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Systemic inflammation among breast cancer survivors: the roles of goal disengagement capacities and health-related self-protection

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Abstract

***Background*: This study examined the associations between breast cancer survivors' capacity to adjust to unattainable goals (through goal disengagement and goal reengagement), health-related self-protection (e.g., positive reappraisals), and low-grade systemic inflammation (i.e., C-reactive protein [CRP]).**

***Methods*: Self-reports of goal adjustment capacities and health-related self-protection were measured and concentrations of the inflammatory molecule CRP were quantified in a cross-sectional sample of 121 female breast cancer survivors (M_{age} 55.53, SD = 10.99 years).**

***Results*: Results from hierarchical linear regression analyses indicated that low levels of goal disengagement capacities predicted higher CRP. Moreover, health-related self-protection buffered the association between failure to disengage from unattainable goals and elevated CRP. These results were independent from potential confounders including age, education, smoking, BMI, cancer stage, and time since diagnosis.**

***Conclusions*: The study's findings suggest that goal disengagement capacities and health-related self-protection can work together in predicting systemic inflammation among breast cancer survivors. Failure to disengage from unattainable goals may trigger health-compromising inflammatory processes, unless breast cancer survivors are able to engage in self-protection to manage their health threats.**

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Introduction

Over 1.4 million new cases of breast cancer (BC) are diagnosed worldwide each year [1]. Despite the high incidence, improvements in detection and treatment have resulted in better prognoses and higher survival rates (87% 5-year relative survival) [2,3]. Unfortunately, many women who survive BC will experience subsequent physical health problems [4,5]. These consequences could be associated with inflammatory processes that often occur in the context of stress. Systemic inflammation represents a major pathway to a number of diseases [6–8], and the proinflammatory biomarker C-reactive protein (CRP) has been associated with distress, serious health conditions (e.g., diabetes, cardiovascular disease), and mortality in BC survivors [9–12]. As such, it is important to examine how BC survivors can prevent systemic inflammation. In this study, we argue that adaptive self-regulation processes could ameliorate inflammatory processes. Identifying psychological constructs may be a viable strategy to help BC survivors mitigate the stressful experience and protect their physical health.

Adjustment to perceived health threats

Health-related declines often emanate from stressful life events and are pronounced if individuals are unable to manage a stressor [13–15]. One particular challenge of BC survivors is to adjust to health threats [4,16], such as treatment effects (e.g., cardiac toxicity) or the possibility of cancer recurrence [17,18]. Because many of these threats are hardly controllable by the individual, survivors may need to change their perceptions of health-related circumstances to effectively cope with them. On the basis of the motivational theory of life-span development [19], this process can be supported by the use of self-protective secondary control strategies. These strategies include positive reappraisals (e.g., silver lining) or self-protective attributions (avoiding self-blame), which are aimed at protecting a person's emotional and motivational resources. Self-protective strategies are adaptive if it is too difficult or impossible for a person to overcome a problem by active control efforts [19]. Past research on the effects of self-protective control strategies examined individuals who encountered low opportunities for overcoming a stressor (e.g., health, financial or loneliness problems in old age, partnership separation in later life). These studies showed that self-protective control strategies can prevent psychological distress and patterns of biological dysregulation (i.e., cortisol and CRP) in these populations [13,20,21].

Although not yet examined in the context of cancer, we think that engaging in health-related self-protection could also benefit BC survivors. For example, positively

reappraising health threats or not blaming oneself for the cancer is likely to prevent a variety of negative psychological states (e.g., regret, depression, or anxiety). As such, self-protective strategies may also mitigate disturbances in inflammatory processes.

Adjustment to goal constraints across life domains

In addition to managing health threats, BC survivors may also confront the challenge of having to change other goal-related aspects of their lives. For example, survivors may need to abandon desired goals, such as working on a promotion, pursuing sexual activities, or traveling [22,23]. In the context of cancer, a variety of goals may become unrealistic either because the cancer made their attainment impossible (e.g., a lack of physical resources) or because BC survivors need their time and energy for managing the health-related consequences of the cancer. In other words, BC survivors may have to make their life goals fit with cancer-related demands, which may require them to give up on some of their goals. If they fail in this task, they may become stretched too thin, expend too many coping resources, and experience stress-related consequences on their physical health.

A psychological construct that could facilitate the latter process relates to individuals' goal adjustment capacities [24,25]. Goal adjustment capacities reflect individual tendencies that have important regulatory functions across different life domains [25]. These capacities include the tendency to reduce effort and commitment from goals that are no longer feasible (i.e., goal disengagement capacities) and to identify, commit to, and pursue other meaningful and attainable goals (i.e., goal reengagement capacities) [25].

We think that goal disengagement capacities become paramount in the context of a demanding life stressor, such as cancer, as they enable individuals to abandon goals that have become constrained by the stressor and to focus their resources on effectively coping with the pressing situation. As a consequence, goal disengagement capacities are likely to prevent accumulated failure and associated psychological distress, which could ameliorate inflammatory processes among BC survivors. In support of this assumption, research examining a variety of vulnerable populations (e.g., older adults, caregivers, parents of sick children) has shown that goal disengagement capacities can forecast fewer depressive symptoms, adaptive endocrine and immune functioning, and better physical health [25–28].

We are less certain about the effects of goal reengagement capacities among BC survivors. Although goal reengagement capacities have been shown to facilitate positive aspects of subjective well-being (e.g., positive affect) [24,25,29], they are often unrelated to psychological distress [30]. In addition, some studies among vulnerable populations (e.g., caregivers or older adults) suggest that goal reengagement capacities may also contribute to psychological distress if they deplete resources necessary for managing the stressful life circumstances [28,31]. As a consequence of these mixed findings, goal reengagement capacities may not be reliably associated with BC survivors' levels of systemic inflammation.

In sum, our theoretical framework suggests that BC survivors may prevent stress-related inflammatory processes (i.e., CRP) if they are able to manage health threats through self-protection or to disengage from unfeasible goals across different domains. Note that these two self-regulation processes may be partially independent of each other and thus could interact in predicting inflammatory processes. In this regard, it would be possible that the combination of high self-protection and high goal disengagement capacity is synergistically associated with particularly low levels of systemic inflammation. Alternatively, it may be sufficient for BC survivors to master one of these challenges, and only the combination of low self-protection and low goal disengagement capacities may relate to particularly high levels of CRP.

We examined these possibilities by analyzing the associations between health-related self-protection, goal adjustment capacities, and CRP in a sample of BC survivors. We hypothesized that health-related self-protection and goal disengagement capacities would predict low levels of CRP. In addition, we examined whether the interaction between health-related self-protection and goal disengagement capacity is associated with levels of CRP. We did not expect to observe effects of goal reengagement capacities on CRP.

Method

Procedures

Female BC survivors were recruited through advertisements and oncologist referrals from medical clinics and hospitals in the Montreal region. Women were eligible if they met the following criteria: (a) at least 18 years of age, (b) first diagnosis of BC within the past year, (c) at least 20 weeks postprimary treatment (i.e., surgery or chemotherapy), (d) ability to provide informed consent, (e) ability to read and speak in English or French, and (f) report no health concerns that prevent them from engaging in physical activities. Women who met the eligibility criteria provided consent and completed questionnaires. Participants were further instructed to collect blood samples using a finger prick. The study was approved by the University and Hospital Ethics boards.

Participants

One hundred and ninety nine BC survivors were recruited. Fifteen participants refused to provide blood, and 62 participants did not provide sufficient blood to analyze

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CRP. On the basis of recommendations from previous research [32], one additional participant was excluded because she had an extremely elevated CRP value (>28). Because these participants had missing data in the outcome variable, the analytic sample is based on 121 women. The excluded participants did not differ statistically from the analytic sample in terms of age, education, smoking, BMI, cancer stage, time since diagnosis, or the main predictor variables ($ps > 0.05$). In the analytic sample, missing data of independent variables did not exceed 5% on any one variable and were replaced with the sample mean [33].

Descriptive sample statistics are presented in Table 1. Study participants ranged in age from young adulthood to old age. The majority of participants had been diagnosed with cancer stage I or II. They were on average 11 months past cancer diagnosis and somewhat overweight (BMI was calculated from objectively assessed weight and height in kilogram per square meter). Participants primarily self-identified as Caucasian (86.80%). The cancer treatments included 63.6% lumpectomy, 60.3% lymph node dissection, 29.8% single mastectomy, 17.4% double mastectomy, 70.2% chemotherapy, 88.4% radiotherapy, 54.5% hormone therapy, and 6.6% reconstructive surgery. Participants reported moderate to high levels of goal adjustment capacities and health-related self-protection, which are comparable with values reported in other studies [e.g., 13,14,20].

Instrumentation

C-reactive protein was measured as an indicator of systemic inflammation. After being instructed by a trained technician, participants collected capillary whole blood using a finger prick at home. Single-use lancets were used to deliver a uniform puncture to the finger, and up to three drops of blood were collected on a filter paper designed for this procedure. The filter paper was allowed to dry and stored in a freezer. After completion of the study, the samples were analyzed in the Laboratory for Human Biology Research at Northwestern University, using a high-sensitive enzyme immunoassay protocol [34,35]. Validation studies measuring CRP from blood drops has shown high correlations with matched CRP samples from blood plasma, as well as good sensitivity and reliability [34].

Table 1. Descriptive statistics and score ranges of study variables

Variable	Score range	Mean (SD)
Age	28–79	55.53 (10.99)
Education	0–5	3.29 (1.43)
Did not complete high school (%)		3.3
High school diploma (%)		14.0
Postsecondary no diploma (%)		7.4
College/technical diploma (%)		23.1
Undergraduate degree (%)		29.8
Postgraduate degree (%)		22.3
Stage of cancer	0–3	1.85 (0.72)
Stage 0 (%)		3.6
Stage I (%)		29.5
Stage II (%)		46.4
Stage III (%)		20.5
Stage IV (%)		0.0
Months since diagnosis	2–20	10.71 (3.48)
BMI	18–50	26.83 (6.13)
Smoking status yes (%)		5.8
Goal disengagement capacities	1–5	2.82 (0.84)
Goal reengagement capacities	1–5	3.73 (0.61)
Health-related self-protection	1–5	4.02 (0.54)
C-reactive protein (mg/L)	0–8	1.43 (1.67)

$N = 121$.

Goal adjustment capacities were assessed using the Goal Adjustment Scale [25]. Previous research has shown that the Goal Adjustment Scale has good reliability and can be associated with well-being and health-relevant outcomes, including lower CRP [e.g., 24,27]. Participants responded to 10 items measuring how they usually react if they have to stop pursuing an important goal. Item responses ranged from 1 (*almost never true*) to 5 (*almost always true*). Four items measured a person's capacity to disengage from unattainable goals (e.g., 'It's easy for me to reduce my effort towards the goal'), and six items measured a person's tendency to reengage with new goals (e.g., 'I seek other meaningful goals'). An average score was computed separately for goal disengagement and goal reengagement capacities. The scales of goal disengagement and goal reengagement showed appropriate reliabilities ($\alpha s = 0.75–0.86$).

Health-related self-protection was assessed by administering three items. These items represent self-protective compensatory secondary control strategies [36] that people can use to manage health threats. The specific item formulations were the following: (a) 'When I am faced with a bad health problem, I try to look at the bright side of things', (b) 'Even if my health is in very difficult condition, I can find something positive in life', and (c) 'When I find it impossible to overcome a health problem, I try not to blame myself'. Participants responded to the items on 5-point Likert-type scales from 1 (*almost never true*) to 5 (*almost always true*). A mean score was calculated for health-related self-protection by averaging the three items. Although previous research showed good reliability ($\alpha = 0.73$) and associations with health-relevant variables (i.e., lower CRP) [13], the scale had only modest reliability in our study ($\alpha = 0.59$).

Covariates

To minimize the possibility of spurious associations, sociodemographic and cancer-related variables that may be associated with the predictors or outcome measure were included in the analyses. Covariates included participants' age, education (from 0 = *did not complete high*

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school to 5 = *postgraduate degree*), smoking (0 = *daily*, 1 = *occasionally*, and 2 = *not at all*), BMI, cancer stage (stage 0 to stage IV), and months since diagnosis.

Data analysis

Preliminary analyses were conducted to examine zero-order correlations between the main study variables in SPSS (version 20.0). The hypotheses were tested by conducting a multiple regression analysis that predicted CRP. In the first step, participant's age, education, BMI, smoking status, stage of BC, and time since diagnosis were entered. In a second step, the main effects of goal disengagement, goal reengagement, and health-related self-protection were tested for significance. In the final step, two interaction terms were entered simultaneously into the regression equation: goal disengagement × health-related self-protection and goal reengagement × health-related self-protection. Predictor variables were standardized prior to conducting the analysis. Significant interaction effects were illustrated by plotting the associations between participants' goal adjustment capacities and CRP one standard deviation above and below the sample mean of health-related self-protection [37,38]. They were followed-up by testing the simple slopes for significance [37].

Results

The zero-order correlations between the main study variables are reported in Table 2. Goal disengagement capacities were correlated with higher levels of goal reengagement capacities, lower levels of CRP, and higher age. CRP was also positively associated with a higher BMI. Smokers had received less education than non-smokers. Older participants were less educated, had a lower cancer stage, and received their diagnosis more recently than their younger counterparts.

The results of the regression analysis for testing the hypotheses are reported in Table 3. The first step of the analysis showed significant effects of the covariates, explaining 11% of the variance in CRP. Of the covariates, only BMI was significantly associated with higher levels of CRP ($\beta = 0.27$, $p < 0.01$).

The second step of the analysis showed that the main effects of goal disengagement capacities, goal reengagement capacities, and health-related self-protection explained an additional 6% of the variance in CRP. However, only goal disengagement capacities exerted a significant main effect on participants' CRP levels, indicating that high levels of goal disengagement were associated with lower levels of CRP ($\beta = -0.19$, $p < 0.05$). The main effects of goal reengagement capacities and health-related self-protection were not significant.

In the final step of the analysis, the two interaction terms accounted for additional 4% of the variance in CRP (Table 3). In support of our hypotheses, only the interaction between goal disengagement capacities and health-related self-protection significantly predicted participants' levels of

Table 3. Regression analysis predicting C-reactive protein by sociodemographic and cancer-related variables, goal adjustment capacities, and health-related self-protection

	C-reactive protein		
Variable	R^2	ß	*p*
Sociodemographic characteristics	0.11		
Age	0.00	−0.04	0.65
Education	0.01	−0.09	0.36
Smoking status	0.00	0.04	0.70
BMI	0.07	0.27**	0.003
Breast cancer stage	0.00	−0.01	0.91
Time since diagnosis	0.02	−0.17	0.10
Main effects	0.06		
Goal disengagement capacities (GD)	0.03	−0.19*	0.04
Goal reengagement capacities (GR)	0.00	−0.04	0.69
Health-related self-protection	0.01	−0.11	0.26
Interactions	0.04		
Health-related self-protection × GD	0.04	0.22**	0.01
Health-related self-protection × GR	0.00	−0.06	0.55

R^2 values represent the unique proportion of variance explained in each step of analyses. ß represents standardized regression coefficient in each step of the analyses.
*$p < 0.05$
**$p < 0.01$

Table 2. Zero-order correlations between constructs used in regression analysis

	1	2	3	4	5	6	7	8	9
1. Goal disengagement capacities	—								
2. Goal reengagement capacities	0.21*	—							
3. Health-related self-protection	0.13	0.12	—						
4. C-reactive protein	−0.22**	−0.14	−0.10	—					
5. Age	0.18*	−0.08	0.15	0.04	—				
6. Education	−0.01	0.08	−0.10	−0.13	−0.18*	—			
7. Smoking status	0.03	0.14	0.17	0.07	−0.01	−0.20*	—		
8. BMI	−0.06	−0.12	0.13	0.26**	0.12	−0.17	0.03	—	
9. Cancer stage	0.04	0.11	0.01	−0.09	−0.20*	0.11	−0.05	−0.04	—
10. Months since diagnosis	−0.03	0.14	0.13	−0.13	−0.23*	−0.05	−0.03	−0.03	−0.13

Correlations are based on 121 participants.
*$p \leq 0.05$.
**$p < 0.01$.

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CRP. The interaction between goal reengagement capacities and health-related self-protection was not significant.

Figure 1 illustrates the significant interaction effect by plotting the associations between goal disengagement capacities and CRP one standard deviation above and below the sample mean of health-related self-protection. The observed pattern suggests that participants who reported both low levels of goal disengagement capacities and low levels of health-related self-protection exhibited the highest levels of CRP. By contrast, relatively lower levels of CRP were observed among participants who reported low levels of goal disengagement capacities but had high levels of health-related self-protection. These lower levels of CRP were comparable with participants who were generally better able to disengage from unattainable goals (independent of health-related self-protection, Figure 1). Analyses of the simple slopes demonstrated that goal disengagement capacities were significantly associated with lower levels of CRP among participants who did not engage in health-related self-protection, $\beta = -0.43$, $p = 0.002$, but not among their counterparts who used health-related self-protection more frequently, $\beta = 0.00$, $p = 0.99$. In addition, health-related self-protection was significantly associated with lower levels of CRP among participants with low levels of goal disengagement capacities, $\beta = -0.34$, $p = 0.01$, but not among participants with high levels of goal disengagement capacities, $\beta = 0.09$, $p = 0.48$.[1]

Discussion

The results of this study demonstrate that BC survivors who are capable of disengaging from unattainable goals had lower levels of CRP than their counterparts who reported more difficulty with goal disengagement. Such benefits may occur because cancer survivors often experience a loss of physical resources and need their time and energy for managing the consequences of the cancer. In turn, they are likely to confront goal constraints across different areas of life (e.g., work, leisure, or other personal goals) [29], which could trigger a stress-related dysregulation of inflammatory processes. Because goal disengagement capacities operate transsituational, they may reduce distress by making it easier to accept that different goals can no longer be pursued [24,25]. In addition, they can provide resources that BC survivors need to effectively cope with their cancer-related circumstances (e.g., engaging in lifestyle changes) [29]. These psychological benefits of goal disengagement capacities may ameliorate stress-related elevations of BC survivors' CRP concentrations. This conclusion is consistent with research in noncancer populations, documenting that goal disengagement capacities can prevent emotional distress, boost endocrine and immune system function, and reduce the likelihood of experiencing physical health problems [27,39].

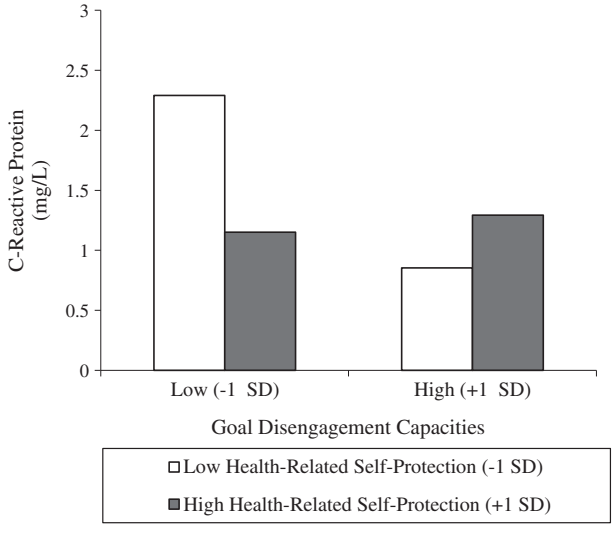

Figure 1. Associations between levels of goal disengagement capacities and C-reactive protein, separately for participants who reported low and high levels of health-related self-protection

In addition, the analyses suggest that the association between failure to disengage from unattainable goals and elevated levels of CRP was enhanced among BC survivors who did not engage in health-related self-protection. This result supports our theoretical framework, postulating that cancer survivors may not only have to adjust to goal constraints across different life domains but also need to cope effectively with specific health threats. The study's findings are consistent with this assumption by suggesting that the use of health-related self-protection was not statistically correlated with cancer survivors' goal disengagement capacities (Table 2). They further show that health-related self-protection can buffer CRP levels among BC survivors who have difficulty disengaging from unattainable goals, just as goal disengagement capacities can be associated with reduced CRP levels among participants who do not engage in health-related self-protection. Such buffering effects may occur because self-protective control strategies are well-suited to provide emotional benefits and prevent a dysregulation of inflammatory processes among individuals who confront threats that are difficult to control through problem-focused strategies (e.g., potential cancer recurrence) [13]. Thus, to avoid high levels of systemic inflammation, BC survivors need to either cope with their specific health threats through self-protection or disengage from unfeasible goals experienced across different areas of life.

The reported results did not show significant effects of participants' goal reengagement capacities. On the basis of previous research, the absence of such effects may be explained by more reliable associations between goal reengagement capacities with positive, as compared with negative, emotional states [30]. Such differential emotional mechanisms may become important if the presence of distress has more severe consequences on physical

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health problems than the absence of positive emotions [40]. In addition, engagement in many (or maladaptive) goals may increase distress by stretching individuals too thin when they encounter demanding stressors [28,30], which could further obscure potential benefits of goal reengagement.

Overall, the reported findings have important implications for theories on physical health and clinical practitioners. First, they show that adjustment to unattainable goals and investment in health-related self-protection are two independent self-regulation processes that work together in predicting health-relevant benefits among BC survivors. Although previous work has shown that broader self-regulation tendencies can unfold their adaptive value by facilitating effective coping with specific stressors [28,41], our findings suggest that these two processes are not necessarily related within individuals. They further imply that the successful management of one challenge can provide biological benefits by compensating for failure in the other challenge. However, if cancer survivors are unable to master either challenge (i.e., disengaging from unattainable goals and engaging in health-related self-protection), they are at a particularly high risk of exhibiting a dysregulation of their immune system, which may have wide-ranging consequences for their physical health [9–12].

Second, the findings from the current study may foster the development of interventions designed to help BC survivors manage perceived health threats and adjust their goals to living with cancer. Given that the use of adaptive health-related control strategies can be improved in therapy [42], clinicians should aim at teaching cancer survivors how to engage in self-protective control strategies (e.g., positively reframing uncontrollable health threats). In addition, given that it is possible to influence adjustment to specific goals [43], practitioners may identify survivors that have difficulty disengaging from unattainable goals and help them to withdraw psychological commitment from specific unfeasible goals. Such targeted interventions could reduce distress among BC survivors and facilitate their biological functioning and physical health.

Limitations and future directions

There are limitations of the study that should be addressed in future research. First, the cross-sectional analysis requires a careful interpretation because the reported analysis cannot document directional associations between self-regulation processes and CRP levels. However, we feel it is unlikely that CRP levels have influenced participants' general self-regulation tendencies and health-specific control strategies, considering that past research has related goal disengagement capacities and health-related self-protection with either changes in, or prospective levels of, CRP [13,27]. Nonetheless, future research should examine this process more thoroughly by enrolling cancer patients at the time of diagnosis and assessing changes in systemic inflammation over time.

Second, to shed light on the generalizability of the proposed theoretical model, it will be useful to examine individuals who confront different types of health challenges. We would expect to replicate the observed pattern of findings for health challenges that involve low levels of controllability (e.g., other cancers or functional disability). However, if individuals confront more controllable health threats (e.g., acute problems such as pain), it could be possible to obtain effects of active health engagement control strategies, such as investments of effort or seeking help from a professionals [44]. Note that our study also included a measure of health engagement control strategies [44]. Supplemental analyses of main and interaction effects showed that health engagement control strategies did not contribute to BC survivors' CRP levels. This finding is consistent with our theoretical framework, postulating that less controllable health threats require individuals to engage in self-protection and not in active control efforts [19].

Third, our analysis included a number of potential confounders; however, there may be other underlying factors (e.g., conscientiousness or optimism) [45–47] that could explain the observed associations. Although our past research has shown that effects of goal disengagement capacities are typically independent of other personality dimensions [30], future research should provide further evidence for the unique contribution of goal disengagement capacities and health-related self-protection to BC survivors' levels of systemic inflammation.

Fourth, the internal consistency of the health-related self-protection scale was only modest. This is surprising because past research has shown a higher reliability of this scale [13]. A lower internal consistency may occur, however, if the different items of a scale (e.g., reappraisals and attributions) assess heterogeneous aspects of a broader construct (i.e., health-related self-protection), serve the same function, but are not particularly highly correlated in a certain population. Supplemental analyses, using the different items separately, showed that only the scale score, but none of the single items, interacted with participants' goal disengagement capacities in predicting levels of CRP. In such circumstances, it may be appropriate to deemphasize internal consistency and highlight content validity to document the inferential usefulness of a scale [48].

Finally, according to our theoretical framework and supporting research [13,39], negative emotional experiences (e.g., depression) and endocrine function (e.g., cortisol secretion) could play a mediating role in the associations between self-regulation processes and immune function. Future analyses should thus examine these possibilities in longitudinal data and predict long-term consequences on physical health outcomes. Research along these lines may illuminate the psychobiological pathways that contribute

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to maintaining psychological and physical health among vulnerable cancer populations.

Conclusions

This study's findings showed evidence that BC survivors can prevent high levels of systemic inflammation if they are able to either disengage from unattainable goals or to engage in self-protective control strategies to manage their health threats. The identification of this mechanism advances theory on the health-related consequences of self-regulation in stressful life circumstances. In addition, it will be helpful for practitioners who work with cancer survivors because modifying self-regulation processes represents a viable nonpharmacological treatment that can improve psychological and physical health [29].

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Conflict of interest

None of the authors has a conflict of interest to declare related to this project.

Note

1. Although our analyses did not control for type of treatment, we note that there were no significant associations between dummy-coded variables of BC treatment type and CRP. In addition, a separate regression model was conducted including treatment type and was compared with the original model. There were no differences in results between the two regression models.

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