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## Reduction in social activities mediates the relationship between diarrhea and distress in rectal/anal cancer survivors

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### 1 INTRODUCTION

Over 45 000 new cases of rectal and anal cancer (RACa) are diagnosed yearly in the United States.<sup>1</sup> Treatment typically requires a combination of surgery, chemotherapy, and radiation and may result in persistent bowel dysfunction.<sup>2,3</sup> Bowel symptoms include increased frequency and urgency, incontinence, leakage/soilage, abnormal sensation or painful bowel movements, evacuation difficulties, and diarrhea. Deterioration of bowel functioning has been described with concurrent disruptions in daily routines, sexual difficulties as well as lowered emotional well-being and quality of life (QOL).<sup>4,5</sup> Symptoms are frequent and can be severe, especially in the first year after treatment but may persist beyond that as well.<sup>2,3</sup> Five years postsurgery, 5% to 63% of patients persistent bowel problems.<sup>6</sup> In colorectal cancer, greater severity of bowel symptoms was related to increased depression and anxiety.<sup>6</sup> Understanding the mechanism by which bowel dysfunction affects psychological variables is an important step to improving RACa survivorship.

The objective of this study was to examine the relationship among bowel dysfunction and the psychosocial variables of social functioning, depression, and anxiety in a sample of RACa survivors. It was hypothesized that greater severity of bowel symptoms would lead to increased depression and anxiety and that disruptions in social functioning would mediate the relationship between bowel dysfunction and increased depression and anxiety. Given the chronic nature of these side effects and associated impairments in daily functioning and QOL, findings may have important implications for posttreatment survivorship care.

### 2 METHODS

As part of a sexual health intervention study, participants completed a baseline (preintervention) assessment questionnaire.<sup>7</sup> Institutional Review Board approval was obtained (#08-073).

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#### SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

## 2.1 Participants

Participants were posttreatment for stages I to III rectal or anal cancer with no evidence of disease, at least 21 years old, and proficient in English. Eligibility criteria also required female participants to have low to moderate sexual satisfaction and male participants to have difficulty with erectile dysfunction, bother related to this difficulty, and to be married or in a committed relationship. All participants gave informed consent.

## 2.2 Measures

The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire<sup>8</sup> and Colorectal Cancer-Specific Module<sup>9</sup> The Diarrhea (1 item) and Social Functioning (2 items) sub-scales were included in this analysis. Responses were on a 4-point scale from “Not at all” to “Very much.” Higher scores indicate *greater* severity of diarrhea and *better* social function.

The Brief Symptom Inventory (BSI)<sup>10</sup> Depression and Anxiety sub-scales were used in this analysis. Respondents rated how much discomfort problems have caused them in the past month on a 5-point scale (“Not at all” to “Extremely”). Higher scores indicate greater depressive and anxiety symptoms.

## 2.3 Analyses

Descriptive statistics characterized the data and Pearson’s correlation tested bivariate relations. Following standard guidelines for establishing mediation,<sup>11</sup> regression analyses tested whether disruptions in social functioning explained relations between diarrhea and depression and anxiety (Figure S1), based on the literature and hypotheses regarding the psychosocial effects of bowel dysfunction. Tests of mediation were conducted separately for depression and anxiety.<sup>11</sup> Models specified diarrhea as the predictor, social function as the mediator, and depression and anxiety as outcome variables (separate analyses), controlling for a priori covariates (age, gender, disease type, time since treatment, and stoma; Table 3).<sup>11</sup>

## 3 RESULTS

Descriptive data for the 144 subjects are provided in Table 1. Participants (51% male) were on average 56 years old ( $SD = 10.3$ ) and 4.6 ( $SD = 3.3$ ) years posttreatment. Clinically significant levels of depression and anxiety were reported by 18% and 19% of participants, respectively.<sup>10</sup> Diarrhea was endorsed by 38% of participants. There were no differences based on gender (male vs female), disease type (rectal vs anal cancer), or stoma status (stoma vs no stoma) in reports of diarrhea, social function, or levels of distress ( $P$ s  $> .05$ ). At marginal significance, women reported higher levels of social function than men ( $M = 80.5$ ,  $SD = 25.5$  and  $M = 72.2$ ,  $SD = 28.8$ , respectively,  $P < .10$ ). Greater severity of diarrhea was associated with worse social function ( $r = -0.52$ ) and higher levels of depression ( $r = 0.36$ ) and anxiety ( $r = 0.29$ ; bivariate relations included in Table S1).

### 3.1 Depression

In separate models, diarrhea was significantly associated with social function ( $\beta = -.53$ ) and depression ( $\beta = .39$ ). Social function was associated with depression ( $\beta = -.57$ ). In the final

test of mediation, the relation between diarrhea and depression was no longer significant ( $\beta = .13$ ) when social function was included in the model ( $\beta = -.50$ ; Table 2; Figure S1a). The hypothesized mediating role of social function to explain the effect of diarrhea on depression was supported. Thirty-two percent of the variance in depression was accounted for in the final model, and no other covariates were related to depression ( $P$ 's > .05).

### 3.2 Anxiety

The same procedure was done with anxiety as the outcome variable. In separate models, diarrhea was significantly related to social function ( $\beta = -.53$ ) and anxiety ( $\beta = .32$ ); and social function was related to anxiety ( $\beta = -.47$ ). When social function was included in the model, the effect of diarrhea on anxiety was no longer significant ( $\beta = .09$ ; Table 2; Figure S1b). Social function remained a significant predictor of anxiety ( $\beta = -.43$ ), supporting the hypothesized role of mediation. The final model accounted for 28% of the variance in anxiety. At marginally significant levels, males reported less anxiety than females and longer time since treatment was associated with greater anxiety.

## 4 DISCUSSION

In this cross-sectional study of 144 RACa survivors who were on average 4.6 years posttreatment, a meaningful percentage reported anxiety and depressive symptoms. While the percent of those reporting anxiety (19%) is considered high and suggestive of significant psychological distress, the percent of patients reporting depressive symptoms (18%) is also strikingly high. Taken together, data present a strong case that RACa survivors should be followed for psychological distress and referred to psychological services if distress levels are high. Psychological distress was related to, and possibly caused by, difficulty with diarrhea reported by a large percentage of survivors (38%). The significant impact bowel side effects can have on the social functioning of these patients is also evident. This is congruent with our clinical work as many patients report withdrawing from social activities for fear that they will have an embarrassing bowel accident. The mediation analysis supports the hypothesized role of social activities as an important mechanism in the relationship among bowel problems and increased anxiety and depression.

### 4.1 Clinical implications

These data signify the importance of targeting distressing and disruptive side effects of RACa treatment to help maintain or improve engagement in social activities and to reduce anxiety and depression posttreatment. Consistent with the literature,<sup>3</sup> survivors in this study were on average more than 4 years posttreatment, demonstrating the persistent and refractory nature of side effects. Rectal and anal cancer treatment has shown excellent efficacy in treating the disease. Unfortunately, treatment leaves a large percentage of patients with persistent bowel difficulties that can impact their life in many ways including reduction of social activities. Surgeons and oncologists who treat RACa continue to test treatments to help address the bowel side effects of these patients. Until they are successful, however, the primary mechanism for helping these patients may be through psychosocial interventions to assist them in coping with distressing and disruptive side effects and better management of their lives posttreatment.

Future work in this area should focus on the development of psychosocial interventions to help RACa survivors build strategies to deal with these persistent symptoms. Fostering social interactions and engagement should be an important piece to these interventions, particularly given the prolonged nature of symptom experiences. Focusing on problem-solving strategies to help patient feel more confidence managing their symptoms, engaging with friends and family, and maintaining social activities could be useful. Teaching patients to manage their worries or fears related to bowel symptom occurrence and reduce avoidance of important activities may also be helpful. A number of therapeutic approaches such as cognitive-behavioral therapy, problem-solving therapy, and acceptance and commitment therapy may be specifically useful for these patients and their concerns. Given the data presented here, the development of these types of interventions should be considered a high priority. Appropriate symptom management, combined with strategies to address worries or fears related to symptom occurrence, may help to mitigate or avoid the social and QOL deficits associated with long-term bowel dysfunction.

Strengths of this study include a relatively large sample size of RACa patients and the assessment of anxiety and depression, which is unique in the RACa literature. Nevertheless, the study also has limitations. The cross-sectional design precludes causal inferences. Second, more comprehensive scales exist for both bowel function and social function and should be used in future studies. Diversity (eg, ethnicity) of the sample was limited and a more diverse sample may demonstrate variability in coping with these side effects. Lastly, the sample included a limited number of stoma patients, and this is a subgroup of survivors with potentially different needs when designing psychosocial interventions. Future work should focus on psychosocial interventions to help survivors cope the persistent bowel symptoms.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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### Key points

- The percentage of rectal and anal cancer survivors reporting clinically significant anxiety (19%) and depressive symptoms (18%) was high, presenting a strong case that patients should be followed for psychological distress after treatment.
- Psychological distress was found to be related to difficulty with diarrhea, and reduction in social activities was found to mediate (account for) this relationship.
- (Alternative: The results suggest that chronic diarrhea is related to a reduction in social activities, which then relate to higher levels of depression and anxiety.)
- These data signify the importance of targeting distressing and disruptive side effects of rectal and anal cancer treatment to help maintain or improve engagement in social activities and to reduce anxiety and depression in these survivors.
- Surgeons and oncologists who treat rectal and anal cancer continue to test treatments to help address the bowel side effects of these patients; however, until they are successful, the primary mechanism for helping patients may be through psychosocial interventions to assist them in coping with side effects and better management of their lives post-treatment.
- Future work in this area should focus on the development of psychosocial interventions to help survivors build strategies to deal with these persistent symptoms and to maintain and foster social interactions and engagement.

TABLE 1

Descriptive characteristics of the study sample (N = 144)

<b>Demographics &amp; Clinical Information</b>	<b>M, SD</b>	<b>%</b>	
Age (mean, SD; y)	56, 10.3		
Male		51	
Race			
White		81	
Hispanic ethnicity		7	
Employed		65	
Annual income			
Less than \$50 000		24	
Partnered		71	
Time since tx (mean, SD; y)	4.6, 3.3		
Cancer type			
Rectal cancer		76	
Anal cancer		20	
Treatment			
Radiation/chemo		71	
Surgery		73	
Permanent stoma		15	
<b>Main variables</b>	<b>M, SD</b>	<b>Range</b>	<b>%</b>
Diarrhea <sup>a</sup>	20.1, 29.3	0–100	38
Social Function <sup>b</sup>	75.6, 27.3	0–100	
Disruptions to family life			43
Disruptions to social activities			52
Psychological Distress <sup>c</sup>			
Depressive symptoms	0.58, 0.71	0–3	18
Anxiety symptoms	0.59, 0.59	0–2.7	19

<sup>a</sup>Higher scores indicate *worse* diarrhea; percentages refer to those who answered “A little,” “Quite a bit,” or “Very much.”

<sup>b</sup>Higher scores indicate *better* social function; percentages refer to those who answered “A little,” “Quite a bit,” or “Very much.”

<sup>c</sup>Higher scores indicate *greater* severity of depressive and anxiety symptoms; percentages refer to validated case rule indicating clinical significance (above the 90th percentile).

Regression models supporting the mediating role of social functioning to explain the relationship between diarrhea and increased depression and anxiety

**TABLE 2**

	<b>B</b>	<b>SE</b>	<b><math>\beta</math></b>	<b>t</b>	<b>Sig.</b>
Depression Model ( $F_{7,125} = 8.45, P < .001; R^2 = 0.32$ )					
Constant	1.50	.36			
Age	.002	.01	.03	.30	.77
Gender (0 = female)	-.17	.11	-.12	-1.56	.12
Disease type (0 = rectal)	-.03	.14	-.02	-.20	.85
Years since treatment	.01	.02	.06	.71	.48
Stoma (0 = no)	-.17	.15	-.09	-1.14	.26
Social function	-.01	.002	-.50	-5.35	<.001
Diarrhea	.003	.002	.13	1.40	.16
Anxiety model ( $F_{7,125} = 7.01, P < .001; R^2 = 0.28$ )					
Constant	1.46	.29			
Age	-.01	.01	-.10	-1.12	.27
Gender (0 = female) <sup>a</sup>	-.16	.09	-.14	-1.70	.09
Disease type (0 = rectal) <sup>a</sup>	-.002	.11	-.001	-.01	.99
Years since treatment	.03	.01	.15	1.83	.07
Stoma status (0 = no stoma) <sup>a</sup>	.17	.12	.11	1.36	.18
Social function	-.01	.002	-.43	-4.44	<.001
Diarrhea	.002	.002	.09	.99	.33

<sup>a</sup>Dichotomized variables with 0 indicating the reference group; categories included male/female for gender, rectal/anal for disease type, and stoma/no stoma for stoma status.