Telemedicine for management of inflammatory bowel disease (myIBDcoach): a pragmatic, multicentre, randomised controlled trial

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Summary

Background Tight and personalised control of inflammatory bowel disease in a traditional setting is challenging because of the disease complexity, high pressure on outpatient clinics, and rising incidence. We compared the effects of self-management with a telemedicine system, which was developed for all subtypes of inflammatory bowel disease, on health-care utilisation and patient-reported quality of care versus standard care.

Methods We did this pragmatic, randomised trial in two academic and two non-academic hospitals in the Netherlands. Outpatients aged 18–75 years with inflammatory bowel disease and without an ileoanal or ileorectal pouch anastomosis, who had internet access and Dutch proficiency, were randomly assigned (1:1) to care via a telemedicine system (myIBDcoach) that monitors and registers disease activity or standard care and followed up for 12 months. Randomisation was done with a computer-generated sequence and used the minimisation method. Participants, health-care providers, and staff who assessed outcome measures were not masked to treatment allocation. Primary outcomes were the number of outpatient visits and patient-reported quality of care (assessed by visual analogue scale score 0–10). Safety endpoints were the numbers of flares, corticosteroid courses, hospital admissions, emergency visits, and surgeries. Analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT02173002.

Findings Between Sept 9, 2014, and May 18, 2015, 909 patients were randomly assigned to telemedicine (n=465) or standard care (n=444). At 12 months, the mean number of outpatient visits to the gastroenterologist or nurse was significantly lower in the telemedicine group (1·55 [SD 1·50]) than in the standard care group (2·34 [1·64]; difference –0·79 [95% CI –0·98 to –0·59]; p<0·0001), as was the mean number of hospital admissions (0·05 [0·28] *vs* 0·10 [0·43]; difference –0·05 [–0·10 to 0·00]; p=0·046). At 12 months, both groups reported high mean patient-reported quality of care scores (8·16 [1·37] in the telemedicine group *vs* 8·27 [1·28] in the standard care group; difference 0·10 [–0·13 to 0·32]; p=0·411). The mean numbers of flares, corticosteroid courses, emergency visits, and surgeries did not differ between groups.

Interpretation Telemedicine was safe and reduced outpatient visits and hospital admissions compared with standard care. This self-management tool might be useful for reorganising care of inflammatory bowel disease towards personalised and value-based health care.

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Introduction

Inflammatory bowel disease is a group of chronic, relapsing inflammatory disorders of the gut, with Crohn's disease and ulcerative colitis being the main subtypes. The clinical presentations of these diseases vary widely among individuals, as shown by variations in disease location and behaviour, relapse frequency, extra-intestinal manifestations, complications, and responses to treatment.[1]

Traditionally, management of inflammatory bowel disease consists of standard scheduled follow-up visits, with a frequency based on medical treatment, but independent of the occurrence of unpredictable flares.[2,3] Until recently, the primary treatment goal was induction and maintenance of clinical remission. However, disease management based on treating symptoms alone did not improve long-term outcomes, defined as the numbers of flares, courses of corticosteroid treatment, hospital admissions, complications, and surgeries.[4,5] Therefore, recent guidelines advocate more stringent management, involving tight control of disease activity and early intervention in patients with intestinal inflammation.[6] Other interventions address aspects of inflammatory bowel disease that might influence disease activity, such as non-adherence to treatment, unfavourable nutritional status, smoking, and psychological factors.[7–9] These interventions were shown to reduce the rates of disease relapse, health-care utilisation including hospital admission, and absence from work in subsets of patients.[7–9] This approach, however, has not been

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Research in context

Evidence before this study

We searched PubMed and MEDLINE for randomised controlled trials of telemedicine in inflammatory bowel diseases published up to Dec 20, 2016, with the terms "telemedicine", "eHealth", "mHealth", "inflammatory bowel disease", "randomised controlled trial", and "adults". This search retrieved two randomised studies, both of which were in patients with ulcerative colitis. The first trial compared self-testing of disease activity and weight measurements versus standard care in 47 patients; no differences were seen between groups in disease activity, medication adherence, and quality of life. The second trial included 333 patients with mild-to-moderate disease treated with mesalazine and found that tight disease monitoring and personalised treatment strategies resulted in an improvement of patient empowerment, quality of life, and medication adherence, and a reduction in outpatient visits and relapse duration compared with usual care. Because both studies reported data on the effects of telemedicine for a specific subgroup, no reliable conclusion could be drawn on the effectiveness of telemedicine for the entire population of patients with inflammatory bowel disease or on which subtypes of patients are likely to benefit most. This shortcoming compromises the use of telemedicine systems in real-world settings.

Added value of this study

Our study includes data on the effects of telemedicine in patients with all subtypes of inflammatory bowel disease, irrespective of phenotype, disease course, or medication use. Telemonitoring in combination with patient-tailored information, a personal care plan, easy, accessible contact with the inflammatory bowel disease nurse, and registration of patient-reported outcome measures resulted in a reduction in health-care utilisation and hospital admissions. Furthermore, the telemedicine system myIBDcoach improved medication adherence and patients reported similar scores for quality of care compared with the standard care group. These results were consistent across different patient subtypes. Our findings accord with those in other chronic relapsing-remitting diseases and suggest that tight disease monitoring and early intervention in case of a relapse can prevent admission to hospital. Trials with a longer follow-up period are required to determine whether telemedicine can change the natural disease course of chronic diseases in the long term.

Implications of all the available evidence

Routine follow-up of patients with inflammatory bowel disease, traditionally consisting of prescheduled visits that are unlikely to correspond with its unpredictable clinical course, puts increasing pressure on outpatient clinics, compromising accessibility and quality of care. Implementation of telemedicine in inflammatory bowel disease care bridges the gap between the health-care workers' requests for tight disease monitoring and continuity of care in an overburdened outpatient setting and patients' demands for more involvement in disease management. Telemedicine is safe, highly accepted by patients and health-care workers, and can be used to reorganise care for patients with all subtypes of inflammatory bowel disease. In our clinic, myIBDcoach will be used in a value-based health-care initiative. Furthermore, patients in remission or with mild disease will be monitored and guided with telemedicine supervised by a specialised nurse to guarantee adequate access to the gastroenterologists' outpatient clinic for those patients with complex disease or in need of urgent action.

systematically implemented in routine care, because acquiring all the necessary information at the right moment for every individual patient remains a challenge. Furthermore, the heterogeneous nature of inflammatory bowel disease, combined with an absence of adequate markers for patient stratification, can lead to the underuse or overuse of resources.

Tight control of disease activity and personalised monitoring of all relevant health parameters during traditional visits put substantial pressure on patients' time and the capacity of outpatient clinics. The incidence of inflammatory bowel disease is increasing and insurance companies, governments, and patient organisations increasingly demand registration of patient-reported outcome measures, patient-reported experience measures, and quality metrics.[10–13] Therefore, reorganisation of health care for patients with inflammatory bowel disease is warranted.

Telemedicine systems, which have been used to manage chronic diseases, such as congestive heart failure and chronic obstructive pulmonary disease, have been shown to improve quality of care and could help optimise the use of available resources.[14,15] Telemedicine allows for the strict and instantaneous follow-up of health parameters and timely, personalised interventions. Moreover, these systems can provide tailored information based on each patient's needs.

At present, few telemedicine systems that can improve disease outcomes, increase patients' empowerment, and reduce health-care utilisation are available for patients with inflammatory bowel disease.[7,16–21] However, these tools were developed for patients with specific subtypes of inflammatory bowel disease, consisting of those with mild-to-moderate disease activity. Studies provide inconsistent results on the effects of these telemedicine systems on disease outcomes, compromising their use in real-world settings.

We therefore developed a telemedicine system (myIBDcoach) that monitors and registers disease activity in patients with all subtypes of inflammatory bowel disease. This system, which can be used in both academic and non-academic hospitals, also monitors other disease-related parameters, including patient-reported outcome measures and quality metrics. This

information is displayed in a manner understood by the user and his or her health-care providers. Integrated care and patient empowerment are promoted by a communication function and a wide range of web-based learning methods. A pilot study showed that integration of myIBDcoach into routine care was feasible and well accepted by patients as well as health-care providers.[22] We postulated that use of this telemedicine system in routine care could reduce health-care utilisation, while ensuring tight disease monitoring and high patient-experienced quality of care. We did a pragmatic, multicentre, randomised controlled trial to investigate the effect of care with this telemedicine system on outpatient visits, patient-reported quality of care, and disease outcomes, and compared these effects with those of standard care.

Methods

Study design and participants

This pragmatic randomised trial was done at four hospitals in the Netherlands: two academic hospitals (Maastricht University Medical Centre and Leiden University Medical Centre), and two large, non-academic, regional hospitals (Zuyderland Medical Centre, Sittard, and St Antonius Hospital, Nieuwegein). Each participating hospital serves 1500–2000 patients with inflammatory bowel disease, had one or two dedicated nurses or nurse specialists, and had an e-mail and telephone consultation structure for patients with inflammatory bowel disease to contact the hospital. Furthermore, each hospital provided patients with the opportunity to consult by telephone with a nurse (at least) three times per week at fixed timepoints. Patients were enrolled at the outpatient clinic of the four participating hospitals. All consecutive patients between 18 and 75 years of age, fulfilling the international diagnostic criteria for inflammatory bowel disease,[23] were eligible for inclusion. Exclusion criteria were an inability to read or understand the informed consent form, and lack of internet access by computer, tablet, or smartphone. Additionally, patients with a hospital admission within 2 weeks before inclusion were excluded for ethical reasons, because these patients were deemed unable to make an informed decision for participation. Patients with an ileoanal pouch or ileorectal anastomosis were also excluded. The study was approved by the medical research ethics committee of the Maastricht University Medical Centre. This approval was applicable to all participating centres. The study protocol is available online in Dutch.

Randomisation and masking

After signing the informed consent form, patients were randomly assigned (1:1) to care via the telemedicine system (intervention) or standard care (control). Randomisation was done with ALEA Screening and Enrolment Application Software using the minimisation method, stratified for medical centre, subtypes of inflammatory bowel disease (Crohn's disease or ulcerative colitis), and treatment (no medication or mesalazine; immunosuppressive drugs; or biological therapy). Participants, health-care providers, and staff who assessed outcome measures were not masked to treatment allocation.

Procedures

The details of the telemedicine system myIBDcoach have been described elsewhere.[22] MyIBDcoach is a secured webpage with an HTML application for tablet or smartphone (figure 1). The system includes monthly monitoring modules, which contain questions regarding disease activity, medication use, treatment adherence, treatment satisfaction, and side-effects, including infections. The system also includes questions on factors affecting disease (including nutritional status, smoking, stress, life events, anxiety and depression, social support, physical exercise, and self-management skills), and patient-reported outcome measures on quality of life and work productivity. In monitoring disease activity, myIBDcoach uses the newly developed Monitor IBD At Home (MIAH) questionnaire, a symptom-based patient-reported outcome measure validated relative to endoscopy. This questionnaire does not require laboratory tests or physical examination, and shows good diagnostic accuracy in screening for patients requiring further assessment of disease activity with biochemical markers, imaging, or endoscopy.[24] When the disease was in remission, defined as three consecutive low monthly MIAH scores, patients were allowed to complete the monitoring module once every 3 months. Furthermore, the system includes intensified monitoring modules (weekly in case of flare), outpatient visit modules (to prepare for an outpatient visit), e-learning modules, a personal care plan, and an administrator page used by the health-care provider (ie, gastroenterologist or nurse). When parameters recorded by the monitoring modules exceeded predefined thresholds, the safety and continuity of care were ensured by the creation of alerts (red flags) on the administrator page of each local hospital. In all participating centres, the administrator page was checked at least twice daily apart from weekend days. If an alert was received, a health-care provider on the local team contacted the patient for further assessment within two working days. Visits to the outpatient clinic were based on the nature and severity of the clinical complaints. At any time, patients were able to communicate easily with their health-care provider by sending a message to the health-care providers' administration office.

Patients assigned to the intervention group received instructions, a username, and a password for the telemedicine system. Participants used the system for 12 months and were instructed to plan at least one routine outpatient visit per year. Additional follow-up visits were scheduled on the basis of alarm symptoms recognised by the telemedicine system or at the requests of individual

For the **myIBDcoach webpage** see http://www.mijnibdcoach.nl

For the **study protocol** see https://mdl.mumc.nl/folders-onderzoek

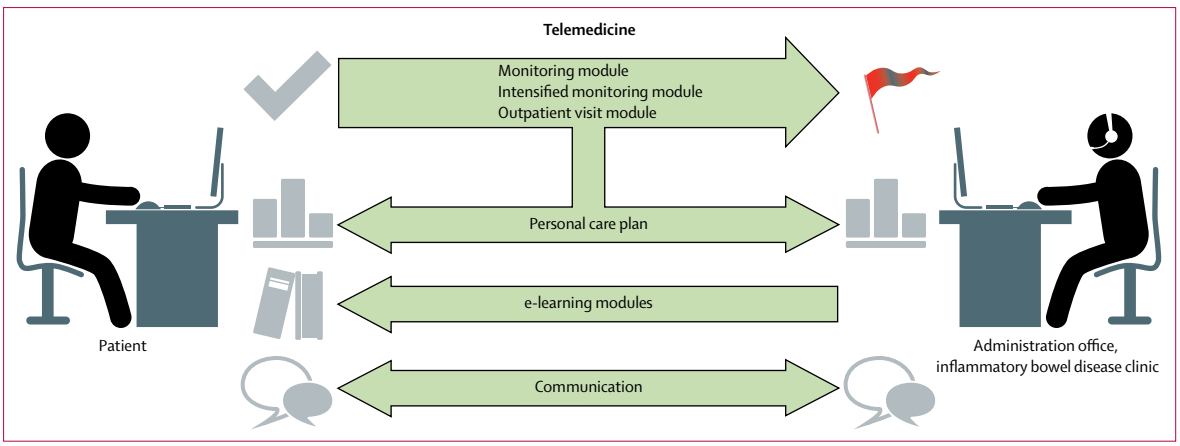

Figure 1: **Overview of the elements of the telemedicine system myIBDcoach**
(1) Modules containing different questionnaires: standard monitoring (every month, or every 3 months when the disease is in remission), intensified monitoring (weekly in case of a flare), and outpatient visit monitoring (to prepare an outpatient visit). When parameters recorded by the monitoring modules exceed predefined thresholds, alerts (red flags) are created on the administrator page of the inflammatory bowel disease clinic. (2) Personal care plan: summary and visualisation of health parameters, patient-reported outcome measures, and quality metrics. (3) e-learning modules: interactive patient-tailored information on topics such as medications, adherence to medication, smoking cessation, (mal)nutrition, methods to prevent or reduce symptoms (self-management), fatigue, work productivity, anxiety, and depression. (4) Communication: secure message connection between patient and health-care providers' administrator page. Figure adapted from de Jong M, van der Meulen-de Jong A, Romberg-Camps M, et al. Development and feasibility study of a telemedicine tool for all patients with IBD: MyIBDcoach. *Inflamm Bowel Dis* 2017; **23:** 485–93. http://journals.lww.com/ibdjournal/Abstract/2017/04000/Development_and_Feasibility_Study_of_a.1.aspx.

patients. Patients in the standard care group continued their routine follow-up visits following the local protocol, with an opportunity to schedule an extra visit if symptoms relapsed. At baseline and after 12 months, all participants received a paper questionnaire regarding perceived quality of care, medication adherence, quality of life, self-efficacy, disease-related and medication-related knowledge, and smoking behaviour.

Outcomes

The primary outcomes were the number of outpatient visits and patient-reported quality of care. The number of outpatient visits and telephone consultations with gastroenterologists and nurses during the 12 month period were retrieved from patients' electronic medical records. Because validated patient-reported quality of care questionnaires have insufficient content validity for telemedicine interventions, patient-reported quality of care was measured with seven relevant domains derived from different questionnaires. These domains included visual analogue scale (VAS) scores (0–10; higher score indicates higher quality) on patient satisfaction with health care, patients' experiences contacting their health-care providers, and the extent to which health care meets patients' expectations. Questions were also included on the health-care workers' timeliness of response to questions and symptoms, health-care workers' fulfilment of agreements and attentiveness to acute situations, and hospital accessibility in case of symptoms. A mean score of 8 out of 10 or higher was predefined as perceived high quality.

Secondary outcomes were adherence to treatment, quality of life, self-efficacy, disease-related and medication-related knowledge, smoking behaviour, and disease outcomes. Disease outcomes were the numbers of flares and inflammatory bowel disease-related hospital admissions, emergency visits, surgeries, and corticosteroid use during the 12 months of follow-up. Flares were defined as clinical symptoms indicative of disease activity with, as a rule, concomitant calprotectin of more than 250 µg/g in the stool or active disease determined by endoscopy, MRI, or CT. In daily practice, in case of clinically severe symptoms suggestive for disease activity, the treating physician occasionally judged these symptoms to be evident enough to adjust therapy. Therefore, to capture all clinical flares, clinical episodes were defined as flares if symptoms suggestive of disease activity resulted in a dose escalation or initiation of a new drug to induce remission. Medication adherence was measured with the eight-item Morisky Medication Adherence Scale,[25] with scores below 6 defined as low adherence, scores between 6 and 8 defined as moderate adherence, and a score of 8 defined as high adherence. Quality of life was measured with the Short Inflammatory Bowel Disease Questionnaire (SIBDQ), a ten-item questionnaire that covers four domains: bowel symptoms, systemic symptoms, emotional health, and social functions.[26] Overall scores on the SIBDQ range from 10 to 70, with a lower score indicating lower quality of life. Self-efficacy, defined as the perception of one's ability to engage in skills required to master a new challenge despite obstacles, was measured with the 29-item inflammatory bowel disease self-efficacy scale (IBD-SES).[27] Questions are grouped into four domains: managing stress and emotions, managing medical care, managing symptoms and disease, and maintaining remission.

Overall scores on the IBD-SES range from 29 to 290, with higher scores indicating higher self-efficacy and thus better self-management and greater patient empowerment. Knowledge of inflammatory bowel disease and medication were both assessed by a VAS score (0–10; higher score indicates better knowledge), whereas smoking behaviour was assessed with a categorical question (non-smoker, active-smoker, or ex-smoker).

Statistical analysis

A sample size of 435 patients per group was estimated as sufficient to detect a difference of one outpatient visit per year (SD 2·4) and 0·5 difference in mean quality of care on a VAS scale (SD 1·4), with 80% power, a 5% significance level, and assuming a 10% dropout rate. Data were analysed on an intention-to-treat basis. Between-group differences in the number of outpatient consultations and disease outcomes were analysed by multivariable linear regression adjusted for the stratification criteria (medical centre [four centres], subtypes of inflammatory bowel disease [Crohn's disease or ulcerative colitis], and treatment [no medication or mesalazine; immunosuppressive drugs; or biological therapy]) and for age (numerical), sex (male or female), disease duration (numerical), disease activity at baseline (remission or active), smoking (non-smoker, active-smoker, or ex-smoker), and educational level (five levels). Because the normality assumption might be violated because of outliers, its effect on the results was checked by comparing the obtained confidence intervals with those after bootstrapping. The multiple imputation method was used for missing outcomes and covariates, in which 20 complete datasets were created using all other variables in the aforementioned analysis model (outcome and covariate, including study group) to impute the missing data. Linear mixed model analyses were used to assess differences in patient-reported outcomes at baseline and 12 months; outcomes analysed included quality of care, quality of life, medication adherence, self-efficacy, and disease-related and medication-related knowledge. An unstructured covariance structure for the two repeated measures was considered and a likelihood based approach was used for missing outcome variables. Results were corrected for stratification criteria and for age, sex, disease duration, disease activity at baseline, smoking, and educational level. The consistency of the intervention effect was assessed across subtypes of sex, age (18–30, 31–50, and >50 years), subtypes of inflammatory bowel disease (Crohn's disease and ulcerative colitis), setting (academic and non-academic), medication (no medication or mesalazine; immunosuppressive drugs; and biological therapy), and disease duration (0–5, 6–10, and >10 years), by post-hoc analyses where interaction terms of these variables with group (intervention and control) were added separately to the aforementioned linear regression and linear mixed models. The adjusted intervention effects that were estimated with these models are reported together with their 95% CI and p values. Logistic regression analysis was used to assess the intervention effect on smoking behaviour (active *vs* non-active [ex-smoker or non-smoker]) and was corrected for baseline smoking behaviour (active *vs* non-active) and educational level. A two-sided p≤0·05 was defined as statistically significant. All statistical analyses were done with SPSS version 22.0. This trial is registered with ClinicalTrials.gov, number NCT02173002.

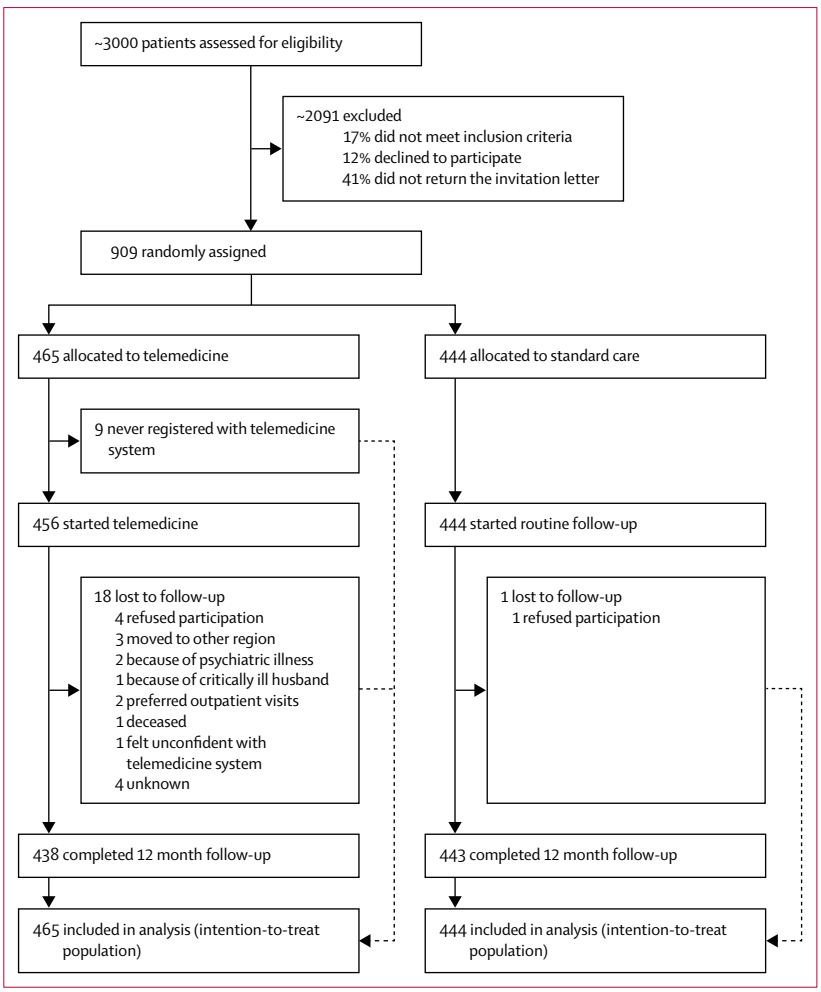

***Figure 2*: Trial profile**
We sent out 3000 invitation letters to patients who had a scheduled outpatient visit. Additionally, a small, but unknown, number of letters were given directly to the patients during outpatient visits, as some patients rescheduled their visit or had not received the invitation letter.

Role of the funding source

The funding source had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

	Telemedicine (n=465)	Standard care (n=444)
Centre		
Maastricht University Medical Centre	133 (29%)	131 (30%)
Leiden University Medical Centre	144 (31%)	152 (34%)
Zuyderland Medical Centre, Sittard	117 (25%)	102 (23%)
St Antonius Hospital, Nieuwegein	71 (15%)	59 (13%)
Sex		
Men	194 (42%)	180 (41%)
Women	271 (58%)	264 (59%)
Age at diagnosis (years)	30·7 (13·5)	30·4 (13·6)
Age at inclusion (years)	44·0 (14·1)	44·1 (14·2)
Disease duration (years)	12·8 (10·4)	13·1 (10·8)
Phenotype		
Crohn's disease*	282 (61%)	262 (59%)
Ileal	87 (31%)	68 (26%)
Colonic	67 (24%)	63 (24%)
Ileocolonic	128 (45%)	131 (50%)
Upper gastrointestinal modifier	34 (12%)	26 (10%)
Non-penetrating, non-stricturing, B1	169 (60%)	152 (58%)
Stricturing, B2	76 (27%)	70 (27%)
Penetrating, B3	37 (13%)	40 (15%)
Perianal disease modifier	67 (24%)	62 (24%)
Ulcerative colitis†	183 (39%)	182 (41%)
Proctitis, E1	26 (14%)	27 (15%)
Left-sided, E2	81 (44%)	70 (38%)
Pancolitis, E3	76 (41%)	85 (47%)
Treatment		
No medication or mesalazine	173 (37%)	147 (33%)
Immunosuppressive drugs	122 (26%)	131 (30%)
Biological therapy	170 (37%)	166 (37%)
Baseline disease activity		
Remission	394 (85%)	380 (86%)
Active disease	71 (15%)	64 (14%)
Smoking		
Non-smoker	157 (41%)	159 (43%)
Active smoker	65 (17%)	50 (14%)
Ex-smoker	157 (41%)	158 (43%)
Missing data	86 (18%)	77 (17%)
Education		
University	54 (14%)	49 (13%)
Higher vocational education	103 (27%)	98 (27%)
Intermediate vocational education	160 (42%)	157 (43%)
Secondary education	56 (15%)	55 (15%)
Primary education	6 (2%)	8 (2%)
Missing data	86 (18%)	77 (17%)

Data are n (%) or mean (SD). *The number of patients with Crohn's disease is used as the denominator for the percentages of each subtype of Crohn's disease. †The number of patients with ulcerative colitis is used as the denominator for the percentages of each subtype of ulcerative colitis.

Table 1: **Baseline characteristics**

See Online for appendix

Results

Between Sept 9, 2014, and May 18, 2015, about 3000 outpatients with inflammatory bowel disease were asked to participate in this study, of whom 17% did not meet the inclusion criteria, 41% did not return the invitation letter, and 12% were not interested, providing reasons such as "too busy", "participating in other studies", "not now", "too much confrontation with the disease", and "impersonality of telemedicine" (figure 2). 909 eligible patients provided written informed consent and were randomly assigned, 465 to the telemedicine group and 444 to the standard care group. Neither protocol deviations nor adverse events related to use of the telemedicine intervention occurred. The baseline characteristics of the two study groups were similar and were representative of the general inflammatory bowel disease population in demographic characteristics and disease activity (table 1).[28] At the end of the 12 month study period, 438 (94%) patients in the telemedicine group continued to use the telemedicine system and 443 (99·8%) in the standard care group continued their routine follow-up visits in the same hospital (figure 2). At baseline, 382 (82%) patients in the telemedicine group and 369 (83%) in the standard care group completed the paper questionnaires about perceived quality of care, medication adherence, quality of life, self-efficacy, disease-related and medication-related knowledge, and smoking behaviour. At 12 months, these questionnaires were completed by 340 (73%) patients in the telemedicine group and 331 (75%) patients in the standard care group. All randomised patients were included in the analyses (intention-to-treat population). One patient in the telemedicine group died because of mucinous colorectal cancer, which was deemed to be unrelated to the study intervention.

At 12 months, the mean number of outpatient visits to the gastroenterologist was significantly lower in the telemedicine group than in the standard care group (1·26 [SD 1·18] in the telemedicine group *vs* 1·98 [1·19] in the standard care group; estimated intervention effect –0·72 [95% CI –0·87 to –0·56]; p<0·0001; table 2). Outpatient visits to the nurse, however, did not differ significantly between groups (table 2). The total number of outpatient visits (gastroenterologist or nurse) was significantly lower in the telemedicine group than in the standard care group (1·55 [1·50] in the telemedicine group *vs* 2·34 [1·64] in the standard care group; estimated intervention effect –0·79 [–0·98 to –0·59]; p<0·0001). The mean number of telephone consultations with the gastroenterologist was also significantly lower in the telemedicine group than in the standard care group, but the mean number of telephone consultations with the nurse did not differ significantly (table 2). These results were largely consistent across patients with Crohn's disease and ulcerative colitis, those treated in academic and non-academic settings, men and women, all age categories, all medication categories, and all disease duration categories (appendix pp 1–2). However, for patients in academic settings, the mean number of outpatient visits to the nurse was lower in the telemedicine group than in the standard care group (appendix pp 1–2).

Patients in the telemedicine and standard care groups reported similar and high scores for quality of care at 12 months (8·16 [SD 1·37] *vs* 8·27 [1·28], respectively; estimated intervention effect 0·10 [95% CI –0·13 to 0·32]; p=0·411; table 3). Results were similar in patients with Crohn's disease and ulcerative colitis, those treated in academic and non-academic settings, men and women, and in all age and disease duration categories. Patients in the telemedicine group using biological therapies reported lower scores for quality of care than did patients in the standard care group (p=0·037; appendix pp 3–4).

Over the 12 month follow-up period, the mean numbers of flares, courses of corticosteroid treatment, emergency visits, and inflammatory bowel disease-related surgeries did not differ significantly between the two groups (table 4). The mean number of hospital admissions was significantly lower in the telemedicine group than in the standard care group (16 unique patients admitted to hospital in the telemedicine group *vs* 29 in the standard care group; estimated intervention effect –0·05 [95% CI –0·10 to 0·00]; p=0·046). Reasons for admission to hospital included exacerbation of disease (six patients in the telemedicine group *vs* eight in the standard care group), surgery (eight *vs* ten), complications of the disease (ie, intestinal obstruction, active perianal disease, or ostomy dysfunction; six *vs* 14), medication side-effects (one *vs* six), and abdominal pain without evidence for active disease (none *vs* five). Analyses per subtype showed no significant differences between groups in numbers of flares, courses of corticosteroid treatment, emergency visits, and inflammatory bowel disease-related surgeries (appendix pp 5–6). However, patients in the telemedicine group with Crohn's disease (estimated intervention effect –0·09 [95% CI –0·17 to –0·02]; p=0·012), or using biological therapies (–0·12 [–0·22 to –0·02]; p=0·025), or with a disease duration of more than 10 years (–0·08 [–0·17 to 0·00]; p=0·045) were less often admitted to the hospital than their respective controls.

Adherence to medication at the end of the trial was significantly higher in the telemedicine group than in the standard care group (table 3). Both groups reported normal values for quality of life and high scores for self-efficacy and disease-related and medication-related knowledge, with no significant differences between groups (table 3). Smoking behaviour at the end of the study period did not differ between groups (odds ratio 0·81 [95% CI 0·33–1·96]; p=0·633; appendix p 7).

	Telemedicine (n=465)	Standard care (n=444)	Estimated intervention effect* (95% CI)	p value
Outpatient visits				
Gastroenterologist	1·26 (1·18)	1·98 (1·19)	–0·72 (–0·87 to –0·56)	<0·0001
Nurse	0·29 (0·68)	0·36 (0·84)	–0·07 (–0·17 to 0·03)	0·173
Total	1·55 (1·50)	2·34 (1·64)	–0·79 (–0·98 to –0·59)	<0·0001
Telephone consultations				
Gastroenterologist	0·58 (0·98)	0·84 (1·11)	–0·26 (–0·40 to –0·12)	0·0003
Nurse	0·70 (1·59)	0·74 (1·90)	–0·08 (–0·30 to 0·13)	0·448
Total	1·28 (2·06)	1·57 (2·44)	–0·34 (–0·63 to –0·06)	0·018

Data are mean (SD) unless otherwise stated. *Adjusted for centre, treatment, subtypes of inflammatory bowel disease, age, sex, disease duration, disease activity at baseline, smoking, and educational level. Bootstrap CIs were similar to those presented here. The estimated intervention effect, 95% CI, and p value were obtained after multiple imputation.

Table 2: **Health-care utilisation**

	Telemedicine		Standard care		Estimated intervention effect* (95% CI)	p value
	Number	Mean score (SD)	Number	Mean score (SD)		
Quality of care						
Baseline	382	8·25 (1·24)	369	8·26 (1·05)	..	..
12 months	340	8·16 (1·37)	331	8·27 (1·28)	0·10 (–0·13 to 0·32)	0·411
Medication adherence						
Baseline	382	6·52 (1·76)	369	6·67 (1·70)	..	..
12 months	340	7·01 (1·40)	331	6·77 (1·61)	0·46 (0·22 to 0·70)	0·0002
Quality of life						
Baseline	382	53·34 (10·29)	369	53·42 (9·95)	..	..
12 months	340	54·44 (9·05)	331	53·71 (9·87)	1·22 (–0·04 to 2·49)	0·057
Self-efficacy						
Baseline	382	224·16 (64·04)	369	222·14 (36·88)	..	..
12 months	340	223·35 (32·11)	331	220·28 (35·08)	2·45 (–6·05 to 10·94)	0·572
Knowledge of inflammatory bowel disease						
Baseline	382	7·66 (1·30)	369	7·57 (1·36)	..	..
12 months	340	8·17 (1·16)	331	7·84 (1·47)	0·20 (–0·19 to 0·41)	0·074
Knowledge of medication						
Baseline	382	7·34 (1·51)	369	7·29 (1·44)	..	..
12 months	340	7·75 (1·58)	331	7·58 (1·51)	0·14 (–0·09 to 0·37)	0·235

Quality of care was assessed by visual analogue scale, medication adherence by the eight-item Morisky Medication Adherence Scale,[25] quality of life by the Short Inflammatory Bowel Disease Questionnaire,[26] and self-efficacy by the inflammatory bowel disease self-efficacy scale.[27] *Adjusted for centre, treatment, subtypes of inflammatory bowel disease, age, sex, disease duration, disease activity at baseline, smoking, educational level, and baseline patient-reported values. Bootstrap CIs were similar to those presented here. The estimated intervention effect, 95% CI, and p value were obtained from linear mixed models based on the likelihood approach for missing outcome data.

Table 3: **Patient-reported outcomes**

Discussion

This pragmatic, randomised controlled trial compared a telemedicine system versus standard outpatient care for patients with inflammatory bowel disease, irrespective of disease course or treatment. Our findings showed that use of the telemedicine system resulted in a reduction in outpatient visits, telephone consultations, and admissions to hospital, and increased adherence to medication. Additionally, the telemedicine system was safe and patient-reported quality of health care remained high.

Ameliorating quality of care for chronic diseases has been defined as improving long-term disease outcomes, creating a healthier population, and reducing health-care costs.[12,29] Our results showed that the use of a telemedicine system reduced the number of outpatient visits, while enabling tight follow-up of disease activity. Disease

	Telemedicine (n=465)	Standard care (n=444)	Estimated intervention effect* (95% CI)	p value
Flares	0·19 (0·42)	0·19 (0·44)	–0·01 (–0·06 to 0·05)	0·819
Corticosteroid courses	0·10 (0·33)	0·12 (0·37)	–0·02 (–0·07 to 0·02)	0·322
Hospital admissions	0·05 (0·28)	0·10 (0·43)	–0·05 (–0·10 to 0·00)	0·046
Emergency visits	0·07 (0·35)	0·10 (0·54)	–0·03 (–0·09 to 0·03)	0·366
Inflammatory bowel disease-related surgeries	0·03 (0·16)	0·03 (0·16)	0·00 (–0·02 to 0·02)	0·786

Data are mean (SD) unless otherwise stated. *Adjusted for centre, treatment, subtypes of inflammatory bowel disease, age, sex, disease duration, disease activity at baseline, smoking, and educational level. Bootstrap CIs were similar to those presented here. The estimated intervention effect, 95% CI, and p value were obtained after multiple imputation.

Table 4: **Disease outcomes**

monitoring with the telemedicine system was safe, because there were no significant differences between groups in numbers of flares, corticosteroid courses, emergency visits, and surgeries. Moreover, use of the telemedicine system resulted in fewer hospital admissions. These results are in line with the improved care and monitoring with telemedicine in other (relapsing-remitting) chronic diseases, such as chronic obstructive pulmonary disease and heart failure.[14,15] However, those studies were done in fairly small and specific patient subgroups, with differences in follow-up times and outcome measures, resulting in inconsistent results. This inconsistency complicates the ability to draw firm conclusions on the effectiveness of telemedicine in larger real-world populations.

To our knowledge, myIBDcoach is the first telemedicine tool for all subtypes of inflammatory bowel disease, irrespective of phenotype, setting, medical treatment, or disease severity. Two previous randomised controlled trials assessed the effect of telemedicine on the management of subtypes of inflammatory bowel disease with mild disease.[19,20] One trial, in 47 patients with ulcerative colitis, compared self-testing of disease activity by questionnaires and weight measurements with standard care, but found no differences between groups in disease outcomes.[20] The other trial, in 333 patients with mild-to-moderate ulcerative colitis who were being treated with mesalazine, showed that tight monitoring of disease activity and personalised treatment strategies reduced outpatient visits compared with usual care.[19] By contrast with our findings, disease activity, relapse frequency, and rates of hospital admission and surgery did not differ in the two groups. However, active self-management shortened relapse duration. As in our study, telemedicine improved adherence to treatment, but we did not find differences in quality of life, self-efficacy, and disease-related and medication-related knowledge, which might have been caused by the high baseline scores on these questionnaires in both the telemedicine and standard care groups.[26,27] Our study was done in four centres with well organised and accessible outpatient clinics with dedicated nurses and an e-mail and telephone consultation structure. As a consequence, rates of outpatient visits were relatively low compared with other European clinics,[30] suggesting that the effect of the telemedicine system on the reduction of outpatient visits might be larger in other clinics.

In addition to disease activity, myIBDcoach also monitors factors that affect disease outcomes, including adherence to treatment, psychosocial factors, smoking, and nutrition. Awareness of these factors and development of standard intervention procedures and educational programmes can further improve the long-term outcome of patients with inflammatory bowel disease. For example, improved medication adherence has been found to improve long-term disease outcomes.[7,8] The telemedicine system offers interactive e-learning modules on various subjects, allowing patients to review modules when they or their health-care providers consider it desirable. The system also registers patient-reported outcome measures on quality of life and work productivity, and quality metrics for value-based health care following the International Consortium for Health Outcomes Measurement recommendations. These findings can immediately be visualised and reported to both individual users and their health-care providers in a personal care plan. Hospitals with value-based health-care programmes could use telemedicine systems to measure patient-reported outcome measures and patient-reported experience measures.[10] Furthermore, systematic registration of quality metrics and aggregation of these metrics from different practices might improve quality of care and reduce practice variability.[11,31]

The main strength of our study was its randomised and pragmatic design. An unselected heterogeneous group of patients, clinicians, and clinical practices were included to maximise the applicability of these results to everyday practice. A potential weakness of the study design was that neither patients nor clinicians were masked to group assignments. We discussed giving all patients the telemedicine system while only monitoring patients in the intervention group. However, we felt that it was not ethical to ask the control group to use the telemedicine system without monitoring possibly relevant information resulting from red flags, nor to instruct those patients to plan follow-up visits only when necessary rather than traditionally booked appointments. The fairly short follow-up period can also be considered a limitation of the study. Intervention trials with 12 month follow-up are, however, regarded sufficient for maintenance drug therapy for registration purposes. Nevertheless, clinicians and patients require time to adapt to an altered clinical workflow. Interventions based on aberrant patient-reported outcome measure values require new procedures and protocols. Trials with longer follow-up periods are required to determine whether the telemedicine system can control costs and improve long-term disease outcomes.

Although telemedicine shows many benefits in managing patients with chronic diseases, few "tele-systems" have been implemented in everyday care.

Among the reasons are the absence of a framework for the development, evaluation, and implementation of eHealth interventions;[18] a disconnect between users and developers of health IT systems;[32] the development of telemedicine programmes aimed at specific subgroups of patients with regard to treatment regimen, disease severity, or health-care setting;[7,19–21] and financial hurdles such as reimbursement of telemedicine consultations by insurance companies. To overcome these barriers, myIBDcoach was developed and pilot-tested with a structured iterative process and through close collaboration between the developer, delegates from the Dutch inflammatory bowel disease patient organisation (CCUVN), nurses, and gastroenterologists working in secondary and tertiary referral centres.[22] Additionally, we deliberately assessed the effects of telemedicine on quality of care in a large unselected population of patients with all subtypes of inflammatory bowel disease, representative of a general inflammatory bowel disease population in a specialised care setting,[28] thereby providing external validity of the results for entire populations of patients with inflammatory bowel disease. Although this study was done in patients with inflammatory bowel disease, the results suggest that telemedicine can measure and improve the quality and value of health care in patients with other chronic relapsing-remitting diseases.

Our results show that telemedicine with myIBDcoach was safe, reduced outpatient visits and hospital admissions, and improved adherence to medication with similar patient-reported quality of care compared with standard care. These results were consistent across different subtypes of inflammatory bowel disease. This telemedicine tool systematically monitors and registers disease activity and factors affecting disease, patient-reported outcome measures, drug side-effects, and quality metrics. In an era of health-care cost reduction and a rising incidence of inflammatory bowel disease, telemedicine systems could be a valuable tool for reorganising inflammatory bowel disease care towards more personalised and value-based health care.

Contributors

MJdJ had full access to the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. MJdJ, AEvdM-dJ, MJR-C, MCB, MC, TM, AAM, DMJ, and MJP contributed to study concept and design. MJdJ, AEvdM-dJ, MJR-C, MCB, JPM, AAvB, NM, WMH, GD, AB, AvT, and MJP contributed to acquisition, analysis, or interpretation of data. MJdJ, AAvB, and MJP contributed to drafting of the report. MJdJ, AEvdM-dJ, MJR-C, MCB, JPM, AAvB, NM, WMH, GD, AAM, AB, DMJ, AvT, and MJP contributed to critical revision of the report for important intellectual content. MJdJ, BW, DMJ and MJP contributed to statistical analysis. MJP supervised the study. All authors approved the final version of the report.

Declaration of interests

MJdJ reports non-financial support from Merck Sharpe & Dohme, outside the submitted work. AEvdM-dJ reports grants and non-financial support from Takeda, personal fees from AbbVie, and non-financial support from Tramedico, all outside the submitted work. AAvB reports personal fees from AbbVie, MSD, Ferring, Tramedico, Takeda, Pfizer, and Janssen, all outside the submitted work. GD reports speaker's fees from Shire, AbbVie, and Takeda, and a grant for investigator-initiated research from Takeda, all outside the submitted work. AAM reports grants from Grünenthal, Zon MW GGG (government), Will Pharma, BioActor, Pentax Europe, Falk Pharma, and Almiral Pharma, all outside the submitted work. AB received research grants to her department from AbbVie, Amgen, and Merck, and advisory board honoraria from Janssen and Sandoz, all unrelated to the current work. MJP reports personal fees from AbbVie, Ferring, Janssen, and Takeda, and grants from Falk, all outside the submitted work. All other authors declare no competing interests.

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References

1 Burisch J, Munkholm P. The epidemiology of inflammatory bowel disease. *Scand J Gastroenterol* 2015; **50:** 942–51.

2 Magro F. Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. *J Crohns Colitis* 2017; published online Feb 2. DOI:10.1093/ecco-jcc/jjx008.

3 Gomollón F. 3rd European evidence-based consensus on the diagnosis and management of Crohn's disease 2016: Part 1: Diagnosis and Medical Management. *J Crohns Colitis* 2016; **11:** 3–25.

4 Jeuring SF, van den Heuvel TR, Liu LY, et al. Improvements in the long-term outcome of Crohn's disease over the past two decades and the relation to changes in medical management: results from the population-based IBDSL cohort. *Am J Gastroenterol* 2016; **112:** 325–36.

5 Jeuring SF, Bours PH, Zeegers MP, et al. Disease outcome of ulcerative colitis in an era of changing treatment strategies: results from the Dutch population-based IBDSL cohort. *J Crohns Colitis* 2015; **9:** 837–45.

6 Colombel JF, Narula N, Peyrin-Biroulet L. Management strategies to improve outcomes of patients with inflammatory bowel diseases. *Gastroenterology* 2017; **152:** 351–61.e5.

7 Pedersen N, Thielsen P, Martinsen L, et al. eHealth: individualization of mesalazine treatment through a self-managed web-based solution in mild-to-moderate ulcerative colitis. *Inflamm Bowel Dis* 2014; **20:** 2276–85.

8 Lakatos PL. Prevalence, predictors, and clinical consequences of medical adherence in IBD: how to improve it? *World J Gastroenterol* 2009; **15:** 4234–39.

9 Reigada LC, Satpute A, Hoogendoorn CJ, et al. Patient-reported anxiety: a possible predictor of pediatric inflammatory bowel disease health care use. *Inflamm Bowel Dis* 2016; **22:** 2127–33.

10 Porter ME. What is value in health care? *N Engl J Med* 2010; **363:** 2477–81.

11 Bradley SM, Rumsfeld JS, Ho PM. Incorporating health status in routine care to improve health care value: the VA Patient Reported Health Status Assessment (PROST) System. *JAMA* 2016; **316:** 487–88.

12 Siegel CA, Allen JI, Melmed GY. Translating improved quality of care into an improved quality of life for patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2013; **11:** 908–12.

13 Melmed GY, Siegel CA, Spiegel BM, et al. Quality indicators for inflammatory bowel disease: development of process and outcome measures. *Inflamm Bowel Dis* 2013; **19:** 662–68.

14 de la Torre Diez I, Garcia-Zapirain B, Mendez-Zorrilla A, Lopez-Coronado M. Monitoring and follow-up of chronic heart failure: a literature review of eHealth applications and systems. *J Med Syst* 2016; **40:** 179.

15 Jonkman NH, Westland H, Trappenburg JC, et al. Do self-management interventions in COPD patients work and which patients benefit most? An individual patient data meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2016; **11:** 2063–74.

16 Aguas M, Del Hoyo J, Faubel R, Nos P. Telemedicine in inflammatory bowel disease: opportunity ahead. *Inflamm Bowel Dis* 2016; **22:** E4–5.

17 Huang VW, Reich KM, Fedorak RN. Distance management of inflammatory bowel disease: systematic review and meta-analysis. *World J Gastroenterol* 2014; **20:** 829–42.

18 Jackson BD, Gray K, Knowles SR, De Cruz P. EHealth technologies in inflammatory bowel disease: a systematic review. *J Crohns Colitis* 2016; **10:** 1103–21.

19 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:** 1652–61.

20 Cross RK, Cheevers N, Rustgi A, Langenberg P, Finkelstein J. Randomized, controlled trial of home telemanagement in patients with ulcerative colitis (UC HAT). *Inflamm Bowel Dis* 2012; **18:** 1018–25.

21 Pedersen N, Elkjaer M, Duricova D, et al. eHealth: individualisation of infliximab treatment and disease course via a self-managed web-based solution in Crohn's disease. *Aliment Pharmacol Ther* 2012; **36:** 840–49.

22 de Jong M, van der Meulen-de Jong A, Romberg-Camps M, et al. Development and feasibility study of a telemedicine tool for all patients with IBD: MyIBDcoach. *Inflamm Bowel Dis* 2017; **23:** 485–93.

23 Lennard-Jones JE. Classification of inflammatory bowel disease. *Scand J Gastroenterol Suppl* 1989; **170:** 2–6; discussion 16–19.

24 de Jong M, van den Heuvel T, Romberg-Camps M, et al. Development of a patient reported disease activity score to screen for mucosal inflammation in inflammatory bowel disease. *J Crohns Colitis* 2015; **9** (suppl 1)**:** S192–93.

25 Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986; **24:** 67–74.

26 Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. *Am J Gastroenterol* 1996; **91:** 1571–78.

27 Keefer L, Kiebles JL, Taft TH. The role of self-efficacy in inflammatory bowel disease management: preliminary validation of a disease-specific measure. *Inflamm Bowel Dis* 2011; **17:** 614–20.

28 van den Heuvel TR, Jonkers DM, Jeuring SF, et al. Cohort profile: the Inflammatory Bowel Disease South Limburg Cohort (IBDSL). *Int J Epidemiol* 2015; published online Jun 4. DOI:10.1093/ije/dyv088.

29 Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff (Millwood)* 2008; **27:** 759–69.

30 Sulz MC, Siebert U, Arvandi M, et al. Predictors for hospitalization and outpatient visits in patients with inflammatory bowel disease: results from the Swiss Inflammatory Bowel Disease Cohort Study. *Eur J Gastroenterol Hepatol* 2013; **25:** 790–97.

31 Feuerstein JD, Castillo NE, Siddique SS, et al. Poor documentation of inflammatory bowel disease quality measures in academic, community, and private practice. *Clin Gastroenterol Hepatol* 2016; **14:** 421–28.e2.

32 Rudin RS, Bates DW, MacRae C. Accelerating innovation in health IT. *N Engl J Med* 2016; **375:** 815–17.