Master's degree
- ☐ Doctoral degree

7. What is your current work status?

- ☐ Blue collar (e.g., construction, factory worker, manual work, etc.)
- ☐ White collar (e.g., administrator, lawyer, director, office work, sales, etc.)
- ☐ Business owner or self-employed
- ☐ Unemployed or retired
- ☐ Student
- ☐ Homemaker/stay at home
- ☐ Medical leave of absence
  - a. If so, what was your employment before? _____
  - b. How long have you been on medical leave of absence? _____

8. What is your current annual family income?

- ☐ Under $20 000
- ☐ $20 000 - $39 999
- ☐ $40 000 - $59 999
- ☐ $60 000 - $79 999
- ☐ $80 000 - $99 999
- ☐ $100 000 - $119 999
- ☐ $120 000 - $139 999
- ☐ $140 000 - $159 999
- ☐ $160 000 - $179 999
- ☐ $180 000 - $199 999
- ☐ $200 000 and above

SDQ-BC

Breast cancer history

The breast cancer history section is divided into two sections. The first one pertains to an initial breast cancer diagnosis and its treatment, the second section pertains to a recurrence in a breast cancer (if this applies) and its treatment.

Initial breast cancer

9. When were you diagnosed with your initial breast cancer? _____ / _____
   Month Year

10. How old were you when you were diagnosed? _____ years old

11. What stage of breast cancer were you diagnosed with?

- ☐ Stage 0 (very early or "in situ")
- ☐ Stage I (localized, no spreading)
- ☐ Stage II (some localized spreading into lymph nodes)
- ☐ Stage III (some localized spreading into lymph nodes)
- ☐ Stage IV (metastases, where the cancer has spread to other parts of the body)
- ☐ Not sure

We would like to know more about the treatment you received for your initial breast cancer diagnosis.

12. What type of surgery did you have?

- ☐ Unilateral mastectomy
- ☐ Bilateral mastectomy
- ☐ Lumpectomy on one breast
- ☐ Lumpectomy on both breasts
- ☐ No surgery

SDQ-BC

13. Did you receive chemotherapy?

☐ No, but I will (please skip to question 14)

☐ No, and I will not (please skip to question 14)

☐ Yes (if yes, answer the questions below)

What type of chemotherapy did you receive?

a. I receive neoadjuvant chemotherapy only (given before surgery to shrink the size of a tumor). ☐ Yes ☐ No

b. I received adjuvant chemotherapy only (given after surgery to reduce the risk of recurrence). ☐ Yes ☐ No

c. I received palliative chemotherapy (used to control the cancer in settings in which the cancer has spread beyond the breast and localized lymph nodes).

☐ Yes ☐ No

What chemotherapy regimen did you receive?

d. Frequency (e.g., once every three weeks): _____

e. Duration (e.g., 5 months): _____

14. Did you receive hormone therapy (or are you still receiving hormone therapy)?

☐ No, but I will (please skip to question 15)

☐ No, and I will not (please skip to question 15)

☐ Yes (if yes, answer the questions below)

a) What type of hormone therapy did you receive (i.e., Tamoxifen)?

_____

b) How long did you receive hormone therapy for (or how long have you been receiving hormone therapy)? _____

15. Did you receive radiation therapy?

☐ No, but I will (please skip to question 16)

☐ No, and I will not (please skip to question 16)

☐ Yes (if yes, answer the question below)

How many sessions in total did you have? _____

16. Have you had breast reconstruction surgery or are you planning on having this surgery?

☐ No, I have not, and do not plan on having breast reconstruction surgery

☐ Yes, I plan on having breast reconstruction surgery

☐ Yes, I have had breast reconstruction surgery

17. Have you experienced a recurrence in breast cancer?

☐ No (please skip to question 26)

☐ Yes

Recurrence in breast cancer

18. When did your recurrence occur? _____ / _____
Month Year

19. How old were you when you were diagnosed with your recurrence? _____ years old

20. What stage of breast cancer were you diagnosed with for this cancer?

☐ Stage 0 (very early or "in situ")

☐ Stage I (localized, no spreading)

☐ Stage II (some localized spreading into lymph nodes)

☐ Stage III (some localized spreading into lymph nodes)

☐ Stage IV (metastases, where the cancer has spread to other parts of the body)

☐ Not sure

SDQ-BC

21. What type of surgery did you have?

☐ Unilateral mastectomy
☐ Bilateral mastectomy
☐ Lumpectomy on one breast
☐ Lumpectomy on both breasts
☐ No surgery

22. Did you receive chemotherapy?

☐ No, but I will (please skip to question 23)
☐ No, and I will not (please skip to question 23)
☐ Yes (if yes, answer the questions below

What type of chemotherapy did you receive? (Please select all the ones that apply):

a. I receive neoadjuvant chemotherapy only (given before surgery to shrink the size of a tumor). ☐ Yes ☐ No

b. I received adjuvant chemotherapy only (given after surgery to reduce the risk of recurrence). ☐ Yes ☐ No

c. I received palliative chemotherapy (used to control the cancer in settings in which the cancer has spread beyond the breast and localized lymph nodes).
☐ Yes ☐ No

23. Did you receive hormone therapy (or are you still receiving hormone therapy)?

☐ No, but I will (please skip to question 24)
☐ No, and I will not (please skip to question 24)
☐ Yes (if yes, answer the questions below)

a. What type of hormone therapy did you receive (i.e., Tamoxifen)?
_____

b. How long did you receive hormone therapy for (or how long have you been receiving hormone therapy)? _____

24. Did you receive radiation therapy?

☐ No, but I will (please skip to question 25)

☐ No, and I will not (please skip to question 25)

☐ Yes (if yes, answer the question below)

a. How many sessions in total did you have? _____

25. Have you had breast reconstruction surgery or are you planning on having this surgery?

☐ No, I have not, and do not plan on having breast reconstruction surgery

☐ Yes, I plan on having breast reconstruction surgery

☐ Yes, I have had breast reconstruction surgery

Other health history

26. Have you been diagnosed with cancer (of any type, other than breast cancer)?

☐ No (if no, please skip to question 27)

☐ Yes. If yes, answer the following:

a. What kind of cancer were you diagnosed with? _____

b. When were you diagnosed? _____

c. How was it treated? Please indicate whether you had *surgery*, *chemotherapy*, *hormone therapy, radiation therapy,* or another treatment:

_____

27. Have you ever had a chronic medical condition (e.g., diabetes, high blood pressure, multiple sclerosis, etc.)?

☐ No (if no, please skip to question 28)

☐ Yes. If yes, answer the following:

a. How much do your worry about this (these) medical condition(s)?

☐ Not at all ☐ A little bit ☐ A lot ☐ All the time

b. Does (Do) this (these) medical condition(s) interfere with your daily activities?

☐ Not at all ☐ A little bit ☐ A lot ☐ All the time

Habits

28. Do you take any prescribed medication(s)?

☐ No (if no, please skip to question 29)

☐ Yes. Please list the name(s) and dose(s):

_____

_____

_____

29. Please indicate the average amount of alcoholic beverages you consume per day.

☐ 0-1 ☐ 2-3 ☐ 4-5 ☐ 6-7 ☐ 8+

30. Please indicate the average amount of caffeinated beverages you consume per day.

☐ 0-1 ☐ 2-3 ☐ 4-5 ☐ 6-7 ☐ 8+

31. Do you smoke cigarettes? ☐ Yes ☐ No (if no, please go to question 32)

a. If yes, please indicate the average amount of cigarettes you smoke per day.

☐ Half a pack or less ☐ 1 pack ☐ 1.5 packs ☐ 2 packs or more

SDQ-BC

32. How often do you brush your teeth?

- ☐ Two or more times per day
- ☐ Once a day
- ☐ Once every two days
- ☐ Less than once every two days

33. When you brush your teeth, is there blood in your saliva?

☐ Always ☐ Often ☐ Sometimes ☐ Never

34. When was your last visit to the dentist?

- ☐ Within the last 6 months
- ☐ Within the last year
- ☐ Within the last 18 months
- ☐ Within the last 24 months
- ☐ More than 24 months ago

35. How often do you do cardiovascular exercise?

- ☐ Once a week or less
- ☐ Two to three times a week
- ☐ Four to five times a week
- ☐ Six to seven times a week
- ☐ More than seven times a week

GEQ-CH

Please use the following scale to indicate how much you agree with the following statements. Circle your response.

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
	1	2	3	4	5
1. I was raised in a way that was Chinese.	1	2	3	4	5
2. When I was growing up, I was exposed to Chinese culture.	1	2	3	4	5
3. Now, I am exposed to Chinese culture.	1	2	3	4	5
4. Compared to how much I negatively criticize other cultures, I criticize Chinese culture less.	1	2	3	4	5
5. I am embarrassed/ashamed of Chinese culture.	1	2	3	4	5
6. I am proud of Chinese culture.	1	2	3	4	5
7. Chinese culture has had a positive impact on my life.	1	2	3	4	5
8. I believe that my children should read, write, and speak Chinese.	1	2	3	4	5
9. I have a strong belief that my children should have Chinese names only.	1	2	3	4	5
10. I go to places where people are Chinese.	1	2	3	4	5
11. I am familiar with Chinese cultural practices and customs.	1	2	3	4	5
12. I relate to my partner or spouse in a way that is Chinese.	1	2	3	4	5
13. I admire people who are Chinese.	1	2	3	4	5
14. I would prefer to live in a Chinese community.	1	2	3	4	5
15. I listen to Chinese music.	1	2	3	4	5

GEQ-CH

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1	2	3	4	5

16. I perform Chinese dance.	1	2	3	4	5
17. I engage in Chinese forms of recreation.	1	2	3	4	5
18. I celebrate Chinese holidays.	1	2	3	4	5
19. At home, I eat Chinese food.	1	2	3	4	5
20. At restaurants, I eat Chinese food.	1	2	3	4	5
21. When I was a child, my friends were Chinese.	1	2	3	4	5
22. Now, my friends are Chinese.	1	2	3	4	5
23. I wish to be accepted by Chinese.	1	2	3	4	5
24. The people I date are Chinese.	1	2	3	4	5
25. Overall, I am Chinese.	1	2	3	4	5

Please use the following scale to answer the following questions. Circle your response.

Very much	Much	Somewhat	A little	Not at all
1	2	3	4	5

26. How much do you speak Chinese *at home*?	1	2	3	4	5
27. How much do you speak Chinese *at school*?	1	2	3	4	5
28. How much do you speak Chinese *at work*?	1	2	3	4	5
29. How much do you speak Chinese *at prayer*?	1	2	3	4	5

GEQ-CH

Very much	Much	Somewhat	A little	Not at all
1	2	3	4	5

	1	2	3	4	5
30. How much do you speak Chinese *with friends*?	1	2	3	4	5
31. How much do you view, read, or listen to Chinese *on TV*?	1	2	3	4	5
32. How much do you view, read, or listen to Chinese *in film*?	1	2	3	4	5
33. How much do your view, read, or listen to Chinese *on the radio*?	1	2	3	4	5
34. How much do you view, read, or listen to Chinese *in literature*?	1	2	3	4	5
35. How fluently do you *speak* Chinese?	1	2	3	4	5
36. How fluently do you *read* Chinese?	1	2	3	4	5
37. How fluently do you *write* Chinese?	1	2	3	4	5
38. How fluently do you *understand* Chinese?	1	2	3	4	5
39. Are you bilingual? (please circle)					
If yes, what languages?			Yes	No	
1) _____					
2) _____					

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GEQ-CA

Please use the following scale to indicate how much you agree with the following statements. Circle your response.

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1	2	3	4	5

1. I was raised in a way that was Canadian.	1	2	3	4	5
2. When I was growing up, I was exposed to Canadian culture.	1	2	3	4	5
3. Now, I am exposed to Canadian culture.	1	2	3	4	5
4. Compared to how much I negatively criticize other cultures, I criticize Canadian culture less.	1	2	3	4	5
5. I am embarrassed/ashamed of Canadian culture.	1	2	3	4	5
6. I am proud of Canadian culture.	1	2	3	4	5
7. Canadian culture has had a positive impact on my life.	1	2	3	4	5
8. I believe that my children should read, write, and speak Canadian.	1	2	3	4	5
9. I have a strong belief that my children should have Canadian names only.	1	2	3	4	5
10. I go to places where people are Canadian.	1	2	3	4	5
11. I am familiar with Canadian cultural practices and customs.	1	2	3	4	5
12. I relate to my partner or spouse in a way that is Canadian.	1	2	3	4	5
13. I admire people who are Canadian.	1	2	3	4	5
14. I would prefer to live in a Canadian community.	1	2	3	4	5
15. I listen to Canadian music.	1	2	3	4	5

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GEQ-CA

Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
1	2	3	4	5

16. I perform Canadian dance.	1	2	3	4	5
17. I engage in Canadian forms of recreation.	1	2	3	4	5
18. I celebrate Canadian holidays.	1	2	3	4	5
19. At home, I eat Canadian food.	1	2	3	4	5
20. At restaurants, I eat Canadian food.	1	2	3	4	5
21. When I was a child, my friends were Canadian.	1	2	3	4	5
22. Now, my friends are Canadian.	1	2	3	4	5
23. I wish to be accepted by Canadian.	1	2	3	4	5
24. The people I date are Canadian.	1	2	3	4	5
25. Overall, I am Canadian.	1	2	3	4	5

Please use the following scale to answer the following questions. Circle your response.

Very much	Much	Somewhat	A little	Not at all
1	2	3	4	5

26. How much do you speak English *at home*?	1	2	3	4	5
27. How much do you speak English *at school*?	1	2	3	4	5
28. How much do you speak English *at work*?	1	2	3	4	5
29. How much do you speak English *at prayer*?	1	2	3	4	5

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GEQ-CA

Very much	Much	Somewhat	A little	Not at all
1	2	3	4	5

	1	2	3	4	5
30. How much do you speak English *with friends*?	1	2	3	4	5
31. How much do you view, read, or listen to English *on TV*?	1	2	3	4	5
32. How much do you view, read, or listen to English *in film*?	1	2	3	4	5
33. How much do your view, read, or listen to English *on the radio*?	1	2	3	4	5
34. How much do you view, read, or listen to English *in literature*?	1	2	3	4	5
35. How fluently do you *speak* English?	1	2	3	4	5
36. How fluently do you *read* English?	1	2	3	4	5
37. How fluently do you *write* English?	1	2	3	4	5
38. How fluently do you *understand* English?	1	2	3	4	5

DSI

Below are listed a variety of events that may be viewed as stressful or unpleasant. Read each item carefully and decide whether or not that event occurred within the past *24 hours*.

If the event *did not* occur, place an "0" in the space next to that item. If the event *did* occur, indicate the amount of stress that it caused you by placing a number from 1 to 7 in the space next to that item (see numbers below).

Did not occur	Was not stressful	Caused very little stress	Caused a little stress	Caused some stress	Caused much stress	Caused very much stress	Caused me to panic
0	1	2	3	4	5	6	7

1. Performed poorly at task _____
2. Performed poorly due to others _____
3. Thought about unfinished work _____
4. Hurried to meet deadline _____
5. Interrupted during task/activity _____
6. Someone spoiled your completed task _____
7. Did something you are unskilled at _____
8. Unable to complete a task _____
9. Was unorganized _____
10. Criticized or verbally attacked _____
11. Ignored by others _____
12. Spoke or performed in public _____
13. Dealt with rude waiter/waitress/salesperson _____
14. Interrupted while talking _____
15. Was forced to socialize _____

DSI

Did not occur	Was not stressful	Caused very little stress	Caused a little stress	Caused some stress	Caused much stress	Caused very much stress	Caused me to panic
0	1	2	3	4	5	6	7

16. Someone broke a promise/appointment _____
17. Competed with someone _____
18. Was stared at _____
19. Did not hear from someone you expected to hear from _____
20. Experienced unwanted physical contact (crowded/pushed) _____
21. Was misunderstood _____
22. Was embarrassed _____
23. Had your sleep disturbed _____
24. Forgot something _____
25. Feared illness/pregnancy _____
26. Experienced illness/physical discomfort _____
27. Someone borrowed something without your permission _____
28. Your property was damaged _____
29. Had minor accident (broke something, tore clothing) _____
30. Thought about the future _____
31. Ran out of food/personal article _____
32. Argued with spouse/boyfriend/girlfriend _____
33. Argued with another person _____
34. Waited longer than you wanted _____
35. Interrupted while thinking/relaxing _____
36. Someone "cut" ahead of you in a line _____

DSI

Did not occur	Was not stressful	Caused very little stress	Caused a little stress	Caused some stress	Caused much stress	Caused very much stress	Caused me to panic
0	1	2	3	4	5	6	7

37. Performed poorly at sport/game _____
38. Did something that you did not want to do _____
39. Unable to complete all plans for today _____
40. Had car trouble _____
41. Had difficulty in traffic _____
42. Money problems _____
43. Store lacked a desired item _____
44. Misplaced something _____
45. Bad weather _____
46. Unexpected expenses (fines, traffic ticket, etc.) _____
47. Had confrontation with an authority figure _____
48. Heard some bad news _____
49. Concerned over personal appearance _____
50. Exposed to feared situation or object _____
51. Exposed to upsetting TV show, movie, book _____
52. "Pet peeve" violated (someone fails to knock, etc.) _____
53. Failed to understand something _____
54. Worried about another's problems _____
55. Experienced narrow escape from danger. _____
56. Stopped unwanted personal habit (overeating, smoking, nail biting) _____
57. Had problem with kid(s) _____

DSI

Did not occur	Was not stressful	Caused very little stress	Caused a little stress	Caused some stress	Caused much stress	Caused very much stress	Caused me to panic
0	1	2	3	4	5	6	7

58. Was late for work/appointment _____

Any stressors that we missed? List below, followed by rating.

59. _____ _____

60. _____ _____

61. _____ _____

62. _____ _____

63. _____ _____

64. _____ _____

65. _____ _____

66. _____ _____

67. _____ _____

68. _____ _____

69. _____ _____

70. _____ _____

PSS

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, you will be asked to indicate *how often* you felt or thought a certain way. Although some of the questions are similar, there are differences between them and you should treat each one as a separate question. The best approach is to answer each question fairly quickly. That is, don't try to count up the number of times you felt a particular way, but rather indicate the alternative that seems like a reasonable estimate.

For each question, choose among the following alternatives:

Never	Almost never	Sometimes	Fairly often	Very often
0	1	2	3	4

1. In the last month, how often have you been upset because of something that happened unexpectedly? _____
2. In the last month, how often have you felt that you were unable to control the important things in your life? _____
3. In the last month, how often have you felt nervous and "stressed"? _____
4. In the last month, how often have you dealt successfully with irritating life hassles? _____
5. In the last month, how often have you felt that you were effectively coping with important changes that were occurring in your life? _____
6. In the last month, how often have you felt confident about your ability to handle your personal problems? _____
7. In the last month, how often have you felt that things were going your way? _____

PSS

For each question, choose among the following alternatives:

Never	Almost never	Sometimes	Fairly often	Very often
0	1	2	3	4

8. In the last month, how often have you found that you could not cope with all the things that you had to do? _____

9. In the last month, how often have you been able to control irritations in your life? _____

10. In the last month, how often have you felt that you were on top of things? _____

11. In the last month, how often have you been angered because of things that happened that were outside of your control? _____

12. In the last month, how often have you found yourself thinking about things that you have to accomplish? _____

13. In the last month, how often have you been able to control the way you spend your time? _____

14. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them? _____

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LES

Listed below are a number of events which sometimes bring about change in the lives of those who experience them and which necessitate social readjustment. ***Please check those events which you have experienced in the recent and indicate the time period which you have experienced each event*****. Be sure that all check marks are directly across from the items they correspond to. Also for each item checked,** ***please indicate the extent to which you viewed the event as having either a positive or negative impact on your life*** **at the time the event occurred.**

Extremely negative	**Moderately negative**	**Somewhat negative**	**No impact**	**Slightly positive**	**Moderately positive**	**Extremely positive**
-3	**-2**	**-1**	**0**	**+1**	**+2**	**+3**

	0 months to 6 months	**7 months to 1 year**	
1. Marriage	☐	☐	-3 -2 -1 0 +1 +2 +3
2. Detention in jail or comparable institution	☐	☐	-3 -2 -1 0 +1 +2 +3
3. Death of spouse	☐	☐	-3 -2 -1 0 +1 +2 +3
4. Major change in sleeping habits (much more or much less sleep)	☐	☐	-3 -2 -1 0 +1 +2 +3
5. Death of a close family member:			-3 -2 -1 0 +1 +2 +3
a) Mother	☐	☐	-3 -2 -1 0 +1 +2 +3
b) Father	☐	☐	-3 -2 -1 0 +1 +2 +3
c) Brother	☐	☐	-3 -2 -1 0 +1 +2 +3
d) Sister	☐	☐	-3 -2 -1 0 +1 +2 +3
e) Grandmother	☐	☐	-3 -2 -1 0 +1 +2 +3
f) Grandfather	☐	☐	-3 -2 -1 0 +1 +2 +3
g) Other: _____	☐	☐	-3 -2 -1 0 +1 +2 +3

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Please rate according to the following scale:

Extremely negative	Moderately negative	Somewhat negative	No impact	Slightly positive	Moderately positive	Extremely positive
-3	-2	-1	0	+1	+2	+3

	0 months to 6 months	7 months to 1 year							
6. Major change in eating habits (much more or much less food intake)	☐	☐	-3	-2	-1	0	+1	+2	+3
7. Foreclosure on mortgage or loan	☐	☐	-3	-2	-1	0	+1	+2	+3
8. Death of close friend	☐	☐	-3	-2	-1	0	+1	+2	+3
9. Outstanding personal achievement	☐	☐	-3	-2	-1	0	+1	+2	+3
10. Minor law violations (traffic tickets, disturbing the peace, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
11. Pregnancy	☐	☐	-3	-2	-1	0	+1	+2	+3
12. Changed work situation (different responsibility, major change in working conditions, working hours, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
13. New job	☐	☐	-3	-2	-1	0	+1	+2	+3

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Please rate according to the following scale:

Extremely negative	Moderately negative	Somewhat negative	No impact	Slightly positive	Moderately positive	Extremely positive
-3	-2	-1	0	+1	+2	+3

	0 months to 6 months	7 months to 1 year							
14. Serious illness or injury of close family member:			-3	-2	-1	0	+1	+2	+3
a) Father	☐	☐	-3	-2	-1	0	+1	+2	+3
b) Mother	☐	☐	-3	-2	-1	0	+1	+2	+3
c) Sister	☐	☐	-3	-2	-1	0	+1	+2	+3
d) Brother	☐	☐	-3	-2	-1	0	+1	+2	+3
e) Grandfather	☐	☐	-3	-2	-1	0	+1	+2	+3
f) Grandmother	☐	☐	-3	-2	-1	0	+1	+2	+3
g) Spouse	☐	☐	-3	-2	-1	0	+1	+2	+3
h) Other: _____	☐	☐	-3	-2	-1	0	+1	+2	+3
15. Sexual difficulties	☐	☐	-3	-2	-1	0	+1	+2	+3
16. Trouble with employer (in danger of losing job, being suspended, demoted, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
17. Trouble with in-laws	☐	☐	-3	-2	-1	0	+1	+2	+3
18. Major change in financial status (a lot better off or a lot worse off)	☐	☐	-3	-2	-1	0	+1	+2	+3

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LES

Please rate according to the following scale:

Extremely negative	Moderately negative	Somewhat negative	No impact	Slightly positive	Moderately positive	Extremely positive
-3	-2	-1	0	+1	+2	+3

	0 months to 6 months	7 months to 1 year							
19. Major change in closeness of family members (increased or decreased closeness)	☐	☐	-3	-2	-1	0	+1	+2	+3
20. Gaining a new family member (through birth, adoption, family moving in, etc.	☐	☐	-3	-2	-1	0	+1	+2	+3
21. Change of residence	☐	☐	-3	-2	-1	0	+1	+2	+3
22. Marital separation from mate (due to conflict)	☐	☐	-3	-2	-1	0	+1	+2	+3
23. Major change in church activities (increased or decreased attendance)	☐	☐	-3	-2	-1	0	+1	+2	+3
24. Marital reconciliation with mate	☐	☐	-3	-2	-1	0	+1	+2	+3
25. Major change in number of arguments with spouse (a lot more or a lot less arguments)	☐	☐	-3	-2	-1	0	+1	+2	+3
26. Change in husband's work outside of home (loss of job, beginning new job, retirement, etc.	☐	☐	-3	-2	-1	0	+1	+2	+3
27. Major change in usual type and/or amount of recreation.	☐	☐	-3	-2	-1	0	+1	+2	+3

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Please rate according to the following scale:

Extremely negative	Moderately negative	Somewhat negative	No impact	Slightly positive	Moderately positive	Extremely positive
-3	-2	-1	0	+1	+2	+3

	0 months to 6 months	7 months to 1 year							
28. Borrowing more than $10 000 (buying home, business, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
29. Borrowing less than $10 000 (Buying car, T.V., getting school loan, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
30. Being fired from a job	☐	☐	-3	-2	-1	0	+1	+2	+3
31. Having abortion	☐	☐	-3	-2	-1	0	+1	+2	+3
32. Major personal illness or injury	☐	☐	-3	-2	-1	0	+1	+2	+3
33. Major change in social activities, e.g., parties, movies, visiting (increased or decreased participation)	☐	☐	-3	-2	-1	0	+1	+2	+3
34, Major change in living conditions of family (building new home, remodeling, deterioration of home, neighborhood, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
35. Divorce	☐	☐	-3	-2	-1	0	+1	+2	+3
36. Serious injury or illness of close friend	☐	☐	-3	-2	-1	0	+1	+2	+3

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Please rate according to the following scale:

Extremely negative	Moderately negative	Somewhat negative	No impact	Slightly positive	Moderately positive	Extremely positive
-3	-2	-1	0	+1	+2	+3

	0 months to 6 months	7 months to 1 year							
37. Retirement from work	☐	☐	-3	-2	-1	0	+1	+2	+3
38. Son or daughter leaving home (due to work, travel, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
39. Ending of formal schooling	☐	☐	-3	-2	-1	0	+1	+2	+3
40. Separation from spouse (due to work, travel, etc.)	☐	☐	-3	-2	-1	0	+1	+2	+3
41. Engagement	☐	☐	-3	-2	-1	0	+1	+2	+3
42. Breaking up with boyfriend/girlfriend	☐	☐	-3	-2	-1	0	+1	+2	+3
43. Leaving home for the first time	☐	☐	-3	-2	-1	0	+1	+2	+3
44. Reconciliation with boyfriend/girlfriend	☐	☐	-3	-2	-1	0	+1	+2	+3

Other recent experiences which have had an impact on your life. Please list and rate:

45. _____ _____ _____	☐	☐	-3	-2	-1	0	+1	+2	+3
46. _____ _____ _____	☐	☐	-3	-2	-1	0	+1	+2	+3
47. _____ _____ _____	☐	☐	-3	-2	-1	0	+1	+2	+3

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BDI-II

This questionnaire consists of 21 groups of statements. Please read each group of statements carefully and then pick out the *one statement* in each group that best describes the way you have been feeling during the *past two weeks, including today.*

Select the number beside the statement you have picked. If several statements in the group seem to apply equally well, select the highest number for that group. *Be sure that you do not choose more than one statement for any group*, including item 16 ("Changes in Sleeping Pattern") or item 18 ("Changes in Appetite").

Sadness	☐ 0. I do not feel sad. ☐ 1. I feel sad much of the time. ☐ 2. I am sad all the time ☐ 3. I am so sad or unhappy that I can't stand it.
Pessimism	☐ 0. I am not discouraged about my future. ☐ 1. I feel more discouraged about my future than I used to be. ☐ 2. I do not expect things to work out for me. ☐ 3. I feel my future is hopeless and will only get worse.
Past Failure	☐ 0. I do not feel like a failure. ☐ 1. I have failed more than I should have. ☐ 2. As I look back, I see a lot of failures ☐ 3. I feel I am a total failure as a person.
Loss of Pleasure	☐ 0. I get as much pleasure as I ever did from the things I enjoy. ☐ 1. I don't enjoy things as much as I used to. ☐ 2. I get very little pleasure from the things I used to enjoy. ☐ 3. I can't get any pleasure from the things I used to enjoy.
Guilty Feelings	☐ 0. I don't feel particularly guilty. ☐ 1. I feel guilty over many things I have done or should have done ☐ 2. I feel quite guilty most of the time. ☐ 3. I feel guilty all of the time.
Punishment Feelings	☐ 0. I don't feel I am being punished. ☐ 1. I feel I may be punished. ☐ 2. I expect to be punished. ☐ 3. I feel I am being punished.
Self-Dislike	☐ 0. I feel the same about myself as ever. ☐ 1. I have lost confidence in myself. ☐ 2. I am disappointed in myself. ☐ 3. I dislike myself.

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BDI-II

Self-Criticalness	☐ 0. I don't criticize or blame myself more than usual. ☐ 1. I am more critical of myself than I used to be. ☐ 2. I criticize myself for all of my faults. ☐ 3. I blame myself for everything bad that happens.
Suicidal Thoughts or Wishes	☐ 0. I don't have any thoughts of killing myself. ☐ 1. I have thoughts of killing myself, but I would not carry them out. ☐ 2. I would like to kill myself. ☐ 3. I would kill myself if I had the chance.
Crying	☐ 0. I don't cry any more than I used to. ☐ 1. I cry more than I used to. ☐ 2. I cry over every little thing. ☐ 3. I feel like crying, but I can't.
Agitation	☐ 0. I am no more restless or wound up than usual. ☐ 1. I feel more restless or wound up than usual. ☐ 2. I am so restless or agitated that it's hard to stay still. ☐ 3. I am so restless or agitated that I have to keep moving or doing something.
Loss of Interest	☐ 0. I have not lost interest in other people or activities. ☐ 1. I am less interested in other people or things than before. ☐ 2. I have lost most of my interest in other people or things. ☐ 3. It's hard to get interested in anything.
Indecisiveness	☐ 0. I make decisions about as well as ever. ☐ 1. I find it more difficult to make decisions than usual. ☐ 2. I have much greater difficulty in making decisions than I used to. ☐ 3. I have trouble making any decisions
Worthlessness	☐ 0. I do not feel I am worthless. ☐ 1. I don't consider myself as worthwhile and useful as I used to. ☐ 2. I feel more worthless as compared to other people. ☐ 3. I feel utterly worthless.
Loss of Energy	☐ 0. I have as much energy as ever. ☐ 1. I have less energy than I used to have. ☐ 2. I don't have enough energy to do very much. ☐ 3. I don't have enough energy to do anything.

BDI-II

Changes in Sleeping Pattern	☐ 0. I have not experienced any change in my sleeping pattern. ☐ 1. I sleep somewhat more or somewhat less than usual. ☐ 2. I sleep a lot more or a lot less than usual. ☐ 3. I sleep most of the day or I wake up 1-2 hours early and can't get back to sleep.
Irritability	☐ 0. I am no more irritable than usual. ☐ 1. I am more irritable than usual. ☐ 2. I am much more irritable than usual. ☐ 3. I am irritable all the time.
Changes in Appetite	☐ 0. I have not experienced any change in my appetite. ☐ 1. My appetite is somewhat less or somewhat greater than usual. ☐ 2. My appetite is much less or much greater than before. ☐ 3. I have no appetite at all or I crave food all the time.
Concentration Difficulty	☐ 0. I can concentrate as well as ever. ☐ 1. I can't concentrate as well as usual. ☐ 2. It's hard to keep my mind on anything for very long. ☐ 3. I find I can't concentrate on anything.
Tiredness or Fatigue	☐ 0. I am no more tired or fatigued than usual. ☐ 1. I get more tired or fatigued more easily than usual. ☐ 2. I am too tired or fatigued to do a lot of the things I used to. ☐ 3. I am too tired or fatigued to do most of the things I used to.
Loss of Interest in Sex	☐ 0. I have not noticed any recent change in my interest in sex. ☐ 1. I am less interested in sex than I used to be. ☐ 2. I am much less interested in sex now. ☐ 3. I have lost interest in sex completely.

STAI

A number of statements which people have used to describe themselves are given below. Read each statement and the select the appropriate answer to the right of the statement to indicate how you feel *right now*, that is, *at this moment*. There are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to best describe your present feelings best.

	Not at all	**Somewhat**	**Moderately so**	**Very much so**	
	1	**2**	**3**	**4**	
1.	I feel calm				_____
2.	I feel secure				_____
3.	I am tense				_____
4.	I feel strained				_____
5.	I feel at ease				_____
6.	I feel upset				_____
7.	I am presently worrying over possible misfortunes				_____
8.	I feel satisfied				_____
9.	I feel frightened				_____
10.	I feel comfortable				_____

STAI

Not at all	Somewhat	Moderately so	Very much so	
1	2	3	4	
11. I feel self-confident				_____
12. I feel nervous				_____
13. I feel jittery				_____
14. I feel indecisive				_____
15. I am relaxed				_____
16. I feel content				_____
17. I am worried				_____
18. I feel confused				_____
19. I feel steady				_____
20. I feel pleasant				_____

STAI

A number of statements which people have used to describe themselves are given below. Read each statement and the select the appropriate answer to the right of the statement to indicate how you *generally* feel.

Almost never	Sometmes	Often	Almost always
1	2	3	4

21. I feel pleasant _____

22. I feel nervous and restless _____

23. I feel satisfied with myself _____

24. I wish I could be as happy as others seem to be _____

25. I feel like a failure _____

26. I feel rested _____

27. I am "calm, cool, and collected" _____

28. I feel that difficulties are piling up so that I cannot overcome them _____

29. I worry too much over something that doesn't matter _____

30. I am happy _____

31. I have disturbing thoughts _____

STAI

Almost never	Sometimes	Often	Almost always
1	2	3	4

32. I lack self-confidence _____

33. I feel secure _____

34. I make decisions easily _____

35. I feel inadequate _____

36. I am content _____

37. Some unimportant thought runs through my mind and bothers me _____

38. I take disappointments so keenly that I can't put them out of my mind _____

39. I am a steady person _____

40. I get in a state of tension or turmoil as I think over my recent concerns and interests _____

CARS

The following questions ask you to tell us about any worries you may have about the possibility of breast cancer recurrence. By recurrence we mean the breast cancer coming back in the same breast or another area of the body, or a new breast cancer in either breast.

Although most women who have been diagnosed with early stage breast cancer will never have another problem with the cancer, we are aware that many women do worry about this possibility. Other women may not worry about recurrence at all. Either way, your answers to these questions are very important to us. We understand that it may be upsetting to think about or answer questions about the possibility of recurrence. However, we need your help to understand how women think about this possibility.

For the following four questions please select the number that comes closest to the way you feel.

1. How much do you spend thinking about the possibility that your breast cancer could recur?

1	2	3	4	5	6
I don't think about it at all					I think about it all the time

2. How much does the possibility that breast cancer would recur upset you?

1	2	3	4	5	6
It does not upset me at all					It makes me extremely upset

3. How often do you worry about the possibility that your breast cancer would recur?

1	2	3	4	5	6
I never worry about it					I worry about it all the time

4. How afraid are you that your breast cancer may recur?

1	2	3	4	5	6
I am not afraid at all					I am very afraid

CARS

Now we are interested in what your concerns are regarding a possible recurrence of breast cancer. Thinking about the possibility of a recurrence, what is it about the possibility that you worry about?

Although each of the following items may be a possible consequence of recurrence, we are really interested in whether you actually worry about any of these things occurring. For example, you may believe that a recurrence of a breast cancer could require further surgery. We would like to know whether you ever actually worry about this possibility.

For the following questions, please select the number indicating how much you worry about each of the following items. If you do not worry about an item or if you think it does not apply to you, please select "0" or "Not at all".

Not at all	A little	Moderately	A lot	Extremely
0	1	2	3	4

I worry that a recurrence of breast cancer would:	
5. Upset me emotionally	_____
6. Keep me from doing the things I had planned to do	_____
7. Threaten my physical health	_____
8. Make me feel I am less of a woman	_____
9. Require chemotherapy	_____
10 Hurt my relationship with friends and family	_____
11. Make me feel that I don't have control over my life	_____
12. Threaten my identity (how I see myself)	_____
13. Interfere with my physical ability to carry out daily activities	_____
14. Threaten my life	_____

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CARS

Not at all	A little	Moderately	A lot	Extremely
0	1	2	3	4

I worry that a recurrence of breast cancer would:

15. Harm my self confidence _____
16. Be more serious than the first diagnosis _____
17. Cause financial problems for me _____
18. Interfere with my sense of sexuality _____
19. Require radiation therapy _____
20. Cause me pain and suffering _____
21. Mean losing my breast(s) _____
22. Interfere with my ability to plan for the future _____
23. Threaten my spirituality or faith _____
24. Keep me from fulfilling important roles (in my job or at home) _____
25. Lead me to feel less feminine _____
26. Require further surgery _____
27. Cause me to die _____
28. Damage my romantic relationship(s) _____
29. Keep me from fulfilling responsibilities (in my job or at home) _____
30. Make me feel badly about how my body looks _____

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SSBS

People help each other out in a lot of different ways. Suppose you had some kind of problem (were upset about something, needed help with a practical problem, were broke, or needed some advice or guidance), *how likely* would (a) members of your *family*, and (b) your *friends* be to help you out in each of the specific ways listed below. We realize you may rarely need this kind of help, but *if you did* would family and friends help in the ways indicated. Try to base your answers on your past experience with these people.

Use the scale below, and indicate one number under family, and one under friends, in each row.

No one **would do this**	***Someone might*** **do this**	***Some*** **family member/friend would *probably* do this**	***Some*** **family member/friend would *certainly* do this**	***Most*** **family member/friend would *certainly* do this**
1	**2**	**3**	**4**	**5**

	Family	Friends
1. Would suggest doing something, just to take my mind off my problems.	_____	_____
2. Would visit with me, or invite me over.	_____	_____
3. Would comfort me if I was upset.	_____	_____
4. Would give me a ride if I needed one.	_____	_____
5. Would have lunch or dinner with me.	_____	_____
6. Would look after my belongings (house, pets, etc.) for a while.	_____	_____
7. Would loan me a car if I needed one.	_____	_____

SSBS

Use the scale below, and indicate one number under family, and one under friends, in each row.

No one **would do this**	***Someone might*** **do this**	***Some*** **family member/friend would *probably* do this**	***Some*** **family member/friend would *certainly* do this**	***Most*** **family member/friend would *certainly* do this**
1	**2**	**3**	**4**	**5**

	Family	Friends
8. Would joke around or suggest doing something to cheer me up.	_____	_____
9. Would go to a movie or concert with me.	_____	_____
10. Would suggest how I could find out more about a situation.	_____	_____
11. Would help me out with a move or other big chore.	_____	_____
12. Would listen if I needed to talk about my feelings.	_____	_____
13. Would have a good time with me.	_____	_____
14. Would pay for my lunch if I was broke.	_____	_____
15. Would suggest a way I might do something.	_____	_____
16. Would give me encouragement to do something difficult.	_____	_____
17. Would give me advice about what to do.	_____	_____
18. Would chat with me.	_____	_____

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SSBS

Use the scale below, and indicate one number under family, and one under friends, in each row.

No one **would do this**	***Someone might*** **do this**	***Some*** **family member/friend would *probably* do this**	***Some*** **family member/friend would *certainly* do this**	***Most*** **family member/friend would *certainly* do this**
1	**2**	**3**	**4**	**5**

	Family	Friends
19. Would help me figure out what I wanted to do.	_____	_____
20. Would show me that they understood how I was feeling.	_____	_____
21. Would buy me a drink if I was short of money.	_____	_____
22. Would help me decide what to do.	_____	_____
23. Would give me a hug, or otherwise show me I was cared about.	_____	_____
24. Would call me just to see how I was doing.	_____	_____
25. Would help me figure out what was going on.	_____	_____
26. Would help me out with some necessary purchase.	_____	_____
27. Would not pass judgment on me.	_____	_____
28. Would tell me who to talk to for help.	_____	_____
29. Would loan me money for an indefinite period.	_____	_____

SSBS

Use the scale below, and indicate one number under family, and one under friends, in each row.

No one **would do this**	***Someone might*** **do this**	***Some*** **family member/friend would *probably* do this**	***Some*** **family member/friend would *certainly* do this**	***Most*** **family member/friend would *certainly* do this**
1	**2**	**3**	**4**	**5**

	Family	Friends
30. Would be sympathetic if I was upset.	_____	_____
31. Would stick by me in a crunch.	_____	_____
32. Would buy me clothes if I was short of money.	_____	_____
33. Would tell me about the available choices and options.	_____	_____
34. Would loan me tools, equipment, or appliances if I needed them.	_____	_____
35. Would give me reasons why I should or should not do something.	_____	_____
36. Would show affection for me.	_____	_____
37. Would show me how to do something I didn't know how to do.	_____	_____
38. Would bring me little presents of things I needed.	_____	_____
39. Would tell me the best way to get something done.	_____	_____
40. Would talk to other people, to arrange something for me.	_____	_____

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SSBS

Use the scale below, and indicate one number under family, and one under friends, in each row.

No one **would do this**	***Someone might*** **do this**	***Some*** **family member/friend would *probably* do this**	***Some*** **family member/friend would *certainly* do this**	***Most*** **family member/friend would *certainly* do this**
1	**2**	**3**	**4**	**5**

	Family	Friends
41. Would loan me money and want to "forget about it".	_____	_____
42. Would tell me what to do.	_____	_____
43. Would offer me a place to stay for awhile.	_____	_____
44. Would help me think about a problem.	_____	_____
45. Would loan me a fairly large sum of money (say the equivalent of a month's rent or mortgage).	_____	_____

If you wish to make any comments about your experience participating in this study, please feel free to write as much or as little as you in the space below.

Thank you for your comments. Please take a minute to look over the next page.

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FUTURE STUDIES

1. Would you like to be contacted for future research studies on the topics covered in this questionnaire and/or today's session?

   ☐ Yes ☐ No

2. Would you like to be contacted for a phone or online interview in future studies on the topics covered in this questionnaire and/or today's session?

   ☐ Yes ☐ No

3. Would you like to be contacted for an in-person interview in future studies on the topics covered in this questionnaire and/or today's session?

   ☐ Yes ☐ No

If you would like to be contacted for future studies, please write your name, email, and/or phone number below. This page will be detached from the questionnaire and stored securely, separate from the data collected today. It will only be accessible by the experimenter.

Name: _____

Email: _____

Tel. No.: _____

Thank you for completing this questionnaire package. Please take a minute to make sure you answered all the questions. When you are finished, please let the experimenter know.

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