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Factors Associated with Anxiety About Colonoscopy: The Preparation, the Procedure, and the Anticipated Findings

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Abstract

Background Previous research has assessed anxiety around colonoscopy procedures, but has not considered anxiety related to different aspects related to the colonoscopy process.

Aims Before colonoscopy, we assessed anxiety about: bowel preparation, the procedure, and the anticipated results. We evaluated associations between patient characteristics and anxiety in each area.

Methods An anonymous survey was distributed to patients immediately prior to their outpatient colonoscopy in six hospitals and two ambulatory care centers in Winnipeg, Canada. Anxiety was assessed using a visual analog scale. For each aspect, logistic regression models were used to explore associations between patient characteristics and high anxiety.

Results A total of 1316 respondents completed the questions about anxiety (52% female, median age 56 years). Anxiety scores > 70 (high anxiety) were reported by 18% about bowel preparation, 29% about the procedure, and 28% about the procedure results. High anxiety about bowel preparation was associated with female sex, perceived unclear instructions, unfinished laxative, and no previous colonoscopies. High anxiety about the procedure was associated with female sex, no previous colonoscopies, and confusing instructions. High anxiety about the results was associated with symptoms as an indication for colonoscopy and instructions perceived as confusing.

Conclusions Fewer people had high anxiety about preparation than about the procedure and findings of the procedure. There are unique predictors of anxiety about each colonoscopy aspect. Understanding the nuanced differences in aspects of anxiety may help to design strategies to reduce anxiety, leading to improved acceptance of the procedure, compliance with preparation instructions, and less discomfort with the procedure.

Keywords Colonoscopy · Anxiety · Pre-procedure · Patient characteristics

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Introduction

Due to increased use of colonoscopies to evaluate symptoms, increased colorectal cancer (CRC) screening, and increased surveillance of those with higher risks of developing CRC, colonoscopy has become a common medical procedure [1, 2]. Patients undergoing an invasive medical procedure commonly experience anxiety [3–6]. While colonoscopies have clear diagnostic benefits, they are uncomfortable and stressful for many patients. Anxiety is a common human emotion, and it is not surprising that people would experience anxiety when faced with this type of procedure.

Community studies suggest that 20–30% of people experience significant levels of health anxiety in general life [7]. People may be particularly susceptible to anxiety around colonoscopy. Previous studies have demonstrated that preprocedure anxiety can be high among a significant proportion of patients undergoing a colonoscopy [8–11]. A study using the Hospital Anxiety and Depression Scale to evaluate anxiety found that 21% of people on the waiting list for colonoscopy scored above the cutoff for moderate to high anxiety, compared to about 13% of people in the general population [8]. In response to an open-ended question, participants identified a wide range of concerns about the procedure itself (concern about the preparation, procedural pain, embarrassment), and more commonly, concern about the eventual results with a high proportion specifically mentioning fear of cancer (11%). It is difficult to directly compare the proportion of people with high anxiety across different studies, because each study defines high anxiety somewhat differently. However, there was a meaningful difference in percent with moderate to high anxiety in this study (21% among those on the colonoscopy waitlist, compared with 13% in the general population). In addition, the participants were completing the survey weeks or months before the scheduled colonoscopy, so one would expect that anxiety may be higher just before the procedure. Another study used the PRIME-MD to identify persons with high levels of anxiety just before the procedure and found that 33% were above the cutoff for generalized anxiety disorder (as a trait) just before the procedure [12].

While there is considerable research on anxiety related to colonoscopy [8–10, 12–16], most previous studies have not considered anxiety related to different aspects of the situation—the bowel preparation, the procedure itself, and the anticipated findings of the procedure. Different measures have been studied to decrease overall anxiety related to colonoscopy, and the findings in this area are quite variable [9, 13, 16, 17]. To successfully develop measures to decrease colonoscopy-related anxiety, it is important to determine the source of anxiety.

Anxiety can negatively affect the success of a colonoscopy in a number of ways, including prolonging the procedure, increasing pain associated with the procedure, and increasing the potential requirement for sedation [11, 18–21]. One study found increased difficulty with pain, cramping and bloating after colonoscopy among those with high anxiety [12]. It is possible anxiety related to bowel preparation may lead to poor or incomplete bowel cleansing. We have recently reported high anxiety about the bowel preparation is indeed associated with reluctance to wake early in the morning to complete bowel preparation [22]. Morning completion of bowel preparation (split-dose bowel preparation) has been shown to lead to better bowel cleansing [23, 24]. Despite its importance, bowel cleansing for colonoscopies has been reported to be poor in up to 20–40% of cases [25]. Poor or incomplete bowel cleansing leads to increased risks of complications, longer procedure times, and increased rates of missed lesions, including colorectal polyps and cancers [26–28].

A better understanding of anxiety related to the various aspects of colonoscopy may help guide the development of resources or strategies to lessen colonoscopy-related anxiety. This, in turn, may help to increase acceptance of the procedure and improve the quality of bowel preparation. For example, strategies to alleviate anxiety about bowel preparation may result in better cleansing and therefore improve patient outcomes. Similarly, strategies to alleviate anxiety about the procedure itself may increase procedure tolerance resulting in a higher likelihood that the patient would be willing to undergo a colonoscopy.

In this study, we assessed anxiety immediately before a colonoscopy about: (1) the bowel preparation, (2) the colonoscopy procedure itself, and (3) the anticipated results of the procedure. We evaluated the associations between patient characteristics and anxiety in each area.

Methods

Study Sample

A self-administered anonymous survey was distributed between August 2015 and June 2016 to adult patients immediately prior to their outpatient colonoscopy in six hospitals and two ambulatory care centers in Winnipeg, Manitoba, Canada. Approximately, 85% of the colonoscopies in Winnipeg are performed in the six hospitals in the city and their affiliated endoscopy units, and the rest in three ambulatory care centers (two of which participated in this study).

Participants were invited into the study if there was enough time before their procedure to complete the survey; that is, this was a convenience sample. Inclusion criteria included patients' willingness to complete the



self-administered survey while sitting in the waiting room and the ability to read and respond in English. The colonoscopy centers were frequently busy and the survey was only distributed when staff had adequate time to explain the survey to patients waiting for their procedure.

Survey

The survey included items on demographic characteristics, reason for the current colonoscopy, previous experience with colonoscopy, whether or not the patient was going direct to colonoscopy (i.e., meeting the endoscopist for the first time on the day of the procedure), type of bowel preparation used, knowledge/information needs around colonoscopy, how willing the patient would be to wake early in the morning to complete the bowel preparation for their next colonoscopy, and anxiety about three aspects of the colonoscopy—the bowel preparation, the procedure itself, and the results of the procedure. The survey took about 10–20 min to complete. The questionnaire was first pilot-tested among eight patients experienced with colonoscopies and eight endoscopists.

A range of anxiety measures have been used in previous research including the State-Trait Anxiety Inventory and the Hospital Anxiety and Depression Scale. These measures have been widely used and provide an overall assessment of anxiety, but they do not allow an assessment of anxiety related to specific aspects of the colonoscopy situation. Consequently, we used visual analog scales (VAS) [29–32] to assess anxiety about the bowel preparation, the colonoscopy procedure, and the results of the procedure. VAS have been used for many decades and have been shown to be a valid and reliable measure of mood and anxiety in a range of different contexts [33, 34]. Each score was obtained by asking the respondent to assess their level of anxiety by placing a mark such as the one below on the scale:

The mark was then translated into a score from 0 to 100 by measuring placement of the line on the scale. The continuous anxiety scales were then dichotomized. A score of 70 or more was chosen to indicate a high level of anxiety, because this score represented approximately the top quartile of the anxiety score among all patients. Previous research indicates that 20–30% of those coming for colonoscopy show levels of anxiety in the clinically significant range [8, 12].

The VAS questions were introduced as follows: "Many people who have a colonoscopy have some nervousness, worry or anxiety about:

- The bowel preparation (using the laxative)
- The colonoscopy procedure itself



• The results of the colonoscopy

Please place a vertical mark on the line below each question to indicate how much nervousness, worry or anxiety you had about each item. Here is an example of how to make the mark:" [an example of the VAS with a mark across the scale to indicate the rating was given].

The first question asked: "How nervous, worried or anxious were you *about the bowel preparation* (using the laxative)?"

The second question asked: "How nervous, worried or anxious are you *about the colonoscopy procedure*?"

The third question asked: "How nervous, worried or anxious are you *about the results of the colonoscopy*?"

Statistical Analysis

The proportion of patients with high anxiety (Score > 70) on each of the three anxiety scores was calculated. Respondents with different background characteristics were compared by the proportion with high anxiety using Fisher's exact tests. We also examined correlations between the three anxiety scores and expressed the results as Pearson correlations between the three continuous anxiety scores and tetrachoric correlations [35, 36] between the binary scores representing high (Score > 70) or low (Score \leq 70) scores.

Logistic regression models were used in our main analyses. We conducted logistic regression to examine associations with the three main outcome variables—high anxiety related to bowel preparation, high anxiety related to colonoscopy procedure, and high anxiety related to colonoscopy results. Potential predictors in the three logistic regression models were demographic characteristics (age, gender, marital status, and education), indication for the colonoscopy (screening, surveillance, or for symptoms), type of bowel preparation used, clarity of information received about the bowel preparation and procedure, and the reported amount of time that the patient spent reviewing information that was received.

Ethical Approval

This study was approved by the University of Manitoba Health Research Ethics Board.

Results

Of the surveys that were distributed, 1580 were returned for an 86% response rate and 1316 (83%) of the respondents completed the questions about anxiety that came at the end of the survey. Of the 1316, 52% were women, and the median age was 57 years (IQR 49–65, range 16–91). The

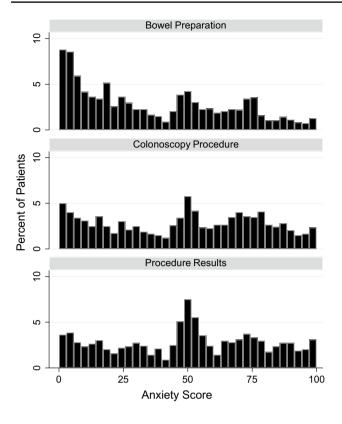


Fig. 1 Distribution of anxiety scores about colonoscopy

anxiety score about bowel preparation was skewed toward lower anxiety (Fig. 1). The anxiety scores about the procedure and the procedure results were fairly evenly distributed across the entire theoretical range (0–100) of the score, though with a somewhat higher density of scores around 50 (Fig. 1). High anxiety (Score > 70) was reported by 18% of respondents about the bowel preparation, 29% about the procedure itself, and 28% about the procedure results. The range of anxiety scores were similar across the eight sites (six hospitals and two ambulatory care sites) of this study.

In bivariate analyses, associations between patient characteristics and the percent with high anxiety on all three aspects of the colonoscopy were similar, but not exactly the same (Table 1). Women were significantly more likely than men to have high anxiety about bowel preparation and the procedure itself (P < 0.01 both), but the gender difference was not significant for anxiety about the procedure results (P = 0.071). Younger people (age 16–39) had higher anxiety than older people (age 40 +) about all three aspects of the colonoscopy, but the difference in proportion with high anxiety was greatest when comparing age groups on anxiety about the procedure itself. Patients about to undergo their first colonoscopy were significantly more anxious about all aspects of the colonoscopy than those who had already had one or more colonoscopies, but the difference in proportion

with high anxiety was narrow on anxiety about the procedure results.

Those with symptoms as an indication for the colonoscopy were significantly more anxious about the procedure and the procedure results than those whose indication was screening, but there was no difference in high anxiety about bowel preparation. Having finished their laxative was associated with being less anxious about the bowel preparation (16% with high anxiety, compared with 28% among those who did not finish, P < 0.01), but was not associated with anxiety about the procedure or procedure results. Finally, patients who found that the bowel preparation instructions that they received were clear were much less anxious about the bowel preparation (15% with high anxiety versus 36% among those who thought the instructions were confusing, P < 0.01) and were also less anxious about the procedure results (27% versus 42%, P = 0.03) and the procedure itself (28% versus 39%, P = 0.04).

Correlations Between Anxiety Scores

Pearson correlations between the three continuous anxiety scores were similar to the tetrachoric correlations between the binary scores representing high (Score > 70) or low (Score < 70) scores. The Pearson correlation between anxiety about bowel preparation and anxiety about the procedure was 0.45 (P < 0.01), between anxiety about bowel preparation and anxiety about the procedure results was 0.30 (P < 0.01), and between anxiety about the procedure and anxiety about procedure results was 0.55 (P < 0.01). Similarly, the tetrachoric correlation between high anxiety about bowel preparation and high anxiety about the procedure was 0.42 (P < 0.01), between high anxiety about bowel preparation and high anxiety about the procedure results was 0.24 (P < 0.01), and between high anxiety about the procedure and high anxiety about procedure results was 0.53 (P < 0.01).

Multivariable Regressions

Although most associations with colonoscopy-related anxiety were the same or similar after controlling for the other variables in the models (Table 2) as they were in bivariate analysis (Table 1), some associations did change. As in bivariate analysis, more women than men were highly anxious in multivariable analysis (logistic regression) about bowel preparation and the procedure itself, but there was not a sex difference in high anxiety about the procedure results. The odds of high anxiety about all three aspects of a colonoscopy were similar across the different age groups. Patients who were undergoing repeat colonoscopies were less likely to be highly anxious about the procedure itself, and those who had undergone exactly one previous



Table 1 Pre-colonoscopy anxiety scores by background characteristics of patients

Variable	N (%)done	Anxiety score					
		Bowel preparation		Procedure		Procedure results	
		Median	> 70 (%)	Median	> 70 (%)	Median	> 70 (%)
Gender	,						
Male	616 (48)	22.5	11	46	23	50	27
Female	680 (52)	44**	25**	55**	35**	51	30
Age in years							
16–39	149 (11)	47	20	60	39	56	34
40–59	604 (47)	28	19	52	31	51	28
60-91	536 (42)	29**	16	45**	25**	50*	27
Education							
<= Grade 12	437 (36)	27	18	50	28	52	32
> Grade 12	770 (64)	33	18	51	30	50	26*
Previous colonoscopies							
0	541 (42)	43	21	60	38	53	31
1	328 (25)	24	14	48	28	49.5	26
2+	433 (33)	26**	16**	38**	20**	50**	26
Indication	, ,						
Screening	327 (25)	27	19	49	28	45	21
Surveillance	268 (21)	22	13	36.5	19	48	27
Symptoms	689 (54)	36.5**	19	54**	34**	54**	32**
Direct to colonoscopy	, ,						
No	776 (60)	30.5	18	51	29	51	27
Yes	521 (40)	29	17	50	29	51	29
Split bowel preparation	- (- /						
No	860 (67)	29.5	17	51	30	50	28
Yes	425 (33)	30	18	50	29	52	29
Finished laxative	- ()						
No	172 (13)	49.5	28	53	33	52.5	28
Yes	1124 (87)	27**	16**	50	29	50	28
Review of scope information	` ′						
Did not receive any	106 (8)	23.5	20	50	31	52.5	30
Did not review/skimmed	55 (4)	48	22	54	33	61	44
Reviewed most/all	469 (37)	29	14	50	29	51	27
Reviewed more than once	628 (50)	32	21*	51	30	50	27
Clarity of bowel prep instruc	` ′				20		
Confusing Confusing	72 (6)	57.5	36	64	39	54.5	42
Somewhat clear	153 (12)	49	25	59	34	53	29
Clear	1055 (82)	27**	15**	49**	28*	50*	27*

^{**}P value < 0.01 (Kruskal–Wallis H test for difference in median anxiety score, Fisher exact test for difference in percent with high anxiety)

colonoscopy were also less likely to be highly anxious about their bowel preparation and procedure results. However, those who were on their third or higher colonoscopy were no longer less anxious about their bowel preparation or procedure results. Patients with symptoms were much more anxious about their colonoscopy results than those who were being screened. However, the indication for the colonoscopy was not associated with anxiety about bowel

preparation or the procedure itself. As was found in bivariate analysis, having finished the laxative was associated with reduced odds of high anxiety about the bowel preparation, but was not associated with either of the other two anxiety scores. Compared with clear preparation instructions, those who felt that the instructions were confusing were significantly more anxious about their bowel preparation (OR 3.5, 95% C.I. 1.9–6.5), procedure itself (OR



^{*}P value > 0.01 and < 0.05

Table 2 Multivariable logistic regressions (OR and 95% C.I.) predicting high anxiety (VAS Anxiety Score > 70) about different aspects of colonoscopy

	Bowel preparation	Procedure	Procedure result
Female gender (ref = Male)	2.7 (1.9, 3.9)	1.8 (1.3, 2.3)	1.1 (0.8, 1.4)
Age in years (ref = $16-39$)			
40–59	1.3 (0.7, 2.2)	0.8 (0.5, 1.3)	0.8 (0.5, 1.3)
60–91	1.2 (0.7, 2.1)	0.7 (0.5, 1.2)	0.8 (0.5, 1.2)
Post-secondary education (ref = Grade 12 or lower)	0.9 (0.6, 1.3)	1.0 (0.7, 1.3)	0.8 (0.6, 1.1)
Previous scopes (ref = 0)			
1	0.6 (0.4, 0.9)	0.6 (0.4, 0.9)	0.7 (0.5, 0.9)
2+	0.8 (0.5, 1.2)	0.4 (0.3, 0.6)	0.8 (0.5, 1.1)
Indication (ref = screening)			
Colorectal cancer surveillance	0.9 (0.5, 1.5)	0.9 (0.5, 1.4)	1.7 (1.0, 2.6)
Symptoms	0.9 (0.6, 1.3)	1.3 (0.9, 1.8)	2.0 (1.4, 2.8)
Direct to colonoscopy (ref = not direct to colonoscopy)	0.9 (0.6, 1.3)	0.8 (0.6, 1.0)	1.1 (0.8, 1.5)
Split bowel preparation	1.0 (0.7, 1.4)	0.9 (0.6, 1.1)	1.1 (0.8, 1.5)
Finished laxative (ref = laxative unfinished)	0.4 (0.3, 0.7)	1.0 (0.6, 1.4)	1.2 (0.8, 1.9)
Review of scope info (ref = did not review	ew or skimmed only)		
Did not receive any	0.7 (0.3, 1.9)	0.8 (0.3, 1.9)	1.0 (0.4, 2.2)
Reviewed most/all	0.5 (0.2, 1.2)	0.9 (0.4, 2.0)	0.7 (0.3, 1.4)
Reviewed more than once	0.8 (0.4, 1.9)	0.9 (0.5, 2.0)	0.7 (0.3, 1.4)
Prep instructions (ref = clear)			
Somewhat clear	1.9 (1.2, 3.1)	1.4 (0.9, 2.1)	1.1 (0.7, 1.6)
Confusing	3.5 (1.9, 6.5)	1.9 (1.0, 3.4)	2.3 (1.3, 4.2)

For convenience, statistically significant odds ratios (OR) are bolded

1.9, 95% C.I. 1.0–3.4), and the procedure results (OR 2.3, 95% C.I. 1.3–4.2).

Discussion

A review conducted by Coombes et al. [17] found that most studies exploring the relationship between a colonoscopy and anxiety did not find elevated average anxiety levels among patients prior to their colonoscopy. On the other hand, a sizeable minority of patients do come to colonoscopy with clinically significant levels of anxiety—a higher proportion have clinically significant anxiety than that in the general population [8, 12]. Our study sheds light on the factors associated with high anxiety for different aspects of colonoscopy.

Although the anxiety scores on three different aspects of a colonoscopy were correlated, the correlations were low enough (0.45, 0.30, and 0.55) to suggest differences in how patients view different aspects of a colonoscopy. That is, the discomfort level of patients about their colonoscopy is not global, but rather related to specific aspects of the colonoscopy. A better understanding of the factors associated with anxiety related to different aspects of colonoscopy may help to design strategies to alleviate the anxiety, and, in so doing,

potentially reduce the proportions declining the recommendation for the procedure, reduce the proportions missing or canceling the procedure, improve bowel preparation, and increase procedure tolerance and satisfaction.

In our study, variables associated with higher anxiety about bowel preparation were female gender, first colonoscopy, not having finished the bowel preparation laxative, and confusing bowel preparation instructions. We were unable to determine in this study whether or not finishing the laxative resulted in higher anxiety about their bowel preparation, or whether patients with higher anxiety about bowel preparation were less likely to finish the laxative. If the latter is the case, then strategies to alleviate bowel preparation anxiety will likely lead to improved bowel preparation. Because of a higher proportion with high anxiety about bowel preparation among those who find instructions confusing and those with first colonoscopy, these groups need extra vigilance in conveying clear and perhaps repeated instructions about bowel preparation. It is also possible that improving the clarity of the instructions in general may reduce the levels of high anxiety about bowel preparation, which may lead to improved bowel cleansing.

Variables associated with higher anxiety about the colonoscopy procedure were female sex and first colonoscopy.



Women generally report higher levels of anxiety than men when assessed in a variety of contexts [37, 38].

Variables associated with higher anxiety about the results of the colonoscopy were first colonoscopy and symptoms being the indication for the colonoscopy. The finding of high levels of anxiety about the results of the colonoscopy is consistent with previous research [8, 14, 39]. The finding of first colonoscopy being associated with high anxiety for all three different aspects of colonoscopy evaluated suggests this group should be a major focus of attempts to allay anxiety about colonoscopy. On the contrary, age and coming direct to colonoscopy were not associated with anxiety about any aspects of colonoscopy, suggesting that strategies to reduce anxiety may apply with similar effectiveness to people of all ages, as well as those coming direct to colonoscopy or not.

A variety of approaches to reduce anxiety concerning colonoscopy have been considered. Educational approaches include providing improved written educational materials before the colonoscopy [17, 40] and video educational materials [16, 41, 42]. Generally, these approaches have been found to reduce anxiety and improve other aspects of the experience, although the impact of the intervention may depend on the quality of the standard procedures to which they are compared. Several interventions during colonoscopy have been evaluated for the impact on anxiety including music [9, 43] and audiovisual distraction [44, 45].

Educational approaches with written and audiovisual material have the advantage that they are relatively low in cost (compared to one-on-one interventions), they can be used well in advance of the colonoscopy (before a patient makes the decision to decline, cancel, or miss the procedure), and they may be easily delivered through Internet-based resources. They can also be tailored to deal with the concerns of patients around fears of pain, embarrassment, discomfort, sedation, and the possibility of a cancer diagnosis [8, 14, 39]. Even for those who are not particularly anxious, well-designed education materials may improve the understanding of the procedure and bowel preparation [17].

Our study must be taken in the context that study participants were all attending their scheduled colonoscopy. A study in China of a colon cancer screening program found that fear of bowel preparation (5%) and pain (11%) were factors in decisions to decline the offer of a colonoscopy [46]. In a recent study of persons who did not attend for scheduled colonoscopy appointments, the patients were contacted for a structured interview [47]. In one center, 25% of patients did not attend and 25% of those interviewed indicated that emotional difficulties (primarily anxiety) were a factor in the missed appointment. In the second center, 15% missed appointments and 10% of those interviewed indicated emotional factors were involved.



The results of this study should be considered in the context of strengths and limitations. The distribution of the survey in the waiting room was partially dependent on how busy the receptionist was and whether it appeared that there would be enough time to complete it before the patient's procedure. The study also started and finished on different dates in different colonoscopy units. During total study period, 14,552 colonoscopies were carried out across the units, 1837 patients were approached about completing the survey, 1580 agreed (86% response rate), and of those 1316 (83%) completed to the last part of the survey where the anxiety questions were placed. This was a convenience sample rather than a random sample. There may have been differences in the tone of the units when the surveys were distributed and when they were not. It is possible that some bias was present in terms of which patients were given surveys to complete. The survey also only included patients who attended their appointments, and it is likely that some patients decline a referral for colonoscopy, cancel their appointment, or do not attend because of problems with anxiety.

Strengths of this study include a high response rate from a large and diverse sample recruited from routine city-wide clinical practices. Participants had a range of previous experience with colonoscopy and a variety of different indications for the procedure, and this is typical of clinical practice. This allowed the evaluation of anxiety of patients with different presenting characteristics. Assessment of anxiety just before the procedure provided for immediacy of the situation and consistency of assessment across the participants is less feasible when questions are administered in the days or weeks before the procedure.

Conclusion

There are unique predictors of anxiety about each colonoscopy aspect. Understanding the nuanced differences in the aspects of anxiety may help to design strategies to reduce anxiety among colonoscopy patients, leading to improved acceptance of the procedure, compliance with preparation instructions, and less loss to follow-up. Coming direct to endoscopy without previously meeting the endoscopist does not enhance patient anxiety.

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Wittmeier, and Singh were involved in the study concept and design. Dr. Shafer performed the analysis and wrote the first draft. Dr. Bernstein is supported in part by the Bingham Chair in Gastroenterology. Dr. Singh has been on advisory board of Pendopharm and Ferring and has received research funding from Merck Canada. Dr. Bernstein has served on advisory boards for Abbvie Canada, Ferring Canada, Janssen Canada, Shire Canada, Pfizer Canada, and Takeda Canada. He has consulted to Mylan Pharmaceuticals and Bristol Myers Squibb. He has received unrestricted educational grants from Abbvie Canada, Janssen Canada, Shire Canada, and Takeda Canada. He has been on speaker's bureau for Abbvie Canada, Ferring Canada, and Shire Canada.

Compliance with ethical standards

Conflict of Interest There are no conflicts of interest for any of the authors

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