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Patient Perceptions of Fecal Microbiota Transplantation for Ulcerative Colitis

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Abstract

Background—Fecal microbiota transplantation (FMT), the delivery of stool from a healthy pre-screened donor to an individual with disease, is gaining increasing recognition as a potential treatment for inflammatory bowel diseases (IBD). Our objective was to describe patient interest in and social concerns around FMT.

Methods—We conducted a survey of adults with ulcerative colitis (UC) seen in outpatient clinic at the University of Chicago IBD Center. All English-speaking patients ≥ 18 years of age were eligible. Subjects completed a written survey in clinic.

Results—95 participants, median age 39, 53% female enrolled. 44% and 49% reported excellent or good/satisfactory medical management of their UC, respectively. 46% were willing to undergo FMT as a treatment for UC, 43% were unsure, and 11% were unwilling to undergo FMT. Subjects who had been hospitalized were more willing to undergo FMT 54% versus 34%, *p=0.035*. Primary concerns included: adequate screening for infections (41%), cleanliness (24%), and potential to worsen UC (18%); 21% reported no specific concerns. For donor selection, an equal number of participants (46%) preferred whomever their doctor recommended or family member/spouse.

Conclusion—In our center despite reporting satisfactory to excellent disease control with their treatments, the vast majority of patients with UC are interested in or willing to consider FMT. Proof of safety and effectiveness, as well as failure of other medical therapies are key issues in considering FMT. Strong interest in this as-yet unproven therapy warrants attention and is a pressing priority for clinical research and education.

Keywords

Ulcerative colitis; fecal microbiota transplantations; ethics; patient preferences

INTRODUCTION

Fecal microbiota transplantation (FMT), also known as stool transplant, is the delivery of stool from a healthy pre-screened donor to an individual with disease. FMT is gaining increasing recognition as a potential treatment for a number of gastrointestinal conditions,

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including inflammatory bowel diseases (IBD).[1-5] The most convincing data is driven by studies of FMT as a treatment for refractory or recurrent *Clostridium difficile* infection (CDI), where it has yielding convincing safety and efficacy data.[6-9] However, critics still have significant concerns about the acceptability of FMT and the ethical issues associated with risk and studying FMT in individuals with severe disease.[10-12]

The theory underlying FMT is based on microbial studies demonstrating significant perturbations in the intestinal commensal microbiota in the setting of CDI.[13-15] FMT is a targeted treatment aimed at restoring healthy commensal bacteria and correcting the intestinal dysbiosis associated with CDI. Intestinal dysbyosis has also been demonstrated in patients with IBD,[16] and therefore FMT may be useful in this patient population.

Despite the progress in studying FMT in CDI, there have been no prospective studies evaluating the safety or efficacy of FMT in IBD. To date, research has been limited by regulatory agencies who are concerned about the potential risks of FMT and those who question whether patients will accept this therapy due to stigma, the “yuck factor”, and safety concerns.[17-20] The lack of safety and efficacy data for FMT in IBD has not dampened patient interest. Recently, we published results from a focus group study demonstrating that patients with colitis as well as parents of patients with colitis were overwhelmingly interested in FMT and were willing to consider treatment with FMT for themselves or their children. Interest in FMT was due in part to a perception that is “natural” and safe compared to conventional therapies.[21] Similar to our colleagues in the field, we receive numerous inquiries about FMT for IBD and other diarrheal diseases. Most concerning however, are the patient internet postings that include “do-it-yourself” home-protocols for FMT as well as patients’ experiences treating themselves with FMT.[22-25]

The strong interest in the approach, the readily available primary product (stool from a donor), and the compelling efficacy data in CDI represent a combination of elements that we believe are potentially dangerous to our patients’ health and to their utility of conventional therapeutic approaches for their ulcerative colitis (UC). Prior to conducting trials of FMT to establish the safety and efficacy of FMT in IBD, it is critical to address the unique social and ethical issues relevant to this vulnerable patient population. We conducted this study to establish quantitative evidence that patients with IBD are interested in FMT and to describe the social and risk concerns patients with UC have about FMT. In addition, given the importance of shared decision making in this potential treatment for IBD we sought to determine patient donor and delivery method preferences.

MATERIALS AND METHODS

Subjects

Participants were recruited from the adult outpatient clinics at the University of Chicago IBD Center between July and November 2011. All patients with UC ≥ 18 years of age were eligible. Subjects who do not speak English or were unable to read/understand the informed consent were excluded. Those who agreed to participate were entered in a random drawing for a $25 gift certificate. Participants were asked to complete the written survey while in clinic before or after seeing their gastroenterologist.

Survey Instrument

The survey instrument was developed based on key findings from our focus group study, and included demographic information and a brief description of FMT using lay terminology, followed by 38 questions about FMT, disease activity, clinical effectiveness and satisfaction with current treatments (see Appendix 1 for full survey). Question formats included multiple-choice, rank order questions, and write-in a short answer. The survey was

piloted by 7 healthy adult volunteers for readability, clarity, and literacy level; modifications in the language and sequence of questions were made based on their feedback to develop the final instrument.

Ethics

This study was approved by the University of Chicago Institutional Review Board (IRB) and all subjects provided written informed consent.

Data Analysis

Study data was entered into Research Electronic Data Capture (REDCap) tools hosted at the University of Chicago.[26] REDCap was used to manage study data and perform descriptive analysis. Contingency squares using two-tailed Fisher's exact test were calculated using the GraphPad QuickCalcs Web site: http://graphpad.com/quickcalcs/contingency1.cfm (accessed August 2012).

RESULTS

100 patients were invited to participate and 95 enrolled and completed the written survey with a 95% response rate for the questions. Subjects were age 19-80 years old (yrs) (median 39 yrs) and 53% female. The median age of symptom onset was 46.5 yrs (range 18-70 yrs), the median age at diagnosis was 40 yrs (range 14-78 yrs) and the median duration of UC in years was 7 (range 0-40 yrs). Self-reported disease severity at the time of the survey was: remission in 59%, mild-moderately active disease in 36%, and severely active disease in 5% (Table 1). Over half of the participants (57%) reported a history of being hospitalized for their UC. Regarding current medical management of their UC, 44% and 49% reported it as excellent or good/satisfactory, respectively. Only 7% reported poor to very poor management of symptoms.

Subjects' self-reported current medications included aminosalicylates, corticosteroids, immunosupressants, anti-tumor necrosis factor alpha (TNFα), and antibiotics. Almost a third of subjects also reported using a complementary or alternative therapy that included special diets, vitamins or supplements, fish oils, relaxation techniques, acupuncture, biofeedback, or other. See Table 1 for complete demographic information.

Regardless of disease activity, almost half (46%) of the subjects were willing to undergo FMT as a treatment for UC, 43% were unsure, and 11% stated that they were unwilling to undergo FMT. There was an association between disease severity and willingness to undergo FMT but even patients in remission were willing to undergo FMT (36%) (Figure 1). Hospitalized patients were more likely to be willing to undergo FMT then subjects who had not been hospitalized for their UC, 55% versus 34% ($p=0.035$). Participants reported effectiveness (38%), safety (26%), failure of conventional medications (21%), and physician recommendation (12%) as the most important factors in considering FMT (Figure 2A).

Primary concerns about FMT included adequate screening of fecal matter for infections (41%), cleanliness (24%), and potential to worsen UC (18%). Twenty-one percent reported no specific concerns about FMT (Figure 2B). Subjects ranked safety of the delivery method (6%) and the potential of FMT to interfere with current treatment (5%) as the least important concerns.

For donor selection, 46% of participants preferred whomever their doctor recommended and 46% preferred to have a family member/spouse as their fecal donor (Figure 3). The preferred method of FMT delivery was by a single sedated colonoscopy (77%) or enema daily for 5 days (20%); single nasogastric tube delivery was preferred only by 3%.

There was no association between medication history and willingness to consider FMT. There was no association between quality of life or the use of complementary/alternative medicine (CAM) and willingness to consider FMT.

DISCUSSION

This is the first quantitative study to explore FMT preferences and concerns. We found the vast majority of patients with ulcerative colitis are interested in and willing to consider FMT, and that this interest was quite strong despite satisfactory to excellent disease control with their current conventional medications and despite the absence of safety or efficacy data for this novel treatment approach.

The findings in this study are striking and reflect what we suspected in our pre-testing hypothesis based on the response to our prior qualitative study and based on the outpouring of unsolicited interest in this topic on the internet and via electronic mail communication to our investigators (SAK and DTR). The profound interest in this approach reflects the perception that FMT is a "natural"' treatment for UC, and resonates with patients who struggle to understand how they developed colitis. A simple (but theoretical) causative explanation that there is dysbiosis as a cause and repopulation with FMT is a treatment or cure makes sense to them. It also reflects, at least in part, patients' dissatisfaction with the absence of a medical cure, and, for many of these patients, their dissatisfaction with chronic medical therapy for a variety of reasons. The stigma or "yuck" factor associated with FMT did not impact patient interest in this therapy.

Disease severity was associated with interest in FMT with 100% of patients with severe UC expressing an interest in FMT, though this was not statistically significant compared to interest in patients with milder disease. However, the association between disease severity and interest in FMT is further supported by the fact that patients who had been hospitalized for UC were significantly more likely to be willing to undergo interested in FMT, 55% versus 34% ($p=0.035$).

We expected that subjects taking medications with an unfavorable side effect profile, such as corticosteroids, or medications with increased risk of serious adverse outcomes such as immunomodulators and biologic therapies would be more interested in FMT. Interestingly, current and prior medication use including corticosteroids, immunomodulators, and biologic therapies did not predict interest in FMT. We also hypothesized that subjects who reported CAM use would be more like to consider this alternative therapy, however, in this study, use of CAM did not correlate with interest in FMT.

Findings from our focus group study suggested that patients were eager to receive FMT because it was more "natural" compared to conventional therapies,[21] our current study population did not report FMT being more "natural" as a primary reason for considering it. In this follow-up study safety and efficacy, were the two most important factors in considering FMT, followed by the need for surgery and physician recommendation. Adequate screening for infections was the most commonly cited concern about FMT. The second most important concern cited was cleanliness/hygiene of the fecal matter; however, we were surprised to find an equal number of subjects reported no specific concerns about FMT.

Currently there is insufficient evidence to identify and match FMT donors and recipients based on their microbiological profiles and as such shared decision making plays a central role in donor identification and selection. Strikingly we found that patients were equally willing to accept a physician recommended FMT donor or a family member/spouse as an FMT donor. This has important implications for FMT protocol development.

One limitation of this study is the fact the subjects were recruited from a single tertiary care center and therefore the results may not be generalizable. Another limitation of the study was the sample size which included less than 100 subjects. However, the aim of our study was to characterize important social and ethical concerns about FMT and as such increasing the sample size or the number of centers would not necessarily have altered these findings. In addition, these data confirm our focus group study findings that patients with UC are very interested in FMT and eager for it to become available.[21]

Finally, it is quite important to acknowledge that the remarkable success of FMT for CDI does not yet translate to meaningful information for the UC population. Obviously, *Clostridium difficile* infection and ulcerative colitis are different diseases, and the implication (by patients or physicians) that efficacy or safety information may be applied from one condition to the other is a mistake, and demands careful explanation and study.

In summary, a majority of these referral center patients with UC are interested in or willing to consider FMT, despite reporting satisfactory to excellent disease control with their current medications. Prior hospitalization for UC and disease severity appear to predict interest in FMT though even patients in remission were interested in FMT. Proof of safety and effectiveness, as well as failure of other medical therapies are key issues in considering FMT. Patients are equally willing to accept family member donors as doctor-recommended ones, and there is a clear preference for colonoscopic delivery. The strong interest in this as-yet unproven therapy for IBD warrants attention to protection of these vulnerable individuals, and is a pressing priority for more clinical research and education.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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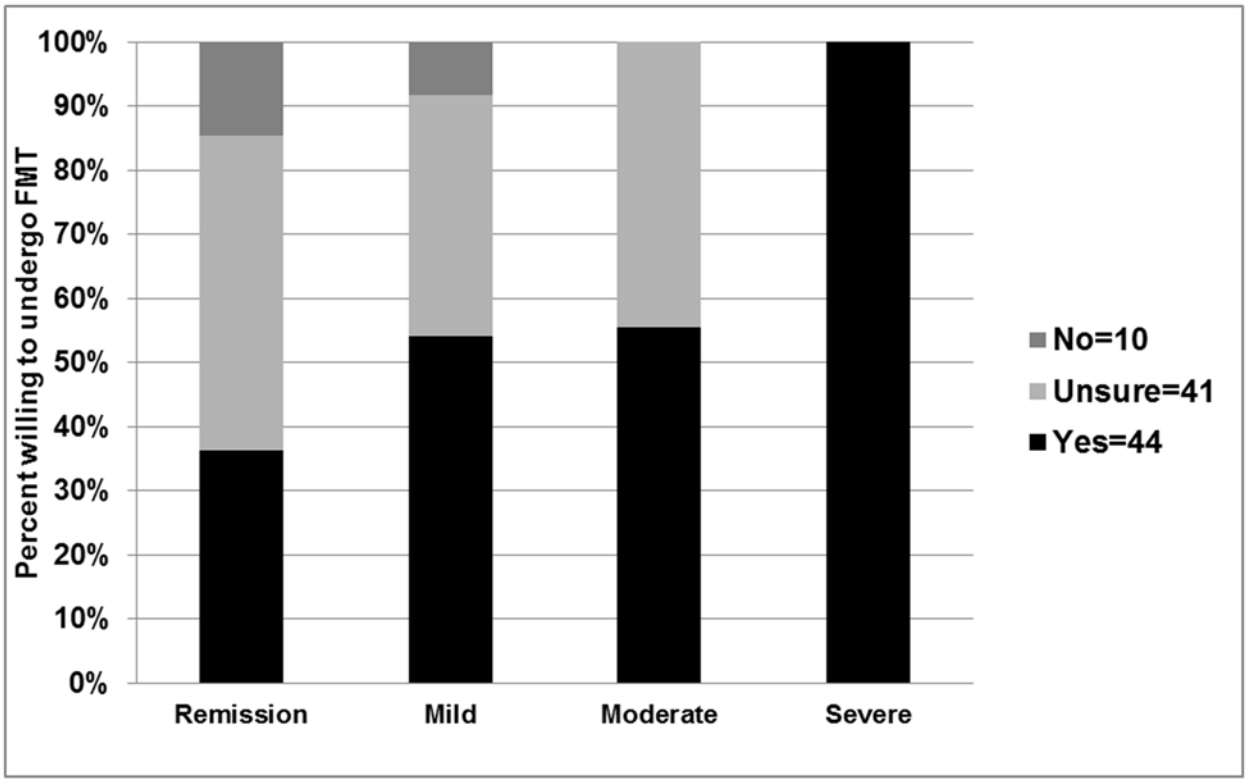
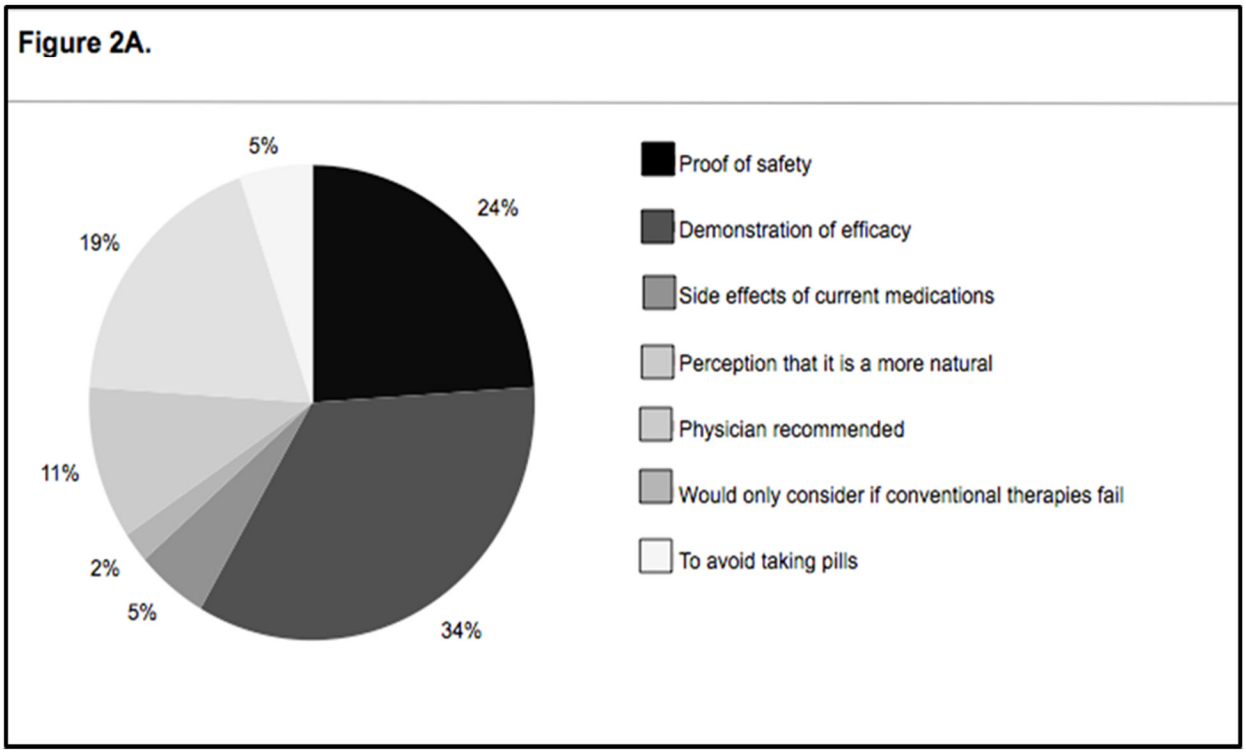


Figure 1.
Participants' self-reported disease severity and willingness to undergo FMT. Patients with more severe disease were more willing to undergo FMT but even patients with mild disease were willing to undergo FMT.



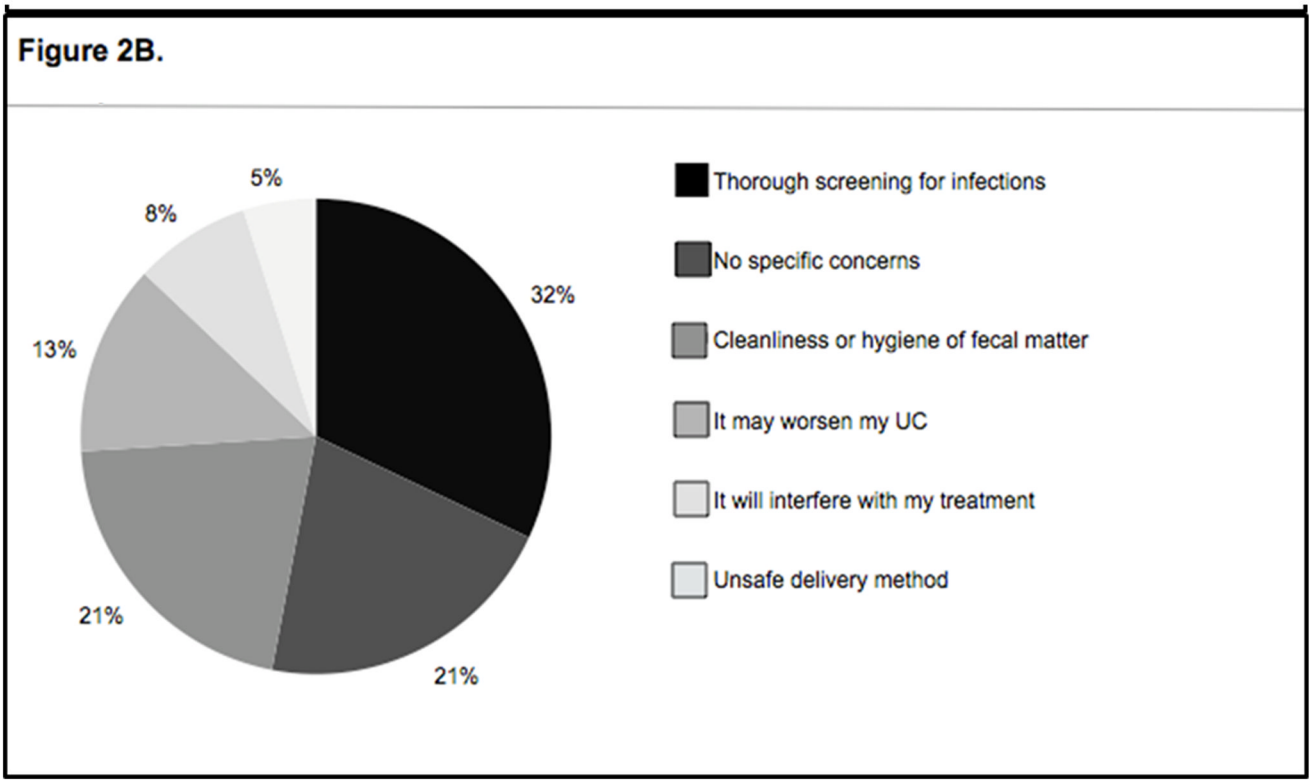


Figure 2.

2A) Major factors influencing patient decision making in FMT and **2B)** Patient-identified concerns about FMT.

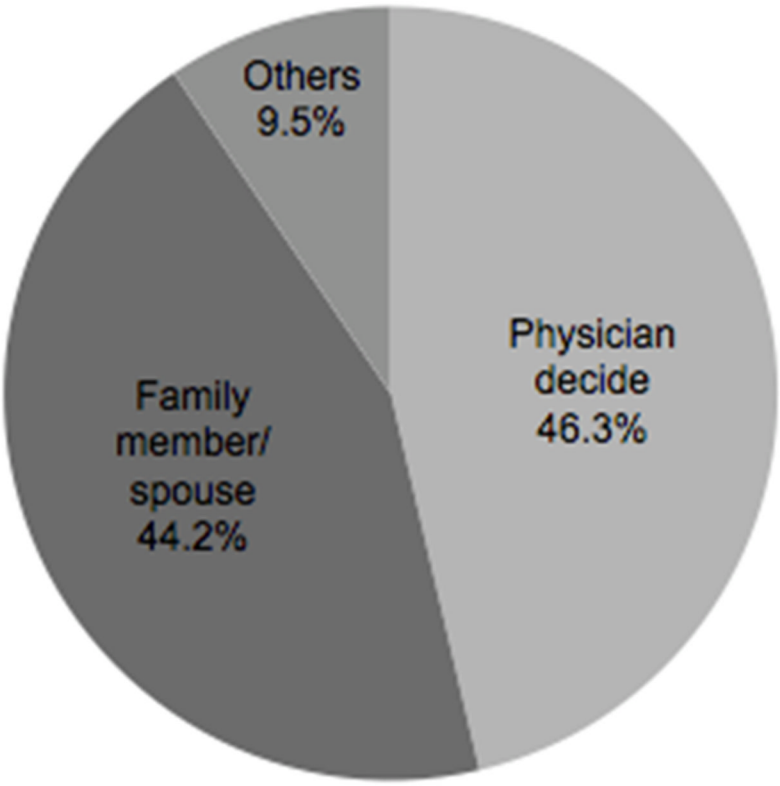


Figure 3.
FMT donor preferences. Participants were equally willing to have their physician select the donor as they were to have a family member or spouse serve as their donor.

Table 1

Demographics, n=95

Age (median years, range)	39 (18-80)
Duration of UC (median years, range)	7 (0-40)
Age of diagnosis (median years, range)	40 (14-78)
History of hospitalization for UC (%)	54 (56.8)
Gender	
Male	45 (47.4)
Female	50 (52.6)
Education	
Graduated high school or equivalent	4 (4.3)
Some college	15 (16.0)
Graduated college	37 (39.4)
Graduate level education	35 (37.2)
Other	3 (3.2)
Ethnicity	
Caucasian	75 (78.9)
African-American	8 (8.4)
Asian or Pacific-Islander	6 (6.3)
Hispanic	5 (5.3)
Native American	0 (0)
Other	1 (1.1)
Marital status	
Single	31 (32.6)
Significant other	5 (5.3)
Married	54 (56.8)
Divorced	5 (5.3)
Widowed	0 (0)
Household income	
Less than $18,400	7 (8)
$18,400 - $50,000	9 (10.2)
$50,000 - $100,000	20 (22.7)
More than $100,000	31 (35.2)
Do not wish to disclose	21 (23.9)
Self-reported disease severity	
Remission	55 (59.1)
Mildly active	24 (25.8)
Moderately active	9 (9.7)
Severely active	5 (5.4)
Effectiveness of current medications at symptom control (self-reported)	
Excellent	39 (43.8)
Good	25 (28.1)
Fair	19 (21.3)
Poor	5 (5.6)
Very poor	1 (1.1)