FEAR OF CANCER RECURRENCE AND SLEEP IN COUPLES COPING WITH EARLY-STAGE BREAST CANCER

by

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ABSTRACT

Objectives: Sleep disturbance and fear of cancer recurrence (FCR) are common in breast cancer (BC) survivors. Yet, few studies have examined a putative link between these two constructs in BC survivors and none among these have also incorporated assessment of their spouses. Focusing on the period surrounding survivors' first post-treatment mammogram, higher survivor and spouse FCR was hypothesized to predict reduced sleep quantity and quality and greater sleep disturbances for both partners. **Methods:** Fifty-seven couples coping with early-stage BC reported sleep duration, quality, and other disturbances each morning for 21 consecutive days spanning survivors' first mammogram post-treatment. Three validated measures of global FCR formed latent survivor and spouse FCR factors. Average daily sleep and sleep on the eve of the mammogram were regressed on both survivor and spouse FCR. **Results:** Survivor FCR was associated with reduced average daily sleep duration and quality for themselves and greater sleep disturbances for their spouse. Spouse FCR was associated with reduced average daily sleep duration for themselves. On the eve of the mammogram, survivor FCR was associated with their own reduced sleep duration and quality as well as greater difficulty falling asleep for their spouse. Spouse FCR was associated with their own reduced sleep duration and quality as well as greater sleep disturbances for their partner. **Conclusions:** Findings supported individual and dyadic associations between FCR and sleep, addressing gaps in knowledge on FCR and health behaviors. FCR interventions may be a strategy for addressing sleep disturbance, and thereby long-term health.

Chapter 1

INTRODUCTION

Due in part to earlier detection and better treatments, breast cancer (BC) mortality has decreased 39% since 1989 (American Cancer Society, 2018). These rapid declines have resulted in a rising number of BC survivors – an estimated 4.5 million alone in the next 10 years (American Cancer Society, 2018). Many of these survivors experience psychosocial challenges, among which fear of cancer recurrence (FCR) and sleep disturbance are top concerns (Custers et al., 2014; Hodgkinson et al., 2007; Ness et al., 2012; Savard & Ivers, 2013; Simard & Savard, 2015; Thewes et al., 2012).

FCR refers to the "fear, worry, or concern relating to the possibility that cancer will come back or progress" (Lebel et al., 2016, p. 3266), and as many as 58% of BC patients report clinically elevated FCR shortly after diagnosis and treatment (Perndorfer, Soriano, Siegel, & Laurenceau, in press; Simard & Savard, 2015). FCR can remain elevated even years after diagnosis and treatment (Deimling, Bowman, Sterns, Wagner, & Kahana, 2006; Koch, Jansen, Brenner, & Arndt, 2013; Mehnert, Berg, Henrich, & Herschbach, 2009; Simard et al., 2013) – for example, FCR was reported as the greatest unmet need by cancer survivors 10 years after diagnosis/treatment (Hodgkinson et al., 2007).

Existing theoretical models of FCR posit influences of pre-existing schemas and traits, the inherent nature of cancer reflecting uncertainty and uncontrollability, and reminders of the possibility of recurrence (e.g., follow-up mammograms), to explain FCR and associated coping responses (Carver, Meyer, & Antoni, 2000; Curran, Sharpe, & Butow, 2017; Fardell et al., 2016; Lee-Jones, Humphris, Dixon, & Bebbington Hatcher, 1997; Leventhal, Diefenbach, & Leventhal, 1992; Mellon, Kershaw, Northouse, & Freeman-Gibb, 2007). To date, no frameworks for conceptualizing FCR have considered its influence on health behaviors apart from body-checking (Curran et al., 2017). Rather, efforts to understand FCR have largely focused on immutable demographic or disease factors (e.g., age, physical symptoms; Simard et al., 2013), personality characteristics (e.g., threat sensitivity; Soriano, Perndorfer, Siegel, & Laurenceau, in press), or psychological outcomes (e.g., distress; Deimling et al., 2006; Dow, Ferrell, Leigh, Ly, & Gulasekaram, 1996).

Only recently has research begun to examine the influence of FCR on health behavior consequences, including body-checking behavior (Soriano et al., 2018) and health care utilization (Champagne, Ivers, & Savard, 2018; Otto, Soriano, Siegel, LoSavio, & Laurenceau, in press). Apart from these few studies, links between FCR and health behaviors, particularly those with known implications for mental and physical health and mortality, remain a critical gap in the understanding of FCR. Sleep is one such health behavior with well-demonstrated associations with health and mortality. Given the high comorbidity between anxiety and sleep disturbance in the general population (Spoormaker & van den Bout, 2005; Taylor, Lichstein, Durrence,

Reidel, & Bush, 2005), the contributing role of psychological factors in insomnia (Bower, 2008), and preliminary evidence of links between FCR and sleep (Berrett-Abebe, Cadet, Pirl, & Lennes, 2015; Matulonis et al., 2008; Mutsaers et al., 2016; Peppercorn et al., 2017; Roth et al., 2003; Taylor et al., 2012), further examination of the relationship between FCR and sleep is warranted.

Sleep disturbance, encompassing a diverse set of symptoms including nonrestorative sleep (i.e., poor sleep quality), difficulties falling asleep (i.e., sleep onset insomnia), difficulties staying asleep (i.e., maintenance insomnia), and waking too early (i.e., terminal insomnia), is commonly reported by cancer survivors (Savard & Morin, 2001). Moreover, sleep disturbance is reported by a greater proportion of patients with BC compared to those with other cancer diagnoses and this effect is not wholly accounted for by gender (Savard, Villa, Ivers, Simard, & Morin, 2009). As many as 65% of early-stage BC patients report sleep disturbance shortly after surgery and treatment (Bower et al., 2011) and a large proportion (23-44%) continue to experience impaired sleep several years post-diagnosis (Couzi, Helzlsouer, & Fetting, 1995; Lindley, Vasa, Sawyer, & Winer, 1998; Savard, Simard, Blanchet, Ivers, & Morin, 2001). Women with BC also report shorter sleep duration compared to healthy, age-matched women (Fiorentino & Ancoli-Israel, 2006). While not necessarily a direct result of cancer itself, psychological and emotional reactions to diagnosis as well as side effects of adjuvant treatment contribute to the development, worsening, and/or maintenance of sleep disturbance, which become chronic for a substantial proportion of BC survivors (Bower, 2008; Savard et al., 2001). Following from this,

BC survivors are at a two-fold risk for clinical insomnia as compared to the general population (Savard, Ivers, Villa, Caplette-Gingras, & Morin, 2011; Savard et al., 2001).

Cancer is a "*we*" disease and its impact extends beyond the patient (Kayser, Watson, & Andrade, 2007). Spouses of cancer survivors, too, report FCR (Boehmer, Tripodis, Bazzi, Winter, & Clark, 2016; Janz et al., 2016; Kent et al., 2016; Kim, Carver, Spillers, Love-Ghaffari, & Kaw, 2012; Perndorfer et al., in press; Schmid-Büchi, Halfens, Dassen, & Borne, 2008; Soriano, Pasipanodya, et al., in press; Soriano, Perndorfer, Otto, Siegel, & Laurenceau, in press; Soriano et al., in press), with levels sometimes exceeding those of patients (Hodges & Humphris, 2009; Mellon et al., 2007). In a recent study of BC patients and their spouses shortly after diagnosis and treatment, 39% of spouses reported clinical levels of FCR (Perndorfer et al., in press). Sleep disturbance among spouses of cancer survivors has received relatively little empirical attention. Spouses experience psychological and emotional reactions to the diagnosis of their partner and often assume caregiving responsibilities for their family. Evidence suggests that spouses also report impaired sleep, with levels of sleep disturbance sometimes matching those of patients (Carney et al., 2011; Chang, Tsai, Chang, & Tsao, 2007).

There are numerous links between sleep and mental and physical health for both the broader, non-diagnosed population and cancer survivors (Irwin, 2015). For example, sleep disturbance is associated with mood disorders (Rumble, White, & Benca, 2015), and impaired cognition (Kreutzmann, Havekes, Abel, & Meerlo, 2015)

in the general population. Individuals with insomnia in the broader population report more health problems, health care utilization, and hospitalizations than those without sleep complaints (Kales et al., 1984; Kaufmann et al., 2013; Simon & Vonkorff, 1997). Impaired sleep is associated with risk for cardiovascular disease (Hoevenaar-Blom, Spijkerman, Kromhout, van den Berg, & Verschuren, 2011), which is particularly relevant for cancer survivors and spouses, who are already at greater risk for developing cardiovascular disease and cardiovascular-related mortality (Bradshaw et al., 2016; Ji, Zöller, Sundquist, & Sundquist, 2012; Kim et al., 2012). Sleep is also implicated in immune function (Irwin et al., 1994; Irwin, 2015), which may be important for preventing cancer recurrence (Standish et al., 2008). Cancer-specific stress reported by spouses of BC survivors has been associated with their own compromised immune functioning (Gregorio et al., 2012), suggesting poor sleep may exacerbate these immune function alterations. Finally, sleep is related to mortality in the general population (Hublin, Partinen, Koskenvuo, & Kaprio, 2007), and for BC patients, sleep disturbance is predictive of both all-cause and BC-related mortality (Palesh et al., 2014; Trudel-Fitzgerald et al., 2017).

Collectively, these literatures suggest that cancer survivors and their spouses commonly report both FCR and sleep disturbance – yet few studies have examined the relationship between these variables in survivors (Berrett-Abebe et al., 2015; Matulonis et al., 2008; Mutsaers et al., 2016; Peppercorn et al., 2017; Roth et al., 2003; Taylor et al., 2012) and none have examined this link in spouses nor cross-partner effects of one partner's FCR on the other's sleep. For men with prostate cancer

and women with ovarian cancer, FCR was associated with global, self-reported sleep disturbance (Matulonis et al., 2008; Roth et al., 2003). Cancer patients receiving follow-up care with moderate to severe insomnia were more likely to report FCR as compared to patients with no insomnia (Peppercorn et al., 2017). In a sample of survivors with mixed-diagnoses, FCR and sleep quality were correlated, such that survivors who reported more FCR were at greater risk for poor sleep (Berrett-Abebe et al., 2015). Having intrusive thoughts about cancer, related to FCR (Curran et al., 2017; Fardell et al., 2016; Lebel et al., 2014; Lee-Jones et al., 1997; Lepore, 2001), was predictive of insomnia symptoms in African-American BC survivors (Taylor et al., 2012). Finally, in a qualitative study, survivors with mixed-diagnoses identified trouble sleeping as one of the consequences of clinical FCR (Mutsaers et al., 2016). Taken together, this preliminary evidence is consistent with the hypothesis that FCR is positively related to sleep disturbance in patients/survivors.

As previously mentioned, no studies have examined cross-partner effects of survivors' FCR on spouses' sleep and vice versa. Historically, sleep has been studied at the individual level. Prior studies of sleep from a dyadic perspective – relatively new in the literature - have focused on couples in which one partner has been diagnosed with a sleep disorder (e.g., obstructive sleep apnea), links between relationship functioning and sleep, and relationships between attachment style and sleep (see Troxel, 2010). However, recently research has begun to examine cross-partner effects of psychological factors on the other partner's sleep. In a sample of healthy, middle-aged couples, husbands' depressive and anxiety symptoms at baseline

were predictive of wives' sleep duration one year later, with greater symptoms predicting shorter sleep duration (Revenson, Marín-Chollom, Rundle, Wisnivesky, & Neugut, 2016). Greater anxiety reported by wives at baseline was predictive of shorter sleep duration for their husbands (Revenson et al., 2016). In a study with Chinese patients with cancer and their spouses, patient and spouse depressive symptoms were positively associated with their partner's sleep disturbance (Chan et al., 2017).

While preliminary studies of FCR and sleep in survivors are a promising development, a number of important conceptual and methodological limitations remain unaddressed. First, reminders of the possibility of recurrence are a central theme in frameworks for conceptualizing FCR (Curran et al., 2017). Despite this theoretical focus on internal (e.g., intrusive thoughts) and external (e.g., mammograms) triggers, very few studies have examined FCR as survivors and spouses face such reminders in everyday life (Soriano, Perndorfer, et al., in press; Soriano et al., in press). Second, preliminary evidence for associations between FCR and sleep disturbance is based on either global, retrospective reports of sleep disturbance or single-item measures of FCR (Berrett-Abebe et al., 2015; Matulonis et al., 2008; Peppercorn et al., 2017; Roth et al., 2003; T. R. Taylor et al., 2012). Moreover, measures of FCR in existing work have not dealt with the issue of measurement error, which can lead to biased inferences. Third, past studies have not considered potential confounds, such as physical symptoms, known to influence both FCR and sleep. Fourth, links between FCR and sleep have not been examined in spouses of cancer survivors nor have cross-partner links between FCR reported by one partner and the other partner's sleep. Patient and spouse FCR are significantly associated (Boehmer et al., 2016; Kim et al., 2012) and cancer-related couple

communication influences FCR (Perndorfer et al., in press; Soriano et al., in press; Soriano et al., 2018). In addition, there is high concordance between partners' sleep, wake, and movements during the night (Gunn, Buysse, Hasler, Begley, & Troxel, 2015; Pankhurst & Home, 1994). Taken together, this evidence points to the importance of studying FCR and sleep disturbance in the interdependent context in which they occur.

Chapter 2

THE CURRENT STUDY

The purpose of the present study was to examine links between FCR and sleep in a sample of early-stage BC survivors and their spouses. FCR and sleep data were collected from both partners and relationships between one partner's FCR and the other's sleep were also examined (partner effects; Kenny, Kashy, & Cook, 2006). FCR was assessed cross-sectionally using three validated scales to create a latent measure. Sleep outcomes, including sleep duration, subjective sleep quality, onset latency (difficulty getting to sleep), and waking after sleep onset (waking in the middle of the night or early in the morning), were assessed daily each morning for 21 consecutive days. Given the focus on threat-related triggers in theoretical models of FCR, the period surrounding the survivor's first follow-up mammogram—an event known to trigger FCR—was of interest (Gil et al., 2004; McGinty, Small, Laronga, & Jacobsen, 2016; Simard & Savard, 2009; Soriano, Perndorfer, Otto, Siegel, & Laurenceau, in press). Relationships between FCR and a) average daily sleep and b) sleep on the eve of the survivor's first post-treatment mammogram were examined.

Research suggests that physical symptoms and treatment type are related to FCR (Crist & Grunfeld, 2013; Simard et al., 2013). Factors that may influence sleep include physical symptoms, medical comorbidities, cancer stage, and cancer treatment (Savard et al., 2001). In contrast to existing studies that did not consider important covariates, the present study examined relationships between FCR and sleep both with and without controlling for survivor and spouse medical comorbidities, survivor

physical well-being, survivor cancer stage, and survivor cancer treatment. Results of associations between FCR and sleep outcomes both before and after the inclusion of these covariates are reported to facilitate comparisons with prior work.

It was hypothesized that greater FCR would be associated with shorter sleep duration and poorer subjective sleep quality for both survivors and spouses. It was hypothesized that survivors and spouses with greater FCR would report more onset latency and waking after sleep onset. Given recent evidence for cross-partner effects of psychological factors on sleep disturbance (Chan et al., 2017; Revenson et al., 2016), it was hypothesized that FCR reported by survivors would be negatively associated with survivors' sleep duration and subjective sleep quality and positively related to survivors' onset latency and waking after sleep onset (partner effects; and vice versa for spouses' FCR and survivors' sleep). These effects were predicted to exist both for average daily sleep and on the eve of the mammogram appointment as well as above and beyond the effect of covariates.

Method

Participants

Female early-stage BC patients who had a positive biopsy and appeared eligible based on data available in electronic health records were invited to participate in a larger longitudinal study, *Surviving Cancer Together*, with Christiana Care Health System IRB approval (FWA00006557; CCC# 33026) (Otto et al., in press; Perndorfer

et al., in press; Soriano, Pasipanodya, et al., in press; Soriano, Perndorfer, Otto, Siegel, & Laurenceau, in press; Soriano et al., 2018). Data from electronic health records were used to identify potential participants (n = 463). Eligibility criteria included patients who: (1) were diagnosed with early-stage BC (Stage 0 – Stage IIIA); (2) received recent BC surgery; (3) had spouses or long-term partners willing to participate; (4) had no prior cancer diagnoses; (5) spoke English; and (6) lived within an hour of the Mid-Atlantic cancer center. Of those identified (n = 463), 110 were ineligible (majority due to being unpartnered) and 82 could not be reached. Of those with confirmed eligibility (n = 271), 192 declined (majority "not enough time" or "spouse/partner did not wish to participate). Seventy-nine couples provided written informed consent for the larger study.

Fifty-seven couples (114 paired individuals) provided data for the study period of current interest. The average age of patients was 58 (*SD* = 9) and the average age for spouses was 60 (*SD* = 10). All but two spouses were male. Most participants identified as Caucasian (87%) and none as Hispanic/Latino. The modal family income was greater than $100,000. Most patients (87%) were diagnosed with Stage I or II BC followed by 12% with stage 0 and 1% with stage IIIA. Seventy-two percent of patients received radiation and 30% received chemotherapy.

Procedure

The larger longitudinal study followed couples from shortly after the patient's BC surgery and treatment until their first follow-up mammogram (approximately one-

year post-diagnosis). The two weeks preceding and one week following survivors' mammogram appointments are of current interest. Additional analyses of this same study period are documented elsewhere, however, this is the first study to focus on sleep as an outcome (Soriano, Perndorfer, et al., in press; Soriano et al., in press).

A cross-sectional survey was scheduled two weeks before each patient's follow-up mammogram. On average, mammogram appointments occurred 12.2 months after diagnosis (*SD* = 1.9). The 21-day daily diary period of current interest was scheduled to span each patient's follow-up mammogram, starting approximately two weeks before her appointment and concluding approximately one week after. On average, the daily diary period began 12 days (*SD* = 5.4) before the mammogram appointment. For both the cross-sectional survey and daily diaries, survivors and spouses were emailed separate links and asked to independently complete the online questionnaires. On each of the 21 daily diary days, participants completed a short morning survey within an hour of waking. On average, participants completed 16.91 (80.52%) of the 21 morning surveys. All but one woman received negative mammography results on the same day as their appointment. After the study's conclusion, this woman was diagnosed with a recurrence. Excluding this couple's data from analyses did not affect the pattern of results reported here.

Measures

Fear of Cancer Recurrence.

FCR was assessed cross-sectionally using three validated measures of FCR (Costa, Smith, & Fardell, 2016; Custers et al., 2017; Mutsaers et al., 2016). While patients reported on concerns regarding their own recurrence, spouses were asked to report on their fears of the patient's BC recurring. The Severity subscale of the Fear of Cancer Recurrence Inventory (FCRI; Simard & Savard, 2009) consists of nine items assessing intrusive thoughts and perceived risk of cancer recurrence. Coefficient alpha was .80 for survivors and .76 for spouses. The Distress subscale of the FCRI consists of four items assessing emotional reactivity to thoughts about recurrence. Alpha was .71 and .91 for survivors and spouses, respectively. For the Overall Fear subscale of the Concerns about Recurrence Scale (CARS; (Vickberg, 2003), participants completed four items assessing the frequency and intensity of FCR and associated distress. Alpha was .76 for survivors and .82 for spouses. All items were rated on a Likert-type response scale and summed for each measure with greater responses indicating greater FCR. The alpha coefficients for each measure reflected, at minimum, acceptable reliability for survivors and spouses. Detailed later, the three measures were used to create latent FCR factors for survivors and spouses.

Sleep Outcomes.

Patients and spouses were asked to complete items within an hour of waking that tapped sleep duration, subjective sleep quality, onset latency, and wake after sleep onset each morning of the 21-day diary period using a brief, in-house survey. Subjective sleep quality was defined as feeling refreshed or rested in the morning, a characterization of good sleep quality used in previous research (Libman et al., 2016). The items for daily onset latency and wake after sleep onset were modeled after a well-validated measure of global, retrospective sleep (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Participants were asked each morning to report on sleep duration and symptoms of insomnia from the previous night. For sleep duration, participants reported the number of hours and minutes (rounded to 15-minute intervals) they slept the previous night. The sleep quality item ("*How refreshed or rested do you feel right now after last night's sleep?*") used a Likert-type response scale ranging from 0 = *Not at all* to 4 = *Extremely*. For onset latency and waking after sleep onset, participants indicated whether (0 = *No*, 1 = *Yes*) they had "difficulty getting to sleep (e.g., within 30 minutes of going to bed)" and whether they "woke up in the middle of the night or early morning when they did not mean to," respectively.

Medical Comorbidities.

Participants indicated if they had current medical illnesses (for survivors, this was apart from their BC diagnosis). Those who endorsed current medical illnesses

(e.g., high blood pressure, diabetes) were asked to list these illnesses and the number of current diagnoses were summed to create a proxy index of medical comorbidities.

Physical Well-Being.

The physical well-being of survivors was assessed cross-sectionally using the Functional Assessment of Cancer Therapy - Breast Cancer Physical Well-Being subscale (FACT-B PWB; (Brady et al., 1997). The FACT-B measures multidimensional quality of life in patients with BC. The PWB scale uses seven items to assess physical side effects of BC as well as their impact on daily life over the past seven days. Items were rated on a Likert-type response scale ranging from 0 = *Not at all* to 4 = *Very Much*, which were summed to create a composite. Cronbach's alpha was 0.73, reflecting acceptable reliability.

Cancer Stage and Treatment.

The stage of each survivor's BC and whether or not they received chemotherapy and/or radiation (0 = *No*, 1 = *Yes*) were obtained from electronic medical records.

Statistical Methods

Primary analyses consisted of Structural equation modeling (SEM) conducted in Mplus (Muthén & Muthén, 1998-2017) using default maximum likelihood estimation. SEM allowed us to examine separately the relationship between an underlying FCR construct and each of the sleep outcomes (sleep duration, subjective sleep quality, sleep onset latency, and wake after sleep onset). The three manifest

indicators (FCRI-Severity, FCRI-Distress, and CARS) were used to create latent FCR factors free of measurement error for both survivors and spouses. To achieve identification and scale the latent factors, the FCRI-Severity subscale (Simard & Savard, 2009) served as the marker variable – with its loading fixed to one. The latent FCR factors for survivors and spouses were allowed to covary. Actor-partner interdependence modeling (APIM; Kenny et al., 2006) was used to account for the interdependence of sleep outcomes - the effect of one participant's FCR on his/her own sleep (actor effects) and on his/her partner's sleep (partner effects) were estimated simultaneously in each model. It was noted that for several models, the actor and/or partner effects for survivors and spouses were similar in magnitude. For parsimony, we constrained these effects to be equal across survivors and spouses when supported by chi-square difference tests.

First, relationships between the latent FCR factors and averages for each of the four sleep outcomes were examined (excluding the night before the mammogram). See Table 2 for associations between FCR and average daily sleep. In each model, average daily sleep outcomes were regressed on both latent survivor and spouse FCR factors. Then, relationships between FCR and each of the four sleep variables were examined specifically for the night before the survivor's mammogram appointment. See Table 3 for associations between FCR and sleep solely on the eve of the mammogram. Again, survivors' and spouses' sleep outcomes on the eve of the mammogram were regressed on both own FCR as well as partner FCR.

These models were then repeated controlling for covariates, including survivor and spouse number of medical comorbidities, survivor physical well-being, survivor cancer stage, and survivor treatment. Standardized results of the models both with and without covariates are reported in Table 4.

Results

Descriptive statistics are detailed in Table 1. To start, a two-factor model was estimated in which the factor loadings for the latent FCR factors for survivors and spouses were freely estimated (χ^2 (8) = 5.384, p = .716). The factor loadings were then constrained to be equal across survivors and spouses (χ^2 (10) = 7.476, p = .680). The deviances of the model with constrained factor loadings did not significantly differ from the model in which the loadings were unconstrained (χ^2 (2) = 2.168, p = .34), suggesting equivalent fit. The results reported therefore make use of a latent FCR factor with a single set of loadings across survivors and spouses reflecting metric (loading) invariance. All standardized factor loadings of FCRI-Severity and Distress and CARS Overall composites were above 0.65 and statistically significant ($p < .001$) for both survivors and spouses. Omega, an index of factor-based reliability, was good for both survivors (α = .86) and spouses (α = .89). There was a moderate, positive correlation between survivors' and spouses' FCR (r = .33, p = .018).

A paired samples t-test was conducted to compare average sleep duration and average subjective sleep quality in the three weeks surrounding the mammogram (excluding the night before the mammogram) with sleep solely on the eve of the

mammogram. Survivors slept for a significantly shorter duration (in hours) on the eve of the mammogram (M = 7.02, SD = 1.59) compared to their average sleep duration on other nights (M = 7.50, SD = 0.93; t (50) = -2.63, p = .011). Survivors also reported significantly worse sleep quality on the night before the mammogram (M = 2.02, SD = 1.04) compared to the other nights (M = 2.26, SD = 0.64; t (51) = -2.18, p = .034). For spouses, there were no significant differences between sleep duration or sleep quality on the night of the mammogram compared to the three weeks surrounding the mammogram appointment.

FCR and Sleep Duration

When modeling average daily sleep duration (Table 2), the survivor and spouse actor effects were similar in magnitude and so were constrained to be equal. The fit of the constrained model was not significantly worse than that of the unconstrained model (χ^2 (1) = 0.025, p = .874). The results of the more parsimonious, constrained model are therefore reported. Results suggested that FCR (constrained across survivors and spouses) was significantly associated with own sleep duration. Specifically, participants with a one-unit greater latent FCR score slept an average of 4.26 minutes less per night across the diary period (B = -0.071, p = .003). Associations between participants' FCR and their partners' (partner effects) sleep duration were not significant. When including medical comorbidities and survivors' physical well-being, cancer stage, and treatment in the model, the actor effects were not similar in magnitude and so were freely estimated. After including these covariates, there was a

marginally-significant, negative association between FCR reported by spouses and their own average daily sleep duration (B = -0.049, *p* = .071). The actor effect for survivors was no longer significant and again, there were no significant associations between survivors' FCR and spouses' average daily sleep duration and vice versa for spouses' FCR and survivors' sleep duration.

Turning to the night before the mammogram (Table 3), the actor effects for survivors and spouses were similar in magnitude and were therefore constrained to be equal. The deviances of the constrained and unconstrained models did not significantly differ for both the model without covariates ($\chi 2$ (1) = 0.016, p = .899) and after including covariates ($\chi 2$ (1) = 0.066, p = .417). The results of the more parsimonious, constrained models are reported. There was a marginally-significant, negative association between participants' FCR and their own sleep duration (B = -0.082, *p* = .053). FCR reported by participants was not significantly associated with their partner's sleep duration on the night before the mammogram. After controlling for medical comorbidities and survivors' physical well-being, cancer stage, and treatment, the marginally-significant actor effect (constrained across survivors and spouses) remained. FCR reported by survivors and spouses was negatively associated with their own sleep duration on the night before the mammogram (B = -0.109, *p* = .060). After including covariates, FCR reported by survivors was not significantly associated with spouses' sleep duration on the night before the mammogram. Spouses' FCR was also not significantly associated with survivors' sleep duration the night before the mammogram.

FCR and Subjective Sleep Quality

When modeling average daily subjective sleep quality, the survivor and spouse actor effects as well as the partner effects were freely estimated. FCR reported by survivors was significantly and negatively associated with their own average daily sleep quality (B = -0.103, $p < .001$). FCR reported by spouses was not significantly associated with their own average daily sleep quality. A significant partner effect emerged such that survivors' FCR was negatively associated with spouses' average daily sleep quality (B = -0.086, $p = .002$). The association between spouses' FCR and survivors' sleep quality was not significant. After including medical comorbidities and survivors' physical well-being, cancer stage, and treatment, the same pattern of effects emerged as the model without covariates. FCR reported by survivors was significantly and negatively associated with their own (B = -0.093, $p = .002$) as well as spouses' average daily sleep quality (B = -0.075, $p = .020$). Spouses' FCR was not significantly associated with their own or survivors' average daily sleep quality.

When modeling subjective sleep quality on the night before the mammogram, the actor effects for survivors and spouses as well as their partner effects were similar in magnitude and so were constrained to be equal. The fit of the model with the constrained actor and constrained partner effects was not significantly worse than the fit of the model with the unconstrained effects (χ^2 (2) = 0.466, $p = .792$). FCR reported by participants (constrained across survivors and spouses) was significantly and negatively associated with their own sleep quality on the eve of the follow-up mammogram (B = -0.093, $p = .002$). There was a marginally-significant constrained

partner effect such that survivors' FCR was negatively associated with spouses' sleep quality and vice versa for spouses' FCR and survivors' sleep quality on the eve of the mammogram (B = -0.055, p = .067). When including covariates in the model, only the actor effects were similar in magnitude. The actor effects were therefore constrained across survivors and spouses and the deviances between this model and the unconstrained model did not significantly differ (χ^2 (1) = 0.66, p = .417), suggesting equivalent fit. The constrained actor effect was significant such that survivors' and spouses' FCR was negatively associated with their own sleep quality on the night before the mammogram (B = -0.073, p = .026), above and beyond the effect of medical comorbidities and survivors' physical well-being, cancer stage, and treatment. After including covariates, the partner effects were not significant when modeling sleep duration on the night before the mammogram.

FCR and Sleep Onset Latency

When modeling average daily onset latency, the actor and partner effects for survivors and spouses were not similar in magnitude and so were left unconstrained. FCR reported by survivors was significantly associated with spouses' onset latency. That is, greater FCR reported by survivors was associated with greater spouses' difficulty getting to sleep across the diary period (logistic B = 0.238, p = .019). Neither the actor effects nor associations between spouses' FCR and survivors' sleep onset latency were significant. After including medical comorbidities and survivors'

physical well-being, cancer stage, and treatment, there were no significant associations between FCR and average daily onset latency.

When modeling sleep onset latency on the night before the mammogram, the partner effects were similar in magnitude. The partner effects were therefore constrained to be equal across survivors and spouses, and this model did not have significantly worse fit than the model with partner effects left unconstrained (χ^2 (1) = 0.048, p = .827). The partner effect, constrained across survivors and spouses, was significant such that participants' FCR was positively associated with their partners' onset latency (logistic B = 0.163, p = .040). The actor effects were not significant. When controlling for medical comorbidities and survivors' physical well-being, cancer stage, and treatment, the partner effects for survivors and spouses were similar in magnitude. The partner effects were constrained to be equal and the deviances of the constrained and unconstrained models did not significantly differ (χ^2 (1) = 0.496, p = .481). Participants' FCR (constrained across survivors and spouses) was significantly associated with their partners' sleep onset latency. Greater FCR reported by survivors was associated with greater difficulty getting to sleep reported by spouses and vice versa for spouses FCR and survivors' onset latency (logistic B = 0.26, p = .041). After including covariates, there was no significant association between participants' FCR and their own onset latency on the night before the mammogram.

FCR and Wake After Sleep Onset

Across all four models for wake after sleep onset, actor and partner effects for survivors and spouses were freely estimated. There were no significant associations between FCR and average daily wake after sleep onset both with and without including medical comorbidities and survivors' physical well-being, cancer stage, and treatment in the model.

For the night before the mammogram, there was a marginally-significant association between spouses' FCR and survivors' wake after sleep onset. Greater FCR reported by spouses was positively associated with survivors' difficulty maintaining sleep on the night before the mammogram (logistic B = 0.238, $p = .073$). After controlling for medical comorbidities and survivors' physical well-being, cancer stage, and treatment, this spouse partner effect became significant. Greater FCR reported by spouses was significantly and positively associated with survivors' wake after sleep onset on the eve of the mammogram, above and beyond associations with covariates (logistic B = .051, $p = .018$).

Chapter 3

DISCUSSION

Despite the prevalence of both FCR and sleep disturbance in cancer survivors, this is the first known study to use daily measures of sleep to examine links between FCR and sleep disturbance in survivors. Additionally, no studies have examined these relationships in spouses of cancer survivors nor cross-partner effects of FCR and sleep disturbance. This study expands prior research by examining links between a measurement error-free factor of FCR and sleep as couples cope with a natural trigger of FCR (Gil et al., 2004; McGinty et al., 2016; Simard & Savard, 2009; Soriano, Perndorfer, et al., in press). Finally, this study examined these relationships above and beyond potential confounding variables. The present work focused on FCR and sleep duration, subjective sleep quality, onset latency, and wake after sleep onset in BC survivors and their spouses as they experience the first mammogram post-treatment. Data were collected from both survivors and spouses and links between participants' FCR and both their own as well as their partner's sleep were examined.

For brevity, only the results of models including covariates will be reviewed here. For sleep duration, results partially supported the hypothesis that FCR is significantly associated with one's own shorter sleep duration. For average daily sleep, there was a marginally-significant association between FCR reported by spouses and their own sleep duration such that greater spouse FCR was associated with shorter sleep. Contrary to hypotheses, there was no association between survivors' FCR and their average daily sleep duration. Turning to the eve of the mammogram, there was a

marginally-significant association between greater FCR reported by both survivors and spouses and their own shorter sleep duration. Contrary to hypotheses, there was no evidence of cross-partner associations for either average daily sleep duration or sleep duration on the eve of the mammogram.

For average daily sleep quality, survivors' FCR was significantly associated with sleep quality for themselves and spouses. That is, greater FCR reported by survivors was associated with their own and spouses' poorer sleep quality. Contrary to hypotheses, there was no association between spouses' FCR and average daily sleep quality for themselves or survivors. For the eve of the mammogram, greater FCR reported by both survivors and spouses was associated with their own poorer sleep quality. There was no evidence for significant cross-partner associations for the eve of the mammogram.

For average daily onset latency, results did not support the hypothesis that FCR is associated with one's own or one's partner's difficulty getting to sleep neither. For the eve of the mammogram, significant cross-partner associations emerged such that greater FCR reported by survivors and spouses was associated with greater difficulty getting to sleep for their partner. Contrary to hypotheses, there was no significant association between participants' FCR and their own onset latency the night before the mammogram.

Finally, for average daily wake after sleep onset, results did not support hypotheses that FCR is associated with one's own as well as one's partner's wake after sleep onset. Turning to the night before the mammogram, results suggested that,

as predicted, spouses' FCR was associated with greater difficulty staying asleep or waking too early for survivors on that single night. Contrary to hypotheses, there were no significant associations between participants' FCR and their own wake after sleep onset or survivors' FCR and spouses' wake after sleep onset the eve of the mammogram.

It should be noted that while several of the hypothesized actor and partner effects were marginal in terms of statistical significance, the standardized coefficients for several of these effects pointed to somewhat large effect sizes, suggesting some degree of practical significance. For example, there was a marginally-significant association between spouses' FCR and survivors' wake after sleep onset on the eve of the mammogram (before including covariates in the model). The standardized results for this same effect ($\beta = 0.41$) suggest that a one-standard deviation increase in spouses' latent FCR is associated with a .41 standard deviation increase in survivors' difficulty staying asleep or waking too early on the eve of the mammogram. Another example, the standardized results for spouses' FCR and their own average daily sleep duration (before including covariates in the model; $\beta = -0.21$) suggest that spouses with a one-standard deviation increase in FCR would be expected to sleep an average of 17.43 minutes less per night across the diary period. Future studies with larger samples would be better powered to detect these effects as statistically significant.

Taken together, these results suggest that greater FCR is associated with sleep disturbance for both cancer survivors and their spouses as they face together a contextual trigger for FCR—the first annual post-diagnosis mammogram. After

including covariates, survivors who reported greater FCR reported shorter sleep duration the eve of the mammogram, poorer average daily sleep quality, and poorer sleep quality the eve of the mammogram. After including covariates, spouses who reported greater FCR reported shorter average daily sleep duration, shorter sleep duration the eve of the mammogram, and poorer sleep quality the eve of the mammogram. Furthermore, FCR experienced by one partner is linked with sleep disturbance experienced by their spouse. After including covariates, greater survivor FCR was associated with spouses' poorer average daily sleep quality and greater difficulty getting to sleep the eve of the mammogram. After including covariates, greater spouse FCR was associated with survivors' greater difficulty getting to sleep and wake after sleep onset the eve of the mammogram.

These relationships highlight critical gaps in existing theoretical models of the antecedents and consequences of FCR (e.g., Lee-Jones et al., 1997), which have not considered sleep outcomes. While the direction of effects between FCR and sleep disturbance cannot be ascertained from this observational study, results suggest that further attention be paid to sleep as a factor in the etiology and maintenance of FCR and/or a consequence of FCR. Future studies should be designed in such a way to allow for examination of the direction of these effects. The role of intrusive and worrisome thoughts in the maintenance of insomnia for the broader, non-diagnosed population is well-established (Harvey, 2005). Following from this, future research should examine intrusive thoughts about recurrence, a component of FCR (Curran et

al., 2017; Fardell et al., 2016; Lebel et al., 2014; Lee-Jones et al., 1997; Lepore, 2001), as a potential mechanism by which FCR may negatively impact sleep.

It is worth noting that existing interventions for psychological distress in cancer survivors do not monitor or address sleep. Results from a meta-analysis suggest that existing interventions demonstrate only small-to-medium effect sizes for cancer-related anxiety (Faller et al., 2013). Given the results of this study, these interventions may be improved by considering relationships between cancer-related anxiety and sleep disturbance. A recent review identified five randomized control trials for interventions for FCR, three of which (a CBT based therapy, a combined meta-cognitive and acceptance and commitment-based therapy, and a psycho-educational intervention) demonstrated clinically significant reductions in FCR (Sharpe, Thewes, & Butow, 2017). These emerging interventions for FCR also do not address or monitor sleep outcomes. Given the strong link between psychological distress and insomnia in the general population, interventions for cancer-related anxiety and FCR may also be effective in treating sleep disturbance, and thereby promote long-term health.

The analysis of partner effects suggests that *couple*- rather than *individual*-focused interventions for FCR and sleep disturbance should be explored. Spouses of cancer survivors also report FCR and sleep disturbance and one partner's FCR was related to the other's sleep. Couple-focused interventions for psychological distress in the context of cancer should assess for and address elevated levels of FCR and sleep

disturbance in both survivors and their spouses, as both can become chronic and are known to be implicated in mental and physical health and mortality.

Several limitations of this study may inform future work as research on FCR and sleep proliferates. First, FCR was assessed cross-sectionally and the direction of effects cannot be determined from this observational study. Future studies should attempt to examine the daily, within-person associations between FCR and sleep, thereby capturing both variables closer in time to when they are experienced. Second, that several of the actor and partner effects were marginally-significant may be due in part to the relatively small sample size. The larger longitudinal study was not designed nor powered specifically to examine relationships between FCR and sleep. Studies with larger samples may be better equipped to detect significant associations between FCR and the sleep outcomes studied here. Third, the sample was homogenous; therefore, future studies should attempt to recruit not only larger but also more diverse or distressed samples to improve generalizability. Finally, sleep outcomes were measured via self-report. Future work should attempt to replicate and extend these results using objective measures of sleep duration, quality, and disturbances using actigraphy or polysomnography.

In conclusion, relationships between FCR and health behaviors are a critical gap in theoretical models and interventions for FCR. FCR is associated with sleep disturbance for both cancer survivors and their spouses as they experience a trigger for FCR, a central factor in frameworks conceptualizing FCR. The relationships that emerged between FCR and sleep disturbance, which has known,

long-term implications for health and mortality, highlight the need for more research on links between FCR and other health behaviors (e.g., medication adherence, physical activity). Such research could inform interventions for improving both FCR and mental and physical health and mortality for the growing population of cancer survivors and their spouses.

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Appendix A

TABLES

Table 1. Descriptive Statistics.

Variable	Survivors		Spouses	
	Mean	*SD*	Mean	SD
FCRI severity	7.19	4.16	4.91	3.59
FCRI distress	1.04	1.57	0.54	1.43
CARS overall	9.51	3.58	8.49	3.84
Average sleep duration	7.51	1.46	7.08	1.37
Average sleep quality	2.25	0.96	2.28	0.98
Average onset latency	0.26	0.14	0.14	0.35
Average WASO	0.61	0.48	0.55	0.49
MMG sleep duration	7.03	1.58	6.87	1.38
MMG sleep quality	2.02	1.03	2.18	1.17
MMG onset latency	0.26	0.44	0.14	0.34
MMG WASO	0.67	0.47	0.63	0.48
Medical comorbidities	0.58	1.31	0.51	0.94
Physical well-being	3.74	3.45	--	--
Cancer stage	1.70	1.30	--	--
Chemotherapy[a]	0.30	0.46	--	--
Radiation[a]	0.72	0.45	--	--

Note. FCRI = Fear of Cancer Recurrence Inventory. CARS = Concerns about Recurrence Scale. WASO = Wake after sleep onset. MMG = sleep outcomes on the eve of the mammogram. [a]Dichotomous variable.

Table 2. Structural Regression of Average Daily Sleep Outcomes on Latent FCR Factors.

Outcome	Estimate	Standard error	*p*	95% *CI*	
				Lower	Upper
		Survivors			
Sleep duration					
Actor effect	-0.071[a]	0.024	.003	-0.119	-0.023
Partner effect	0.038	0.033	.257	-0.028	0.104
Sleep quality					
Actor effect	-0.103	0.024	<.001	-0.151	-0.055
Partner effect	0.023	0.022	.297	-0.020	0.066
Onset latency					
Actor effect	0.153	0.116	.187	-0.074	0.380
Partner effect	-0.041	0.099	.679	-0.236	0.154
WASO					
Actor effect	0.059	0.115	.610	-0.167	0.284
Partner effect	0.056	0.103	.587	-0.147	0.249
		Spouses			
Sleep duration					
Actor effect	-0.071[a]	0.024	.003	-0.119	-0.023
Partner effect	-0.036	0.025	.159	-0.085	0.014
Sleep quality					
Actor effect	-0.015	0.021	.485	-0.056	0.027
Partner effect	-0.086	0.028	.002	-0.141	-0.032
Onset latency					
Actor effect	0.012	0.093	.895	-0.170	0.195
Partner effect	0.238	0.101	.019	0.040	0.437
WASO					
Actor effect	-0.010	0.092	.910	-0.192	0.171
Partner effect	0.098	0.121	.417	-0.139	0.335

Note. WASO = Wake after sleep onset. CI = confidence interval. [a]Coefficients constrained to be equal across survivors and spouses.

Table 3. Structural Regression of Sleep Outcomes for the Eve of the Mammogram on Latent FCR Factors.

Outcome	Estimate	Standard error	*p*	95% *CI*	
				Lower	Upper
		Survivors			
Sleep duration					
Actor effect	-0.082[a]	0.043	.053	-0.166	0.001
Partner effect	-0.029	0.065	.655	-0.156	0.059
Sleep quality					
Actor effect	-0.093[b]	0.030	.002	-0.151	-0.035
Partner effect	-0.055[c]	0.030	.067	-0.113	0.004
Onset latency					
Actor effect	0.066	0.102	.599	-0.135	0.267
Partner effect	0.163[d]	0.079	.040	0.008	0.318
WASO					
Actor effect	0.005	0.097	.962	-0.186	0.195
Partner effect	0.238	0.132	.073	-0.022	0.497
		Spouses			
Sleep duration					
Actor effect	-0.082[a]	0.043	.053	-0.166	0.001
Partner effect	0.035	0.054	.517	-0.072	0.142
Sleep quality					
Actor effect	-0.093[b]	0.030	.002	-0.151	-0.035
Partner effect	-0.055[c]	0.030	.067	-0.113	0.004
Onset latency					
Actor effect	-0.097	0.129	.451	-0.349	0.155
Partner effect	0.163[d]	0.079	.040	0.008	0.318
WASO					
Actor effect	0.154	0.111	.165	-0.063	0.372
Partner effect	0.000	0.092	.999	-0.180	0.180

Note. WASO = Wake after sleep onset. [a, b, c, d] Coefficients constrained to be equal across survivors and spouses.

Table 4. Standardized Associations Between FCR and Sleep Outcomes.

Outcome	Survivors	Spouses
Average sleep duration		
Actor effect	-0.299**/0.090	-0.306**/-0.213†
Partner effect	0.152/0.184	-0.160/0.218
Average sleep quality		
Actor effect	-0.644***/-0.093**	-0.074/-0.017
Partner effect	0.135/0.023	-0.461**/-0.075*
Average onset latency		
Actor effect	0.257/-0.033	0.019/-0.058
Partner effect	-0.068/-0.078	0.386*/0.216
Average WASO		
Actor effect	0.095/0.065	-0.014/-0.023
Partner effect	0.087/0.072	0.140/-0.067
MMG sleep duration		
Actor effect	-0.194†/-0.189†	-0.209†/-0.199†
Partner effect	-0.064/0.034	0.095/0.034
MMG sleep quality		
Actor effect	-0.347**/-0.269*	-0.273**/0.222*
Partner effect	-0.189†/-0.226	-0.172†/0.030
MMG onset latency		
Actor effect	0.125/-0.091	-0.178/-0.198
Partner effect	0.293*/0.210*	0.315*/0.270*
MMG WASO		
Actor effect	0.009/-0.042	0.283/0.224
Partner effect	0.413†/0.373*	0.000/-0.158

Note. WASO= Wake after sleep onset. MMG = Sleep outcomes on the eve of the mammogram. Standardized regression coefficients before the slash are without controls; coefficients after the slash control for medical comorbidities as well as survivors' physical well-being, cancer stage, and treatment. $^{\dagger}p < .10$, $*p < .05$, $**p < .01$, $***p < .001$