Development of an Internet-based Cohort of Patients with Inflammatory Bowel Diseases (CCFA Partners): Methodology and Initial Results

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Background: The widespread use of the Internet allows for unique research opportunities. We aimed to develop and follow an Internet-based cohort (e-cohort) of patients with self-reported inflammatory bowel diseases (IBD) over time.

Methods: We established an e-cohort of adults with IBD (CCFA Partners) by recruiting through Crohn's and Colitis Foundation of America (CCFA) email rosters, CCFA Website promotion, social media, and other publicity mechanisms. The baseline survey included modules on disease course and activity, diet and exercise, and patient-reported outcomes (PROs). Baseline characteristics of the cohort are summarized using descriptive statistics.

Results: A total of 7819 adults with IBD joined CCFA Partners through August, 2011. The median age was 42 years (interquartile range [IQR] 30–54), 5074 (72.3%) were female. A total of 4933 (63.1%) had Crohn's disease (CD), 2675 (34.2%) had ulcerative colitis (UC), and 211 (2.7%) had IBD unspecified. For CD, the mean short CD Activity Index (CDAI) was 151.9 (standard deviation [SD] 106.4), with 2274 (59.4%) in remission. For UC, the mean simple clinical colitis activity index (SCCAI) was 3.6 (SD 2.8), with 937 (42.9%) in remission. The mean short IBD questionnaire (SIBDQ) score was 48.7 (SD 11.8). SIBDQ was inversely correlated with disease activity ($P < 0.01$). The mean Morisky medication adherence score (MMAS) was 4.93 (SD 1.9). MMAS scores were inversely correlated with disease activity ($P < 0.01$).

Conclusions: CCFA Partners is a novel e-cohort. Enrollment is ongoing, with surveys twice yearly. CCFA Partners represents a unique resource to study PROs and changes in disease management over time.

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Key Words: inflammatory bowel disease, patient reported outcomes, quality of life, Internet, cohort, disease activity

Crohn's disease (CD) and ulcerative colitis (UC) are chronic, relapsing inflammatory disorders that exact a considerable personal and economic burden on affected individuals. Despite extensive research, the etiology remains largely unknown. There is considerable variation in healthcare utilization by age, gender, geographic region, and insurance type that is poorly understood.[1–3]

Most longitudinal cohort studies of CD and UC have relied on administrative data or retrospective review of clinical records. Such studies often lack important clinical data that can only be collected directly from the patient. Examples include detailed smoking history, use of over-the-counter medications, dietary patterns, exercise, and quality of life (QoL). Other important patient-reported outcomes (PROs) such as depression, well-being, sleep, and fatigue are often lacking. Traditionally, prospective cohort studies have been extraordinarily expensive to conduct due to the need for large personnel resources to recruit and follow patients over time. The availability and widespread use of the Internet creates an unparalleled opportunity to create an online community of inflammatory bowel disease (IBD) patients that could be used for education programs and research at dramatically reduced costs.

Here we describe the development of CCFA Partners, a longitudinal Internet-based cohort (e-cohort) of IBD patients established to 1) facilitate studies of the natural history of disease in a large, diverse population; 2) serve as

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a platform for additional studies of disease mechanisms, treatments, and outcomes; and 3) potentially influence disease management through educational interventions focusing on quality improvement and prevention.

MATERIALS AND METHODS

We first developed a survey including important information on various patient-reported components of living with IBD that we piloted in 1000 individuals on the Crohn's and Colitis Foundation of America (CCFA) email roster to determine feasibility of recruitment for an Internet-based cohort. We then expanded the invitation to include all individuals on CCFA rosters, and employed additional means of recruitment including social media and print advertisements, a link from the CCFA Website, word of mouth from other participants, and promotion at local CCFA chapter meetings. The email invitations to join the cohort were released in waves in June and July 2011. For those who did not join the cohort, or who did not complete a total of two modules, email reminders were sent at 2 weeks after the initial invitation and again at 3 months. Any individual could access the cohort entry portal through the Website www.ccfapartners.org or through a specific email link if they were on CCFA email rosters. How the individual joined the cohort (via email link vs. direct Website access) was also tracked. Only those who met inclusion criteria were able to join the cohort.

Eligibility and Inclusion Criteria

During the first recruitment wave we excluded individuals under age 18 and those who did not have self-reported IBD (CD, UC, or indeterminate colitis). Individuals also had to have Internet access to join the e-cohort and complete the surveys. There were no other exclusion criteria for participation.

Baseline Survey

The complete CCFA Partners baseline survey is available online at the CCFA Partners website: www.ccfapartners.org, under the ''For Researchers'' tab. The survey was available only in English. The baseline survey instrument featured three modules that each targeted different aspects of living with IBD. All participants received Module 1. Participants were then randomized to receive either Module 2 or Module 3 in equal proportions. After completion of their second module, all patients were given the opportunity to complete an optional third module (whichever module they did not receive as #2) (see Fig. 1).

Module 1

Module 1 included information on demographics, disease phenotype, prior and current medication use, health-related behaviors, family history of IBD, extraintestinal manifestations of IBD, disease activity, and prevention. Validated disease activity measurements were used, including the Simple Clinical Colitis Activity Index (SCCAI)[4] for UC and the short Crohn's Disease Activity Index (sCDAI) for CD.[5] The SCCAI has been validated in a longitudinal cohort study of patients

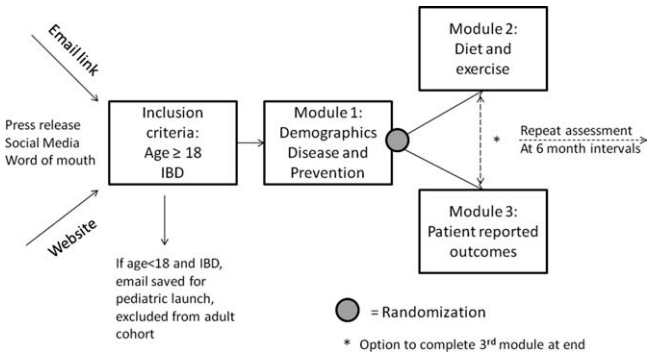

FIGURE 1. CCFA Partners study flow.

with UC undergoing colonoscopy. It was found to have excellent psychometric validity and moderate to good performance validity.[6] A SCCAI score of 5 or more defines a relapse of UC.[7] A SCCAI score of $\leq$2 is associated with UC remission.[8] The SCCAI has also been validated with self-report.[7] The validity, reliability, and responsiveness of the sCDAI has been shown to be comparable to the original CDAI using data from nine clinical trials of budesonide. The sCDAI accounted for 82.4% of the variance of the original CDAI in this validation study.[5] Also within this module, patients reported prevention activities such as vaccine utilization, calcium and vitamin D supplementation for bone health, skin testing for tuberculosis (TB), Pap smears for women, skin examinations and sunscreen use, and colonoscopy surveillance in those with colonic disease of greater than 10 years duration.

Module 2

Module 2 consisted of questions on diet and exercise. This module used a National Cancer Institute (NCI) food frequency questionnaire developed in 2010 and a separate food avoidance questionnaire developed specifically for the IBD population. The dietary results will be reported separately. Exercise was assessed via the validated Godin Leisure Time Exercise Index.[9,10] The Godin Index contains questions on frequency of strenuous, moderate, and mild exercise, with one question on how often the individual "works up a sweat." Increasing points are awarded based on levels of strenuous exercise. The Godin Index has been validated with self-report.[11]

Module 3

Module 3 consisted of patient-reported outcomes (PROs). PRO is the term used to describe health data provided by the patient through a system of reporting. A PRO consists of a patient's feedback on their feelings or how they function as they deal with chronic diseases or conditions. We measured three separate PRO scales on medication adherence, QoL, and other physical and emotional domains. We collected self-reported medication adherence using the Morisky Medication Adherence Scale (MMAS). The MMAS consists of eight questions, each worth 1 point. Each question focuses on a different aspect of adherence, such as forgetfulness and actual self-

reported missing of doses over various time periods (i.e. yesterday, or over the past 2 weeks). The MMAS is categorized as 1–5 (low), 6–7 (medium), and 8 (high) adherence.[12] This scale has been validated in the IBD population.[13] We also collected data from an IBD-specific QoL instrument: the validated Short IBD Questionnaire (SIBDQ).[14] This scale has been previously shown to correlate with disease activity in the IBD population. The scores for the SIBDQ range from 10–70. A score of 10 correlates with poor health-related quality of life (HRQOL) and a score of 70 correlates with optimum HRQOL. Finally, we asked questions on the specific domains of fatigue, sleep, physical function, and emotional distress. These questions were taken from the Patient Reported Outcome Measurement Information System (PROMIS). PROMIS is a system of highly reliable, precise measures of patient-reported health status for physical, mental, and social well-being (http://www.nihpromis.org/). The questions have been validated in the general population and population-based norms are available.[15–17] The PROMIS results will be reported separately.

Data Collection and Management

The data were collected entirely in a Web-based format, allowing for real-time implementation of range and consistency checks. Therefore, missing data were minimized at point of entry. The data management system was implemented using a suite of reusable metadata-driven tools that facilitated rapid development of the protocol and good computing practice. Some examples of these tools include questionnaire version change auditing, data change auditing, dynamic form generation, and data validation. The program provided important validation including single-variable range checks and cross-variable and cross-form logic checks that identified logical inconsistencies in the data. For example, an individual would be prompted if they reported IBD duration as longer than their current age. The user interfaces for the Web-based system were generated dynamically from metadata and programmed within the central database. The Web forms were accessible from any machine running a modern Internet browser with an active connection to the Internet; no special software was required.

Statistical Analysis

Descriptive statistics were used to characterize the population, including proportions and 95% confidence intervals, medians and interquartile ranges, means and standard deviations (SD) as appropriate. Bivariate statistics were used to compare outcomes by CD versus UC when applicable, including Pearson's chi-square test statistic, Fisher's exact, Wilcoxon rank sum, and Student's *t*-test as appropriate. Spearman's correlation was used to evaluate the association between scales of ordinal data. STATA v. 10.0 (College Station, TX) was used for all analyses and $P < 0.05$ was considered statistically significant. The study protocol was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill.

RESULTS

A total of 7819 individuals with self-reported IBD joined CCFA Partners through August 19, 2011. Of these, the majority 7609 (97.3%) entered the survey through a direct email link sent to the CCFA email roster and 210 (2.7%) entered independently via the CCFA Partners Website. Among those who entered independently, reported mechanisms or recruitment included: an Internet search (10), CCFA Website advertisement (92), their physician (13), CCFA newsletter (40), CCFA social media outlet (27), a friend (7), a family member (8), or a CCFA meeting or event (3). Cohort members included individuals from over 250 nations and territories throughout the world; however, the vast majority (96.4) were from within the United States. The median age within the cohort was 42 years (interquartile range [IQR] 30–54). The majority of the population were female, 5074 (72.3%). A total of 4933 (63.1%) had CD, 2675 (34.2%) had UC, and 211 (2.7%) had indeterminate colitis (IC) / IBD unspecified. The characteristics of the population are shown in Table 1 by CD or UC status. While age was similar for CD and UC populations, those with CD had longer duration of disease.

Medication Use

The most common class of medications used in the cohort was the 5-aminosalicylate (5-ASA) class. A total of 1465 (34.3%) of the CD patients were currently using oral 5-ASA medications, while 1421 (60.4%) of the UC population were currently using oral 5-ASA medications. The cohort also demonstrated considerable use of immunosuppressant and biologic medications for both CD and UC. Approximately a quarter of patients with CD and UC were currently on thiopurines. Forty percent of CD patients and 17% of UC patients reported current biologic use (Table 1).

Distribution of Involvement and Extraintestinal Manifestations

The distribution of involvement by CD is shown in Table 2. The majority of individuals had colonic and/or ileal involvement, although upper tract involvement was also represented in the cohort in up to 24% of individuals. Painful joints were the most common extraintestinal manifestation among the CD population. Table 3 shows disease location and extraintestinal manifestations among the UC patients. A total of 34% of those with UC reported pancolitis. Again, painful joints were the most common extraintestinal manifestation.

Disease Activity

When the population was categorized into remission versus active disease based on validated cutoffs for the SCCAI and the sCDAI, slightly less than half of the CD

TABLE 1. Characteristics of the Population by Crohn's Disease vs. Ulcerative Colitis Within CCFA Partners Cohort

	Crohn's Disease (n=4933)		Ulcerative Colitis (n=2675)	
Characteristic	n	%, Median (IQR)	n	%, Median (IQR)
Age	4389	42 (30-54)	2411	42 (31-54)
Age at IBD diagnosis	4321	24 (18-34)	2373	28 (21-40)
Disease duration of IBD (yrs)	4300	12 (6-24)	2357	9 (4-17)
Gender (% female)	3195	72.7	1739	71.7
Heath care visits in prior year				
Primary care physician (% yes)	1885	71.6	1140	73.6
Gastroenterologist (% yes)	3863	90.3	2017	85.1
Ever smoking (% yes)	1720	39.5	881	36.8
Current smoking	419	9.7	104	4.4
Prior bowel surgery	2242	53.0	392	16.6
Current ostomy	366	8.8	81	3.5
Current medications				
5-ASA (oral)	1465	34.3	1421	60.4
5-ASA (rectal)	108	2.6	347	15.0
Prednisone	404	9.5	253	10.8
Entocort (budesonide)	268	6.3	39	1.7
Ciprofloxacin	123	2.9	52	2.3
Metronidazole	131	3.1	34	1.5
Thiopurine (6-MP/azathioprine)	1071	25.7	465	20.4
Methotrexate	179	4.3	37	1.6
Cyclosporine	22	0.5	14	0.6
Biologic (any)	1648	40.3	373	16.9
Adalimumab	725	17.7	91	4.1
Infliximab	703	17.1	282	12.6
Certolizumab pegol	240	5.9	21	0.9
Natalizumab	32	0.8	12	0.6
Medication in a clinical trial	48	1.2	27	1.2

population was in remission, and slightly greater than half of the UC population was in remission. These differences in remission rates between CD and UC are shown in Table 4. Within the CD population, the mean short CD activity index (CDAI) was 151.9 (SD 106.4). Within the UC population, the mean SCCAI was 3.6 (SD 2.8). We also asked patients to self-report their own level of disease activity in a separate question. For those with CD, 1064 (25.4%) reported remission, 1478 (35.3%) reported minimal activity, 858 (20.5%) reported mild activity, 573 (13.7%) reported moderate activity, and 211 (5.0%) reported severe activity. For UC, 821 (35.2%) reported remission, 726 (31.1%) reported minimal activity, 495 (17.4%) reported mild activity, 273 (11.7%) reported moderate activity, and 109 (4.7%) reported severe activity. When the validated indices, SCDAI and SCCAI, were compared with the individual question on grading of disease activity, there was significant correlation for both CD and UC. For CD, the Spearman's correlation was 0.77, $P < 0.001$. For UC, the Spearman's correlation was 0.69, $P < 0.001$.

Prevention

The status of prevention within both the CD and UC populations is shown in Table 5. Less than two-thirds of the population received an influenza vaccine over the prior year and approximately one-third had ever received a pneumococcal vaccination. We also investigated reasons for lack of influenza vaccine in the IBD population as a whole. These reasons included: personal refusal 1044 (45.7%), never offered the vaccine 267 (11.7%), other 602 (26.4%), allergy to eggs 78 (3.4%), and don't know 292 (12.8%). With regard to bone health, among the population of prior or current corticosteroid users ($n = 5841$), approximately half of individuals with IBD had ever had a dual-energy x-ray absorptiometry (DEXA) scan test ($n = 3007$, 55.1%). In this population of prior or current corticosteroid users, a

TABLE 2. Disease Location (Ever Involvement) and Extraintestinal Manifestations in Patients with Crohn's Disease Within CCFA Partners Cohort

Characteristic	*n*	Percent
Disease location		
Esophagus	526	12.6
Stomach	720	17.3
Duodenum	1006	24.2
Jejunum	945	22.8
Ileum	2872	68.0
Terminal ileum	2968	70.8
Colon	2577	61.7
Rectum	1675	40.6
Extraintestinal manifestations		
Painful joints	2170	52.3
Erythema nodosm	273	6.6
Pyoderma gangrenosm	99	2.4
Aphthous ulcerations	437	10.6
Eye inflammation	432	10.4
Primary sclerosing cholangitis	37	0.9

total of 53.6% were on calcium, 60.7% vitamin D supplementation, and 7.4% on a bisphosphonate. We also assessed skin examination among those on current or prior immunosuppression (including immunomodulators or biologic medications). In the past 3 years, less than half of these individuals had a skin examination by a dermatologist. We additionally asked about skin protective measures in those on immunosuppression, such as sunscreen use. A total of 661 (16.0%) reported always wearing sunscreen, while 1529 (37.1%) only wore sunscreen most of the time, 1496 (36.3%) sometimes, and 438 (10.6%) never. Among those with current or prior biologic medication use the majority reported a prior screening test for TB (88.3%). In the population of patients with prior colonic inflammation and disease duration >10 years, nearly 80% of both CD and UC patients reported a colonoscopy within the past 2 years. In those with a history of primary sclerosing cholangitis (PSC) and IBD, without prior colectomy, yearly surveillance colonoscopy is recommended. In this group, 69.0% had a colonoscopy within the past year.

TABLE 3. Disease Location (Ever Involvement) and Extraintestinal Manifestations in Patients with Ulcerative Colitis Within CCFA Partners Cohort

Characteristic	*n*	Percent
Disease location		
Rectum ("proctitis")	125	5.0
Rectum and sigmoid ("proctosigmoiditis")	337	13.4
Rectum/sigmoid/descending ("left")	635	25.2
Rectum/sigmoid/descending/transverse ("extensive")	171	6.8
Entire colon ("pancolitis")	857	34.0
Don't know	394	15.6
Extraintestinal manifestations		
Painful joints	1132	47.2
Erythema nodosm	95	4.0
Pyoderma gangrenosm	35	1.5
Aphthous ulcerations	212	8.9
Eye inflammation	192	8.0
Primary sclerosing cholangitis	42	1.8

TABLE 4. Disease Activity in Crohn's Disease and Ulcerative Colitis Within CCFA Partners Cohort

	Crohn's Disease		Ulcerative Colitis		
Disease Activity[a]	*n*	%	*n*	%	*P* value[b]
Remission	937	42.9	2274	59.4	<0.01
Active Disease	1249	57.1	1554	40.6	

[a]Measured by short CDAI for CD and simple clinical colitis activity index (SCCAI) for UC, scores of <150 and ≤2 associated with remission, respectively, patients with ostomy excluded.
[b]Pearson's chi-square test statistic.

Exercise

The overall median total energy score (ENERT) score on the Godin scale in the IBD population was 26 (IQR 12–25). There was a significantly lower median score of 25 (IQR 10–44) in those with CD as compared with those with UC 29.5 (IQR 15–49), $P < 0.01$.

Medication Adherence

The MMAS is categorized as 1–5 (low), 6–7 (medium), and 8 (high). Within the overall IBD population a total of 2149 (52.8%) had low adherence, 1842 (45.3%) had medium adherence, and 79 (1.9%) had high adherence on the MMAS scale. The overall mean MMAS was 4.93 (SD 1.9). When evaluated by IBD subtype, there was no difference in adherence by CD or UC status (4.91 [SD 2.0] for CD vs. 4.98 [SD 1.9] for UC, $P = 0.30$). We then evaluated medication adherence in quartiles of disease activity for both CD and UC populations. For both CD and UC, medication adherence rates were better in the lowest quartile of disease activity, and worsened significantly with higher levels of disease activity ($P < 0.01$ for both CD and UC; Fig. 2). Additional analyses evaluating categories of medication adherence by the clinically significant cutpoint of active disease as compared with remission (defined as

TABLE 5. Status of Prevention in Patients with IBD, Overall, and by Crohn's Disease vs. Ulcerative Colitis Within CCFA Partners Cohort

	IBD Overall		CD		UC		
Preventive Measure	*n*	% yes	*n*	% yes	*n*	% yes	*P* value[a]
Vaccinations							
Pneumococcal[b]	2521	37.8	1695	40.6	757	32.7	<0.01
Influenza[c]	4244	63.9	2725	66.1	1399	60.9	<0.01
DEXA[d]	3007	55.1	2071	59.4	867	47.3	
Pap smear[e]	3926	94.0	2466	94.2	1351	93.8	0.60
Skin exam[f]	1623	39.6	1170	39.7	423	39.5	0.91
TB skin test[g]	2628	88.3	2052	89.2	520	85.5	0.02
Colonoscopy[h]							
Colonic CD	—	—	1017	79.8	—	—	NA
UC	—	—	—	—	739	79.0	NA
PSC	20	69.0	—	—	—	—	NA

[a]Pearson's chi square comparing CD to UC.
[b]Ever.
[c]Within the past year.
[d]Ever, among those with prior or current corticosteroid use.
[e]Among women, within the past 3 years.
[f]Within the past 3 years, among those on current or prior immunosuppression.
[g]Ever, among those on current or prior biologic anti-TNF.
[h]Within past 2 years among those with intact colon, prior colonic inflammation, disease duration of >10 years, or within past 1 year with intact colon and ever diagnosis of PSC.
NA, not applicable.

sCDAI <150 for CD and SCCAI ≤2 for UC) also showed that active disease was associated with significantly lower medication adherence for CD and UC ($P < 0.01$ and $P = 0.02$, respectively).

Quality of Life

The SIBDQ ranges from 10 (poor) to 70 (optimum). In the overall IBD population, the median SIBDQ score was 50 (IQR 41-58). For those with CD, the median SIBDQ score was 50 (IQR 40–58) and for those with UC, the median score was 52 (42–59), $P < 0.01$. When evaluated in quartiles of disease activity, higher QoL was inversely correlated with disease activity ($P < 0.01$ for both CD and UC; Fig. 3). When QoL was compared within quartiles of disease duration, the SIBDQ significantly increased with increasing duration of disease (data now shown). Using logistic regression to control for disease activity, disease duration remained significantly associated with SIBDQ for both CD and UC (beta coefficient 0.07, 0.06 respectively, $P < 0.01$). SIBDQ in UC patients with more active disease (defined as SCCAI > median) was significantly lower than SIBDQ in UC patients status postcolectomy with pouch formation; 40.8 (SD 10.2) vs. 50.1 (SD 11.9), $P < 0.01$.

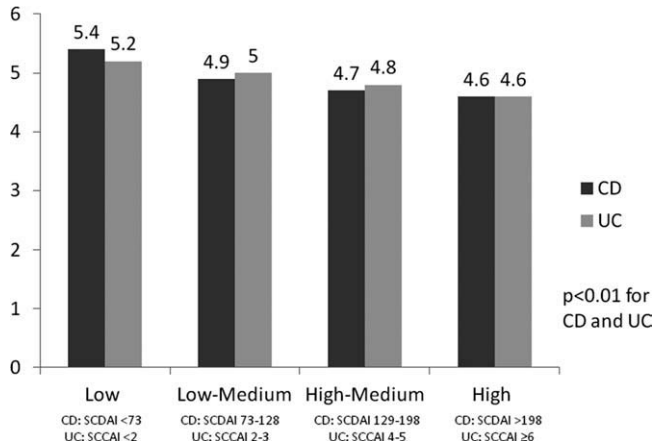

FIGURE 2. Self-reported medication adherence by levels of disease activity (in quartiles) within the CCFA Partners cohort.

DISCUSSION

We have demonstrated the feasibility of developing and recruiting an online cohort of IBD patients to study important patient-reported exposures and outcomes. Recruitment of almost 8000 participants from 250 nations over a 2-month period provides strong evidence of the interest in participation by the IBD patient community. Longitudinal follow-up of this large, diverse cohort of invested participants will facilitate studies evaluating the complex associations between health behaviors, medical treatments, and disease course measured by patient-reported outcomes.

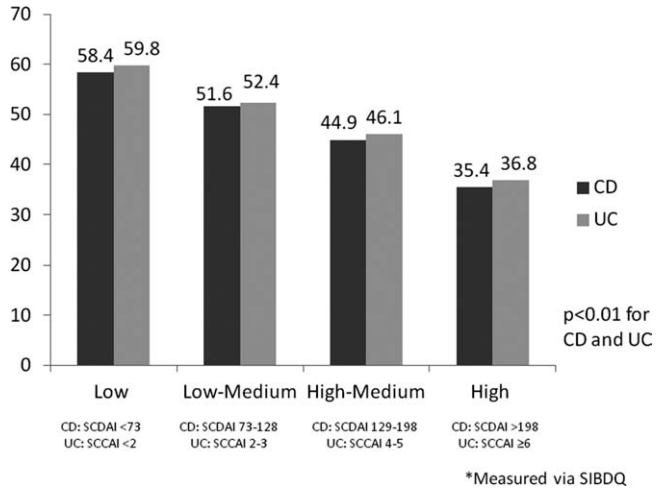

FIGURE 3. Quality of life measurements by levels of disease activity (in quartiles) within the CCFA Partners cohort.

Additionally, we also designed the CCFA Partners to be a scalable and modular platform upon which interventional studies and translational studies can be built. By maintaining the contact information of study participants, we have the ability to evaluate health behavior interventions, request biospecimens to study genetic, microbiological, and immunological factors, and combine the patient-reported data from CCFA Partners with physician-reported data from medical records, research registries, and clinical trials.

Given widespread Internet access (68.7% of U.S. households according to 2009 census[18]; 81% of IBD patients[19]), Web-based epidemiological studies offer a number of advantages over traditional print survey methods, including cost savings, efficiency in data collection and management, convenience for the participant, improvements in data quality, and a greater degree of anonymity for the participant.[20] Completion rates of surveys have been reported to be similar, regardless of Internet or print-based format.[21] Although individuals without Internet access may be different from those with access, therefore limiting the external generalizability of e-cohorts, many suggest that the bias associated with collecting information over the Web is no greater than that introduced by traditional paper methods.[21] As a result, e-cohorts such as ours have become an increasingly well-accepted study design. Examples include a military cohort with over 20 years of planned follow-up[20] and Black Women's Health study, which substituted Web-based surveys for paper surveys as an alternate means of follow-up.[22] Prior studies in IBD have utilized the Internet for various phases of follow-up within cohort studies. Wolters et al[23] used an Internet-based data acquisition tool to successfully attain follow-up information on a Western-European and Israeli multicenter 10-year study of patients with IBD. Others have used the Internet to share data acquisition tools within studies of IBD.[24] To our knowledge, we are among the first to undertake a large, prospective cohort of patients with IBD entirely via the Internet.

The strengths of this study include the large sample size, geographic diversity of the study population, the use of validated indices, and the ease of participation for individuals within the cohort. Additionally, the Web-based format allowed for enhancement of data quality through point of entry quality and range checks and electronic skip patterns.

A limitation of this e-cohort is that all data are based on participant self-reporting. We are unable to confirm the diagnosis of IBD itself, nor any of the other clinical or phenotypical aspects of disease. However, we believe that the strong focus on patient-reported exposures, health behaviors, and outcomes is an important complement to more traditional research that has relied solely on physician-reported data via retrospective chart reviews or prospective clinical registries. Additionally, it will be possible to combine the patient-reported data collected here with other data sources including medical records or data collected in other observational or interventional studies. Reassuringly, we were also able to confirm previously reported associations within this e-cohort, thus supporting the internal validity of patient-reported data. For example, Irvine et al[14] previously reported reductions in QoL scales with increased disease activity. We found this same association within our study. Prior studies have demonstrated that QoL improves for individuals with active UC after undergoing colectomy for refractory disease.[25,26] We found similar results within our e-cohort, where QoL scores were higher for individuals after colectomy than for those with more active UC (SCCAI $>$ median). We also found a strong positive correlation between patient global assessment rating of disease severity and symptom-based indices such as the sCDAI and SCCAI.

Due to methods of recruitment, interest in participating, requirement for English language, and the technology required to join our e-cohort, this sample is not necessarily representative of the IBD population as a whole. As expected, our study contains relatively few elderly participants; however, we did recruit a total of 556 over the age of 65. Additionally, over 70% of those enrolled in the cohort are female, whereas gender frequencies of CD and UC in the U.S. are more equal. Regardless of potential for enrolment bias, internal comparisons and longitudinal analyses will be valid as long as there is not differential loss to follow-up. Indeed, the selection bias in this cohort is essentially no different than in traditional cohorts such as Framingham[27] or Nurses Health Study,[28] where the value lies with continued follow-up. We have learned a great deal from the aforementioned traditional cohorts, and have the potential to similarly learn from this IBD-specific e-cohort at a fraction of the cost.

In summary, this is the first large-scale Internet-based cohort of individuals living with IBD. This cohort represents a unique method of recruiting and following individuals with IBD over time. Every 6 months, individuals will be contacted to update their status within the cohort. CCFA Partners has been designed to be both modular and scalable. In this regard, we anticipate that it will be a valuable research platform for the scientific community. We anticipate this platform will support a variety of research designs including: 1) survey-based research administered to the entire cohort, or subpopulations selected on the basis of prespecified criteria; 2) translational studies combining CCFA Partners data and with biospecimens collected from subpopulations of the cohort; 3) additional clinical studies and trials facilitated by merging CCFA Partners patient-reported data with medical record, registry, or trial data; and 4) studies of Internet-based health behavior interventions to promote adherence, preventive measures, and patient-activation. Researchers interested in utilizing the CCFA Partners cohort in future studies should register at the "for researchers" section at www.ccfapartners.org. The possibilities for future collaborative epidemiologic studies within this population are extraordinary.

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