# Age Modifies the Association Between Depressive Symptoms and Adherence to Self-Testing With Telemedicine in Patients With Inflammatory Bowel Disease

Kenechukwu Chudy-Onwugaje, MBBS, MPH,\* Ameer Abutaleb, MD, MS,\* Andrea Buchwald, PhD,†
Patricia Langenberg, PhD,† Miguel Regueiro, MD,‡ David A. Schwartz, MD,§ J. Kathleen Tracy, PhD,†
Leyla Ghazi, MD,¶ Seema A. Patil, MD,\* Sandra Quezada, MD, MS,\* Katharine Russman, BA,\* Sara Horst, MD,§
Dawn Beaulieu, MD,§ Charlene Quinn, RN, PhD,† Guruprasad Jambaulikar, MBBS, MPH,¶ and
Raymond K. Cross, MD, MS\*

**Background:** Depression is common in patients with inflammatory bowel disease (IBD) and is known to be associated with poor adherence in the usual care setting. In the last decade, there has been an increase in the use of information technology (IT) for the delivery of IBD care, but the association between depressive symptoms (DS) and adherence to self-testing in this context is not known. We aimed to investigate this association among IBD patients managed via a text messaging—based telemedicine system.

**Methods:** This was a prospective study of participants in the 2 intervention arms of the Telemedicine for Patients with IBD (TELE-IBD) trial. Depressive symptoms were measured at baseline, and then participants received periodic text messages to initiate IBD-specific self-testing. Treatment plans were similarly conveyed, and adherence to self-testing was evaluated at the end of 1 year. Regression analyses were performed, and age-stratified models were constructed to evaluate for effect modification.

**Results:** Of the 193 study participants, 48% had DS at baseline. Overall, there was no significant association between DS and adherence to self-testing. However, upon stratification by age, adherence increased with depressive symptoms in those that were 40 years and younger (P = 0.02), but there was no association between depressive symptoms and adherence in the older group (P = 0.53).

**Conclusions:** Younger IBD patients with DS have high adherence when managed in a text messaging—based telemedicine program. Telemedicine interventions have the potential to improve health outcomes in this demographic—a group that is often thought to be difficult to manage due to nonadherence.

Key Words: inflammatory bowel disease, telemedicine, depression, adherence to self-testing, age

Received for publications January 3, 2018; Editorial Decision April 16, 2018.

From the \*Division of Gastroenterology and Hepatology, Department of Medicine, and †Department of Epidemiology and Public Health, University of Maryland, Baltimore, Maryland; †Division of Gastroenterology, Hepatology and Nutrition, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania; †Division of Gastroenterology, Hepatology and Nutrition, Department of Medicine, Vanderbilt University, Nashville, Tennessee; †Department of Gastroenterology and Hepatology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire; †Department of Emergency Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Conflicts of interest: None.

Supported by: the Litwin Pioneers Program at the Crohn's and Colitis Foundation (431257), the Agency for Healthcare Research and Quality (1R01HS018975-01A1), and the University of Maryland General Clinical Research Centers Program. Dr. Chudy-Onwugaje and Dr Abutaleb were also supported by a T32 Research Grant (DK067872-11) from the National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases.

Address correspondence to: Raymond K. Cross, MD, MS, 685 West Baltimore Street, Suite 8-00, Baltimore, MD 21201 (rcross@som.umaryland.edu).

© 2018 Crohn's & Colitis Foundation. Published by Oxford University Press. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com.

doi: 10.1093/ibd/izy194 Published online 28 May 2018

## **INTRODUCTION**

Inflammatory bowel disease (IBD) is a significant cause of morbidity in the United States and consumes a disproportionate amount of health care resources.<sup>1, 2</sup> Depression is a prevalent condition in IBD, with 49% of IBD patients having depressive symptoms (DS) in a recent analysis of US population data from the National Health and Nutrition Examination Survey.<sup>3</sup> Depression compounds morbidity in IBD and has been shown to be associated with nonadherence to medications and medical counsel.<sup>4</sup> Poor adherence is correlated with suboptimal health outcomes in IBD patients and has been associated with an increase in the risk of disease flares, the development of colorectal cancer, and the need for hospitalizations.<sup>5-8</sup>

In recent years, there has been a gradual shift from the delivery of IBD care in the traditional physical spaces of hospital and clinics to computerized platforms. This use of information technology (IT) for the remote delivery of care, also known as telemedicine, has been shown to result in improved outcomes, better quality of life, and decreased health care use in IBD.9-12 Using web- and mobile-based technology, telemedicine has been adapted for patient education, disease and side effect monitoring, and the delivery of medication and disease staterelated prompts. In this setting, active patient engagement is vital for good health outcomes. Self-testing in telemedicine refers to the performance of clinical tasks by the patient and transmission of the resulting data to the health care team to affect patient care. Self-testing is necessary in telemedicine as history-taking, physical examination, and other disease-specific clinical processes that are the bedrock of the traditional in-person encounter are not possible with the remote delivery of health care. Specifically, participants are often expected to monitor their symptoms, perform home-based tests, and make reports to their providers through predefined communication channels. However, as is seen in the usual health care space, maintaining adherence to selftesting can be challenging in telemedicine patients.

Depression is known to be associated with nonadherence in the traditional care setting, but this relationship has not been studied in IBD patients managed via telemedicine. A better understanding of this association is important, as it could inform the appropriate selection of patients for telemedicine interventions in the future and promote the clinical design of effective and responsive IT programs for IBD patients. As telemedicine becomes more common place, the efficient use of digital resources could result in substantial health care savings.

We hypothesized that depression would be correlated with decreased adherence to self-testing in telemedicine patients and aimed to investigate the association between DS and adherence to self-testing in IBD patients managed via text messaging—based telemedicine.

## **METHODS**

## **Study Design and Participants**

This was a prospective study of the cohort in the intervention arms of the Telemedicine for Patients with Inflammatory Bowel Disease (TELE-IBD) study.<sup>13</sup> The TELE-IBD study was a 12-month, multicenter randomized clinical trial comparing disease activity and quality of life in IBD patients receiving standard care vs text message-based telemedicine. It was conducted at 3 university medical centers: University of Maryland (UMB), University of Pittsburgh Medical Center (UPMC), and Vanderbilt University (VU). For inclusion in the TELE-IBD study, participants had to meet the following criteria: be 18 years of age or older, have documented IBD on the basis of usual diagnostic criteria, and have had at least 1 documented exacerbation of disease symptoms in the 2 years preceding the initial study visit. The exclusion criteria for the study were as follows: uncontrolled medical or psychiatric disease, inability to speak and/or read English, pregnancy, history of short bowel syndrome, imminent surgery, and presence of an ileoanal pouch, ileostomy, ileorectal anastomosis, or colostomy. Participants were randomized to 1 of 3 care groups: telemedicine

every week, telemedicine every other week, and standard care. The TELE-IBD system was a web-based, database-driven system developed by investigators at UMB in collaboration with MedAdherence LLC (now CircleLink Health). It was designed for 2-way communication and collection of secure clinical data and consisted of mobile phones for patients and a decision support server and website for health care providers.

Participants for the present study included all those in the 2 intervention arms of the TELE-IBD study. Depending on group assignment, they received weekly or every-otherweek text messages to initiate self-testing over a 1-year period. At each session, they were prompted to respond to a series of simple text messages regarding IBD symptoms, medication side effects, and body weight. To assess disease activity, for example, they were expected to grade their symptoms with a focus on certain core areas: overall well-being, abdominal pain, number of bowel movements, and the presence of blood in stool. Participants were also prompted to assess their body weight using an electronic scale that was provided at enrollment. At the end of each self-testing session, health care providers were able to access patient data on a secure portal. Based on text responses and predetermined thresholds, a clinical impression was made of each participant's overall health, and treatment plans were conveyed via text messaging. Nurse coordinators were alerted if patients reported significant symptoms of IBD or side effects from treatment.

# **Assessment of Depressive Symptoms**

Depressive symptoms were self-reported and measured at study enrollment using the Mental Health Index 5 (MHI-5) scale.<sup>14, 15</sup> This is a 5-item validated measure of DS that is a subscale of the Short Form 36 (SF-36) survey, and its items were designed to evaluate symptoms in the month before administration. Each item is graded on a Likert scale with responses ranging from "all the time" to "none of the time" and scored as 1 to 6 points, with the scores for items 3 and 5 reversed. Individual item scores are summed up and transformed to obtain a total MHI-5 score on a scale that ranges from 0 to 100. Lower scores denote more severe DS.<sup>16, 17</sup> Consistent with prior studies, participants with scores below 76 were classified as depressed, and those with scores of 76 or higher were considered nondepressed.<sup>18, 19</sup>

### **Assessment of Adherence**

The primary study outcome was adherence to self-testing, and this was assessed at the end of the 12-month study period. We treated this as a dichotomous variable and defined adherence to self-testing as completion of at least 80% of self-testing sessions. The 80% cutoff was chosen because this benchmark has been commonly used to define good adherence in IBD studies. Completion of self-testing was recorded in the TELE-IBD portal at the end of every session, and the research team had access to the interval and aggregate adherence data

for each participant. For participants in the weekly self-testing group, adherence was calculated by assessing the number of completed self-testing sessions against a high of 52. For those in the every-other-week group, it was calculated against a maximum total of 26 sessions.

#### **Covariates**

Sociodemographic information was collected on age, race, ethnicity, sex, health insurance, and smoking status. Clinical data were collected for each participant and included IBD type and behavior, age at diagnosis, medication use, inflammatory markers, and disease activity scores (Harvey-Bradshaw index [HBI] for Crohn's disease and the Simple Clinical Colitis Activity Index [SCCAI] for ulcerative colitis). TELE-IBD-specific information such as frequency of self-testing and recruitment site was also collected.

# **Statistical Analysis**

The mean and standard deviation were estimated for continuous variables, and categorical variables were expressed as proportions. Comparisons were made between groups using the Student t test for continuous variables and the Pearson chisquare or Fisher exact test for categorical variables. Odds ratio (ORs) and 95% confidence intervals (CIs) were calculated by logistic regression analysis using unadjusted and multivariable models to test the association of DS with adherence to self-testing. To assess for effect measure modification, stratified analyses were performed to determine if the association between DS and adherence varied within the strata of a third variable. The effect of the interaction between age (categorical variable: 18-40 years and >40 years) and DS on adherence was tested by including an interaction term in the model. Covariates were considered for inclusion as confounders if they were supported by our review of the literature and were either associated with both exposure and outcome or met the 10% cutoff of our change-in-estimate criterion after calculating the difference between a variable-adjusted OR and the crude OR. Statistical analyses were performed using SAS 9.3 for Windows (SAS Institute Inc., Cary, NC, USA), and a P value <0.05 was considered statistically significant.

#### **Ethical Considerations**

This study was conducted under a protocol approved by the institutional review boards at the 3 study sites: UMB Human Research Protection Office, UPMC Office of Research, and the VU Human Research Protection Program.

#### **RESULTS**

Of the 230 participants eligible for this study, 183 were included in the final analysis.

Those who did not complete the study (n = 37) were excluded, and the most common reasons for noncompletion were loss to follow-up and withdrawal due to pregnancy or

surgery. Information on DS was incomplete or missing for 10 participants, and they were also excluded.

The mean age of the sample (range) was 39 (18–79) years, and the mean disease duration was  $12.5 \pm 9.0$  years. Women made up 56% of the cohort, and 66% of the sample had Crohn's disease. A majority of the participants were Caucasian (95%), and only 9% of the population were current cigarette smokers. At baseline, and based on the MHI-5 score cutoff of 76, DS were present in 48% of the sample. The demographic and clinical characteristics of study participants, according to DS, are summarized in Table 1. We did not observe any significant differences in the distribution of age, sex, race, IBD type, or frequency of self-testing between those with and without DS.

Sixty percent of participants (n = 110) were adherent to testing at the end of the 12-month study period. Adherent participants were more likely to be female (P = 0.03) and to have received text messages every other week (P = 0.003). They also tended to have a higher mean erythrocyte sedimentation rate (P = 0.09). On crude analysis, there was no significant association between DS and adherence to self-testing (OR, 1.51; 95% CI, 0.83–2.74; P = 0.17), and this remained after controlling for age, sex, erythrocyte sedimentation rate (ESR), serum albumin, and frequency of receipt of text messages (OR, 1.59; 95% CI, 0.80–3.15; P = 0.18).

We observed a significant interaction between DS and age on adherence to self-testing (P = 0.05). Upon stratification of the population by age (Table 2), adherence increased with DS in individuals aged 18–40 years (OR, 2.48; 95% CI, 1.12–5.50; P = 0.02), but there was no association between DS and adherence in individuals older than 40 years (OR, 0.74; 95% CI, 0.29–1.89; P = 0.53). Overall, the group of participants who were young and with DS had the highest adherence in comparison with others (young and without DS, old and with DS, and old and without DS). Adjusting for confounding factors did not change these findings (Table 3).

Further, we performed a subgroup analysis to investigate the effect modification by age on the relationship between DS and adherence. We compared participants in the 2 age groups according to depression status and found that among those between age 18 and 40 years, DS were positively associated with markers of more severe disease (Table 4). Young participants with DS had a higher ESR (P = 0.01), higher HBI (P < 0.001), and lower serum albumin (P = 0.04) compared with their peers who did not have DS. Similar findings were also observed in the older age group, where DS were positively associated with higher disease activity scores (HBI, P = 0.001; SCCAI, P = 0.03).

# **DISCUSSION**

In the present study, we prospectively assessed the relationship between DS and adherence to self-testing in IBD patients managed via text messaging—based telemedicine. We did not observe an overall association between DS and adherence

**TABLE 1:** Baseline Characteristics of Study Participants, by Depression Status

Variables	Depressive Symptoms (n = 89)	No Depressive Symptoms (n = 94)	P	
Age group, No. (%)				
18–40 y	51 (57.3)	57 (60.6)	0.65	
>40 y	38 (42.7)	37 (39.4)		
Sex, No. (%)				
Female	56 (62.9)	47 (50.0)	0.08	
Male	33 (37.1)	47 (50.0)		
Caucasian, No. (%)	85 (95.5)	89 (94.7)	0.80	
Study site, No. (%)				
University of Maryland	54 (60.7)	56 (59.6)	0.97	
University of Pittsburgh	26 (29.2)	29 (30.9)		
Vanderbilt University	9 (10.1)	9 (9.5)		
Health insurance coverage, No. (%)				
Commercial	50 (64.9)	51 (63.7)	0.77	
Medical assistance	1 (1.3)	1 (1.3)		
Medicare	4 (5.2)	2 (2.5)		
None	0 (0.0)	1 (1.3)		
Other	22 (28.6)	25 (31.2)		
Diagnosis, No. (%)				
Crohn's disease	62 (69.6)	59 (62.8)	0.44	
Ulcerative colitis	25 (18.1)	34 (36.1)		
Indeterminate colitis	2 (2.3)	1 (1.1)		
Cigarette use, No. (%)				
Current or former	36 (40.9)	33 (36.3)	0.52	
Never	52 (59.1)	58 (63.7)		
Frequency of self-testing, No. (%)				
Week	43 (48.3)	48 (51.1)	0.71	
Every other week	46 (51.7)	46 (48.9)		
Current medication use, No. (%)				
Aminosalicylates	26 (29.2)	30 (32.9)	0.59	
Corticosteroids	15 (16.9)	16 (17.0)	0.97	
Immunomodulators	35 (39.3)	25 (27.1)	0.08	
Anti-TNF agents	49 (55.7)	59 (65.6)	0.18	
Natalizumab	1 (1.1)	0 (0.0)	0.49	

in the study cohort. However, we found that age modifies this association. In the younger age group (18–40 years), adherence to self-testing increased with DS; in the older age group (>40 years), there was no significant association between DS and adherence to self-testing. The effect modification by age on the association between DS and adherence was unexpected.

In comparing our findings with the published literature, we found that previous articles on this subject have focused on adherence to medications as the outcome of interest and were conducted mostly in non-telemedicine-based settings. To our knowledge, this study is the first to prospectively study the relationship between DS and adherence to self-testing in a text messaging—based telemedicine context. The overall lack of an association between DS and adherence in our study is

in contrast with the findings of a majority of previous studies, which have generally shown that adherence is poor in IBD patients with depression. In a cross-sectional survey of 1069 IBD patients in France, depression and anxiety were found to be associated with poor adherence to prescribed IBD medications, with only anxiety remaining significant on multivariable analysis.<sup>23</sup> Similarly, in a prospective study of IBD patients on immunomodulator therapy, nonadherence was found to be higher among those with depression.<sup>24</sup> Investigators made the same observation in a cross-sectional study on adherence to thiopurines.<sup>25</sup> Here, compliance with thiopurine therapy was objectively assessed using metabolite levels, and they found that a higher depression score was significantly associated with poor adherence. In another study using variables comparable to the

**TABLE 2:** Modification of the Effect of Depressive Symptoms on Adherence to Self-Testing by Age

	No Depressive Symptoms		Depressive Symptoms		
	No. Adherent/	OR (95% CI) <sup>a</sup>	No. Adherent/ Nonadherent	OR (95% CI) <sup>a</sup>	OR (95% CI) for Depressive Symptoms Within Strata of Age Group
Age 18–40 y	28/29	1.0 (ref)	36/15	2.48 (1.12–5.50) P = 0.02	2.48 (1.12–5.50) P = 0.02
Age >40 y	24/13	1.91 (0.82-4.48) $P = 0.13$	22/16	1.42 (0.62-3.26) $P = 0.40$	0.74 (0.29-1.89) $P = 0.53$

\*Odds ratios (95% confidence intervals) were computed in comparison with the reference group of younger age and no depressive symptoms.

present study, Tabibian et al. examined the association between perceived stress in IBD patients and general adherence (to medications and IBD-specific medical counsel).<sup>26</sup> They found that general adherence was significantly lower in subjects with higher levels of stress. Of note, 1 study did not find a relationship between depression and adherence, in keeping with our overall findings. Using the Hospital Anxiety and Depression Score to measure depression and the Medicine Adherence Report Scale to assess adherence, Selinger et al. did not find an association between depression and adherence to maintenance medication in 356 study participants.<sup>27</sup>

We found that the presence of DS was associated with increased adherence to self-testing in the younger age group, but there was no association between DS and adherence to self-testing in older participants. This effect modification of age on the relationship between depression and adherence was an unexpected finding, and the reasons for this are unclear. We theorize that the increased adherence seen among young participants with DS is explained by an interplay of the greater familiarity and affinity for interaction with technology in younger persons, with the increased health-seeking behavior seen in severe disease. Severe disease is known to be associated with improved adherence in IBD,<sup>20</sup> and as our subgroup analyses indicate,

**TABLE 3:** Multivariate Adjusted Odds Ratio for the Association of Depressive Symptoms With Adherence to Self-Testing According to Age Group

		Depressive Symptoms		
	Age Group, y	No	Yes	
Adherence to self-testing	18–40 >40	1.0 (ref) 1.70 (0.64–4.52)	2.74 (1.10–6.80)* 1.31 (0.51–3.38)	

Data are expressed as odds ratio (95% confidence interval) compared with the reference group of younger age and no depressive symptoms, and adjusted for sex, erythrocyte sedimentation rate, serum albumin, and frequency of self-testing. \*P < 0.05.

young participants with depressive symptoms had evidence of more severe disease in comparison with their nondepressed peers. They had increased biologic markers of disease activity and higher disease activity scores (Table 4). This correlation of depression with more severe disease in IBD patients has also been described by Kochar et al.<sup>28</sup> On additional analyses, we found that young and old participants with DS had comparable disease severity (Table 4), yet the relationship between DS and adherence was divergent in these 2 groups. We posit that improved adherence to self-testing was only seen in young participants with DS because their greater technological adeptness made for the expression of health-seeking behavior through greater engagement with text messaging—based care.

High uptake of telemedicine in young IBD patients has been noted in previous studies. In a prospective study of pediatric IBD patients, use of 2-way interactive text messaging to remind participants of medication administration was associated with an improvement in adherence to oral medications when compared with a control group.<sup>29</sup> Among young people with DS, recent research has also demonstrated the utility of telemedicine in symptom monitoring and in improving overall outcomes.30,31 In a recent pilot study of adolescent patients with depression, researchers explored the use of automated text message interventions for monitoring of DS.32 Standardized messages were sent periodically to participants, and in response to this, alerts could be triggered and targeted educational messages could be sent. At the conclusion of the study, the researchers found that the weekly response rate was excellent among participants. More importantly, they found that suicidal ideation was detected earlier using this telemedicine modality—even before family members and case managers were aware of these. Another study by Gray et al. on adherence in young patients in the usual care setting is instructive and may provide some elucidation of the improved adherence noted in young and depressed patients in the present study.<sup>33</sup> In a sample of 79 patients with IBD, they found that DS moderated the relationship between barriers to adherence and medication adherence. Of note, the most common barriers to medication adherence were forgetfulness (85%) and "wasn't home" (43%).

TABLE 4: Comparison of Study Participants by Depression Status, According to Age

	Age 18–40 y			Age >40 y		
	Depressive Symptoms (n = 51)	No Depressive Symptoms (n = 57)	P	Depressive Symptoms (n = 38)	No Depressive Symptoms (n = 37)	P
Mean age (SD), y	$31.2 \pm 5.1$	$30.1 \pm 5.7$	0.30	$51.2 \pm 9.5$	$51.7 \pm 9.0$	0.81
Female, No. (%)	32 (62.8)	27 (47.3)	0.11	24 (63.2)	20 (54.0)	0.42
Crohn's disease, No. (%)	36 (70.6)	39 (68.4)	0.63	26 (68.4)	20 (54.0)	0.10
Perianal involvement, No. (%)	9 (26.5)	10 (26.3)	0.99	9 (36.0)	3 (13.6)	0.08
Mean age at disease onset (SD), y	$21.5 \pm 7.3$	$21.7 \pm 5.4$	0.89	$34.1 \pm 10.9$	$33.9 \pm 11.7$	0.94
Mean time since diagnosis (SD), y	$9.7 \pm 6.9$	$8.4 \pm 5.4$	0.30	$17.4 \pm 9.7$	$17.9 \pm 10.6$	0.84
Mean time since last flare (SD), y	$0.66 \pm 0.80$	$0.63 \pm 0.55$	0.82	$0.53 \pm 0.49$	$0.75 \pm 0.61$	0.09
Laboratory parameters, mean (SD)						
ESR, mm/h	$17.2 \pm 17.4$	$10.2 \pm 9.7$	0.01	$19.8 \pm 18.9$	$20.1 \pm 20.9$	0.97
CRP, mg/L	$12.9 \pm 27.0$	$6.8 \pm 16.9$	0.18	$3.9 \pm 6.9$	$5.4 \pm 6.8$	0.41
Serum albumin, g/dl	$4.2 \pm 0.4$	$4.4 \pm 0.4$	0.04	$4.1 \pm 0.4$	$4.2 \pm 0.5$	0.12
Disease activity scores, mean (SD)						
HBI	$4.6 \pm 3.6$	$1.95 \pm 2.5$	0.0004	$5.7 \pm 3.6$	$2.5 \pm 2.9$	0.001
SCCAI	$3.6 \pm 2.9$	$2.2 \pm 2.8$	0.19	$3.5 \pm 2.6$	$1.6 \pm 1.6$	0.03

Nonadherence due to refusal to take medications (11%) or due to side effects (6%) was rare. Here we see that the prevalent barriers in this demographic are potentially modifiable, and this can be accomplished with a system that engages with and provides reminders to young patients in an effort to improve adherence. The 2-way text message—based telemedicine system used in our study served this exact purpose.

In review of the literature, we did not find any studies that specifically examined the association between depression and adherence to self-testing in telemedicine patients with comparable chronic medical conditions, and there were no studies that evaluated this relationship by age. It is important to note, however, that a greater affinity for mobile technology among young telemedicine patients has been seen in other medical conditions. A pair of recent studies highlighted this observation in those with chronic kidney disease. In a study by Reber et al., affinity to mobile technology was evaluated among renal transplant recipients.34 Affinity to mobile technology was measured using the Technology Experience Questionnaire (TEQ), and they found that young patients (<40 years of age) had significantly higher mobile technology affinity in comparison with older patients. They also noted an inverse association between age and mobile technology affinity, with the middle-aged group (40-59 years) having a higher affinity in comparison with the oldest age group (60 years or older). Similar findings were also reported in another study that evaluated the opportunity for the use of technology among 708 patients with chronic kidney disease. Here, they found that in comparison with the older group, younger subjects had a greater likelihood of use and proficiency with mobile technology.<sup>35</sup>

To our knowledge, this is the first study to comprehensively and prospectively examine the association between DS and adherence to self-testing using mobile-based technology in IBD patients. Our uncovering of the effect modification of age on the relationship between depression and adherence is a novel one and has important implications for clinical practice. In this IBD cohort, we have demonstrated that young depressed patients are the most likely to be adherent to text messaging—based interventions. If telemedicine becomes more widely adopted in IBD care, as expected, health care resources will be more effectively spent if channeled to more responsive subgroups. Our findings suggest that text messaging—based telemedicine is a veritable means to reach and engage young persons with DS—a demographic that is considered difficult to manage in the usual care setting due to poor adherence.<sup>36</sup>

This study has several strengths. First, the quality of measurement of the outcome variable was high as adherence to self-testing was automatically captured in the TELE-IBD portal. This degree of objectivity in the assessment of adherence is a major strength. Previous medication adherence studies in IBD patients have mostly relied on more subjective measures of adherence such as self-reporting, and these are prone to white coat adherence. Second, the prospective design of this study was advantageous in establishing temporality. Our study also has some limitations. There was a potential for recall bias, as assessment of DS was based on self-reporting using the MHI-5 instrument. The addition of another means to ascertain depression status—such as a comprehensive clinical assessment or a review of medication records for antidepressant use—could have reduced this likelihood. Furthermore, all 3 study sites are

referral centers for IBD treatment and, as such, are more likely to see patients with DS and more severe IBD. Our findings may therefore not be generalizable to the IBD population at large.

In conclusion, our results show that age modifies the association between DS and adherence to self-testing. Specifically, the association between DS and adherence was strongly positive in participants aged 18-40 years, but there was no association in those older than 40 years. Young IBD patients with DS bear a double burden, with the co-existence of 2 chronic and potentially debilitating conditions, but it appears that they are highly responsive to, and are therefore excellent targets for, telemedicine interventions. Looking to the future, additional studies are needed to examine the disease-specific outcomes of text messaging-based telemedicine care in this group. Additionally, the feasibility of delivering Tele-IBD care and Tele-psychiatry care on an integrated IT platform should be explored in young and depressed IBD patients. This will ensure the efficient use of health care resources and reduce the fatigue and attendant lack of engagement that may arise from receiving care for 2 chronic conditions through separate providers.

#### **REFERENCES**

- Kappelman MD, Rifas-Shiman SL, Porter CQ, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US children and adults. *Gastroenterology*. 2008;135:1907–1913.
- Gibson TB, Ng E, Ozminkowski RJ, et al. The direct and indirect cost burden of Crohn's disease and ulcerative colitis. J Occup Environ Med. 2008;50:1261–1272.
- Bhandari S, Larson ME, Kumar N, Stein D. Association of inflammatory bowel disease (IBD) with depressive symptoms in the United States population and independent predictors of depressive symptoms in an IBD population: a NHANES study. Gut Liver. 2017;11:512–519.
- Graff LA, Walker JR, Bernstein CN. Depression and anxiety in inflammatory bowel disease: a review of comorbidity and management. *Inflamm Bowel Dis*. 2009;15:1105–1118.
- Kane S, Huo D, Aikens J, Hanauer S. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. Am J Med. 2003;114:39–43.
- Moody GA, Jayanthi V, Probert CS, et al. Long-term therapy with sulphasalazine protects against colorectal cancer in ulcerative colitis: a retrospective study of colorectal cancer risk and compliance with treatment in leicestershire. Eur J Gastroenterol Hepatol. 1996;8:1179–1183.
- Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut. 2001;48:526–535.
- Carter CT, Waters HC, Smith DB. Impact of infliximab adherence on Crohn's disease-related healthcare utilization and inpatient costs. Adv Ther. 2011;28:671–683.
- Jackson BD, Gray K, Knowles SR, De Cruz P. Ehealth technologies in inflammatory bowel disease: a systematic review. J Crohns Colitis. 2016;10:1103–1121.
- Cross RK, Cheevers N, Rustgi A, et al. Randomized, controlled trial of home telemanagement in patients with ulcerative colitis (UC HAT). *Inflamm Bowel Dis*. 2012;18:1018–1025.
- Elkjaer M, Shuhaibar M, Burisch J, et al. E-health empowers patients with ulcerative colitis: a randomised controlled trial of the web-guided 'constant-care' approach. Gut. 2010;59:1652–1661.
- Pedersen N. Ehealth: self-management in inflammatory bowel disease and in irritable bowel syndrome using novel constant-care web applications. Ehealth by constant-care in IBD and IBS. Dan Med J. 2015;62:B5168.
- Cross RK, Jambaulikar G, Langenberg P, et al. Telemedicine for patients with inflammatory bowel disease (TELE-IBD): design and implementation of randomized clinical trial. *Contemp Clin Trials*. 2015;42:132–144.

- Cuijpers P, Smits N, Donker T, et al. Screening for mood and anxiety disorders with the five-item, the three-item, and the two-item mental health inventory. *Psychiatry Res.* 2009;168:250–255.
- Strand BH, Dalgard OS, Tambs K, Rognerud M. Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). Nord J Psychiatry. 2003;57:113–118.
- van den Beukel TO, Siegert CE, van Dijk S, et al. Comparison of the SF-36 fiveitem mental health inventory and Beck Depression Inventory for the screening of depressive symptoms in chronic dialysis patients. Nephrol Dial Transplant. 2012;27:4453–4457.
- Friedman B, Heisel M, Delavan R. Validity of the SF-36 five-item mental health index for major depression in functionally impaired, community-dwelling elderly patients. J Am Geriatr Soc. 2005;53:1978–1985.
- Kelly MJ, Dunstan FD, Lloyd K, Fone DL. Evaluating cutpoints for the MHI-5 and MCS using the GHQ-12: a comparison of five different methods. BMC Psychiatry. 2008;8:10.
- Ananthakrishnan AN, Khalili H, Pan A, et al. Association between depressive symptoms and incidence of Crohn's disease and ulcerative colitis: results from the Nurses' Health Study. Clin Gastroenterol Hepatol. 2013;11:57–62.
- Kane SV, Cohen RD, Aikens JE, Hanauer SB. Prevalence of nonadherence with maintenance mesalamine in quiescent ulcerative colitis. Am J Gastroenterol. 2001;96:2929–2933.
- Lachaine J, Yen L, Beauchemin C, Hodgkins P. Medication adherence and persistence in the treatment of Canadian ulcerative colitis patients: analyses with the RAMO database. BMC Gastroenterol. 2013;13:23.
- Shale MJ, Riley SA. Studies of compliance with delayed-release mesalazine therapy in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2003;18:191–198.
- Nahon S, Lahmek P, Saas C, et al. Socioeconomic and psychological factors associated with nonadherence to treatment in inflammatory bowel disease patients: results of the ISSEO survey. *Inflamm Bowel Dis.* 2011;17:1270–1276.
- Campos S, Portela F, Sousa P, Sofia C. Inflammatory bowel disease: adherence to immunomodulators in a biological therapy era. Eur J Gastroenterol Hepatol. 2016;28:1313–1319.
- Goodhand JR, Kamperidis N, Sirwan B, et al. Factors associated with thiopurine non-adherence in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2013;38:1097–1108.
- Tabibian A, Tabibian JH, Beckman LJ, et al. Predictors of health-related quality
  of life and adherence in Crohn's disease and ulcerative colitis: implications for
  clinical management. *Dig Dis Sci.* 2015;60:1366–1374.
- Selinger CP, Eaden J, Jones DB, et al. Modifiable factors associated with nonadherence to maintenance medication for inflammatory bowel disease. *Inflamm Bowel Dis.* 2013;19:2199–2206.
- Kochar B, Barnes EL, Long MD, et al. Depression is associated with more aggressive inflammatory bowel disease. Am J Gastroenterol. 2018;113:80–85.
- Miloh T, Shub M, Montes R, et al. Text messaging effect on adherence in children with inflammatory bowel disease. J Pediatr Gastroenterol Nutr. 2017;64:939–942.
- Stasiak K, Hatcher S, Frampton C, Merry SN. A pilot double blind randomized placebo controlled trial of a prototype computer-based cognitive behavioural therapy program for adolescents with symptoms of depression. *Behav Cogn Psychother*. 2014;42:385–401.
- Kobak KA, Mundt JC, Kennard B. Erratum to: integrating technology into cognitive behavior therapy for adolescent depression: a pilot study. *Ann Gen Psychiatry*. 2016;15:2.
- Chen RY, Feltes JR, Tzeng WS, et al. Phone-based interventions in adolescent psychiatry: a perspective and proof of concept pilot study with a focus on depression and autism. *JMIR Res Protoc*. 2017;6:e114.
- Gray WN, Denson LA, Baldassano RN, Hommel KA. Treatment adherence in adolescents with inflammatory bowel disease: the collective impact of barriers to adherence and anxiety/depressive symptoms. J Pediatr Psychol. 2012;37:282–291.
- Reber S, Scheel J, Stoessel L, et al. Mobile technology affinity in renal transplant recipients. *Transplant Proc.* 2018;50:92–98.
- Bonner A, Gillespie K, Campbell KL, et al. Evaluating the prevalence and opportunity for technology use in chronic kidney disease patients: a cross-sectional study. BMC Nephrol. 2018;19:28.
- Ediger JP, Walker JR, Graff L, et al. Predictors of medication adherence in inflammatory bowel disease. Am J Gastroenterol. 2007;102:1417–1426.