FEAR OF CANCER RECURRENCE, CHECKING BEHAVIOR, AND TRIGGERING EVENTS IN THE DAILY LIVES OF BREAST CANCER SURVIVORS

by

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ABSTRACT

Fear of cancer recurrence (FCR) is a top ongoing concern of breast cancer (BC) survivors and thus the focus of recent intervention development. According to prominent theory, certain events trigger FCR, which, in turn, leads to specific behavioral responses, including checking the body for signs or symptoms of cancer (Lee-Jones, Humphris, Dixon, & Hatcher, 1997). Links between triggering events, FCR, and checking behavior have not yet been studied in the context of daily life. The goal of this study was to examine whether FCR has a within-person link with daily checking behavior and whether FCR mediates the link between triggering events and checking behavior. Seventy-two early-stage BC survivors completed daily diaries over a 21-day period approximately five months after BC surgery. FCR, checking behavior, and triggering events were assessed each evening. Multilevel modeling results indicated that FCR predicted greater odds of same-day, but not next-day, checking behavior. Checking behavior had a positive but non-significant effect on next-day FCR. We found that daily FCR significantly mediated the same-day effect of triggering events on checking behavior. These average within-person effects varied substantially between patients and were not explained by negative affect. The results support the within-person sequence of triggering events, FCR, and checking behavior posited by guiding theory, and can inform FCR intervention development.

Chapter 1

INTRODUCTION

Fear of cancer recurrence (FCR) is defined as "fear, worry, or concern relating to the possibility that cancer will come back or progress" (p. 3266; Lebel et al., 2016). Particularly for cancers with high survival rates, such as breast cancer (BC), FCR can become a permanent fixture in the lives of patients whose cancer has been treated successfully. For the 3.6 million women who are BC survivors in the United States (Miller et al., 2016), the possibility of recurrence is often the top ongoing concern (Baker, Denniston, Smith, & West, 2005; Simard, Thewes, & Humphris, 2013; Vickberg, 2003). Indeed, FCR can be best understood as a chronic rather than acute experience, as it has been shown to persist years following BC treatment (Deimling, Bowman, Sterns, Wagner, & Kahana, 2006; Mellon, Kershaw, Northouse, & Freeman-Gibb, 2007). A growing literature points to numerous negative outcomes of FCR, including psychological distress (Deimling et al., 2006; Simard & Savard, 2009), worse quality of life (Mehnert et al., 2009; Simard, Thewes, & Humphris, 2013), and anxiety (Deimling et al., 2006).

1.1 The Self-Regulation Model of Illness

The most prominent and comprehensive theoretical framework for conceptualizing FCR is an adaptation of Leventhal's Self-Regulation Model of Illness (SRM; Leventhal, Diefenbach, & Leventhal, 1992) by Lee-Jones and colleagues (Lee-Jones, Humphris, Dixon, & Hatcher, 1997). The SRM posits a comprehensive network

of processes that represent a holistic context for understanding FCR, beginning with its antecedents or triggers and ending with its consequences. Triggers of FCR include internal cues, such as experiencing pain and other physical symptoms, and external cues, such as annual cancer screenings and commercials for cancer treatment. When FCR comes online, the SRM suggests several behavioral consequences, including checking for signs or symptoms of cancer, as well as psychological consequences, such as anxiety.

Substantial effort has put into defining the experience of FCR itself (see Lebel et al., 2016) and identifying its psychological correlates (e.g., Simard, Thewes, & Humphris, 2013). However, there have been few empirical tests of the remaining components of the SRM. In terms of the theorized triggers of FCR, numerous studies have demonstrated cross-sectional associations between FCR and internal cues including pain, physical symptoms, fatigue, and changes in appearance (for a review, see Crist & Grunfeld, 2013; Simard et al., 2013). Results from these studies indicate that patients who experience more physical symptoms, treatment side effects, or changes to their appearance tend to be the same patients who also report greater FCR. The research on external triggers of FCR is less developed. Qualitative work suggests that common external triggers include doctor appointments, hearing about someone else having cancer, and annual mammograms (Gil et al., 2004; Simard & Savard, 2009).

Behavioral consequences of FCR have received little empirical attention. One theorized behavioral consequence is checking the body for signs or symptoms of cancer (Lee-Jones et al., 1997). It is thought that when a patient experiences FCR, one way she may attempt to regulate the distress is to seek confirmation that no new signs

or symptoms have surfaced. When she gains this confirmation by checking her body, she may be, in the moment, reassured that her cancer has not progressed or recurred. Thus, checking behavior serves to temporarily attenuate distress associated with FCR. When FCR inevitably returns, the patient will be more likely to use this distress-reducing strategy again. For patients who experience FCR frequently, checking behavior may become excessive, problematic, and even compulsive. Over the past several decades, scholars have frequently described and drawn upon this theorized process (e.g., Fardell et al., 2016; Ghazali et al., 2012; Lasry & Margolese, 1992; Stark & House, 2000; Ziner et al., 2012). In fact, excessive checking behavior is an explicit target of a recent intervention designed to reduce FCR (Humphris & Ozakinci, 2008).

Checking behavior is a seemingly fundamental element of the conceptualization of FCR, as it may serve ultimately to reinforce the distressing experience. Importantly, self-examination is not necessarily a certain or straightforward method for assessing signs or symptoms of cancer progression or recurrence, especially when performed in an emotionally aroused state (Fardell et al., 2016; Miller, 1995; Taylor, Richardson, & Cowley, 2011). National guidelines recommend monthly breast self-examination for BC survivors (Khatcheressian et al., 2013) based on evidence that a greater frequency increases rates of invasive procedures resulting in benign findings, but does not improve rates of mortality (Thomas et al., 2002). Thus, checking in response to FCR may actually evoke more uncertainty about disease status or lead to preventable or unnecessary doctor appointments and formal screenings. Taken together, checking behavior may not only

have significant implications for the well-being of cancer survivors, but also the health-care delivery system and federal healthcare spending and policy.

1.2 Matching Method to Theory

Unfortunately, the strong theoretical and intuitive interest in checking behavior does not currently correspond to its empirical support as a consequence of FCR. Only two studies, to our knowledge, have assessed FCR and checking behavior in BC patients. In a cross-sectional study, Thewes and colleagues (2012) found that for BC patients who recently finished treatment, greater FCR was associated with more frequent self-reported use of breast self-examination. In another relevant cross-sectional study, BC survivors who had more severe FCR reported more frequent use of checking as a strategy to cope with FCR when it came up (Custers et al., 2016).

Although preliminary cross-sectional support of the SRM as applied to FCR is encouraging, these studies do not speak to the within-person, temporal unfolding of triggers, FCR, and consequences that comprise the model. The SRM posits an internal or external trigger that reminds a patient of cancer, which in turn activates illness representations of her cancer and the possibility of recurrence. The patient experiences FCR, which leads her to check her body for signs or symptoms of cancer as a means of reassurance. A BC patient likely moves through this entire sequence within a relatively small window of time (e.g., potentially within minutes, hours, or possibly several days). FCR interventions are intended to map onto this within-person process in order to interrupt the patient's maladaptive pattern. For example, a recently developed FCR intervention involves identifying the patient's personal sequence of FCR and checking and challenging the proximal reasons for and consequences of the checking response (Humphris & Ozakinci, 2008).

To unravel the experience of FCR and validate the SRM, it is crucial to examine these processes at the level at which we believe they unfold. While limited cross-sectional findings suggest that individuals with higher FCR tend to report checking more frequently, global and retrospective assessment may only distally capture the processes of the SRM. Global cross-sectional methods are vulnerable to retrospective biases (Shiffman, Stone, & Hufford, 2008) and do not address the directionality of an association or rule out unmeasured between-person confounding variables (Bolger, Davis, & Rafaeli, 2003; Bolger & Laurenceau, 2013; Laurenceau & Bolger, 2005). Behavioral consequences of FCR, including checking behavior, have not yet been examined prospectively and at the within-person level, despite the fact that checking behavior is targeted in FCR-specific interventions. Moreover, FCR triggers hypothesized to initiate the SRM sequence, while well studied cross-sectionally, have also not yet been examined at this level.

Intensive longitudinal methods, which involve repeated measurements of individuals over time (e.g., daily diaries; Bolger & Laurenceau, 2013), can provide valuable information that maps onto our theoretical and intuitive understanding of FCR. This approach can bypass retrospective biases associated with global self-report of behaviors or feelings over a span of time, and provides a clearer picture of the processes that flow into and flow from FCR (Bolger et al., 2003; Bolger & Laurenceau, 2013; Laurenceau & Bolger, 2005; Shiffman et al., 2008). Furthermore, intensive longitudinal data also offer the potential of identifying the directionality and sequence of effects (Bolger et al., 2003; Bolger & Laurenceau, 2013). For example, one can examine whether a particular effect carries over from one measurement interval to the next, which could provide insight into the potency and duration of the

effect. This level of insight can be easily translated and applied to the development and refinement of FCR interventions.

1.3 The Present Study

In the current study, we examined the links among triggering events, levels of FCR, and checking behavior posited by the SRM on a daily, within-person level, which has not been previously examined. Daily diary data from early-stage BC patients were used to accomplish several aims. Our first aim was to determine whether FCR was associated with checking behavior on the same day. Based on the SRM, we hypothesized that patients who reported greater FCR on one day would be more likely to check for signs or symptoms of cancer on that same day.

We also sought to explore the directionality of the association between FCR and checking behavior by examining the carryover of the effect in both directions from one day to the next. No prior research has attempted to delineate the timeline for these effects. Further, it has been suggested that checking behavior may reinforce and strengthen FCR, but this has also not been examined empirically. Thus, an exploratory aim was to investigate whether FCR was associated with a greater likelihood of checking the next day, and vice versa.

Finally, we examined the posited sequence of triggers predicting FCR, in turn, leading to checking behavior. Therefore, our second aim was to determine the extent to which the effect of daily triggers on checking behavior is mediated by FCR. Based on the SRM, we hypothesized that FCR would mediate the within-person association between triggers and checking behavior. To rule out the possibility that feelings of negativity could explain the hypothesized links among these variables, we included momentary negative affect as a within-person covariate in all tests.

Chapter 2

METHOD

2.1 Participants

Participants were early-stage BC patients recruited from a community cancer center for a larger longitudinal study. Patients were asked to participate if they met the following inclusion criteria: (1) diagnosed with Stage 0 (lobular/ductal carcinoma in situ), I, II, or IIIA breast cancer, (2) had recent breast cancer surgery, (3) in a committed romantic relationship with a partner who also agreed to participate, (4) English-speaking, and (5) lived within an hour of the recruitment site. Exclusion criteria included prior cancer diagnoses and diagnoses of serious mental illness. Patients who had a recent positive breast biopsy and appeared to be eligible based on their electronic medical records were sent a letter about the study and then contacted by phone. Note that although the larger study obtained data from both patients and their partners, only patient data are used in the current study.

Of the 1161 patients who had a recent positive breast biopsy, 698 were identified as ineligible based on their medical records. The 463 potentially eligible patients were mailed a letter and contacted by phone. Of those patients who were contacted, 117 agreed to participate, 110 were identified as ineligible based on patient-provided information, 82 were unable to be reached, and 154 declined to participate. Those who agreed to participate by phone were mailed a consent form to return to the study staff. Seventy-seven patients provided informed consent and participated, six patients provided consent but did not participate, and 34 did not return the consent

form. The present study examined one assessment period of the larger longitudinal study, to which 72 participants contributed data, resulting in a final sample of 72 patients described here.

Approximately 89% of patients identified as Caucasian, 10% as African American, and 1% as Asian. All patients identified as non-Hispanic. The average age of patients was 54.54 years (SD = 9.48), and 94% of patients were married. In terms of occupational status, about 43% reported not working, 39% reported working full time, and 18% reported working part time. The majority of patients (73%) reported an annual household income over $60,000. Fifteen percent of patients were diagnosed with Stage 0 breast cancer, 49% Stage IA, 24% Stage IIA, 11% Stage IIB, and 1% Stage IIIA. In terms of adjuvant treatment, the majority of patients did not receive chemotherapy (67%) but did receive radiation therapy (71%) and hormonal therapy (81%).

2.2 Procedure

Patients were recruited as soon as possible after their initial BC surgery. After providing informed consent, patients completed a series of baseline questionnaires, including a demographic questionnaire. The baseline assessment took place an average of three months after initial BC surgery (SD = 1.56, range = 1 – 8). Data for the current study came from a daily diary period that took place after the baseline assessment, as soon as possible after the end of adjuvant treatment. This particular period was targeted for intensive study of FCR based on evidence suggesting that FCR emerges soon after the end of adjuvant treatment, when patients begin seeing their healthcare providers less frequently and often feel as though they are no longer actively fighting the cancer (King, Kenny, Schiel, Hall, & Boyages, 2000; McKinley,

2000). Patients who did not receive adjuvant chemotherapy or radiation therapy were asked to complete the daily diary period as soon as possible after the completion of their baseline questionnaire. Patients started the daily diary period an average of five months after their BC surgery (SD = 2.09, range = 2 – 12).

The daily diary period took place over 21 consecutive days. Over the course of the daily recording period, patients were asked to complete a short survey every evening within about an hour of going to sleep. Before the diary period began, patients were provided with a website link to access and complete the same survey from their home each evening. The evening survey was designed to be brief and took patients 13 minutes on average to complete. Since several survey items asked patients about the events of their day, compliance with the requested time for completion was monitored via the online survey software. Data were only included in analysis if the evening survey took place between 6:00pm and 3:00am. On average, patients completed the surveys on 17 out of the 21 days (81% compliance rate).

2.3 Measures

2.3.1 Daily triggers

Eight internal and external triggers were assessed in each evening survey. Patients indicated whether each trigger occurred that day. Five internal triggers were assessed, including “noticed skin irritation,” and “tingling or loss of sensation in hands or feet.” Three external triggers were also assessed, including “had a long wait in doctor’s office” and “received negative news from physician.” Internal and external triggers were summed to represent the number of triggers experienced daily.

2.3.2 Daily fear of cancer recurrence

Six items from the Fear of Cancer Recurrence Inventory (FCRI; Simard & Savard, 2009) were adapted for daily use. One item assessed how much time patients spent thinking about the possibility of cancer recurrence that day, with responses ranging from zero (*"I didn't think about it at all"*) to four (*"several hours"*). The remaining items, drawn from the FCRI severity and psychological distress subscales, tapped emotion states associated with the possibility of cancer recurrence (e.g., *"I felt helpless or resigned about the possibility of cancer recurrence."*). The latter five items were rated from zero (*"not at all"*) to four (*"extremely").* The six items were summed to create a daily FCR composite. Coefficient omega estimated strong within-person reliability of the daily FCR scale ($\omega = .91$).

2.3.3 Daily checking behavior

One item assessed whether patients engaged in daily checking behavior: *"Today, did you examine yourself physically or symptoms of cancer?"* Patients responded *"yes"* or "*no*."

2.3.4 Momentary negative affect

Momentary negative affect was measured using seven items from the Positive and Negative Affect Schedule (PANAS-X; Watson & Clark, 1994), which were averaged to create a composite. Patients indicated the extent they experienced each affective item *"at this moment"* from zero (*"not at all"*) to four (*"extremely"*). Coefficient omega estimated acceptable within-person reliability of the momentary negative affect scale ($\omega = .79$).

Chapter 3

RESULTS

3.1 Data Analytic Approach

Multilevel modeling was used to accommodate the nested structure of the daily diary data (i.e., days nested within patients). Multilevel analyses were conducted in R (version 3.3.2; R Core Team, 2016) using the *lme4* package (version 1.1-12; Bates, Maechler, Bolker, & Walker, 2015). In all primary analyses, time was entered as a covariate to control for any linear effect of time during the diary period. In addition, a random intercept was estimated in each model, allowing for person-to-person variability in levels of the outcome. Random slope effects for focal predictors were estimated when possible. Time-varying predictors were person-mean centered and person-level predictors were grand mean centered (Bolger & Laurenceau, 2013).

To address our first aim, we examined the concurrent daily association between FCR and checking behavior (a binary outcome variable) by estimating a multilevel logistic regression model. Daily checking behavior was regressed on daily FCR, controlling for time and momentary negative affect. In addition to the within-person effect of primary interest, we also estimated the between-person effect by including average FCR over the course of the diary period as a person-level predictor. A random intercept effect and random slope effect for daily FCR were estimated.

To explore the directionality of the association between FCR and checking behavior (our exploratory aim), we examined whether FCR predicted not only concurrent checking behavior, but also future checking behavior, and vice versa. An

additional set of multilevel regression models was conducted in which the outcome was set one day after the predictor. First, next-day checking behavior was regressed on same-day FCR while controlling for same-day checking behavior and momentary negative affect. We then regressed next-day FCR on same-day checking behavior, including same-day FCR and momentary negative affect as covariates. A random slope effect for the focal predictor of each model (i.e., FCR or checking behavior) was also estimated.

To address our second aim, we conducted a 1→1→1 multilevel mediation analysis (Bauer, Preacher, & Gill, 2006; Kenny, Korchmaros, & Bolger, 2003; Krull & MacKinnon, 2001), in which the predictor (triggers), mediator (FCR), and outcome (checking behavior) were all time-varying variables (i.e., measured daily). The hypothesized mediation model is depicted in Figure 3.1. Because FCR was modeled as a count outcome and checking behavior was modeled as a binary outcome, the standard test of the mediated effect (i.e., the product of the indirect paths; Baron & Kenny, 1986) is an incorrect approach. We used a more general approach to mediation analysis (Imai, Keele, & Tingley, 2010) based on the counterfactual, or potential outcomes, framework (Imai, Jo, & Stuart, 2011; Rubin, 2005). It can be useful to exemplify this approach making use of a dichotomized predictor that takes the value of X = 0 or X = 1, and a mediator which is defined based on the value of X (i.e., mediator when X = 0 or X = 1). In this general mediation framework, the average direct effect is defined as the expected value of the outcome when the predictor has changed (from X = 0 to X = 1) but the mediator is held constant. The average mediated effect is defined as the expected value of the outcome when the mediator has

changed from its potential value at X = 0 to X = 1, while holding the predictor constant.

The average direct and mediated effects sum to equal the average total effect, as in traditional approaches to mediation. However, this more general approach to mediation analysis accommodates conditions that traditional approaches do not, such as interactions between the predictor and mediator variables and non-linear outcome distributions (e.g., in the current study, checking behavior is a binary outcome variable and was modeled using multilevel logistic regression; Valeri & VanderWeele, 2013). The *mediation* package in R was used to test our hypothesized mediated effect and obtain estimates of the average direct, mediated, and total effects (version 4.4.5; Tingley, Yamamoto, Hirose, Keele, & Imai, 2014).

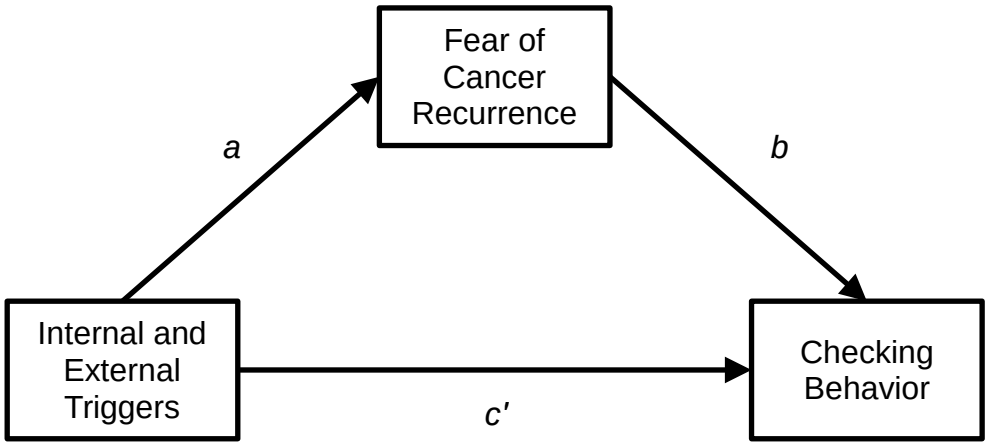

Figure 3.1: Hypothesized Multilevel Mediation Model. The *a* path was estimated by regressing FCR on daily triggers, controlling for momentary negative affect, average triggers, and time, with a random slope estimated for daily triggers. The *b* and *c′* paths were estimated by regressing checking behavior on daily FCR, daily triggers, controlling for momentary negative affect, average FCR, average triggers, and time. Random slope effects for the *b* and *c′* paths were not able to be estimated due to convergence problems.

3.2 Preliminary Results

Descriptive statistics are displayed in Table 3.1. On average, patients reported the occurrence of about one trigger event per day. Daily FCR was low on average and positively skewed, with a large proportion (57.8%) of zero scores. As a result, FCR was modeled as a multilevel count outcome with a Poisson distribution in subsequent analyses. Patients reported checking on 19% of their diary days on average. Some patients did not endorse checking behavior on any days, while others reported checking on as many as 18 of the 21 diary days.

Table 3.1: Descriptive Statistics and Bivariate Correlations of Primary Variables

	Fear of recurrence	Checking behavior	Triggering events	Negative affect
Fear of recurrence	–	.39	.51	.74
Checking behavior	.25	–	.25	.23
Triggering events	.26	.08	–	.30
Negative affect	.25	.02	.16	–
Mean	2.09	0.19	0.86	0.17
Within-person *SD*	2.53	0.32	0.76	0.26
Range	0 – 20	0 – 1	0 – 7	0 – 2.71
Intraclass correlation	.43	.35	.55	.45
Number of observations	1282	1278	1280	1281

Note. Within-person correlations are displayed below the diagonal, and between-person correlations are displayed above the diagonal.

3.3 Daily Link Between FCR and Checking Behavior

We first examined whether FCR predicted checking behavior on the same day, by regressing checking behavior on FCR while controlling for time and momentary negative affect. Results are displayed in Table 3.2. FCR emerged as a significant within-person predictor of checking behavior, indicating that when a patient experiences a one-unit increase in FCR, compared to what is typical for her, the odds are 32% greater that she will check for signs or symptoms of cancer the same day. The random effect variance for the slope was 0.03 (*SD* = 0.18), indicating that the slopes of about 95% of patients fell between -0.07 (odds ratio (OR) = 0.93) and 0.64 (OR = 1.89). This suggests that for some patients, the effect of FCR on checking behavior approached zero, while for others, the effect of FCR on checking behavior was much greater than the average effect. In addition, average FCR over the course of the diary period was a significant predictor of average checking behavior, $\gamma = 0.37$, OR = 1.45, $z = 3.18$, $p = .002$. This between-person effect indicated that patients who tend to report higher average daily FCR also tend to report checking more frequently.

3.4 Prospective Link Between FCR and Checking Behavior

We examined whether FCR predicted checking behavior the next day, controlling for same-day momentary negative affect, same-day checking behavior, and time. Results are shown in Table 3.2. We did not find evidence that FCR predicted future checking behavior (OR = 1.04, $p = .473$). Thus, our results suggest that FCR is a strong predictor of checking behavior the same day, but does not have a detectable effect on checking behavior the next day (above and beyond its same-day effect). The random slope for FCR estimated a variance of 0.03 (*SD* = 0.17), indicating that 95%

of individual patient slopes in the population fall between -0.29 (OR = 0.75) and 0.38 (OR = 1.46).

We also examined whether checking behavior predicted next-day FCR, controlling for same-day momentary negative affect, same-day FCR, and time. Results (shown in Table 3.2) suggested a positive but non-significant effect of checking behavior on next-day FCR (rate ratio (RR) = 1.37, p = .112). When a patient checked, regardless of her FCR score on that same day, she was predicted to have a 1.37 times greater FCR score the next day. The random slope for checking behavior also pointed to substantial variability in this effect (variance = 0.73, SD = 0.85), indicating that 95% of patients had slopes between -1.40 (RR = 0.25) and 2.02 (RR = 7.53).

Table 3.2: Multilevel Regression Results of Concurrent and Prospective Link Between FCR and Checking Behavior

Effect	Estimate	*SE*	Odds/rate ratio	*p*	95% CI	
					Lower	Upper
Concurrent link: FCR → Same-day checking behavior*						
FCR	0.28	0.06	1.32	<.001	0.162	0.398
Negative affect	-0.57	0.42	0.57	.171	-1.393	0.253
Time	0.01	0.02	1.01	.546	-0.029	0.049
Prospective link: FCR → Next-day checking behavior*						
FCR	0.04	0.06	1.04	.473	-0.078	0.158
Negative affect	-0.24	0.40	0.79	.574	-1.024	0.544
Time	-0.01	0.02	0.99	.710	-0.049	0.029
Prospective link: Checking behavior → Next-day FCR†						
Checking behavior	0.31	0.20	1.37	.112	-0.082	0.702
Negative affect	0.28	0.06	1.32	<.001	0.162	0.398
Time	-0.01	0.00	0.99	.005	-0.018	-0.002

*Poisson regression estimates are exponentiated to obtain rate ratios. †Logistic regression estimates are exponentiated to obtain odds ratios. Note. The same-day level of the outcome was also included as a covariate in prospective models (data not shown). FCR = daily fear of cancer recurrence.

3.5 Within-Person Mediation Model

The results of the tests of the hypothesized mediation model (depicted in Figure 3.1) are displayed in Table 3. The *a* path was estimated by regressing FCR on daily triggers, momentary negative affect, average triggers, and time, with a random slope estimated for daily triggers. As expected, triggering events were a significant and positive predictor of same-day FCR. Specifically, on a day a patient experienced one additional triggering event (compared to the average number of daily triggers she typically experienced), she was predicted to have a 1.51 times greater FCR score that same day. The random effect variance of this fixed effect was 0.14 (*SD* = 0.37), indicating that about 95% of patient slopes in the population fall between -0.32 (RR = 0.72) and 1.15 (RR = 3.16). In addition, average number of triggers over the course of the diary period significantly predicted higher average FCR, $\gamma = 0.71$, RR = 2.04, $z = 3.76$, $p < .001$.

Next, we tested the *b* and *c′* paths by regressing checking behavior on daily FCR, daily triggers, momentary negative affect, average FCR, average triggers, and time. Random slope effects were not able to be estimated in this model due to nonconvergence. Results (shown in Table 3) indicated a significant positive effect of FCR on checking behavior (*b* path), suggesting that when a patient experiences a one-unit increase in FCR, compared to what is typical for her, the odds are 33% greater that she will check for signs or symptoms of cancer the same day. The effect of triggers on checking behavior was not statistically significant (*c′* path).

The R *mediation* package uses these models to produce the mediated effect estimates, which are provided in probability units (shown in Table 3). The average mediated causal effect was 0.02. This estimate indicates that when a patient

experiences one more daily trigger relative to what is typical for her over the diary period, there is a 2% increase in the probability of reporting checking behavior on the same day that is due solely to increases in FCR. The average direct effect was 0.01, suggesting that a one-unit increase in daily triggers results in a 1% increase in the probability that the patient will exhibit checking behavior that is not explained by increases in FCR. The average proportion mediated effect is 0.66, indicating that 66% of the total effect of FCR triggers on checking behavior is explained by FCR.

Table 3.3: Results of the Multilevel Mediation of the Link Between Triggering Events and Checking Behavior by FCR

Effect	Estimate	*SE*	Odds/rate ratio	*p*	95% CI	
					Lower	Upper
Mediator model: FCR triggers → FCR*						
FCR triggers (a path)	0.41	0.08	1.51	<.001	0.259	0.568
Negative affect	0.42	0.05	1.52	<.001	0.313	0.518
Time	-0.02	0.00	0.98	<.001	-0.023	-0.009
Outcome model: Triggers and FCR → Checking behavior†						
FCR (b path)	0.28	0.04	1.33	<.001	0.203	0.365
FCR triggers (c' path)	0.10	0.13	1.11	.414	-0.146	0.354
Negative affect	-0.60	0.39	0.55	.119	-1.363	0.155
Time	0.01	0.02	1.01	.448	-0.019	0.042
Mediation effects						
Average mediated effect	0.02			<.001	0.01	0.04
Average direct effect	0.01			.42	-0.02	0.04
Total effect	0.04			.03	0.00	0.07

Table 3.3 continued

Proportion mediated effect	0.66		.03	0.22	2.65

*Poisson regression estimates are exponentiated to obtain rate ratios. †Logistic regression estimates are exponentiated to obtain odds ratios. *Note*. Mediation effect estimates are displayed in probability units. FCR = daily fear of cancer recurrence.

Chapter 4

DISCUSSION

Although there has been increasing research documenting FCR as a top concern, we are aware of no published work examining antecedents and consequences of FCR within the daily context of lives of BC survivors. The present study examined daily checking behavior, a behavioral consequence of FCR implicated by prominent theory (Lee-Jones et al., 1997) and a target of existing interventions for reducing FCR (Humphris & Ozakinci, 2008). Checking behavior has long been theorized as a consequence of FCR that provides short-term distress reduction but ultimately maintains FCR and reinforces checking behavior (e.g., Fardell et al., 2016; Ghazali et al., 2012; Lasry & Margolese, 1992; Lee-Jones et al., 1997; Stark & House, 2000; Ziner et al., 2012). Surprisingly, the link between FCR and checking behavior has only been examined in one cross-sectional study (Thewes et al., 2012). Despite the lack of empirical support, emerging FCR interventions draw heavily on the SRM and explicitly target excessive checking behavior (Humphris & Ozakinci, 2008). Using daily diary data from BC patients, the current study addresses this gap in the literature by examining the proximal (FCR) and distal (FCR triggering events) predictors of daily checking behavior proposed by the SRM. Our use of intensive longitudinal methodology provides the first test of the within-person, temporal processes outlined in the SRM and targeted in FCR interventions but not captured in the existing literature, which is based almost exclusively on global and cross-sectional assessments (e.g., Custers et al., 2016).

Results provided support for our hypothesis that patients who experience greater FCR on one day would be more likely to report checking their bodies for signs or symptoms of cancer. We found that on a day that a patient reports a one-unit increase in FCR, the odds are 32% greater that she will check for signs or symptoms of cancer the same day. Moreover, this effect was not explained by momentary negative affect during the evening survey. This significant fixed effect was also found to vary between patients, such that for some, the estimated effect was near zero, while for others, the estimated effect was over twice the size. These results point strongly to the potential role of moderating variables that attenuate or intensify the effect of FCR on checking behavior. While the current study was not designed or sufficiently powered to examine moderators of this effect, future studies should investigate variables that may explain why some patients exhibit checking behavior when they experience FCR and others do not.

Based on our finding that FCR and checking behavior were linked concurrently (i.e., were positively associated on the same day), we could conclude that FCR took no longer than the period of a day to evoke checking behavior (or vice versa). However, given the lack of empirical or theoretical work on the timescale of the SRM, we also explored the possibility of carryover effects of FCR on checking behavior the next day, which would also provide stronger evidence for the direction of this effect. We did not find evidence of an effect of FCR on next-day checking behavior (controlling for checking behavior the previous day). This finding does not support or conflict with the hypothesized causal role of FCR, but does suggests that future studies must involve more frequent assessments (e.g., multiple daily measurements) in order to determine the directionality and temporal sequence of these

momentary experiences. Intuitively, it seems likely that the effect of FCR on checking behavior occurs within a shorter time frame than one day, making it impossible for a daily diary design to capture. In addition, there was evidence for variability in the effect among patients, such that greater FCR on one day predicted increased odds of checking the next day for some patients, and decreased odds of checking the next day for others.

It has been suggested that checking behavior may maintain or exacerbate FCR (Fardell et al., 2016; Ghazali et al., 2012; Lasry & Margolese, 1992; Lee-Jones et al., 1997; Stark & House, 2000; Ziner et al., 2012). We explored this idea by examining whether checking behavior on one day predicted FCR the next day, controlling for FCR and momentary negative affect the previous day. On average, patients who checked on one day were predicted to have a 1.37 times greater FCR score the next day. Although this effect did not reach statistical significance, it warrants further study. There was also substantial variability in this effect, with effects estimated for some to be strongly negative and others strongly positive. While many have conceptualized checking behavior as a FCR-reinforcing compulsion, more research is necessary to determine for whom and under what conditions this may ring true. Again, more frequent assessments are needed to work out the sequence and cycle of FCR and checking behavior over time.

Finally, we tested a multilevel mediation model representing the full FCR sequence posited by the SRM, in which internal and external triggers predict FCR, which predicts checking behavior. The results supported our hypothesis, indicating that the effect of daily triggers on checking behavior was significantly mediated by daily FCR. The direct effect of daily triggers on checking behavior not attributed to

the effects of FCR was not statistically significant. These results support the antecedents, FCR, and consequences posited by the SRM at the same momentary, within-person level that inherently defines the model. Further, the methods employed minimize retrospective bias and eliminate the possibility of person-level confounding variables. Taken together, the methodological strengths and results of the current study provide strong support for the SRM that has not been previously reported.

4.1 Limitations and Future Directions

We attempted to address directionality and temporal precedence in the association between FCR and checking behavior by examining the effects from one day to the next. We did not find strong support for FCR predicting next-day checking behavior, or vice versa. It is therefore possible that checking behavior temporally precedes FCR. Similarly, we cannot rule out the possibility that checking behavior leads to increased sensitivity or awareness of daily triggering events. As described earlier, it seems likely that our failure to find temporal precedence was a result of incongruence between the timeframe of assessments and unfolding of effects. Future studies should be designed to capture these processes that may unfold over minutes or hours.

Our use of intensive longitudinal methodology allowed us to quantify the heterogeneity in the within-person effects among the patients in our sample. Although the current study was not designed to explore and explain variability in the effects, our results suggest that this is a ripe area for future research. It will be important to understand the individual characteristics and contextual factors that attenuate or intensify the effect of FCR on checking behavior. For example, perhaps patients who perceive themselves at higher risk of recurrence are more likely to actively assess for

symptoms of recurrence in response to FCR (McCaul, Schroeder, & Reid, 1996). Trait anxiety may also differentiate the patient who has this behavioral response to FCR from the patient who does not (Cameron, Leventhal, & Love, 1998; Cohen, 2002; Stark & House, 2000). Patients who use other adaptive coping strategies, such as disclosing concerns about recurrence to a supportive and responsive loved one, may also be less likely to result in checking behavior.

Furthermore, our results do suggest that at least for some women, checking behavior does predict greater FCR prospectively, but this effect varied across our sample. Future work must further explore the notion that checking behavior can function as a FCR-reinforcing compulsion. To address this, a larger and more diverse sample is necessary. Patients in the current sample were largely high-functioning and typically reported low levels of daily FCR. Despite this, we did find an average positive effect of checking behavior on next day FCR, which suggests a complex process that is not likely explained by severe FCR alone. Understanding the rebound effect of checking behavior has crucial implications for both mental and medical healthcare. FCR interventions that target checking behavior will be more effective and efficient if guided by empirical evidence of the distinction between adaptive and maladaptive checking behavior, and how and for whom this behavior perpetuates a cyclical process. Future work in this area may also inform the guidance and education about self-examination that physicians and nurses provide to patients.

Finally, the impact of checking behavior on other domains is largely unknown. The excessive checker may be more vulnerable to false positives that result in unnecessary health care utilization. Although the role of health care utilization is a crucial component of the FCR framework, extant research in that area is surprisingly

limited. The results of the few studies that have examined FCR and health care utilization point to inconsistent associations across different forms of health care (Lebel, Tomei, Feldstain, Beattie, & McCallum, 2013; Sarkar et al., 2015; Thewes et al., 2012). Thewes and colleagues (2012) found that greater FCR was significantly associated with more frequent self-checking behavior but less frequent formal screenings, such as mammograms and ultrasounds. Another study found that FCR was predictive of more outpatient and emergency room visits, but unrelated to specialist visits and other healthcare appointments (Lebel et al., 2013). More work on this topic is needed to gauge the extent and domains of the individual- and system-level consequences of FCR.

4.2 Conclusion

The SRM is a widely used framework for the conceptualization of FCR and development of FCR interventions. This was the first study to move beyond global and cross-sectional tests of the model and examine the daily within-person processes that are inherent in the guiding framework. Our findings support the posited sequence of triggering events, FCR, and checking behavior that may unfold within just a day. We found that FCR predicted the behavioral response of checking behavior, which in turn, for some patients, backfired and predicted greater next-day FCR. These findings have potential implications for healthcare utilization, information and instruction about self-checking provided to BC patients, and FCR intervention development.

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Appendix

INSTITUTIONAL REVIEW BOARD APPROVAL

CHRISTIANA CARE
Institutional Review Board
FWA00006557

Helen F. Graham Cancer Center & Research Institute
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MEMORANDUM

DATE: January 11, 2016

TO: Jean-Philippe Laurenceau, PhD
Oncology Research
Christiana Hospital

FROM: Wendy Bassett WB

RE: ***CCC# 33026*** **- Surviving Cancer Together: (DDD# 601576)**

This is to officially inform you that the Continuing Review with Consent to your protocol which was received on 01/08/2016 was reviewed by Expedited Review and approved by Jerry Castellano, Pharm.D, CIP, Corporate Director of the Christiana Care Health System Institutional Review Board, on **01/11/2016**.

Approval was extended for a period of one year, through **01/10/2017.**

Our records indicate this study is OPEN.

If you have any questions or concerns, please contact the IRB Office.

Thank you.