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Review Article

EHealth Technologies in Inflammatory Bowel Disease: A Systematic Review

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Abstract

Background and Aims: Electronic-health technologies (eHealth) such as Web-based interventions, virtual clinics, smart-phone applications, and telemedicine are being used to manage patients with inflammatory bowel disease (IBD). We aimed to: (1) Evaluate the impact of eHealth technologies on conventional clinical indices and patient-reported outcome measures (PROs) in IBD; (2) assess the effectiveness, cost-effectiveness and feasibility of using eHealth technologies to facilitate the self-management of individuals with IBD, and; (3) provide recommendations for their design and optimal use for patient care.
Methods: Relevant publications were identified via a literature search, and 17 publications were selected based on predefined quality parameters.
Results: Six randomized controlled trials and nine observational studies utilizing eHealth technologies in IBD were identified. Compared with standard outpatient-led care, eHealth technologies have led to improvements in: Relapse duration [($n = 1$) 18 days vs 77 days, $p < 0.001$]; disease activity ($n = 2$); short-term medication adherence ($n = 3$); quality of life ($n = 4$); IBD knowledge ($n = 2$); healthcare costs ($n = 4$); the number of acute visits to the outpatient clinic due to IBD symptoms ($n = 1$), and; facilitating the remote management of up to 20% of an IBD cohort ($n = 2$). Methodological shortcomings of eHealth studies include heterogeneity of outcome measures, lack of clinician/patient input, lack of validation against conventional clinical indices and PROs, and limited cost–benefit analyses.
Conclusions: EHealth technologies have the potential for promoting self-management and reducing the impact of the growing burden of IBD on health care resource utilization. A theoretical framework should be applied to the development, implementation, and evaluation of eHealth interventions.

Key Words: EHealth; inflammatory bowel disease; remote consultation; self-management; telemedicine

1. Introduction

Inflammatory bowel diseases (IBDs) including Crohn's disease (CD) and Ulcerative Colitis (UC) are chronic inflammatory disorders of the gastrointestinal tract that are associated with significant morbidity and mortality.[1,2] IBD is characterized by intermittent flares of disease activity requiring invasive medical investigations, adjustments

in medication, frequent outpatient clinic visits, hospitalizations, and surgeries.[3] IBD is also associated with an increased prevalence of psychological morbidity and adversely affects quality of life (QoL), societal interaction, and functioning.[4,5]

The increasing incidence of IBD over the past decade has resulted in increased demands on limited health care resources and longer specialist outpatient waiting lists.[4,6,7] The burden of IBD on the health care system is likely to increase based on the evidence that: (1) the incidence of IBD is increasing worldwide, and; (2) these chronic illnesses require increasingly more complex integrated models of health care.[8–10]

Traditional approaches to the management of IBD care based on treating symptoms alone and managing 'flare-ups' of disease has not changed the natural history of disease.[11,12] A more 'proactive' rather than 'reactive' approach to disease management is required.[13] Engaging patients in their self-care using novel approaches such as participatory health care models may facilitate a more 'proactive' approach to management. Further, patient-oriented participatory health care models may also be likely to be more successful in targeting several key drivers of active disease, such as medication nonadherence and smoking.[14,15]

Electronic-health technologies represent a vehicle to facilitate participatory medicine, a movement in which networked patients move from being merely passengers to responsible drivers of their health.[16–20] 'EHealth' has consequently been defined as 'health services and information delivered or enhanced through the Internet and related-technologies', 'characterizing not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve health care by using information and communication technology'.[21]

The principle underlying the remote management of patients via eHealth is the incorporation of a component of patient self-management whereby patients share information about their state of health with a program or health care team, on the basis of which patients are provided with management recommendations.[4] Patients can adjust their therapy based on predetermined algorithms or seek medical assessments. Self-management has been shown to improve symptoms, psychological well-being, and health care utilization.[22] EHealth technologies, therefore, have the potential to facilitate patient engagement, greater monitoring of disease activity, and earlier intervention than traditional outpatient-based models of care. However, the application of eHealth technologies to the IBD setting has been relatively limited.[23–28]

The peak incidence of IBD is in the second to fourth decade of life.[7] Due to the relatively young age of onset, the majority of patients with IBD are likely to be familiar with eHealth technologies. Moreover the Internet is now widely available in the developed world.[29] Patients are now increasingly using the Internet to access health web sites and physician web pages.[30–33] In a study by Panes *et al.*, 84% of patients (*n* = 172) expressed an interest in having access to an IBD-specific support web-site overseen by their gastroenterologist, and 65% were prepared to pay for the additional service.[34] Young patients' inclination to utilize eHealth technologies in their day-to-day lives for non-health-related purposes, together with the fact that they are widely accessible, makes the use of such technologies a potentially practical resource for supporting IBD management.

This systematic review summarizes the current literature on eHealth use in patients with IBD and focuses on Web-based interventions, smart phone apps, telemedicine, virtual clinics (VCs) and social media. The primary objective of this review was to evaluate the impact of eHealth technologies on conventional clinical indices and patient-reported outcome measures in IBD. The secondary objectives were to assess the effectiveness, cost–effectiveness, and feasibility of using eHealth technologies to facilitate the self-management of individuals with IBD, and to provide recommendations for their design and optimal use for patient care.

2. Methods

2.1. Search strategy for identification of studies

A structured electronic search of the literature was conducted in October 2015 according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines using Medline (EBSCOhost) (1950–2015), EMBASE, and the Cochrane Controlled Trials Register (CENTRAL) to identify articles on the use of eHealth in IBD. Any trial or report using eHealth technologies and recruiting adult patients with IBD were eligible. Abstracts from international conferences (Digestive Diseases Week, European Crohn's and Colitis Organisation Congress and United European Gastroenterology Week) from 2000–2015 (where applicable) were also reviewed. Internet publications were searched using the Google search engine (http://www.google.com). All search strategies used the terms 'eHealth,' 'mHealth,' 'telemedicine,' 'self-care,' 'self-administration,' 'patient education,' 'internet,' 'social media,' 'VCs,' 'remote consultation,' 'telenursing,' 'inflammatory bowel disease' alone or in combination as free-text and MeSH headings. All abstracts were screened independently and the relevant reports, abstracts and publications were identified (Figure 1). Additional publications were identified via a manual review of the reference list of identified studies and review articles.

2.2. Criteria for study inclusion

Given the rapidly evolving nature of eHealth technologies and considering that few controlled trials have evaluated eHealth interventions, this review assessed any eHealth intervention in IBD (including Web-based management, telemedicine, mobile telephone apps, VCs, email use, and social media) from a broad range of study designs and included reports of eHealth use in abstracts from international conferences. Those reports without a component of self-management were also included to evaluate the breadth of eHealth technologies currently used in IBD. Reports of development of an eHealth technology without a dedicated study were also included in this review. The main outcome measures evaluated in the review were: Disease activity, QoL, medication adherence, work productivity, cost-efficacy, depression, anxiety, and IBD knowledge. The search was limited to clinical studies on adolescent or adult participants. No restrictions were applied with regard to language of publication.

2.3. Data collection

Two reviewers (BDJ and PDC) independently identified studies for eligibility where outcome data was extracted, and any discrepancy between the two reviewers was resolved by discussion in order to reach a consensus.

2.4. Quality assessment

Randomized controlled trials (RCTs) were assessed for risk of bias using the following characteristics described in the Cochrane handbook[35]: method used to generate the randomization schedule; method used to conceal treatment allocation; implementation of blinding of outcome assessment; completeness of follow-up, and;
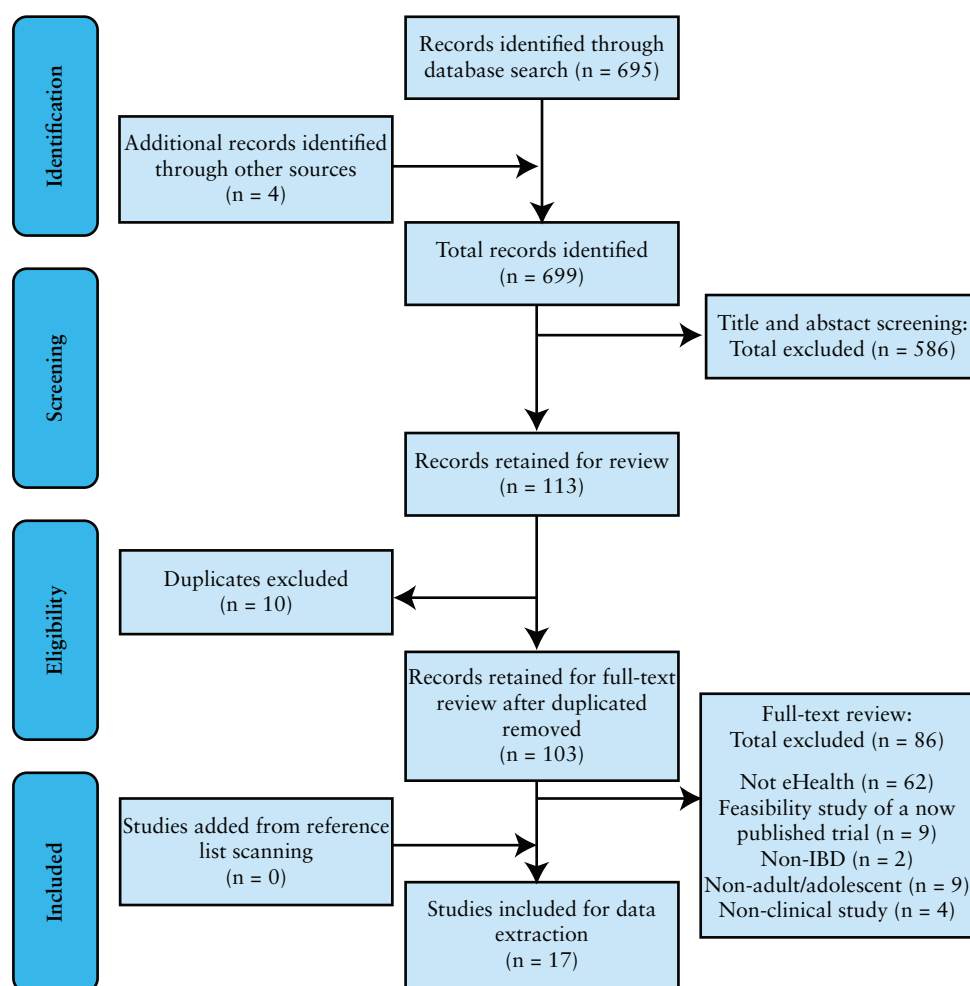
Figure 1. PRISMA flowchart illustrating published studies or abstracts included in the systematic review.

conduct of an intention-to-treat analysis. Observational studies were similarly assessed using the Effective Public Health Practice Project quality assessment tool for quantitative studies.[36] Each parameter of trial quality has been graded as low risk of bias, high risk of bias, or unclear risk of bias, with an overall assessment of each trial agreed upon by the reviewers (BDJ and PDC).

2.5. Thematic analysis

Studies were subsequently categorized into major types of eHealth technology used. Studies in each category were then summarized in terms of their reporting of factors connected with impacts on clinical indices, patient-reported outcomes, effectiveness, cost–effectiveness, and feasibility for self-management.

3. Results

3.1. Study selection

A total of 695 articles were identified by the electronic search strategy (Figure 1). After exact duplications were removed and titles and abstracts were screened, 112 articles remained. Of these, 86 were excluded for the following reasons: (1) Non-eHealth interventions; (2) non-IBD studies; (3) nonclinical studies; (4) nonadult or adolescent studies; and (5) feasibility study of a now published trial, resulting in 17 reports of eHealth use in IBD. A meta-analysis was

not undertaken due to methodological differences between the studies, particularly with respect to types of design (not all studies were RCTs), interventions, populations studied, and outcomes measured. Critical appraisal was conducted based on gastroenterology-specific recommendations adapted from Knowles *et al.*[37]

3.2. Study characteristics

Study characteristics are documented in Tables 1 and 2. EHealth technologies in IBD have been evaluated in RCTs, cohort studies, and case series. These studies have included self-described Web-based interventions, telemedicine, VCs, smartphone applications, e-mental health interventions, email use, and the application of social media. There has been a significant time delay between the introduction of eHealth technologies and the evidence supporting their use in IBD (Figure 2). Of the 17 reports, five were Web-based interventions, three were VCs, and three used telemedicine. The majority of the studies were implemented in hospital settings with UC patients. Of the 17 reports of eHealth interventions in IBD, the duration of interventions ranged from 6 weeks to 12 months. Three eHealth interventions were compared with standard care. In addition to the 17 reports, Calvert *et al.* has developed a Web-based management system in Manchester for IBD patients, called 'My IBD Portal', with the aim of supporting patients' in self-management of their IBD.[38] Although the latter self-management, Web-based system has been implemented and is

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Table 1. Summary of eHealth Web-based interventions for patients with IBD

Investigators	Intervention	IBD type	Study Design	Number of patients	Control	Outcome measures	Duration of follow-up	Study findings and/or conclusions
McCombie et al. (New Zealand) IBD, 2015	Web-based Psychological intervention	UC and CD	RCT	231 patients	Treatment as usual	**Primary** IBD-Health Related QoL **Secondary** Generic QoL Depression and Anxiety Stress Social functioning Neuroticism Coping strategies Disease activity using HBI and SCCAI	12 weeks (intervention) 6 months (question-naires)	Improved QoL at 12 weeks only F = 6.38 $p = 0.01$ At Week 12, SF-12 mental score improved F = 5.00 $p = 0.03$ At 6 months, reduction in religion (adaptive emotion-focused coping strategy) F = 4.66 $p = 0.03$
Pedersen et al. (Denmark) IBD, 2014	Web-guided mesalazine therapy	Mild-moderate UC	Cohort study	95 patients	N/A	**Primary** Efficacy of mesalazine treatment in inducing deep remission Adherence to therapy **Secondary** QoL Patient satisfaction	3 months	Reduction in disease activity from 4.6 to 1.6 (total inflammatory burden score) $p < 0.001$ Improved adherence $p < 0.001$ QoL improvement $p < 0.001$ All patients were satisfied with the intervention
Pedersen et al. (Denmark) APT, 2012	Web-based intervention for infliximab infusion timing	CD (Infliximab)	Cohort study	27 patients	N/A	Assessment of efficacy and safety Inflammatory burden QoL Cost Adherence to web program Antibodies to infliximab	12 months	Efficacious and safe No change in disease activity (inflammatory burden 2.4 baseline, 2.2 at 52 weeks, $p = 0.4$) No change in QoL Cost saving of 699 EUR per patient 86% adherence to web program No difference in antibodies to infliximab between baseline and end of study
Cross et al. (USA) IBD, 2012	Home telemanagement system	UC (using UC-HAT)	RCT	47 patients	Best available care	**Primary** Disease activity Adherence QoL	12 months	No change in disease activity but reduction in disease activity by 11.9 (Seo index) from baseline ($p = 0.08$) after adjustment for QoL No change in medication adherence Improved QoL $p = 0.04$

Table 1. Continued

Investigators	Intervention	IBD type	Study Design	Number of patients	Control	Outcome measures	Duration of follow-up	Study findings and/or conclusions
Elkjaer et al. (Denmark & Ireland) Gut, 2010	Web-based intervention (Constant Care)	Mild-moderate UC	RCT	333 patients randomized 1:1	Standard care	**Primary** Feasibility **Secondary** Patient compliance Disease outcomes QoL Knowledge Costs Safety	12 months	88% feasibility compared with conventional care (OR 1.6) Improved compliance with treatment only at 4 weeks (73% vs 42%, $p = 0.005$ Denmark; 73% vs 29%, $p = 0.03$ Ireland) No change in disease activity (OR 2.74, non-significant) Longer time to relapse (88 days in Danish web arm vs 77 days in Danish controls, $p < 0.001$) Improved QoL in Danish group only ($p = 0.04$) Improved knowledge (30–40% improvement) Cost saving 189 EUR/patient/year Safe intervention
McCormick et al. (USA) IBD, 2010	Web-based intervention	UC and CD adolescent females	RCT	24 patients	Standard outpatient care	Coping skills Abdominal pain Somatic symptoms	6 weeks	No change in abdominal pain Reduction of somatic symptoms from pre-treatment to post-treatment ($p = 0.009$) Improved adaptive coping skills

Table 2. Summary of eHealth telehealth, virtual clinics, smartphone apps, and other non-Web-based interventions for patients with IBD

Investigators	Intervention	IBD type	Study design	Number of patients	Control	Outcome measures	Duration of follow-up	Study findings and/or conclusions
Vinding et al. (Denmark) IBD, 2015	Smartphone app + faecal calprotectin kit	UC and CD	RCT	221 patients	ELISA-based faecal calprotectin kit	Faecal calprotectin score	6 months	Smartphone FC kit correlated well with the ELISA FC kit correlation coefficient 0.685
Atreja et al. (USA) JMIR, 2015	Smartphone app	UC and CD	RCT	300 intended patients	Education application	**Primary** Number of quality indicators met including eHealth literacy and patient engagement **Secondary** QoL Quality of care Patient adherence Disease control Resource utilization (emergency visits, hospitalizations)	24 months	N/A
Cross et al. (USA) Contemporary Clinical Trials, 2015	Telemedicine using mobile phone texts to communicate with patients	UC and CD	RCT	375 intended patients	Standard outpatient care	**Primary** QoL Disease activity **Secondary** Health care utilizations Patient knowledge Social constraint Self-efficacy Locus of control General QoL Client satisfaction	12 months	N/A
Regueiro et al. (USA) IBD, 2014	Telehealth using video-link to communicate between centres	UC and CD	Case series	11 US centres	N/A	The degree to which the conference changed practice	5 years	Successful multidisciplinary communication that has changed practice
Lichtenstein and Rubin (USA) Not published, 2014	Virtual clinic using an online portal for clinician data entry and education	For IBD clinicians	N/A	N/A	N/A	N/A	Not specified	N/A
Choi et al. (USA) ECCO Abstract, 2014	Twitter account and Facebook page	Available to anyone with or without IBD	N/A	N/A	N/A	Re-tweets Facebook 'likes' Facebook posts	15 months	Twitter and Facebook are valuable tools for the IBD community

Table 2. Continued

Investigators	Intervention	IBD type	Study design	Number of patients	Control	Outcome measures	Duration of follow-up	Study findings and/or conclusions
Plener et al. (Canada) Can JJGH, 2014	Email use for patients and clinicians	UC and CD	Case series	137 patients	N/A	Emails sent; Hours lost from work; Distance travelled; Specialist clinic visits; Hours taken per appointment; Anxiety scale; Patient preference	6 months	90% of patients prefer a combined model of care with email communication and clinic attendance
Johnson et al. (United Kingdom) Gut, 2013	Virtual clinic (patient portal with traffic-light feedback management; staff contact patients 1–2 times per year to assist online management)	Stable IBD	Case series	Not specified	N/A	Costs; Patient satisfaction	Not specified	Cost saving of 130 000 pounds per year; Satisfied patients
Hommel et al. (USA) EJGH, 2013	Telehealth (using video-link to review patients)	UC and CD	Case series	9 patients	N/A	Feasibility; Medication non-adherence; Costs	Not specified	Feasible; ↑adherence for 5-ASA from 62% to 91%; Time consuming; Saves $100 in mileage + 4 h of travel time per patient
Hunter et al. (United Kingdom) Postgrad Med J, 2012	Virtual clinic (using annual blood tests and questionnaires; patients are only reviewed in person if they meet specific criteria)	Stable IBD	Case series	Not specified	N/A	Clinic attendance	Not specified	Reduced clinic attendance (20% of patients transferred to the virtual clinic)
Krier et al. (USA) AJG, 2011	Telehealth (using video-link to review patients)	UC and CD	RCT	34 patients	Standard outpatient encounter	Patient satisfaction; Wait time; Throughput	9 months	High level of patient satisfaction; No difference in wait time (2.5 telehealth vs 18 standard care, $p = 0.31$) or appointment duration (60 telehealth vs 59 standard care, $p = 0.81$)

Figure 2. Timeline for the evidence supporting the use of eHealth technologies in IBD.

currently being used in routine clinical practice, outcome data related to this Web-based intervention are yet to be reported; hence, this was not analyzed in this review. A separate study evaluating telepathology for the diagnosis of dysplasia in chronic UC by Odze *et al.* has also been omitted from this review because it did not focus on conventional clinical indices or PROs.[39] Carlsen *et al.* are currently undertaking a Web-based eHealth intervention in adolescent and pediatric patients; however, the latter study is yet to be completed and published and, hence, was not analysed in this review (NCT01860651).

3.3. Quality assessment of eHealth technologies in IBD

The risk of bias varied among the Web-based studies. With the exception of the study by Cross *et al.*, four of the five Web-based studies were judged to have a low risk of bias. Two RCT studies (Elkjaer *et al.* and Cross *et al.*) presented approved randomization procedures and allocation concealment. Cross *et al.* reported blinding of outcome assessors; however, blinding of outcome assessors was not reported on in the other Web-based studies. All five studies included all participants in analyses, including those lost to follow-up. Only two of the five studies presented power analyses prior to the study commencement; however, the latter study by Cross *et al.* failed to recruit an adequate sample size for statistical power and experienced a high attrition rate in the Web-based group, resulting in a high risk of bias. The risk of bias was difficult to measure in the small cohort pilot studies. The RCT by Krier *et al.* used a randomization procedure; however, allocation concealment was not discussed, nor was blinding of outcome assessment. There was no attrition and, therefore, an intention-to-treat analysis was not required. Hence the RCT by Krier *et al.* was considered to be at low risk of bias. McCormick *et al.* randomized and concealed participants prior to study commencement; however, the randomization process was not detailed, indicating a possibility of bias in randomization. Blinding of outcome assessors did not occur during analysis. A large attrition rate occurred (14/20, 70%) in the intervention group due to the researchers being unable to contact the participants. An intention-to-treat analysis was not performed, suggesting a high risk of bias.

3.4. Web-based interventions in IBD

3.4.1. Impact of Web-based management in IBD on clinical indices of disease activity

The impact of a Web-based intervention on disease activity has been explored in two RCTs and two cohort studies in the IBD setting. In 2010 Elkjaer and colleagues conducted the largest RCT to date using Web-based management in IBD.[24] A total of 333 patients (233 patients in Denmark and 100 patients in Ireland) with 'stable' mild-to-moderate UC, treated with aminosalicylates (5-ASAs), were randomized to either 'Constant care', a Web-based management program, or a standard care control group, which was also compared with 106 patients in a historical cohort group. Eighty-eight percent of the Web group patients found the eHealth intervention feasible (the primary end point) and preferred the eHealth approach to conventional care (Odds ratio [OR] 1.6). No significant difference in disease activity, a secondary outcome of the study, based on the Simple Clinical Colitis Activity Index (SCCAI) was found between the Web-based group and the control group at 12 months (OR 2.74, p = nonsignificant). Moreover there was no significant difference in relapse frequency, hospitalization, surgery, or adverse events between the two groups. However, there was a decrease in the duration of relapse via the traffic light–guided management system [18 days in the Danish Web arm vs 77 days in the Danish control group ($p < 0.001$)].

In contrast to the study by Elkjaer *et al.*, a single-centre study from Baltimore randomized 47 patients with UC, stratified by disease activity, to Web-based management using UC-HAT (Home Telemanagement in Patients with UC) or standard care (comprised of active controls who were provided with educational fact sheets and individualized written action plans). Although no significant difference was found between the Web-based intervention and the standard outpatient-based care, after adjustment for baseline QoL, disease activity (using the Seo Index score) at 12 months in the Web-based intervention arm did decrease from baseline compared with the standard care arm [(11.9 ± 6.6 points (p = 0.08) compared with 1.2 ± 6.0 (p = 0.84)]. In contrast to the two controlled trials undertaken, a cohort study of 95 patients with mild-to-moderate UC on melsalazine undertaken by Pedersen *et al.* was able to demonstrate a significant reduction in the mean SCCAI over a 3-month period, from 4.6 at Week 0 to 1.6 at Week 12 ($p < 0.001$).[28] A separate cohort study by the same authors, which followed 27 patients with CD on infliximab (IFX) using Web-based management found no difference in disease activity based on inflammatory burden [using the Harvey Bradshaw Index (HBI) and faecal calprotectin (FC)] between baseline and end of follow-up (mean 2.4 vs 2.2, p = 0.4).[27]

McCombie *et al.* recently performed a RCT in 199 [CD *n* = 137; UC *n* = 54; IBD-unclassified (IBD-U) *n* = 80] patients that compared a Web-based psychological intervention designed to improve stress management and coping skills with standard outpatient-based care.[40] No significant difference in disease activity (measured using the SCCAI and HBI), a secondary outcome of the trial, was found between the intervention group and the standard care group when comparing baseline scores 12 weeks after the intervention. The nature of the Web-based interventions, study designs, and primary and secondary outcome measures have varied between each of these

studies, making it difficult to compare the effectiveness of Web-based intervention between studies. Nonetheless, taken together, these studies suggest that Web-based management may reduce the duration of relapse; however, the impact of Web-based management on disease activity appears modest and most likely to be of benefit to patients with mild-to-moderate UC.

3.4.2. Impact of Web-based management in IBD on patient-reported outcomes

Patient-reported outcome measures or 'PROs' are validated surveys that quantify patient-reported qualitative data and reflect a patient's state of well-being and/or their ability to function.[41–43] PROs that have been evaluated in IBD Web-based interventions include QoL, work productivity, depression, and anxiety.

3.4.2.1. Web-based management and quality of life

Health-related quality of life (HRQoL) is a global measure of the patient's perceptions, illness experience, and functional status, which incorporates social, cultural, psychological, and disease-related factors and has become an integral part of patient care.[44] Quality of life has been the focus of PROs measured in eHealth interventions and has been the only PRO for which eHealth interventions have consistently demonstrated a benefit.[23,24] Elkjaer *et al.* measured the impact of 'Constant care' on QoL, using a modified short version of the IBD questionnaire (s-IBDQ) in conjunction with the short form generic health survey (SF-36) and found a significant improvement in disease specific QoL ($p = 0.04$) in the Danish intervention group, but not in the Irish intervention group. Cross *et al.* measured the impact of UC-HAT on disease-specific QoL using the IBD questionnaire (IBDQ) and found that although the intention-to-treat analyses did not demonstrate improved disease-specific QoL compared with the control group, after adjustment for baseline disease knowledge, there was an improvement in QoL at 12 months compared with baseline scores ($p = 0.04$). In their UC cohort study, Pedersen *et al.* (2014) found a significant improvement in QoL using both the s-IBDQ (mean 47 at baseline vs mean 58 at Week 12, $p < 0.001$) and SF-12 (physical health summary measure mean 226 at baseline vs mean 253, $p < 0.01$; mental health summary measure mean 218 vs mean 248, $p < 0.01$). In Pedersen *et al.*'s study examining a Web-based strategy to manage CD with IFX, no change was observed in QoL measured by the s-IBDQ between baseline and end of follow-up at 12 months. McCombie *et al.* used a self-administered computerized cognitive behavioral therapy in patients with IBD to assess HRQoL using the IBDQ.[40] There was a 25.7% completion rate in the intervention arm (29/113 patients), with an increased QoL (using the IBDQ) compared with the standard care arm at 12 weeks ($p = 0.01$); however, the improved HRQoL was not maintained at 6 months. Baseline levels of depression (adjusted OR 0.29; CI 0.06–1.38); biologic use (adjusted OR 0.15; CI 0.02–1.17); baseline IBDQ scores >160 (adjusted OR 2.02; CI 0.77–5.30); and an absence of corticosteroid use (unadjusted OR 4.12; 1.02–16.55) were all factors that predicted dropout. Overall, these findings suggest that Web-based interventions do result in improvements in QoL, and therefore morbidity associated with IBD, especially among UC patients with mild-to-moderate disease severity. However, cultural biases, baseline levels of depression, and disease severity may influence the impact of Web-based interventions on QoL.

3.4.2.2. Web-based management and work productivity/absenteeism

The impact of Web-based interventions on work productivity has been measured in two studies, both directly using a validated index of work productivity [the Work Productivity and Activity Impairment Index (WPAI)] and indirectly (via rates of absenteeism and health care utilization). Although Elkjaer *et al.* did not directly evaluate work productivity, they did evaluate the impact of 'Constant care' on health care utilization and absenteeism and found no significant difference in number of days lost through illness and hospital admissions between the two groups; instead, a significantly reduced number of acute visits to the outpatient clinic due to UC symptoms was found (21 acute visits in the intervention arm vs 107 in the control arm; 35 vs 92 routine visits) ($p < 0.001$).[24] In their CD study, Pedersen *et al.* (2012) assessed work productivity using the Work Productivity and Activity Impairment for CD (WPAI-CD), but they did not find a change in: time missed from work due to CD; impairment due to CD while working; or overall work impairment due to CD ($p = 0.35$; $p = 0.96$; and $p = 0.47$, respectively). McCombie *et al.*, Cross *et al.*, and Pedersen *et al.* (2014) did not assess work productivity or absenteeism in their interventions. The data to support the impact of Web-based management on work productivity is, therefore, currently equivocal and needs to be further characterized, given its potential to reduce the need for face-to-face outpatient reviews.

3.4.2.3. Web-based management and psychological outcome measures

Despite there being several psychological eHealth intervention studies for gastrointestinal disease,[37] there have only been two studies that have evaluated the efficacy of a Web-based, psychologically oriented intervention in IBD.[45] McCormick *et al.* assessed a 6-week Web-based psychological intervention on coping skills in adolescent females, using reduction in abdominal pain (via the Abdominal Pain Index) and other somatic symptoms (using the Child Somatization Inventory) as a composite primary outcome. Parental perceptions were also assessed. No significant differences in abdominal pain or somatic symptoms were found between the 20 patients who underwent Web-based treatment over the 6 weeks compared with the 11 patients who underwent standard wait-list treatment commencing at 6 weeks. The Web-based psychological intervention was, nonetheless, associated with significant reductions in somatic symptoms among the adolescents from pretreatment to posttreatment ($p = 0.009$).[45] Moreover, the Web-based treatment reduced parent-reported somatic symptoms ($p = 0.021$) and was associated with a significant improvement in the parent-reported adolescent approach to general coping ($p = 0.006$), pain-specific coping strategies ($p = 0.005$), and parental irrational cognitions regarding their daughter's pain ($p = 0.048$).[45] The impact of eHealth interventions on psychological processes was also assessed by Elkjaer *et al.*, using the Hospital Anxiety and Depression Scale; however, no specific psychological intervention was undertaken. The Web-based intervention in 'Constant care' was associated with nonsignificant reductions in anxiety and depression (OR 1.6) at 12 months follow-up.[24] In their Web-based psychological intervention comparing computer-based cognitive behavioural therapy (CCBT) with standard-care, McCombie *et al.* assessed depression and anxiety using the Hospital Anxiety and Depression Scale (HADS), stress using the Perceived Stress Scale (PSS), and ability to cope using the Brief Coping Operations Preference Enquiry (Brief COPE) scale. Although there was no significant difference in each of these outcome measures at 12 weeks following completion of the intervention, at 6 months, the use of religion as an adaptive emotion-focused coping strategy reduced more in the standard-care group than in the CCBT group (F = 4.66, $p = 0.03$). Taken together, these data indicate that eHealth interventions may not benefit all patients

with IBD from a psychological view-point, particularly if they have comorbid baseline depression—patient selection may be an important factor in identifying which patients are most likely to benefit from Web-based psychological interventions.

3.4.2.4. Web-based interventions and other PROs
Fatigue and disability, which are considered important PROs in IBD, are yet to be assessed in eHealth interventions for IBD.[46,47] Although Elkjaer *et al*. demonstrated qualitative improvements in patient empowerment with their Web-based management compared with standard care, a validated measure of patient empowerment and engagement such as the patient activation measure was not used.[48] Additional PROs are required to assess IBD management within eHealth interventions as clinical measures of improvement in disease activity may not necessarily correlate with improvements in a patient's ability to perform daily activities.[49]

3.4.2.5. Correlating patient-reported outcomes with objective markers of disease activity in Web-based interventions
The majority of eHealth interventions for IBD rely on patients self-reporting their symptoms and mental well-being. However, PRO measures cannot be used exclusively to assess or manage a patient's disease activity using eHealth interventions. Objective markers of disease activity are, therefore, needed to corroborate which PROs are driven by disease activity and which symptoms may be functionally or psychologically related. Faecal calprotectin and routine blood tests (erythrocyte sedimentation rate [ESR], hemoglobin and albumin) have been the objective markers of inflammatory disease activity utilized in eHealth interventions, but data regarding the value of blood tests [including C-Reactive Protein (CRP)] in eHealth monitoring have not been reported. In their Web-based intervention, Elkjaer *at al*. undertook both serial FCs at fixed time-points and at symptom relapse (characterized by increased stool frequency and/or the presence of blood in the stool) and found that in the Danish group, 70% of Web-patients versus 78% of control patients had FC levels >50 µg/kg. In contrast, in the Irish group 45% percent of Web-based patients at baseline and 22% of Web-based patients at 6 months vs 45% of control patients had FC levels >50 µg/kg. Comparison between FC levels at baseline and at 12 months was not possible due to small numbers. Cross *et al*. did not report their use of objective markers of disease activity. In their Web-based study of UC patients, Pedersen *et al*. utilized a combination of SCCAI and weekly FC measurement to devise a total inflammatory burden score, which was then used to guide Web-based therapy. Remission was regarded as total inflammatory burden score of <2 [as denoted by a combined FC cut-off of <100 µg/g (0 points) together with an SCCAI score of 0–2.] Using such a score to step-up the 5-ASA dose resulted in an improvement in luminal disease activity as measured by FC, suggesting that combining SCCAI and FC is a feasible guide for Web-based therapy. A similar approach by Pedersen *et al*., using the HBI and FC to calculate an inflammatory burden index, was used in their Web-based study of CD patients. An FC level of <200 mg/kg was given a score of 0, and >200 mg/kg was given a score of 2. No difference in inflammatory burden score was found between baseline and end of follow-up, suggesting that FC may not be as effective in guiding Web-based intervention in patients with CD. Taken together, these results suggest that while FC may correlate with luminal disease activity in UC, the uptake of FC is variable among patients; the cut-off level of FC that correlates with true luminal disease activity with PROs in both UC and CD is yet to be determined.

3.4.3. Impact of Web-based management of IBD on other outcome measures

3.4.3.1. Web-based management and medication adherence
One of the main purported benefits of Web-based management is in its potential to improve medication adherence rates.[50,51] In their randomized controlled trial of Web-based patient management, Elkjaer *et al*. measured adherence rates using an investigator-developed compliance questionnaire (CQ). Although no statistically significant difference in adherence rates between the web and control groups was observed at 12 months, short-term adherence with acute treatment up to 4 weeks did improve significantly in the intervention arm in Elkjaer *et al*.'s study compared with the control arms [(73% versus 42% in Denmark, *p* = 0.005) (73% versus 29% in Ireland, *p* = 0.03)]. It was also noted that at the time of relapse, 100% of the Web-based intervention arm in the Danish group commenced treatment with high-dose 5-ASAs compared with only 10% in the control arm (*p* < 0.0001). Despite the increased adherence with high-dose 5-ASAs in the Web-based intervention arm in Denmark, only 15% of patients in the intervention arm in Ireland commenced high-dose systemic 5-ASAs compared with 10% in the control arm. In contrast to Elkjaer *et al.*, Cross and colleagues evaluated adherence using the Morisky Medication Adherence Score.[52] No significant difference was found between the groups in adherence rates at baseline (45% in the control group compared with 40% in the UC-HAT group, *p* = 0.71) compared with at 12 months (68% in the control group compared with 44% in the UC-HAT group, *p* = 0.10). Pedersen *et al*.'s mesalazine study (2014) reported that of 95 patients, 82 (86%) were adherent to 5-ASA therapy [according to the Medical Adherence Rate Scale (MARS) and a visual analog scale (VAS) using the Web], with a statistically significant difference in adherence by VAS and MARS at baseline compared with at 12 weeks [VAS median 88 (range 10–100) at baseline vs median 100 (range 60–100) at 12 weeks, *p* < 0.001; MARS median 23 (range 5–25) at baseline vs median 24 (range 15–25) at 12 weeks, *p* < 0.001]. Although adherence to drug administration of IFX was not directly measured by Pedersen *et al*., adherence to their Web-based program was observed in 86% of CD patients. McCombie *et al*. did not measure medication adherence; however, adherence to the psychologically based intervention was measured indirectly via an analysis of attrition rates. Although the rates of adherence have been inconsistent between studies, it seems that Web therapy can help to improve adherence to therapy in an acute flare of disease, when patients are regularly reminded via an eHealth intervention of the need to take 5-ASA medication. However, there may be Web literacy, and cultural and behavioral differences patients that influence adherence rates.

3.4.3.2. Web-based management and IBD knowledge
Patient knowledge and understanding about IBD is thought to play a key role in a patient's ability to be an active participant in his or her own management. The impact of Web-based management on patient knowledge about IBD has been assessed using a validated questionnaire, The Crohn's and Colitis Knowledge Score (CC-KNOW).[53] In the study by Elkjaer *et al*., Web-based management resulted in a significant improvement in patient knowledge in patients in Denmark (but not in Ireland) when compared to the control arm. Cross *et al*. only examined IBD knowledge using the CC-KNOW at baseline. There was no difference between the Web-based management group and the control group (*p* = 0.83). Assessment of UC-HAT literacy prior to study commencement took 30–40 min and was reported in a previous study by Cross *et al*.[54] Pedersen *et al*. (2012) demonstrated

a significant improvement in IBD knowledge in patients on IFX using 'Constant care' over the course of the study period, using CC-KNOW (17 at baseline vs 23 at Week 52, $p < 0.001$). However, neither Pedersen *et al.* in their mesalazine study nor McCombie *et al.* in their Web-based psychological intervention study measured IBD knowledge. Although not evaluated in all studies these data in combination indicate that IBD knowledge may improve following a Web-based intervention.

3.4.3.3. Web-based management and health care costs

Inflammatory bowel disease is associated with high direct costs due to its chronic, relapsing, and remitting disease course.[55–58] The cost-effectiveness of Web-based management has been evaluated in two studies to date. Elkjaer *et al.*'s Web-based management system resulted in a cost saving of 189 EUR/patient/year. Similarly, Pedersen and colleagues found a significantly lower cost of Web-administered IFX treatment per patient (11.502 EUR) compared with IFX treatment administered in the outpatient clinic (12.062 EUR) ($p = 0.001$). Web-based management has the potential to significantly reduce direct costs when replacing standard outpatient care.

3.4.4. Uptake rates in the Web-based interventions

The method used to invite patients to participate in Web-based interventions has varied among studies. Elkjaer *et al.*, who used letter-based invitations, reported that 50% of 485 invited patients did not respond to letter invitations to participate in the study. From 167 eligible patients, 113 refused to participate in the Cross *et al.* study after invitation by letter or during a clinic review. The reason for refusal was not specified. Pedersen *et al.* telephoned eligible UC patients and were able to recruit 95 patients from 120 eligible patients for the mesalazine study using telephone-based invitations. In Pedersen's IFX for CD study, 27 patients were eligible, and all were invited and enrolled in the study; however, the invitation method was not specified. The recruitment method employed by McCombie *et al.* involved direct invitation of adult IBD patients attending gastroenterology outpatient clinics. Reminders to participate in the study were then sent by email, text message, letter, and telephone call. Of the 589 patients who were assessed for eligibility, 227 were excluded due to time constraints, lack of reply to mail, or other unspecified reasons. A further 131 patients were ineligible for the study as per the inclusion and exclusion criteria, resulting in randomization of 231 patients. Patient engagement strategies were not described in any of the Web-based intervention studies. Of the methods used to invite patients to participate in Web-based intervention studies, a more personal invitation via direct face-to-face contact or a phone call to participate in the study seems to entice more patients to participate in and take up Web interventions compared with letter-based invitations.

3.4.5. Attrition rates in the Web-based interventions

Attrition is a phenomenon that has been observed frequently in Web-based management strategies and has the potential to reduce the effectiveness of the intervention.[59] Attrition rates have varied across the Web-based interventions trialed in IBD. In the Danish arm of the Elkjaer *et al.* study, 89/117 (76%) patients randomized to the Web intervention and 97/116 (84%) patients randomized to the control arm completed the study, whereas in the Irish arm of the study, 40/52 (77%) patients in the Web-based group and 38 of 48 (79%) in the control group completed the study. The 20% attrition rate was due to failure to attend the baseline visit ($n = 18$), change in diagnosis ($n = 6$), failure to meet the inclusion criteria after randomization

due to immunomodulator commencement ($n = 9$), change in location ($n = 9$), and refusal to participate ($n = 6$). Sample size calculations and expected attrition rates were not provided in the study by Elkjaer *et al.*; hence, it was difficult to appreciate to what extent the investigators allowed for the 20% attrition rate.

In the study by Cross *et al.*, of the 47 patients randomized in the study to Web-based management and controls, only 1 of the 22 patients in the control arm discontinued the study. Three patients in each group withdrew from the study after the baseline visit. Compared with the anticipated 10% attrition rate, a higher attrition rate of 44% (11 from 25) in the intervention arm was observed, with 8 patients discontinuing the intervention during the study period, possibly impacting on their results. Four participants were withdrawn by the research team because they were non-adherent with the weekly self-testing (administration of questionnaires regarding disease activity), two participants withdrew due to a change of mind about participating in the study, one participant withdrew due to moving abroad, and one participant developed a comorbidity during the study and was therefore withdrawn. The requirement for weekly self-testing and home installation may have contributed to this high attrition rate.

In Pedersen *et al.*'s study investigating Web-based management in IFX-treated patients, 4 of 27 were excluded from analysis due to nonadherence with the Web program pregnancy, or need for urgent surgery. Of 23 patients, 17 completed the 12-month follow-up and the remaining 6 patients completed at least 26 weeks of follow-up on the web portal. In Pedersen *et al.*'s mesalazine study, 86% of patients (82 of 95) completed the 3 months of web-guided therapy, with 12 patients noncompliant to Web-guided therapy and 1 patient becoming pregnant during the study.

Of the 131 patients randomized to the psychological intervention in the RCT by McCombie *et al.*, 113 completed the baseline questionnaires in the intervention arm compared with 86 participants in the standard care arm. Only 65/113 patients (57.5%) in the intervention arm and 78/86 patients (90.7%) in the standard care arm answered the primary outcome questionnaire at 12 weeks, with a greater number of patients in the intervention arm dropping out of the study in the first 12 weeks compared with patients in the standard care arm (42.5% vs 9.3%, $p = 0.048$). Fifty-three participants (46.9%) in the intervention arm and 66 participants (76.7%) in the standard care arm completed the primary outcome questionnaire at 6 months. The high attrition rate in the intervention arm was attributed to the lack of direct contact with a therapist, as has been demonstrated in previous on-line CBT studies.[60,61] Overall attrition in Web-based intervention studies appears to be a significant issue, with a number of contributing factors, including noncompliance or refusal to use the Web-based management program, change in disease activity, IBD subtype, patients' location, and a lack of direct contact in some studies with the health care provider.

3.5. Virtual Clinics in IBD

Virtual clinics refer to a planned contact that is generally prearranged between a health care professional and a patient for the purposes of clinical consultation, advice, and treatment planning, in lieu of face-to face contact.[62] It may also be referred to as a telephone contact, telemedicine, teleconference, or videolink and may integrate with a Web-based patient portal for the uploading of patient information and results.[62] The contact generally needs to be auditable (for health care delivery purposes and not administrative purposes).[62] Three VCs in IBD have been reported.[63–65]

3.5.1. Impact of virtual clinics in IBD on clinical indices of disease activity

Whilst evaluation of disease activity has not yet been reported in any of the VCs in IBD using conventional clinical indices, it has been evaluated indirectly. In particular, Johnson *et al.* measured the impact of their VC, IBD Supported, Self Help and Management Programme (IBD-SSHAMP), on disease activity by reporting the numbers of disease flares as an outcome measure.[63] After 3 years of IBD-SSHAMP, 550 of 2004 IBD patients have been transferred from the outpatient clinic to the Web-based management portal. Of the 550 patients managed using IBD-SSHAMP, 43 patients have flared, with only 16 patients requiring corticosteroids (most of which has been directed by telephone) and none of the patients have required hospital admission, suggesting that IBD-SSHAMP may be a feasible alternative for facilitating disease management in a cohort of stable patients.[63]

In contrast to IBD-SSHAMP, which integrates its VC with a Web-based patient portal, Hunter and colleagues in Southampton, UK, have devised a VC system for patients with an established diagnosis for >2 years, who have been stable for >1 year, who do not have primary sclerosing cholangitis, and who are willing to give their informed consent to be entered into the VC system. The impact of the VC on disease activity using conventional clinical indices has not as yet been assessed; however, screening for 'alarm symptoms' (such as presence of blood in stools, nocturnal symptoms and diarrhoea, together with gastrointestinal symptoms and need for medications such as steroids) is undertaken in order to assess the feasibility of remote management versus escalation to face-to-face outpatient visits. If stable, patients are reviewed face-to-face at a minimum of every 4 years in the clinic.[64] The Southampton IBD service has transferred 20% of their IBD patients from their standard outpatient clinic to their VC, thereby increasing the availability of clinic space for patients who require face-to-face contact. Whilst the impact of the VC system on disease activity remains to be demonstrated, it has freed up an estimated 400 outpatient clinic appointments over the course of a year for the management of patients who are either having a flare or who have complex disease.

3.5.2. Impact of virtual clinics in IBD on patient-reported outcomes

Evaluation of the impact of VCs on PROs has not yet been formally reported in the literature. However, the influence of VCs on patient satisfaction has been measured, despite its lack of validation as a PRO. In particular IBD-SSHAMP has recently been found to improve patient satisfaction, although the extent to which the latter has occurred compared with standard outpatient-led care is yet to be reported.[63] Similarly, Hunter *et al.* found that 90.9% of patients who responded to their follow-up questionnaire preferred the VC follow-up to traditional outpatient review, with 84.7% and 75.7% either agreeing or strongly agreeing that VC follow-up reduced interference with work and social life.[64]

3.5.3. Impact of virtual clinics in IBD on other outcome measures

Although the impact of VCs on adherence has not been assessed, there are preliminary data to support the preventive care aspects of IBD management and the cost-effectiveness of a VC. In particular, the Southampton VC provides a more structured reliable system for the efficient follow-up of patients on surveillance pathways, including surveillance endoscopy, and it ensures that the most up-to-date surveillance guidelines are observed.[66]

Virtual clinics have been demonstrated to be cost-effective. Johnson *et al.* found that their VC saved an estimated 130 000 pounds per year compared with traditional outpatient-led management.[63] On a personal level, Hunter *et al.* found that their VC reduced the economic burden to the individual, with 83% of patients reporting decreased personal cost of using the VC versus the traditional outpatient clinic.[64]

The impact of a VC on improving patient knowledge of their disease has not as yet been assessed. Nonetheless an alternative version of a VC, which seeks to enhance physician knowledge of IBD management via case-based learning, has been devised by Lichtenstein and colleagues.[65] However, its efficacy in improving clinician knowledge and, therefore, patient management is yet to be demonstrated.

Common themes among all the IBD VCs are their requirement for adequate integration of computer technology, a well-maintained database, and IBD nurse support. Preliminary data suggest that IBD VCs have the potential to reduce the demand on outpatient clinics and thereby save costs as well as improve communication between primary and secondary care providers. However, data regarding their efficacy has been limited to nonvalidated, qualitative patient questionnaires. Therefore their capacity to improve patient outcomes remains to be proven.

3.6. Telemedicine use in IBD

Telemedicine, a term coined in the 1970s, which literally means 'healing at a distance',[67] signifies the use of information and communication technologies (ICTs) to improve patient outcomes by increasing access to care and medical information. The terms 'telemedicine' and 'telehealth' can be used interchangeably.[68] Given that the Tele-IBD study by Cross *et al.* encompassed a Web-based interface, it has been described in detail in the Web-based intervention section. Three other telemedicine studies have been undertaken in IBD, including one RCT [25,26,69].

3.6.1. Impact of telemedicine in IBD on disease activity

With the exception of the Web-based telemedicine RCT undertaken by Cross *et al.*, the impact of telemedicine-directed intervention on disease activity outcomes has not yet been reported. Although baseline disease activity was measured by Hommel *et al.* (using the Partial HBI and the Pediatric UC Activity Index) and Krier *et al.* (using the HBI and The Ulcerative Colitis Disease Activity Index), disease activity was not used as an outcome measure for either study.

3.6.2. Impact of telemedicine in IBD on patient-reported outcomes

Patient-reported outcomes have not been formally evaluated in telemedicine interventions, other than in the Web-based telemedicine RCT undertaken by Cross *et al.* However, Krier *et al.* compared patient experience and satisfaction in 34 IBD patients who were randomized to telemedicine or standard care.[26] Patient satisfaction with telemedicine was rated highly, both by the patients and the clinicians, using a validated Ware Specific Visit questionnaire. Both groups rated the clinic experiences highly, with a mean rating of 1.2 ± 0.4 [telemedicine group (TE) 1.2 ± 0.4 vs standard care group (SE) 1.3 ± 0.5, on a 1–5 scale: 1 excellent, 5 poor; $p = 0.53$]. All major clinical satisfaction end points were similar between the two groups, including indices of attention to patient concerns (TE vs SE, 1.2 ± 0.4 vs 1.3 ± 0.7; $p = 0.63$), bedside manner (1.1 ± 0.2 vs 1.1 ± 0.3; $p = 0.83$), and perceived skill level of the doctor (1.1 ± 0.3

vs 1.0 ± 0; *p* = 0.2). The use of telemedicine in IBD resulted in a similar patient experience and satisfaction to standard outpatient-led care.

3.6.3. Impact of telemedicine in IBD on other outcome measures

Waiting time, appointment duration of the telehealth consultation, medication adherence, cost, and change of practice have all been evaluated in separate telemedicine studies.[25,26,69]

3.6.3.1. Telemedicine and wait time and appointment duration
Krier *et al.* compared wait time and appointment duration in telemedicine with that in standard outpatient-led care. No difference in wait time (TE 25 ± 25 min vs SE 18 ± 14.5 min; *p* = 0.31) or appointment duration (TE 60 ± 14 min vs SE 59 ± 10 min; *p* = 0.81) was identified between the two groups.[26]

3.6.3.2. Telemedicine and medication adherence and cost-effectiveness
Hommel *et al.* (2013) evaluated a telehealth pilot and feasibility clinical trial using an individually tailored treatment protocol depending on the patient's disease activity score and current medication regimen in nine adolescent patients with IBD. An increase in adherence from 62% to 91% for mesalazine, but a decreased adherence for immunomodulators (6-mercaptopurine/azathioprine) from 61% to 53% was observed after four weekly intervention sessions using the tailored telemedicine approach.[25] The telehealth pilot study by Hommel *et al.* was able to achieve a cost saving of USD $100 in mileage and 4 h of travel time per patient.[25]

3.6.3.3. Telemedicine and change of practice
A different approach to the use of telemedicine in IBD care was undertaken by Regueiro *et al.*, who evaluated the use of telemedicine to facilitate the multidisciplinary management of IBD patients across 11 institutions, using IBD Live Interinstitutional Interdisciplinary Videoconference Education (IBD Live) conferences (which hosted up to 73 participants).[69] Although participants overall responded positively in relation to whether the teleconference changed management, no other qualitative or quantitative data regarding the efficacy of the teleconference in facilitating patient management have been reported.

Although telehealth appears feasible and acceptable to some patients and physicians, due to the limited number of studies, their relatively small samples sizes, and heterogeneous outcomes, robust conclusions cannot be drawn about the effectiveness of telemedicine in IBD.

3.7. Other eHealth interventions in IBD

3.7.1. Mobile telephone applications in IBD
The extensive use of smartphones among young adults has raised the possibility that smartphone apps may provide a useful adjunct to the monitoring and management of patients with IBD. A recent systematic review by Con and De Cruz of the content and tools of 26 existing IBD apps (10 Android; 8 on iOS platforms; and 8 on both) found that while 14 of 26 apps (53.8%) had diary functionalities and 10 of 26 (38.5%) provided health information about IBD, none of the apps offered decision support for facilitating self-management, only 5 of 26 (19.2%) had professional medical involvement in their design, and only 37.5% provided complete coverage of international

IBD consensus statements.[70] Most apps do not offer management advice, but rather are applications for symptom logging, dietary reporting, medication reminders, and education. These apps may empower patients to self-manage their IBD, enable symptom monitoring, and improve adherence and knowledge; however, the current available apps are limited in professional medical input and lack of coverage of international consensus guidelines.[70] To date, there have been no prospective studies that have demonstrated the efficacy of mobile smartphone apps as a tool to facilitate self-management of IBD. However, two methods papers have reported on planned RCTs using smartphone apps to facilitate self-management.[71,72]

3.7.1.1. Impact of mobile telephone applications in IBD on disease activity
To date, nine mobile IBD applications have been reported to contain a symptom logging function; however, none have used validated clinical indices to measure disease activity and none have offered decision support.[70] Of the two studies that are planned to evaluate smart-phone apps for IBD, one study aims to use mobile telemedicine with a mobile telephone for patients as a management interface and a decision-support server and Web site for study coordinators.[71] Cross *et al.* aims to enrol 375 patients to compare disease activity (using the HBI and SCCAI), QoL (using IBDQ and SF-36), and health care utilization over 12 months in IBD patients who have had a flare of their disease in the previous 2 years, including steroid-dependent patients.[71] The participants will be randomized to standard care or one of two interventions consisting of weekly or every other week assessment of subjective disease activity and medication use, stratified by disease type and disease activity, with management advice via text message.

The utility of smartphone apps in corroborating disease activity by using FC as an objective marker has been recently reported by Vinding *et al.*, who compared a smart-phone FC kit to an ELISA-based FC kit in 221 patients (115 UC and 106 CD). The smartphone–based kit and ELISA-based kit correlated well (with a correlation coefficient of 0.685 with an optimal cut-off at 150 µg/g).[73] These preliminary data suggest that mobile applications in IBD can be combined with FC to objectively measure disease activity in IBD; however, further data are required to determine their utility for supporting self-management in clinical practice.

3.7.1.2. Impact of mobile telephone applications in IBD on patient-reported outcomes
Mobile telephone applications have not yet evaluated PROs. However, the two planned mobile applications for IBD (Cross *et al.* and Atreja *et al.*) will assess PROs in the form of QoL. In particular the planned RCT by Atreja *et al.* aims to determine the impact of the 'HealthPROMISE' app in improving a number of quality indicators (QoL, quality of care, patient adherence, disease control, and resource utilization) in IBD patients compared with a patient education application.[72] One hundred and fifty patients randomized to the 'HealthPROMISE' app arm will be able to update their information and receive disease summary, QoL scores, and resource utilization over time, enabling providers to collaborate with the patients in decision-making, using a unique cloud-based PRO tool.

3.7.1.3. Impact of mobile telephone applications in IBD on other outcome measures
Mobile telephone applications have not yet evaluated health care costs, IBD knowledge, or patient satisfaction. Although medication

tracking is currently available in eight mobile IBD applications, medication adherence has not been evaluated or reported. Ten existing applications provide health information about IBD; however, few of these applications have had medical professional input, and none have reported outcomes on patient knowledge. Although the future of mobile app utilization in self-management of IBD appears promising, further development and data are required to support their use as tools to facilitate self-management in clinical practice.

3.7.2. Social media in IBD

Social media in IBD is another eHealth tool that has the potential to promote patient engagement, communication, and education and may enable providers to better recognize patients' interests. A study on social media in IBD has been conducted by The University of California in Los Angeles, using a Twitter and Facebook profile page.[74] The study aimed to describe the strategies and experiences of an IBD tertiary referral center developing a social media presence among patients (using Twitter and Facebook) and its outcomes 12 months after establishing a Twitter and Facebook page for the center. After 15 months there were 2212 Twitter followers, of which 44% were IBD patients, and 469 Facebook 'likes'.[74] The most popular Retweeted Twitter topics were risk factors (70%), surgery (63%), and complications/symptoms (62%). The most favoured Twitter topics were about sex/fertility (92% liked), value in health care (90% liked), and therapies (91% liked). The Facebook posts that drew the most comments were posts on diet (2.7 comments per post, 67% commented on). Photographs were the lost 'Liked' media format of postings (7.9 Likes per photograph, 90% Liked). Social media in Twitter and Facebook appear to be valuable tools for enabling the IBD community to engage and communicate with each other. Although it is acknowledged that the Crohn's and Colitis Foundation of America and the Mayo Clinic have YouTube channels for individuals to obtain information about IBD, and that patients themselves have used, and continue to use social media such as YouTube to post videos, Facebook to set up IBD groups/discussion forums, and Twitter to express their everyday feelings and thoughts about IBD, there have been no other formalized studies to date evaluating the impact of social media on IBD outcomes.[75]

3.7.2.1. Impact of social media in IBD on disease activity

Disease activity was not evaluated as an outcome measure in the single study of social media in IBD. User preference in relation to privacy or desire to share personal information with their online community is likely to influence the extent to which social media is able to influence disease activity management.

3.7.2.2. Impact of social media in IBD on patient-reported outcomes

Patient-reported outcome measures have not yet been studied using social media, although the integration of PROs into Facebook and Twitter would appear to be feasible. Further data is required to validate 'Tweets', 'Retweets' and 'Likes' as potential PROs that may serve as indicators as to the extent to which patients engage with social media.

3.7.2.3. Impact of social media in IBD on other outcome measures

Medication adherence, IBD knowledge, and patient satisfaction have not been formally measured using social media. Although

data regarding social media in IBD management are currently limited, social media represents another eHealth medium that has the potential to disseminate information regarding IBD. Knowles *et al.* recently concluded that although through these media patients may develop a sense of normality and comfort because they can attract like-minded individuals, social media may facilitate misinformation about IBD and its treatment and, thus, cause distress. Hence the utility of social media needs to be weighed-up against its potential negative impacts. Furthermore, its potential to facilitate self-management in IBD remains to be seen.

3.7.3. Email communication in IBD

Email communication in IBD has the potential to assist in the management of IBD patients. Email communication has been studied in a small cohort (n = 74) in Toronto.[76]

3.7.3.1. Impact of email communication in IBD on disease activity and patient-reported outcomes

The impact of email communication in IBD on disease activity and PROs has not been assessed. Further studies are required to assess these outcome measures using email as a means of communication for IBD patients.

3.7.3.2. Impact of email communication in IBD on other outcome measures

Plener *et al.* assessed emails sent, hours lost from work, distance travelled, specialist clinic visits, hours taken per appointment, anxiety scale, and patient preference in their study on email communication in IBD. Seventy-six percent of email-managed IBD patients estimated that they made at least one to two fewer visits to the clinic due to email communication.[76] A majority (77%) of patients reported that email communication reduced stress levels regarding their IBD management, and 90% preferred a combined model of clinics and email rather than clinics alone.[76] Email is convenient, free, facilitates physician approval of self-managed actions, and reduces outpatient clinic waiting times, but it may result in misuse of information, and privacy concerns exist regarding confidentiality of patient information. Patients may also have an expectation that replies occur in a timely manner, which may be unrealistic given physician time constraints. Therefore, although email communication can be advantageous compared with regular outpatient reviews, the optimal use of email as an adjunct to clinical care remains to be demonstrated.

4. Discussion

This is the first systematic review to evaluate the entire spectrum of eHealth interventions used for IBD management.[37,77,78] The outcome measures used to evaluate eHealth technologies in IBD have been heterogeneous, which may reflect the dichotomy between what physicians prioritize in relation to disease activity and medication adherence and what patients prioritize, which seems to be convenience and QoL. Despite the heterogeneity of outcome measures, eHealth interventions appear promising and have been reported to facilitate the remote management of approximately 20% of patients in tertiary referral centers. EHealth interventions have produced consistent improvements in QoL. However, data regarding the impact of eHealth interventions on disease activity, medication adherence, cost-efficacy, and patient engagement and empowerment are either conflicting or lacking. Given their complexity, a considered and staged approach to the design, review, and implementation of

eHealth interventions ought to be undertaken before they can be recommended as tools to facilitate self-management.

4.1. Impact of eHealth interventions on clinical indices

EHealth interventions may have an impact on disease activity, but disease subtype and severity appear to be important factors in determining the extent to which patients benefit. Disease activity outcomes are limited to Web-based interventions alone.[23,24,27,28] The majority of the studies evaluating eHealth interventions have included patients with UC, as opposed to CD, most likely because the majority of patients with UC have less complex disease that is more amenable to (noncorticosteroid) induction therapy with 5-ASAs and is less likely to require immunosuppressive therapy, thereby limiting the need for physician intervention.[79–82] Disease severity at study inclusion also plays an important role in the feasibility and efficacy of eHealth interventions. A possible contributing factor to the negative outcomes in the Cross *et al.* study was the greater disease severity at baseline and higher rates of immunomodulator use in the Web-based intervention arm compared with the control arm. In contrast, Elkjaer *et al.* only included patients with stable disease and excluded those on immunomodulators or tumor necrosis factor (TNF) inhibitors. The efficacy of the Web-based intervention in Elkjaer *et al.*'s study in reducing time to relapse suggests that whilst the impact of Web-based interventions on disease activity may overall be modest, patients with stable, mild-to-moderate UC who do not require immunomodulators are those most likely to benefit from Web-based management in relation to their disease activity.

4.2. Impact of eHealth interventions on patient-reported outcomes

Patient-reported outcomes have become an integral patient of eHealth technologies and clinical trials because they quantify the impact of disease on patients beyond the effect of the disease activity alone.[41,83] Quality of life is the only PRO that has consistently been demonstrated to improve using eHealth Web-based interventions. The impact of Web-based interventions on QoL may be influenced by cultural biases, as demonstrated by the differences in outcomes between Danish and Irish patients in the study by Elkjaer *et al.*[24] The extent to which Web-based interventions impact on QoL also appears to be influenced by disease subtype, with improvements to date experienced by patients with UC, but not those with CD.[27] Baseline QoL scores also appear to influence the impact of Web-based interventions on disease activity.[23] The ability of eHealth interventions to improve patients' QoL appears promising but the impact of eHealth interventions on other PROs such as disability and fatigue is unknown and requires further evaluation.[83]

4.3. Relationship between patient-reported outcomes and objective markers of disease

Patient-reported outcomes cannot be used exclusively to assess or manage patients using eHealth intervention studies. The ability to distinguish between PROs driven by disease activity and those influenced by psychological distress is likely to ensure that drug- or psychology-based interventions are appropriately targeted to the patient's needs. Correlating PROs with objective markers of luminal disease activity in IBD is particularly important given the evidence demonstrating a poor correlation between symptoms and endoscopically identifiable disease activity.[84] A 'treat-to-target' strategy using FC [85] as a surrogate marker of luminal disease activity in order to maintain tight disease control has, therefore, been advocated as an optimal management approach for IBD.[83] Surrogate biomarkers of inflammation, including (CRP and FC, have been utilized in the eHealth setting[86,87]; however, the optimal cut-offs for CRP and FC that can be used to guide Web-based management are yet to be determined.

4.4. Cost-efficacy of eHealth interventions in IBD

EHealth interventions are often portrayed as a method of health care delivery that will reduce costs compared with standard outpatient base management.[88] However, the actual results of eHealth interventions are somewhat disappointing, sometimes increasing costs.[89] Health economics data for eHealth interventions in IBD are lacking. Although Elkjaer *et al.* and Johnson *et al.* have described cost savings from 'Constant care' and IBD-SSHAMP respectively, the cost savings described have related to the direct costs and not the indirect costs associated with implementation, maintenance, and quality improvement of the eHealth intervention, which are considerably large.[89] Further work to characterize both the direct and indirect costs associated with eHealth interventions is required in order to appreciate whether or not they are cost-effective.

4.5. Feasibility of eHealth interventions for self-management

The reliability of self-reporting of symptoms has been raised as an issue that may influence the accuracy with which eHealth solutions are able to facilitate self-management. The majority of eHealth interventions for IBD rely on patients self-reporting their symptoms and their mental well-being. Knowledge about the disease is considered to be an important factor in the accuracy of self-reported information, with greater IBD knowledge correlating with more accurate self-reporting.[90] Patient-reported outcome measures that quantify patient-reported qualitative data may overcome the limitations that patient knowledge may have on self-reporting.

4.6. EHealth interventions and evidence for self-management for a patient with IBD

EHealth interventions incorporate the principle of self-management. However, none of the eHealth intervention in this review has formally evaluated the impact of eHealth interventions on self-management using validated indices such as the patient-enablement instrument.[91] Self-management itself is defined as 'the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a chronic condition'.[92] Patient self-management in chronic disease has been found to promote a sense of well-being and, therefore, has the potential to optimize a person's ability to live as well as possible.[93] A positive patient/physician relationship has been shown to be a key factor in the success of guided self-management.[94,95] Tools that improve patient self-management and empowerment are also likely to be supported by funding bodies if they can be shown to reduce long-term disability and therefore improve IBD quality of care.[96] Given self-management can improve symptoms, psychological well-being, and health care utilization,[22] more evidence of patient empowerment, engagement, and self-care, using validated indices with eHealth interventions in IBD, should be sought to demonstrate improvements in self-management.

The success of an eHealth intervention relies on high adherence and small attrition rates.[59] Adherence to any specified intervention may be related to characteristics of the intervention, characteristics

of the user, or characteristics of the condition addressed by the intervention.[97] Characteristics of the intervention that may improve adherence include a strong theoretical foundation, perceived personal relevance to the user, perceived effectiveness, tailoring, frequency of data entry, persuasive technologies, credibility, social networking, and regular 'push factors', including human support and/or periodic prompts (e.g. by email or telephone).[97] There is no consistent known user characteristic that is associated with greater adherence to Web-based interventions. Although McCombie *et al.* found that patients with more severe disease and baseline depression appear to do poorly with eHealth psychological interventions,[40] it is unknown which patients do well with nonpsychological interventions. After its development, the success of an eHealth intervention depends on an adequate uptake of users. Elkjaer *et al.* demonstrated that a large proportion of patients were unwilling to participate in eHealth interventions, a finding that has been replicated in other chronic diseases where low uptake of eHealth interventions has occurred, despite considerable implementation efforts.[98] It therefore remains to be seen whether eHealth interventions have will adequate traction in patients with IBD to be of any practical use to facilitate care.

4.7. Models of design for eHealth interventions in IBD

Despite the efficacy of eHealth interventions in promoting behavioral changes, medical knowledge, self-management, and improving clinical outcomes, few efficacious eHealth interventions are adopted and sustained in real-world settings beyond the scope of the research project.[99] This may be due to the fact that many eHealth modalities are lacking a framework to enable the intervention to be effective as well as functional in the outpatient and inpatient setting. EHealth interventions can increase error rates if not well designed and implemented.[100] The lack of translation of some eHealth interventions into the real-world setting may be due, in part, to the use of predominantly explanatory (efficacy) research methods (which do not usually evaluate external validity) and to issues with limited reporting of intervention details (cost and contextual factors of implementation) that would allow for replication.[20,101] Further work is needed to determine why some interventions work and others do not. There may be certain demographic, psychological, or clinical factors that promote or inhibit success. Some behaviors or clinical problems may be more amenable to change by computer-based interventions.

The likelihood of adopting an eHealth solution successfully into real-world practice may be increased by applying a framework for planning, designing, evaluating, and implementing complex interventions.[97,102–104] This includes having a strong theoretical foundation, developing a proposed mechanism or pathway of action, ensuring that the evaluation adequately reflects this proposed pathway, and considering implementation from the beginning of the development process.[102,103] Resolving barriers to implementation, and understanding patients' resistance to change will ensure a more successful intervention that is effective, safe, technically robust, accessible, and usable. Therefore, designing eHealth tools from the ground up, rather than based on developers' preconceptions is recommended.[103] A phased approach should be developed for all interventions, starting with systematic reviews to identify the known literature, followed by theoretical work to establish an appropriate theoretical foundation. Modelling studies should follow to identify potential barriers to implementation and population impact, followed by qualitative studies to determine acceptability and feasibility, and finally pilot studies to optimize both the intervention and the trial parameters.

Only when both the intervention and the trial parameters have been developed should researchers proceed to a RCT to establish the effectiveness of the intervention. Both Cross *et al.* and Elkjaer *et al.* were able to demonstrate sequential phases in the development of their respective interventions. Evaluating performance at each of these phases is critical to the overall success of the intervention[105] and to ensure that these systems are safe, beneficial, and not a waste of scant resources.[106] The present systematic review confirms that theoretically informed eHealth interventions are more likely to be effective than those without a theoretical foundation.

A framework that integrates robust, clinical care models with emerging participatory care models may help refine the design, development, and implementation of future eHealth strategies and thereby overcome some of the issues that have been raised in this systematic review. A participatory health model of care should be informed by participatory design of the technologies employed by the eHealth solution.[107] Patients should be involved in all stages of the design process to ensure that the participatory health care model remains patient-centered and engaging to help mitigate the risk associated with attrition.[16] Participatory medicine principles, therefore, represent a good fit with participatory design approaches to technologies in health.[107] The collaboration on patients' health between patient and physician that underpins a participatory model of care should also involve a patient–physician partnership in the design and implementation of the eHealth intervention. Ultimately, the eHealth intervention should have a positive impact on two axes: the interaction between the patient and the eHealth interface, and the interaction between the patient and the physician.

5. Conclusions

EHealth interventions present unique opportunities to enhance chronic disease prevention and IBD management by increasing accessibility of the intervention and tailoring information and management to patients' needs. However, many eHealth interventions are lacking robust research data to prove the effectiveness of their implementation in the IBD setting. The evidence supporting eHealth interventions in IBD has been largely limited to studies that have included patients with mild-to-moderate disease severity with inconsistent improvements demonstrated in disease activity. Methodological shortcomings include heterogeneity of outcome measures, lack of clinician and patient input, lack of validation against conventional clinical indices and relatively limited cost–benefit analyses. Robust outcome data are required if we are to understand which modalities are most effective and which patients are most likely to benefit from eHealth technologies. The application of a framework for development, evaluation, and implementation of complex interventions, together with a greater use of theory could improve the efficacy and implementation of eHealth interventions. Extensive population-based clinical testing is then warranted to ensure that they not only function in clinical management, but are also useful tools that help enhance the experience of IBD patients as they participate in their self-management.

Conflict of Interest

BDJ has received educational support from Shire, Ferring, Norgine, and Janssen. SRK has received educational support, consulted on advisory boards

Author Contributions

PDC is the submission's guarantor. BDJ and PDC performed systematic review, drafting of the manuscript, and critical revision of the manuscript. KG and SRK performed critical review of the manuscript. All authors approved the final version of the manuscript.

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