University of Southampton

Faculty of Medicine
Primary Care and Population Sciences

Utilising new technologies and supported self-management to enhance the inflammatory bowel disease patient pathway: pilot, feasibility and development studies

by

Dr Nicola Taylor MBChB(hons) MRCP

Thesis for the degree of Doctor of Medicine

March 2020

University of Southampton

Abstract

Faculty of Medicine
Primary Care and Population Sciences

Thesis for the degree of Doctor of Medicine

Utilising new technologies and supported self-management to enhance the inflammatory bowel disease patient pathway: pilot, feasibility and development studies

by

Dr Nicola Taylor MBChB(hons) MRCP

Inflammatory bowel disease (IBD) is a lifelong relapsing/remitting condition. Early diagnosis and treatment can have a considerable impact on disease course and quality of life. Traditionally, IBD is managed in a specialist outpatient setting, however outpatient review may not always coincide with times of greatest need. The growth of eHealth technology has led to the development of new interactive self-management websites or 'portals' which allow remote self- monitoring and communication between patients and health providers. New diagnostic technologies for IBD are also becoming increasingly available. Faecal calprotectin (FC) testing can sensitively detect bowel inflammation and is used to aid diagnosis of IBD and predict disease flare in existing IBD. Recently, home-testing kits have been developed which, combined with a smartphone app, can provide rapid assessment of IBD activity.

The aim of this thesis is to present three projects which explore the development and use of new diagnostic and self-management technologies to enhance the traditional IBD outpatient pathway: piloting the use of FC testing in primary care and its impact upon general practitioners' plans to refer, assessing the feasibility and acceptability of using the My Medical Record (MyMR) digital patient portal and home FC testing for disease monitoring in patients who have stopped a treatment for IBD, and developing a digital Virtual Clinic for remote follow-up of more stable patients. These projects were informed by a systematic review of the literature exploring if interactive digital self-management interventions improve patient outcomes for IBD.

The primary care pilot study confirmed the clinical utility of FC testing as a screening tool when differentiating IBD from irritable bowel syndrome (IBS). It was observed that a negative calprotectin appeared to reverse a significant proportion of initial GP plans to refer to secondary care. In the feasibility study, recruitment was challenging but qualitative work demonstrated that home monitoring using MyMR and FC testing was acceptable and provided significant reassurance to a potentially vulnerable group of patients at greater risk of disease flare. A novel fully digital Virtual IBD clinic was established to oversee monitoring and support for more stable IBD patients. Normalisation Process Theory helped to reflect on barriers and facilitators to developing and implementing this new technology, particularly the need for greater engagement of key clerical and nursing stakeholders in the project. These studies explore how both FC and supported self-management via a digital portal have the potential to modernise and enhance key areas in the IBD patient pathway from diagnosis through to monitoring, but also highlight the challenges of implementing new technologies into established models of care.

Table of Contents

Table of Tables

Table of Figures

Author's declaration

I, Dr Nicola Sarah Taylor, declare that this thesis and the work presented in it are my own and has been generated by me as the result of my own original research.

Title of Thesis: Utilising new technologies and supported self-management to enhance the inflammatory bowel disease patient pathway: pilot, feasibility and development studies

I confirm that:

1. This work was done wholly or mainly while in candidature for a research degree at this University.
2. Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
3. Where I have consulted the published work of others, this is always clearly attributed.
4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
5. I have acknowledged all main sources of help.
6. Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.
7. None of this work has been published before submission.

Signed: 

Date: 19/11/2020

Acknowledgements

There are many people who supported me throughout my DM to whom I am extremely grateful.

I would like to thank my research supervisors: Dr Fraser Cummings, who inspired a passion for inflammatory bowel disease early on in my career – thank you for your enthusiasm and guidance over many cups of coffee. To Professor Sue Latter, for guiding me through qualitative research with such kindness and patience; and to Professor Hazel Everitt, for your endless encouragement and advice about managing work, research and family life. You have all given much of your time to help and support me to keep going and I am so thankful to you.

Thank you to all the nursing, research and clerical staff which make UHS IBD Team so wonderful. You gave me a home in your office during my research and spent so much time spent developing MyMR and the virtual clinic. You are all fantastic at what you do, and I am proud to have been part of your team.

To Jo Watts, Natalie Steel, Kevin Hamer and all the UHS IT team: thank you for all your help and positivity in developing MyMR – I hope that it continues to grow and develop into even more a of a fantastic resource for patients and staff alike.

Thank you to Graham Johnson at BioHit Healthcare for training me in using QuantOn Cal and providing supplies and technical support for the feasibility study.

Thank you to all the patients and healthcare professionals who kindly took part in all stages of the research and without whom none of this would be possible. You shared the trials and tribulations of life with IBD which I hope will give me the insight to make me a better doctor.

Lastly, to my family: to my wonderful husband Jamie for your love and good humour, and to Samuel and Beatrix, who are the best possible reasons for this thesis taking a little longer than planned – I love you.

Definitions and abbreviations

AHSN – Allied Health Science Network

ALT – alanine transferase

ALP – alkaline phosphatase

Anti-TNF – anti-tumour necrosis factor

API – application processing interface

ART – anti-retroviral therapy

ASCA – anti-Saccharomyces cerevisiae antibodies

BSG – British Society of Gastroenterology

CBT – cognitive behavioural therapy

CCG – clinical commissioning group

CCUK – Crohn's and colitis UK

CD – Crohn's disease

CDAI – Crohn's disease activity index

CDEIS – Crohn's disease endoscopic index score

CENTRAL - Cochrane Central Register of Controlled Trials

CI – confidence interval

CINAHL - Cumulative Index of Nursing and Allied Health Literature

CNS – clinical nurse specialist

CONSORT - Consolidated Standards of Reporting Trials

COPD – chronic obstructive pulmonary disease

CRP – C-reactive protein

CTE – computed tomography enterography

CTIMP - clinical trial of investigational medicinal product

DEXA – dual energy x-ray absorptiometry

DM – Doctor of Medicine

DNA – did not attend

ELISA – enzyme-linked immunoassay

EOW – every other week

ESR- erythrocyte sedimentation rate

FBC – full blood count

FC – faecal calprotectin

FHb – faecal haemoglobin

FIT – faecal immunochemical test

GCSE – general certificate of secondary education

GDE – global digital exemplar

GDPR – general data protection regulation

GI – gastrointestinal

GORD – gastroesophageal reflux disease

GP – general practitioner

GRIPP2-SF – guidance for reporting involvement of patients and public 2 – short form

GT – grounded theory

HADS – hospital anxiety and depression score

Hb – haemoglobin

HE – Professor Hazel Everitt

HRA – high risk adenoma

HRQoL – health-related quality of life

HTE – high telephone encounter

IBD – inflammatory bowel disease

IBS – irritable bowel syndrome

ICHOM – International Consortium on Health Outcome Measures

IFX – infliximab

iOS - Internet Operating System

IQR – interquartile range

ISRCTN - international standard randomised controlled trials number

IT – information technology

JFC – Dr J Fraser Cummings

kDa – kilodaltons

LOS – length of stay

MD – medical doctorate

MDT – multidisciplinary team

MeSH -medical subject headings

MIAH – monitor IBD at home

MRC – Medical Research Council

MRE – magnetic resonance enterography

MTX - methotrexate

MyMR – My Medical Record

NHS – National Health Service

NICE – National Institute for Health and Clinical Excellence

NPT – normalisation process theory

NPV – negative predictive value

NSAID – non-steroidal anti-inflammatory drug

NT – Nicola Taylor

NVQ – national vocational qualification

OD – once daily

OGD – oesophagogastroduodenoscopy

PBA – person-based approach

PC – personal computer

PCT - primary care trust

PDF – print-downloadable format

PGA – physician global assessment

PIC – patient-initiated clinic

PIL – patient information leaflet

PK – pyruvate kinase

PKB – Patients Know Best

POC – point of care

PPI – patient and public involvement

PPV – positive predictive value

PPRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROM – patient-reported outcome measure

QoC – quality of care

QoL – quality of life

RCT – randomised controlled trial

SCCAI - simple clinical colitis activity index

SES-CD – simple endoscopic score for Crohn's disease

SF36 – short-form 36

SIBDQ – short inflammatory bowel disease questionnaire

SL – Professor Sue Latter

SMS – short message service

SRQR – standards for the reporting of qualitative research

STT – straight to test

TECCU - Telemedicine Crohn's disease and ulcerative colitis

TIBS – total inflammatory burden score

TNF – tumour necrosis factor

TTG – tissue transglutaminase

UC – ulcerative colitis

UCEAI – UC endoscopic activity index

UC HAT – ulcerative colitis home automated telemanagement

UHS – University Hospitals Southampton

UK – United Kingdom

UKCRN – United Kingdom clinical research network

UKIBDQ – United Kingdom inflammatory bowel disease questionnaire

USA – United States of America

VAT – value-added tax

VC – Virtual Clinic

5-ASA – 5-aminosalycylic acid

µg/g – micrograms per gram

1 Introduction

This thesis presents three associated projects which explore the development and use of new diagnostic and management technologies to enhance current IBD outpatient care: from referral to secondary care, to disease monitoring and then longer term follow-up, with a focus on supporting patients to take greater control in managing their health.

This chapter introduces an overview of IBD, conventional care pathways from diagnosis to outpatient management, faecal calprotectin-monitoring, supported self-management in inflammatory bowel disease and other chronic illness, the My Medical Record digital self-management intervention that forms the basis of much of this research, and finally the structure aims of the thesis and research timeline.

1.1 Inflammatory bowel disease

Inflammatory bowel disease (IBD) (which includes Crohn's disease (CD) and ulcerative colitis (UC)), is a lifelong condition with an unpredictable relapsing-remitting disease course and wide-ranging severity. UC is characterised by inflammation and ulceration of the colon and rectum. CD can occur anywhere in the digestive tract and affects the full thickness of the bowel which may lead to stricturing and fistulisation to adjacent organs. The physical symptoms are extensive and may include diarrhoea, rectal bleeding, abdominal pain and fatigue.

Living with inflammatory bowel disease can be a significant challenge, both physically and psychologically. The physical and psychological burden of IBD results in reduced quality of life and most patients require medical attention throughout their lives. As a result, the lifetime medical costs are comparable to those of other major chronic diseases such as diabetes mellitus or cancer(2). Qualitative researcher(3) has identified fatigue, incontinence, body image, uncertainty about the future and lack of information from healthcare professionals as key concerns of patients that may contribute to poorer outcomes. Experience of stigma surrounding inflammatory bowel disease results in patients reporting a reluctance to disclose information about their illness, which can result in feelings of isolation and exclusion(3).

UC and CD have a UK prevalence of approximately 240 and 157 per 100,000 people respectively(4). The UK incidence of inflammatory bowel disease is approximately 10 per 100,000 population per year(2). IBD care poses significant annual costs to the NHS (National Health Service) of up to £470 million(2). There is no cure, and treatment is aimed at maintaining disease

remission and early treatment of disease 'flare-ups'. Flare-ups represent a period of increased symptoms due to uncontrolled inflammation and must be recognised and treated promptly to reduce the risk of significant complications including the need for surgery. Disease remission may be demonstrated by improved symptom scores, biochemical indices such as C-reactive protein or faecal markers such as calprotectin, as well as by endoscopic or radiologic appearances.

The diagnosis of inflammatory bowel disease can be challenging, especially in cases with mild clinical activity or significant overlap with the functional symptoms of irritable bowel syndrome, which may lead to underestimation of the underlying disease by patient and physician. Delays to diagnosis of IBD are common - in a large online survey of almost 5000 patients with IBD, 20% of Crohn's patients received a diagnosis 5 years after symptomatic disease onset, with consequent impairment in their quality of life(5). Delays are more marked in patients with Crohn's disease compared with UC, which may be due to the wide range of potential symptoms(6). In contrast, the frequent symptoms of rectal bleeding in UC patients can be perceived as more alarming and may lead to earlier referral to a physician. The length of diagnostic delay directly correlates with an increased risk of bowel stenosis and Crohn's-related intestinal surgery(7). Delay to diagnosis in both CD and UC can lead to reduced quality of life(6) and increased extent and severity of disease can impact upon future colorectal cancer risk(8). Early treatment and mucosal healing are associated with improved clinical outcomes in both CD and UC and therefore strategies for improving time to diagnosis are very important for IBD patients(9, 10).

1.2 Disease classification and activity

The gold standard for diagnosis of inflammatory bowel disease is with endoscopic (usually colonoscopy) and histological examination. Ulcerative colitis (UC) may be differentiated from Crohn's disease by continuous extension of bowel inflammation from the rectum to more proximal bowel. Up to 3% of patients with ulcerative colitis demonstrate 'rectal sparing' more typically seen in Crohn's disease(11). The presence of a 'caecal patch' (isolated caecal inflammation discontinuous with more distal disease) or 'backwash ileitis', found in 20% of patients with extensive colitis can also cause diagnostic uncertainty(12). Multiple 'mapping biopsies from the rectum to the terminal ileum(13) are recommended to obtain a diagnosis, and small bowel imaging should be used to exclude Crohn's disease in the event of any uncertainty. No single histological feature is pathognomonic of UC(14), but the combination of diffuse crypt atrophy and distortion, villous surface irregularity and mucus depletion favour a diagnosis of UC. By contrast, Crohn's disease is characterised by discontinuous segments of disease known as 'skip lesions', Ileal involvement, more proximal disease, and the presence of granulomata(14). In 5–

15% of IBD patients, a differentiation between CD and UC cannot be made, and thus a classification of IBD-unclassified (IBD-U) is given(15).

Both UC and CD affect different areas within the gastrointestinal tract and typical patterns allow for phenotypical classification which helps to guide treatment and categorise for research purposes. UC may be classified phenotypically using the Montreal classification(16) which grades disease based upon extent (proctitis/left-sided disease/extensive) and severity (remission/mild/moderate/severe). There are numerous disease activity scores for UC including the Mayo Score(17) (combined clinical and endoscopic assessments), partial Mayo score(18) (non-invasive), and endoscopic indices such as the Ulcerative Colitis Endoscopic Activity Index(19) (UCEAI). Crohn's disease is also widely classified using the Montreal classification(20) which uses age at diagnosis, disease location, disease behaviour (non-stricturing or penetrating /stricturing/penetrating/perianal). CD activity may be measured using the Crohn's disease activity index(21) (CDAI)with a score of <150 suggesting remission. It has a number of limitations which include the need for a significant amount of data entry, a focus on diarrhoea (not always a feature for some patients) and it is not validated in patients post-surgery or those with stomas. The Harvey Bradshaw Index(22) (remission <4) also tends to focus heavily on diarrhoeal symptoms. Although well-validated, such scoring tools do not always consider the impact of IBD on quality of life and increasingly patient-reported outcome measures (PROMs) are being used clinically and in a research context. Disease may also be scored endoscopically – indices such as the Crohn's Disease Endoscopic Index of Severity(23) (CDEIS) and the less complex Simplified Endoscopic activity Score for Crohn's disease(24) (SES-CD) are both reliable markers of disease activity. The Rutgeert's score(25) is used specifically to assess the neo-terminal ileum endoscopically post-surgical resection.

1.3 Investigation

1.3.1 *Endoscopic and radiological investigation*

Ileocolonoscopy is utilised for both diagnosis and assessment of IBD activity. In Crohn's, up to a fifth of patients may have isolated small bowel disease not identified by ileocolonoscopy therefore it is important to consider cross-sectional imaging such as magnetic resonance enterography (MRE) and computed tomography enterography (CTE)(26) to identify more proximal disease. Small bowel ultrasound is an increasingly utilised diagnostic tool with diagnostic equipoise compared with CTE and MRE and a high sensitivity and specificity of 85-95%(27). Upper GI Crohn's is less common in adults and its usually present in conjunction with lower GI disease(28). Nonetheless, it has been reported in as many as 13-16% of patients with CD(29) and

oesophagogastroduodenoscopy (OGD) is therefore important in patients presenting with upper GI symptoms. Capsule endoscopy provides detailed images of small intestinal mucosa not accessible by standard endoscopy and is well-tolerated by patients(30). Data suggest capsule endoscopy is superior to MRE at detecting small bowel inflammation in Crohn's disease, particularly for proximal or superficial small bowel lesions(31), although a 2017 meta-analysis did not find any statistically significant difference in diagnostic yield between MRE and capsule endoscopy(32).

1.3.2 *Serum markers of IBD*

Patients presenting with GI symptoms should receive testing for full blood count (FBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and coeliac disease antibody testing(33). Other serum markers such as leucocyte, platelets and albumin can also suggest disease. Increased CRP levels are associated with better treatment response rates in IBD and normal CRP levels predict high placebo response rates in clinical trials with biologicals(34). CRP is however non-specific and can be elevated in conditions other than IBD, and normal inflammatory markers may not exclude endoscopic disease activity.

Antibody tests have the potential to aid diagnosis and different diagnostic antibody markers have been targeted for study. Autoantibody pANCA (perinuclear anti-neutrophil cytoplasmic antibody) has been detected in up to 70% of UC patients, whilst microbial antibodies such as ASCA (anti-saccharomyces cerevisiae antibody) anti-Omp C antibody, Anti-Cbir1 antibody and Anti-I2 antibody have been detected in 55-70% of patients with CD(35). None of these markers are in routine use in the investigation of IBD but are exciting areas for further study of non-invasive means of diagnosing IBD.

1.3.3 *Faecal markers of IBD*

1.3.3.1 Faecal Calprotectin

In recent years, the development of non-invasive faecal markers of intestinal inflammation such as faecal calprotectin (FC) has enabled physicians to stratify risk of significant pathology such as IBD and reduce unnecessary investigations and referrals to secondary care. FC-testing is recommended by NICE (National Institute of Health and Care Excellence) to help differentiate between IBS and IBD in adults with recent onset lower GI symptoms for whom specialist assessment is being considered(36), where cancer is not suspected, and locally agreed care pathways are in place.

FC is a reliable, non-invasive marker that detects histological inflammation in the bowel and has clinical utility in diagnosing IBD, monitoring, and informing treatment decisions. In pooled meta-

analyses, it has high sensitivity and specificity of 93% and 96% respectively(37). In some circumstances it can be elevated prior to the onset of clinical symptoms, making it a very useful tool for monitoring in IBD(38). Although sensitive, FC is not specific to IBD and can be elevated in other conditions such as infection and malignancy(38), which must be considered when interpreting results.

There is no clear international consensus on what constitutes an elevated faecal calprotectin which may be in part due to inter-assay variability. Generally, when used in primary care to identify patients with altered bowel habit who require colonoscopy for possible IBD, use of the upper limit of the 'normal range' for assays (usually 50 μg/g) as the threshold for referring for colonoscopy, may result in large numbers of unnecessary procedures. Several authors, including NICE, have therefore proposed the use of an intermediate calprotectin, ranging between 50 to 200 μg/g(39). NICE recommend that thresholds should be set based upon local audit data and quality assurance processes. There is a need to balance sensitivity and specificity. A higher threshold will result in fewer investigations but increase the risk of missing IBD cases. Specificity may be improved by repeating FC testing for patients in the indeterminate range(40). FC is discussed in more detail in Chapter 4.

1.3.3.2 S100 proteins

S100s are a family of 25 proteins involved in a diverse range of functions controlling degenerative, inflammatory and neoplastic processes. Calprotectin, mentioned above, is a heterodimer composed of two S100 proteins. The 3 components of the S100 family involved in IBD are also known as calgranulins as they can bind calcium and are secreted in granulocytes(41). Calgranulins are very specific to bowel inflammation as they are produced by the inflamed tissue itself as opposed to another organ (for example C-reactive protein is produced by the liver).

S100A12 (calgranulin C) is a calcium-binding cytoplasmic protein expressed by granulocytes and secreted by activated neutrophils. It is a chemoattractant of monocytes, macrophages and neutrophils. S100A12 can be measured in both serum and faeces. High sensitivity (96% to 97%) and specificity (92% to 100%) have been reported for S100A12 in differentiating IBD from normal gut(41). Although very sensitive, there are several limitations to S100A12. As with FC, S100A12 correlates poorly with small bowel disease on capsule endoscopy(42). It is nonspecific to IBD—with levels also being elevated due to other illness such as infection (elevated levels may be seen in viral or bacterial gastroenteritis, diverticulitis, polyposis, colon cancer, celiac disease and immunodeficiency) as well as increased age, obesity, and physical inactivity(41).

1.3.3.3 Lactoferrin

Lactoferrin is neutrophil-derived protein secreted from mucosal surfaces and may be found in most body fluids including serum and synovial fluid(43). Like calprotectin, it is stable at room temperature for several days(44). It is antimicrobial and appears to have both pro- and anti-inflammatory properties. A meta-analysis of faecal lactoferrin as a biological marker in IBD found that the sensitivity and specificity were lower than FC for detecting active inflammation (80% and 82%), which may explain a lack of more recent research into its clinical utility(45). Lactoferrin has also been shown to be useful in identifying pouchitis in patients with ileo-anal anastomosis(46). As with FC, there is a stronger correlation between UC activity and lactoferrin than in Crohn's disease(47). No additional diagnostic benefit was conferred in studies where faecal calprotectin and lactoferrin were combined(45).

1.3.3.4 Dimeric Pyruvate kinase

Pyruvate kinase (PK) is a glycolytic enzyme present in normal cells as tissue-specific isoenzymes (liver pyruvate kinase in liver, M1-PK in muscle and brain etc.) These isoenzymes exist as tetramers, but in rapidly dividing cells a dimeric form has been described (M2-PK). Cell turnover is increased in the GI tract of patients with IBD and hence M2-PK has been studied as a marker of IBD. M2-PK has been reported to have a sensitivity of 73% and a specificity of 74% for the identification of organic disease and had significant correlation with faecal calprotectin (r=0.7)(48). In a paediatric study faecal M2-PK had a sensitivity of 71% and a specificity of 97% for distinguishing between children with IBD and those without any detectable pathology(49).

1.3.3.5 Faecal haemoglobin

The faecal immunochemical test (FIT) is a quantitative faecal occult blood test used to screen for colorectal cancer. It can measure the concentration of haemoglobin (Hb) in faeces and, consequently, the amount of blood from the injured intestinal mucosa by using a specific antibody against human haemoglobin(50). A small study demonstrated a significant difference in faecal Hb between active and inactive disease in 26 CD patients and 36 UC patients ($P < 0.01$)(51). FIT can be used as marker of mucosal healing and endoscopic activity. Nakarai et al(52) showed that a negative FIT was able to predict mucosal healing in a cohort of 152 UC patients with 92% sensitivity and 71% specificity. Inokuchi et al(53) assessed FIT in a cohort of 71 patients with CD and showed a significant correlation of FIT with endoscopic activity ($r = 0.54$) comparable with that of FC ($r = 0.67$), but not in patients with small bowel lesions alone ($r = 0.42$ and 0.78). The sensitivities of FIT and FC for predicting mucosal healing were similar (96% and 87%, respectively), but FIT was less specific (48% and 71%, respectively), particularly in patients with disease limited

to the terminal ileum (40% and 80%, respectively). As with FC, FIT may rise 1 to 2 months prior to clinical disease relapse in a proportion of patients(54).

1.3.3.6 Summary

Although numerous biomarkers continue to be explored, faecal calprotectin appears to have the best overall sensitivity and specificity in a wide range of applications and is now widely commercially available, making its use in clinical and research settings widespread. Alternative markers (e.g. FIT, lactoferrin) showed a high sensitivity and specificity and correlated with disease activity, response to therapy, and mucosal healing, with potential utility in the prediction of clinical relapse. Variability in their accuracy in assessment of intestinal inflammation suggests the need for further studies.

No single measure gives the complete picture in IBD. In practice, a combined approach encompassing patient-reported outcomes, clinical scoring tools and more objective measures such as stool markers, serum indices and endoscopic assessment should be used to guide diagnosis and treatment decisions(13).

1.3.4 *Medical therapies for IBD*

Patients with IBD require long-term treatment to maintain control of their disease. In the event of a disease flare-up, patients may require short-term treatment with oral (or intravenous) corticosteroids. The high side-effect profile (both short- and long-term) of steroids means they are not suitable for longer term treatment of IBD. Treatment goals are therefore aimed at achieving 'steroid-free' disease remission where possible using one or a combination of medications.

1.3.4.1 5-ASA

5-Aminosalicylic acids (5-ASA) (mesalazine and sulfasalazine) are the mainstay of treatment for patients with mild UC. Aminosalicylates reduce gut inflammation by moderating the release of a variety of lipid mediators, inflammatory cells and cytokines from gut epithelial cells(55). They can be administered either via controlled-release oral tablets or sachets, or topically to the distal bowel via enemas and suppositories. Sulfasalazine intolerance can occur in 10-45% of patients and is dose dependent. Mesalazine is better tolerated, but diarrhoea, headache, nausea or rash still occur in up to 15% of patients(13) which can lead to patients stopping treatment. All aminosalicylates are associated with an increased risk of nephrotoxicity (interstitial nephritis and nephrotic syndrome). Patients should therefore have yearly renal blood tests(56).

1.3.4.2 Immunomodulators

Patients with moderate to severe IBD usually require treatment with an immunomodulator medication (thiopurines such as azathioprine and mercaptopurine, or methotrexate), and/or anti-TNF medication (infliximab, adalimumab etc.). Thiopurines modulate the immune system by inducing T cell apoptosis(57) and are useful for both inducing and maintaining steroid-free disease remission, and preventing the formation of antibodies against biological agents. They commonly cause flu-like symptoms, and there is a risk of more serious side effects including profound leucopenia, hepatotoxicity and pancreatitis. Methotrexate (MTX) metabolites inhibit dihydrofolate reductase and cytokines, exerting an anti-inflammatory effect. Side effects lead to drug discontinuation in 10-25% of MTX treated patients(58). Symptoms most often include gastrointestinal upset, but more serious hepatotoxicity and pneumonitis may also rarely occur. Patients established on these medications are required to undergo blood monitoring at least every three months(13).

Thiopurines are known to increase the risk of non-melanomatous skin cancers(59). In the largest case-control study conducted thus far on lymphoma and IBD (80 lymphoma patients and 159 matched controls), immunosuppressive therapy was associated with an increased the risk of lymphoma (OR 4.20, 95% CI, 1.35–13.11, p = 0.01). Decisions to continue treatment must take this small but important risk into account. Average 1-year relapse rates for UC patients stopping azathioprine or mercaptopurine (for patients in remission) have been observed at 53% (range 35%–77%)(10), with average rates in CD patients of 38% (range 21%–41%), therefore the need for recognition of increased disease activity and retreatment is high.

1.3.4.3 Biologics

In recent decades biological agents have had a huge impact on the maintenance treatment of patients who have moderate to severe IBD and have a vital role in the management of acute severe disease. Infliximab and adalimumab are well-established and commonly prescribed anti-TNF medications with a UK licence to treat moderate to severe Crohn's not responding to conventional treatment. Infliximab is a chimeric anti-tumour necrosis factor alpha (TNFα) monoclonal antibody typically administered every 8 weeks and requires a 1–2 hours infusion in a hospital day unit. Adalimumab is a recombinant human immunoglobulin anti-TNFα monoclonal antibody and by contrast is usually self-administered subcutaneously every fortnight by the patient in their own home. In recent years more biological treatments have become available with Golimumab (UC), Vedolizumab (CD and UC) and Ustekinumab (CD and UC) licenced to treat moderate to severe UC or Crohn's(13) in the UK. Golimumab is also an anti-TNF but current data

comparing the relative efficacy of infliximab, adalimumab and golimumab is conflicting. Vedolizumab is a gut-specific monoclonal antibody that binds specifically to the α4β7 integrin which is expressed on gut-homing T helper lymphocytes and causes a reduction in GI inflammation and therefore has reduced systemic immunosuppressant effects. Ustekinumab is an antagonist of the inflammatory p40 subunit of interleukin-12 and interleukin-23 and may be used in induce and maintain remission in both UC and CD. Tofacitinib, a janus-kinase inhibitor given in tablet form, also has a place in therapy where other biological medications have failed(13) but has an increased risk of venous thromboembolism which patients must be counselled about. It is not uncommon for patients to require multiple different biological treatments and close monitoring is essential to establish safe monitoring and assess treatment response.

Biologic use has grown rapidly in recent years. At the time of writing, over 500 patients were receiving biologic therapies for IBD in Southampton General Hospital, compared with just 90 patients in 2010(13). Biologics are costly, ranging from £5,000 to £20,000 per patient annum. NICE recommend that treatment should be reviewed at around 3 months' post-induction of therapy to assess for primary treatment response, and again at 1 year to ensure appropriateness of ongoing treatment. If evidence of non-response, treatment should be stopped. An audit of biologic practice at Southampton General Hospital(60) showed that 165 patients had their biologic treatment discontinued over 3 years for reasons including lack of efficacy, side effects as well as patient's being in deep remission.

The long-term safety of these medications has been questioned due to a risk of serious side effects including infection, infusion reactions and increased risk of cancer but there is insufficient data to make definitive recommendations on when/in whom to stop treatment(61). Risks of stopping treatment include potentially serious disease flare-ups and difficulty reinstating treatment with anti-TNF medications due to the development of anti-bodies against them. Decisions to stop treatment are usually base upon a combination of clinical symptoms, endoscopic and radiological findings, and patient preference, and must be based upon a risk-benefit analysis. Relapse rates are significant - the STORI study(62) of 115 patients with luminal Crohn's disease found relapse rates of 44% one year following cessation of infliximab.

There is a huge amount of literature on the role and effectiveness of these medications which is beyond the scope of this introduction. For all IBD treatments, there is a need for systems to support patients in both monitoring the effects of continuing/stopping medications to detect disease relapse early and ensure prudent prescribing.

1.3.5 *Surgery for IBD*

Over 50% of patients with Crohn's Disease will undergo surgery within 10 years of diagnosis, and over 70% may require surgery during their lifetime(13, 63). Total lifetime surgery rates in UC may be as high as 20-30%(64). Surgical options vary depending on disease extent and location. In most cases, clear indications for surgery are medical treatment failure or disease complications, but decisions regarding the precise timing and specific procedure required are often difficult. In Crohn's disease, the pan-enteric nature of the disease leads to significant recurrence rates post-surgery, but in UC, a colectomy (with eventual completion proctectomy) can be curative(65).

1.4 Conventional outpatient pathways for IBD

Lower gastrointestinal (GI) complaints are a common indication for presentation to general practice and it can often be difficult to differentiate between symptoms of irritable bowel syndrome (IBS) and IBD. Where clinical suspicion of organic pathology is high (particularly if 'red flag' symptoms such as weight loss, anaemia, and raised inflammatory markers are present), referral to secondary care should be made. Patients with suspected IBD should be referred urgently for assessment and seen by a secondary care physician with a specialist interest in IBD within 4 weeks(13) but only 73% of UK gastroenterology services report seeing all urgent referrals within 4 weeks. Only 30% had guidance in place to help local GPs identify and refer suspected IBD cases.

Colonoscopy is traditionally the investigation of choice to distinguish between IBD and IBS but can be an invasive and unpleasant procedure for patients. IBD is an independent risk factor for colonic perforation even when adjusted for age, sex, endoscopic dilatation and other comorbidities, and perforation rates are estimated to be almost tenfold(66) in IBD populations compared with healthy populations. The financial costs are considerable, with an NHS tariff of at least £474 for a diagnostic colonoscopy with biopsy(36).

Once a diagnosis of IBD is established, follow-up comprises regular (at least yearly) outpatient appointments with a specialist physician or nurse(13). To maintain remission, most patients with IBD receive medication indefinitely and are monitored by a specialist. Sometimes drugs may be stopped due to side effects, patient preference or disease remission, but there is a high (up to 50%) risk of disease relapse when drugs are stopped in patients with more severe IBD(67). Complex patients need close outpatient monitoring but the unpredictable relapsing/remitting nature of IBD and pressures on outpatient resources mean that it is difficult to coordinate outpatient review with the periods of greatest need. As NHS resources are becoming increasingly

stretched, finding ways of optimising diagnosis and longer-term management of IBD are vital to improve patient experience and outcomes.

In a bid to relieve outpatient pressures and avoid inconvenience to patients, local experience has led to the development of the Southampton Virtual IBD Clinic. Patients with an established IBD diagnosis are entered onto the Virtual Clinic (VC) database and sent a yearly blood test and postal questionnaire. If these suggest active disease, patients telephone the IBD specialist nursing team on a dedicated 'Flareline'. Approximately 15-20% of IBD patients at University Hospital Southampton NHS Foundation Trust are followed up using this method, freeing up over 400 clinic appointments a year to be used by more complex patients or those experiencing a disease flare(68). This is discussed on more detail in Chapter 7.

It is recognised that there could be improvements in time to new diagnosis of IBD and IBD flares. At UHS, direct access IBD-physician delivered flexible sigmoidoscopy in established IBD patients (following call to an IBD flareline) has been recently established. Changing the model of service delivery combining IBD physician delivered endoscopy with proactive management decisions resulted in a change of management in 84.9% of patients. This reduced overall IBD follow up outpatient appointments by 52.2%(69). Although 'straight-to-test' flexible sigmoidoscopies are often arranged for appropriate new gastroenterology referrals, this is dependent on the practitioner vetting the referrals and there is no standardised process in place.

The IBD Standards for care of patients with IBD(2) recommend strategies to improve outpatient care, including supporting patients in self-management when appropriate, as well as the need for clear pathways and protocols between primary and secondary care (including the use of faecal biomarker tests in primary care) to aid rapid diagnosis (Appendix A.1).

1.5 Point of care and home faecal calprotectin monitoring

As faecal calprotectin is increasingly established in both the diagnosis and monitoring of IBD, new ways of delivering this technology to patients and providers are being explored. In 2017 NICE appraised the new technology of point of care (POC) and home-use faecal calprotectin testing, across 6 studies with a total of 558 patients and found comparable accuracy to ELISA laboratory testing, with greater patient satisfaction for both(70). The cost of point-of-care and home-use faecal calprotectin tests varies, ranging from £23.25 to £85.85 per unit (exclusive of VAT), and although expensive, the cost could be offset if their use reduces colonoscopies and clinical appointments. Point of care tests come as single-use, disposable kits which are usually used with

a dedicated, reusable reader (connected to a computer) and are delivered in a healthcare setting. The tests use lateral flow immunoassays specific to FC.

Home-use tests allow patients with established IBD to monitor their own FC levels and transmit the results directly to their healthcare professional. Most home-use tests need a smartphone with camera, and generally consist of a stool sample collection kit, a sample extraction tube, FC extraction solution, the test plate, a smartphone camera calibrator and a smartphone app to interpret and transmit the results. To use the tests, the user logs into an app on their smartphone. A stool sample is collected, a small sample of which is placed into an extraction tube with some extraction solution. The tube is agitated, and 1 or 2 drops of the sample are released from the sample tube (by turning a lever or squeezing the tube) onto the test plate. The test is left to develop, and the smartphone camera is used to capture an image of the completed test. The app interprets the test and provides the user with the test results and transmits them to a healthcare professional if needed. The test itself takes 10 to 15minutes to complete.

There are currently 4 tests on the market for at-home calprotectin testing (Table 1). Point of care tests such as Quantum Blue® (Buhlmann), Calprosmart® Office (Calpro) and Calfast® (Eurospital) are also available but are operated in a healthcare setting by a trained professional.

Table 1: Available home faecal calprotectin test kits

Test	Manufacturer	Range
IBDoc®	Buhlmann	Range 30 to 1,000µg/g. Can be presented in a traffic light rating scale with patient-specific thresholds established by the clinician
Calprosmart®	Calpro	Range 70-1500µg/kg
QuantOn Cal®	Biohit	Range 25-2000µg/g
Cal Detect®	Biohit	Semi-quantitative Range 50µg/g or 200µ/g

In a UK study (abstract poster presentation), Parr et al(71) conducted a prospective single-centre pilot study 54 adults with IBD (23 people with CD and 31 people with UC). IBDoc® FC was monitored monthly at home for a 4 month period and compared with laboratory ELISA (Buhlmann) results. Strong positive correlation of numerical FC results was reported between the

2 methods (r=0.77, p<0.0001). 63% of respondents preferred using IBDoc® for routine testing, provided with the assurance that they could obtain contact from their designated healthcare professional within 1–3 days of receiving an abnormal IBDoc® test result. A further 22% preferred the IBDoc® test and stated that they did not think further contact before their next scheduled appointment was necessary.

In a larger 2016 study, Vinding et al(72) compared CalproSmart ® (home use and POC) against standard ELISA at 2 different laboratories (Buhlmann and Calpro). 221 adults with IBD (115 with UC and 106 with CD) participated in a prospective, single centre randomised control trial in Denmark. CalproSmart® had reasonably high sensitivity and specificity (82% and 85% respectively). Educational status appeared to be linked to a significant difference in the correlation between results: CalproSmart® completed by people with postgraduate degrees aligned more significantly with the laboratory ELISA test. This could suggest that some users found the home testing more difficult. A significant limitation of the study was that tests were performed in an outpatient clinic simulating a home environment with patients using a phone provided by the researchers and not their own.

El-Matary et al(73) examined point-of-care and home faecal calprotectin tests for monitoring treatment response in inflammatory bowel disease in 77 children with IBD in a retrospective single-centre study in Canada. They compared the use of Quantum Blue® (POC) testing against standard monitoring practice, including ESR, CRP and clinical outcomes. Monitoring was mostly non-invasive with only 12% of children having colonoscopy, the gold standard for diagnosing active disease. 86% of abnormal FC tests resulted in a treatment change that significantly improved clinical outcomes. 83% of children with normal FC measurements demonstrated maintained remission on follow-up 3–6months later. 88% of treatment decisions were based solely on FC testing. The children were prescribed a range of different medications and the performance of FC testing across different treatment regimens was not discussed. Unlike most of the literature, in this study, FC testing did not correlate with CRP.

Heida et al(74) presented a comparison of IBDoc® (home testing) and Quantum Blue® (POC) with laboratory ELISA (Buhlmann) in 101 children (over 10 years) and adults in a prospective single-centre comparative study in The Netherlands. Correlation was 0.94 for results obtained by IBDoc® versus Quantum Blue and 0.85 for IBDoc® versus ELISA. Discordant test result pairs (IBDoc® versus ELISA or IBDoc® versus Quantum Blue®) that could potentially lead to different treatment outcomes occurred in 6 of 152 stool samples (4%). 87% of respondents (only 62% responded to

invitation) surveyed said the test was not difficult and 97% were interested in using the home test in the future.

Ungar et al(75) published a poster abstract of 52 adults with CD in a prospective, single-centre study, in Israel in 2017 therefore limited information about study design is available. They compared IBDoc® (home-use, under guidance from trained personnel therefore not performed independently) and Quantum Blue® (POC). There was a strong correlation between results for both assays ($r=0.924$, $p<0.0001$). Level of education or age did not significantly influence the correlation between tests results ($r>0.92$, $p<0.0001$, for both comparisons). However, in 27 out of 52 tests the difference in quantitative result of the paired tests was more than 25%.

More recently, Haisma et al(76) performed a head to head comparison study of three at-home smartphone calprotectin tests (IBDoc®, QuantOn Cal® and CalproSmart®) and companion ELISA tests (fCAL, IDK-Calprotectin and Calprotectin-ALP) to establish if measurement pairs agreed sufficiently. Medical students (albeit without any specific laboratory training) carried out the home tests thus study conditions did not truly replicate standard home use by patients. The primary outcome of the study was test agreement (defined as percentage of paired measurements within predefined limits of difference). 1440 smartphone readings and 120 ELISA tests were performed. In the low calprotectin range (≤500 µg/g) IBDoc®, QuantOnCal® and CalproSmart® showed 87%, 82% and 76% agreement with their companion ELISAs. In the high range (>500 µg/g) the agreement was 37%, 19% and 37%, respectively. Whilst these levels of agreement for the lower range are acceptable in terms of prompting a referral for investigation of IBD, a lack of agreement for the higher ranges could have significant implications for monitoring of IBD. This study reinforces the importance of staying within manufacturer when performing serial calprotectin measurements.

Puolanne et al(77) conducted a 12 month prospective randomised controlled trial evaluating home monitoring with a rapid semi-quantitative faecal calprotectin test (CalDetect®, Preventis) combined with a quality of life questionnaire in patients with colonic IBD in a real-life setting. They randomized 180 patients to study and control groups. The home monitoring patients performed the faecal calprotectin test and filled in a symptom questionnaire every second month and in cases with increasing symptoms. The control patients filled in the symptom questionnaire at baseline and at 6 and 12 months as well as for the appointment at the outpatient clinic. Just 38% of the study group and 20% of controls continued the study for 12 months. Patients were not sent reminders or prompts to complete monitoring which could explain why adherence to the self-monitoring program was low. Patients with a higher disease burden were more adherent

than patients with better health-related quality of life. Although there were no significant differences in disease course between groups, the home monitoring group had fewer contacts with the hospital outpatient department which may free-up resources to be used for more unstable patients.

In 2017 Bello et al(78) conducted a small usability study of home faecal calprotectin testing in 58 patients with IBD. They measured FC levels using smartphone technology CalApp (IBDoc®) (as well as ELISA lab FC) every 2 weeks for the 8 weeks study period and filled usability questionnaires (System Usability Scale (SUS: 0–100) and the Global Score of Usability (GSU: 0–85)). 42 patients (72%) of recruits completed at least one FC measurement and 47% all FC tests. The testing demonstrated good usability (even at first use) with a median (interquartile range; IQR) SUS at the first and last use of 85 (78–90) and 81 (70–88), respectively; the median (IQR) GSU at the first and last use were 74 (69–80) and 77 (68–83), respectively. Adherence to the planned measurements and usability of the tool were higher in females and in less severe disease. The intra-class correlation coefficient between home-based and centrally measured ELISA FC was 0.88.

Wei et al(79) also evaluated the performance of the IBDoc® home testing system in 51 patients with IBD in clinical remission and obtained their feedback as an objective patient-reported outcome. FC in the same stool sample was assessed by using both the laboratory test (Quantum Blue® calprotectin test) and home test (IBDoc®). Semi-quantitave correlation between the 2 tests was good: by using 250 μg/g as the cut-off, the agreement between home test and laboratory results was 80%, and by using 600 μg/g as the cut-off, the agreement increased to 92%. In addition, the patients were asked to fill a questionnaire based on their experience. After the test, just 56% patients reported finding IBDoc® easy to perform, but 96% were satisfied with it. It should be noted that the app is in English, the second language to the Taiwanese participants, which may have been a factor in usability. 80% reported strong (>70%) probability to use it for future monitoring if the price was acceptable.

In 2019 Ankersen et al(80) examined whether an eHealth assessment for disease activity in IBD should be scheduled every third month (3M) or on demand (OD), according to patient preference. Disease activity was assessed using home measured the CalproSmart® FC smartphone application and a disease activity score (SCCAI or HBI) giving a combined total inflammatory burden score (TIBS). 88 (86%) patients completed the study (n = 43 3M; n = 45 OD). No statistical differences were detected in either group for compliance, fatigue, quality of life scores, mean time in remission and overall FC relapse rates. Both patient directed and routine scheduled screening

were equally good in recognising relapse and the patient directed OD screening used fewer home test kits per patient and could be argued as therefore more cost-effective.

In addition to the above studies there are several studies registered on clinicaltrials.gov that appear to be ongoing:

- Home-based Faecal Calprotectin Measurements (IBDoc®) Predicting Adalimumab Induction Destiny (HELP-AID) (ClinicalTrials.gov identifier: NCT02634060). The study appears to be ongoing and is currently recruiting according to clinicaltrials.gov and the University of Gent website.
- Home Versus Postal Testing for Faecal Calprotectin (IBDoc®): A Feasibility Study (ClinicalTrials.gov identifier: NCT02542917. Remains unpublished.
- Are Rates of Colectomies, Resections, Mortalities and Cancer Reduced by Home Monitoring of IBD Patients (Calprosmart®) (ClinicalTrials.gov identifier: NCT03038984. Appears to be ongoing and currently recruiting as a side arm of a wider study of home monitoring of IBD with completion expected in 2026.

In summary, there are several point-of-care and at-home faecal calprotectin test kits commercially available. Inter-assay variability amongst FC test kits was frequently observed and it is therefore important to ensure consistency when measuring FC and to use the same assay over time to ensure reliability. Test kits are expensive, but it is possible that these costs can be offset through a reduction in invasive procedures such as colonoscopy and outpatient appointments. There may be a place for targeting their use in 'at-risk' patients who are more likely to experience disease flare and/or require early intervention. Patient compliance with home-testing seems to be variable and further work is needed to explore this.

1.6 Supported self-management

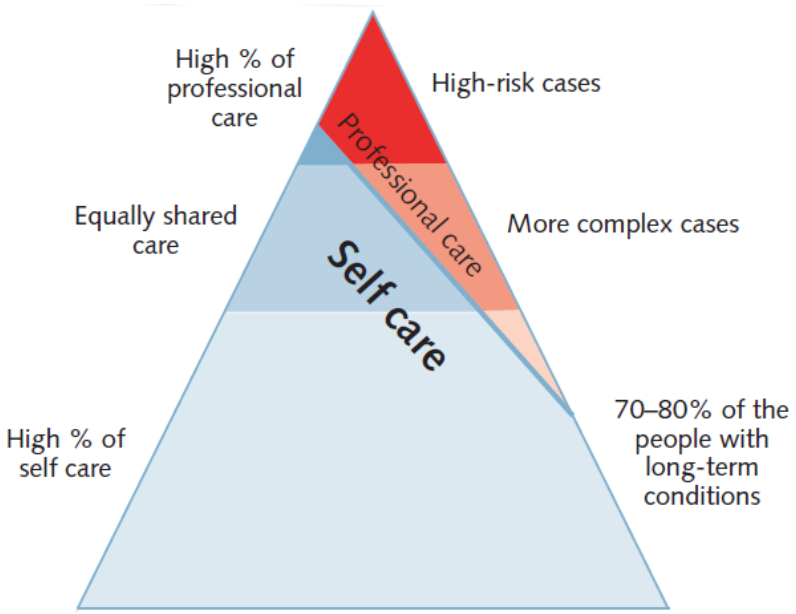
Over recent decades, there has been a considerable shift from traditional outpatient-based management of chronic diseases towards an appreciation that patients themselves do most of the day-to-day management of their chronic disease, are now actively encouraged to take on greater responsibility for their care. The concept of self-management evolved during the 1960's and 70's alongside the widely recognised self-help movement which arose through changes in societal values about people's responsibility for their health and well-being(81). Since then, a large body of evidence regarding its use in many chronic diseases has been collated.

Self-management has been defined as "the individual's ability to manage the symptoms, treatment, physical and psychosocial consequences, and lifestyle changes inherent in living with a

condition(82)". Audulv(83) established 3 key principles of supported self-management (SSM) that guide this process. Firstly, despite being due to different pathological processes, chronic diseases often share a common set of consequences or symptoms, for example pain or fatigue. Secondly, people with chronic conditions should be active partners in the management of their disease. And finally, in order to be an active manager of their health, patients need to have the relevant skills, information/resources and the confidence to use them. Self-management may not be appropriate for all patients due to a number of factors such as complex disease, vulnerability, mental health problems, and limited language skills/understanding(84). Other patients may simply prefer a traditional management approach, favouring regular contact with their health provider.

A key theoretical model that describes the overall impact of a long-term condition on people's lives and sense of self is the Corbin and Strauss model(85) which describes three areas of work required by those affected: illness work, everyday life work, and biographical work. This leads to three areas of self-management: medical management (e.g. remembering to take medications regularly, managing healthcare appointments, eating healthily and exercising, and stopping harmful behaviours such as smoking or drinking; emotional management (e.g. managing the many cognitions and emotions of chronic disease such as anger, fear, anxiety); and role management (e.g. managing the biographical disruption and changes to identities and roles required by living with a long-term condition), with all three areas being equally essential. Self-management interventions can provide strategies to remediate the effects of these impacts and is becoming an increasingly important part of how we manage chronic illness (Figure 1).

Figure 1: Empowering and enabling patients to take control (Source: Department of Health)



There is a wealth of literature on supported self-management (SSM) covering many different chronic and recurring conditions. The most prevalent topics appear to be diabetes mellitus, asthma and chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, congestive cardiac failure, recurrent urinary tract infections, multiple sclerosis, irritable bowel syndrome, and even physiological conditions such as pregnancy and its associated symptoms. The unifying factor in most of these conditions appears to be their chronicity and variability, i.e. the "acute-on-chronic" episodes. Many of these conditions share similar symptoms such as pain or fatigue, therefore there are lessons to be learned for SSM in inflammatory bowel disease. Skills and techniques can be used interchangeably between chronic conditions. Self-management employs a broad range of techniques and skills and literature is available regarding the use of patient initiated clinics, self-help manuals and groups, patient education programmes, illness "guidebooks", telecommunication (telephone, email, remote monitoring), internet tools, websites, virtual clinics, mobile phone messaging and applications, and even alternative strategies such as hypnotherapy. Several of these methods are often used simultaneously in research interventions.

1.6.1 *Patient-initiated clinics*

Patient-initiated clinics (PICs) are one of the simplest forms of SSM and may be scheduled by the patient according a self-determined need for clinical input. They are particularly pertinent to

relapsing diseases such as rheumatoid arthritis and IBD. As well as the cost benefits of minimising non-attendance at hospital appointments, they are more responsive to patients' needs during disease fluctuations. UK patient surveys have found that scheduling an appointment at a convenient time is more important to patients than speed of access, unless they are presenting with a new health problem(86). PICs have been studied in primary care and have had mixed findings. A systematic review(87) of 24 studies examined advanced access scheduling in the primary care setting. All but two of these (both UK studies) were based in the United States of America (USA). Only one was a randomised controlled trial. 8 of these studies evaluated and showed a reduction in time to the third-next-available appointment (range 1.1-32 days), but only 2 of the trial interventions successfully achieved a third-next-available appointment in less than 48 hours. Time to third-next appointment is a measure used to reduce bias in determining waiting times as it excludes appointments made available by last-minute cancellations (usually first or second next available) and gives a more accurate overview of expected waiting times. Longer waiting times in primary care may explain why out of the four studies examining overall patient satisfaction, only 1 reported statistically significant improvements.

There have been several UK studies comparing PIC in secondary care with routine, clinician-led follow up systems. The most common disease groups studied were rheumatoid arthritis and inflammatory bowel disease. Like IBD, rheumatoid arthritis has periods of painful flare up and a responsive clinic service can be beneficial. In the largest randomised controlled study in in rheumatoid arthritis, Hewlett et al(88) assessed the impact of patient-initiated direct access clinics. After 6 years, there was only one significant difference between the two groups in clinical outcomes measured (deterioration in range of movement in elbow was less in direct access patients), however satisfaction and confidence in the system were significantly higher in the direct access group at two, four, and six years. Patients in the direct access group had 38% fewer hospital appointments ($P < 0.0001$) and there were no significant differences between groups for median change in psychological status, suggesting that deviation from the traditional follow up approach did not have negative effects on psychological wellbeing.

There have been three studies incorporating the use of PICs in IBD, all UK-based. Williams et al(89) conducted a pragmatic randomised controlled trial assessing the impact of outpatient follow up of patients with inflammatory bowel disease through open access compared with traditional outpatient follow up on health related quality of life, total resource use, and patient and general practitioner preference. No differences were detected in generic or disease specific quality of life between the control and intervention groups. Open access patients had fewer outpatient visits (4.12 vs 4.64 per patient per year, $P<0.01$), but some patients had difficulty

obtaining an urgent appointment. There were no significant differences in specific investigations undertaken, inpatient days, general practitioner surgery or home visits, drugs prescribed, or total patient-borne costs. Mean total costs in secondary care were lower for open access patients ($P<0.05$), but when primary care and patient-borne costs were added there were no significant differences in total costs. Overall, general practitioners and patients preferred the open access strategy.

Not all the studies solely examined PIC but incorporated a few other SSM strategies. In one of the most pivotal guided self-management trials in recent decades, Robinson et al(90) randomised 203 UC patients to receive either traditional outpatient follow-up or an intervention comprising patient-centred self-management training and outpatient follow up on request. Patients were given personalised self-management plans developed with their consultants to follow in the event of a disease flare. They were also provided with a telephone helpline number to call for advice and requested to initiate a clinic appointment if self-treatment had not resulted in symptom improvement within 7 days, if symptoms relapsed upon treatment cessation, if they required more than 2 courses of steroids within a year, if they exhibited any “red flag” symptoms (unexplained weight loss or rectal bleeding between flares), or if at any time they wanted a consultation. The combination intervention reduced both the number of primary care (0.3 vs 0.9 per patient per year) and hospital visits (0.9 vs 2.9 per patient per year) and had no detrimental impact upon quality of life scores. Disease relapses were treated more promptly in the intervention group with a mean time to treatment of 14.8 hours vs 49.6 hours in controls (difference 34.8 hours, 95% CI 16.4-60.2).

Kennedy et al(91) used patient-initiated clinics as part of a comprehensive randomised controlled trial assessing the use of a self-help guidebook and patient-centred consultation on disease management and patient satisfaction in 700 patients with IBD. Guidebooks on ulcerative colitis and Crohn's disease were developed with patients prior to the study. Patients were issued with this disease-specific guidebook and together with physicians prepared a written self-management plan to follow in the event of a disease flare, and self-referred to clinic based upon self-evaluation of their need for medical input. After 1 year, the intervention resulted in fewer hospital visits (difference −1.04 (95% CI −1.43 to −0.65); $p<0.001$), with no change in the number of primary care visits. Patients felt more able to cope with their condition. The intervention did not reduce quality of life (QoL) and did not raise anxiety levels. The intervention group reported fewer symptom relapses and 74% of these patients preferred the patient-initiated system indicating good acceptability.

Widespread adoption of the PIC approach would require significant changes to the way outpatient clinics are run in the UK. Physicians would need to be willing to accept the shift in responsibility that comes with patients acting as self-managers. All three studies reported clinician satisfaction with the new system. Equally, patients need to be comfortable with the intervention but would also need to recognise their limitations in managing their disease, particularly in complex cases of IBD. Outpatient clinics would require considerable reorganisation to accommodate appointments at short notice, requiring the cooperation of clerical and clinical staff to make this work. The costs of this restructuring would be more than compensated by the cost-savings of reduced overall outpatient attendances(91). What is not yet clearly evident from these studies is whether PICs can affect the clinical course of IBD and alter disease outcomes, and this is an area for future study.

1.6.2 *Patient education and guidebooks*

In many chronic diseases such as diabetes, asthma, and hypertension,(92-94) patient education has been shown to improve patient lifestyle behaviour and drug adherence, which in turn can decrease disease complications and health resource use. Patient education is an important aspect of SSM and is as an integral part of most self-management interventions. Patients can often be dissatisfied with information given to them, particularly in time-pressured clinic situations(95). The results of educating patients are very positive, although it should be considered that for some patients, particularly in serious or chronic disease, an increased knowledge of their disease can actually lead to higher levels of anxiety and lower QoL initially(95). The provision of written information has been proven to be a key factor in conveying information to IBD patients and can aid decision-making(96).

There have been several studies based upon the provision of information and education of patients with irritable bowel syndrome (IBS) in order to promote self-management of symptoms. Ringstrom et al(97) randomised 143 patients with Rome-II criteria IBS in primary and secondary care to receive an IBS education booklet or partake in a structured education programme called 'IBS School' consisting of 6 weekly sessions led by health professionals (nurse, gastroenterologist, physiotherapist and psychologist). Those in the IBS School intervention group displayed statistically significant improvements in IBS knowledge (74 vs 40 on visual analogue scale at 6 months, $P < 0.001$) compared with the booklet intervention group. Gastrointestinal specific anxiety levels improved, but not IBS QoL scores or anxiety and depression.

Saito et al(98) conducted a larger study of 298 patients referred to a tertiary gastroenterology clinic with IBS. Patients took part in a single educational class conducted by professionals on

gastrointestinal physiology, diet and exercise, stress management, breathing and muscle relaxation techniques. The study was not randomised, and no primary outcome measure was identified. Patients were instead compared with a cohort of 46 patients who did not attend the class. Overall, 29% of class attendees who met Rome criteria for IBS at baseline no longer met these criteria at follow-up, compared with 7% of non-attendees, suggesting a symptomatic benefit. The educational intervention was associated with improvement in health-related behaviours (measured using the Health-Promoting Lifestyle Profile scores; $P < 0.05$) but not with change in pain, quality of life, patient satisfaction, or health care utilisation.

In a randomised controlled trial of self-help interventions in 420 patients with a primary care diagnosis of irritable bowel syndrome, Robinson et al(99) compared the use of an IBS guidebook or the guidebook plus a "self-help" group meeting against usual care. Use of the guidebook resulted in a 60% reduction in primary care consultations ($p<0.001$) and also a reduction in perceived symptom severity when compared with the control group ($p<0.001$).The self-help group did not confer any additional benefits. Although self-help groups have been shown to be beneficial in supporting self-management in a wide range of chronic diseases(100), some patients may find it embarrassing to discuss symptoms regarding bowel habit in a public setting. Others may prefer the more anonymous environment of online forums.

Patients with IBD tend to feel inadequately informed about their disease(101). One important consequence of not providing patients with sufficient education is medication non-adherence, crucial to successfully controlling IBD. Reported rates of medication non-adherence range between 43 and 72% among patients with IBD(95). The most common reasons cited for non-adherence in IBD are resolution of symptoms, thereby assuming medications can be stopped, and adverse drug effects, both of which may reflect inadequate IBD-related knowledge. Patient education has been demonstrated to be successful in increasing treatment adherence(102, 103), an important aspect of self-management. Patients who have a better understanding of their illness are less likely to report psychological distress and have fewer disease-related concerns(104).

A Canadian randomised controlled trial by Waters et al(104) assessed the effects of an educational intervention (pamphlet plus ad hoc physician education) versus standard care in 69 IBD patients. IBD knowledge and QOL were assessed at baseline, immediately after education and eight weeks later. Participants documented medication adherence and health care use in personal diaries. The education group had higher knowledge scores ($P<0.001$) and patient satisfaction ($P=0.001$). There were lower rates of medication non-adherence and health care use in the

education group, although these differences were not significant. No changes in QoL indices were observed. As expected from previous study, significant correlations were found for increased health care use in patients with poorer medication compliance.

Kennedy et al(105) developed a dedicated guidebook for ulcerative colitis in conjunction with patient groups. The guidebook was a culmination of patient experiences including information patients with IBD felt they most needed, evidence-based medicine, and input from healthcare professionals including physicians, specialist nurses, pharmacists and dieticians. Guidebooks were individualised using personal disease information and self-management plans. The concept of individualised information is particularly important in IBD given its highly variable nature across time and individuals. Educational interventions which have an individualised behaviour modification element are more likely to be successful in changing behaviour in chronic disease compared with structured programmes(106). The results of the cluster RCT showed that patients using the guidebook demonstrated significantly better knowledge of their ulcerative colitis at 1 month, which persisted at 9 months, than patients in the control group. Anxiety and QoL scores were unchanged throughout, although encouragingly, findings at 9 months of follow up suggested than overall improvements in quality of life may occur over a longer time period.

1.6.3 *Telemedicine*

Telemedicine is the provision of healthcare services through use of information and communication technology. It encompasses a variety of amenities such as telephone advice lines, email communication, and videoconferencing between health professionals and/or patients and has expanded hugely in recent decades. More recently it has taken the form of email and web-based systems, which are fast overtaking more traditional methods.

Telephone interventions play a key role in the outpatient management of chronic disease. The advent of the specialist nurse role has advanced this area and patients now have a key health professional to contact when guidance is necessary. Telephone communication is utilised informally to communicate rapidly with patients and allows a two-way interaction between patient caregiver and can therefore facilitate self-management. Ramos-Rivers et al(107) conducted a prospective study examining patterns of telephone encounters between patients and nurse co-ordinators in a tertiary IBD centre. Approximately half of the 54,646 calls over a 2-year period (mean 10.5 calls per patient) were initiated by patients. 15% o of patients were stratified into the High Telephone Encounter (HTE) group (>10 calls per year). Factors associated with HTE included female sex, patients with Crohn's disease, greater number of previous IBD surgeries, steroid use, elevated inflammatory markers, opiate use, psychiatric comorbidities and chronic

abdominal pain. Anti–tumour necrosis factor (anti-TNF) use was associated with HTE for CD but not for ulcerative colitis. Not surprisingly, HTE patients were more likely to have a diminished quality of life defined by an S-IBDQ score of less than 50 compared with low telephone users. Interestingly, the investigators assessed that patients who had 8 or more telephone encounters in a month were four times more likely to be hospitalised than patients with only one telephone encounter. This finding has applications in the use of self-management interventions. The use of a "red flag" system for these patient subgroups or repeated contact with support services could serve as a safety net for self-managers to enable extra vigilance and prompt recognition and treatment of those who are deteriorating.

In chronic heart failure, patients can suffer relapses and worsening of symptoms that can often require inpatient treatment. A systematic review by Clark et al(108) examined the literature comparing remote monitoring programmes for heart failure in the community versus usual care. They included several telemonitoring interventions (daily transmission of pulse and blood pressure observation, weight, and symptoms at various time points to healthcare providers) and structured telephone consultations. Of 14 trials, remote monitoring programmes reduced chronic heart failure hospital admission rates by 21% (95% CI 11% to 31%) and all-cause mortality by 20% (CI 8% to 31%). These improvements can be explained by the early detection of clinical deterioration by telemonitoring and rapid medical intervention, and by early recognition of deterioration by an experienced nurse at the end of the telephone with prompt intervention. Of the six trials evaluating health related quality of life three reported significant benefits with remote monitoring, and of the four studies examining healthcare costs with structured telephone support three reported reduced healthcare costs and one had no effects on costs. The authors selected only studies which used a "structured" telephone consultation approach, i.e. a system of scheduled telephone appointments as opposed to an "as needed" basis as dictated by the patient, so is perhaps less of a self-management approach than some other systems. Both approaches would be highly applicable in inflammatory bowel disease.

A very large, randomised quality improvement trial of over 174,000 subjects in the USA(109) assessed the effects of a telephone-based self-management strategy on resource utilization and medical costs. 'Health coaches', comprising specialist and non-specialist nurses, dieticians, respiratory therapists, and pharmacists, contacted subjects with chronic medical conditions as part of a usual care programme. The intervention group received 'enhanced support' by way of greater attempts to contact the patients by telephone (5 versus 3 attempts in the usual care model). Subjects were then given coaching on a number of areas such as medication regimes to aid adherence, to explain and reinforce any discharge instructions after recent hospital stays, to

help motivate patients to make behavioural changes, and to engage in shared decision-making. At baseline, medical costs and resource utilization were similar in the two groups. The cost of this intervention program was less than $2.00 per person per month. After 12 months, 10.4% of the enhanced-support group and 3.7% of the usual-support group received the telephone intervention. The average monthly medical and pharmacy costs per person in the enhanced-support group were 3.6% ($7.96) lower than those in the usual-support group ($213.82 vs. $221.78, P = 0.05); a 10.1% reduction in annual hospital admissions (P<0.001) accounted for the majority of savings. Although US healthcare models differ from the UK, the intervention may be transferable and the potential total cost savings significant.

Email correspondence is considered a form of telemedicine and is universally used in professional and personal contexts however little has been published in the context of gastroenterology. There are a number of benefits to using email to support self-management(110) including enhanced convenience, improved documentation and provision of an audit trail of encounters, improved specialist availability for non-urgent communications, cost-savings, reduced ecological impacts, and 'freeing up' of clinic resources for more complex patients. There are potential disadvantages to email communication. Patients and physicians have concerns about privacy and misuse of sensitive information. There may be also be issues surrounding the potential for increased workload, financial burden of setting up such a system, difficulties in placing a financial value on the new workload, potential misuse of email for urgent matters, and medico-legal issues such as informed consent(110).

Patients with chronic diseases are increasingly turning towards the Internet in order to learn more about their illness and communicate with others (patients and health care providers) about their disease. Patients with inflammatory bowel disease who use the internet tend to have more severe disease, are often younger, and have higher levels of education than those who do not use the internet(111). Internet-use has contributed to the change in dynamic of the doctor-patient relationship and the concept of the 'expert patient'. Care needs to be taken when recommending the internet as a source education given the highly variable content and unregulated nature of many of the websites available. The internet may not be an appropriate self-management tool for all patients – obvious barriers include poor language and reading skills, access to the internet, and receptiveness to using the internet. Older age may not necessarily be a barrier to internet use. A study by Crabb et al(112) examined the extent to which older patients in a primary care setting are receptive to using internet resources to manage chronic disease. In a sample of 50 patients over the age of 65 (range 65-95, mean 80.3 years), nearly three quarters were regular internet users, and over half had used the internet to search for health information. Although the majority

of older patients were receptive to using the internet to get information (78%) and use email to communicate about health matters (75%), participants were less interested in using internet interventions to keep track of health symptoms (64%) or health-related behaviours (50%). This should be borne in mind when designing and recruiting older patients to internet-based management systems.

Researchers have objectively assessed the quality of IBD information available on the internet. Promislow et al(113) specifically evaluated online information regarding self-management of inflammatory bowel diseases. They found that most websites had little or no information regarding self-management, and those that did had low information scores. It could be argued that given the unreliable nature of many websites, unguided self-management using inadequate educational materials could be damaging. The authors again emphasise the importance of tailored information for specific patient groups (children, adults, varied reading levels). The use of supplementary media such as illustrations and videos can help convey information on the complexities of IBD more effectively by presenting personalised data in a more usable format.

In the UK, the official IBD charity, Crohn's and Colitis UK has a comprehensive website(114) for patients and healthcare providers, providing accurate, evidence-based, up to date information on IBD. They also take advantage of social media to reach a wider audience to help people manage their IBD with links to Twitter and Facebook. Patients need to be guided towards reliable Internet sources such as Crohn's and Colitis UK to reliably inform and enable them to make wise health choices.

1.6.4 *Mobile phone interventions*

EHealth, is a paradigm encompassing all of the information and communication technologies necessary to make the health system work(115). With the increasing sophistication of mobile phones comes a new branch of eHealth - mobile health (mHealth). It is estimated that up to one third of the UK population owns a smart phone – a mobile telephone incorporating computer technology which allows it to perform a variety of advanced functions. The portability of mobile devices makes continuous and/or regular monitoring more convenient compared with personal computer (PC)-based programmes. This is particularly pertinent in the large number of patients of working age affected by IBD. Patients need to be able to maintain daily routines and successful self-management interventions must fit conveniently into day to day life where possible. Mobile devices allow temporal synchronisation of the intervention delivery and can claim people's attention when most relevant.

O'Neill et al(116) conducted the first review of quality of smartphone apps in colorectal diseases in 2012 and found that expert opinion is often lacking. They found 63 apps, 29 of which were targeted towards patients, the remainder towards healthcare workers. 6 of the patient-directed apps were for patients with inflammatory bowel disease and were used mainly to record data to aid self-management such as diet, symptoms, bowel habit, disease triggers, medication, as well as reminders for upcoming appointments. Although all were favourably reviewed by users, only one had named medical professional involvement. One interesting bowel preparation app asked users to enter their bowel preparation prescription and provided prompts on how and when to consume the preparation, a useful application in IBD. Although there is no robust peer-review process for smartphone apps yet, carefully developed evidence-based apps could play a key role in self-management.

Most of the literature in this field explores the efficacy of mobile phone messaging in chronic disease management but there is little evidence on the efficacy of mobile phone apps. SMS interventions have been demonstrated to improve drug adherence and smoking cessation(117). Short message service (SMS) reminders can improve adherence to anti-retroviral therapy(ART)(118). 431 patients who had recently initiated ART within 3 months were randomly assigned to a control group or the intervention. Participants in the intervention groups received SMS reminders sent at a daily or weekly frequency. In intention-to-treat analysis, 53% of participants receiving weekly SMS reminders achieved adherence of at least 90% during the 48 weeks of the study, compared with 40% of participants in the control group (P=0.03). Participants in groups receiving weekly reminders were also significantly less likely to experience treatment interruptions exceeding 48 h during the 48-week follow-up period than participants in the control group (81 vs. 90%, P = 0.03). Medication adherence is a particular challenge in IBD. Many medications are taken at infrequent intervals, for example methotrexate on a weekly basis, or adalimumab fortnightly. Regular text reminders could help to improve the rates of missed or late doses in these patients. Similar techniques could be used to remind patients to have regular blood monitoring tests. SMS reminders are already currently being used in many hospitals to improve clinic attendance rates.

Although there are definite positive trends, there appears to be limited evidence of large, robust randomised controlled trials on the use of telemedicine in the management of chronic disease. A 2010 Cochrane review(119) assessed the use of telemedicine and its effects on professional practice and health care outcomes. Of seven trials involving more than 800 subjects, five were concerned with the provision of care at home or patient self-monitoring of disease, for example blood sugar levels in diabetic patients or hypertension, with readings sent remotely to physicians.

None of these RCTs were in the area of IBD. The authors concluded that although the trials appeared to be well conducted and all aspects of the interventions were well accepted by patients, patient numbers were small in all but one study. Although the interventions showed no detrimental effects on subjects, nor did they show any clinical benefits. None of the studies included any formal economic analysis of the self-care intervention.

1.6.5 *Digital self-management systems (portals)*

Delivering self-management interventions digitally has the potential to lead to better health outcomes, better healthcare and lower costs(120) and are therefore an important area for exploration. Web-based patient management systems, or "portals" feature more prominently in recent literature. Back in 2005, a Cochrane review(121) explored the use of Interactive Health Communication Applications (IHCAs) in people with chronic disease, identifying 24 randomised controlled trials with 3739 participants (adults and children) which covered a variety of illnesses including asthma, diabetes and cancer. ICHAs were defined as computerised, usually web-based, information packages for patients that combine health information with at least one of social support, decision support, or behaviour change support. The review found that ICHAs have significant positive effects on knowledge, social support and behavioural and clinical outcomes, and are more likely than not to have significant positive effects on self-efficacy. The authors supported continued cautious investment in IHCAs, coupled with a rigorous programme of evaluation. They highlighted a need for further research into the effects of IHCAs on health service utilisation and thus financial implications of their use – for example, they questioned if motivated, active patient users of ICHAs demand more from the health service (more medication, more preventive care) and if so, is the cost of this demand offset by reductions in complications or emergency care?

Since the Cochrane review, self-management platforms have been explored further in numerous different conditions. Diabetes lends itself well to self-management given then need for regular monitoring of blood sugars and lifestyle modification. Like IBD, diabetes can affect all age-groups, and interventions need to be flexible to accommodate a wide variety of needs. Most of the literature in this area focuses on using web-based technology to support blood glucose monitoring, with patients uploading regular blood sugar readings for physicians to review and then adjust insulin doses accordingly. Patient web portal interventions appear to improve communication between patients and providers, increase overall satisfaction with care, and can improve disease management and patient outcomes(122). Computer-based programmes appear to have small statistically significant benefits on glycaemic control (pooled mean effect on

glycosylated haemoglobin A1c (HbA1c) -2.3 mmol/mol or -0.2% (95% CI -0.4 to -0.1). Interestingly, the effects on HbA1c were greater in the subgroup of patients using mobile phone-based web interventions (mean reduction in HbA1c -5.5 mmol/mol or -0.5% (95% CI -0.7 to -0.3). There was no RCT evidence that recent web-based diabetes management interventions can improve health related quality of life or depressions scores(123).

Patients with rheumatoid disease share characteristics with IBD, benefit from many of the same drugs and subsequently undergo regular drug monitoring. Lorig et al(124) used a password-protected interactive online platform to provide web-based teaching via a learning centre, a bulletin board discussion group, and tools that patients could use individually to monitor their disease such as exercise logs, medication diaries and tailored exercise programmes. In addition, they provided access to the educational 'Arthritis Help book', a virtual equivalent of a patient guidebook. The web portal was focused upon the reduction of pain and improvement of function. Patients were requested to login regularly to complete 6 weekly learning modules, supported by a panel of peer moderators who provided reminders, encouragement and supervision. Management plans were individualised by providing tailored exercises suggested via automated algorithms for each participant based on their answers to an online questionnaire designed to assess problems with each major joint function. Randomised intervention participants (n=433) were compared with usual care controls (n=422) at 6 months and 1 year. 4 health status measures (health distress, activity limitation, self-reported global health, and pain) showed statistically significant improvements, as did self-efficacy scores, but health behaviours such as exercise and stress management, and health utilisation including hospital visits did not alter significantly. Other studies of similar interventions this field have however shown reduced healthcare cost, primarily due to a reduced number of physician visits(125).

In 2011, Krier et al(126) performed a prospective randomized controlled pilot study at a Veterans Affairs hospital, assigning patients into two groups: telemedicine encounter, with the IBD specialist remotely located, and standard encounter. Telemedicine involved clinicians using a new computerized system called Collaborative Imaging, to deliver telemedicine. Patients did not access the system or upload data themselves, instead it was used to facilitate a telemedicine encounter with the patient. The authors enrolled 34 patients, undertaking 57 telemedicine encounters in 9 months and the intervention was very well received, with the two groups similarly rating as excellent their clinic experience and the major clinical satisfaction indices of attention to patient concerns, bedside manner, and perceived skill level of the doctor.

In the past decade, there has been a slow but steady increase in the number of digital self-management platforms available for use in inflammatory bowel disease, with most literature coming from Denmark, The Netherlands, USA, the UK and Spain. The Danish Constant Care(1, 127) platform has been at the fore of digital interventions for IBD since 2010, initially for stable, and then in more complex and unwell patients. They have also used faecal calprotectin monitoring (laboratory based) from the outset as an adjunct to remote monitoring. They have found digital platforms to be safe, feasible, and produce significant cost savings. Subsequent studies across Europe and the USA have demonstrated a variety of improved outcomes such as medication adherence, reduced health resource utilisation, and in the majority, although few studies have shown improved quality of life, most demonstrate no reduction in quality of life in what is an alternative means of management to traditional outpatient follow-up(128-133).

1.6.5.1 Development of digital self-management interventions

Digital self-management interventions are complex. Dack et al(120) described the development of a self-management intervention for diabetes called HeLP-Diabetes, using the MRC framework for development of complex interventions(134) as a guide and described three key developmental processes: 1) identifying appropriate theory – to better understand illness behaviour in chronic disease. 2) collecting primary qualitative research to identify target users' needs – e.g. using focus groups where users trialled different self-management websites and fed back on usability and ways to improve. 3) identifying existing research evidence in order to determine the content to be included within HeLP-Diabetes by way of systematic review. The MRC Framework is described in greater detail in 2.3.1. Digital interventions, as with all complex interventions take time to develop, test, refine and establish, and development is an iterative process. This is demonstrated by the available literature with studies reported from the same authors over several years, in one group reporting over a decade-long period from feasibility study to randomised controlled trial(129, 135). Each study describes new developments made to an existing digital platform, with increasingly complex patients and interventions included in study. This significant timeframe is important to consider when developing digital interventions and makes it important to share learning to move the field forward. Digital interventions for IBD are described in greater detail in the systematic review in Chapter 3.

1.7 My Medical Record

My Medical Record (MyMR) is a locally developed interactive self-management digital portal for which forms the basis for much of the service development and research in this thesis. MyMR was created in 2012 by the University Hospitals Southampton informatics team in collaboration with

clinical staff and software supplier Get Real Health®. The site initially fed into Microsoft's HealthVault® – an online tool which enables patients to store a range of health information for personal use and to share with care providers. UHS NHSFT now host the MyMR service through the Microsoft Azure cloud-based platform. This approach supports the scaling of the service and results in benefits from the inherent security within Azure whilst also ensuring business continuity (e.g. ensuring appropriate capacity). The Azure instance that supports the MyMR service is within a Microsoft data centre that is based in the UK. To support the MyMR service a dataset is also stored within the UHS NHSFT network.

In its earliest format, MyMR initially comprised a personal patient record where patients or healthcare professionals could enter data on personal information, medication and disease history, as well as viewing clinic appointments and recent clinic letters. Following on from initial successes in the field of prostate cancer, the IBD team were early adopters of MyMR, and it has since been developed for numerous other disease specialties. In recent years, UHS has been the recipient of a multi-million-pound Global Digital Exemplar (GDE) award(136) and as a result IT systems such as MyMR have received financial and staffing investment.

A GDE is defined as an "internationally recognised NHS provider delivering improvements in the quality of care, through the world-class use of digital technologies and information"(137). Exemplars share their learning and experiences through the creation of blueprints to enable other trusts to follow in their footsteps as quickly and effectively as possible. Lessons learned through the development and research processes involving MyMR can therefore be disseminated to other trusts beyond Southampton, where the MyMR is commercially available for use and has been taken up by several other trusts in the region.

MyMR now provides a two-way interactive platform where patients and healthcare providers can upload and share patient reported outcomes, monitor disease activity, view laboratory, radiology and endoscopy results, access information regarding IBD, communicate via e-messaging, as well as a clinical management system designed to oversee virtual outpatient clinic review. This development is explained in more detail in Chapters 5 and 7.

1.8 Summary

Inflammatory bowel disease is a complex illness with wide-ranging severity and patient needs. There are numerous means of diagnosing and monitoring IBD, and no single diagnostic test or scoring system is perfect. Instead, diagnosis and monitoring should be approached by drawing together information from different sources. Healthcare delivery is becoming increasingly digitalised to try and improve delivery and quality of patient care in chronic illness. There are

numerous different methods of supporting patient to self-manage, from simple guidebooks through to more complex digital interventions, with varying strength of evidence in their favour. Lessons can be learned from such interventions in both IBD and other chronic diseases, but the use of web-portals in the management of inflammatory bowel disease is still an emerging field. The current literature on digital self-management platforms in IBD is explored further in a systematic review of the literature in Chapter 3.

1.9 Structure and aims of thesis

This thesis describes 3 projects that aim to explore how the IBD patient pathway may be improved by integrating faecal calprotectin and self-management technologies for patients with suspected IBD in referral from primary to secondary care, monitoring and detection of disease flare-ups in established IBD, and longer-term monitoring/follow-up in stable disease.

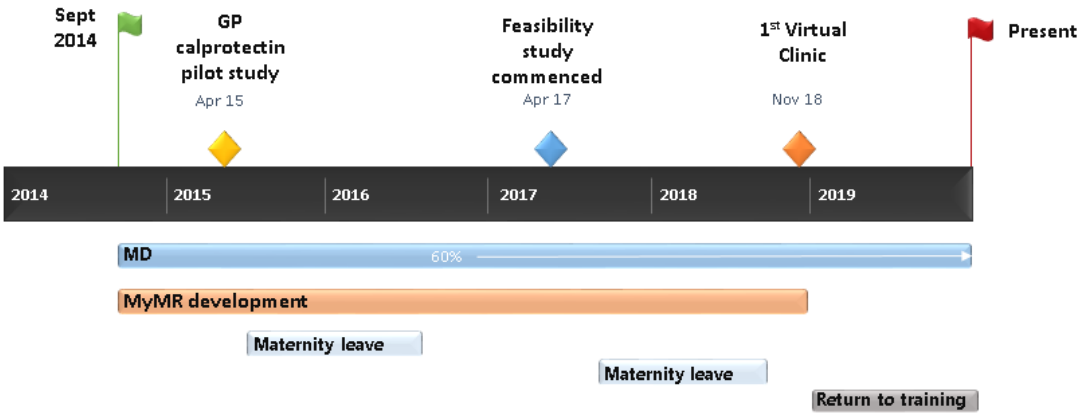
The key objectives for this thesis are:

- Critically appraise the literature on the effects of digital self-management interventions in IBD on patient outcomes (Chapter 3)
- Assess a pilot of general practitioner (GP) access to FC testing when referring patients with suspected IBD to secondary care and develop a pathway for a Positive Calprotectin Clinic (Chapter 4)
- Assist in the development of My Medical Record (MyMR) supported self-management website for IBD and describe the integration of home calprotectin test procedures into the website (Chapter 5)
- Assess the feasibility and acceptability of combined home smartphone FC testing and MyMR to monitor IBD patients who have recently stopped a medication for IBD (Chapter 6)
- Assist in the development of a digital virtual IBD clinic using MyMR and explore barriers and facilitators to change during its implementation (Chapter 7)

1.10 Thesis Timeline

This research was conducted part-time between September 2014 and December 2018, the majority of which was undertaken at 60% full-time equivalent. This period incorporated two year-long periods of maternity leave. During the research period, I continued my clinical work providing out-of-hours medical registrar cover at University Hospital Southampton and returned to clinical training in January 2019. Figure 2 presents a Gannt chart broadly illustrating when key elements were undertaken.

Figure 2: Thesis timeline



2 Methodology

2.1 Introduction

Methodology is the strategy or design underlying the choice of research methods. In other words, how does one go about finding knowledge and why choose particular methods?(138) The research in this thesis involves using mixed methods to explore new technologies to support diagnosis and self-management in inflammatory bowel disease. The thesis presents a combination of service development which underpins the technologies used in the research, as well as original systematic review and mixed quantitative and qualitative research.

When conducting research it is important to understand and select the most appropriate methodology, and also to have an understanding of one's own philosophical stance in order to reflect upon how the role of researcher may impact upon the study. It is also important to explore relevant theory that may aid interpretation of findings.

This chapter presents established philosophical positions encountered in qualitative research and my reflections on my own philosophical stance. I describe the MRC framework for developing complex interventions(134), the different methodologies used across various chapters of this thesis, and the process and rationale behind systematic review as a means of informing the research (Chapter 3). I also explore different methodologies for analysing qualitative data from the perspective of a novice qualitative researcher (Chapter 6) and the differences between involvement in qualitative research and patient and public involvement (PPI). Finally, I introduce the theory behind developing complex interventions like MyMR digital self-management platform and how change occurs via Normalisation Process Theory (Chapter 7).

2.2 Philosophical stance

Mixed methods studies combine elements of both qualitative and quantitative research approaches to give breadth and depth to understanding in research(139). My experience to date as a clinician has been of largely quantitative research, critically appraising the available evidence to inform my clinical practice. In undertaking this qualitative research, I have been exposed to a completely new way of approaching and interpreting evidence – by first considering my philosophical position and how this might influence how I conduct and analyse qualitative research.

To conduct high quality qualitative research, it is important that transparency be maintained in not just the research itself, but also the researcher's mindset. This includes the 'researcher's

paradigm', or theoretical frame of reference(140). The research paradigm is "the set of common beliefs or agreements shared between scientists about how problems should be understood and addressed"(141). It can be broken down into 3 main components: ontology, epistemology, and methodology(142).

i. Ontology – one's view on the nature of reality.

• Relativists believe that knowledge is a social reality that is laden with values and only comes to light through our individual interpretation.

• Realists see reality as something that is 'out there' as a law of nature waiting to be found.

• Critical realists believe things exist 'out there' but as humans our presence as the researcher can impact upon what we are trying to measure.

ii. Epistemology – one's perceived relationship with the knowledge that one is uncovering. Am I part of the knowledge or am I external to it?

iii. Methodology – how does one go about finding the knowledge?

Numerous different research paradigms have been described(138) and incorporate a combination of the above components. 3 core research paradigms have been described:

i. Positivism - viewing knowledge as discoverable through objective research, seeking out the facts of a single reality such as cause and effect, and then trying to draw conclusions from this. It is therefore most often employed in quantitative research. Positivism is based upon reason, truth and validity and there is a focus purely on facts, gathered through direct observation and experience and measured empirically using quantitative methods and statistical analysis(143).

ii. Constructivist/Interpretivism - this position was described by Blaikie(143) as 'post-positivist' as it countered that there are fundamental differences between the natural world and the social world. It views knowledge as constructed by the subjective meaning that people place on their world. Meaning is constantly reconstructed over time due to multiple individual experiences and interpretations. People, their interpretations and their perceptions are the primary data source(144) and as such this philosophy often underpins most qualitative research. The close relationship between the researcher and their research within this paradigm, means that self-reflection is an important part of the research process.

iii. Realism borrows from both positivist and interpretivist philosophies. Whilst realists are concerned with studying social objects and how they behave objectively and 'scientifically', they also recognise realities that are simply claimed to exist or act, whether proven or not. Realists take the view that researching from multiple approaches can contribute to understanding since reality can exist on multiple levels and hence realism may be seen as inductive or theory building(145).

These paradigms represent a spectrum, and most researchers will fall somewhere between depending on the value placed on finding 'fact' or 'meaning' when conducting research. It is important to understand one's epistemological and ontological views when presenting qualitative research so that both the reader, and the researcher, can understand the perspective from which they are approaching the research. The researcher should consider any preconceptions or personal beliefs they may have about the research topic and take these into consideration when designing and evaluating research(146). It is important to note that there is no 'right' or 'wrong' philosophical view. I feel I approached my research from a critical realist perspective. This allowed me scope to conduct a mixed methods feasibility study in Chapter 6, with a focus first on more positivist methodology collecting directly observed quantitative data to help determine feasibility (for example FC testing completion rates etc.), but then to explore from a more interpretivist stance by researching participants' experiences and reflections, as well as reflecting upon my own influences on the study, particularly as the sole researcher.

2.3 Methodology

Several different projects are described in this thesis. This section introduces the rationale for and key methodologies employed in the studies.

2.3.1 *MRC Framework for the development of complex interventions*

Much of the research and service development in this thesis revolves around My Medical Record, an interactive digital intervention used for inflammatory bowel disease and other chronic conditions. Complex interventions are widely used in the health service and are conventionally defined as interventions with several interacting components. Complexity may arise through the number of and interactions within the intervention, variability of users of the intervention, and degree of flexibility in the intervention permitted. They present challenges for researchers, in addition to the practical and methodological difficulties that any successful evaluation must overcome. Many of these challenges relate to the difficulty of standardising the design and delivery of the interventions, their sensitivity to features of the local context, the organisational and logistical difficulty of applying experimental methods to service or policy change, and the

length and complexity of the causal chains linking intervention with outcome. In 2000, the MRC published a Framework for the Development and Evaluation of RCTs for Complex Interventions to Improve Health(134), to help researchers and research funders to recognise and adopt appropriate methods. This was subsequently updated in 2019 following further development in the field.

The MRC recommend that a good theoretical understanding is needed of how an intervention causes change, so that weak links in the causal chain can be identified and strengthened. Key elements of the development and evaluation process include development, feasibility/piloting, evaluation (including understanding change processes), and implementation. These steps will not always follow a linear or even cyclical sequence. Best practice is to develop interventions systematically, using the best available evidence and appropriate theory, then to test them using a carefully phased approach, starting with a series of pilot studies targeted at each of the key uncertainties in the design, and moving on to an exploratory and then a definitive evaluation. In practice, evaluation takes place in a wide range of settings that constrain researchers' choice of interventions to evaluate and their choice of evaluation methods. Where there are significant non-health benefits associated with receipt of an intervention, the ethics of withholding or delaying receipt of an intervention in order to study its health impact need careful consideration. Given the cost of such interventions, evaluation should still be considered: 'best available' methods, even if they are not theoretically optimum, may yield useful results, but these must be interpreted with caution. For this research, MyMR was already and established intervention, and an alternative to traditional outpatients may have significant cost benefits to consider.

Before undertaking a substantial evaluation, the MRC recommend one should first develop the intervention to the point where it can reasonably be expected to have a worthwhile effect. This provides rationale for the different elements of this thesis. First identifying the evidence base, ideally through systematic review. It is important to identify/develop appropriate theory on the process of change the likely process of change, by drawing on existing evidence and theory, supplemented (if necessary) by new primary research, for example interviews with 'stakeholders. This was conducted in my research through PPI with patients and nurse stakeholders when developing MyMR, as well as qualitative research as part of a feasibility study. Modelling a complex intervention prior to a full-scale evaluation can provide important information about the design of both the intervention and the evaluation, before assessing feasibility and piloting methods, and this guided the choice of conducting a feasibility study incorporating MyMR. Finally, the complex intervention should be evaluated. Ideally this will take place using a randomised trial

but, in some circumstances, for example if an intervention is already being widely implemented within an organisation, in this case non-experimental evaluation should still be considered.

MyMR is an established but developing intervention at our hospital trust, and this, combined with time and financial limitations of conducting DM part-time, influenced the choice of research methods. Using the MRC guidelines as a framework for my research involving MyMR, I conducted a systematic review to gather knowledge, utilised patient and public involvement, conducted qualitative research, and explored barriers and facilitators to change using Normalisation Process Theory. These methodologies are discussed below.

2.3.2 *Systematic review*

Healthcare decisions for individual patients and for wider public health policies should be informed by the best available research evidence. Systematic reviews aim to identify, evaluate, and summarize the findings of all relevant individual studies over a health-related issue, thereby making the available evidence more accessible to decision makers. A systematic review is a summary of the primary research literature on a particular area, using explicit and reproducible methods to systematically search, critically appraise, and synthesize data on a specific issue. Strict scientific design is required to ensure methods are carried out reproducibly and results are reliable(147). Systematic reviews can demonstrate where knowledge is lacking which can then be used to guide future research. A meta-analysis combines quantitative data from multiple independent studies to produce a single estimate such as the effect of a treatment or intervention could do with a reference. As such it relies on a degree of homogeneity in terms of the initial primary studies and quant outcome measures employed. An initial search highlighted that because of the limited number and heterogeneity of studies exploring the use and effectiveness? of digital management platforms in IBD, a meta-analysis was not possible.

There are several steps to conducting a systematic review. First, the question must be defined. In Chapter 2, the systematic review addressed the question – “Do interactive digital self-management interventions improve patient outcomes for IBD?” Search terms must then be defined. The literature must then be reviewed by searching scientific resources such as electronic databases, clinical trials registers, as well as the “grey literature” (thesis, internal reports, websites), references listed in primary sources, and raw data from published trials. Studies identified through the searches must then be sifted through to select the studies relevant to the research question and meeting inclusion/exclusion criteria. Results should be presented using a PRISMA diagram(148) detailing the selection process. The quality of the studies must then be assessed by critically appraising. Quality of trial reporting can be assessed using scoring systems

such as the CONSORT checklist(149) to assess quality of reporting. For non-randomised controlled trials, CONSORT extensions are available(149). CONSORT checklists for systematic review papers can be found in Appendix B.1.

The systematic review question addressed a relatively narrow field in the IBD literature. This was felt to be an appropriate focus for the purposes of a DM thesis. There are different methods of analysing and synthesising data produced from systematic review. The resulting papers identified from the review encompassed a range of study designs from randomised controlled trials to pilot studies and had multiple different outcome measures. For this reason, a meta-analysis was not possible and instead a narrative synthesis was presented. Narrative syntheses are commonly used to examine complex interventions which commonly include data from different study designs or have captured a wide range of interventions. Narrative reviews can provide a first step in looking systematically at and organising data(150). Rather than grouping the small number of studies into type (RCT, pilot etc.), I presented the studies chronologically to better reflect how digital platforms have progressed over time.

2.3.3 *Qualitative data analytical strategies*

Within the research paradigm of a realist, and in-keeping with the MRC guidance(134) I conducted a mix of quantitative and qualitative research to better my understanding, and reflected on my influence on the data as a researcher and IBD physician. For the qualitative component of the feasibility study (Chapter 6), I conducted qualitative interviews to explore the use of self-monitoring via MyMR and home calprotectin testing.

I considered three common analytic approaches to determine whether self-monitoring in the form of home stool testing and website use was acceptable to patients; grounded theory (GT), thematic analysis, and framework analysis.

2.3.3.1 Grounded Theory

GT was developed by Glaser and Strauss(151) in the 1960's when social researchers were questioning the tenets of positivism. At that time, most theory development was conducted prior to collecting and analysing data. GT incorporates a package of analytic procedures with the aim of generating or developing new theory from the data collected. It comprises a repetitive inductive cycle, or constant comparative analysis, where theory can emerge directly from data and is ultimately tested ('grounded') against 'the real world'. It tends to be used in new areas that have not been explored previously. It involves the researcher moving back and forth between the data collection and analysis, involving multiple iterations. With each iteration, the researcher collects

data, analyses, and a theory takes shape. Based upon this theory the researcher decides how next to sample, a process called theoretical sampling. This process continues until no new themes emerge; a point known as 'saturation'. Due to the small sample size involved in the feasibility study, I did not anticipate being able to proceed further than one or two iterations of the GT process, and hence I did not consider GT to be a suitable option for analysis.

2.3.3.2 Thematic analysis

Thematic analysis is popular amongst qualitative researchers, and has been described as one of the simplest forms of qualitative data analysis(152). It is the process of identifying patterns or themes in qualitative data. Braun and Clarke(153) suggest that thematic analysis can be a good starting point for novice qualitative researchers as it "provides core skills that will be useful for conducting many other kinds of analysis". They developed a straightforward 6-step framework for analysis: familiarization with the data, coding the data, generating themes, reviewing themes, defining and labelling themes, and finally writing up.

Data can be analysed at two thematic levels – semantic and latent(154). Semantic themes are the more superficial or explicit meanings of the data - the analyst is not looking beyond what the subject has said. It is important to not simply summarise the data, for example by using the interview guide to generate themes, which has been described as a common pitfall(154). By contrast, the latent level explores the underlying ideologies that shape and inform the semantic content of the data, which provides a more in-depth analysis. Thematic analysis can be conducted by an inductive approach that is driven by the data itself ('bottom-up'), or it can be driven by the research question and aims of the researcher ('top-down')(155, 156). Being new to qualitative research, I felt that thematic analysis would be a prudent choice for analysing my interview data and would allow me some flexibility. To answer the question of acceptability, I adopted a 'top-down' approach to my thematic analysis, coding each segment of data that was relevant to or captured something of interest to the research question of acceptability. I used open coding, developing and refining the codes as I worked through the process. I also explored participants' views on stopping a medication and self-management in IBD, and for this I used a more inductive approach, allowing themes to emerge from the data itself following more general discussions with patients.

2.3.3.3 Framework analysis

The Framework Analysis Method(157) is more highly structured approach to analysis and may be incorporated under the umbrella terms of thematic analysis or qualitative content analysis. This

approach aims to identify commonalities/differences in qualitative data. It uses a defining 'matrix' comprising rows (cases), columns (codes) and cells of summarised data to provide a structure into which the data can be systematically reduced before being analysed. Analysing the data by case and by code prevents individuals' views from being lost within the wider theme. The structured, methodical nature of this method of analysis means that it can provide consistency where large volumes of data are being analysed or when a number of different researchers are coding the data(158), and for these reasons I would consider adopting this technique in future in a larger scale study.

2.3.3.4 Qualitative data reporting

In 2014, the Standards for Reporting of Qualitative Research (SRQR)(159) were developed, aiming to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research, facilitating manuscript preparation and critical review of qualitative research. Items that should be reported include the qualitative approach and research paradigm of the researcher, researcher characteristics and reflexivity, research context sampling strategies, data collection methods, instruments and processing, results and discussion of trustworthiness and limitations. (A SRQR checklist for the feasibility study in Chapter 5 can be found in Appendix B.2, although in practice these items are spread across the body of the thesis, for example in the methodology chapter.)

2.3.4 *Normalisation process theory*

To better understand the processes involved in integrating MyMR and the new digital virtual clinic into everyday practice, and any barriers or facilitators to this change, I used the principles of normalization process theory(160). (NPT) as a framework to present the evolution of the service during its development (Appendix F.4). NPT is an 'action theory', which means that it is concerned with explaining what people do, rather than their attitudes or beliefs. It can be used as a tool to identify and better understand process problems and structural problems concerning the integration of new systems of practice into existing healthcare settings(161).

NPT comprises 4 core constructs: coherence, cognitive participation, collective action, and reflexive monitoring. Each core construct is further divided into 4 components and represents a mechanism by which a social action is generated; the work that people do to effect a change. The constructs tend to occur in the order above, but there can be movement between the constructs as subjects do not always to conform to rigid patterns of behaviour(160).

2.3.4.1 Coherence

Coherence can be defined as the 'sense-making' work that people do (individually or collectively) when faced with integrating a new set of practices into their routine. Its 4 components are:

- Differentiation – the understanding of how a set of practices and their components are different from each other.
- Communal specification – making sense of a new practice requires people to work together to build a shared understanding of the aims, objectives and expected benefits of the practice.
- Individual specification – making sense of a new practice requires individuals to participate in coherence work to understand what their specific task and responsibility will be for a new practice.
- Internalization – the work that people do to understand the benefits and importance of a new practice.

2.3.4.2 Cognitive participation

Cognitive participation is the relational work that people do to build and foster a community of practice around a new intervention. Its 4 components are:

- Initiation – when a new service is implemented, a key area for address is whether core participants are working to drive to service forward.
- Enrolment – is about building communal engagement to organize or reorganise staff to deliver a new practice to deliver it collectively.
- Legitimation – is the relational work that is carried out to ensure participants in the service believe it is right for them to be involved.
- Activation – once the development in underway, participants need to collectively define the work needed to sustain the new practice and to stay involved.

2.3.4.3 Collective action

Collective action is the operational work that professionals do to enact a set of practices to implement a new technology. Its 4 components are slightly different to the other constructs as the names reflect the qualities of the technology itself, rather than the character of the work involved, however as in all the other constructs they are used to help define actions. The 4 components are:

- Interactional Workability – this is the interactional work that people do with each other and with elements of the new technology when they seek to put them into everyday practice.
- Relational Integration – this is the knowledge work that people do to build accountability and sustain confidence in a new technology and in their team.
- Skill-set Workability – this is the knowledge work that facilitates the appropriate division of labour when implementing a new technology in a real-world scenario.
- Contextual Integration – this is the work of managing resource allocation for a new set of practices. This is typically seen as a management role where the power to allocate resources normally lies in a healthcare setting?

2.3.4.4 Reflexive monitoring

Reflexive Monitoring describes the appraisal work that is carried out at a group and individual level to assess and understand the effects of a new technology. Its 4 components are:

- Systematization – this is how stakeholders seek to collect information about how effective and useful a new technology is to them and others.
- Communal Appraisal - this describes the informal and formal work participants do together to evaluate the worth of a new practice, drawing on both experiential and systematized information.
- Individual Appraisal – this is the work that individuals do to examine the effect of a new technology on them and their personal practice.
- Reconfiguration – this is the modification of a new practice or technology in response to appraisal work by a group/individual to make it more workable in practice.

NPT has been used in a number of interventions including feasibility studies, retrospective documentary analyses, and process evaluations(161). In emedicine, it has been used to examine the implementation of numerous digital/telecare interventions for conditions such as chronic back and dermatological conditions(162, 163), stroke medicine(164), and web-based cognitive behavioural therapy (CBT)(165). Interventions which focus on action and education (for example educational outreach, audit and feedback) which act upon the NPT constructs of collective action and reflexive monitoring, tended to have more positive outcomes than those that do not address these constructs(166).

NPT was developed as a flexible tool and the authors encourage its creative use in any aspect of research and service development. I used it as a framework to present the development of MyMR

and the virtual clinic and reflect on barriers and facilitators to change during implementation. It helped me to reflect on the service development (which took place over several years) and to draw the process events together.

2.3.5 *Patient and public involvement versus qualitative research participation*

Involvement of patients is key when implementing new health technologies, particularly when developing self-management interventions with patients the key user of the technology. The projects in the thesis required the use of both patient and public involvement and qualitative research participation. Both PPI and qualitative research aim to incorporate deeper understanding of the research problem and ensure greater relevance of the findings to wider society. Both were used to gather information to help in the design of the MyMR intervention and feasibility study. PPI is predominantly involved in the tasks of research and is a two-way exchange of knowledge that may influence how a study is designed, whereas qualitative research is predominantly intended to advance understanding and therefore involves the researchers being informed by the participants(167). PPI is more likely to take place over an extended period and involve multiple meetings and is more likely to draw on established networks of people interested in contributing to research, and this is demonstrated in this thesis through consultation with the IBD patient panel at various stages of the development of MyMR. Qualitative research is more likely to involve a one-time data collection session.

PPI has been combined with the Person-based approach (PBA)(168) when developing health-related behaviour change interventions to give a wider range of feedback than either technique would provide alone. The Person-Based Approach (PBA) to developing health interventions utilises iterative qualitative research at every stage of developing and testing to ensure the intervention is meaningful, useable, and engaging to the people who will use it. PBA adapts and integrates methods from user-centred design and in-depth qualitative research to enable a deep understanding of the views of the intervention users, the contexts within which they are engaging with the intervention, and their experiences of using the intervention. This knowledge the then informs the planning, optimisation and evaluation of behavioural health interventions. PBA identifies “guiding principles” – the intervention design objectives, and the key features of the intervention that can achieve these objectives (169).

PBA can enhance the acceptability and feasibility of interventions. There are several different PBA activities useful in the various stages of planning and intervention and assessing its feasibility and acceptability. When planning, it is useful to synthesise previous qualitative studies of user experiences of similar interventions and conduct original qualitative research to elicit user views

of the planned intervention (such as previous experience, barriers and facilitators to change). In design, themes arising from the planning stage should be used to identify key issues, needs and challenges that the intervention must address before developing the guiding principles Finally, it is important to elicit and observe user reactions to every element of the intervention (for example using think-aloud techniques), iteratively modifying the intervention to optimise acceptability and feasibility, and if possible to carry out detailed longitudinal mixed methods case studies of independent intervention usage. These activities may be carried out iteratively, concurrently or in a different order, and it is recognised that it may not be necessary or possible to undertake every element. This is relevant to my research which was limited by time and resources, and this is addressed in the Discussion in Chapter 8. Other activities relevant to PBA recommended by the developers include consultation with experts and stakeholders (e.g. members of user groups, practitioners), examining evidence from previous trials, observing real-life context of intended intervention and piloting the intervention using mixed methods to evaluate acceptability and feasibility(170).

While the patient and public involvement (PPI) evidence base has expanded in recent years, the quality of reporting within papers is often inconsistent, limiting our understanding of how it works, in what context, for whom, and why. The GRIPP-2 (short form, SF) is used to report on PPI involvement in any study (whereas the long form is used where the focus of the study is patient involvement) and represents the first international evidence based, consensus informed guidance for reporting patient and public involvement in research. Short form requirements for reporting include the aim of PPI in the study, the methods used for PPI conduct, results of the PPI, the extent to which the PPI influenced the study overall, and critical reflection on the study. PPI was an iterative process throughout the various projects in this thesis, and I have reflected on its use in the discussion sections.

2.3.6 *Summary*

In this chapter I explored different research paradigms and presented my philosophical perspective as a critical realist. I introduced the MRC for complex interventions and how this guided elements of this thesis, explained the process of systematic review, qualitative data analytical techniques, and how both qualitative research and PPI contribute to the methodology. I explored the use of Normalisation Process Theory as a flexible tool to better help me gain knowledge relating to barriers and facilitators encountered when developing a new digital service.

3 Digital IBD portals - Systematic literature review

3.1 Introduction

There are many different electronic tools for supporting patients to manage their inflammatory bowel disease (discussed in Chapter 1), ranging from mobile phone text messaging, disease monitoring apps, online education, and more recently, interactive digital platforms, also known as 'portals'. Portals allow two-way communication and exchange of information between patient and provider. Information can include patient-reported outcomes, blood tests, radiology and endoscopic results. Many portals also allow electronic messaging communication, often between patients and nurse specialists. This is an evolving field and date there have been few studies of self-management portals in the context of IBD and little is known on their effects on IBD outcomes. This chapter describes a systematic review of the literature which explores if interactive digital self-management interventions improve outcomes for patients with IBD. This review helped to inform the feasibility study undertaken in Chapter 5.

3.2 Aims and objectives

The aims of this chapter are:

1. Conduct a systematic review of the literature which answers the question: "Do interactive digital self-management interventions improve patient outcomes for IBD?"
2. Explore how FC may be used as an adjunct in interactive digital interventions.

3.3 Methods

A structured electronic search of the literature was conducted in October 2018 using Pubmed (1966–2019), CINAHL, Embase (1996-2019), OvidMEDLINE (1996-2019) ISRCTN registry, Clinicaltrials.gov, UKCRN Portfolio database, and the Cochrane Controlled Trials Register (CENTRAL) to identify studies on the use of electronic self-management portals in adult patients with IBD. Any trial or study of any type using internet technologies with a two-way interaction between adult IBD patients and healthcare providers were eligible. Abstracts from national and international conferences (British Society of Gastroenterology, Digestive Diseases Week, European Crohn's and Colitis Organisation Congress and United European Gastroenterology Week) from the last 5 years (2015–2019) were also reviewed. Internet publications were searched using the Google search engine (http://www.google.co.uk) and google scholar (https://scholar.google.co.uk). All search strategies used the terms: 'IBD', 'internet', 'self-care', 'self-management', 'eHealth', 'telemedicine,' 'telehealth', 'website' and 'portal', alone or in combination as free-text and MeSH headings. Article reference lists from returned search papers

were manually searched for additional publications. A further final search using the above terms was conducted in September 2019 to look for additional literature updates and verified for the previous timeframe in June 2020. Articles were screened by NT. Due to limited resources; it was not possible for double screening to take place.

Due to the focused scope of the research project and relatively small amount of literature in the field, all types of study design, using adult participant and published in English, were eligible for review. There were no limitations on duration of intervention, but digital interventions that did not allow two-way interaction were not included in the review (but were discussed).

Quality of reporting of randomised controlled trials was assessed using the CONSORT 2010 checklist (http://www.consort-statement.org). CONSORT extensions (http://www.consort-statement.org/extensions) were used to guide review of non-randomised trials. CONSORT checklists for each study can be found in Appendix B.1.

3.4 Results

3.4.1 *Published studies*

493 studies were identified through initial database searches after duplicates were removed. Abstracts were screened for eligibility by NT. 9 full text articles were initially identified as being suitable for review (figure 3). One was excluded as although it described a study involving a website, interaction was not possible between patients and healthcare providers and the website was used a decision support tool for physicians and nurses(129). This is discussed further below. Of the 8 studies included in the review, 4 were randomised controlled trials (127, 128, 132, 133) (for one of which only the study protocol is available), 3 were pilot studies(1, 130, 131) (one of which (131) was identified on the updated search in 2019), and one was described as a prospective open label study(171). 1 study registered on ClinicalTrials.gov is currently in progress and was not included as part of this review but will be discussed later.

The studies identified for review explored a wide range of complex interventions with different outcome measures therefore a meta-analysis was not possible. Instead I used a narrative approach, describing the studies and commenting on strengths and weaknesses. An overview of study characteristics and conformation to CONSORT(149) checklists is presented in Table1.

Figure 3:PRISMA flowchart

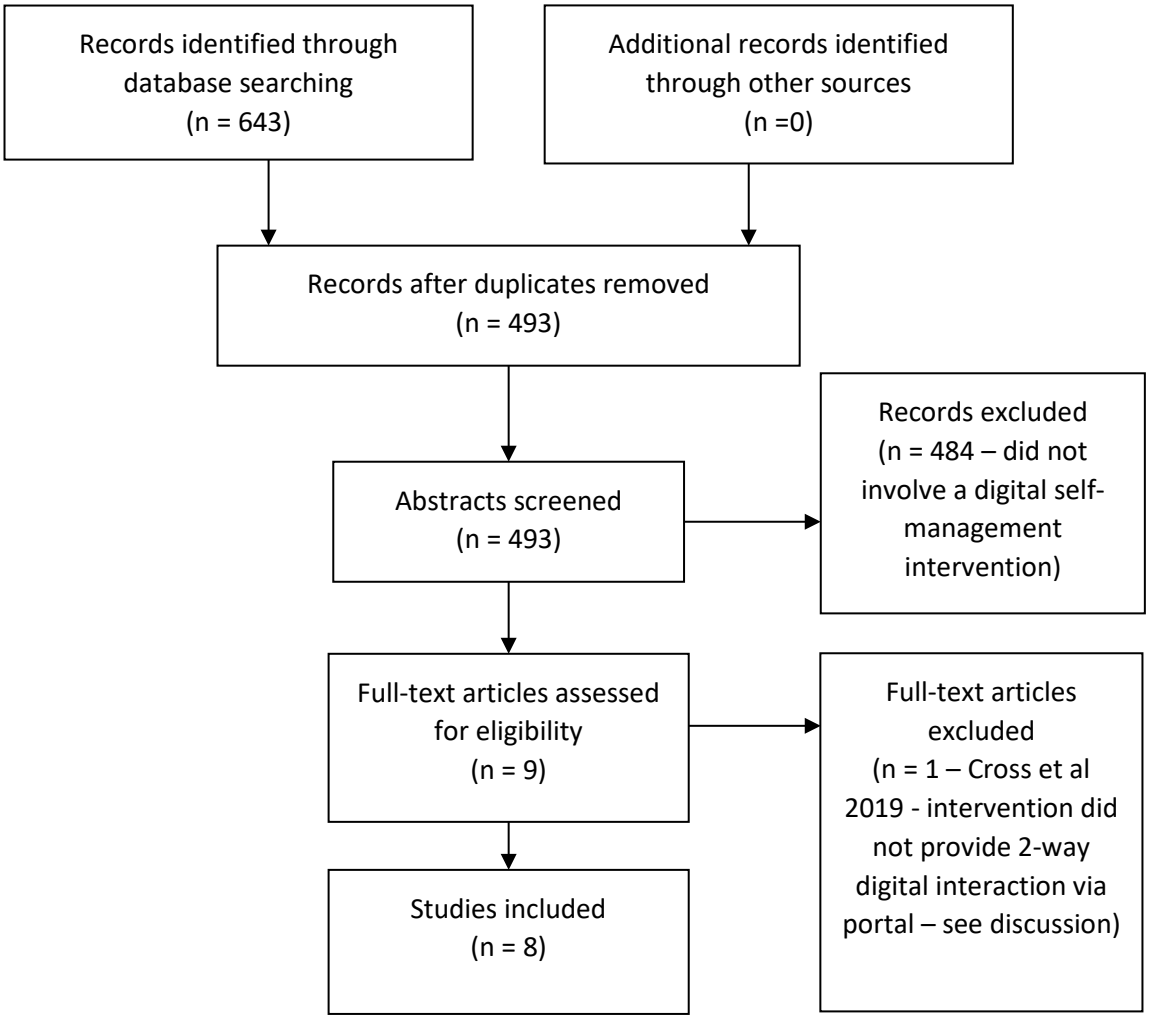


Table 2: Summary of systematic review study characteristics

Authors	Study design	Intervention	Patients	Outcome measures	Summary of main findings	Faecal calprotectin use	CONSORT checklist
Elkjaer et al. (Denmark & Ireland) 2010(127)	RCT 12 months	Constant Care (Web-based portal)	Mild to moderate UC 333	Compliance Satisfaction CCKNOW QoL HADS FC Disease activity	Feasible Improved adherence Longer time to relapse Improved QoL (Denmark) Increased knowledge scores Cost-saving	Patients asked to send in stool samples (to laboratory) in case of relapse and again 7 days after absence of relapse symptoms	25/35 applicable checklist points completed
Cross et al. (USA) 2012(128)	RCT 12 months	UC HAT (Home telemanagement system)	UC 47	Disease activity Adherence QoL	No change in disease activity No change in medication adherence No change in QoL	Not used	30/37 applicable checklist points completed
Pedersen et al. (Denmark) 2012(1)	Open label pilot study 12 months	Constant Care (Web-based portal – focus on individual interval timing of infliximab infusion)	CD 27	Efficacy and safety Inflamm. burden QoL Cost Adherence to web program Antibodies to infliximab	Safe No change in disease activity No change in QoL Cost saving of 699 euros per patient 86% adherence No difference in antibodies	Weekly FC testing (lab) commencing 1 month after each IFX infusion until inflammatory burden score exceeded threshold	22/32 applicable checklist points completed
Pedersen et al. (Denmark) 2014(171)	Prospective open label study 12 months	Constant Care (Web-based portal guiding mesalazine therapy)	Mild to moderate UC 95	Efficacy of mesalazine treatment in inducing deep remission Adherence to therapy	Reduced disease activity Improved adherence Improved QoL Patient satisfaction Reduced FC	Weekly FC testing by patient sent to laboratory and registered onto website. Used to calculate inflammatory burden score	13/15 applicable checklist points completed
Atreja et al. (USA) 2017(132)	RCT study protocol 12 months	Health PROMISE	UC and CD 320	Symptom burden App usage QoL QoC parameters	Improved quality of care (interim data) Improved quality of life (interim data)	Not known	n/a
de Jong et al. (Netherlands) 2017(133)	RCT 12 months	My IBD Coach	UC and CD 909	Disease activity Medication adherence Side effects, Nutrition Smoking QoL Depression Stress Anxiety Life events Work	Improved medication adherence Reduced health resource utilisation	Not used in monitoring	34/35 applicable checklist points completed
Walsh et al (UK) 2017(130)	Pilot study 6 months	UC True Colours	UC 66	Recruitment Retention Questionnaire adherence	High adherence to questionnaire (76% daily and 94% fortnightly)	Monthly home FC smartphone testing	19/30 applicable checklist points completed

				FC adherence Qualitative interview	Retention almost 90%. Recruitment rate less than 30%		
Del Hoyo et al (Spain) 2018(131)	Pilot RCT 24 weeks	TECCU (Telemonitoring of Crohn's disease and ulcerative colitis) vs nurse-assisted telephone care vs standard care	UC and CD (active disease) 60	Clinical remission at 24 weeks HRQoL Medication adherence Work, productivity and activity impairment Healthcare resource utilisation Study compliance Patient satisfaction	Higher remission rates, larger reductions in FC and lower health resource utilisation in TECCU High compliance across all groups. Higher QoL and patient satisfaction in all groups	Assessed at baseline, 12 and 24 weeks (laboratory)	30/35 applicable checklist points completed
Cross et al. (USA) 2019(129) (No two-way interaction)	RCT 12 months	TELE-IBD (mobile phone-based decision support server and website) vs usual care 348	IBD Mild to moderate disease in last 2 years	Disease activity Quality of life Health resource utilisation	Increased healthcare utilisation in all Decreased disease activity in all Less IBD-hospitalisations in intervention Increased QoL in all groups	Nil	23/31 applicable checklist points completed

Patient management websites, or 'portals' have started to feature more prominently in recent IBD literature. One of the first and most comprehensive studies to date regarding the use of a web-based tool to support self-management used the Danish 'Constant Care' platform(127). The key elements of this online programme included generation of an automated score based upon patients' answers on selected items from the Simple Clinical Colitis Activity Index (SCCAI)(172) and the Short IBD Questionnaire (S-IBDQ)(173). When patients completed these, the web program displayed results based upon a 'traffic light' system of disease activity and guided the patient to a self-initiated 5-ASA treatment plan. Patients were monitored daily by investigators until remission was achieved, at which point the system recommended a maintenance treatment. Patients were also provided with a 5-ASA specific e-learning programme to improve their knowledge. Patients were able to contact their physician via email or SMS.

333 patients with mild-moderately active UC on 5-ASA treatment from hospitals in Denmark and Ireland were randomised (1:1) to receive either the Constant Care web-intervention, or best usual care for 12 months. In the case of relapse, patients were asked to send in an initial stool sample for microscopy, culture and sensitivity, and for FC. The authors gave no description of sample size

calculation. Calprotectin was repeated one week after cessation of symptoms. The intervention was widely accepted, with 88% of the web patients preferring the new approach. Adherence to 4 weeks of acute treatment was increased by 31% in Denmark and 44% in Ireland compared to the control groups. In Denmark IBD knowledge and QoL were significantly improved in web patients. Most strikingly, the median relapse duration was significantly lower in the web group at 18 days (95% CI 10 to 21) versus 77 days (95% CI 46 to 108) in the control group. The number of acute and routine visits to the outpatient clinic was lower in the web than in the control group, which resulted in a saving of 189 euros/patient/year. No differences in the relapse frequency, hospitalisation rates, surgery or adverse events were observed. The authors noted that compliance with faecal samples during relapses was very low in Irish patients and suggested this may have been due to patients receiving the FC results only at the end of the study, leading to misunderstanding of the importance of this aspect, or perhaps a reluctance to supply a sample of stool and this could be an area for future qualitative study.

In 2012, Pedersen et al(1) used the Constant-care platform to individualise infliximab dosing in patients with CD and this was found to be both feasible and safe. Twenty-seven CD patients on 8-weekly infliximab maintenance therapy were recruited to receive standardised disease education and web-training to use Constant Care. The inflammatory burden (IB) score described above was updated using the new technology of at-home FC testing. For the home test, patients took a picture of a lateral flow device (onto which a solution containing a stool sample had been applied) using a mobile phone with a 3.2-m pixel autofocus camera. The software package on the smartphone sent the picture to a server in Oslo (CALPRO Inc ®.) via mobile internet. The result appeared on the phone screen after 15 seconds(174). Patients recorded their disease activity and FC online weekly, from one month after each infliximab infusion. Weekly samples for FC testing were also sent by the patient to the research laboratory where FC was measured by a quantitative scanning test. Testing commenced 1 month after each IFX infusion. The IB score placed patients in the green, yellow or red zones of a 'traffic light' system. If placed in the yellow or red zones, the computer directed these patients to consult their physician for their next infusion, which was scheduled for within 72 hours. 17 patients (63%) completed 52 weeks of follow-up, 6 (22%) completed 26 weeks and 4 (15%) were excluded due to loss of response, patient decision or non-adherence. 121 infliximab infusions were given with a median interval of 9 (range: 4–18) weeks. Only 10% of infusions were given at 8-week intervals, whereas 39% were administered with shorter and 50% with longer intervals, respectively. The mean IB and the QoL remained stable during the web-treatment, with the authors concluding that this appeared to be a practical and safe concept for the individualised scheduling of maintenance treatment with IFX in patients with

Crohn's disease, however acknowledged that numbers were small and further study needed. This method of scheduling could be challenging in other centres due to limited spaces available at infusion units and may not be feasible outside of a research setting. The increasing use of therapeutic infliximab antibody and drug level monitoring also now provides an alternative (and likely more accurate) means of individualising anti-TNF treatments.

In 2014, Constant-care was further used to perform a prospective, open-label, study of 3 months of web-guided 5-ASA therapy for 95 patients with mild-to-moderately active UC(171). Patients taking immunosuppressant therapies such as azathioprine, methotrexate, anti-TNF etc were excluded. Patients were instructed to register completed weekly simple clinical colitis activity index scores (SCCAI) and to send weekly FC samples to the hospital laboratory. FC level in stool was measured weekly by patients using a home-administered kit subsequently sent to the research laboratory by mail and analysed by a quantitative enzyme immunoassay (CALPRO ® calprotectin ELISA). FC results were promptly registered onto the website, and the system sent an SMS (short message service) to the patients with a request to log in to the Constant-care website to view their TIBS (total inflammatory burden scores) and the automated web treatment advice. 86% of patients were adherent to web therapy, completing 3 months of guided therapy according to TIBS. There was a significant reduction in mean symptom scores (SCCAI 4.6 vs 1.6, $p<0.001$) and mean FC (437 vs 195 mcg/g, $p<0.001$) at week 0 and week 12, respectively. Almost 90% of patients had decreased their dose of 5-ASA by week 12 of the study. Of the 82 adherent patients, 72 (88%) continued mesalazine and 10 (12%), a significant proportion, needed rescue therapy. The authors do not elaborate on what rescue therapy entailed (i.e. corticosteroids or biologic therapy). This is a surprisingly high number of patients given that the study included just 3 months of follow-up. It would be of interest to know the outcomes of those patients who required rescue therapy and whether it was felt the monitoring helped to provide early warning of flaring patients and hence treatment escalation. Although no qualitative work was conducted with patients to ascertain attitudes to weekly self-testing, the 86% adherence rates suggests the intervention was very acceptable to patients, although it remains to be seen if this would be sustainable over a more prolonged period or if the use could be focused to patients at higher risk of disease flare.

In 2012 Cross et al(128) reported a RCT of the UC Home Telemanagement (UC HAT) system, randomising 47 patients to UC HAT (n=25) or usual care (n=22) for 12 months. The authors hypothesized that UC HAT would improve disease activity and disease specific QoL scores compared with best available care through improved monitoring, medical adherence, and participant knowledge. The intervention group (n=25) received the HAT system which comprised considerable equipment: a laptop computer, electronic weight scale, and decision support server,

linked via a web portal to the clinical team. Patients were also given an action plan and had access to an electronic messaging system. The decision support server analysed clinical data uploaded by the patient against individualized thresholds, and if certain clinical conditions were met, the server generated an alert to a case manager who reviewed the information and consulted the patient to implement management changes. 22 control subjects received "best available care" comprising a comprehensive assessment, therapy plan, scheduled and as-needed clinic visits and telephone calls, and educational fact sheets. The study did not demonstrate any significant improvements in disease activity, QoL, or adherence in participants using UC HAT. Due to difficulties in recruiting, the study was underpowered to detect any small differences in outcome measures. Over a third of patients withdrew from the study. The authors reflected that recruitment difficulties may have been due to using a system that requires installation in the home. Newer telemedicine systems that can be accessed from anywhere via the Web may enhance recruitment.

In 2015 a USA team undertook a pragmatic RCT of HealthPROMISE(132), a cloud-based PROM and decision support tool delivered by a mobile phone app and have presented the study protocol and interim results for a single centre randomised controlled trial. 320 patients were enrolled at the time of presenting. Those in the HealthPROMISE arm could update their clinical information and receive a summary of their disease and graph trends in IBD-related QoL over time. The primary outcome of the RCT is to measure the effects on quality of care and quality of life (measured by S-IBDQ) compared with standard care (plus access to an educational app). Data were entered every 2 weeks by patients which are available to view by the healthcare team through electronic hospital patient record. Interim results of the study are promising. At one year, 75% of participants continued to log in to HealthPROMISE biweekly. Both quality of care and quality of life improved in those patients randomised to HealthPROMISE at a median follow up time of 495 days (+/- 135). QoL started to improve within 5 months and was consistently above the control arm. Quality of care parameters (for example surveillance colonoscopy, smoking cessation advice) significantly increased in the intervention group compared to the control group using the educational app (28% increase vs. 9%, $P<0.01$). The results of the full RCT have not yet been published.

A large, well-reported (conforming to 34/35 applicable CONSORT checklist items) 2017 study by de Jong et al(133) randomised 909 IBD patients to receive care via telemedicine (n= 465) or usual outpatient care (n=444) and found that telemedicine was safe and reduced outpatient visits and hospital admissions compared with standard care. Telemedicine was administered via

MyIBDCoach, a self-management website that monitors disease activity in patients with both UC and Crohn's disease, differentiating it from some sites developed solely for UC patients. It was also designed for use in patients across the spectrum of IBD disease severity. Participants were required to complete monthly monitoring 'modules', comprising questions regarding symptoms, medication use, treatment satisfaction and side effects, as well as other factors that may affect disease such as nutrition, life events, stress, social support, exercise and self-management skills. The authors used the MIAH (Monitor IBD at Home, developed by the study's authors) questionnaire, a symptom-based outcome measure which has been validated against endoscopic assessment. It does not require any laboratory tests or physician input to predict which patients may require further assessment in hospital. Remission was defined as 3 consecutive monthly low MIAH scores, at which point patients could switch to 3-monthly monitoring. Conversely, flaring patients were escalated to weekly monitoring. If preset parameters were exceeded, the clinical team were automatically alerted via myIBDcoach. Patients could communicate with providers via online messaging, checked twice daily by an administrator and outpatient review arranged based upon clinical need. Patients in the standard care control group continued their routine follow-up visits following their local protocol, with an opportunity to schedule an extra visit if symptoms relapsed. The authors do not state what routine follow up entails in each of the 4 participating hospitals. Despite the requirements for monthly (or weekly) module completion, study retention was excellent with 94% of the telemedicine group continuing to use it at 12 months. This may have been aided by the fact that study patients could reduce their monitoring frequency to 3-monthly if stable. 82% of telemedicine patients and 83% of controls completed the baseline paper questionnaires about perceived quality of care, medication adherence, quality of life, self-efficacy, disease- and medication-related knowledge, and smoking behaviour. At 12 months, these questionnaires were completed by 73% of telemedicine patients and 75%of control patients. 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). Patient reported quality of care was similarly high in both groups.

In Oxford, a team of researchers adapted TrueColours(175), a software package originally designed for use in bipolar disorder, to be used in monitoring and remotely managing ulcerative colitis patients (and is currently being adapted for use in Crohn's). A pilot study of TrueColours IBD was conducted in 66 patients over 6 months in 2016. Inclusion criteria were broad and any patients with UC between the ages of 18 and 65 years with UC of any severity in possession of a

smartphone were deemed eligible. Email prompts encouraged patients to complete daily SCCAI questionnaires, fortnightly QoL scores, monthly home FC (IBDoc®®)) and 3-monthly ICHOM(176) questionnaires. ICHOM is the International Consortium for Health Outcomes Measurement who devised a set of standard outcome metrics deemed by international consensus to be important measures of IBD-health such as weight, prednisolone use etc, and more recently IBD-Control 8(176).

The authors used the IBDoc® faecal calprotectin test kit, produced by Buhlmann Laboratories. This is a pre-packaged kit that provides the equipment and instructions to allow patients to test their own stool at home. A series of steps is required to transfer some stool to a test "cassette" and the smartphone camera may be used as a cassette reader, scanning the cassette and calculating a quantitative calprotectin level. Results were then transferred to a clinician-facing IBDoc® web portal and its associated 'application processing interface' (API) - a list of formatted commands allowing individual programmes to communicate with one another directly. This allowed graphical representation of FC in TrueColours UC, with daily secure requests made from the TrueColours UC server to the IBDoc® Portal to pull through and update results. This integration was reported to be successful with no significant concerns reported.

Results were coded into a traffic light system of disease activity based upon responses. Feasibility was demonstrated with 76% adherence to daily SCCAI and 95% adherence to fortnightly QoL questionnaires, and 75% adherence to monthly FC. One of the strengths of the study was a mixed methods approach, and it is one of few studies to explore the impact of a digital intervention qualitatively in a broad mix of UC patients. Combined qualitative interviews and questionnaires demonstrated an overarching theme of empowerment, with increased levels of disease awareness and control, as well as improved communication with healthcare providers.

In 2018, Del Hoyo et al conducted a high quality 3-arm pilot randomised controlled trial (complying with 30/35 applicable CONSORT checklist items) to evaluate the impact of remote monitoring using a Web system—Telemonitoring of Crohn's Disease and Ulcerative Colitis (TECCU)—compared to standard and telephone care on health outcomes and health care in patients with complex IBD. These patients were all initiating treatment for active disease, which may justify closer monitoring. They recruited 63 adult patients (enrolled over 21 months) with IBD receiving immunosuppressants and biological agents from a tertiary university hospital. Participants were randomized to receive remote monitoring (TECCU), nurse-assisted telephone care (NT – regular telephone consultations with IBD nurses), or standard care with outpatient clinic visits (control) over 24 weeks.

TECCU was described as a secure webpage accessible by mobile phone, tablet, or computer. Patients connected to the platform and completed questionnaires, received advice, reminders, educational material about their disease, and information on prevention of disease flares. This information was received by the case managers and filtered using an 'intelligent prioritization system' with generation of alerts and push notifications according to an integrated intervention protocol. Patients in the TECCU group answered questions relating to their IBD symptoms and possible adverse effects since the last evaluation via text messaging. A strength of the TECCU intervention was the creation of individualized alerts and action plans based on the answers to questions about the activity index, adverse effects, and blood biochemistry results. As in previous studies, a traffic light value was assigned to each alert allowing triage of cases. After receiving an alert, IBD physicians and nurses used the general recommendations of the action plans to guide medication adjustments (including biological agents), with telephone calls or clinic visits when necessary. Once the disease was in remission again (green zone), the patient continued with the initially programmed follow-up. Patients treated with immunosuppressants alone or in combination with biological agents were monitored every 1-2 weeks during the first month, every 2-4 weeks between months 1 to 3, and every 4 weeks from month 3 until the end of follow-up. Patients treated with biological agents alone were monitored every 2-4 weeks during the entire follow-up period.

The primary outcome was the percentage of patients in remission at 24 weeks, with secondary outcome measures of quality of life, medication adherence, adverse effects, satisfaction, social activities and health resource use. 21 patients were recruited to each group. Compliance was good: 85.7% (18/21) in the TECCU group were compliant with the intervention vs. 90.5% (19/21) in control and 95.2% in NT. After 24 weeks, the percentage of patients in remission was higher in TECCU (17/21, 81%) than in NT (14/21, 66.7%) and the control (15/21, 71.4%), although sample sizes were too small to achieve statistical significance. This was recognised by the authors as a weakness of the study; however, this was a pilot, and a smaller sample is expected. The authors do not comment on enrolment but the average recruitment rate of 3 patients per month in this pilot study needs to be taken into consideration in a larger study. A multicentre approach may help increase the potential recruitment pool which is already limited compared with previous study by recruiting only patients flaring and initiating new treatment for unstable disease. A higher improvement in disease activity was observed in TECCU than in controls in terms of the Harvey-Bradshaw/Mayo indices but was not statistically significant (odds ratio=0.12, 95%

CI=0.003-2.162, P=0.19). IBDQ-9 scores of patients from all 3 groups improved after 24 weeks (median IBDQ-9 scores increased from 38.5 to 53 in controls, from 37.5 to 53 in NT, and from 42 to 52.5 in TECCU (overall intervention effect on the IBDQ-9 score: OR=8.42, 95% CI=3.98-17.81, P<.001) but the improvement in IBDQ-9 was not significantly different among groups (TECCU vs control: OR=1.25, 95% CI=0.49-3.15, P=.64; NT vs control: OR=0.79, 95% CI=0.32-1.98, P=.62).

Faecal calprotectin levels were assessed at baseline, 12 and 24 weeks but it did not feature in the study in monitoring (which was predominantly symptom-based). FC could be a useful addition to subsequent full RCT particularly in assessing treatment response in this group of potentially unstable patients who have recently commenced/escalated IBD treatment. As a pilot the results are very encouraging but further larger-scale study is required to determine whether digital SSM interventions can improve the long-term course of IBD in a more-complex setting.

A 2019 study by Cross et al(129) was considered for inclusion but did not fit the criteria of utilising a 2-way digital interactive portal as participants simply responded to text messaging from their healthcare team. It did however utilise a web-based decision support server for healthcare providers not dissimilar to that used in other portals and has therefore been included for discussion separately. Following on from their initial study of the UCHAT telemedicine intervention for UC in 2012(128), Cross et al conducted a 2019 large, multicentre RCT of telemedicine for IBD (TELE-IBD) with 348 participants, all of whom had had active disease in the preceding 2 years. 117 were controls, 115 received telemedicine every other week (EOW) and 116 telemedicine weekly. Engagement was good with 259 (74.4%) completed the study after 1 year. Outcomes included disease activity, quality of life and health resource utilisation.

TELE-IBD was designed using a mobile phone for participants and a decision support server and website for healthcare staff who could individualize alerts and action plans for each participant. If pre-determined criteria were met after testing, simultaneous action plans and email alerts were sent to the participant and nurse, respectively. Participants in the intervention groups were prompted to respond to a series of texts grading their IBD symptoms (HBI and SCCAI). After answering questions about their symptoms, participants received a list of medication, dose and directions. They did not access a website or decision support server.

In CD, all groups experienced a decrease in disease activity (control -5.2 +/- 5.0 to 3.7 +/- 3.6, TELE-IBDEOW 4.7 +/- 4.1 to 4.2 +/- 3.9, and TELE-IBD weekly 4.2 +/- 4.2 to 3.2 +/- 3.4, p< 0.0001 for each of the groups). In UC, only controls had a significant decrease in disease activity (control 2.9 +/- 3.1 to 1.4 +/- 1.4, p= 0.01, TELEIBD EOW 2.7 +/- 3.1 to 1.7 +/- 1.9, p= 0.35, and TELE-IBD Weekly 2.5 +/- 2.5 to 2.0 +/- 1.8, p= 0.31). QoL increased in all groups; the increase was significant

only in TELE-IBD EOW (172.3 +/- 33.1 to 181.5 +/- 28.2, p= 0.03). Unadjusted and adjusted changes in disease activity and QoL were not significantly different among groups. Healthcare utilization increased in all groups. TELE-IBD weekly were less likely to have IBD-related hospitalizations but more likely to have non-invasive diagnostic tests and electronic encounters compared to controls which may suggest closer monitoring and action relating to flare-ups. Disease activity and QoL, although improved in all participants, were not improved further through use of the TELE-IBD system. This is contrast to the Constant Care study(1) Discussed in Chapter 2 but it is difficult to draw a direct comparison between mobile phone telemedicine versus a two-way interactive web-portal which may perhaps add the next level of bespoke care.

3.4.2 *Registered studies*

There is currently 1 study registered with the ClinicalTrials.gov and ISRCTN trials registers that will complement the existing literature. IBD and Me (ClinicalTrials.gov Identifier: NCT03695783)(177) is a pragmatic multicentre randomised controlled trial in outpatient IBD care which compares the use of an online shared -decision making tool that allows patients to explore decisions around choice of biologic therapy at their own pace, versus high quality IBD educational material from the Crohn's and Colitis Foundation. The researchers aim to recruit 152 patients and hypothesise that by optimising shared decision-making they can make incremental benefits to patient care. Outcomes include patient perceptions of shared decision making and decisional conflict, patient satisfaction, IBD-control and quality of life (all measured via questionnaire), as well as initiation or switch of treatment. No results are yet available.

3.4.3 *Other available digital portals*

3.4.3.1 Patients Know Best

Patients Know Best (PKB)(178) is an NHS-endorsed digital management platform that is being adopted by multiple UK health providers. It allows patients and clinicians to upload, view and edit various health data (e.g., symptoms, medications, diagnoses, test results, and body measurements). In addition, it provides features that are traditionally not part of a health record, such as electronic messaging, video conferencing, and file management. PKB can be tethered to the EHR of a hospital, so that both systems can interact, and data shared. In the context of IBD, a qualitative Cumbrian case study(179) of PKB examined usage of PKB by stakeholders in an NHS Foundation trust amongst inflammatory bowel disease patients by conducting qualitative interviews and a patient survey. Clinicians reported PKB to be a useful new way of managing stable patients, facilitating clinical and cost-effective use of specialist nurses; improved two-way communications, and more optimal use of outpatient appointments and consultant time. For

patients, the system was reported to be a source of support when unwell and facilitated improved communication with specialists. Three main barriers to adoption were identified: concerns over security, risk averse attitudes of users and problems with data integration.

3.4.3.2 MyIBD portal

In Salford (UK), healthcare and IT teams collaborated with local patients and the IBD charity Crohn's and Colitis UK to create MY IBD portal(180) – a web-based IBD management platform. The portal incorporates access to personalised patient record, links to information about IBD, access to investigation results, disease monitoring tools and an electronic messaging system with email triggers when disease activity scores are high. As of 2018, 720 IBD patients were recorded as using the portal. In a poster presentation of a service evaluation(181), clinic attendances were reduced from an average of 2.9 attendances per patient per year to 0.6 attendances per year for self-management users which was estimated to release over 500 clinic appointments. Although formal study of the portal effects has not yet been published, early user data reported 98% of users rating the process as either good or excellent.

3.4.3.3 UCLA eIBD

UCLA (University of California, Los Angeles) developed a 2012 which is downloadable from iTunes/Google Play for patients at the UCLA Centre for IBD although little has been published on its use in a research context. The system utilises predefined symptoms thresholds which trigger automated alerts to a nurse specialist. Investigators validated two 4-question, patient-reported outcome questionnaires used in the UCLA eIBD mobile app to remotely monitor disease activity in 566 IBD patients(182) and were able to demonstrate that patient-reported disease activity was an independent predictor of clinical disease activity. There is no mention in the limited available literature as to whether two-way interaction is possible via the app and it does not appear to be searchable on UK app stores and equivalent.

3.4.3.4 My IBD Care

My IBD Care mobile phone application was developed by Ampersand Health in partnership with Crohn's & Colitis UK and the gastroenterology teams at King's College Hospital and Barts Health(183). It is marketed as helping people with IBD to access support and resources, set medication and appointment reminders, and self-report their condition giving a greater sense of empowerment. The app uses a cloud-based dashboard which allows healthcare professionals to view information uploaded by patients. In a small survey among patients patient users, 85% reported stated they would prefer to use the app as their preferred method of clinical contact for

routine check-ups, echoing previous study of other web-platforms proposed as a means of providing patient-centric care and freeing up outpatient resources.

3.5 Summary

This systematic review demonstrates a small but increasing amount of research on the effects of digital supported self-management interventions in IBD on patient outcomes. Strengths of the review include the use of comprehensive search terms and multiple sources including databases, reference lists, conference proceedings and clinical trials databases. Restriction to English-language databases however may have led to missed studies. The use of CONSORT checklists provided an objective means of assessing study reporting quality. A significant limitation to the review was the lack of double screening of papers which was unfortunately not possible due to limited resources. Due to the small number of available studies for review, I included studies of any type, including pilot studies. This, combined with a wide range of outcome measures, meant that a meta-analysis was not feasible.

Based upon CONSORT criteria, study reporting quality was variable, but more recent large studies such as de Jong et al (133) provide more robust evidence. Whilst only two of the studies discussed in this review demonstrated statistically significant improvements in QoL because of self-management interventions(132, 171), none demonstrated any deterioration in QoL which is important to consider when implementing new technologies. Self-management websites appear to be acceptable to both patients and healthcare providers (127, 132, 133, 135). They have the potential to better disease outcomes by improving medication adherence (127, 133, 171) and disease knowledge(127) although little is known on the longer term effects on IBD outcomes. Two studies were able to demonstrate significant cost-savings, predominantly through saved outpatient appointments and a reduction in expensive biologic drug use(1, 127) which provides a strong rationale for the use of self-management so that resources can be fed back into patient care.

The review has highlighted potential gaps in the knowledge surrounding the use of digital self-management interventions in IBD. Except for Del Hoyo et al(131) who examined a digital intervention in patients with active disease starting new treatments, most studies examined patients with established or stable disease. There is therefore scope to explore digital interventions in in a slightly higher risk population of IBD patients (such as those with active disease or those stopping a treatment) who may be more vulnerable to disease flare. Just one study (130) explored in detail how a digital intervention and home testing impacted upon patients' quality of life and well-being through qualitative research. The use of FC monitoring,

particularly home test kits, has increased the scope of self-management websites by providing selected patients with a rapid, objective additional means of assessing disease activity. Whilst some studies found regular calprotectin testing (either self-administered or sample collected at home and sent to a laboratory) testing to be a feasible adjunct to self-monitoring(1, 171, 175), adherence to testing was not always high and this warrants further research into acceptability of home-testing. These are areas for future study. Home FC monitoring is discussed in more detail in Chapter 4.

4 Pilot FC-testing for suspected IBD in Primary Care

4.1 Introduction

This chapter describes a pilot study of faecal calprotectin testing for suspected IBD in primary care. Diagnosis forms the first step in the IBD patient's healthcare pathway. This can sometimes be delayed due to patient and healthcare factors and can result in poor outcomes in IBD patients. This chapter examines how access to faecal calprotectin testing (previously a specialist secondary care test) may influence GP referrals to secondary care.

Patients commonly present to primary care with lower gastrointestinal (GI) complaints(184). It can be difficult to differentiate between symptoms of irritable bowel syndrome (IBS) and more serious pathology such as IBD. Delayed diagnosis of IBD can have a significant negative impact upon patients' quality of life and longer term health outcomes(184). Traditionally, most patients referred to GI clinics undergo lower GI endoscopy, which is invasive, costly, and carries a risk of complications(66). The development of non-invasive markers of intestinal inflammation such as FC have enabled physicians to stratify risk of significant pathology and potentially avoid unnecessary referral to secondary care(36) as well as giving greater confidence in making a positive diagnosis of IBS. The IBD Standards for the care of people with IBD(2) recommend that "clear pathways and protocols for investigating children and adults with persistent lower gastrointestinal symptoms should be agreed between primary and secondary care and should include guidance on the use of faecal biomarker tests in primary care to aid rapid diagnosis"(Appendix A.1). In this chapter I describe pilot access to FC testing for suspected IBD amongst local general practitioners (GPs) and evaluate its impact on GP referral practice to secondary care.

4.2 Background

4.2.1 *Faecal calprotectin*

FC is a reliable, non-invasive marker that detects bowel inflammation, even in the presence of macroscopically normal endoscopic appearances, normal biochemistry (e.g. C-reactive protein (CRP)), or in the absence of symptoms. Calprotectin is a stable 36-kDa calcium and zinc binding protein that accounts for about 60% of total proteins in the cytosol fraction in neutrophil granulocytes(185). It has antimicrobial activity and is involved in the regulation of inflammatory reactions. It is released into the faeces at any site where neutrophils gather in the presence of intestinal inflammation. It remains stable in stool samples for up to seven days at room temperature and one sample of less than 5g is sufficient for a reliable measurement.(186) FC is

not specific for IBD and may also be increased in infectious gastroenteritis, colonic neoplasia, diverticulitis, polyps, and non-steroidal anti-inflammatory drug use (187).

FC-testing can be useful in both the diagnosis and in monitoring of established IBD. As a screening tool for IBD, low FC cut-offs give high sensitivity for IBD but poor specificity. Sensitivity is consistently high across studies (83-100% at levels under 50 micrograms/g), but specificity is more varied at a cut-off of 50 micrograms/g (51–100%)(36). This could potentially result in a significant number of patients without IBD being referred for colonoscopy and as a result, NICE have recommended an intermediate range defined from 50 to as much as 200mcg/g of stool where repeat interval testing may be appropriate, but add that until further evidence is available, thresholds should be determined locally based on audit data and clinical assessment(36). A number of different commercially available calprotectin assays exist with the potential for inter-assay variability, however in a comparison study of six different assays for FC, all assays showed comparable clinical performance for diagnosis of IBD(188). For monitoring of IBD, it is recommended that the same assay is used where possible to ensure consistency(36).

In primary care, FC-testing is recommended by NICE to support differentiation between IBS and IBD in adults with recent onset lower GI symptoms for whom specialist assessment is being considered(36). Testing can be performed qualitatively, semi-quantitatively or quantitatively using either laboratory-based ELISA (enzyme-linked immunosorbent assay) or 'point of care' testing (POC, e.g. CalDetect®, QuantonCal®) methods. There is only a small difference in cost between laboratory-vs POC testing. NICE conducted an economic analysis as part of the development of their 2013 FC diagnostics guideline NICE(36). The 2013 per person costs of an ELISA test and POC test (CalDetect®) were estimated to be £22.79 (based on an assumption of 40 patient samples per 96-well plate, plus an average 11–12 minutes of staff time at band 6/7) and £24.03 (test list price plus cost of 15 minutes of GP practice-nurse time) respectively. This compares to around £480 for a colonoscopy(36).

4.2.2 *Faecal calprotectin use in primary care*

Most research on FC comes from secondary care populations and its use in assessing response to treatment and detecting disease activity. There is a limited but growing body of literature describing the use of diagnostic FC-testing in primary care, exploring both lab-based and POC-testing in GP surgeries, with a focus on differentiating between IBS and IBD.

In 2013, supported by the NHS Technology Adoption Centre, Dhar et al(189) were one of the earliest UK adopters of FC-testing in primary care. They developed a pilot programme to assess the feasibility of POC FC testing (Caldetect®, Preventis, GmbH) and its impact upon GP referrals to

secondary care. Approximately 253 referrals are made annually to secondary care in the Durham Dales primary care trust (PCT) to assess patients < 60 years presenting with diarrhoea, with associated costs of around £119,000. A pathway for investigating chronic diarrhoea using semi-quantitative FC testing was designed and implemented in the community (population 150,000) for a 7-month period in 2011/12. 142 Caldetect® tests were carried out in primary care during this pilot phase: 89 (59%) were negative (<15 µg/g), 36 (25%) were positive (> 60 µg/g), 3 (2%) tests were intermediate and 14 (10%) tests could not be accurately reported, quite a high rate of loss in testing. Patients with negative results were managed in primary care as IBS. Significant annual cost savings of £73,200 were made from outpatient consultation and endoscopy tariffs. Based on current literature, it would be expected that although the sensitivity would be very high, the specificity for IBD would be low at the above levels. The study authors have subsequently presented (unpublished)a post-implementation audit of faecal calprotectin level and diagnosis in 122 patients, and suggest a higher cut-off level of 100 µg/g (sensitivity 98%, specificity 74% at 50ug/g, vs sensitivity 94%, specificity 82% at 100ug/g)(190) may be more appropriate.

In 2016, a UK Somerset team of community dieticians, primary and secondary care physicians, and the local clinical commissioning group (CCG) published an audit of a new best practice pathway with a focus on aiming to achieve timely diagnosis and effective treatment for patients with IBS(191). They hypothesised that better primary care educational resources for diagnosing IBS, combined with an effective management pathway, should lead to direct NHS savings allowing secondary care gastroenterology services to utilise their limited resources more effectively. The team implemented 3 interventions: education for GPs (diagnostic/management algorithms for IBS in the form of a desktop 'app' and GP teaching sessions), primary care provision of FC testing for patients aged 16-45 (no referral if <50µg/g), and a community dietetic-led service offering dietary intervention for patients diagnosed with IBS. Over 12 months, there was a 36% reduction in referral of patients with likely IBS from GP to secondary care, resulting in estimated annual savings of around £120,000 because of reduced outpatient clinics and endoscopies. Over 2 years, 308 FC samples were requested by primary care. GPs were contacted to inquire as to the health of any patients who were not referred despite a FC of >50µg/g. In 12/13 patients with a FC of 50-150µg/g where referral did not take place, GPs reported no further contact from the patient and it was assumed by the team that patients would have contacted their GP should symptoms have persisted. The authors justify the decision not to pursue this any further because of a previous analysis that showed that significant pathology was highly unlikely unless the FC level was >150µg/g. 38/63 (60%) of patients in this 50-150µg/g bracket were referred and seen in

secondary care but only 1 potential IBD case diagnosed. For those patients diagnosed with IBS, dietetic input proved successful, with all symptom scores (pain, bloating, urgency etc.) showing statistically significant reduction (all p values <0.001). The intervention was certainly successful in reducing secondary care referrals and increasing cost-savings. It would be of benefit to re-audit outcomes for patients in the future to determine if any of the patients managed in primary care were ultimately referred to secondary care further down the line, but the improved IBS symptom scores are encouraging, and dietary interventions can be continued by the patient long-term. The authors suggest the introduction of more holistic approaches such as hypnotherapy and cognitive behavioural therapy¸ as endorsed by NICE in 2008(33).

In 2016, York teaching hospital published their implementation of a primary care pathway for suspected significant organic bowel disease (IBD, microscopic colitis, diverticular disease, gastroenteritis, coeliac disease, pancreatic insufficiency, and significant adenoma) incorporating the use of FC in 262 patients aged 18-60 years (192). Patients with a FC < 100 µg/g were assumed to have IBS and managed with positive reassurance, NICE guidance-based treatments, plus a GP review at 6 weeks and routine referral to gastroenterology services only if still symptomatic. Turnaround times for FC results (lab-based) were around 7 days. Indeterminate FC results (100-250 µg/g) were repeated at 2 weeks and referral made only if rising to over 250 µg/g. Those remaining between 100 and 250 µg/g were referred routinely to gastroenterology services. Cases with FC results of >250 µg/g were directed to a 'straight to test' (STT) colonoscopy. Those patients with a poorer performance status (≥3) received an urgent outpatient appointment to assess fitness for colonoscopy. Results for the pathway group were analysed against a comparator group in a neighbouring hospital trust. Implementation of the pathway resulted in an average of 4 referrals to secondary care per week. It is not known if this is in addition to usual caseload, or if these patients would have been referred eventually. The mean time from referral to diagnosis of IBD was 20 days, well within recommended standards(4). 82% of patients had a FC of less than 100µg/g however a high proportion (30%) of these remained symptomatic at 6 weeks and were ultimately referred to secondary care. Organic intestinal disease was found in 8% of patients with FC<100 mcg/g, all of whom were 50 years and older and had a FC>50 mcg/g. The FC was 100–250 mcg/g in 6.5% of patients (on repeat testing), of which 23% had organic intestinal disease. FC was >250 mcg/g in 11.5% of patients with a diagnostic yield of 36% for IBD and 53% for all organic intestinal disease. A FC>250 mcg/g had a sensitivity of 89% for IBD however the investigators did not report on specificity for IBD. This is a high cut-off in the context of current IBD literature, but the investigators are applying it in the context of a broad age-ranging population (where risk of significant disease is expected to be higher as age increases) and in identifying different

diagnoses. Feedback from GPs was positive, with 90% agreeing/strongly agreeing that the FC test had been useful in their clinical decision-making when considering organic bowel pathology (not specifically IBD). 71% agreed that a result <100 μ/g would prevent the need for a referral. There is still debate surrounding optimal cut-off level of FC to ensure adequate detection of IBD whilst utilising limited resources and minimising unnecessary investigation in low-risk groups(36).

One particularly impactful study of faecal calprotectin in the diagnostic pathway for IBD was "The New Faecal Calprotectin Care Pathway" published in 2018 via the NICE shared learning database(193). Turvill et al, in collaboration with the Yorkshire & Humber Academic Health Science Network (AHSN), developed a new pathway for utilising FC testing in line with the NICE 2013 guidance DG11(36). The cut off for the faecal calprotectin (FC) assay proposed in the NICE Guidance (50μg/g) was found to increase the number of referrals to secondary care as the specificity at that cut off was not sufficient to prevent a high number of patients with IBS being unnecessarily referred to secondary care. The NICE guidance includes a research recommendation which states: "Further research is needed on the impact of faecal calprotectin testing on clinical decision making when added to current practice. This includes research into optimal cut off values for tests and the investigation of repeat testing strategies in people with intermediate levels of faecal calprotectin. Development of a consistent definition for the 'intermediate range' is encouraged".

The York pathway increased the recommended FC cut-off level to 100μg/g (Buhlmann assay) and provided risk assessment tools and a pack of resources support GPs (template business case, leaflets, education video) to use their clinical judgement on whether a referral was necessary, with the aim of reducing pressures on secondary care endoscopy and outpatient services, improving patient experience and health economics. The authors found this increased adherence to the pathway to 85% (the pathway previously used in Leeds had a reported adherence of 11%). The pathway has been rolled out to multiple other regions across England.

Reported barriers to adoption included reluctance and hesitance of gastroenterologists in the trusts, how this would fit with other pathways and how FIT testing would affect the future of FC testing. Despite this, the cost benefits have been clear with an economic evaluation demonstrating savings of £100,000 to £160,000 per 1000 patients tested; this equated to a saving of £2.5 million in the Yorkshire and Humber region alone. The evaluation also found that the pathway saves one unnecessary colonoscopy and outpatient appointment per 4-6 patients tested (147-262 colonoscopies per 1000 patients). The sensitivity and specificity of the new pathway was found to be 94% and 92% respectively versus 94% and 61% for the other pathway mentioned in

the NICE guidance. One key piece of learning reported was that when developing an implementation plan with CCGs, that having a clinical champion speak at GP education events was key to better GP understanding of and adherence to the new pathway.

4.3 Aims/objectives

The aims and objectives of this chapter are:

i. To explore the impact of a local programme of pilot primary care FC-testing on GP referral of patients with suspected IBD to secondary care.
ii. To develop a proposed care pathway combining primary care FC testing and a local secondary care 'Positive Calprotectin Clinic'.

4.4 Methods

My research supervisor Dr Fraser Cummings devised the pilot study. I collected and analysed the initial data, wrote to GPs to establish outcomes of patients with positive calprotectin who were not referred to secondary care, and wrote the protocol for the new 'positive calprotectin clinic'. This pilot study was conducted as part of a service evaluation (confirmed using the HRA/MRC decision tool(194)) and ethical approval was therefore not sought.

4.4.1 *GP recruitment*

University Hospital Southampton NHS Foundation Trust serves a population of 1.3 million people, receiving referrals from within Southampton City and around half of West Hampshire CCGs. In April 2015, Dr Cummings presented the proposed pilot at a local educational GP meeting and invited all 64 GP practices within area via email and local GP newsletter to opt in to FC testing in patients under the age of 45 who they were considering referring to secondary care with suspected IBD. GP plans to refer were recorded, as well as whether the referral ultimately took place on receipt of the FC result.

FC was requested electronically using the existing GP requesting system (ICE®). A series of mandatory questions were designed to prompt appropriate use of the test and allowed data collection for audit. If the response to any of the first 4 questions was 'no' then the request was automatically cancelled and the requester unable to proceed.

Figure 4: Mandatory-requesting audit questions

1. Patient age <45 years? Yes/no
2. IBD is suspected or possible? Yes/no
3. Low suspicion of colorectal cancer? Yes/no
4. No NSAID (including aspirin) for the last 6 weeks? Yes/no
5. If FC was not available would you have referred this patient to secondary care? Yes/no
6. Are you planning to refer this patient to secondary care even if FC is normal? Yes/no
7. Duration of symptoms (weeks)?
8. Abdominal pain? Yes/no
9. Pain improves with defecation? yes/no
10. Change in stool frequency? Yes/no
11. 24hr stool frequency? Yes/no
12. Change in stool appearance/frequency? Yes/no
13. Change in stool consistency? Yes/no
14. Rectal bleeding? Yes/no
15. Unintentional bleeding? Yes/no
16. Nocturnal symptoms? Yes/no
17. Family history of IBD? Yes/no
18. Family history of bowel or ovarian cancer? Yes/no
19. Alcohol? (units per week)

The following guidance was issued to GPs via an automated prompt when interpreting FC results:

- Positive: FC≥100 µg/g faeces - referral to Gastroenterology recommended.
- Negative: FC<50 µg/g faeces - IBD unlikely, consider primary care IBS management.
- Indeterminate: FC 50-99µg/g faeces - check for NSAID use. If symptoms persist re-test FC after 4-6 weeks. If on re-test FC ≥50 µg/g faeces referral to Gastroenterology is recommended.
- If clinical concern despite a negative FC - do not repeat but refer as usual, including result in the referral letter and stating features of concern.

4.4.2 *Laboratory procedures*

FC samples were processed in the UHS laboratory using the EliA® calprotectin assay (Thermo Fisher®), an enzyme fluoro-immunoassay using mouse monoclonal antibodies to calprotectin. It is most cost-efficient to process these samples in batches therefore there can be a turnaround time of 1-2 weeks locally. EliA® shows good sensitivity and specificity for IBD with a FC cut off of ≤50µg/g (97.7% and 89.8% respectively) and is comparable to other commercial FC assays (188, 195).

4.4.3 *Data collection*

Data on GP responses to mandatory questions on ICE and FC levels were extracted by the UHS informatics team and linked to patient hospital numbers. Electronic patient records were then

screened for clinical information on endoscopic investigation, clinic letters, and imaging results pertaining to the patients' diagnosis.

4.4.4 *Follow up of non-referred patients*

For patients who were not referred to UHS despite having a positive FC, GPs were contacted via letter with a brief questionnaire inviting them to respond with further information and an invitation to refer the patient if they felt this was necessary. Responses were sent back to the Gastroenterology Department in a stamped, addressed envelope.

4.5 Results

4.5.1 *Uptake of testing*

59/64 (92%) invited GP surgeries took part in pilot FC testing. 435 FC samples were received by the laboratory over 15 months between April 2015 and June 2016. Of these, 410 (94%) were suitable for processing. Reasons for non-processing of samples included unlabelled specimens, undated specimens, and contamination of specimen through leakage. GP usage of FC was relatively modest with an average of 29 samples received by the laboratory each month. To put this into context, during the 15-month pilot, an average of 187 referrals were received by specialist gastroenterology services per month (not including hepatology), of which around a quarter to a third might be expected to be for investigation of lower gastrointestinal symptoms, in which case a FC might be a relevant test.

4.5.2 *Results by FC level*

66/410 (16.1%) yielded a positive calprotectin (FC ≥100 µg/g), 33/410 (8.0%) were indeterminate (FC 50-99 µg/g), and 311/410 (75.9%) were negative (FC <50 µg/g). The mean calprotectin in the positive group was 1307.2 µg/g (range 104-6000 µg/g). Table 3 gives a summary of results by FC category.

Table 3: Summary of results by FC category

Item		All	Negative FC <50	Indeterminate FC 50-99	Positive FC ≥100
		n *(%)*	n *(%)*	n *(%)*	n *(%)*
Patients		410 *(100)*	311 *(75.9)*	33 *(8.0)*	66 *(16.1)*
Sex (F:M)		241:169	192:119	18:15	31:35
Age	*Mean*	30	29	31	30
	Median	29	28	30	31
	Range	16-45	16-45	17-45	17-45
FC	*Mean*	228.5	16.1	72.4	1307.2
	Median	29	28	73	571.5
	Range	3.8->6000	3.8-49	50-99	104->6000
Low suspicion of colorectal cancer?		410*(100)*	311*(100)*	33*(100)*	66*(100)*
Symptom duration (weeks)	*Mean*	74.9	80.9	68.7	49.3
	Median	26	30	50	10
	Range	1-520	1-520	1-350	1-400
Abdominal pain		369*(90)*	282*(90.7)*	30*(90.9)*	57*(86.4)*
Pain improved with defaecation		224*(54.6)*	168*(54.0)*	20*(60.6)*	36*(54.5)*
Change in stool frequency		356*(86.8)*	269*(86.5)*	29*(87.8)*	58*(87.9)*
24-hour stool frequency	*Mean*	4.3	4.2	4.7	4.65
	Median	4	4	3	4
	Range	0-25	1-25	0-20	1-12
Change in stool appearance		355*(86.6)*	267*(85.9)*	29*(87.9)*	59*(89.4)*
Rectal bleeding		140*(34.1)*	91*(29.3)*	9*(27.3)*	40*(60.6)*
Unintentional weight loss		77*(18.8)*	47*(15.1)*	6*(18.2)*	24*(36.4)*
Nocturnal symptoms		139*(33.9)*	96*(30.9)*	12*(36.4)*	31*(47.0)*
Family history of IBD		60*(14.6)*	51*(16.4)*	4*(12.1)*	5*(7.6)*
Family history bowel or ovarian cancer		43*(10.5)*	34*(10.9)*	1*(3.0)*	8*(12.1)*
Alcohol units/week	*Mean*	4.5	4.48	4.45	4.73
	Median	1	1	7	1.5
	Range	0-175	0-175	0-50	0-25
Lower GI endoscopy	All	68*(16.6)*	17*(5.5)*	4*(12.1)*	47*(71.2)*
	Colonoscopy	54*(13.2)*	10*(3.2)*	4*(12.1)*	40*(60.6)*
	OGD & colonoscopy	6*(1.5)*	5*(1.6)*	0*(0)*	1*(1.5)*
	Flexible sigmoidoscopy	7*(1.7)*	2*(0.6)*	0*(0)*	5*(7.6)*
	Capsule endoscopy	1*(0.2)*	0*(0)*	0*(0)*	1**(1.5)*

* (recent normal colonoscopy)

4.5.3 *Endoscopic evaluation and diagnoses*

4.5.3.1 Negative FC

311/410 (75.9%) of patients tested had a negative FC (<50 µg/g). 35/311 (11.3%) patients with negative FC were referred to secondary care. 2 further patients were already under outpatient care of gastroenterology. Lower GI endoscopic evaluation was undertaken in almost half of referred patients with a negative FC (n=17, 48.6%), suggesting that the secondary care physician felt the referral for further investigation appropriate. Table 4 shows the diagnoses of those patients who were referred to secondary care.

Table 4: Negative FC cases referred to secondary care: diagnoses in all cases and in those undergoing lower gastrointestinal endoscopy

Diagnosis	**All cases with negative FC n=35**	**Cases with negative FC undergoing lower GI endoscopy n=17**
	n *(%)*	**n *(%)***
IBD	0	0
IBS	23 *(65.7)*	10 *(58.8)*
NSAID-associated damage	1 *(2.9)*	1 *(5.9)*
GORD	1 *(2.9)*	0
Microscopic colitis	2 *(5.7)*	2 *(11.8)*
Idiopathic bile salt malabsorption	2 *(5.7)*	2 *(11.8)*
Coeliac	3 *(8.6)*	2 *(11.8)*
Unknown	2 *(5.7)* (x1 DNA, x1 no appointment)	0
Post-infectious IBS	1 *(2.9)*	0

Whilst most patients (23/35, 65.7%) were ultimately diagnosed with IBS, some significant alternative diagnoses were made – namely bile salt malabsorption, coeliac disease and microscopic colitis, all of which require specialist input. Although these 4 patients make up 11.4% of the cohort of referred patients with negative calprotectin, it is not known if this rate is representative of the remaining, non-referred cohort. It should also be noted that although significant diagnoses in terms of the effect of symptoms on patients and potential for treatment, unlike IBD, the long-term serious risks to patients with bile salt malabsorption or microscopic colitis (e.g. cancer, surgery) are not significantly elevated (196).

4.5.3.2 Indeterminate FC

9/33 (27.3%) patients with indeterminate FC were referred to secondary care. 4 of these patients (44.4%) underwent colonoscopy. 1 case of IBD was identified. Table 5 illustrates the diagnoses observed.

Table 5: Indeterminate FC cases referred to secondary care: diagnoses in all cases and in those undergoing lower gastrointestinal endoscopy

Diagnosis	**All cases with intermediate FC n=9**	**Cases with intermediate FC undergoing lower GI endoscopy n=4**
	n *(%)*	**n *(%)***
IBD	1 *(11.1)*	1 *(25)*
IBS	4 *(44.4)*	1 *(25)*
GORD	1 *(11.1)*	0
Microscopic colitis	1 *(11.1)*	1 *(25)*
Infection (acute)	1 *(11.1)* (C. difficile)	1 *(25)*
Unknown	1 *(11.1)* (DNA)	0

Of the 33 patients with indeterminate FC, 14 (42.4%) had repeat FC testing, 3 of which were >100 µg/g. Of the 3 repeat elevated readings (901 µg/g,152 µg/g,231 µg/g), all were referred to secondary care with one diagnosis of IBD made (FC 901 µg/g). These cases are included in the positive FC section below.

4.5.3.3 Positive FC

52/66 (78.8%) patients with a positive FC were referred. 47/52 (94%) underwent lower GI endoscopic evaluation (colonoscopy or flexible sigmoidoscopy). Table 6 illustrates the diagnoses made.

Table 6: Positive FC cases referred to secondary care: diagnoses in all cases and in those undergoing lower gastrointestinal endoscopy

Diagnosis	**All cases with positive FC n=52**	**Cases with positive FC undergoing lower GI endoscopy n=47**
	n *(%)*	**n *(%)***
IBD	21 *(40.4)* (CD 8, UC 10, IBDU 3)	21 *(44.6)*
IBS	17 *(31.5)*	17 *(36.1)*
NSAID associated damage	1 *(1.9)*	1 *(2.1)*
Infection (acute)	1 *(1.9)*	1 *(2.1)*
Post-infective IBS	4 *(7.4)*	4 *(8.5)*
Bile salt malabsorption	1 *(1.9)*	1 *(2.1)*

Coeliac	1 *(1.9)*	0
Unknown	6 *(11.5)* (2 suspicion of IBD – keep under review, x2 no appointment, x2 DNA)	2 *(4.3)*

Almost half (21/47, 44.6%) of patients with a positive FC who underwent lower GI endoscopy had a diagnosis of IBD. 14 (21.2%) patients with positive FC were not referred to secondary care services. One patient was admitted to hospital with acute severe UC as an inpatient, obviating the need for referral. For the remaining 13 patients, 10/13 (76.9%) GPs responded to a postal invitation (Appendix C.1) to supply further information on outcomes (Table 7). Only 1 additional case of IBD was identified from this enquiry.

Table 7: Outcomes of patients with positive FC not referred to secondary care (UHS)

Patient	Sex	Age at referral	Reason not referred	Diagnosis
1	F	20	Referral made. No appointment received. No request to reschedule	Unknown
2	F	41	Symptoms resolved	Unknown
3	F	45	Referred privately	Distal UC
4	M	32	GP called patient and left voicemail, no further contact	Unknown
5	M	35	Referred privately	Unknown
6	M	27	Symptoms resolved	Campylobacter enteritis
7	M	19	Symptoms resolved	Likely infective gastroenteritis
8	M	35	GP requested patient to repeat sample. No further contact.	Unknown
9	M	27	Normal colonoscopy at Care UK	IBS
10	M	35	Referred to another NHS hospital. Normal flexible sigmoidoscopy. Raised TTG.	Coeliac disease.

4.5.4 *Impact on GP referral practice*

4.5.4.1 GP plans to refer versus completed referrals

Almost a quarter of patients undergoing FC testing (96/410, 23.4%) were referred. Less patients were referred than initially indicated by GPs (23.4% vs 50.0%). When asked (pre-testing): "if FC was not available, would you have referred this patient to secondary care?" GPs responded "yes" 205/410 (50.0%) times, but only 62 (30.2%) of these patients were referred after FC testing. On 34 occasions GPs responded "no" but did ultimately refer 5 of these patients (14.7%). On 171/410

(42.0%) occasions GPs responded “unsure” and referred 29 of these patients (17.0%). This is illustrated in Table 8.

Table 8: Response to “If FC was not available would you have referred this patient to secondary care?” vs actual referrals

Number of patients GPs planned to refer	**Number of patients referred**			
“If FC was not available would you have referred this patient to secondary care?”	**All**	**Negative FC**	**Indeterminate FC**	**Positive FC**
	n *(%)*	**n**	**n**	**n**
Yes (n=205)	62 *(30.2)*	21	5	36
Unsure (n=171)	29 *(17.0)*	12	3	14
No (n=34)	5 *(14.7)*	2	1	2
Total	96	35	9	52

When asked a further question: “are you planning to refer this patient to secondary care even if FC is normal?” in 55/410 (13.4%) cases GPs responded “yes”, but only 27 (49%) of these patients were referred. In 175/410 cases GPs responded “no” but did ultimately refer 29 (16.6%) of these patients. This is illustrated in Table 9.

Table 9: Response to “Are you planning to refer this patient to secondary care even if FC is normal?” vs actual referrals

Number of patients GPs planned to refer	**Number of patients referred**			
“Are you planning to refer this patient to secondary care even if FC is normal?”	**All *(%)***	**Negative FC**	**Indeterminate FC**	**Positive FC**
Yes (n=55)	27*(49.0)*	10	1	16
Unsure (n=180)	40 *(22.2)*	12	4	24
No (n=175)	29 (16.6)	13	4	12
Total	96	35	9	52

Of the referred patients whom the GP had planned to refer even if the FC was normal, more had a positive FC compared with negative FC (16 positive vs. 10 negative). Of those referred whom the GP would refer even if FC were not available, more had a positive FC compared with negative FC (36 positive vs. 21 negative), suggesting these may be patients of higher concern to the GP.

GPs reversed initial decisions not to refer despite FC (“are you planning to refer this patient to secondary care even if FC is normal?”) on 29/175 (16.6%) occasions. This occurred in similar numbers irrespective of whether the FC was ultimately positive or negative (12 positive FC vs 13 negative FC, 4 indeterminate). GPs reversed plans to refer a total of 28/55 (50.9%) times. The

majority of these (24/28, 85.7%) had a negative FC, with 4 indeterminate. No plans to refer were reversed if the FC was positive.

4.5.4.2 Time from GP referral to outpatient appointment and endoscopy

Full electronic data were available for 87/96 (90.6%) referrals to secondary care. 68 endoscopy appointments took place, of which 55 (80.1%) occurred after secondary care review. 13 endoscopy appointments occurred prior to secondary care review, of which 7 had already taken place prior to the GP referral being made so were not included in the time to endoscopy analysis.

The mean time from GP referral to outpatient appointment (Table 10) was less for patients with positive FC than for negative FC (58.2 vs 76.6 days), as was time from outpatient review to endoscopy (31.6 vs 43.9 days). Mean time from GP referral to outpatient appointment was lower for IBD versus all diagnoses (39.9 vs 70.6 days), as was time from GP referral to endoscopy (71.3 vs 88 days). In some cases, there was a significant delay to endoscopy ranging up to 309 days from GP referral.

Table 10: Time from GP referral to outpatient appointment and endoscopy

		All FC/diagnoses	Negative FC	Indeterminate FC	Positive FC	Confirmed IBD
Time from GP referral to outpatient appointment (days)		*n=87*	*n=32*	*n=9*	*n=46*	*n=20*
	Mean	70.6	76.6	100.9	58.2	39.9
	Median	60	80.5	99	50.5	62
	Range	0-288	11-153	29-288	0-154	0-131
Time from outpatient appointment to endoscopy (days)		*n=55*	*n=14*	*n=4*	*n=37*	*n=16*
	Mean	36.1	43.9	49.3	31.6	38.8
	Median	21	33.5	42	15	27.5
	Range	1-268	5-173	19-94	1-268	1-268
Time from GP referral to endoscopy (days)		*n=62*	*n=18*	*n=4*	*n=40*	*n=17*
	Mean	88	99.1	138	78	71.3
	Median	75.5	99.5	140.5	62.5	89.5
	Range	0-309	24-214	110-161	0-309	9-309

4.5.5 *Sensitivity, specificity and predictive values of FC*

Sensitivity and specificity were calculated for the 68 patients who underwent lower GI endoscopic investigation, the 'gold standard' for IBD diagnosis. These were like other reported figures, but as

expected, varied depending on FC cut-off levels (Table 11). For a cut-off of ≤50µg/g, sensitivity and specificity were 100% and 27.9% respectively. For FC ≤100 µg/g, the sensitivity was 95.8% with a specificity of 45.5%. For 150 ≤µg/g the sensitivity remained at 95.8% with a slightly higher specificity of 52.3%. At ≤200 µg/g, sensitivity dropped to 91.7% and although specificity rose to 85.3%, the concern of missing cases of IBD increases.

Table 11: FC sensitivity and specificity by cut-off level

FC cut-off (µg/g)	% Sensitivity	% Specificity
≤50	100	27.9
≤100	95.8	45.5
≤150	95.8	52.3
≤200	91.7	85.3
≤250	91.7	75

Negative predictive values were high (93.5-100%) with varying FC cut-off levels from 50µg/g up to 250µg/g but positive predictive values were considerably lower (Table 12).

Table 12: Positive predictive value (PPV) and negative predictive value (NPV) by FC cut-off level

FC cut-off(µg/g)	% Positive predictive value	% Negative predictive value
≤50	47.0	100.0
≤100	48.9	95.2
≤150	52.3	95.8
≤200	59.5	93.5
≤250	66.7	94.3

4.6 Discussion

4.6.1 *Summary of observations*

Uptake of FC testing across GP practices was excellent with 92% engaging. An average of 29 samples were received each month (compared with 187 patient referrals to gastroenterology per month). There is little available data on what proportion of referrals to secondary care gastroenterology services are for IBD. Locally, gastroenterology new outpatient reviews are all coded under the umbrella of 'gastroenterology' and are not disease-specific, so it is difficult to access exact figures. There is surprisingly little data available on indications for referral to gastroenterology from primary care. One UK study(197) (published as a poster abstract) examined unselected new patient referrals to a single gastroenterologist's outpatient clinic during a 2-year period, reviewing clinical letters and outcomes of investigations to establish final diagnosis. For 397 referrals, 102 (25.7%) reported diarrhoea. 26.5% were diagnosed with IBS, 14.7% with bile acid malabsorption, and 11.8% had inflammatory bowel disease. It is not known the size of hospital, demographic mix, or number of other gastroenterologists to help ascertain a typical

referral caseload, but this illustrates the case mix and how common diarrhoea may be as a presenting complaint. A Spanish study(198) conducted a retrospective observational study of referrals to gastroenterology secondary care in nearly 2000 patients and found the most common reasons to be dyspepsia (27.7%), high-risk of colorectal cancer (17.1%), disturbance of bowel rhythm (18.2%), abdominal pain (16%), and gastroesophageal reflux (11.2%). In a 2018(199) UK study of the impact of a formal gastroenterology clinical assessment referral process, the most common reasons for referral to GI clinics (including hepatology) were dyspepsia (20%), abdominal pain (19%) and diarrhoea (12%). One could therefore tentatively conclude that around at least a fifth of referrals to gastroenterology would be for bowel symptoms (predominantly diarrhoea and pain) which could be associated with IBD.

UHS serves a population of 1.9 million people. The UK incidence of inflammatory bowel disease is approximately 10 per 100,000 population per year(2). It could therefore loosely be estimated that there would be around 190 new cases (any age) of IBD diagnosed in the Southampton catchment each year (although this does not consider local incidence). We identified 22 cases of IBD over a 15-month period through primary care calprotectin testing (in 18-45-year olds). It is difficult to say however if the number of calprotectin tests carried in the GP study was above or below those expected as a large number of new cases of IBD identified will be outside of the age range for FC testing. There are also other routes of diagnosis of new IBD such as emergency hospital admission, incidental findings, or radiological diagnoses, for example. There were also limitations placed upon GPs when testing patients – those over the age of 45 were excluded, as were those with suspected colorectal cancer or taking NSAIDs (although re-testing off NSAID was recommended).

A significant proportion of patients with negative FC were referred to secondary care (more than 1 in 10), but still lower than in a similar study quoting 30% (192). Almost half of this group underwent endoscopy, implying that at a significant proportion of these referrals were still considered appropriate by the secondary care physician. It should be noted however, that no cases of IBD were identified in this group and this reinforces the utility of FC as a valuable screening tool. Reducing potentially unnecessary referrals is important to minimise risk to patients in undergoing invasive investigations and for outpatient services; the current stresses on which are evidenced by the significant waiting time to see a specialist. Time from GP referral to secondary care outpatient review was less in the positive FC group, as was time from outpatient review to endoscopy. Although the mean time to specialist assessment in patients diagnosed with IBD was less than the overall mean for all diagnoses (39.9 vs 70.6 days for outpatient clinic review), this still falls short of the 30 day target for specialist assessment of suspected IBD cases

proposed by NICE(4). Time from GP referral to endoscopy was even longer at a mean of 71.3 days for patients diagnosed with IBD. For patients with severe IBD, this delay to diagnosis and subsequent treatment could have life-altering consequences.

One of the findings of interest was that a negative FC appeared to influence GPs' plans to refer patients to secondary care. Reversal of plans to refer occurred 28/55 (43.6%) times, of which the majority (85.7%) were when FC was negative. Although there are numerous reasons why decisions could change, for example new information coming to light (e.g. positive stool culture, resolution of symptoms, etc.) this could suggest that a negative FC may help to influence GP decision-making. The negative predictive value of FC as a screening test for IBD is high, even at higher (>200µg/g) cut-offs in our population and this should be emphasised when offering the test. Although there has been some study of the impact of FC on decision-making in established IBD(73), there have been no studies to date on how it might impact upon pre-diagnosis decision-making. A larger sample and the addition of qualitative research with GPs would help to shed further light on this observation of reduction in referrals.

4.6.2 *Strengths and limitations*

Strengths of this study include the size of the pilot, with over 400 FC samples processed (a similar pilot study had 142 samples)(189). This allowed me to examine trends in FC levels and referral practice. Follow up of outcomes for the patients who were not referred was felt to be an important aspect of patient safety and showed that GP management was thorough and very appropriate. Conversely, a limitation of the study is that although the records of patients with a negative FC were screened for subsequent secondary care input (suggesting a later diagnosis of IBD). Not all patients underwent the 'gold standard' test of colonoscopy so I cannot state definitively that non-referred patients did not have IBD. One would assume that in the presence of persistent or worrying symptoms that these patients would have been referred regardless, and this is an accepted caveat of screening tests.

Although not one of the main objectives of study, I observed the sensitivity and specificity of FC in differentiating between IBD and non-IBD varied depending upon the FC 'cut-off' value used to define a positive result. In a 2013 meta-analysis of FC testing(36), the overall pooled results (531 patients) for IBD compared with non-IBD showed very high sensitivity of 99% but moderate specificity of 74% at a cut-off of 50 µg/g. It was therefore expected that a FC cut-off value of either 50 or 100 µg/g would provide the best sensitivity and specificity in our cohort, however specificity was very low at these cut-offs in our cohort (27.9% and 45.5% respectively). This may be explained by the calculation of sensitivity and specificity based upon the 68 patients who

underwent endoscopic investigation (as a means of determining a definitive diagnosis) which make up only 16.6% of the entire cohort of patients and therefore these values may not truly reflect the cohort. It must also be considered that a normal lower GI endoscopy does not always exclude a diagnosis of Crohn's disease and often other investigations may be required (e.g. small bowel imaging).

The requirement to complete compulsory screening questions before requesting FC levels ensured appropriate use of the test and provided the opportunity to collect data on this group of GPs and patients but may have deterred some GPs from utilising the test. No formal feedback was gathered from GPs on this aspect of the study as to whether the screening questions were acceptable or not. It is possible that more interested GPs with greater knowledge of IBD may have tended to utilise the test, and therefore results may not be generalizable to the whole GP community. Future work should include qualitative research into barriers and facilitators for implementing the test, and GP attitudes to testing.

4.6.3 *Implications for research/existing practice*

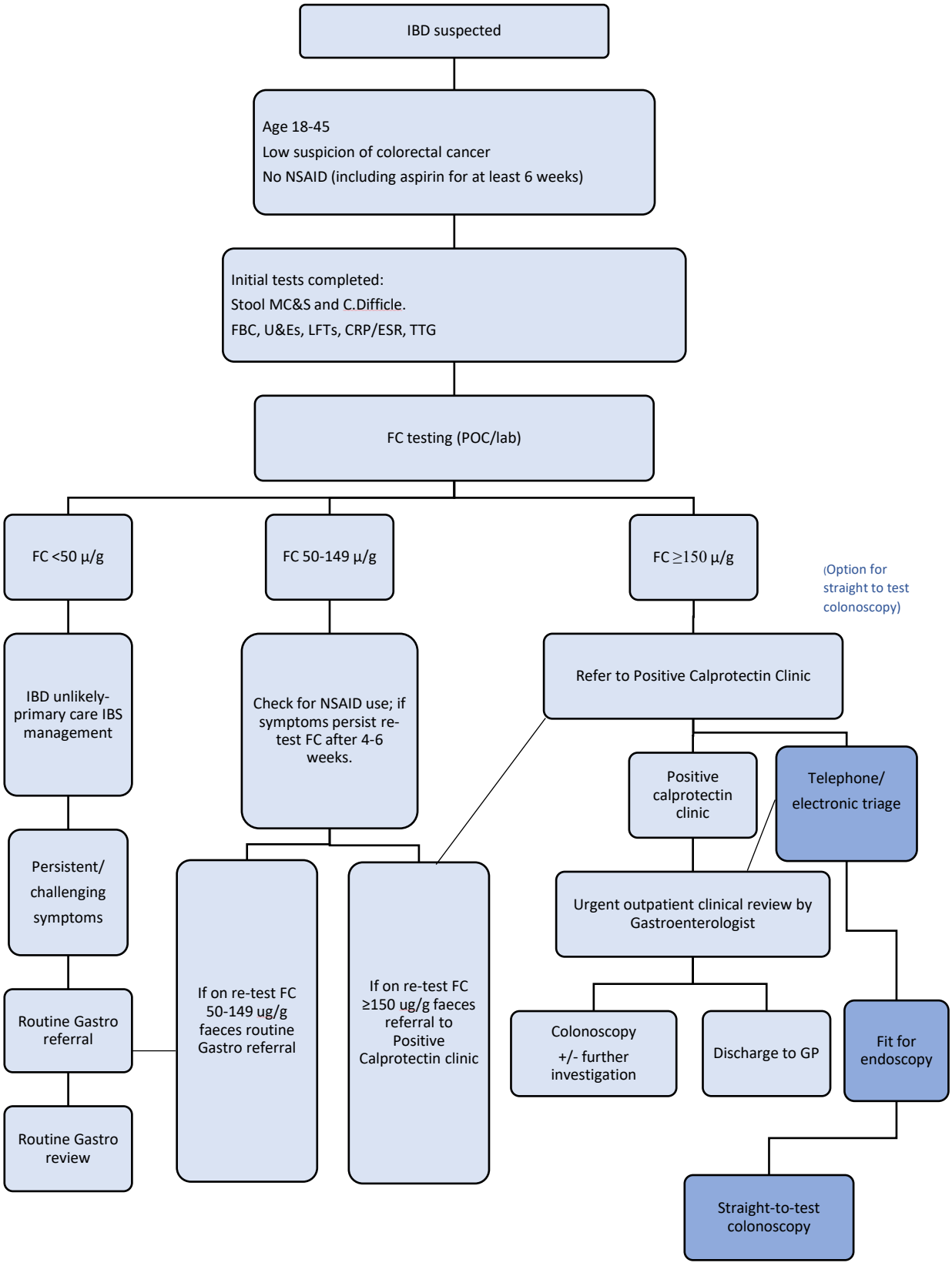
Providing responsive services for complex diseases such as IBD in the current NHS climate is challenging. I observed delays in both time to specialist review and from specialist review to endoscopic assessment. The development of a 'one-stop' approach to diagnosing IBD is a potential step towards helping to streamline the process and reduce delays via a dedicated 'Positive Calprotectin Clinic', where the patient is referred directly by the GP on receipt of a positive FC sample, has a specialist review and appropriate tests (stool, blood, +/- flexible sigmoidoscopy), before a decision is made to proceed to further testing (colonoscopy, capsule endoscopy, radiology etc.). Patients with a negative FC could be referred more routinely via the traditional route, thereby prioritising those 'at-risk' patients with a high FC (Figure 5). Faecal calprotectin thresholds remain contentious but in our population a cut-off value of 150 ≤µg/g provided the best sensitivity for IBD.

A modified route would be to consider a 'straight to test' referral pathway(196) (particularly in this younger age group where the relative risk of adverse events post-colonoscopy is lower), with a protocol-led telephone/online triage system to screen patients for contraindication to bowel preparation. This strategy has proved successful in meeting diagnostic and treatment targets for 2-week wait referrals for suspected colorectal cancer (200, 201) but may raise concerns amongst physicians who may feel a full 'face-to-face' assessment and examination is required before committing the patient to an invasive investigation. Both these options would also require full

economic costing locally to ensure appropriate use of resources and feed any potential savings back into patient care.

At the time of writing. faecal calprotectin testing remains available to primary care physicians locally. A re-audit of current practice would be valuable to establish current uptake in primary care and if there has been a demonstrable change in referrals and time to diagnosis as its use becomes more established.

Figure 5: Proposed pathway for positive primary care FC testing



4.7 Conclusions

FC is a useful tool to help differentiate between IBD and IBS. This study suggests that FC results may influence GP referrals to GI clinics, but numbers were modest and so further work would be needed to confirm this. A FC test may give greater confidence in making a positive diagnosis of IBS without further investigation or referral to secondary care if negative and confirm the need for referral if positive, supported by a consistently high NPV across numerous studies. Our finding that there were no cases of IBD identified in any patients referred to secondary care who had a negative (<50µg/g) FC is reassuring, however 49% of these patients underwent endoscopy with some receiving alternative (non-IBS, non-IBD) diagnoses – so it is likely that many of these were still 'appropriate' referrals, but could perhaps have been triaged for less urgent review compared with those with positive calprotectin. It could also be argued that once a patient has reached a secondary care setting there is also an expectation that further specialist investigation will be undertaken.

The ultimate goals of pre-hospital FC testing are to help GPs identify higher risk patients, reduce the need for unnecessary/invasive investigation, and improve how we use our limited specialist resources so that cases of IBD (and other significant pathology) are identified and treated more promptly. Further measures are required to improve awareness and uptake of FC testing in primary care, as well as streamlining the processes involved in triaging and reviewing patients with positive calprotectin, potentially through the implementation of a dedicated 'Positive Calprotectin Clinic' and considering 'straight to test' colonoscopy in those at higher risk of significant pathology.

5 Development of My Medical Record supported self-management website and home FC testing

5.1 Introduction

This chapter describes the development of My Medical Record (MyMR; https://mymedicalrecord.uhs.nhs.uk/), a local supported self-management website or 'portal', developed at University Hospital Southampton (UHS). MyMR provides an interactive platform which allows patients to access their electronic health records, test results and information about IBD, as well as self-management tools such as the IBD-Control survey(202) and the IBD e-messaging service. This chapter also describes the establishment of home FC testing and how this was linked to MyMR. These technologies form the basis for an exploratory feasibility study described in Chapter 5.

5.1.1 *My Medical Record*

My Medical Record (Figure 6) was created in 2012 by the UHS informatics team in collaboration with clinical staff and software supplier Get Real Health®. The site feeds into Microsoft's HealthVault® – an online tool which enables people to store a range of health information for personal use and to share with care providers. In its earliest format, MyMR initially comprised a personal patient record where patients or healthcare professionals could enter data on personal information, medication and disease history, as well as viewing clinic appointments and recent clinic letters. Following on from initial successes in the field of prostate cancer, the IBD team were early adopters of MyMR, and it has since been developed for numerous other disease specialties. In recent years, UHS has been the recipient of a multi-million-pound Global Digital Exemplar award(136) and as a result IT systems such as MyMR have received financial and staffing investment.

The early development of the patient-facing version of MyMedicalRecord (MyMR) is described in this chapter, with further development of the clinical version of the website (used by healthcare professionals to manage patients) described in Chapter 6. MyMR is a continually developing service than can be adapted to the needs of specific groups of patients. Other technologies can 'link' to the website to share data, and this has already been utilised within our IBD service using electronic weight scales to monitor IBD patient nutritional status remotely via MyMR. To help patients monitor their IBD and facilitate earlier recognition and treatment of disease flares, I collaborated with our UHS IT team, Biohit® healthcare (suppliers of QuantOn Cal® calprotectin

testing) and Immunodiagnostik® (developers of QuantOn Cal®; Appendix D.1) to link at-home FC monitoring with the MyMR platform.

Figure 6: My Medical Record icon

5.1.2 *Home FC testing*

Faecal calprotectin (FC) is a non-invasive biochemical marker of gut inflammation and has been described in detail in Chapter 3. FC is a useful tool for diagnosis of IBD but also in monitoring disease activity and response to changes in treatment. Data from the STORI study(62) (patients had their anti-TNFα treatment stopped electively and were then followed up with serial FC measurement) suggests that FC increases before a flare becomes clinically apparent, allowing intervention before patients develop symptoms. Interventions may include checking treatment adherence, optimising medication dosing, or restarting/initiating treatment.

The use of home FC kits has been explored in Chapters 1 and 3. A major barrier to the widespread adoption of FC testing is the nature of the specimen required, with challenges in both the collection and processing of stool samples. Traditionally FC has been carried out in pathology laboratories with results being sent to patients' clinicians. Current local turnaround times are up to 2 weeks for a FC sample to be processed and results conveyed to the clinical team with the potential to cause subsequent delay in decision-making and treatment. Quantitative home FC testing could reduce these barriers by providing a test that patients can conduct in the privacy of their own home which gives immediate feedback, thus allowing implementation of management plans promptly with appropriate support from clinical teams.

FC has been developed as a 'point of care' test kit (QuantOn Cal® by Immunodiagnostik®) which involves extraction of faeces and application to a lateral flow device (like that seen in a standard home pregnancy test kit), which is then scanned and processed using a smartphone camera and 'app'. QuantOn Cal® is a validated calprotectin test method which shows good validity versus laboratory ELISA testing(203). QuantOnCal® kits currently retail at a list price of £40.00 + VAT. They are not routinely available as part of routine NHS care. Home FC testing may not be appropriate for all patients; the cost and time involved in its implementation means that it's use should be targeted, for example in patients with more severe disease or in whom there has been a recent change in treatment.

5.2 Aims and objectives

The aims of this chapter are to:

i. Describe the work I contributed to the development of My Medical Record
ii. Explain how the MyMR website and home calprotectin test procedures work as a basis for the exploratory feasibility study described in Chapter 6.

5.3 Methods

My contributions to MyMR since 2014 have helped to form it into a more interactive resource for patients and IBD staff. I designed and provided content for patient-facing features including the patient information pages, messaging function, diary monitoring, IBD Control survey, and test results, linked at-home FC testing. I also collaborated with the IT and clinical teams to produce the clinician-facing version of MyMR used to conduct the Virtual IBD Clinic which is described in Chapter 7. I conducted a patient focus group as well as more informal developmental work with IBD nursing and medical colleagues in 2015 and 2016 to aid the service development. Prior to research, I worked as a specialist registrar in the IBD department and my knowledge of the workings of the department and rapport with members of the team helped to facilitate developmental work. The status of the project as a service development was confirmed using the Health Research Authority "Is my study research?" decision tool(194) and therefore ethical approval was not sought.

5.3.1 *Patient focus group*

UHS holds an annual IBD Open Day for patients and families affected by IBD. I invited members of the Patient Panel (a group of interested IBD patients who meet regularly with the IBD clinical team to develop IBD services) via email to attend a 'breakaway' focus group conducted during the 2015 IBD Open Day.

I used a semi-structured guide (Appendix D.2) to engage panel members in discussion about aspects of the MyMR website such as layout and content (including test results, IBD control survey, FC) and explored their thoughts on the proposed changes to improve and develop the site. I used a test login to the site to demonstrate current and developmental functions in real time. The session was digitally audio-recorded with verbal permission from patients. Patients also gave permission for anonymised quotes to be used in material pertaining to the MyMR service development. The recording was uploaded to a password protected UHS trust computer and was deleted following transcription.

5.3.2 *Development of the patient facing MyMR IBD site*

Developmental work on the patient-facing MyMR site was guided by both formal (as an item for discussion on the agenda of a fortnightly IBD general team meeting) and informal (day-to-day) discussion with nursing and medical members of the IBD team. These meetings involved a combination of up to 4 senior IBD nurses, 3 IBD consultants, and 3 specialist registrars, and often a member of the patient panel. I had monthly meetings with members of the IT team to feedback from the clinical team and approve IT developments. I also met with the MyMR project manager monthly. Their role in overseeing the development of MyMR is described in more detail in Chapter 6. Between meetings I maintained regular email communication with the above parties regarding any modifications to MyMR. Website development was an iterative process which is still ongoing at the time of writing as feedback and experience help to improve the site.

5.4 Results

5.4.1 *MyMR patient focus group*

4 patient panel members (all female, age range 29-46) attended the MyMR focus group in January 2015. They were a mix of established and new users of MyMR, as well as experienced and relatively new patients less familiar with IBD. Discussions were based around a topic-guide (Appendix D.2) and included the basic features of MyMR at that time, as well as proposed uses such as the electronic virtual clinic. I did not perform a full qualitative analysis on this service development data as the intention of the exercise was to gain general feedback to aid developments to the MyMR site prior to conducting formal research.

Participants highlighted areas which they felt could be improved, particularly the monitoring tools such as the stool and nutritional diaries. There was an emphasis on the importance of any data entered being viewed by the clinical team, and not just for self-management purposes. Patients were also keen that alerts be developed to highlight if any data was entered which caused concern.

> 42F: "…I was thinking when I came to clinic that (he) would be looking and would know what was going on, but (he) didn't know what was going on…So I stopped doing it, thinking oh well, no-one's looking at it"

> 42F: "What I was hoping is that if a patient is suffering and is going downhill, that a little alert will come up saying: this patient is going downhill"

Participants acknowledged that due to the individual variability of IBD it was difficult to design a 'one size fits all' intervention and set parameters for these alerts. They recognised that there were variations in 'normal' when it comes to subjective markers such as symptoms, as well more objective markers of disease activity such as CRP.

> 29F: "with personalised care, it's not always the same for one person. As one person who goes [to the bathroom] three times a day and that's their norm shouldn't be flagging up, whereas someone who goes every other day and is now going three times a day, well that should flag up as being wrong."

This supported the implementation of the IBD Control questionnaire(202), a 16 point validated survey which uses more general questions on the impact of IBD on daily living, as opposed to discrete variables to signify disease flare. This is discussed in more detail in section 4.4.2.

We discussed how patients would like to access their blood test results, how different patients may like to access different levels of detail and how to explain test results to patients.

> 29F: "Perhaps we could have it, so you expand it, so you could click 'see all', and then if anybody who isn't interested doesn't have to request it."

There was a worry that providing more significant test results directly to patients could cause undue worry, particularly for new patients:

> 46F: "Quite often your colonoscopy is often the first time that you find out that you've got cancer. You have to be careful that patients don't actually get that information before it's been explained to them."

Again, the option of bespoke information provision was suggested:

> 29F: "Yeah and maybe you should be able to opt in and out of different things? Like if all you want is your clinic letters you should be able to say I do not want reports, I don't want referrals, I don't want history sheets."

38F: “Yes a lot of people don’t want to know about their illness, so they don’t want everything that’s related to it.”

How this information is presented to patients was felt to be important, with all in agreement that presenting results graphically was much more user-friendly:

40F: “But a little graph, I love that because you can actually see it and not just having it all written down, so I’d like that.”

They really valued being able to access information about their care such as appointments and letters, but at times they were slow to be made available:

29F: “There is such an issue with letters getting to patients.”

46F: “Well I find that frustrating because sometimes you find you need your letter, and instead of hassling the secretaries for it, you can just download it”

Security concerns were raised by one participant, but most felt trust for the systems already in place:

38F: “My husband was asking how do you know if somebody’s going to be looking at your documents? Is there security? And he was really worried about that. But you know what you’re doing, the hospital.”

46F: “I mean it’s probably no different to anything else you do…any to other systems you use, like the internet.”

29F: “Yeah, you’ve got that risk everywhere you go.”

There was a lot of support for the messaging system, which as one of the earliest developments of the site was already in use:

46F: “Yes I’ve found that the most useful part of the whole thing, the messaging. She can do so many more of those than if you phone somebody. It can save you going to A&E. I

had an allergic reaction and it saved me going to A&E. It's like, that saved a few thousand pounds for the NHS!"

When asked their views on the proposed electronic blood forms, participants were all very supportive. They were very keen that the whole intervention would be fully virtual, to include the provision of electronic blood test requesting and forms:

> 46F: "To be able to print out your blood forms! Because I needed a blood test, so I had to come in to get my blood form… if I'd been able to print out my own blood forms, then I could have gone to [another more local] Hospital."
>
> 42F: "There could be some way where you have it the app on your phone, and you go to the GP surgery, and you show them your phone."
>
> 46F: "Yeah like you do with cinema tickets."

Because of the patient focus group, several developments were made to the website. Other developments are also planned, but limitations to IT software and resources have meant that these have not yet occurred (Table 12). The development of these changes is described in more detail in section 4.4.2.

Table 13: Implemented and planned changes to patient facing MyMR site

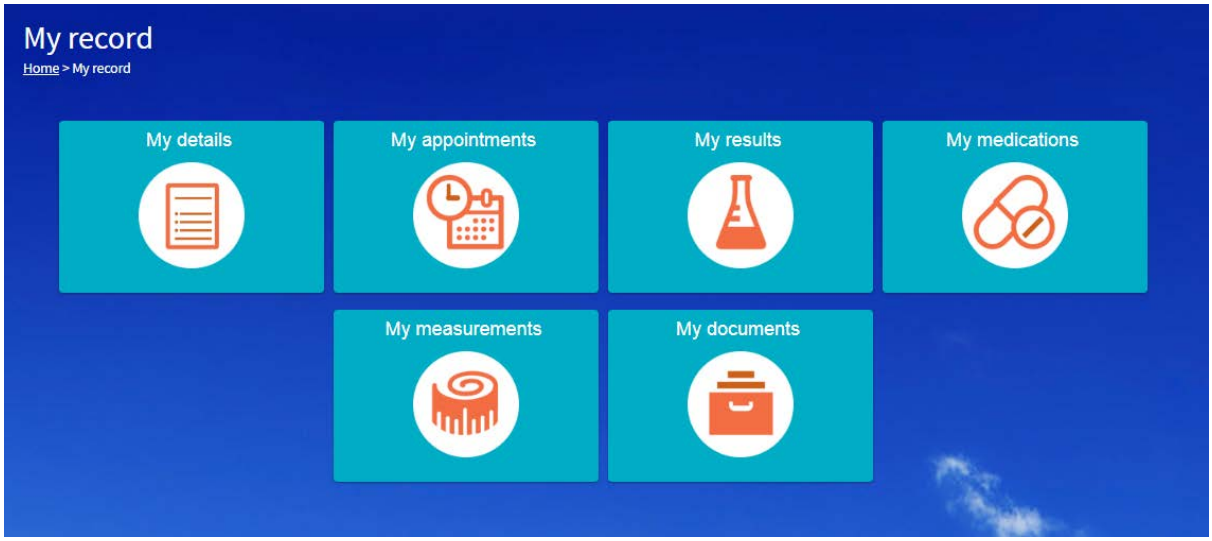
Feedback/concern	**Implemented changes *(planned changes*)**
Individualised disease- monitoring	IBD Control questionnaire
Making test results user-friendly	Graphical representation of test results
Reducing anxiety around test results	Provision of brief lay explanation of test External link to peer-reviewed lab-test online site for greater detail
Data not being viewed by healthcare team	Improved presentation of test results Clinician-facing version of MyMR (Chapter 7) *(Development of alerts in response to IBD Control outcome)*
Security	Migration of MyMR data to The Cloud (Chapter 7)
Need for fully electronic service	Implementation of electronic Virtual Clinic (Chapter 7) *(Electronic blood test requesting)*

5.4.2 *Current functionality of MyMR and home FC-testing*

This section details the current functionality of the MyMR and home calprotectin technologies following the above developmental work.

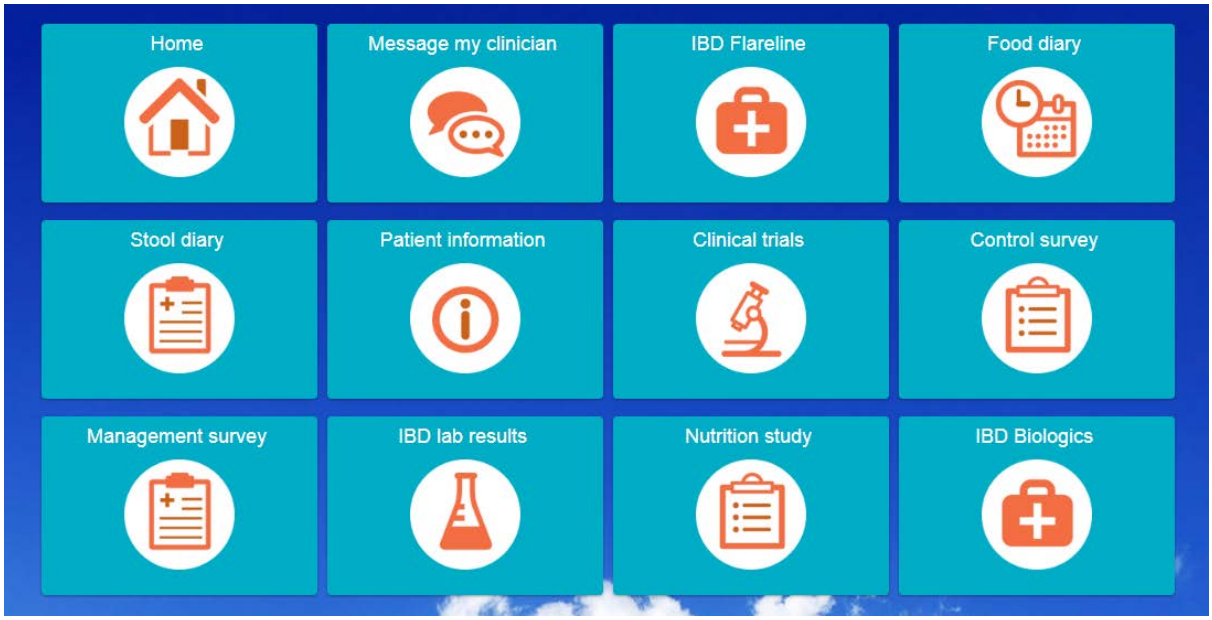
When first logging in to MyMR, patients are presented with an overview of their health record (Figure 7) and upcoming appointments.

Figure 7: View of 'My Record' home screen



The home screen for the IBD pages of MyMR (Figure 8) comprises 12 different buttons known as 'widgets' which take the user to various functions of the IBD site.

Figure 8: View of IBD Home Screen



Message my clinician

'Message my clinician' allows patients to contact the IBD team with any queries pertaining to their IBD and is intended to largely replace the existing IBD telephone flareline. Patients can view both sent and received messages. Important messages are marked 'clinically relevant' by the IBD team and are automatically saved to the electronic letters system (eDocs) used by the trust. This was

felt by the clinical team to be an important feature in terms of audit and accountability, as well as ensuring clinically activity replacing the telephone flareline was recognised financially (see Chapter 6).

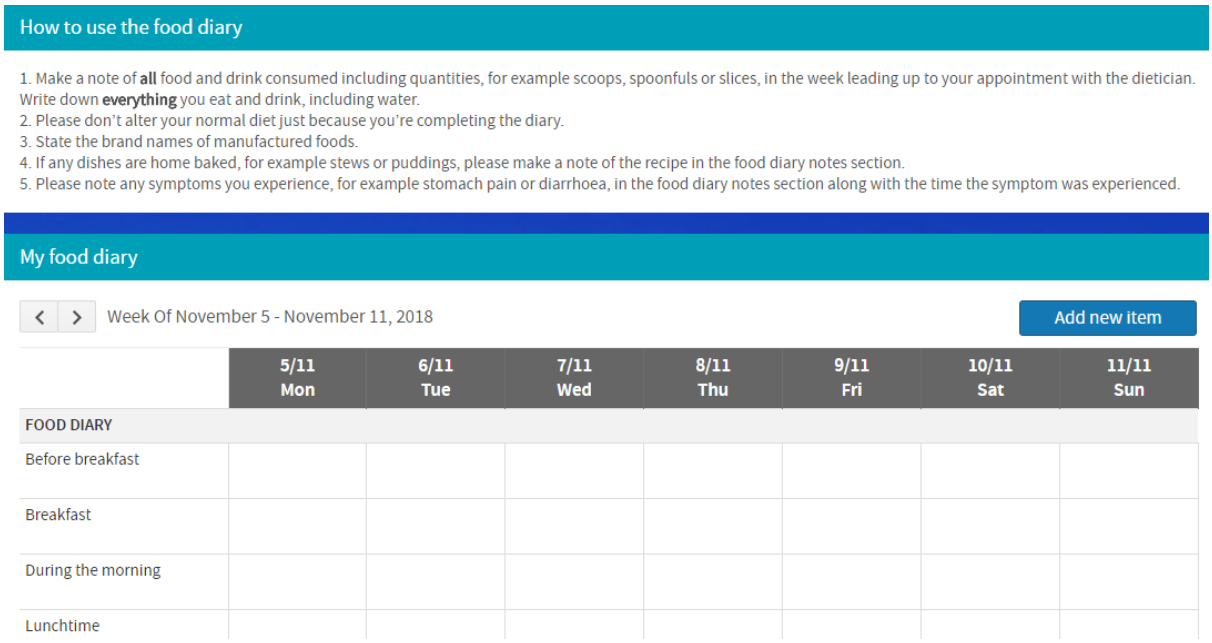
IBD Flareline

The flareline page provides users with details of the existing IBD flareline telephone number.

Food Diary

The food diary (Figure 9) provides a tool for monitoring the intake of patients with nutritional concerns. The data is mainly intended to be utilised by a dietician but can also allow patients to reflect on their diet and help establish any flare triggers.

Figure 9: View of Food Diary page



Stool Diary

The stool diary (Figure 10) was developed to allow patients to monitor their stools and any additional symptoms. It is primarily intended for patients to record and reflect upon their symptoms but can be referred to by healthcare professionals when assessing response to treatment.

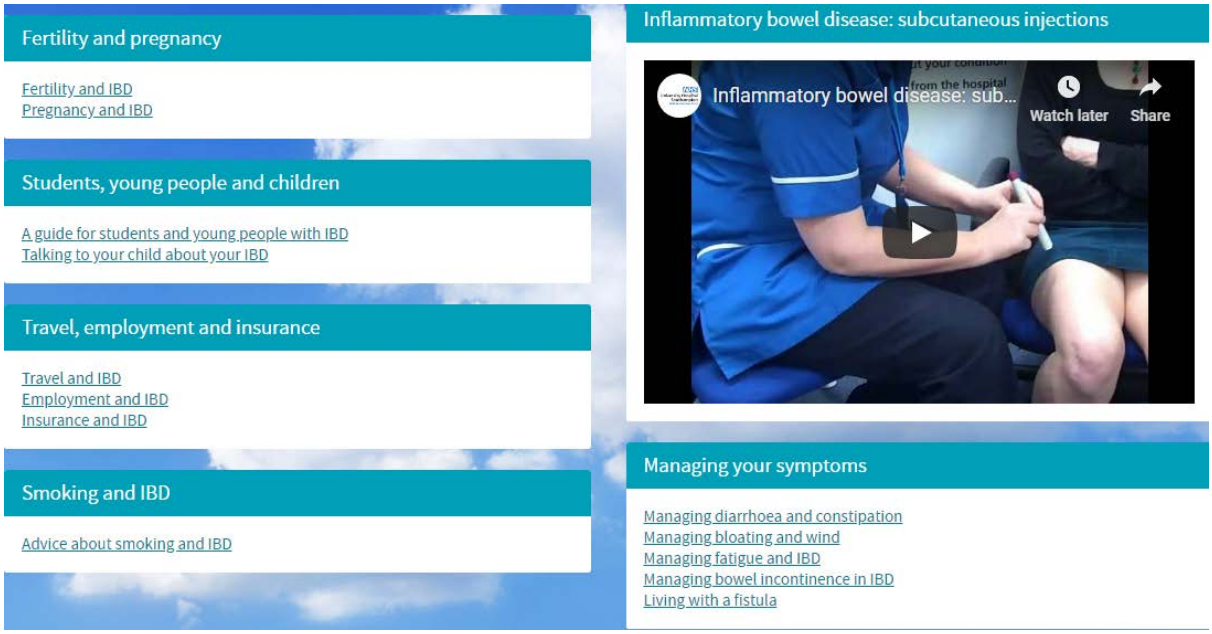
Figure 10: View of Stool Diary page

	5/11 Mon	6/11 Tue	7/11 Wed	8/11 Thu	9/11 Fri	10/11 Sat	11/11 Sun
STOOL DIARY							
Based on the Bristol Stool Chart below, what type of stool have you passed lately?	Type 7 09:30 Type 7 10:00 + Add New	Type 7 09:00 Type 7 15:00 Type 7 19:00 + Add New	Type 7 09:00 Type 7 11:00 Type 7 15:00 Type 7 19:00 + Add New				
Is there any blood in your stools?	Yes 09:30 + Add New	Yes 09:00 + Add New	Yes 09:00 + Add New				
Is there any mucus in your stools?	Yes 09:30 + Add New	Yes 09:00 + Add New	Yes 09:00 + Add New				
How would you rate the amount passed?	Large 09:30 + Add New	Large 09:00 + Add New	Large 09:00 + Add New				

Patient Information

The 'Patient Information' page (Figure 11) allows patients to access information relating to IBD all under one page. I sourced links to the Crohn's and Colitis UK (CCUK) website which provides comprehensive, reliable patient literature from a trustworthy source. After discussion with medical and nursing colleagues in the IBD team and our IBD patient panel, it was felt there would be no benefit to duplicating this information by developing local literature as the CCUK information is extensively peer/patient reviewed and evidence-based.

Figure 11: View of Patient Information page



Clinical Trials

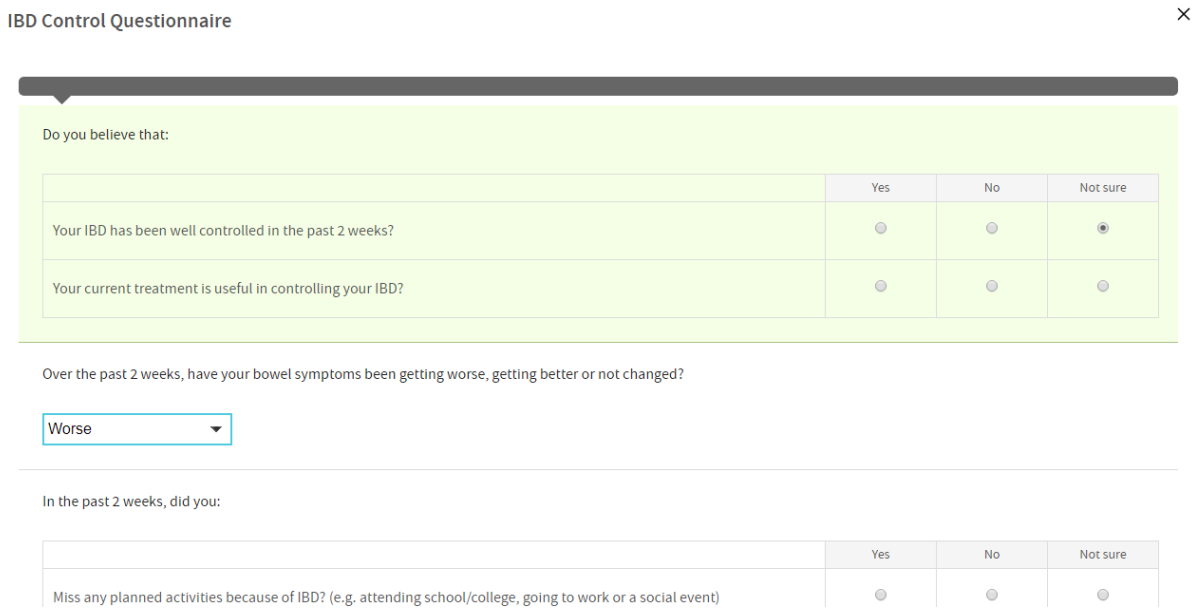
The Clinical Trials page provides links to the trust website's research pages with up to date information on how to participate in clinical research. The page will be developed further in future in collaboration with the IBD research team to include an overview of current IBD research studies and eligibility criteria.

IBD Control Survey

Incorporating the IBD Control(202) survey (Figure 12; Appendix D.3) was one of the more technical elements of the MyMR development process. Self-management outcomes have previously been assessed from a service perspective (e.g. clinic attendance, hospital admissions, and financial savings) or from a patient health perspective (symptom scores, quality of life) but to date no IBD guidelines endorse the use of a specific outcome measure(202). Many of the tools use scoring systems that refer to physical symptoms or disease activity (e.g. Harvey Bradshaw Index(22), Crohn's disease activity index (CDAI)(21)). Without addressing measures such as disability and function, the true impact of IBD may not be accurately assessed.

Patient-reported outcome measures (PROMs) provide the opportunity to assess the impact of chronic disease and management interventions from the patient's perspective and are increasingly advocated as a means of supporting patient-centred care and improving service quality. IBD Control(202) is a 16-item IBD PROM designed to quickly and reliably assess disease activity and quality of life from a patient's perspective. The IBD Control Sub score 8 (a combined score from 8 of the 16 questions) has been fully validated to give a rapid assessment of disease comparable to lengthier quality of life outcome measures such as UK-IBDQ(204) and disease activity indexes including the Physician Global Assessment(205), Harvey Bradshaw Index(22), ulcerative colitis disease activity index(206), and S-IBDQ(207). Patients from the focus group were in favour of this rapid, easy to use means of assessing disease activity and our IT team were able to incorporate the survey into MyMR. Patients can enter their data rapidly and are then presented with a disease activity score and explanation. Limitations within the existing MyMR software means that the survey is conducted via a pop-up window in which the user answers IBD-Control questions. This then generates a PDF (print downloadable format) copy of the survey with a cumulative score at the bottom (0= worst control, 16= best control) which is stored on MyMR.

Figure 12: View of portion of sample IBD Control PDF


IBD Control Questionnaire

Do you believe that:

	Yes	No	Not sure
Your IBD has been well controlled in the past 2 weeks?	○	○	◉
Your current treatment is useful in controlling your IBD?	○	○	○

Over the past 2 weeks, have your bowel symptoms been getting worse, getting better or not changed?

Worse

In the past 2 weeks, did you:

	Yes	No	Not sure
Miss any planned activities because of IBD? (e.g. attending school/college, going to work or a social event)	○	○	○

As the results of the IBD Control-8 sub score are presented in PDF format, they are easily viewable by patients but unfortunately it is not currently possible to present the results graphically, however this is planned for future development so that patients and clinicians can view change over time.

Traffic-light systems have been shown to be a useful visual indicator for disease activity in IBD (208) in the context of actioning self-management plans. The IBD Control subscore-8 by shows good validity when compared with the Physician Global Assessment (PGA)(202, 209). The creators do not provide a numerical categorisation for severity of IBD based upon IBD Control, however it has been demonstrated to be sensitive in detecting patients with quiescent disease at a score of ≥13(210), therefore patients with a score of ≥13 are advised that their disease is under good control (green) and they are encouraged to continue with current management, with the caveat of messaging the IBD team should they have any queries.

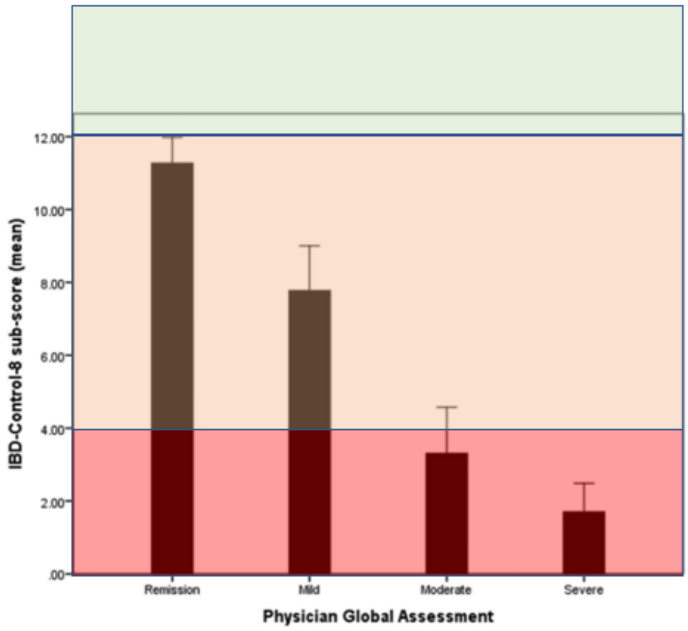
Differentiating between moderate or severe disease was less clear. I utilised the developers' validated comparison of IBD Control versus PGA to guide the categories of moderate and severe (Figure 13). In the validation work by Bodger et al(202), there was little difference in mean scores for those rated as moderate or severe disease on the PGA scale (mean scores of around 3 and 2 out of 16 respectively). When discussed with the IBD nursing team (4 experienced senior nursing colleagues), consensus opinion was that they would be very concerned with anyone falling into moderate/severe disease (according to PGA) and would therefore wish to be informed about these patients, so a score of 4 or less was categorised as 'red'. By default, anyone scoring between

5 and 12 was classified as ‘amber’. This system provides a safety net as any patients other than those defined as having quiescent disease (≥13) (i.e. ‘amber’ or ‘red’ scores) will be prompted to seek help if concerned. These parameters will need to be reviewed for appropriateness in time in clinical use. Similar traffic light methods of displaying disease activity have been employed in other digital portals (Constant Care(208), using SCCAI and s-IBDQ score and True Colours(130), using SCCAI only) and have been found to be good indicators of disease activity and usable tools. The benefit of using IBD-Control is its simplicity versus more traditional disease measures.

Current software limitations do not enable automated notifications based upon IBD-Control scores. As a compromise, an automated notification can be provided to the IBD nurses if 2 key questions are answered unfavourably (if the patient answers “no” to their IBD being under control or “no” to if they feel their treatment is working). These questions were identified as being of importance by the nursing team and signified significant loss of control of IBD which they would wish to be informed about. Ultimately, the nursing team will be notified based upon the traffic light scoring described above to enable triaging of patient need but this function was still under development at the time of writing. The current triggers for action are therefore:

1. IBD Control score ≤12 – patient advised to contact IBD Team if concerned
2. Answer of “no” to either “Is your IBD under control” or “Do you feel your current treatment is working” – automated alert to IBD nurses

Figure 13: Proposed IBD Control traffic light scoring system

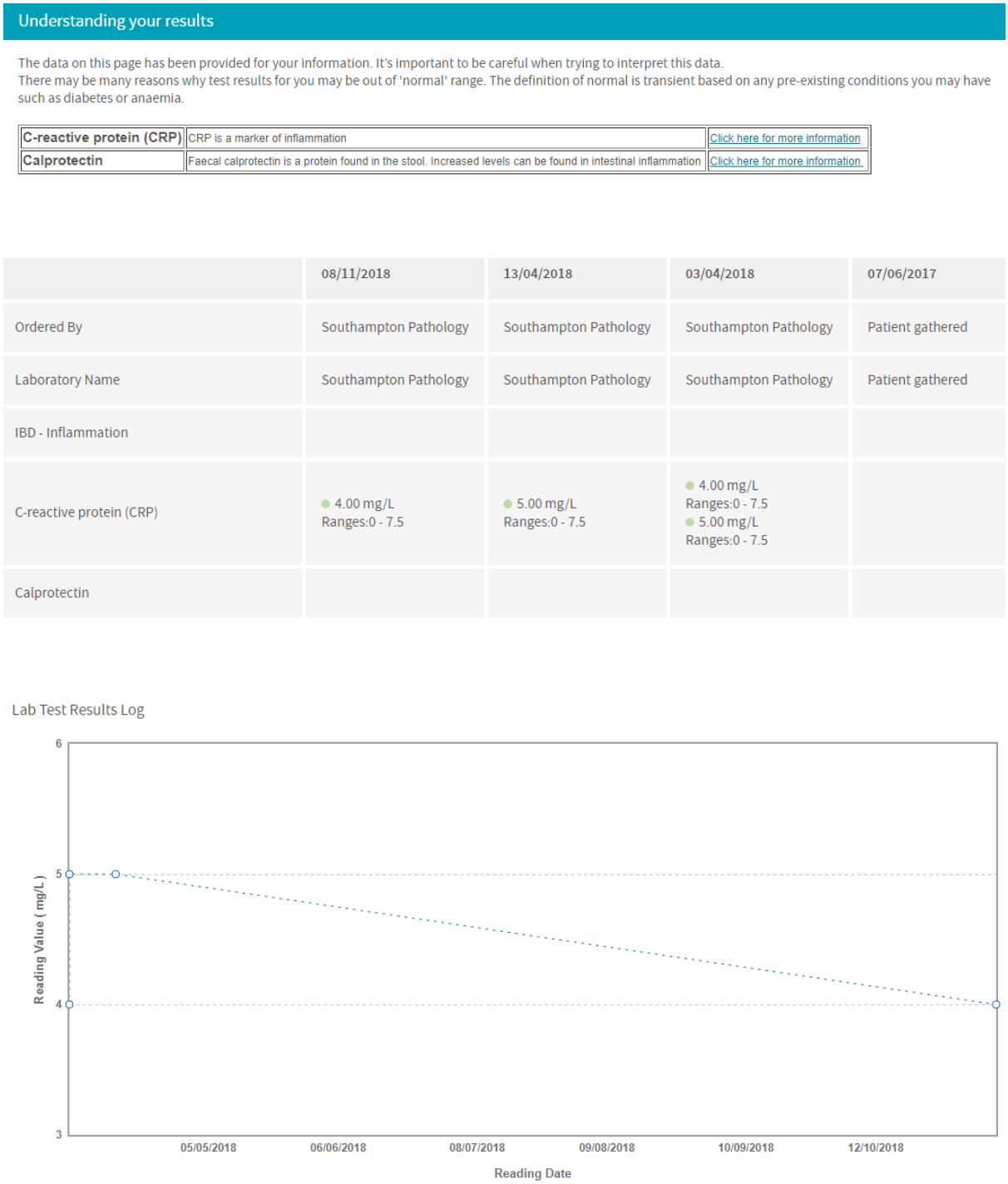


IBD Results

I discussed presentation of blood test results with IBD nursing/medical staff at a formal MyMR clinical user meeting (comprising 3 senior nurses, 1 IBD consultant, 2 specialist registrars and 1 member of the IT team) and patients at the focus group about which blood tests should be made available to patients to view. It was felt by both patients and staff that all the main tests conducted as part of IBD routine practice should be included but that this should be kept as simple as possible to reduce any confusion or anxiety for patients. Patients are provided with a brief explanation of the significance of the test (Figure 14) and can click on an external link to labtestsonline.org.uk, a peer-reviewed, non-commercial, website which provides comprehensive explanations of lab tests.

Results feed into MyMR from the hospital electronic results database and are presented in both table form and graphically for a more visual representation. There was debate amongst the IBD team about whether patients should be able to access test results before their physician may have viewed them. At UHS, results come through to the requester electronically before they are 'acknowledged' by the requester and appropriate action taken. It was ultimately felt that to empower patients and prevent delays in care they should be able to access their results as soon as they were processed with the proviso that appropriate explanations are provided. This decision was guided by discussions at the patient focus group and following debate at our fortnightly IBD group meetings. This is supported by evidence that providing patients with full access to medical records can increase satisfaction without increasing anxiety, even in patients with newly diagnosed cancer(211).

Figure 14: View of Results page



Understanding your results

The data on this page has been provided for your information. It's important to be careful when trying to interpret this data.
There may be many reasons why test results for you may be out of 'normal' range. The definition of normal is transient based on any pre-existing conditions you may have such as diabetes or anaemia.

C-reactive protein (CRP)	CRP is a marker of inflammation	Click here for more information
Calprotectin	Faecal calprotectin is a protein found in the stool. Increased levels can be found in intestinal inflammation	Click here for more information

	08/11/2018	13/04/2018	03/04/2018	07/06/2017
Ordered By	Southampton Pathology	Southampton Pathology	Southampton Pathology	Patient gathered
Laboratory Name	Southampton Pathology	Southampton Pathology	Southampton Pathology	Patient gathered
IBD - Inflammation				
C-reactive protein (CRP)	4.00 mg/L Ranges:0 - 7.5	5.00 mg/L Ranges:0 - 7.5	4.00 mg/L Ranges:0 - 7.5 5.00 mg/L Ranges:0 - 7.5	
Calprotectin				

Lab Test Results Log

5.4.2.1 Home FC testing

This section provides an overview of home FC testing and how this was linked to our MyMR platform so that patients could conduct testing at home with results immediately available to their IBD team.

Home testing (QuantOnCal® by Immunodiagnostik®) involves extraction of faeces and application to a lateral flow device, which is then scanned and processed using a smartphone camera and

app. QuantOn Cal® were provided free of charge by Biohit® Healthcare. I received a one-hour training session from a Biohit® representative in use of the kits and QuantOn Cal® web interface (which presents FC results via a secure 'Doctor's Portal'). I was shown how to set up a QuantOn Cal® 'competence centre' from which UHS physicians could register new QuantOn Cal® users and create their unique identifying number and barcode for them to use in setting up the QuantOn Cal® app on their smartphone. QuantOn Cal® and the associated doctor's portal site is fully established and available for use to any healthcare provider (https://quantoncal.com/en). Biohit® and Immunodiagnostik® provided IT and technical support throughout the development stages and later in the feasibility study (Chapter 5).

Each QuantOn Cal® test kit comprises a detailed instruction leaflet (with a link to an instructional online video), paper stool catcher, sample collection tube containing buffer solution (Figure 15), and one test cassette (Figure 16).

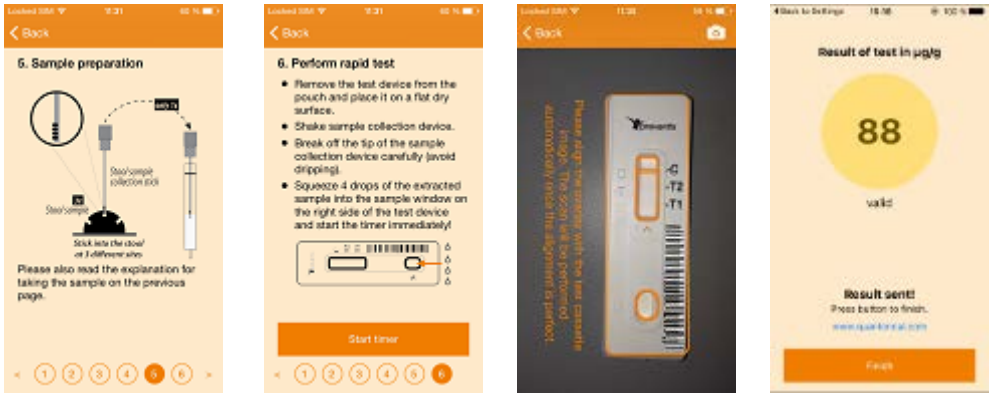
Figure 15: Contents of QuantOn Cal® test kit

Figure 16: Test cassette

Smartphone users can download the QuantOn Cal® app free of charge via their app store and complete a camera test to ensure the camera resolution is sufficient to successfully complete the test. To register the app for the QuantOn Cal® program the participant scans their personal barcode (downloaded from the doctor's portal and then printed out by their physician/nurse) using their smartphone camera and the QuantOn Cal® app matches the scanned barcodes with the registered competence centre. Data and test results uploaded to the doctor's portal from the app are pseudonymised and no identifiable patient details transmitted.

Participants are then taken through the steps of the test kit via the app (Figure 17; see Appendix D.4 for full test procedures). The stool sample is collected using the enclosed adhesive paper stool catcher. The sample collection stick is inserted into the stool sample at 3 different points and returned to the sample collection tube containing an extraction buffer solution once and shaken well. The test device is placed on a flat, dry, light surface. The tip is broken off the (plastic) sample tube and 4 drops are squeezed onto the round sample application window of the test device. The timer of the QuantOn Cal® app is started immediately. During the incubation time, fluid runs across the results window of the rapid test. This fluid turns red depending on calprotectin level and forms the measuring signal, which is later evaluated by the QuantOn Cal® app. As with the camera test, participants see the camera image on their screen, as well as the orange-coloured outline of a test device. The smartphone is aligned so that the outline is aligned with the test device. The camera is held steady in this position, until the QuantOn Cal® app takes the photo automatically and switches to the analysis screen.

Figure 17: Test procedures via QuantOn Cal® app



.

FC results are automatically sent to the physician from the QuantOn Cal® competence centre via email and can also be viewed on the QuantOn Cal® website (Figures 18 and 19).

Figure 18: Sample Doctor's Portal graphical view of patient test results

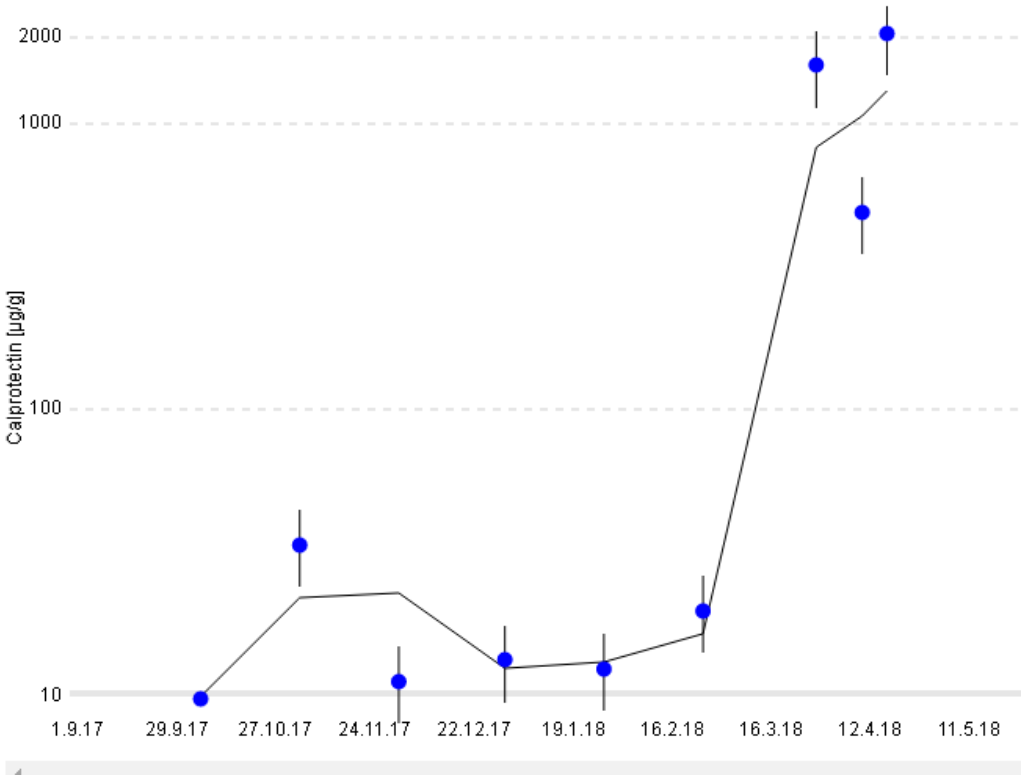


Figure 19: Sample Doctor's Portal table view of patient test results

Test date	Valid	Camera check		Result µg/g	Therapeutic	Functions
19 Apr 2018 7:54	✓	✓	!	> 2000		
12 Apr 2018 16:50	✓	✓	!	476		
30 Mar 2018 8:15	✓	✓	!	1548		
26 Feb 2018 7:56	✓	✓	!	< 25		
29 Jan 2018 7:53	✓	✓		< 25		
1 Jan 2018 9:19	✓	✓		< 25		
2 Dec 2017 7:45	✓	✓		< 25		
4 Nov 2017 8:50	✓	✓	!	33		
7 Oct 2017 10:11	✓	✓		< 25		

To effectively manage any short or longer-term flare-ups, it was important to ensure that all members of the healthcare team could access patients' calprotectin test results, not just those directly involved in the study. To enable this, a link was established by the UHS IT team between the QuantOn Cal® interface and the eQuest results server at UHS. This was first set-up and tested on a 'demo' site, using test patient results before going live onto the real results server. Results were labelled as 'POCT' (point of care test) FC to make it clear that the source of the test was outside of hospital and differentiate these from samples analysed in the laboratory. Patients could therefore have all their relevant IBD results at their fingertips.

5.5 Discussion

One of the strengths of the development work was the use of patient feedback from a dedicated patient focus group which led to direct improvements (and planned improvements) to the site. Ideally this would be an ongoing process with continual patient feedback and testing of the implemented changes to ensure user-friendliness, had time and resources allowed. In practice, changes were reviewed by a patient panel member (also a healthcare professional) who provided valuable patient insight but may not be strictly classed as a lay person. Work commitments and time constraints on our healthcare team meant that it was challenging to conduct many formal developmental sessions and most of the discussions around web content took place informally around clinical commitments. PPI was used throughout the development of MyMR and would benefit from more structured planning using the GRIPP-2 criteria as a guide to ensure this was conducted in a more systematic way.

IT developments were limited by the capabilities of the current software. For example, plans for the generation of alerts in response to IBD Control score were limited to a compromise of trigger question-generated alerts and the safety net of advising patients to get in touch in the event of an unfavourable IBD Control score. The need for clinical staff to oversee and act upon patient-

entered data was felt to be an important area for improvement by members of the patient focus group and therefore the generation of alerts will continue to be developed. The receipt of the multi-million-pound Global Digital Exemplar award in recent years means that local IT systems such as MyMR now have further resources to make the proposed developments. These are discussed further in Chapter 7.

More work is needed to establish whether the proposed traffic light system for categorising IBD Control scoring is appropriate. Our nurses felt they would wish to be informed of anyone scoring less than 13. i.e. anyone without quiescent disease in which case results could simply be classified into 'green' (≥13) and 'red' (≤12), with automated alerts for any patient scoring in the 'red' zone. Although this could mean earlier detection and intervention for disease flares, it could have the consequence of inundating them with alerts and potentially overwhelming an already stretched service. A solution to this could be giving patients back control an encouraging them to self-monitor and get in touch in the event of falling IBD Control scores, and this was the strategy adopted in the feasibility study in Chapter 6.

The provision of access to all test results, whilst welcomed by patients, was met with some reservation by health professionals during discussions about what test results to release and when to do so and this is not unusual. Patient health records are slowly becoming accepted in other countries. In 2015, a trial of OpenNotes, a system for sharing doctors' notes from appointments and visits with patients, took place in United States (212). 105 primary care physicians completed the study. Two-thirds of patients reported a better understanding of their health and medical conditions and that they were taking better care of themselves, improving medication compliance, and feeling more in control of their care. There was some concern over the workload increased health queries might pose: for clinicians, only 3% spent more time answering patient questions outside visits but 11% spent more time writing or editing notes—with a fifth reporting changes to the way they wrote about cancer, mental health, substance misuse, or obesity. After the trial, some 99% of patients and 75% of doctors wanted to continue using OpenNotes. The Canadian University Health Network, carried out a similar trial to make laboratory results, diagnostic imaging reports, pathology reports, clinic notes, and mental health notes available in real time(213). It found the move had no significant adverse effect on patient anxiety. Clinical and service efficiency were improved because of fewer telephone calls about results and appointment schedules and fewer requests for copies of health records; 96% of patients using the portal said they preferred real time access to their health record, even before seeing their doctor.

5.6 Conclusions

This service development describes the changes made to the existing MyMR site to both improve the IBD service and develop it to a level required to conduct the feasibility study detailed in Chapter 5. In 2014 MyMR already provided basic services to patients such as the provision of medical records and electronic messaging and our IBD and IT teams have worked together to improve upon this, providing greater access to clinical information such as test results, detailed information about IBD, a patient-reported outcome tool (IBD-Control), and now the IT capability to provide home-FC monitoring.

MyMR continues to improve and develop. The linkage of remote technologies such as at-home FC testing provides an exciting opportunity to empower patients to collect and act upon their own data, as well as allowing them to share this with their healthcare team. More work is needed to examine feasibility and patient views of incorporating these technologies into routine clinical practice and this provides the rationale for the feasibility study of home FC testing and MyMR use described in Chapter 6.

6 Feasibility and acceptability of an IBD supported self-management website and home faecal calprotectin-testing in treatment cessation

6.1 Introduction

This chapter describes a mixed-method ethically approved exploratory study of the feasibility and acceptability of using home FC-testing and the MyMR website to monitor and support self-management. It aims to complement the existing literature by combining these technologies and examining their use in patients who have stopped a medication and are thus at increased risk of flare.

There are an increasing number of therapeutic options for IBD ranging from topical and oral anti-inflammatory drugs to potent intravenous or subcutaneously administered biological agents. Immunosuppressant treatments for IBD are costly and the long-term safety of these medications has been questioned due to a risk of serious side effects including infection, infusion reactions and increased cancer risk. International guidelines suggest that current data is insufficient to make definitive recommendations on when/in whom to stop treatment (214). Risks of stopping treatment include potentially serious disease flare-ups (occurring in around 50% (61, 67, 215)) and difficulty reinstating treatment with anti-TNF medications due to the development of anti-bodies. Decisions to stop treatment are usually based upon a combination of clinical symptoms, endoscopic and radiological findings, and patient preference, and must involve a careful risk-benefit analysis. Several studies have examined disease relapse rates at one year following cessation of infliximab treatment in Crohn's' patients. The STORI study(62) of 115 patients with luminal Crohn's disease found relapse rates of 44% one year following cessation of infliximab and several retrospective studies have found even higher relapse rates of 55-85%(61, 67, 215). Early detection and management of a relapse is extremely important as delays to treatment can prolong and increase the severity of a flare. Although FC testing in the context of self-management websites has been studied in stable IBD patients(127), its use in the subgroup of patients stopping a treatment has not yet been explored. Little is known about how patients feel about stopping treatments for IBD and how access to home-testing and support might affect their attitudes to stopping a medication.

Before considering a full trial exploring the effects of the new and potentially complex technologies of MyMR and home calprotectin testing on patient outcomes, it was important first

to explore how these technologies would work in practice, as well as how patients would find using them. The Medical Research Council (MRC)(216) emphasise the importance of focusing adequate attention on the developmental stages and practicalities of implementation of complex interventions, and not just on outcomes, and this lead to the development of a mixed methods exploratory feasibility study.

As healthcare becomes increasingly IT-driven, the rising prevalence and cost of IBD make it important to conduct this study to assess this new technology and how it might fit into traditional outpatient methods of managing IBD. I designed, led and carried out this research with support from my research supervisors and the UHS IT and nursing teams.

6.2 Aims and Objectives

- To explore the feasibility of monitoring patients (who have recently stopped a medication) remotely using a combination of MyMR self-management website and home FC-testing by collecting data on study recruitment, compliance and retention which could inform a randomised controlled trial
- To explore the acceptability of self-monitoring via patient questionnaires and qualitative interviews

6.3 Methods

6.3.1 *Study design*

To better understand how home monitoring would work in a selected IBD population, I devised an exploratory feasibility study, applied for ethical approval and conducted the feasibility study comprising 2 parts:

i. Study recruitment and 26 weeks of disease self-monitoring and questionnaires
ii. Qualitative patient interviews to explore views on self-management as a concept, as well as the acceptability of home monitoring.

It was not appropriate at this stage to conduct a pilot RCT. The MyMR and home FC testing/linkage to MyMR were both in their early stages and further exploration of how these technologies would work in practice was required. The use of an exploratory feasibility study approach allowed me to explore the feasibility of a study in this area, how well the technologies worked and how feasible it was to recruit and collect data.

6.3.1.1 Ethical approval

The study was granted HRA approval on the 7th February 2017 (South Central - Hampshire A Research Ethics Committee reference 17/SC/0002; Appendix E.2). The University of Southampton Research Governance Office reviewed and approved the submission on the 6th March 2017 (ERGO reference 25830; Appendix E.3). The study is registered on clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03671980).

6.3.1.2 Funding

FC test kits were provided free of charge by BioHit Healthcare® who had no input into the study design or analysis (Appendix E.1). With support from my supervisors, I designed, undertook and analysed the study. My research time was funded by providing medical registrar out of hours cover at the University Hospital Southampton for 2 weeks out of every 6 as part of a rolling rota. IBD specialist nurses supported study patient care which was within the scope of their usual clinical practice and therefore did not require additional funding.

6.3.1.3 Study participants

The study took place at University Hospital Southampton, a large Foundation Trust teaching hospital serving a population of around 1.9 million people. Adult patients receiving inpatient or outpatient care at UHS with a diagnosis of ulcerative colitis or Crohn's disease who had recently (within the last 8 weeks) stopped one or more IBD treatments were invited to participate. The decision to include only those patients who had recently stopped a treatment for IBD was taken as these patients are at higher risk of disease flare. FC has been demonstrated to rise before the clinical symptoms of a flare become apparent(217, 218), allowing early treatment to be implemented. Limited resources mean that novel interventions such as home FC testing need to be targeted to those patients most likely to gain benefit from them.

6.3.1.4 Researcher Characteristics

I was the sole researcher in the study, the implications of which are discussed later in the discussion section. My role at the time of research was as an IBD research fellow, conducting IBD clinics and medical registrar on call shifts. I had no previous direct clinical contact with research participants but did develop a rapport during the study requirements which should be considered in the analysis of the qualitative research.

6.3.1.5 Inclusion criteria

The following inclusion criteria were required for participation:

- Adults aged ≥ 18 years currently under secondary care outpatient follow up for IBD.
- Diagnosed with IBD at least one year prior to study enrolment (to ensure familiarity with disease and treatment).
- Stopped one or more treatments for IBD (for any reason) within the last 8 weeks (time frame selected to ensure patients were unlikely to have flared yet).
- Able to understand English and provide written consent (the current version of MyMR does not support multilingual use. The resources available to the study did not allow for the cost of translation or interpreters. The study was reliant upon individuals being able to access the website independently and at their convenience. Given the demography, I did not anticipate that this would lead to the exclusion of a significant number of participants however it is important that MyMR is accessible to all and further developmental work is planned in future to support multi-lingual use).
- Own, or have regular (at least weekly) access to a smartphone +/- personal computer with internet connection (minimum requirement of monthly testing but participants encouraged to use website as frequently as desired).

6.3.1.6 Exclusion criteria

The following exclusion criteria were implemented:

- Inability to read or understand informed consent.
- Inability to use a smartphone (successful participation was dependent on being able to independently negotiate smartphone and home test-kit functions).
- Likely requirement of IBD surgery within the study period (this could potentially mean a period away from home and access to personal computer/smartphone. Many of these patients may also undergo bowel resection and ileostomy formation, in which case FC measurement may be less reliable(219)).
- Pregnancy or planned pregnancy within next 6 months (increased supervision and clinical input potentially required).
- Terminal illness with limited (< 1year) life expectancy.
- Current participation in another IBD research study (one of study requirements was that patients would not have any routine follow up appointments during the study period which is usually a requirement of other research studies).

6.3.1.7 Sample size estimation

This was a feasibility study and I therefore took a pragmatic approach to sample size estimation. Two IBD clinics take place in UHS each week with around 100 patients attending in total. Based upon my previous study of biologics drug use(60), it is anticipated that at least 60 patients will stop biologic drug treatment (infliximab, adalimumab etc.) each year. Local physician experience suggests conservatively that around 60 patients will stop other immunomodulator treatment (azathioprine, methotrexate etc.) each year, and at least 20 will discontinue aminosalicylate medication. Based upon 40-50% positive recruitment rates for similar studies (127), I anticipated average recruitment of 5 of these patients per month, aiming for a target sample size of 30 patients after 6 months. With an anticipated drop-out rate of around 20-25% (127, 220), I projected this would leave an estimated 24 participants for analysis at the end of the study. Around 50% of patients stopping treatment for IBD will experience a disease flare up in any given 12 month period(61), so it was estimated that up to a quarter of recruited patients might have a rise in FC level and/or symptoms of a disease flare over 6 months. This would provide a sufficient sample to explore the feasibility aims of this study highlighted above and provide valuable information to inform a more substantial study.

6.3.1.8 Identification and recruitment of study participants

Following receipt of ethical approval, I advertised the study to patients and healthcare professionals via several routes:

1. Email introducing study to all physicians and nurses on gastroenterology team.
2. Face-to-face explanation of study to all consultants, registrars and nurses involved in the care of IBD patients.
3. Small, laminated postcard-sized summary of study placed by computers in clinic and endoscopy rooms.
4. Colour posters in lifts and stairwells of main hospital introducing study to patients and providing contact details for researcher (Appendix E.4).

Patients were introduced to the study by their attending nurse/physician, and if interested, were given an invitation letter (Appendix E.5) and patient information leaflet (PIL; Appendix E.6) and invited to contact the researcher via email or telephone to discuss participation. Reasons volunteered by patients and clinicians for patient non-participation were documented with the patient's permission. Written informed consent from patients was sought during the initial study visit (Appendix E.7), prior to collection of any baseline measures. Patients' general practitioners were informed in writing of their participation in the study (Appendix E.8).

6.3.1.9 Initial study visit

Once a patient had confirmed their interest in participating (via telephone/email), an initial telephone conversation was scheduled to discuss the study and plan an initial study visit to take place either at UHS or in the patient's own home, the latter being preferable for participant convenience and to set up home testing in the environment in which it would take place. I registered participants to the MyMR website and provided them with their log in details via text (password) and email (username). They were also invited to download the QuantOn Cal® app prior to the visit, to ensure that their phone model was compatible.

Home visits took place in accordance with the University of Southampton lone researcher policy (https://www.southampton.ac.uk/hr/services/lone-working/index.page) and lasted approximately 1 hour. In most cases I had already had telephone interaction with the patient which helped to establish a rapport, and I talked to members of the clinical team who knew the patient to establish if there might be any concerns about conducting a home visit. In all cases, I provided a nominated member of the clinical team (usually an IBD nurse) with the patients address, contact numbers, as well as an agreed telephone 'distress code' to indicate to the contact that help was required. I then 'called in' to confirm I had safely left the address and was on my way back to base.

- Provision of information and consent

During the visit, I gave the participant the opportunity to ask any questions before informed consent was sought and the consent form signed. The patient was then provided with the following:

- 7 QuantOn Cal® FC test kits
- One single page information sheet outlining the schedule of requirements of the study (e.g. monthly IBD Control, monthly FC, blood tests, questionnaires) and useful contact details
- Blood forms x2
- Copy of competence centre barcode

- MyMR and QuantOn Cal® training

I taught the participant how to:

- Login to MyMR website, view results and letters, access information about IBD, contact their IBD team in event of flare/problem via email messaging, and complete the IBD Control questionnaire.
- Login to and use the QuantOn Cal® app – this included scanning the competence centre code to link the patient to the UHS system, complete the camera scan tests, and perform an initial demo FC test. The patient was shown how to do this using a pre-loaded demo test cassette and demo app on my smartphone. This demo app allowed me to skip the usual 15-minute incubation period required for the test. No faecal samples were required.

- Baseline questionnaires:
  After the visit was complete, I sent the patient an email link to complete baseline IBD knowledge and quality of life (QoL) questionnaires via SurveyMonkey® at week 0.
    - CC-KNOW(221) (Appendix E.9). CC-KNOW is a well-established measure of IBD knowledge. It is a self-administered 24-item questionnaire and psychometric tests have shown it to be valid, reliable and readable(221). A higher score reflects increased knowledge of IBD.
    - Short-IBDQ(207) (Appendix E.10). The S-IBDQ consists of the 10 questions derived from the 32 question IBDQ(222) concerning health-related quality of life (HRQL), and covers four areas: bowel symptoms, systemic symptoms, emotional wellbeing, and social functioning. The total score ranges from 10 to 70 (best QoL). Higher values reflect better HRQL. Based on findings from a previous study of patients with Crohn's disease, a clinically meaningful improvement in a patient's health has been estimated as an increase of 9 points in the SIBDQ total score(173)-.

6.3.1.10 Ongoing study requirements/ monitoring

Participants were required to complete:

- Monthly FC testing at weeks 0, 4, 8, 12, 16, 20, and 24 and to contact the IBD team via MyMR in the event of a FC ≥150µg/g, symptoms suggestive of a flare up, or any clinical cause for concern. A FC ≥150µg/g has been shown to be strongly predictive of relapse in UC and Crohn's (223).

- Log in to the MyMR website at least once per month to record a monthly IBD Control score(202) (patient-reported measure of IBD activity, Appendix D.3), message IBD nursing team if IBD Control score ≤12.

- Use any other features of the MyMR website such as the health journals, viewing test results etc. as often as desired.
- Blood tests (conducted at either their local GP surgery or UHS phlebotomy department), occurring at:
    - Week 0 - full blood count (FBC), urea and electrolytes (U&E), liver function tests (LFT), C-reactive protein (CRP), vitamin B12, folate, ferritin, and vitamin D.
    - Week 26, end of study (tests as above)
    - For any additional blood test required as part of usual care (for example 3-monthly azathioprine blood monitoring), blood forms were provided to the patient to perform as usual.

  Frequency of blood tests were standard for IBD outpatient monitoring and were considered in-keeping with routine care.
- Blood results were made available to patients via the MyMR website accompanied by simple explanations of their meanings. I monitored blood results remotely and contacted the patient via email if they had not initiated contact with the IBD team within 7 days of receipt of any significantly abnormal FC results (sooner if clinical need warranted this).
- Participants received a follow-up outpatient appointment with an IBD doctor or nurse at around week 26 on completion of the monitoring element of the study. Current IBD guidance recommends minimum yearly review (63) in stable patients, but most patients, particularly those undergoing changes to treatment, will be seen more frequently than this.
- If the need for additional face-to-face outpatient review or telephone consultation arose due to clinical need, this was arranged between the patient and specialist nurse using the messaging feature of MyMR.

6.3.1.11 Remote monitoring

I monitored patients remotely over the 6-month study period. Participants were expected to complete one QuantOn Cal® test and IBD Control questionnaire per month as a minimum requirement of the study and were encouraged to use other elements of MyMR as often as they wished (messaging service, results, clinical info). If these tasks were overdue by one week, I sent the participant up to 2 separate email reminders.

6.3.1.12 Management of abnormal test results

Abnormal stool and blood test results were managed by me or a specialist IBD nurse (depending on availability and who the patient contacted) according to best clinical practice and up to date IBD guidance, with consultant input where necessary.

6.3.1.13 End of study questionnaires and qualitative interviews

At 26 weeks participants were sent an end of study online questionnaire comprising a mix of closed and open-ended questions to gather mixed data (Appendix E.11) to assess acceptability of the intervention and repeat CC-KNOW(221)(Appendix E.9) and SIBD-Q(207)(Appendix E.10) questionnaires. The end-of-study questionnaire was researched(224) and developed by me to help answer the research objectives and was reviewed and amended by my research supervisors (HE, SL) and approved by the South Central - Hampshire A Research Ethics Committee.

Qualitative interviews took place via telephone within 12 weeks of completion of the monitoring element of the study to evaluate acceptability of both the website and home FC monitoring and were based around a semi-structured interview guide (Appendix E.12) using largely open-ended questions to encourage patients to describe their experiences in detail and allowing me to follow up on interesting responses. A semi-structured approach allows a balance between developing a rapport with participants and maintaining scientific rigour. This method typically consists of a dialogue between researcher and participant, guided by a flexible interview protocol and supplemented by follow-up questions, probes and comments. It allows the researcher to collect open-ended data, to explore participant thoughts, feelings and beliefs and to delve deeply into personal and sometimes sensitive issues(225). I developed the interview guide after attending a course on Qualitative Interview Skills at the University of Surrey. This was reviewed and amended by my research supervisors (HE, SL) and approved by the South Central - Hampshire A Research Ethics Committee. Interview questions evolved over the course of subsequent interviews if they were felt to require further clarity for participants or were not generating sufficient data. For example, a question regarding patient views on self-management appeared to cause some confusion in early interviews and was adapted slightly to include an explanation of what 'self-management' may mean. Interviews were audio-recorded and transcribed with advance written consent which was confirmed verbally at time of interview.

6.3.2 *Data collection and analysis*

6.3.2.1 Primary Outcome measures

Primary outcome measures were selected to provide information on measures of feasibility which could inform a randomised controlled trial.

Feasibility was determined by:

- Recruitment rates
    - Target 5 patients per month (based upon sample size estimation, see section 5.3.1.5).
    - Data on feedback given for non-participation were also collected to help identify factors which may limit/improve recruitment.
- Number of patients achieving adherence to FC testing schedule
    - Target 5 out of 7 tests completed – i.e. greater than 70% completion of testing
- Number of patients achieving adherence to website use
    - Minimum login target: x1 per month – to ensure monthly IBD Control(202) scoring as a minimum.
- Study retention rate
    - Target 80% (Anticipated dropout rate of 20% based upon similar studies(127, 128)).
    - Study retention was defined as successful completion of at least 5 out of 7 home FC tests, with no periods without login to website of greater than 3 consecutive months.
- Response rates to questionnaires
    - Target >60%(226) based upon acceptable rates from similar studies.

Acceptability was determined by:

- An end-of study questionnaire exploring participants' experiences of using both home FC testing and the self-management website.
- Outcomes of qualitative interviews undertaken in a purposive sample of patients.

6.3.2.2 Secondary outcome measures

Data was collected during the exploratory feasibility study on the following outcomes:

- Socio-demographic and disease data: gender, age at diagnosis, age at time of inclusion, type of IBD, disease location, disease behaviour, disease activity score, treatment at time

of inclusion, smoking status, education, marital status, occupation, ethnic origin, computer/smartphone use.

- FC levels at 0, 4, 8, 12, 16, 20, and 24 weeks (monthly monitoring).
- IBD-Control scores at 0, 4, 8, 12, 16, 20, and 24 weeks (monthly monitoring).
- Frequency of disease relapse over 26 weeks
    - Defined by rise in FC level >150 and/or IBD control score ≤12.
- Mean quality of life (S-IBDQ(207)) scores at 0 and 26 weeks
    - Data was collected on completion rates as well as SIBDQ score.
- Mean IBD knowledge scores (CC-KNOW(221)) at 0 and 26 weeks
    - Data was collected on completion rates as well as CC-KNOW score.
- Frequency of IT helpdesk contact
    - Number of patient-initiated contacts with IT via email (reported by IT team on completion of study).
- Frequency of contact with healthcare providers for IBD-related illness
    - GP visits (patient self-report).
    - A&E visits (UHS electronic database)
    - Hospital admissions (UHS electronic database)
    - Outpatient appointments (UHS electronic database)
    - Flareline telephone calls (UHS electronic database)
    - MyMR messaging (UHS electronic database)
    - Adverse events
        - Any unfavourable or unintended consequences relating to the study, reported by patients, IBD staff, or researchers.
        - This did not include IBD flare-ups which were anticipated in the study protocol to be an expected occurrence.
        - Any serious adverse events (SAEs) were to be submitted to the local REC using a Non-CTIMP (clinical trial of investigational medicinal product) safety reporting form within 15 days of the chief investigator (NT) becoming aware of them.

6.3.2.3 Quantitative data collection and analysis

Quantitative data on primary and secondary outcome measures were gathered using a combination of patient self-report, questionnaires, interrogation of the existing UHS electronic medical record (via the Charts® computer application) and via MyMR. Simple descriptive analysis

was performed for primary and secondary outcome measures and any other additional observations.

6.3.2.4 Qualitative data collection and analysis

Qualitative data were collected in the form of open-ended questions from end-of-study questionnaires and audio-recordings from qualitative interviews. Interviews took place via telephone at a time convenient to the participant and lasted between 20 and 40 minutes. All recordings were conducted via telephone using a handheld digital recorder. Patient consent to recording was re-confirmed at the onset of the interview before any interview schedule questions were asked and participants were reminded about confidentiality. Immediately after the interview was complete, I re-played the recording to ensure sound quality was adequate. I transcribed all interviews and following this the recordings were destroyed in keeping with South Central - Hampshire A Research Ethics Committee specification.

NVIVO qualitative data software was used to analyse interview data. Data were analysed using thematic analysis(153) using the steps detailed below:

1. Become familiar with the data - I listened to the interviews several times before transcribing verbatim and re-reading systematically, recording initial preliminary codes and thoughts
2. Generate initial codes - I went through the data systematically generating codes and identifying patterns concerning themes
3. Search for themes - Codes were divided into themes and subthemes
4. Review themes - Themes were reviewed once more to determine their core themes. Any themes that displayed significant overlap were amalgamated into themes/subthemes
5. Define themes - I defined themes, considering their application to the research question
6. Write-up - I described and reflected upon themes and used pertinent quotes for illustration.

The SRQR checklist for the qualitative element of the study can be found in Appendix B.2.

6.3.2.5 Patient and public involvement

Members of the Southampton IBD Patient Panel, a group of interested patients (including a regional patient representative of the Crohn's and Colitis UK charity) were consulted during the development of the study proposal to gain a lay perspective on the proposed feasibility trial and to ensure it addressed issues relevant to patients with IBD. The panel fully supported the initiative and contributed to the development of the study protocol by providing insight on how patients would be likely to use the website and respond to the requirements of the study (for example acceptable burden of questionnaires). Panel members were consulted during preparation of patient literature for the study.

The proposed study was presented at the IBD Open Day for patients, family and carers. Feedback from this session was used to develop the protocol and MyMR website. For example, patients felt strongly that to maximise uptake and use of the web intervention it was important that the website could be accessed by both computer and smartphone which supported development of a MyMR app by the IT team. Outcomes from the patient focus group is described in section 5.4.1.

6.4 Results

6.4.1 *Recruitment*

The study was open for recruitment for 22 weeks from the 4th of April 2017. The final potential participant was referred on the 22nd August 2017. Recruitment closed before the target number of patients were recruited to the study because of maternity leave and a lack of available resources to fund training of additional researchers to recruit and conduct initial study visits.

38 patients (25 female, 13 male) were referred from different sources (research team, IBD nurses, IBD consultants/registrars, and self-referral) during this period. 36/38 (95%) of patients were referred from outpatient clinics, with just one inpatient referred following an inpatient admission and one whilst attending endoscopy. The most common treatment ceased was azathioprine (Table 14; 42% of referred patients, 64% recruited patients). The most common reason for treatment cessation was disease remission (Table 15; 58% referred patients, 91% recruited patients). The most common sources of referral were from IBD physicians (Table 16; 42% referred patients) and IBD specialist nurses (39%).

Table 14: Treatment cessation in potential participants

Treatment ceased	Patients referred (n=38)	Patients recruited (n=11)

Azathioprine	16	7
Infliximab	7	0
Adalimumab	4	2
Mercaptopurine	3	1
Methotrexate	2	1
5-ASA	2	0
Vedolizumab	2	0
Nil	2	0

Table 15: Indication for treatment cessation

Indication	Patients referred (n=38)	Patients recruited (n=11)
Remission	22	10
Treatment failure	2	0
Pregnancy/fertility	3	0
Side effects	9	1
Unknown	2	0

Table 16: Referral source for potential participants

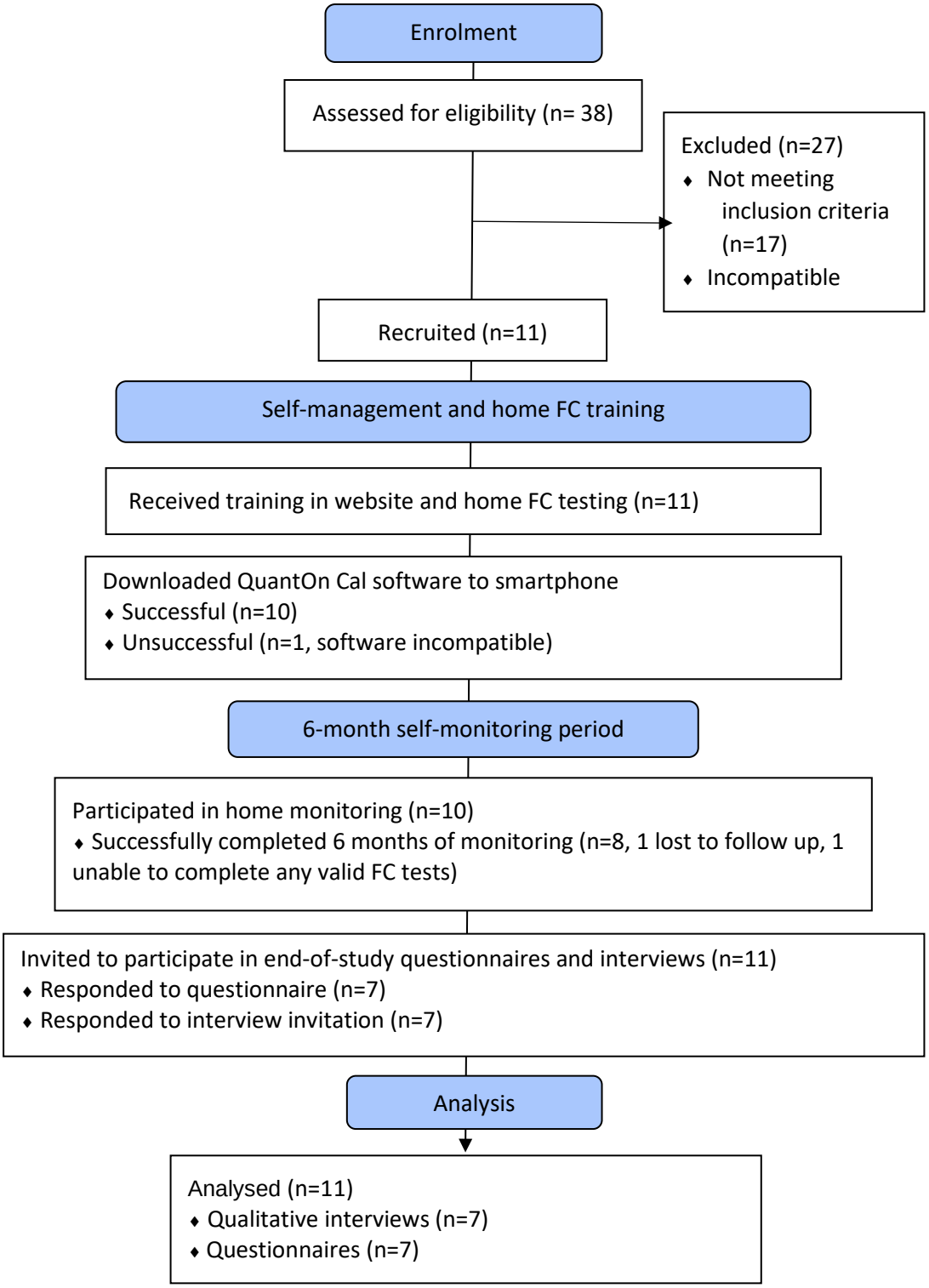
Referral source	Patients referred (n=38)	Patients recruited (n=11)
IBD nurses	14	5
IBD physicians	16	6
Clinical trials coordinator	5	0
Self-referral	3	0

Of the 38 patients screened, 21 (55%) were considered eligible according to inclusion/exclusion criteria for the study. 11/21 (52%) were ultimately recruited to the study. Reasons for non-eligibility are documented in Table 17. 10 eligible patients were not recruited. 3 of these were keen to participate but unfortunately their smartphones were not compatible for QuantOn Cal® use. The remaining 7 did not respond to follow up invitations to participate.

Table 17: Reasons for ineligibility of potential participants

Reason not eligible	Patients referred (n=38)
IBD diagnosis not established	2
Patient out of area	1
Stopped treatment > 8 weeks go	2
Undergoing surgery	2
Pregnancy or planned pregnancy within next 6 months	2
Treatment escalated (despite x1 treatment stopped)	3
Did not stop treatment	5

Figure 20: CONSORT diagram detailing flow of patients through the study



6.4.2 *Baseline characteristics*

Table 18 summarises the baseline characteristics of participants recruited to the study. Females outnumbered males at 8:3. The median age at participation was 38 with the oldest participant 71 years of age. 5 patients had Crohn's and 6 UC. All except 1 used a smartphone daily and the majority owned iPhone models (9/11, 82%).

Table 18: Description of baseline characteristics of participants recruited to the study

Characteristic	**n=11**
Gender, male: female	3:8
Median age at inclusion (range, mean), years	38 (27-71, 41)
Median disease duration (range, mean), years	5 (1-21, 7)
Diagnosis	
Crohn's	5
Median HBI (range, mean)	1 (1-6, 2.25)
Ulcerative colitis	6
Median UCDAI (range, mean)	0.5 (0-1, 0.5)
Disease extent	
Pan-colonic	2
Left-sided colonic	5
Proctitis	1
Terminal ileal	1
Ileocolonic	2
Smoking status	
Smoker	1
Ex-smoker	6
Never smoked	4
Median alcohol intake, units/week (range)	2 (0-10)
Education	
Secondary school - GCSE	1
Secondary school - College	4
University	6
Employment	
Unemployed	0
Employed	10
Retired	1
Ethnic origin	
White British	10
White Irish	1
Computer usage	
Daily	7
Weekly	3
Monthly	0
Less than monthly	1
Never	0
Tablet usage	
Daily	5
Weekly	1
Monthly	0
Less than monthly	0
Never	6
Smartphone usage	

Daily	10	
Weekly	1	
Monthly	0	
Less than monthly	0	
Never	0	
Smartphone make		
iPhone	9	(models 4-7)
Samsung	2	
Other	0	

6.4.3 *Blood indices*

All patients were provided with blood forms to have a full set of routine IBD blood tests at study onset and completion. All 11 patients undertook the initial blood test, and 9/11 (82%) patients undertook the end of study blood test (Table 19). Mild abnormalities were observed in white cell count/neutrophils in 4/11(36%), in keeping with current or recent immunomodulator use. Ferritin levels were frequently observed to be low (less than 50µg/L considered low in an IBD population) and occurred in 8/11 (73%) of study recruits. Low vitamin D levels were observed in 4/11 (36%) recruits. Two patients had a mildly elevated alanine transferase (ALT), one of whom (P5) underwent further investigation with ultrasound scan and liver screen bloods which yielded a diagnosis of fatty liver disease. The other ALT (P2) was very mildly raised and subsequently normalised. One patient was found to have low platelets for which she had already been referred to haematology and which subsequently normalised. I contacted all patients with clinically significant blood abnormalities and arranged for replacement of vitamin D, vitamin B12 and ferritin as appropriate via the general practitioner.

6.4.4 *FC testing and IBD Control*

11 participants were recruited to home monitoring. One patient (P2), despite having access to a compatible smartphone (Samsung Galaxy s6) was unable to scan the barcode required to provide his unique QuantOn Cal® patient identifier to link to the competence centre. The phone operating system was up to date and various attempts were made to scan in different locations and lighting with no success. I offered to arrange a support visit however as the phone belonged to his partner who did not live locally this proved challenging to arrange and ultimately, he decided to withdraw from the study. Another patient (P3) eventually abandoned testing at month 5 due to repeated difficulties and was unable to perform any valid tests despite several attempts each month. I arranged for a second home visit after month 1 and was able to complete a trial test using the participant's phone but unfortunately subsequent attempts by the participant remained

unsuccessful. This participant remained in the study and was able to discuss his difficulties during the qualitative interviews.

9/11 (82%) patients successfully completed their first self-directed FC test and proceeded to the 6-month period of FC testing for which results can be seen in Table 20. 7/9 (78%) completed all 7 FC tests required for the study, with the remainder completing 3 and 4 of the 7 tests, respectively. 2 patients completed all their FC testing without requiring any email prompts, while the remainder required between 1 and 7 prompts over the study period to complete overdue testing (mean 3).

Of the patients who were unable to complete all 7 FC tests, two had trouble conducting the testing largely due to being unable to get their smartphone camera to successfully scan the test cassette within the two-minute window. Another patient (P1), whilst managing to perform several valid tests, was undergoing an extensive house renovation and found it very challenging to find the space or time required to undertake the testing. A third patient (P8) completed their first 4 FC tests and IBD control surveys very punctually but following this completely ceased any further study participation. Reasonable attempts were made to contact this participant by post, telephone and letter with no response. I noted that this patient failed to attend other outpatient hospital appointments not related to the study, so it is possible that a major life event or perhaps move out of area occurred.

Table 19: Study participant FC test results

Participant number	FC1	FC2	FC3	FC4	FC5	FC6	FC7
1	12	x	14	x	14	x	x
2	x	x	x	x	x	x	x
3	-	-	-	-	-	x	x
4	18	22	21	43	13	16	12
5	189	1415	34	33	10	24	510
6	16	10	10	8	10	9	9
7	19	23	26	12	20	13	13
8	12	10	11	27	x	x	x
9	10	18	29	105	31	11	9
10	10	33	11	13	12	1548	7429
11	201	10	13	20	13	14	12

(- F C test invalid, x FC test not performed)

FC levels of greater than or equal to 150µg/g were considered significantly elevated. 5/9 (56%) patients' FC levels remained under 150 µg/g throughout the monitoring period. All participants except two had an initial FC level of <25 µg/g. One participant (P10) had a single reading of 201 (valid test confirmed) but all subsequent tests were <25 µg/g and she reported no change in

symptoms and remained clinically well. One participant (P5) had an initial FC of 189 and subsequently went on to have elevated and normal FC levels that corresponded well with IBD symptom relapse and remission (see section 5.4.5). It is noted that he was the only participant who had not ceased a treatment for disease remission, but for side effects, and could therefore immediately be considered at high risk of relapse as he was known to have ongoing active disease.

Figures 21-29 present paired individual patient FC and IBD-Control 8 scores. There was insufficient data for patient 2 and 3 to chart results. Active disease is represented by high FC levels but low IBD-Control 8 scores. Patients 5, 8 and 10 demonstrated falling IBD Control in tandem with rising FC levels most clearly.

Figure 21: Patient 1 FC and IBD Control-8 scores

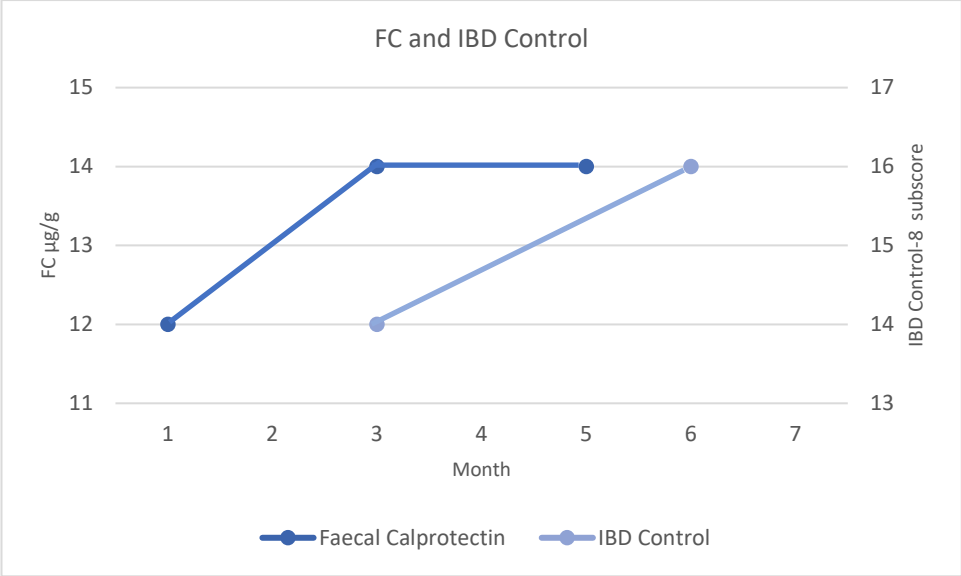


Figure 22: Patient 4 FC and IBD Control-8 scores

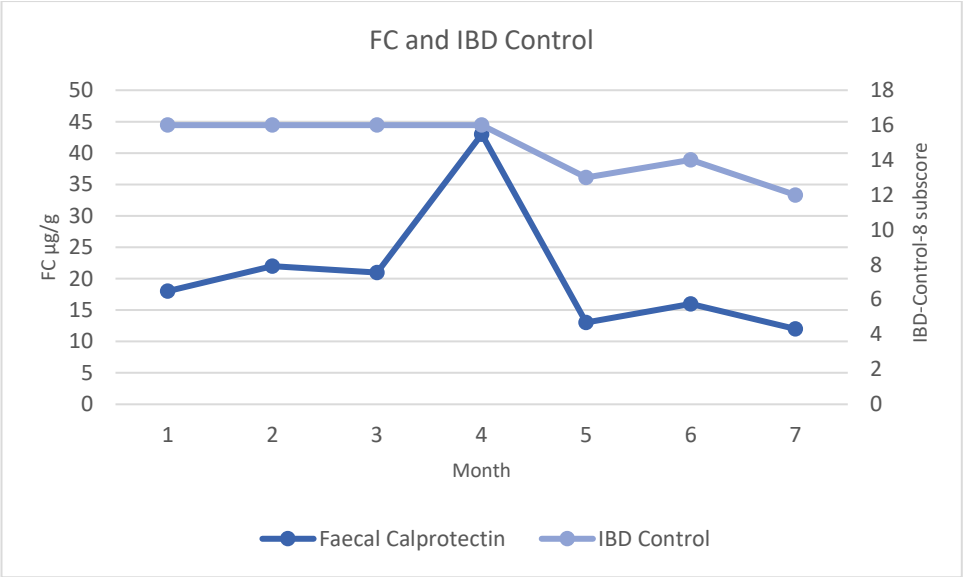


Figure 23: Patient 5 FC and IBD Control-8 scores

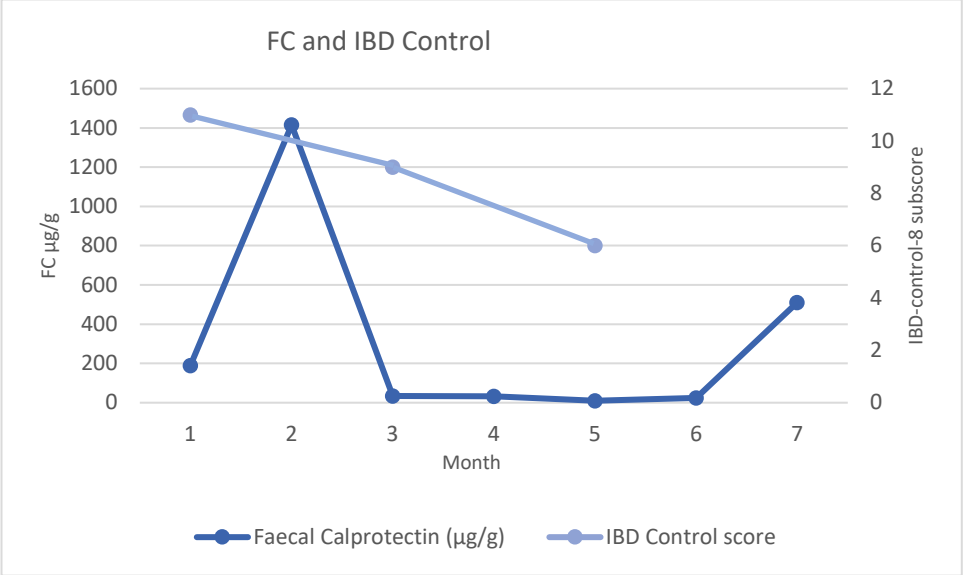


Figure 24: Patient 6 FC and IBD Control-8 scores

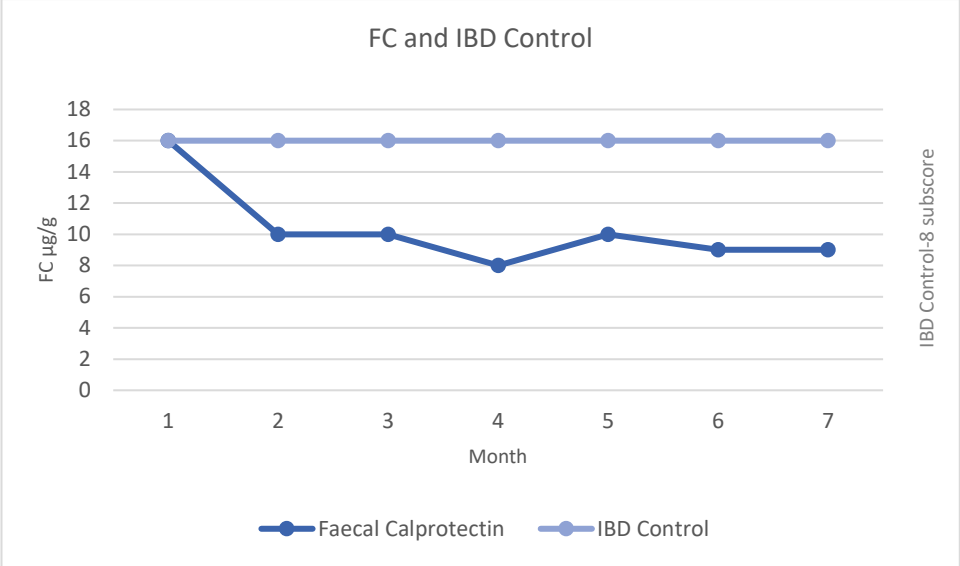


Figure 25: Patient 7 FC and IBD Control-8 scores

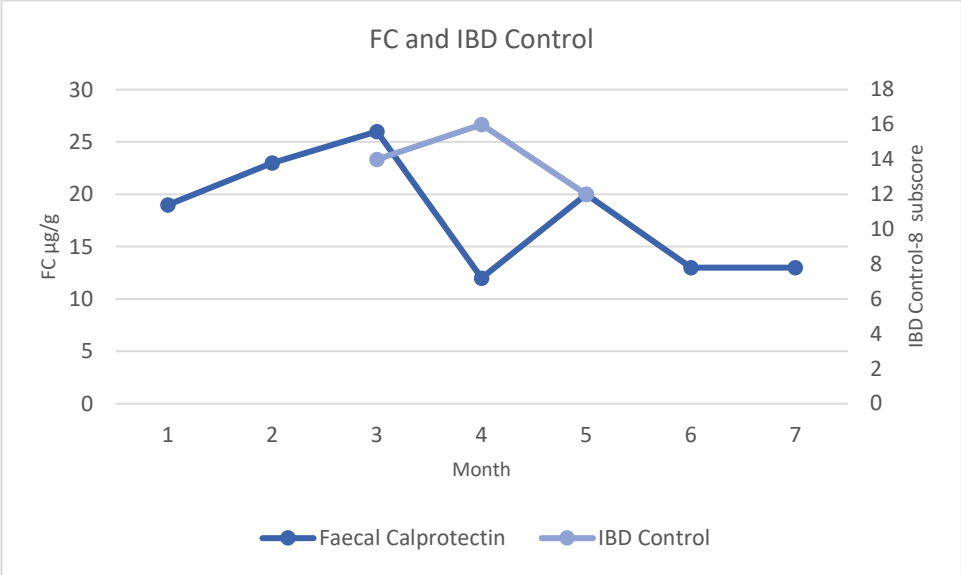


Figure 26: Patient 8 FC and IBD Control-8 scores

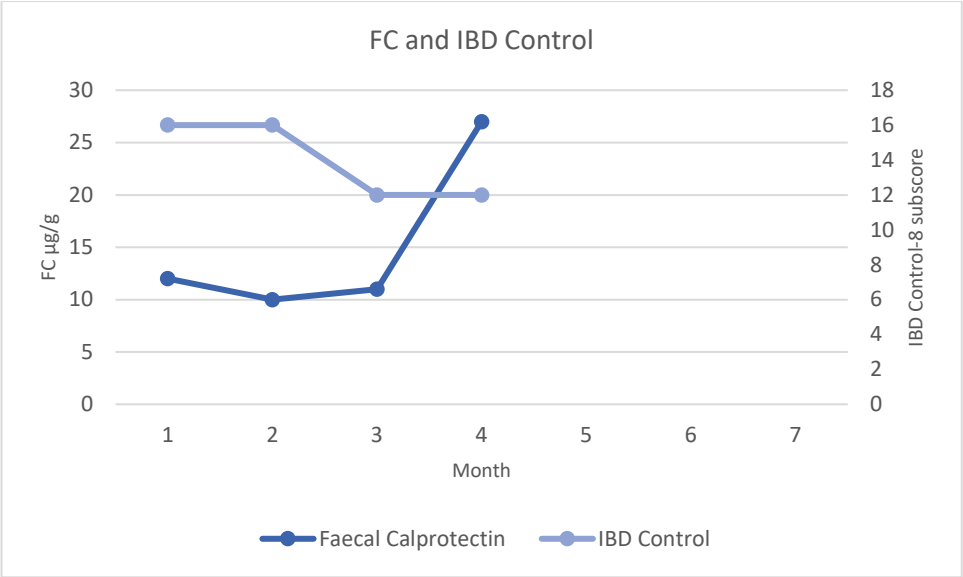


Figure 27: Patient 9 FC and IBD Control-8 scores

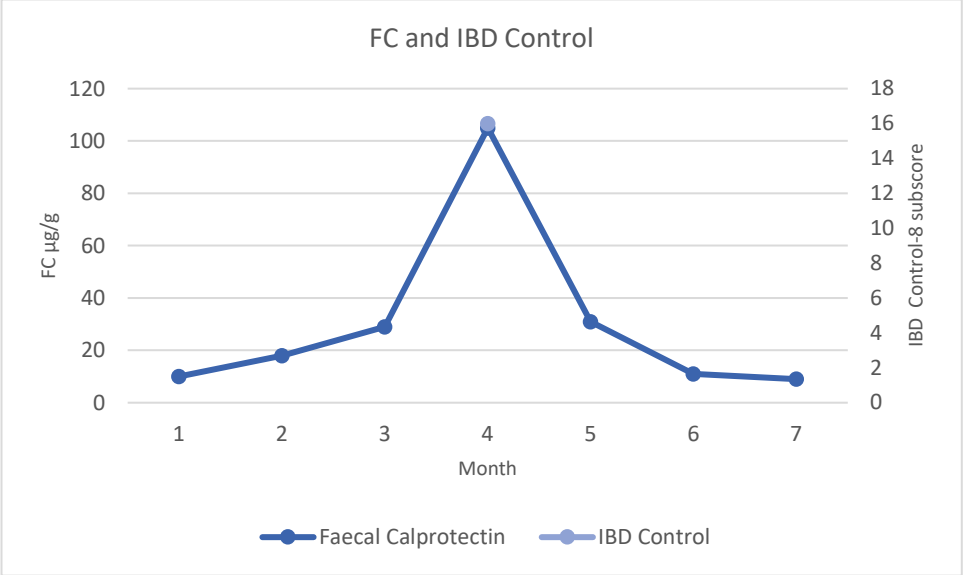


Figure 28: Patient 10 FC and IBD Control-8 scores

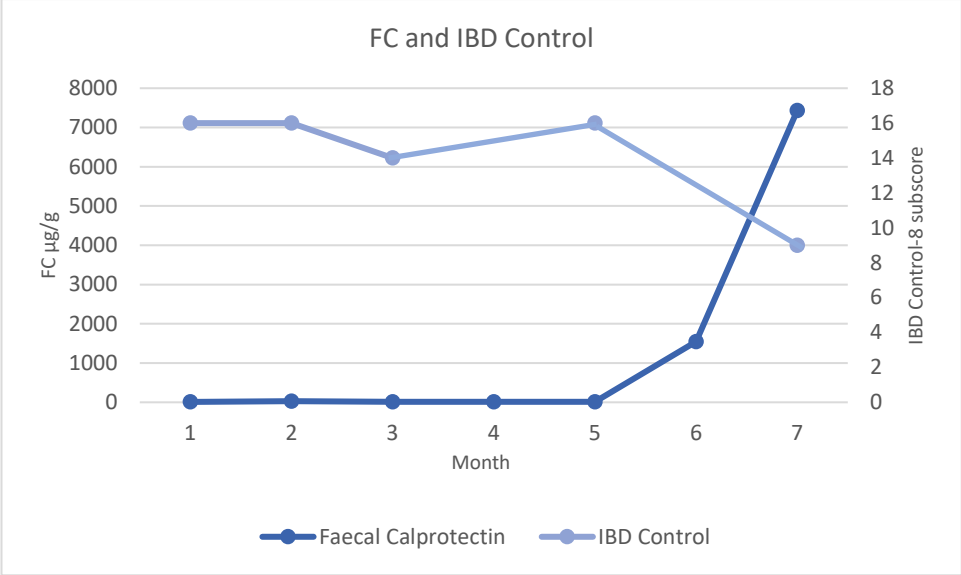
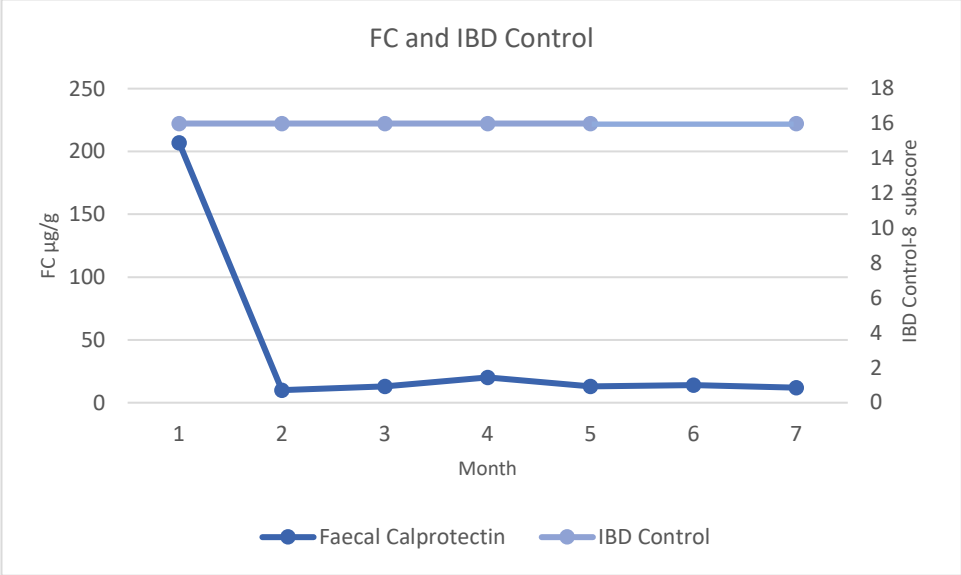


Figure 29: Patient 11 FC and IBD Control-8 scores



Overall, adherence to website usage and IBD Control completion was poorer than FC testing with a median of 3.5 IBD Control questionnaires completed over 6 months (range 1-7). Only one patient (P6) completed all 7 IBD Control questionnaires. This participant also completed all their FC tests.

6.4.5 *Clinical performance*

Two out of the ten continuing study patients had both objective (FC) and subjective (symptoms) evidence of disease flare. P5 (colonic Crohn's) stopped adalimumab treatment due to sleep and severe mood disturbance and had his treatment de-escalated to methotrexate, a less potent immunosuppressant. He was known to have active colonic Crohn's disease and had ongoing

abdominal pain and diarrhoea despite 8 weeks of methotrexate therapy. His FC had been abnormal from study onset at 188µg/g and climbed to over 1000µg/g within a month. This coincided with falling IBD Control 8 scores. He used the MyMR messaging system to contact the IBD specialist nurses who promptly initiated treatment escalation with infliximab. His FC rapidly normalised and remained under 40µg/g for 4 months during infliximab treatment, however the development of further sleep disturbance meant the infliximab treatment had to be ceased. This was reflected in a rapid rise in calprotectin to a final level of 510µg/g. After study completion, he was commenced on prednisolone and Ustekinumab treatment and regained good control of his symptoms.

P10 (ulcerative colitis) stopped methotrexate for disease remission but continued adalimumab. She remained well for the first 4 months of the study with a maximum FC level of just 32µg/g. She was unwell with an upper respiratory tract infection and suspended her adalimumab for a brief period (due to its immunosuppressant effects). She then noted a sharp rise in FC to 1548µg/g in association with abdominal pain which she described as not typical for her IBD. She contacted the IBD specialist nurses via MyMR who arranged for a flexible sigmoidoscopy to investigate further. This was normal and showed good remission of her IBD despite her FC rising to 7429µg/g. She was reviewed by a consultant during the procedure who felt that her pain could be renal colic and arranged an ultrasound scan of her kidneys. Subsequent calprotectin levels beyond the study period normalised without treatment escalation. There is some evidence that FC can rise during concurrent upper respiratory tract infections due to the ingestion of airway-derived calprotectin(227), which could explain P10's elevated reading or perhaps she may have had a self-limiting gastrointestinal infection.

P8 (ulcerative proctitis) contacted the IBD nursing team via MyMR with mild symptoms of proctitis and exchanged several messages regarding escalating topical treatment with suppositories and gained good symptomatic control. This flare period corresponded with a fall in IBD Control from 16 to 12. Her FC remained normal throughout (FC may not always rise in cases of limited proctitis(217)) and she was subsequently unfortunately lost to follow-up despite several attempts to make contact.

6.4.6 *CC-KNOW, SIBDQ and end of study questionnaires*

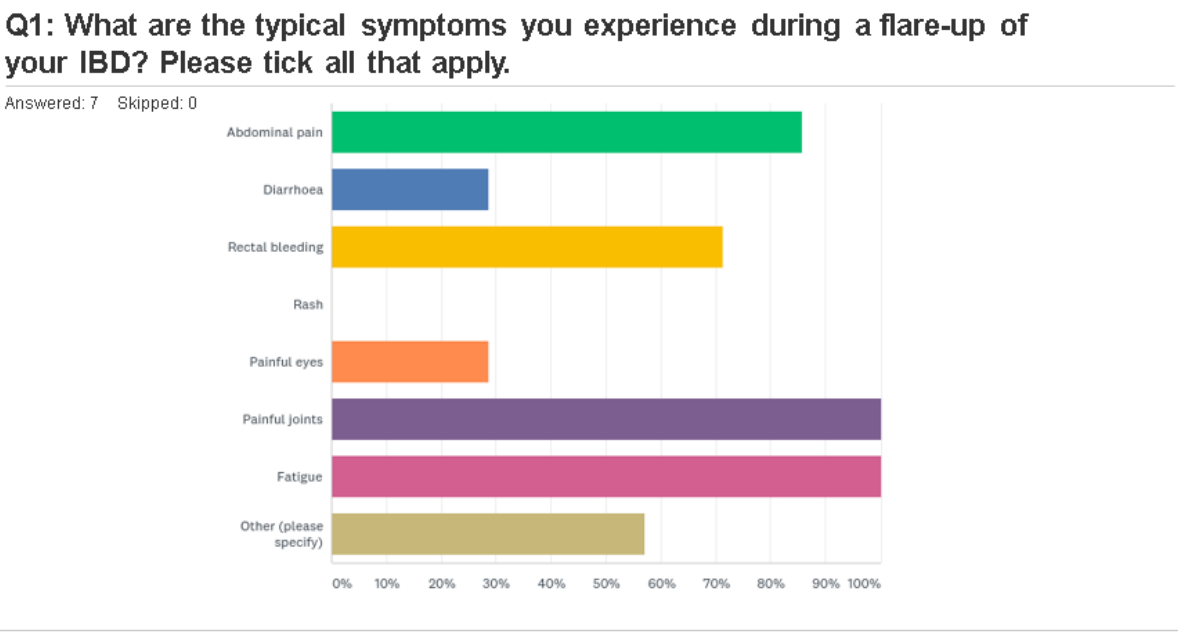
In addition to IBD Control(202) questionnaires, participants were requested to undertake pre- and post-study questionnaires (CC-KNOW(221), SIBDQ(207) and an end of study questionnaire (Appendix E.11)) which were administered via SurveyMonkey®. 11/11 patients completed these at study onset. After one patient withdrew, 7/10 patients completed the second round of

questionnaires at the end of the study, giving 7 sets of pre-and post-study questionnaires to compare (Appendices E.13-17). Mean CC-KNOW scores at 0 months where 53.4 (range 27-83, median 60), and 60.8 (range 17-93, median 63)) at 6 months. Mean SIBDQ scores were 83 (range 70-91, median 84) at 0 months, and 80 (range 54-94, median 86) at 6 months. A change in SIBDQ of more than 9 points is felt to be clinically meaningful(173). Participants reported a median of 5 (mean 6.1, range 1-20) flare-ups since diagnosis of IBD, and a median of 0 (mean 1.7, range 0-10) flare-ups during the study.

Patient-reported data on healthcare contact confirmed x1 GP appointment, x2 GP telephone appointments, and x2 IBD flareline consultations amongst participants. 2 patients reported x1 visit to IBD outpatients during the study however these visits were the planned end-of-study follow up appointments. 3 MyMR messages were reported by the participants who completed questionnaires which were confirmed on reviewing the MyMR messaging system. A further 4 messages were sent by P8 who did not participate in the end of study questionnaires. 2 participants have continued to use the messaging service actively since study completion.

The 7 end of study questionnaire respondents answered questions regarding their use of the MyMR website and home FC testing (Appendices E.11 and E.17, Figure 30). Of these respondents, 6 completed the study requirements for monitoring, but 1 was unable to complete the initial home calprotectin testing. Responses to these questions are presented below and were explored in greater detail in the qualitative interviews.

Figure 30: Survey Monkey end of study questionnaire results Q1.



Q1: What are the typical symptoms you experience during a flare-up of your IBD? Please tick all that apply.

Answered: 7 Skipped: 0

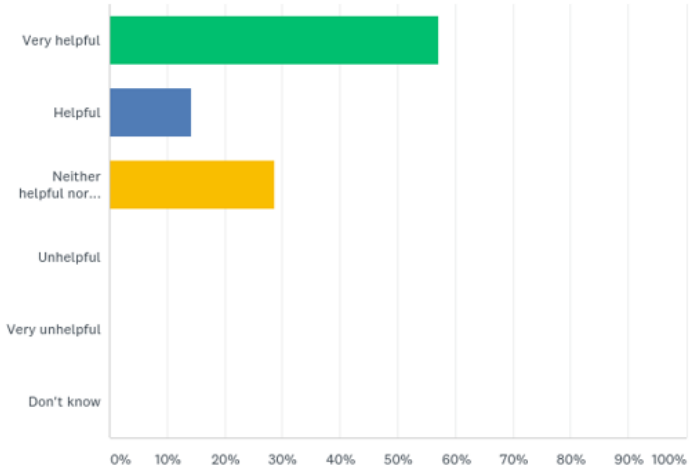
ANSWER CHOICES	RESPONSES	
Abdominal pain	85.71%	6
Diarrhoea	28.57%	2
Rectal bleeding	71.43%	5
Rash	0.00%	0
Painful eyes	28.57%	2
Painful joints	100.00%	7
Fatigue	100.00%	7
Other (please specify)	57.14%	4
Total Respondents: 7		

Question 1 was a general question regarding IBD symptoms. The most common symptoms experienced by respondents were painful joints and fatigue (100%) and abdominal pain (86%). Interestingly, only 2 respondents experienced diarrhoea as part of their disease flare, showing how “flares” can vary from individual to individual.

Figure 31: Survey Monkey end of study questionnaire results Q2

Q2: When it comes to managing your IBD, how helpful did you find viewing your tests results on the MyMR website?

Answered: 7 Skipped: 0



Q2: When it comes to managing your IBD, how helpful did you find viewing your tests results on the MyMR website?

Answered: 7 Skipped: 0

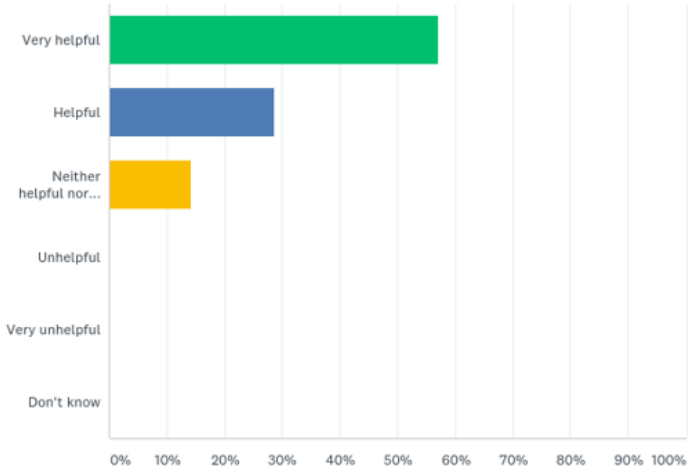
ANSWER CHOICES	RESPONSES	
Very helpful	57.14%	4
Helpful	14.29%	1
Neither helpful nor unhelpful	28.57%	2
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	0.00%	0
TOTAL		7

5/7 (71%) respondents found viewing test results to be either very helpful or helpful in managing their IBD.

Figure 32: Survey Monkey end of study questionnaire results Q3

Q3: When it comes to managing your IBD, how helpful did you find looking at your clinic letters on the MyMR website?

Answered: 7 Skipped: 0



Q3: When it comes to managing your IBD, how helpful did you find looking at your clinic letters on the MyMR website?

Answered: 7 Skipped: 0

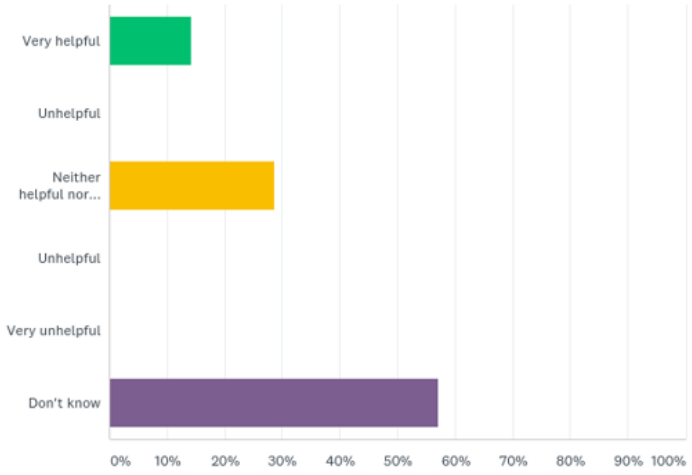
ANSWER CHOICES	RESPONSES	
Very helpful	57.14%	4
Helpful	28.57%	2
Neither helpful nor unhelpful	14.29%	1
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	0.00%	0
TOTAL		7

6/7 (86%) respondents found being able to view their clinic letters either very helpful or helpful in managing their IBD.

Figure 33: Survey Monkey end of study questionnaire results Q4

Q4: When it comes to managing your IBD, how helpful did you find using the email messaging service on the MyMR website?

Answered: 7 Skipped: 0



Q4: When it comes to managing your IBD, how helpful did you find using the email messaging service on the MyMR website?

Answered: 7 Skipped: 0

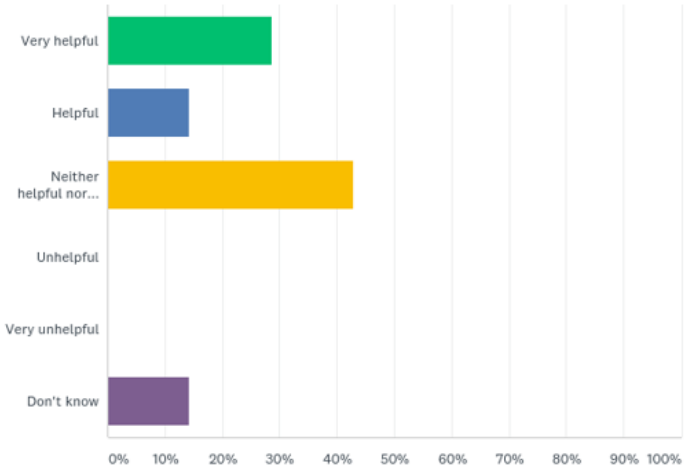
ANSWER CHOICES	RESPONSES	
Very helpful	14.29%	1
Unhelpful	0.00%	0
Neither helpful nor unhelpful	28.57%	2
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	57.14%	4
TOTAL		7

Only 1 respondent reported finding the messaging service helpful in managing their IBD. 4/7 (57%) respondents selected “don’t know”, suggesting they may not have used the service yet. This was supported by question 6 regarding speed of messaging reply where 6/7 (86%) respondents replied that this was not applicable.

Figure 34: Survey Monkey end of study questionnaire results Q5

Q5: When it comes to managing your IBD, how helpful did you find reading the IBD educational material on the MyMR website?

Answered: 7 Skipped: 0



Q5: When it comes to managing your IBD, how helpful did you find reading the IBD educational material on the MyMR website?

Answered: 7 Skipped: 0

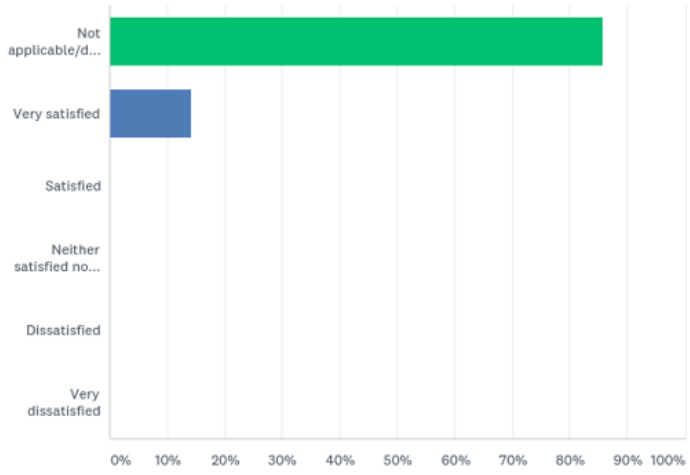
ANSWER CHOICES	RESPONSES	
Very helpful	28.57%	2
Helpful	14.29%	1
Neither helpful nor unhelpful	42.86%	3
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	14.29%	1
TOTAL		7

Only 3 (43%) of respondents reported finding the educational material either very helpful or helpful in managing their IBD.

Figure 35: Survey Monkey end of study questionnaire results Q6

Q6: When using the email messaging service on the MyMR website, how satisfied where you with the speed of response from the IBD team?

Answered: 7 Skipped: 0



Q6: When using the email messaging service on the MyMR website, how satisfied where you with the speed of response from the IBD team?

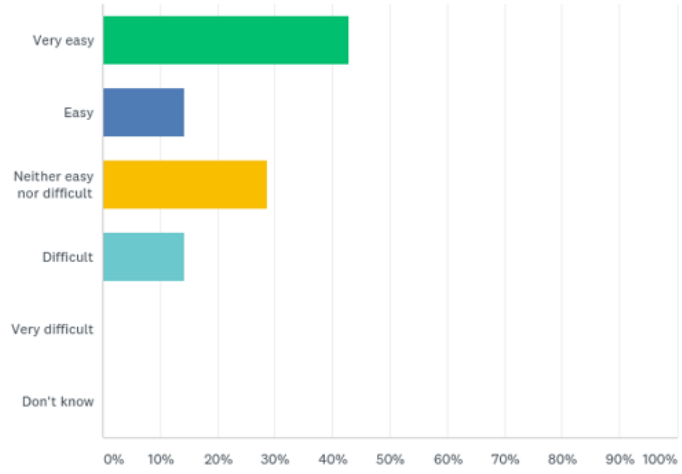
Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Not applicable/didn't use this service	85.71%	6
Very satisfied	14.29%	1
Satisfied	0.00%	0
Neither satisfied nor dissatisfied	0.00%	0
Dissatisfied	0.00%	0
Very dissatisfied	0.00%	0
TOTAL		7

Figure 36: Survey Monkey end of study questionnaire results Q7

Q7: How easy or difficult was the home faecal calprotectin test to use?

Answered: 7 Skipped: 0



Q7: How easy or difficult was the home faecal calprotectin test to use?

Answered: 7 Skipped: 0

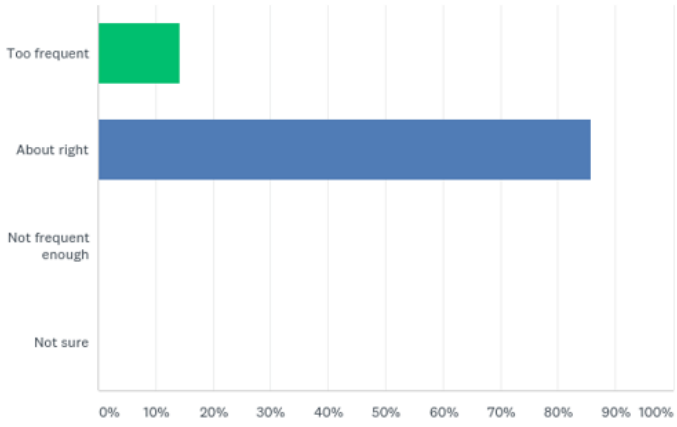
ANSWER CHOICES	RESPONSES	
Very easy	42.86%	3
Easy	14.29%	1
Neither easy nor difficult	28.57%	2
Difficult	14.29%	1
Very difficult	0.00%	0
Don't know	0.00%	0
TOTAL		7

4/7 (57%) of respondents found the home calprotectin testing very easy or easy to use, 2/7 (29%) found it neither easy or difficult, and 1 respondent found it difficult.

Figure 37: Survey Monkey end of study questionnaire results Q8

Q8: Was monthly faecal calprotectin-testing appropriate?

Answered: 7 Skipped: 0



Q8: Was monthly faecal calprotectin-testing appropriate?

Answered: 7 Skipped: 0

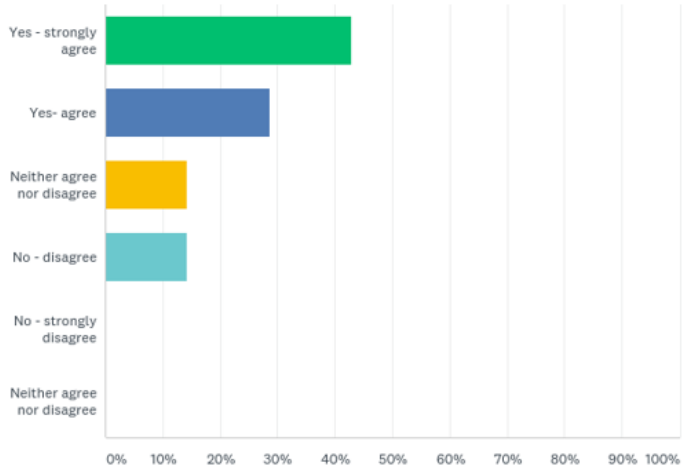
ANSWER CHOICES	RESPONSES	
Too frequent	14.29%	1
About right	85.71%	6
Not frequent enough	0.00%	0
Not sure	0.00%	0
TOTAL		7

6/7 (86%) respondents found monthly testing to be “about right”, but 1 respondent felt this was too frequent.

Figure 38: Survey Monkey end of study questionnaire results Q9

Q9: Did home faecal calprotectin monitoring improve your confidence in stopping a medication for your IBD?

Answered: 7 Skipped: 0



Q9: Did home faecal calprotectin monitoring improve your confidence in stopping a medication for your IBD?

Answered: 7 Skipped: 0

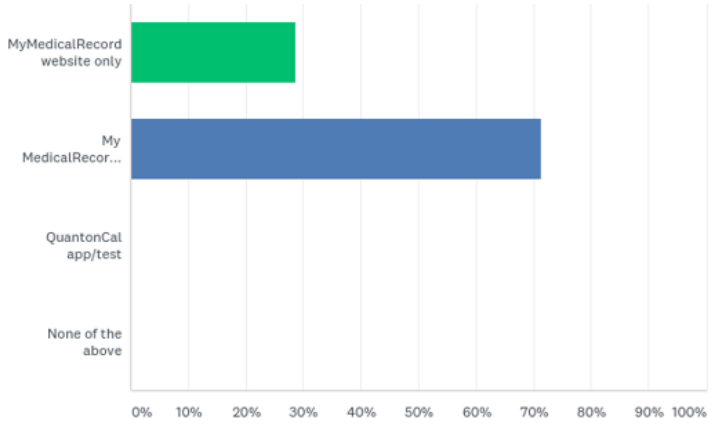
ANSWER CHOICES	RESPONSES	
Yes - strongly agree	42.86%	3
Yes- agree	28.57%	2
Neither agree nor disagree	14.29%	1
No - disagree	14.29%	1
No - strongly disagree	0.00%	0
Neither agree nor disagree	0.00%	0
TOTAL		7

5/7 71% agreed or strongly agreed that home calprotectin monitoring improved their confidence in stopping an IBD medication.

Figure 39: Survey Monkey end of study questionnaire results Q10

Q10: Which (if any) self-management tools would you consider continuing to use after the study ends?

Answered: 7 Skipped: 0



Q10: Which (if any) self-management tools would you consider continuing to use after the study ends?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
MyMedicalRecord website only	28.57%	2
My MedicalRecord website plus QuantonCal app/test	71.43%	5
QuantonCal app/test	0.00%	0
None of the above	0.00%	0
TOTAL		7

All respondents expressed interest in continuing to use home monitoring after the study end, with 5/7 (71%) wishing to continue using both MyMR and home calprotectin.

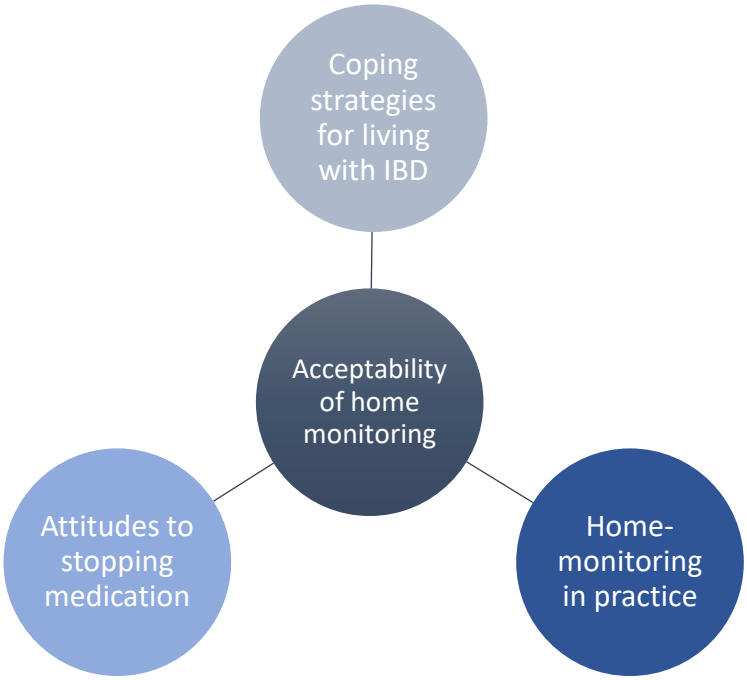
6.4.7 *Qualitative interview data*

7 participants agreed to telephone interview (3 male, 4 females, median age 38, mean 53, range 32-71 years). Interviews lasted between 20 and 40 minutes. Data from 7 semi-structured interviews were analysed using thematic analysis as described previously. I explored two main areas in the qualitative interviews (Appendix E.12): the acceptability of stopping a medication and using home monitoring as part of a research study, and thoughts on self-management using home monitoring. Three key themes emerged (Table 21), and I divided each into further sub-themes.

Table 20: Themes and subthemes generated through thematic analysis

Theme	Subtheme
1. Coping strategies for living with IBD	a. Acceptance/avoidance b. Overcoming embarrassment c. Self-knowledge d. Need for support
2. Attitudes to stopping medication	a. Fear of a flare b. Need for reassurance
3. Home-monitoring in practice	a. Usability b. Fitting it into daily life c. Worry about getting it right d. Future applications

Figure 40: Themes and subthemes generated through thematic analysis



Living with IBD

During the interviews, patients frequently referred to, or were identified as using various strategies to cope with having a chronic illness.

Figure 41: Thematic analysis: Coping strategies for living with IBD theme

Acceptance/avoidance

Acceptance of chronic illness is an important part of living with IBD but avoiding acknowledging symptoms and subsequently adapting to a poorer quality of life featured prominently in the qualitative analysis and emerged as a theme. One patient found that home monitoring helped them to acknowledge their symptoms more:

> P7 (on IBD Control 8 questionnaire): "it was good because it helped me to sort of think back over the past month which I don't often take the time to do. You just, you know… accept each day"

Other examples of acceptance or avoidance included:

> P1 "I do take things in my stride and tend to get on with them rather than paying them attention"

> P6: "I've got a habit of just saying ah it'll be alright, it'll be alright…and before you know it, I'll be on my knees"

> P4: "I didn't actually realise when I was pretty much at death's door, like really fatigued, couldn't move, getting really low. I didn't realise that it was that. Yeah, I just kind of kept battling on, which in hindsight wasn't the right thing to do but I didn't really know any different."

Sometimes this acceptance of poor quality of life due to ill health seemed to be due to not wanting to bother healthcare professionals with what patients worried might be perceived as trivial or unimportant, when it was clear that they were important to the patient and their health. Having simple ways to access support, such as email messaging for example, helped to overcome this.

> P4: "you just feel like you're a bit of a pain or wasting time. So at least if I send an email, that was for me a facility that I felt comfortable doing."

One participant described starting to feel more empowered to seek help earlier:

> P5: "I think the more as a patient you know, and the more kind of informed you feel, the more empowered you feel to do that."

Overcoming embarrassment

IBD can be associated with symptoms relating to bowels and toileting that can be very embarrassing for patients. Interview participants frequently used humour as a tool to help

overcome this embarrassment, for example when reflecting on the challenges of the stool specimen collection kit:

> P2: “I’m not being nasty, but when you’ve got Crohn’s… when you’ve gotta go you’ve gotta go. Yeah, you’re not gonna stop and that hammock ain’t gonna stop nothin’ (laughs)”

> P6: “The hammock was a bit like a chocolate fireguard (laughs)”

Often participants made light of symptoms despite them clearly being very troubling for them:

> P6: “my bowel feels unstable if that makes sense. It feels like it’s threatening to let me down!” (laughs).

Another patient joked about the impact of limiting his dietary intake before going on to discuss how a serious reaction to medications left him with such severe sleep and mental health disturbance he worried about causing harm to others, shedding light on the seriousness of his underlying worries.

> P2: “I miss me curries, miss me beer” (laughs) “There’s nothing left in life now! What else can you do?”

I explored with patients about how they felt about dealing with the potentially unpleasant or embarrassing task of collecting and processing their own stool samples as part of the home monitoring. Almost all spoke about becoming accustomed to dealing with these things over time and no longer feeling the embarrassment that they once did.

> P1: “when you’ve got to do these things you do them and I’ve got a system of doing it and well, it’s no problem”

One patient who had had IBD for over a decade spoke of having to deal with using enemas at a very young age and getting help from her partner:

> P4: “when you have something like this you kind of just change your whole mind-set on it and you find ways of dealing with it… I was 18 when I had really bad flare up and I was having to get my other half to help me with like enemas and things and since then I was like, you know what? Actually, there are more important things”

There seemed to be an appreciation that unpleasant tasks such as these were simply part of living with IBD and having periods of such ill health put things into perspective.

P5: “I think you just kind of get over it. I feel by this point, especially at this point when you’ve been ill as well, you’re kind of just like: I’m done, I can do whatever”

Need for support

The need for support featured highly in patients’ priorities and reinforces the importance of support in self-management and home monitoring. Participants often leaned on family members for technical help ranging from borrowing a compatible smartphone to logging into MyMR and completing data entry on the patient’s behalf.

P2: “I had my ‘secretary’ (referring to wife) again using it for me (laughs)”

P1: “My wife’s got medical problems and she does all her... you know... it keeps her on top of it. And my daughter, she’s local, she helps us no end”

Patients spoke of feeling supported because of participating in the study itself and having the extra layers of support provided by both myself and the online messaging communication with the nurses that hadn’t previously been available.

P6: “thank you as well for sort emailing randomly to see how I am. It’s nice. Because sometimes you can just feel a bit alone and then just to know that someone’s sort of just saying, how are you? It’s quite nice”

P7: “In the past I’ve felt a bit sort of not really in control, especially doing the virtual clinic. Because over three years I think you don’t actually see anyone”

IBD knowledge

The importance of knowledge (of IBD and of self) emerged from the data. Patients were very aware of what was ‘normal’ for them and appreciated that this could vary from individual to individual. Some patients expressed a great interest in their health and what was happening with their bodies, whereas others preferred to leave decisions regarding their care to healthcare professionals or family members.

Participants spoke frequently of knowing when their IBD was going to flare based upon previous experience and what was typical for them, as well as triggers for flares, from food to stress.

P2: “the only reason I know me Crohn’s has flared is ‘cos me back hurts…so basically with my Crohn’s, my back problems were how I knew whether I was flaring up or not”

P2: “I always watch what I eat anyway, basically vegetables and a bit of meat. I don’t drink. I’ve packed in smoking. I don’t have any spices or anything like that. It’s all plain food…. I think spices probably play a key role in… em yeah that turmeric, that’s sends me doolally nowadays”

P4: “I think I had a couple of blips going through, but nothing major…it was kind of after a stressful time or after a couple of nights out when there was a bit of alcohol involved”

P4: “after like 6 months or a year once you know what is feeling like normal”

They understood that experiences of IBD for one patient could be very different to those of another and that often it takes time and experience for patients to further their self-knowledge when it comes to their illness.

P4: “…actually what works, or the symptoms for one person is completely different for another person anyway isn’t it? It is sort of difficult if you get a symptom I’m thinking, ‘is that going to be a flare-up?’ or is it not and I’m still sort of learning even though I’m quite a few years on, is it…how bad does I need to get before it’s a flare up or is it just a twinge, but again that’s not really information you guys can give, that’s just learning to live with the condition”

One participant reflected on the empowerment that knowledge and experience could bring to patients:

P5: “I’ve now got to the point where I know you should ask a question about this. I think the more as a patient you know, and the more kind of informed you feel, the more empowered you feel to do that. And I think that’s always great.”

They also appreciated that there is often a lot of uncertainty in IBD for both patients and healthcare professionals in diagnosing a flare.

P1: “I’ve had the camera down, and the camera up again, and they, they found a bit of inflammation at the entry, but not a lot. I do confuse them at times I suppose (laughs)”

P6: “I don’t know what’s going on to be honest really. It all just seems to be a bit weird…I kind of…my body’s threatening a flare but then, it’s kind of not doing it in the way that it usually does. There’s no bleeding there but my bowel feels unstable”

Some patients were very interested in what was going on with their health and again referred to the theme of knowledge empowering patients.

> P7: (referring to MyMR website) "I looked at all the IBD bits and checked all my blood results…Yeah, I quite enjoyed that (laughs). Yeah, I loved it! … it gave me a bit more power"

> P6: "I go on it loads! I find it really useful because everything's on there… I can actually look now to see if all my levels are in normal range…It's got all my letters on there. It's got all my appointments so if I forget an appointment date, I just go on there."

Another patient was very motivated to know more about her health, taking the initiative by suspending her medications during an acute infection and actively managing her IBD.

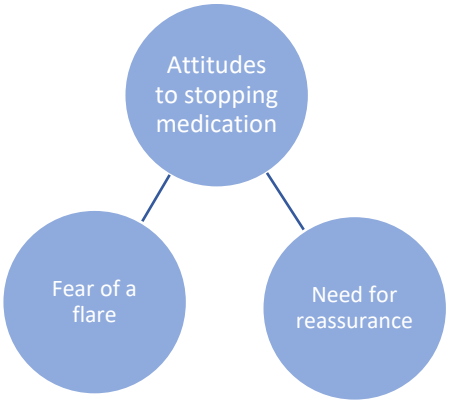
> P6: I like to know what's going on with my body. I can't believe other people haven't found it useful! Since my results are on there, I've been going through all my bloods, seeing what's what. I'm that sad I've even googled some of them to see what they are!"

> P6: "I had that like that horrible bug where I felt really run down and kept getting sore throats and thought I'd better not take it because I felt really run down, and I only missed…I only missed two, so it's not like a lot."

Attitudes to stopping medication

Home monitoring in the context of having recently stopped a treatment was a key part of this project. This has not been studied before in other literature therefore it was important to explore how patients felt about stopping medication and if they felt home monitoring might influence this.

Figure 42: Thematic analysis: attitudes to stopping medication theme



Fear of a flare

Stopping medication can be difficult for patients, particularly if they have been taking it for a long time or have enjoyed a long period of good health.

> P7: "I was quite worried initially because I'd been on them so long, and they just told me to just stop, so yeah, it's a bit worrying but it helped me, you know, not to worry about it."

Patients described a range of feelings about avoiding a flare up, ranging from simply wanting to keep things under control to real distress at the thought of a flare up and the impact this might have on their life.

> (NT: "So every month when you got your result how did you feel?")
>
> P7: "Relief really (laughs). All under control"
>
> P1: "I want to keep on top of it just in case it escalates"

The excerpt below really illustrates the devastating effect IBD flares can have not just on health but upon work and family life too and why monitoring and detection of flares is important:

> P6: "I panic about having a flare. I mean I've had such nasty ones and they last for about a year…It literally stops my life. I can't go to work. I can't take the kids to school. I can't leave the house."

One participant reflected upon the significant impact fear of a flare had upon his mental health in the past due to the uncertainty of his symptoms and accessibility of a bathroom and the anxiety that this created. He described how home-monitoring had helped this:

> P5: "I've had flare ups that have had huge impact on kind of mental health stuff, because you are worried about where can I go? Where is the nearest toilet going to be? Am I going to be able to commit to doing this activity because am I going to feel like rough and all that kind of thing…Actually that was quite a big…the impact lasted way beyond any of my other symptoms. You know, that feeling of worry. And you still…you still…even months…years later you still get those moments where you go 'oh! Can I do that?' and then I go: I can, its fine. And those tests are actually helping in that moment and you can go no no, you don't need to worry about that, that's fine. It's really really… it's great."

Need for reassurance

I discussed with patients how they felt about stopping medication and whether home monitoring had affected their confidence in doing so. One of the strongest themes that emerged was that patients felt they benefitted from the reassurance that having a normal FC level and/or normal blood test results provided them. The phrase "peace of mind" occurred frequently when referring to home testing.

> P3: "It was kind of reassuring to me to know that I was all looking good…. It's given me peace of mind that, you know, things are being tracked and watched… I think it's given me peace of mind really, to come off the medication."

> P7: "I was quite worried initially because I'd been on them so long, and they just told me to just stop, so yeah, it's a bit worrying but it helped me, you know, not to worry about it……I'm really grateful just to have been able to take part, you know it did give me a lot of peace of mind coming off the medications"

Other patients, particularly those who had found the process straightforward, expressed disappointment that they wouldn't be able to continue with the monitoring beyond the study and enjoyed the reassurance that it had provided.

> P6: "It's been so good being able to do that and monitor it…I found it really easy to use and really useful. It's a shame I can't carry on. I'd like a lifetime supply of kits!"

P5: “It was such an easy thing to do and it actually gave me confidence that things were being checked and it only took like 15 minutes at a time…I mean I felt so comfortable with it I’m a little bit gutted that it stopped really.”

All patients felt that monthly testing was appropriate for the monitoring. For example:

P5: “Monthly - I think I was happy with. Any later than that I think I’d be panicking that things might have changed in that time. I think…And I would do it always within the first week if that month…I think it’s actually an amazing thing and it’s made such a difference to me over the last 6 months”

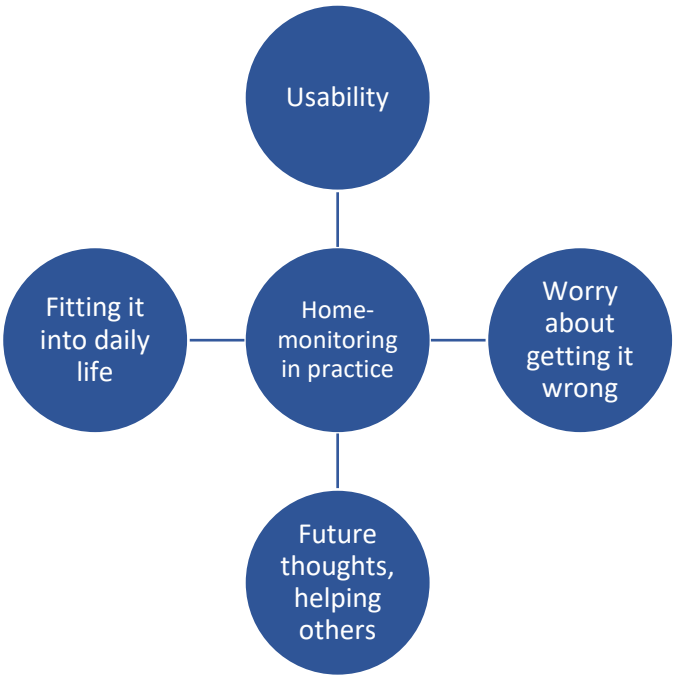
This patient felt the testing was a huge reassurance to her, particularly when undertaking major life events without fear of a flare hanging over things:

P5: “absolutely amazing 6 months and I just appreciate the chance to have been on the trial. Honestly, it made the difference that I could get married and go on my honeymoon without any sort of worries getting out of control. I done it a week before I went and had peace of mind.”

Home-monitoring in practice

I explored participants’ views on home-monitoring and how they put this into practice using the stool test and MyMR.

Figure 43: Thematic analysis: Home monitoring in practice theme



Fitting it into daily life

Patients developed and adapted their own techniques for making monitoring work. For example, doing testing at the same time every month to ensure the light was satisfactory for the camera, moving from room to room to establish the best site for completing the testing, and deferring testing for a few days until the weekend when testing would be easier to fit in with their schedule. Patients again sought support from family, from borrowing mobile phones with compatible software, to getting a spouse to attempt the test when it proved challenging.

> P7: "in the end I worked out certain times of the day…And to adjust each month (laughs) as it got lighter!"
>
> P5: "I try and do it every 4 weeks as I get paid every 4 weeks and I knew that once I got paid I had to do it the following week (laughs) at some point…It was just an easy way for me to remember"
>
> P3: "I found that the best room was in the bathroom near the window, but I think it just helps with the whole lining it all up…And I think it's better to start from a height and come down"

Unfortunately, despite trying multiple different approaches one patient was unable to perform the FC test successfully, which proved understandably frustrating and potentially added stress to his current situation.

P1: “You know, it just didn’t seem to work. And of course, when you’re moving from room to room, you run out of time. We had problems doing the photograph and plus the wife was taken to hospital and there were lots of other things going on. It just seemed a bridge too far at one stage, didn’t it?”

When things didn’t go so well (for example the piece of paper used in the toilet pan for catching stool specimens was universally felt to be inadequate), patients were good at adapting and improvising other techniques to collect their sample.

P1: “I just collect in in a Tupperware box and take the stool from it, then go through the procedure that way. Then empty the box, wash it all out for the next time, rather than messing with those paper things.”

P6: “It’s a case of just…I had to just improvise and collect it”

P3: “I found it better catching it in the tissue and then bringing it up sort of thing”

Each patient seemed to find a time or day which worked best for them when testing:

P7: “I mean if it was coming up to the weekend then I’d just wait a few days and do it then.”

P6: “I would just do it first thing in the morning…get the timer on while I was getting ready for work.”

P3: “Most of them I managed to do when I’m the first one up in the morning, all the family is asleep, so I could do it quite privately on my own, so it was fine”

Patients seemed to appreciate both the flexibility that home-testing afforded compared with traditional methods of dropping off samples to GP surgeries or hospital departments, and the immediacy of getting a result and then carrying on with your day:

P5: “When I’ve had to drop stool samples off to the GP before you know it’s gotta be at a certain time, there’s a time limit between when you can take it and when you can drop it in.”

Usability

I explored participants' views on the usability of both the website and stool testing. Reviews of the website were mixed, with some participants finding it very straightforward, and others struggling with layout and accessing relevant areas of the site.

> P6: "It's a bit…I had a bit of trouble finding the questionnaire. It's a bit…There's quite a lot of button pressing to find it."

> P4: Yeah again when you go to 'IBD' it was all self-explanatory and especially sort of emailing the gastro nurses and that.

Similarly, there were mixed opinions on the IBD Control questionnaire, with some patients enjoying the time and opportunity to take a few minutes to reflect on their health over the past week.

> P5: "it felt like it was quite clear that that's what it was getting at. That was quite nice actually, because sometimes you know they're not actually the questions that are most pertinent to ask are they, but actually it's quite nice to be able to actually reflect in that stuff. And have a moment to have that be seen and be heard."

Others found it a little repetitive and less useful.

> P6: "it's very repetitive. Yeah it kind of just sort of asks you in the last sort of 2 weeks kind of thing. Well in the last 2 weeks I've been fine, its' just...I... some of it seems kind of a little bit irrelevant."

When discussing what worked and didn't work with the FC testing, most of the participants commented, often with good humour, on the inadequacy of the stool specimen collection paper:

> P2: "Well that hammock thing is a load of rubbish; you might as well throw that in the bin (laughs)…you're not gonna stop and that hammock ain't gonna stop nothin'!"

> P6: "The hammock was a bit like a chocolate fireguard (laughs)…Yes it was like plop! And then it's gone. The whole thing down the toilet! And blocks your toilet!"

Participants had mixed views on the usability of the application itself, with some finding it very straightforward:

> P4: "It was so easy! The actual process of it and actually doing it was so easy."

P5: “Yeah that was all fine, yeah that was great. And actually, you know that way of doing it feels quite natural, you know, easy”

But others struggled to get their smartphone camera to scan the FC test cassette

P6: “Yeah, I found that a lot of the time it took a good 6-7 times to scan it. It just kept coming up with a big cross and I don’t know whether it was my camera, but every time…I think it’s really hard to hold your phone so steady”

P4: “So sometimes it worked first time, and other times I sort of had to scan it 5 or 6 times and then I thought. I’m getting a bit fluttery. Am I going to do it in time?”

This resulted in participants feeling frustrated, and in one case the interviewee expressed feelings of ‘failure’ at not having done more regarding the study.

Worry about getting it wrong

The worry of getting the testing wrong, although not mentioned in great frequency, stood out amongst participants and several spoke of the anxiety that they might not complete the test before the time limit expired. When they spoke of this it was usually countered by a statement that things ultimately turned out well.

P4: “Am I going to do it in time...? You can see it counting down and you’re going ‘quick, quick, quick!’ And you’re running around the house finding the place… You do get a bit fluttery when you’ve done it a few times and you’re like no it’s bad and you’re like come on!”

P3: “you feel like it’s a ticking time bomb (laughing) but apart from that it’s been fine”

P6: “It just kept coming up with a big cross”

This sense of worry and failure seemed quite marked for one gentleman who was unable to complete the testing:

P1: “I do feel quite guilty…. I hope other patients were far more forthcoming than I was…I mean you’ve been very good, the hospital’s been very good…The only thing I can say is going back to the photograph, I’ve just wasted your time and a lot of other people’s time, but I just couldn’t get it right”

The email messaging function of MyMR seemed to help reduce worry. Patient-initiated care is an important aspect of self-management and patients spoke about past worry about not knowing

when they should seek help about their IBD and not wanting to bother anyone by telephoning the flareline.

> P5: “now I know that I should reach out rather than thinking ‘should I ask a question about that? (laughs)”

> P4: “I always feel that if it is just like minor symptoms then I don’t like really calling them because I feel a bit more of a pain… So at least if I send an email, that was for me a facility that I felt comfortable doing.”

Future thoughts, helping others

Patients were enthusiastic about the project and were already thinking of the future of home-testing and volunteered ideas about how it could be used elsewhere to help others.

The importance of ‘joining up’ with GP resources to facilitate communication was suggested.

> P6: “it would be nice if you could request medication on there. You can’t, can you? At the moment... Like if I could have sent a thing, like a repeat of my omeprazole”

> P3: “if there was any way it could be linked with your local GP as well. I don’t know if that was something that might be done in the future? So, if you had like a blood test or something at the GP it could be linked up, you know”

Patients displayed altruism not only in taking part in the research, but also in how they envisaged MyMR and home FC testing being utilised by other patients, in particular those who were just setting out on their IBD journey and learning about their illness.

> P4: “it would be good if that was sort of something accessible to a lot of people, especially if they were starting out or learning how to control it. It really could help.”

> P3: “maybe more at the beginning of a diagnosis when it’s really hard to find out what medication works, and you end up trying a couple of different medications until you find the one that works, so yeah it could be useful for that, definitely.”

Patients also showed (unprompted) an appreciation of the limited resources for providing outpatient clinics for patients and the need to find alternative means of managing patients were possible.

> P3: “I know that we have, like, outpatient appointments, but sometimes you do feel like it’s not necessary and someone else could use that appointment. Given it takes half a day and because they’re always running behind”

P4: “Even if it’s every 6 months or a year or something then it would reduce the hospital appointments”

These excerpts illustrate the 3 key themes which emerged from the qualitative data analysis: how patients use coping strategies to live with IBD, patients’ attitudes to stopping medication, and how self-monitoring strategies work for them in practice. Patients did experience some technical issues when conducting both FC testing and using the website, but most of the feedback regarding was positive. Key findings and areas for reflection on the feasibility study discussed below.

6.5 Discussion

6.5.1 *Summary of main findings and comparison with existing literature*

6.5.1.1 Recruitment

Recruitment to the study proved challenging. The initial target sample size for the study was 30 participants, with an end sample size of 24 participants (allowing for a 20-25% drop out rate(127, 220)). Although 38 patients were referred for consideration in the study, the final recruitment number of was just 11 patients (29% of referrals). Due to maternity leave I was limited to a shortened recruitment period of 4-months. Although disappointing, the rate of recruitment was in-keeping with other similar studies (127). Increased awareness of the study amongst staff over time and referrals of potential participants improved month on month so it is possible that recruitment rates may have picked up over time.

Focusing the study on only those patients who had stopped a treatment recently was intended to add to the current body of evidence surrounding supported self-management by examining its effects in this ‘at-risk’ subgroup of IBD patients, in whom SSM has not yet been closely examined. It also meant that the limited resource of home calprotectin testing was provided to those who were potentially most in need of this new technology due to higher risk of disease flares. In reality, this meant that I limited the potential pool of participants compared with other SSM studies (228). Whilst this may have limited recruitment, it did make for a novel cohort of patients in which to explore this new technology and attitudes to stopping medication. Compared with very stable patients with mild disease, this at-risk cohort may have greater potential to benefit from closer monitoring for flares, with the majority having disease that has been sufficiently severe in the past to require immunosuppressant treatment. This is reflected in the qualitative work which highlighted the significant negative impact fear of a disease flare can have on IBD

patients. The relative expense of home calprotectin monitoring may mean this technology needs to be utilised in a focused manner.

Other barriers to recruitment lay in my exclusion criteria. Pregnancy ruled out two otherwise eligible study participants. The initial reason for excluding this group is that they are often quite complex and due to the importance of monitoring both the health of the mother and the baby. Whilst it was felt that it was important to continue face-to-face routine follow up in this group, it could be argued that they could benefit from participation in the study due to the ability to monitor their disease even more closely at home. Pregnancy can be a common patient reason for stopping IBD medications and the inclusion of this group could improve recruitment and provide a useful resource for this group. Pregnancy has been demonstrated to have no significant effect on FC levels (229).

A small number of patients were ineligible as they were identified over 8 weeks from treatment cessation. We know that up to half of patients stopping anti-TNF medication (62) may experience a disease flare in the year following treatment cessation (for disease remission). RCT evidence for Crohn's disease relapse rates when stopping azathioprine/6-mercaptopruine is as high as 41% at 1 year(61). The median time to relapse has been found to be around 7 and 4 months in CD and UC respectively(230), therefore extending the acceptable period from cessation of treatment to 3 months, for example, could potentially improve recruitment whilst involving more patients pre-relapse.

For further study I would consider changing the term 'treatment cessation' to treatment de-escalation'. Several study patients stopped a treatment but continued a second, less potent immune suppressant (for example stopped infliximab but continued methotrexate). They de-escalated treatment and were therefore still at increased risk of relapse. I would therefore also consider including patients who had reduced a treatment dose (but not completely stopped it) for reasons such as side effects/intolerance, as these patients have also de-escalated treatment and are at increased risk of disease relapse.

Whilst I did exclude those patients with an ileostomy from the study (FC measurement is thought to be of limited value in isolated small bowel Crohn's(217)), I did not exclude patients with proctitis, which in hindsight, I would consider in future study. FC is often not elevated in cases of active proctitis as the stool has little chance to mix with the limited section of inflamed bowel mucosa(217). This is illustrated in the case of P8 whose FC remained normal despite contacting the IBD team with a symptomatic disease flare.

6.5.1.2 Baseline characteristics

11 patients took part in the study, with a median age of 38. More female patients took part in the study compared with males (8 vs 3). Similar studies also show a female recruitment preponderance (72). There is no literature surrounding gender -based reasons for non-participation in IBD research however more generally women are more likely to participate in research than men(231). Very few eligible patients who did not participate in the research cited reasons for non-participation (most simply didn't reply to the invitation letter) but lack of time or difficulty scheduling the initial study meeting were the most common reasons. All participants were educated to at least GCSE (plus NVQ), with over half having a university degree. It is well-known that individuals possessing a higher education are more likely to take part in research(231). 5 of the 11 participants were employed in health and social care roles allied to medicine which may perhaps lend an increased awareness and support for research. Most patients (9/11, 82%) had stopped an oral immunomodulator treatment (azathioprine, methotrexate or mercaptopurine) which have a small but significant increased risk of malignancy in long term treatment(232).

6.5.1.3 Feasibility

One of the main feasibility issues encountered was that in some cases the potential participant's smartphone could not support the QuantOn Cal® app. In some cases, this was rectified by the patient borrowing a spouse or family member's smartphone, and as the test was only conducted monthly, this did not seem too much of a problem for participants. As mobile phone technology improves, and people upgrade their smartphones this will be less of an issue. As of September 2019, QuantOn Cal® was supported by a much broader range of mobile phone makes and models (see Appendix E.17) compared with during the recruitment period. 9/11 participants owned an Apple iPhone and 2 used a Samsung Galaxy. These 2 brands dominate the UK smartphone market (iPhone 48%, Samsung 35%(233)). Smartphones are expensive, costing on average £250(234). This could be viewed as a significant feasibility issue and must be considered a potential inequity of access to the study, however smartphone use is expanding rapidly, with 78% of British adults using smartphones to access the internet in 2018(235).

The target for study retention rate was 80%, defined as successful completion of at least 5 out of 7 home FC tests, with no periods without login to MyMR of greater than 3 consecutive months. Retention was therefore good with 80% (8/10) participants successfully completing a minimum of 5 FC tests and 7 of these patients completing all tests. 7/10 participants (70%) completed the minimum requirement for completion of both FC test and MyMR log in. In a previous patient

workshop during the development of MyMR, I discussed with patients the circumstances in which they might use MyMR and patients frequently commented that they would find it useful when they were unwell but when well, were less likely to feel the need to input data about their condition as they couldn't see an immediate benefit to themselves. By contrast, FC testing uptake was better, reflecting the positive feedback from the qualitative interviews on the immediate reassurance this provided. Future methods to improve inputting of IBD Control data could include combining this with the home FC testing all under one mobile phone application to obviate the need to login to 2 different applications.

The feasibility target for response rates to questionnaires was >60%(226). Whilst 100% (11/11) of patients completed both initial questionnaires (CC-KNOW and SIBDQ), 70% (7/10) participants completed follow-up questionnaires, some requiring reminders. I took measures to ensure as high a return rate as possible by personalising invitations, including a direct hyperlink to the survey, and following up with 2 subsequent personalised email reminders(236). It is possible that with the study now over, the incentive (i.e. the FC testing) to complete further paperwork had gone for some patients, but the target was achieved.

Just 2 patients completed all FC testing without any email prompts or reminders, with some patients requiring up to 7 prompts over the study period. Whilst manageable in a small study population such as this, overseeing testing in a larger group of patients would not be feasible without significant resources. My experience in this study was that the patients who were most likely to complete testing were motivated and did so with little input from me, and those that were less motivated or struggled with the test did not complete much of the monitoring even with frequent reminders. The benefit of reminders could therefore be questioned. Prompts also detract from the self-directed goals of the study and could be considered to remove responsibility for self-care from the patient. It would be worth considering removing test reminders from a future study altogether however this would need to be carefully considered against possible reduction in study retention rates. An alternative solution would be to develop the IT results system further to generate an automated reminder in the event of non-completion of a test.

6.5.1.4 Questionnaires

Mean CC-KNOW scores increased over the study period, but numbers were too small to attribute any statistical significance to this. It could reflect patients becoming more knowledgeable about their disease or perhaps simply being more familiar with the questions asked. Mean S-IBDQ scores fell slightly over the study period from 83 to 80. This may be explained by the two flaring patients whose SIBDQ scores dropped significantly. End of study questionnaires showed accurate

self-report of participant contact with healthcare professionals when corroborated with hospital IT records (telephone, flareline, email messaging).

Participants' views on home FC testing, the MyMR website and self-management in general were sought using open-ended questions in the questionnaire. However, as all questionnaire respondents but one also participated in interviews where these responses were explored in more detail, questionnaire responses did not contribute significant additional data. A questionnaire approach may still be useful in a larger study where it would not be feasible to interview all participants.

6.5.1.5 Qualitative interview findings

6.5.1.5.1 Coping strategies for living with IBD

IBD is a disabling disease that can have a significant negative impact upon physical, psychological, and social well-being(237). A number of key concerns of patients have been identified through qualitative research and include: loss of energy, loss of control, negative body image, fear, isolation, not being able to reach their full potential, feeling dirty, and lack of information from the medical community(237), all of which can lead to a reduced quality of life when living with this condition.

Lazarus defined coping as "cognitive and behavioural efforts to manage specific external or internal demands (and conflicts between them) that are appraised as taxing or exceeding the resources of a person"(238). Coping mechanisms can be classified in numerous different ways, the most commonly utilised being the 'problem-focused' versus 'emotion-focused' framework(239). Problem-focused coping aims to alter or remove the source of stress, for example reading a leaflet about IBD to gain better insight into the problem or calling up the healthcare team to ask advice. Whereas emotion-focused coping aims to reduce the emotional stress caused by the problem by using techniques such as avoidance or distraction.

Acceptance of a chronic condition is a necessary part of living with disease, however in clinical practice we often observe that patients adapt to and tolerate a lower than average quality of life, often by ignoring or avoiding their symptoms, and this becomes their 'normal'. This notion repeatedly emerged during the qualitative interviews and could be considered an adaptive coping mechanism, allowing patients some degree of normality and thus function, but may also be maladaptive, potentially resulting in harm by not dealing with ill health promptly. Maladaptive coping behaviours such as avoidance strategies have been shown to negatively correlate with quality of life(240). The concept of 'health-related normality' in IBD has been explored, with

patients often maintaining appearance of normality as a means of coping(241). It has been proposed that healthy people define themselves in terms of activity and ill people define themselves in terms of appearing 'normal'(242).

Due to the characteristics of the illness, feelings of shame and embarrassment are common amongst IBD patients(3, 237). When it came to talking about their bowels and dealing with stool specimens, participants acknowledged that although they may have struggled previously in the past to talk about bowel habits et cetera, over time they had become so accustomed to this they no longer found it a significant source of embarrassment. Patients reported feeling very comfortable processing their own stool samples, and in some cases preferred dealing with this in the privacy of their own home as opposed to bringing a sample to the GP or hospital. This was a universal finding amongst interview participants but may not be considered wholly representative as these patients agreed to take part in research where they most likely expected to talk about their bowels, and this openness may not reflect non-participants. It would be interesting to study whether patient perceptions and coping in IBD differed according to the length of their illness. In other chronic disease such as chronic fatigue syndrome(243), those with a longer illness duration group reported higher use of active coping, positive reframing, planning, and acceptance, and lower use of behavioural disengagement than those with shorter illness duration, and this ties in with my (limited) findings.

Participants frequently used humour as an emotion-focused strategy when talking about the demands of life with IBD and bowel-related issues. There is little research on humour and IBD, but it has been studied in other chronic and acute illness. Humour is known to have directly beneficial physiological effects on pain and the cardiovascular and immune systems(244). Indirectly, it can have beneficial effects in moderating stress and enhancing social competence and support (the indirect humour-health hypothesis)(244), so it is understandable that patients use it as a means of coping with IBD.

Seeking out knowledge can be viewed as a problem-focused coping strategy. It is well-known that providing patients with high quality information can empower them to be more involved in their own care and can ultimately improve disease control in chronic illness (245, 246). Providing easy to access information (for example through the information pages on MyMR) can help to address a key patient concern of lack of information provision(237). Study participants also displayed knowledge of self when talking about their IBD, and reinforced the concept of the 'expert patient' discussed previously(247). They had a strong appreciation for what was normal for them and reflected upon how this could be different for other IBD sufferers. This finding is replicated in a

2012 meta-synthesis(248) of the health and social care needs of IBD patients, which demonstrated participants voicing the theme of "knowing my body", with accounts of knowing when their illness flared up better than their doctor. The concept of individual knowledge also supports the use of the IBD Control questionnaire(202) as part of the self-monitoring element of the study as IBDC focuses upon the personal impact of IBD on the individual, as opposed to the previous assessors of disease activity(22, 206) which have focused more upon quantitative measures like bowel frequency. Several patients spoke of how it can take time and experience for patients to become familiar with their IBD, recognising flare-ups and disease triggers, and this reinforces the decision to include only patients who had been diagnosed a least one year previously in the study.

Two main themes emerged when exploring patients' attitudes to stopping their medication and the impact that home-monitoring had on this: fear of a disease flare, and the need for reassurance. Participants spoke candidly of the detrimental effect that a flare-up of IBD could have on their life and this provided some of the most powerful qualitative data. They were particularly anxious about stopping a medication if they had been on it for a long time or if they had enjoyed a long period of disease remission. One participant described the real lasting effects that fear of a flare can have on mental health, and how this fear persists long after the physical symptoms of a flare-up have subsided. 'Fear' was a recurrent theme in the 2012 meta-synthesis by Kemp et al(248) with frequent reference to fear of incontinence, complications, and of letting others down due to a disease flare. These feelings are common to al IBD patients but could be heightened in those who have stopped a medication and are thus at increased risk of a flare up.

Participants spoke of the need for reassurance to reduce this fear. The theme of reassurance was very strong when patients were speaking about the impact self-monitoring had on them, with numerous utterances of the phrase "peace of mind" across almost all participants. It appeared that this reassurance was the number one motivator for patient's carrying out their home testing and the reason many of them wished to continue with self-monitoring beyond the study. Patients felt reassured not only by a negative FC result, but also by easy access to their IBD nursing team (with prompt responses) and enhanced support as they undertook the research. Unpredictability has been cited as a key concern of patients with IBD(249) and having the means to predict disease flares could help to alleviate this concern.

6.5.1.6 Self-monitoring in practice

Patients were adept at developing techniques to fit monitoring into their daily lives. Those patients who described their methods of remembering to do the testing were more likely to

consistently comply with the requirements of the study (website and FC testing). Ultimately, how patients make self-testing fit in with their lives will come down mostly to the patient, their circumstances, and their motivations. The flexibility the home testing afforded seemed popular amongst patients, by reducing the amount of administrative time required in providing/processing a sample, as well as the immediacy of gaining a result) in under ten minutes. In other chronic diseases, access to 'point of care' testing has been linked to improved adherence to treatment, particularly where there may not be other signs and symptoms to indicate response to treatment, for example in hypertension or anticoagulant monitoring(250) and adherence would be an interesting area for study in IBD.

Questions exploring the usability of both the FC test and website yielded mixed responses. The majority of patients found it straightforward to process the stool specimen, but many struggled to get the camera to scan the cassette to give a valid test result, although this did get easier over time, It is not clear whether this problem was operator or device dependent – to determine this I would need to study patients performing the FC test in the same conditions but with different smartphone devices. Those with more advanced smartphones (for example iPhone 7 vs iPhone 6) did seem to find the test more straightforward but this was not universal (nor rigorously tested to be able to draw a firm conclusion). One older gentleman struggled with the testing and found it difficult to hold the smartphone camera steady enough to scan the test cassette (this was also mentioned by younger participants) and an element of dexterity is required for the testing to be successful.

There is little qualitative research on factors that might help patients to comply with self-management in IBD as this is a relatively new field. More qualitative work has been carried in prevalent chronic diseases such as heart failure (251) and chronic obstructive pulmonary disease (COPD) (252). Professionals praised telemonitoring for promoting compliance with medical advice and encouraged patients to exercise personal responsibility within clinical parameters but expressed concerns about promoting the sick role and creating dependence on telemonitoring. Patients considered that telemonitoring empowered self-management by enhancing their understanding of COPD and providing additional justification for their decisions to adjust treatment or seek professional advice.(251, 252). Engagement of professionals with overseeing self-management and responding to patients' data was cited as an important feature for continuing engagement in self-management in the preliminary MyMR development work with our patient panel. In a 2010 qualitative study by Cooper et al(253) amongst 30-40 year olds with IBD (similar to our cohort), participants felt that being able to share control of IBD with specialist

health care staff was beneficial. The collaborative nature of 2-way interactive platforms such as MyMR may help engagement, and this is an area for further qualitative exploration.

6.5.2 *Strengths and limitations*

The feasibility study was originally intended to recruit around 30 patients and therefore the ultimate figure of 11 was well below anticipated and a significant limitation. Several eligible patients were unable to participate as they did not possess a compatible smartphone for the QuantOn Cal® app. I tried to facilitate this where possible, for example updating patients who had previously been unable to participate with any changes to the compatible smartphone list. This list has expanded significantly since the study onset with many more smartphone makes and models now eligible. The lower numbers also were in part due to time and resource constraints, however had recruitment continued I feel that rates would have improved as they were on upward trajectory as more staff were aware of and identifying potential study participants.

Acting as the sole researcher on the study could be considered both a strength and a weakness. Study procedures and data collection were both consistent throughout, however this did put completion of the study at risk if I had been unable to complete it. I therefore ensured that handover measures were in place prior to my maternity leave detailing study procedures as well as the details of the study participants that were under active monitoring to ensure continuity of the study, as well as participant safety. The administration required to oversee patient self-monitoring and website use and issue reminders, although manageable for this small number of patients, could prove a challenge in a larger scale study. It would be prudent to utilise our increasingly sophisticated IT systems, for example developing automated reminders for patients.

10 patients who commenced home-FC testing were invited via email to participate in qualitative interviews, of whom 7 responded. As numbers were small, I did not feel that a point of data saturation had been reached in all the subthemes. Despite this, some strong themes about patient experiences of IBD and the self-management intervention emerged. Interviews took place on the telephone. Relatively few qualitative research studies have used telephone-based interviews in the past due to concern of the loss of contextual and nonverbal data, and subsequent interpretation of responses(254). There has been limited study into how the differing interview modes may affect outcomes, for example a greater disclosure of substance misuse has been observed in face to face versus telephone interview(255). The use of telephone interview mode has a number of advantages over face to face, including lower costs, less time intensive (travel), researcher safety, unobtrusive note taking, and coverage of more sensitive topics with less awkwardness(256). I felt that we were not discussing highly sensitive topics, and I had already

established a good rapport with the participants during the initial study visit and subsequent communications that enabled me to conduct the telephone interviews comfortably. This also supports naturalism, one of the key principles of qualitative research whereby the observation(s) take place in the participant's own environment(146). I considered conducting a patient focus group however felt that due to the personal nature of the discussions surrounding toileting that one-to-one interviews would gain more open responses.

I tried to adapt my interview schedule accordingly for subsequent interviewees and found I was getting more comfortable with the process but could have benefitted from continuing to refine my technique had more participants been available. I performed all transcriptions myself. I found doing this to be of benefit as spending time listening to the recordings in detail helped me familiarise myself with the data and interpret the tone of the interviewee. For example, it was easy to recall when transcribing if a patient was making a light-hearted statement having just had the conversation with them myself. This familiarity with the data helped me to develop themes during the subsequent analysis and this is a recognised benefit of self-transcribing(257). A possible downside to this method is that the data may not be an unbiased representation of events, instead reflecting my own interpretation of the data (258) in line with my research paradigm and there would be an argument for further coding by other researchers if time/finances had allowed.

Finally, generalisability of the study and its procedures for use in a wider context must be considered. QuantOn Cal® currently retails at a list price of around £40 plus VAT per test kit (with potential cost reductions for bulk purchase). This compares to a per person cost of £22.79 for an ELISA test (based on an assumption of 40 patient samples per 96 well-plate, costed at the list price, plus an average 11–12minutes of staff time at grade6/7)(36). There is clearly a significant cost difference between lab and home-based testing but there are potential cost savings of home monitoring from the patient perspective with reduced travel costs. Home monitoring through calprotectin and MyMR has the potential to reduce the need for both outpatient appointments (£164 per person) and potentially colonoscopy (£480 per person(36)) however other factors such as IT support and infrastructure, as well as nursing support for home monitoring would need to be factored into overall costing and a full economic analysis will be an important aspect of any future larger studies.

6.6 Conclusions

This exploratory feasibility study, whilst small, adds to the existing knowledge base surrounding electronic supported self-management in IBD by exploring the use of a digital self-management

intervention and FC testing in a group of patients who have recently stopped a medication for IBD. The study explored patient perspectives on the impact of stopping IBD medications and how SSM may help these patients through this challenging time. Whilst other studies have often focused on supporting patients to self-manage stable disease, patients who have stopped a treatment are at a higher risk of disease relapse are particularly in need of tools to monitor their disease. The qualitative arm of this work illustrates the significant negative impact that fear of a disease flare can have on IBD patients' quality of life, and it is therefore important to continue exploring methods to mitigate this. The study was very limited by under-recruitment and inclusion criteria may need to be revised for any future study, perhaps by increasing the window in which medications were stopped, or including patients who are pregnant (a common reason for stopping medication), for example. The resources required to oversee a larger study may be considerable, but this could be significantly improved by further IT developments to the MyMR site to ultimately support automated reminders and alerts between both patients and staff. Whilst the intervention of MyMR and home FC monitoring appeared to be acceptable to participants, it is likely to be a very selected sample of motivated individuals and the small numbers make it difficult to extrapolate the wider IBD population. Although I observed themes emerging from the qualitative interviews I do not feel that I reached data saturation, however, I found these interviews to be the most interesting aspect of the study and they provided powerful insight into living with IBD that I will take with me onwards in my clinical career. The increasing burden on outpatient resources across the NHS mean that it is important to continue exploring modern, cost-effective means of patient self-management using IT to improve patient care and allocation of resources.

7 Developing a digital Virtual IBD Clinic – service development and implementation

7.1 Introduction

This chapter describes the development and early experiences of the digital Southampton Virtual IBD Clinic service. It follows on from Chapter 3 by exploring methods of modernising the outpatient care of more stable IBD patients using MyMR. I followed the Squire 2.0 guidelines(259) (Appendix F.1) to present the service development and used Normalisation Process Theory(160) (NPT; see section 2.3.4) as a means of better understanding the processes involved in its implementation. NPT is an 'action theory', which is concerned with explaining what people do, rather than their attitudes or beliefs. It can be used as a tool to identify and better understand implementation of new ways of organizing healthcare

7.1.1 *Problem description*

Conventional IBD outpatient clinics are often over-stretched and may struggle to flexibly accommodate the needs of patients requiring increased support. Conversely, some patients can remain well for many years and may not require such close supervision during this time. Alternative pathways to traditional outpatient management have been developed to ease pressures on outpatient services and offer a more flexible service for patients. These can include 'virtual' or remote methods such as nurse-led telephone clinics, patient-led self-management programmes, and more recently digital patient 'portals' which offer a modern way of helping patients and healthcare professionals to work together as partners in their care.

The original Southampton IBD virtual clinic (VC)(260) was developed in 2010 and used a combination of postal and telephone nurse-led follow-up for stable patients. Patients with an established diagnosis of IBD for >2 years, who had been stable for more than 1 year, did not have primary sclerosing cholangitis (increased risk of liver complications and cancer requiring close follow up) were entered into the VC system. Two months before their annual follow-up was due, they were sent a blood test form and questionnaire to complete. If they met any of the criteria on the questionnaire, they were advised to telephone the specialist IBD nursing team for support. Blood test results and the patient's medical record were reviewed by a specialist nurse who arranged any surveillance investigations that might be required such as a colonoscopy or DEXA (dual emission x-ray absorptiometry) scan. The patient and their GP then received a letter informing them of their management plan.

Over 10% of the estimated 5000 IBD patients under the care of UHS were followed up using this method and the system was well-liked by patients. One of the limitations of this pathway was that there was no direct documented feedback from the patient demonstrating they were well. A growing population of IBD patients and limited staffing also meant that annual VC reviews were falling behind schedule. Developments within the UHS trust IT (information technology) system provided the opportunity for modernisation of the VC, by fully 'virtualising' it, utilising the digital self-management platform of My Medical Record (MyMR).

7.1.2 *Available knowledge*

There are numerous modes of delivery of remote monitoring of patients, some of which (digital self-management portals and telephone-based follow up for IBD) are described in Chapter 1. Virtual clinics are widely used in the United Kingdom for the review of patients with IBD. The term 'virtual clinic' tends to be used to describe an annual multidisciplinary team discussion with minimal patient interaction(261, 262) and little has been published in a formal trial setting. The most comparable service to our proposed digital virtual clinic is that used by the Danish Constant Care group(208) described in Chapter 3. Stable UC patients received a 3-hour education and training session, then were asked to log in to a self-management website and input data monthly, except in the event of a flare during which daily data input was required as well as management via a self-initiated treatment plan of 5-ASA treatment escalation. Investigators monitored flaring patients daily and were automatically notified in the event of unfavourable disease activity score using a traffic light warning system. The system was well-liked by patients and QoL, anxiety, depression and general well-being did not show any significant difference after the intervention(208).

Outside of a study environment, there have been no reports of the development and use of such interventions in a 'real world' clinical IBD setting. I therefore sought to explore the implementation of our digital virtual clinic in this context and any barriers or facilitators to this new way of delivering our service.

7.1.3 *Rationale*

The patient facing MyMR site is described in Chapter 5. It provides patients access to up to date IBD information, diagnostic results and clinic letters, shared journals for symptom monitoring and online messaging with the IBD team. The clinical version can be accessed by medical, nursing and administrative staff. It provides an overview of all currently registered patients on a customizable dashboard known as a 'patient tracker' which allows remote management of patients using bespoke care plans (protocols) based upon their current health.

The digital virtual IBD clinic builds upon the existing paper/telephone process and relies upon patients inputting data on their current health via MyMR and nurse specialists managing their care via the MyMR clinical portal.

7.1.3.1 Medical Research Council guidance on complex interventions

The development and evaluation of My Medical Record were guided by the MRC Guidance on complex interventions(134) which emphasise the importance of focusing adequate attention on the developmental stages and practicalities of implementation, stating "a good theoretical understanding is needed of how the intervention causes change, so that weak links in the causal chain can be identified and strengthened". Understanding the processes involved in change can provide insight into why an intervention might fail unexpectedly or why a successful intervention might work. This chapter therefore primarily focuses on the lessons learned from the development of MyMR and the implementation of the virtual IBD clinic.

7.1.4 *Objectives*

The objectives for this project were:

i. To understand the current pathways involved in the existing virtual IBD clinic and the needs of key staff involved
ii. To describe the development of the digital virtual clinic via MyMR
iii. Reflect on barriers and facilitators to change using Normalisation Process Theory(160)
iv. Collect data on initial registration to MyMR and early use of the digital VC

7.2 Methods

7.2.1 *Context*

University Hospitals Southampton NHS Foundation Trust (UHS) serves a population of 1.3million people living in Southampton and South Hampshire. It provides IBD services to over 5000 local patients as well as those from further afield as a tertiary referral centre. Over 600 of these patients are managed with annual review via the existing virtual IBD clinic. In 2016 UHSNHSFT was awarded the status of Global Digital Exemplar (GDE)(216) which has provided increased funding (and new job roles including a MyMR project manager) to further develop IT services.

7.2.2 *Interventions*

My work on developing the digital virtual clinic took place between 2016 and 2018. The digital virtual clinic was fully implemented beyond a test environment in November 2018. I conducted 2 key work packages:

1. Exploratory work – to better understand current VC processes and the needs of key staff stakeholders (IBD clinical nurse specialists (CNS), IBD secretaries, IT specialists and the MyMR project manager) and current VC processes
2. Development and implementation– MyMR clinical portal and the digital VC

7.2.2.1 Exploratory work

To gain a better understanding of how the current virtual system works, I conducted preliminary exploratory work with 2 key stakeholder groups: nursing and administrative staff. Together with the MyMR project manager, I conducted a diary monitoring exercise and focus group among IBD nursing staff to better understand their role and priorities for work prior to the implementation of a significant change to their practice. The MyMR project manager established the current administrative practices involved in the paper-based virtual IBD clinic using process-mapping.

7.2.2.1.1 IBD Clinical Nurse Specialist (CNS) diary monitoring

I conducted a week-long diary-monitoring exercise with the 4 IBD nurse specialists. They were provided with a diary card with each day broken into half hour sessions and a key (Appendix F.2) from which to fill out their activities for the day over a 'typical' working week. The key divided activities into 3 duties: clinical, administrative, and non-working. Diaries were collated, and average working patterns calculated for the nursing team. The diary exercise will be repeated once the new virtual clinic is fully established to assess if this has had a significant impact upon CNS working patterns.

7.2.2.1.2 IBD CNS workshop

I conducted a workshop with the MyMR project manager and the 4 IBD nurse specialists who are responsible for the clinical side of MyMR to better understand their role and identify their priorities for areas for improvement within the service. The nurses were asked 6 key questions about their role as IBD nurse specialists and how they might improve the IBD service:

1. What is important about the role of the IBD CNS?
2. What do you enjoy most about your role?
3. What do you not enjoy about your role?

4. What aspects of your team-working are important?
5. How would you change your service to improve it?
6. What patient outcomes would you like to improve?

The nurses were asked to note down short anonymous answers on post-it notes. These were then reviewed and grouped into core themes.

7.2.2.1.3 Administrative process mapping methods

To better understand the processes involved in the existing virtual clinic and how these might evolve for the digital virtual clinic, the MyMR project manager conducted a mapping exercise to identify and record the processes involved in administering a virtual clinic, observing and documenting the individual process steps taken by secretarial and nursing staff to create a flow chart (Figure 55; "process map").

7.2.2.2 Development and implementation work

7.2.2.2.1 Development of MyMR clinical portal and the digital virtual clinic

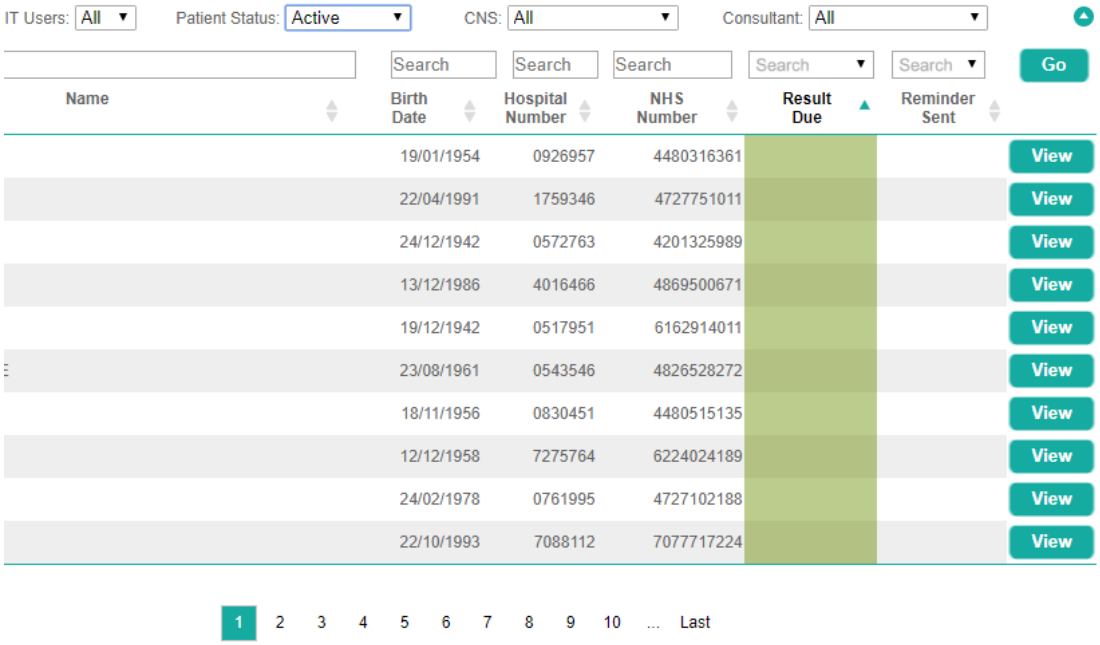
The MyMR clinical portal was initially created to allow members of the patient's team to view patient-entered data on medications, diaries, and messaging. I worked with the IT team to develop the clinical site to include more detailed information on the patient's history on the patient's home page so that staff could access all relevant information within one IT system. The new content includes drop down menus to input patient demographics (pulled through automatically from existing digital patient systems), GP details, clinical team (named nurse specialist and consultant as per current IBD standards(2)), disease and extent, medical and surgical treatments, lab/radiology/procedural results, and IBD control scores. At the bottom of the patient home screen a list of tasks can be selected, for example generating a patient results letter, reminder or updating records.

UHS Virtual Clinic follow-up requires patients to complete a predictable standardised regime of blood tests and questionnaires, with additional tasks as required. This allowed me to design templates or 'protocols' for VC requirements with the IT team (Appendix F.3). These protocols can be set by the CNS to automatically generate a yearly reminder to both patients and the CNS team for the requirements of the virtual clinic for that year.

The clinical team can view an interactive list of all their patients under virtual clinic follow up in date order on a 'dashboard' (Figure 42) using a colour-coded system adapted from earlier work by the prostate cancer team. Patients are colour-coded according to whether they have completed

their protocol or if this is overdue. ‘Green’ is set (showing the virtual clinic due date) when the patient is registered for virtual clinic. An ‘amber alert’ is generated when an incomplete test in the patient's assigned protocol is on or before that day or if a reminder letter has been sent to the patient. A ‘red alert’ appears when an incomplete test in the patient's assigned protocol is overdue by at least 14 days or if the patient has received a reminder letter following a previous amber alert.

Figure 44: Virtual clinic dashboard



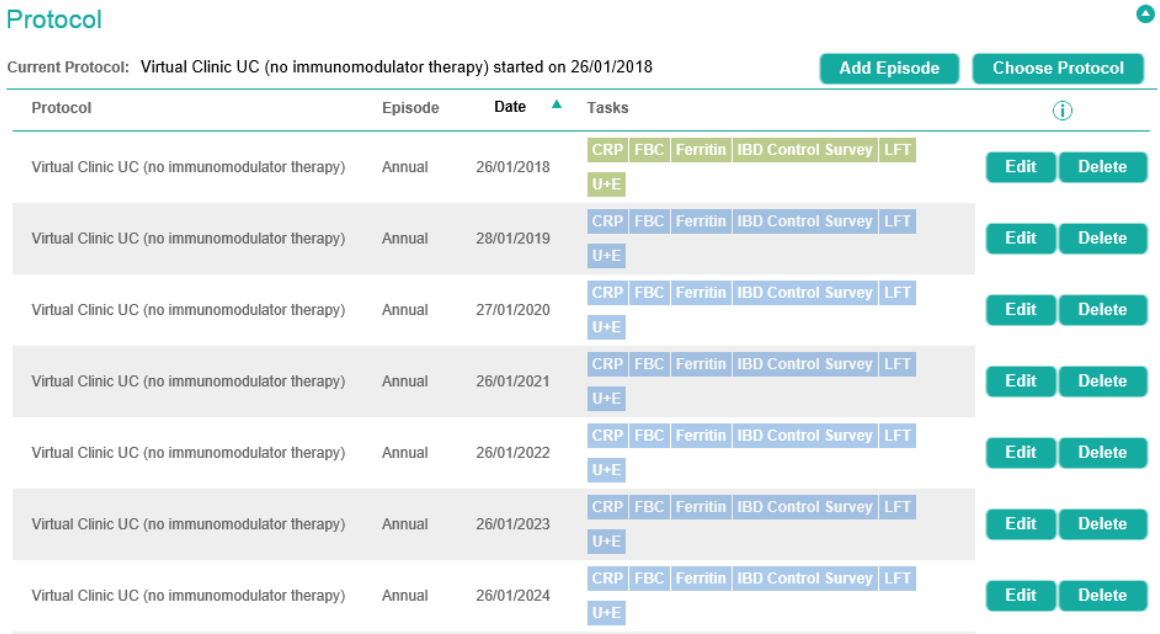
I designed set protocols (Table 21; Appendix F.3) based upon medication: immunomodulator therapy vs non-immunomodulator (e.g. 5ASA). The rationale for this differentiation is that patients taking immunomodulator therapies are required every 4th year to attend a face-to-face outpatient appointment to review whether treatment should be continued considering the increased side effect profile and cancer risk with these medications(232). Follow-up requirements are therefore slightly different. Protocols were also divided onto Crohn’s disease and ulcerative colitis due to variations in the blood tests required. Protocols were designed to span 5 years (to accommodate surveillance colonoscopy frequency which is usually every 1,3, or 5 years depending upon outcome of previous colonoscopy(263)) but can continue recurring indefinitely. DEXA (dual emission x-ray absorptiometry) scan frequency is decided by the CNS based upon previous results and risk factors for osteoporosis.

Table 21: Example protocol 1: Non-immunomodulator, Crohn's

Month	Interval (mths)	CRP	FBC	U&E	LFTs	Ferritin	B12	Folate	Vit D	IBD Control Survey	Colonoscopy (1,3,5 yr interval)	DEXA scan
0	0	+	+	+	+	+	+	+	+	+		(+)
12	12	+	+	+	+	+	+	+	+	+	(+)	
24	12	+	+	+	+	+	+	+	+	+		
36	12	+	+	+	+	+	+	+	+	+	(+)	
48	12	+	+	+	+	+	+	+	+	+		
60	12	+	+	+	+	+	+	+	+	+	(+)	

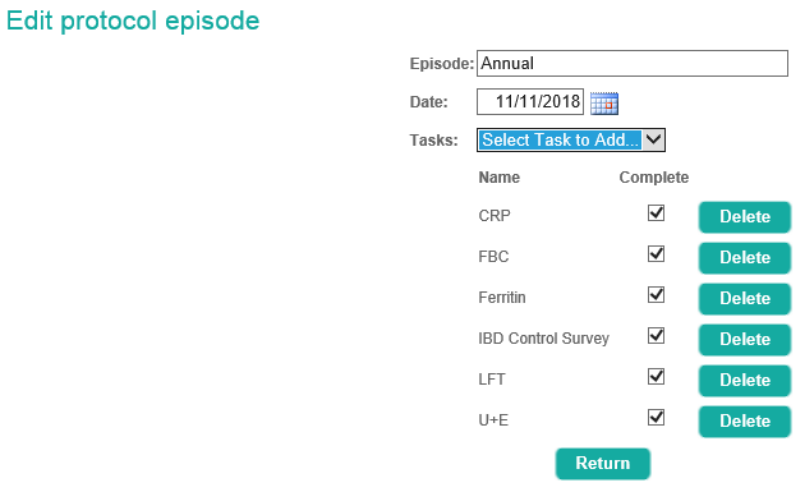
At the time of virtual clinic review, protocols can be set for the patient for the next and subsequent years. Set protocols can be edited to include any additional testing felt necessary. Once set, the requirements for that year's virtual review can be viewed (in green, amber or red according to completion), with subsequent years' in blue (Figure 45).

Figure 45: Protocol translated onto clinical tracker



The CNS conducting the VC review can click on the edit button to mark the tasks complete, as well as add any additional tasks required at the next VC review.

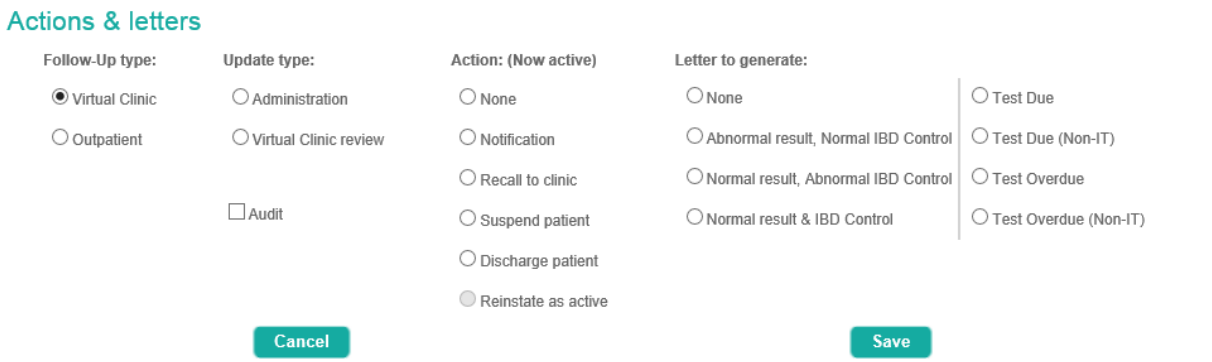
Figure 46: Edit protocol function



We created a list of actions to be conducted on completion of a virtual clinic review based upon the existing letter templates normally sent out via post to VC patients (Figure 47). These include inputting the next follow-up type (virtual or outpatient), update type (VC review or update - if for example a new piece of information needs to be added the patient record or new protocol set, without completing the virtual clinic review), action (e.g. recall to clinic, if for example a patient has been unstable in between virtual reviews they may need additional clinical input and virtual clinic may not be appropriate at that time), suspend patient (e.g. if not fulfilling VC requirements despite reminders), letter to generate (normal/abnormal result/IBD Control), reminder letter (e.g. if test overdue).

All letters were intended to be sent electronically via email. I designed these letters to try to minimise the time required to feedback results and follow up plans to the patient by creating templates for 'Normal result and IBD Control', 'Abnormal result and normal IBD Control' etc. Not all patient reviews will fit neatly into the pre-generated text therefore free text boxes where built into the letters where users can add additional detail. I reviewed the protocols and letters regularly with the nursing and IT teams to check appropriateness, and protocols were subject to modifications over the course of the implementation of the digital virtual clinic as improvements were made.

Figure 47: Outcome and action functions



.

7.2.3 ***Measures and analysis***

7.2.3.1 Exploratory work

Nurses recorded their reflections on their role on post-it notes during the CNS workshop. These were then transcribed and analysed using NVivo to identify themes. Due to limited nature of the data, it was analysed on a semantic level(154). Investigation of more latent themes would require more extensive qualitative work outside of the scope of this project. Data from this exercise was used to guide resource allocation during the implementation of the VC.

The MyMR project manager made notes during the virtual clinic administration mapping exercise and transcribed these to make a process map.

7.2.3.2 Developmental work

7.2.3.2.1 Normalisation Process Theory

The 4 tenets of NPT were used as a template to present barriers and facilitators to change encountered during implementation of the digital virtual clinic and was used as a reflective tool.

7.2.3.2.2 NoMAD survey

The NoMAD survey(160)(Appendix F.5) is a key component of the NPT toolkit and can be used to explore stakeholder's views about how a new service impacts upon their work, and whether it might become a routine part of their work.

I invited all clerical and nursing colleagues from the IBD team to complete the NoMAD questionnaire in November 2018, in the early months of the virtual clinic going 'live' in clinical

practice. In line with the guidance provided by the tool's creators, individual and group responses were examined but total scores for the NoMAD were not calculated(160).

7.2.3.3 Implementation measures

Data were collected on the following measures and analysed using simple descriptive analysis:

- Monthly patient registration to MyMR
- Monthly VC registration (IT users and non-IT users)
- MyMR IBD patient website usage
- E-messaging utilisation
- Telephone flareline usage

7.2.4 *Ethical considerations*

The main ethical issue considered was the change in care for patients using the existing paper-based virtual clinic. The digital VC provides existing VC services delivered electronically, plus the additional services available through use of MyMR. We considered those patients who may not have internet access or may not wish to access the digital virtual clinic by continuing to provide a paper-based service to 'non-IT' users. This also ensured equity of access to IBD services for those patients who may not be able to access internet/computing services.

7.2.5 *Safety*

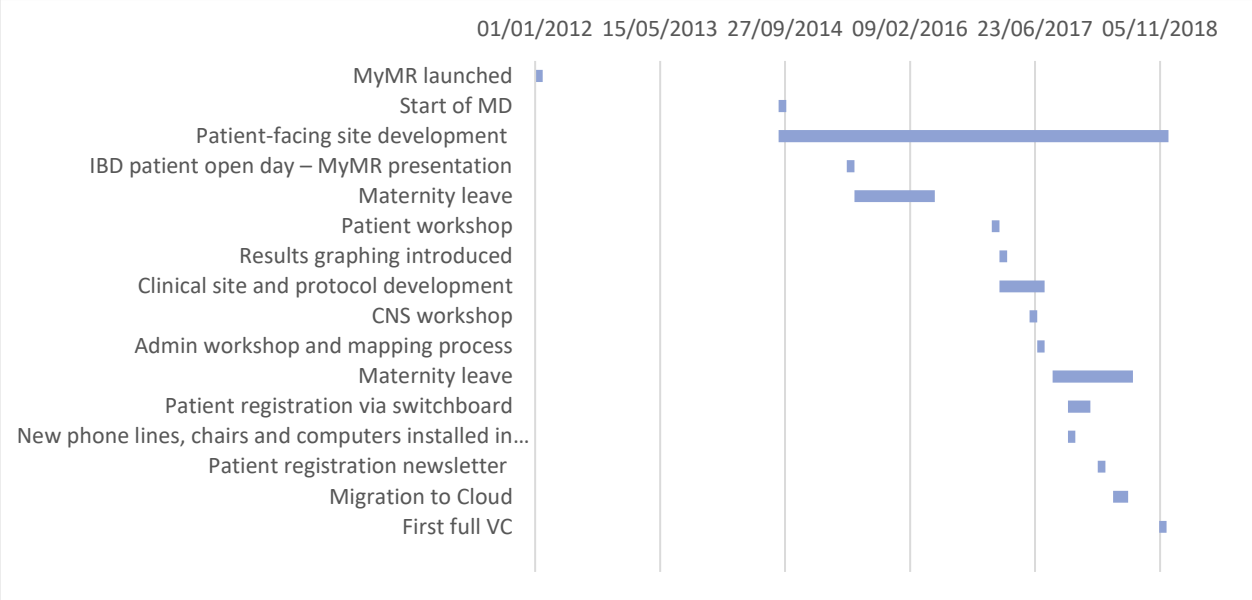
Consent and data security were important aspects to consider in developing MyMR and the VC, and strict security protocols were adhered to in line with the Caldicott principles(264) and the 2016 GPDR(265) (General Data Protection Regulations). Informed consent to data being stored securely outside of trust IT systems is sought automatically during the registration process for MyMR required to participate in the digital VC.

7.3 **Results**

The main developmental work on the MyMR clinical site and developing the digital VC took place in 2016 and 2017 (Figure 48). IT developments migrating MyMR to The Cloud delayed progress which meant that the first patients were registered to the live digital VC in November 2018.

7.3.1 *Timeline of key events*

Figure 48: Timeline of key events



7.3.2 ***Preliminary work***

Results of the IBD CNS diary monitoring exercise, CNS workshop, and administration mapping exercise are presented in this section.

7.3.2.1 Participants

4 clinical nurse specialists took part in the diary monitoring and workshop exercises. All participants were experienced senior nurses (Band 7 or 8), female, with IBD experience ranging from 2 to over 15 years. All 4 nurses were known to me, having previously worked as a specialist registrar in the department.

7.3.2.2 IBD CNS diary monitoring

All 4 members of the IBD CNS team completed diary monitoring for a one-week period in July 2017. 3 out of 4 nurses spent a greater proportion of time on clinical tasks than administrative tasks but the time spent on administrative tasks was substantial, ranging from 37.2-53.3% (Table 33). The diary monitoring exercise will be conducted again following full establishment of the new digital VC (after allowing time to 'bed in') to assess if this has impacted upon CNS working patterns.

Table 22: Individual clinical nurse specialist diary monitoring

CNS	Clinical time (%)	Admin time (%)
CNS 1	62.8	37.2
CNS 2	46.7	53.3
CNS 3	59.8	40.2
CNS 4	64.0	36.0
Mean	*58.17*	*41.83*

7.3.2.3 IBD CNS workshop

The workshop lasted 90 minutes and took place during a normal working day. Questions were intended to explore general views on their role, the current IBD service, and how this might be improved. All 4 nurses actively contributed. Brief answers were recorded by the nurses on post-it notes, transcribed into NVivo data analysis software and grouped into core themes.

Question 1 – What is important about the role of the IBD CNS?

4 main themes emerged on what nurses viewed to be important about the CNS role: their skillset, enhancing the provision of IBD care, working together and patient relationships.

Figure 49: Question 1 themes – What is important about the role of the IBD CNS?

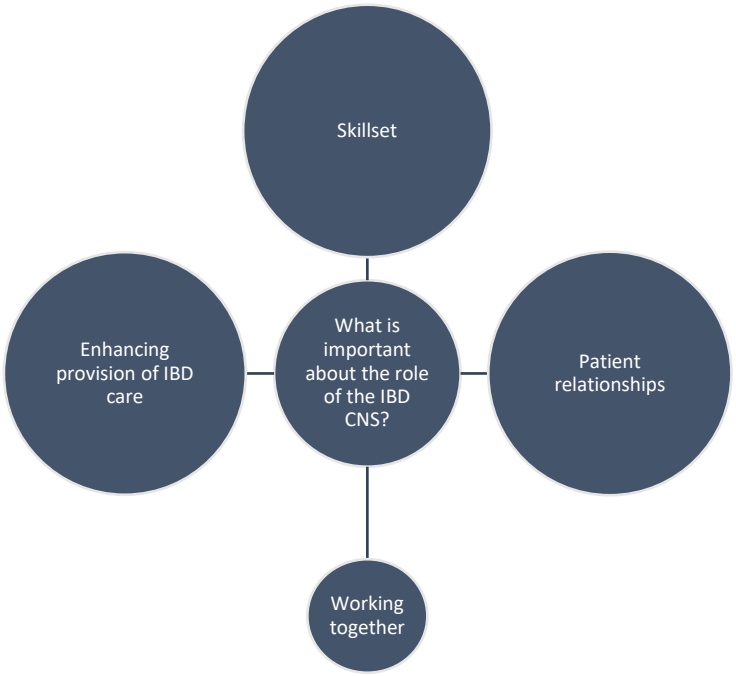


Table 23: Question 1 themes and individual answers: What is important about the role of the IBD CNS?

Individual answers	Themes derived from these answers
"Expertise" *"Specialist advice"* *"Knowing the IBD Cohort"* *"Knowledge"* *"Access to investigations, tests and treatment options"* *"Safety and reduction of doctors"* *"Education"*	Skillset
"Building trust" *"Point of contact for patients"* *"Patient centred care "* *"Patient support"* *"Direct access to CNS to advise on treatment – contact"* *"Increasing patient experience"*	Patient relationships
"Teamwork "	Working together
"Admission avoidance " *"Reducing admissions Virtual clinics – helping patients avoid hospital visits and parking charges"* *"Encourage patient involvement in services"* *"Quick Follow up"*	Enhancing provision of IBD care

Question 2 - What is most enjoyable about the role of the IBD CNS?

There were many things the nurses identified as being enjoyable parts of their role, with again a focus on relationships with colleagues and with patients.

Figure 50: Question 2 themes: What is most enjoyable about the role of the IBD CNS?

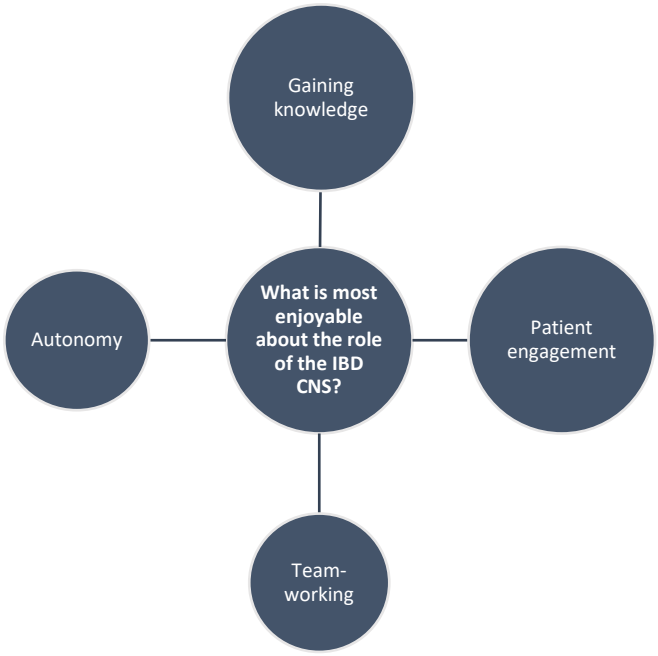


Table 24: Question 2 themes and individual responses: What is most enjoyable about the role of the IBD CNS?

Individual answers	Themes derived from these answers
"Opportunity for learning" *"Developing my knowledge and experience"* *"The increased knowledge"* *"The topic of IBD"* *"Research"*	Gaining knowledge
"Seeing patients in clinic/ward review – face to face" *"Making a difference to patients and family"* *"Providing information and advice to patients"* *"The contact with patients and making a difference"* *"Clinic reviews"*	Patient engagement
"Nurse-led clinic" *"Autonomy while working within a supportive team"* *"The hours – no nights"*	Autonomy
"My colleagues" *"The team I work with"* *"The team"* *"Working with my colleagues"*	Team-working

Question 3 – What is not enjoyable about the role of the IBD CNS?

This question revealed the frustrations felt by the nursing team about the difficulties of facing a high workload compounded by challenging healthcare systems and a lack of resources.

Figure 51: Question 3 themes: What is not enjoyable about the role of the IBD CNS?

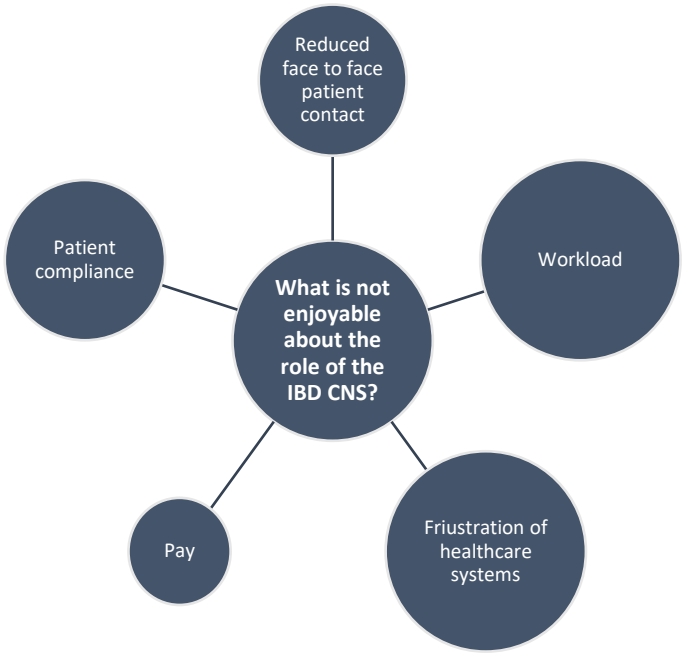


Table 25: Question 3 themes and individual responses: What is not enjoyable about the role of the IBD CNS?

Individual answers	Themes derived from these answers
"Miss face to face contact with patients" *"Reduced face to face time with patients"* *"Lack of clinical hands on practice"*	Reduced face to face patient contact
"High volume workload / chance that something will be missed" *"Back-log of virtual clinic that hasn't been completed"* *"High volume of calls on helpline"* *"Volume of prescriptions"* *"Pressure of referrals"* *"Pressure with reduced staff and increased workload"* *"Can seem like just do helpline calls for IBD"*	Workload
"Lack of connection to community – delays" *"Reduced access to endoscopy and clinic appointments"*	Frustration of health care systems

Individual answers	Themes derived from these answers
"Reduced access in clinic to see and advise patients on treatment – leading to delays" *"NICE (2016) frustrating with treatment options"*	
"Poor pay"	Pay
"Non-compliant patients"	Patient compliance

Question 4 – What aspects of your team working are important?

There were recurring themes of the importance of multidisciplinary team-working and providing/receiving support from each other, as well as the importance of communication which is integral to any effective team-working. The working environment was mentioned by just one respondent but for the subsequent question on improving the IBD service the working environment featured more prominently.

Figure 52: Question 4 themes: What aspects of your team working are important?

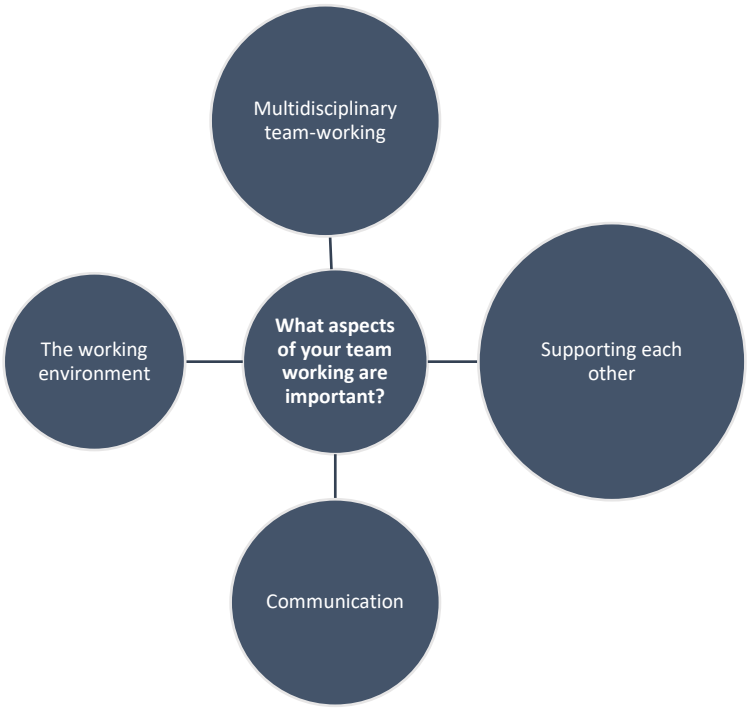


Table 26: Question 4 themes and individual responses: What aspects of your team working are important?

Individual answers	Themes derived from these answers
"Good communications with all members of Multidisciplinary team (MDT)" *"MDT approach"* *"MDT Working"* *"Team decisions"* *"MDT"* *"IBD focus group"* *"Good working relationships"*	Multidisciplinary team-working
"Advice" *"Colleagues"* *"Encouragement"* *"Have a laugh (even when you want to cry!)"* *"Listening to each other"* *"Pick each other up"* *"Support"* *"Support"* *"Support"*	Supporting each other
"Approachability" *"Communication"* *"Communication"* *"Communication"* *"Negotiation"*	Communication
"Environment"	The working environment

Question 5 – How would you change your IBD service to improve it?

This question gained the most responses from the nursing staff. There was an overwhelming theme of improving capacity, with a need identified for more doctors, nurses and clinical staff. There also several themes relating to equipment and IT improvements.

Figure 53: Question 5 themes: How would you change your IBD service to improve it?

Table 27: Question 5 themes and individual responses: How would you change your IBD service to improve it?

Individual answers	Themes derived from these answers
"More IBD nurses" *"More nurses and doctors"* *"More consultants"* *"More nurses"*	Clinical capacity
"More admin" *"Extra admin support for letter dictation; work etc."* *"More admin support to help secretary"*	Administrative capacity
"Updated computer networking e.g. national" *"Better IT – computer speed increased and not crashing"*	IT systems
"Larger and better equipped office" *"Reduce need to share computers and desks"* *"Environment – more comfortable"* *"Better office space"* *"New telephone with headset"* *"A telephone per nurse"* *"Better seating in office"* *"Headsets"*	Office environment and equipment
"Facilities – infusion centre" *"IBD specific unit"* *"Better patient facilities"*	Clinical environment

Individual answers	Themes derived from these answers
"Better outpatient department/ Infrastructure"	
"Other services working hours – blood at weekend, access to pharmacy" *"Less red tape i.e. Not wait for drug approval"*	Access to other related services
"Time to complete clinics" *"More clinic availability"* *"Flexibility for patients"* *"Outpatients drop-in clinics"*	Outpatient clinic capacity

Question 6 – What patient outcomes would you like to improve?

The nursing team had many ideas about how patient outcomes could be improved, such as speeding up IBD timelines (diagnosis, hospital stay, treatments etc.) as well as how we access resources.

Figure 54: Question 6 themes: What patient outcomes would you like to improve?

Table 28: Question 6 themes and individual responses: What patient outcomes would you like to improve?

Individual answers	Themes derived from these answers
"Clear path – sooner from referral to diagnosis"	Reducing time to diagnosis
"Fewer admissions" *"Reduce admissions"* *"Reduce admissions"* *"Reduce LOS (length of stay)"* *"If admitted reviewed by IBD team promptly"* *"In an ideal world: less flares (but this probably won't happen!)"*	Reducing inpatient time in hospital
"Clinic appointments – shorter waiting lists" *"An increase in outpatient reviews – IT reviews?"* *"Reduce backlog of virtual clinic"*	Reducing waiting time for IBD outpatient appointments
"Have more drug options that can be initiated sooner" *"Reduce the cost of prescriptions"* *"Right treatment at the right time"* *"Top down approach to treatment"* *"Time of starting biologics – availability of space / prescription requesting time"* *"Treat to target"*	Improved access to and use of medical therapies
"Endoscopy appointments for urgent/flaring patients being available in less than 2 weeks" *"Seamless care"* *"Continuous care"*	Improved interface with other services
"Funding to help patients get back to work"	Reducing the impact of IBD on personal life

7.3.2.4 Administration process-mapping

There are 4 key IT applications employed by UHS in running outpatient services – eCaMIS® is an electronic patient administration system used by clerical staff in managing outpatient appointments, HICCS® is an integrated clinical support system which allows both clinical and administrative staff to input data and view patient records electronically, eQuest® is an electronic requesting and results-reporting system, and eDOCS® provides paper-free access to outpatient clinic letters and other patient documents. Some of these systems can pull data from and communicate with each other but not all, and staff will frequently have several applications running concurrently when completing tasks.

The mapping project demonstrated the complex administrative processes involved in running the virtual clinic for both clerical and clinical staff – there are over 50 potential steps in the administrative pathway involving multiple staff members (Figure 55). The system is also extremely 'paper-heavy', with a potential maximum of 14 letters being sent either to the patient or between IBD staff per patient for every yearly virtual clinic.

The new process for virtual clinic cut the possible number of steps involved in the process of administering a virtual clinic from up to 50 to a maximum of 20, with a potential for 3 paper letters for initial invitation to virtual clinic and correspondence. At the time of writing, a fully digital system for letters and conveying VC results to GPs was under development, with the goal of being a completely paperless system.

Figure 55: Process map for standard VC (adapted with permission from work by N Steel, MyMR project manager)

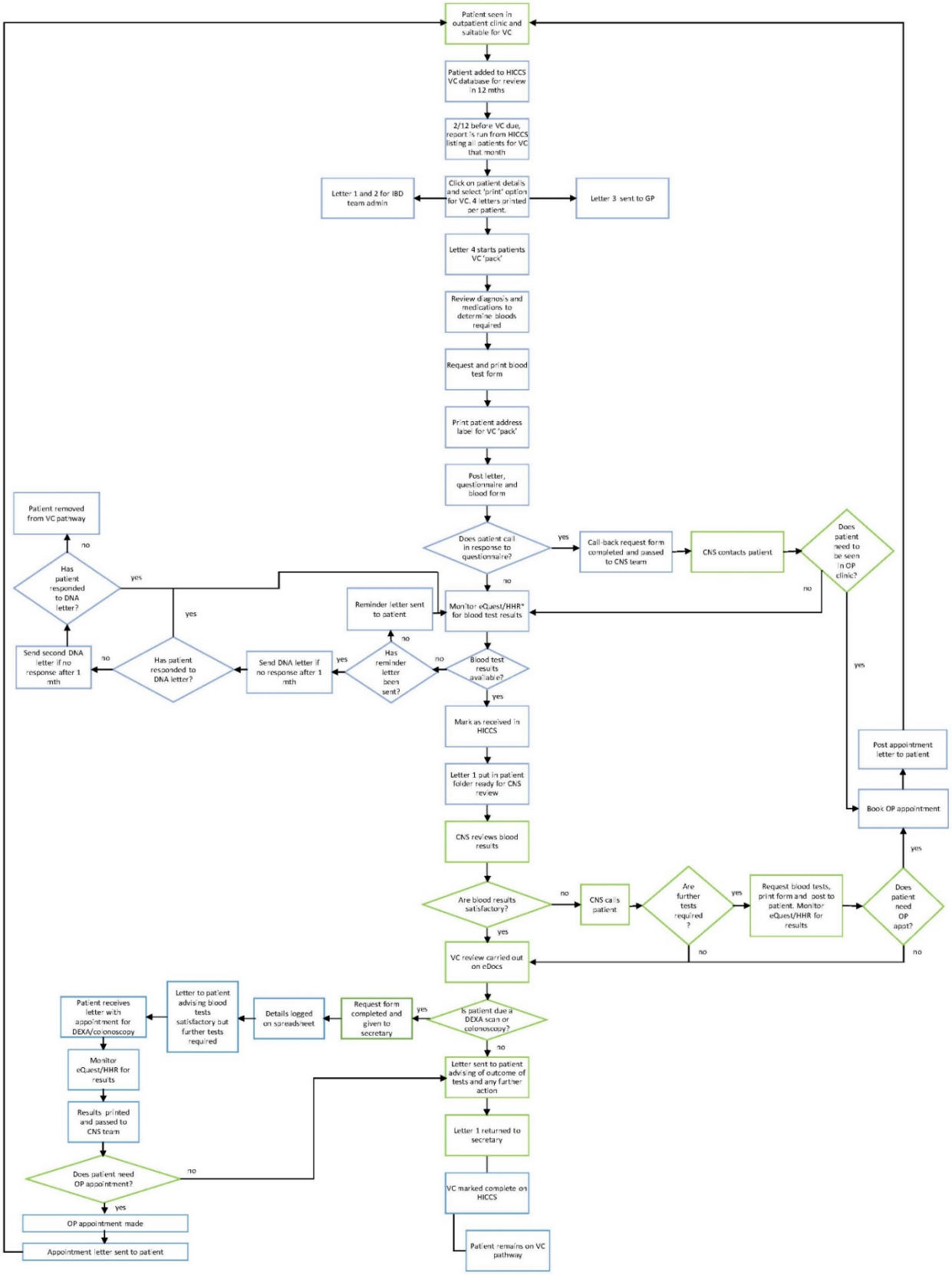
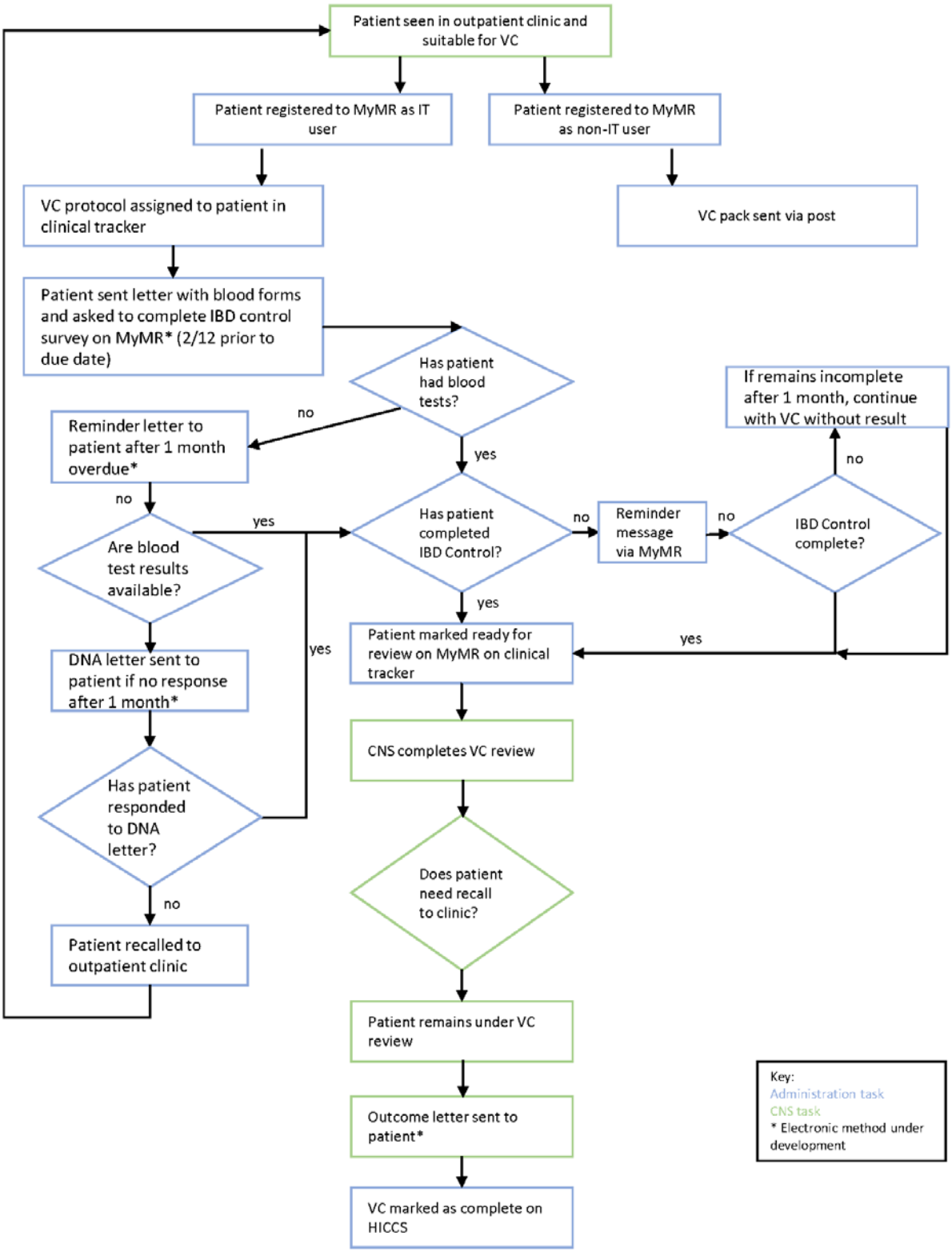


Figure 56: Process map for new digital virtual clinic



7.3.3 *Implementing MyMR for IBD and the digital VC*

7.3.3.1 NPT reflection on implementation

This section presents examples to illustrate each of the NPT constructs and components. Although several key stakeholder groups were involved in developing the new service, I have focused on the key group of nursing and clerical staff, on whom the implementation of the digital VC has impacted most upon, prior to being rolled out to patient users. I used NPT as a retrospective tool to present and reflect upon our experiences of implementing the digital virtual clinic using MyMR.

1. **Coherence**

a. Differentiation

What work did we do to understand the differences between the existing VC and digital VC via MyMR?

The MyMR patient focus group (Chapter 5) explored attitudes to the current virtual clinic service and how the proposed changes might affect patients. We reviewed our existing VC methods through process-mapping and communicated this back to nurses and clerical staff, allowing the team to have a better understanding of the processes involved in current practice. This also highlighted the significant administrative burden of the existing paper-based VC. We conducted a MyMR workshop with representatives from IT, nursing and medical teams to introduce the concept of the digital VC and clinical tracker and obtain feedback from these key users which was used to further develop the service.

b. Communal specification

How did we work together to build a shared understanding of the aims and benefits of the digital VC?

We conducted exercises with key stakeholders to better understand the potential benefits of the digital VC. I led the nursing diary monitoring exercise which illustrated a high proportion of time spent on administrative tasks and telephone contact which the current VC was contributing to. The CNS workshop helped us to better understand how the IBD service could be improved, for example the significant backlog of VC reviews was causing stress, and current working environments were not felt to be fit for purpose with insufficient access to phone lines. This helped provided rationale for the development of the digital VC and guided allocation of resources.

c. Individual specification

What did we do to help understand our specific tasks and responsibilities for managing patients on MyMR?

Process-mapping laid out the precise steps and responsibilities of staff involved in running the existing and digital VC allowing better understanding of individual and colleague's roles and an appreciation of the time invested in each step of the process. I met with nursing and IT colleagues to run through the proposed VC step by step using a demo site, generating debate about who should be responsible for patient protocol allocation and issuing blood tests which had traditionally been designated a clerical task. Despite the IBD secretary being very experienced with VC monitoring requirements, clinical staff countered that reviewing case histories to determine treatment plans should be considered a clinical task but given current nursing workload, these tasks would need to remain a clerical duty, with support where needed from clinical team members.

d. Internalization

What work did we do to attribute worth to this new way of working?

Worth was attributed to the project largely in terms of potential financial and time-savings. At the beginning of the project there were no standards in place for charging for activity undertaken through MyMR. By consulting with the trust finance department and CCG (clinical commissioning group), the MyMR project manager was able to establish a financial tariff for virtual clinic reviews for the 2018/19 contract. The tariff for a virtual clinical review via MyMR is £70 and a message thread per patient per month is £25. The potential time-saving benefits of the project are yet to be realised. Because of the initial up-front increase in workload generated by the new VC system (practising with test patients, troubleshooting etc.), it has proved difficult to visualise the potential time-saving worth of the VC.

2. <u>Cognitive participation</u>

a. Initiation

What key participants worked together to drive the VC forward?

Multiple key participants worked to drive forward the implementation of MyMR and the digital VC. Although it was rare that all participants came together at any point in the process, both the MyMR project manager and I liaised with all stakeholders to coordinate and communicate ideas. The informatics and technology team were very responsive to requests from the clinical team, although this was dependent upon time and financial resources. Interested patients such as those

of the patient panel helped to progress patient-facing site content. The nursing and administrative teams provided valuable clinical insight on the practicalities of running the virtual clinic and championed the MyMR website to patients, enrolling them opportunistically during clinic visits and telephone consultations. At times it was challenging to engage the nursing and administrative teams to drive the project forward because of the initial burden of increased workload whilst the new system was trialed and refined. When this occurred, the MyMR project manager was key in picking up momentum by responding to feedback from clinical teams and liaising with the IT team to ensure any changes that might improve working practice were implemented as swiftly as possible.

b. Enrolment

What work did we do to build engagement of stakeholders to deliver the new service collectively?

As illustrated by the nurse monitoring diary exercise, a large proportion of nursing time is spent on administrative tasks. When the digital VC was implemented, the need to register patients, add clinical data, and select protocols before first use, meant an increase in administrative tasks. The pre- and post- digital VC workflows show a marked decrease in the number of tasks required to complete a digital VC review. Reflecting these workflows back to the nursing and admin teams helped to better understand the rationale for the project and aid engagement.

The CNS workshop identified key areas that might improve working conditions for the nurses were identified. Health Foundation funding was used to provide new office equipment (chairs, headsets, dual screen monitors) which the nurses and IBD secretaries felt improved their working environment and aided efficiency. When conducting clinic reviews, nurses often have several different IT systems at once and dual screens allowed simultaneous use.

Engaging clerical staff was more challenging as enrolment involved questioning established methods of running the VC. It was very important to acknowledge the expertise of clerical staff in the use of complex administration systems and involve them in key decision-making. This required a shift in thinking away from separate clinical and clerical teams, acknowledging all as part of the same team. This resulted in regular participation of clerical staff at fortnightly IBD focus group meetings at which aspects of MyMR development were discussed.

Legitimation

What work was done to ensure that participants believed that it is right for them to be involved and that they could make a valid contribution to MyMR and the VC?

The mapping exercise illustrated the significant clerical input required to run the virtual clinic successfully, legitimizing their involvement in the service development both to the clerical and wider members of the team. It also highlighted the complexity of these processes which were largely completed by one individual secretary, prompting the development of a standard operating procedure to enable others to conduct the VC if required and ensure resilience of the system. An extra secretary was employed to support the process change, again reinforcing the legitimation of the clerical role. IBD secretaries were provided with additional access rights for MyMR password resetting and troubleshooting which provided them with increased ownership and control of the service and transitioned the day to day running of MyMR for IBD from the IT team to the IBD team.

d. Activation

How did we collectively define the actions and procedures needed to sustain momentum of implementation of the MyMR VC?

The MyMR project manager was crucial to sustaining the momentum of the implementation of MyMR and the digital VC, unhindered by clinical commitments. We met monthly to define targets for implementation, review progress and provide clinical advice. The project manager produced monthly MyMR newsletters on registration and development updates and circulated these to clinical and clerical staff. In 2018, due to the continuing expansion of MyMR, a trust-wide steering group was formed to oversee MyMR as a whole, as well as individual specialty projects.

3. <u>Collective action</u>

a. Interactional workability

What interactional work did we do with each other and with other elements of MyMR when we sought to implement it?

Our interaction with patients has changed with the development of MyMR and the virtual clinic, with increased use of email-communication. Whilst the e-messaging system was well received by patients and staff alike, there have been teething problems with occasional delay of messages. This was communicated to the IT team and swiftly rectified. The IBD telephone flareline remained in situ as a back-up (and for patients who may need to communicate via telephone). To ensure

important information appears on patient records outside of MyMR (for example on the trust document store 'eDocs'), the IT team developed a function that allows the team to mark messages as 'clinically relevant'. A star appears next to these on the MyMR dashboard, and the message appears on eDocs so that other members of the team can view it. It was also agreed with commissioners that these marked conversations should command a tariff equal to that of the telephone flareline and this data is fed automatically to the finance department, adding additional worth to the messaging service.

b. Relational integration

What knowledge work did we do to build confidence in MyMR and in each other?

Communication was key in building confidence in MyMR and in each other. The current messaging system allows patients to communicate with the whole IBD team (rather than individual professionals) to ensure that someone will always be available to answer queries. The nurses communicate each day to decide who will be responsible for responding to messages for the day to ensure no messages will be missed.

Despite running virtual clinics in an initial test environment, the complexity of the intervention meant that when this was attempted in a live environment, new challenges came to light which did lead to a loss of confidence in MyMR. As patient registration numbers grew, the system slowed, and it took longer for the patient dashboard to load when exiting one patient record and entering another, at times reported by the nurses to be up to 2 minutes of buffering. This problem was in part rectified by the IT team when the data storage for MyMR was migrated to The Cloud and current delays are under 10 seconds. Although a significant improvement, the delay is still frustrating when trying to pass quickly from patient to patient.

c. Skill set workability

What allocation work underpinned the division of labour that is built up around a set of practices as they are operationalized in the real world?

The bulk of labour running the virtual clinic is carried out by the clerical and nursing teams, with input from physicians when additional advice is required. The process mapping exercise demonstrated that the preparatory work is done primarily by admin staff, including chasing up test results and sending reminders, whereas clinical decision-making and management plans were actioned by the nursing staff. It was agreed between the nursing and admin teams during focus

group meetings that this division of labour remained appropriate and should be continued. The nurse monitoring exercise showed that a large proportion of nursing time is already taken up with administrative tasks and it is important to protect and utilise their clinical skills as much as possible.

d. Contextual integration

How was MyMR managed through allocation of different kinds of resources?

The financial resources required to develop MyMR and the VC came largely from funding derived from the wider Global Digital Exemplar (GDE)(136) awarded to the trust, with additional use of funding from a Health Foundation Innovating for Improvement(266) grant. We explored using funding to provide nursing support during the VC integration. The role would require specialist IBD knowledge from an experienced nurse (band 6 or above) limited to a short-term secondment from a permanent post, however current pressures on ward-staffing meant it was difficult to release staff. Instead, funding was put to practical use to improve working conditions for nursing and clerical staff (chairs, dual monitors, telephone headsets etc.), areas identified for improvement in the nursing workshop. Additional clerical support to help the transition was funded for 6-month period and led to a permanent post within the IBD secretarial team.

IT resources were at times limited. Over the last few years, numerous other medical specialties and healthcare trusts have adopted MyMR and required IR support. GDE funding led to rapid expansion of the IT team to help accommodate this. In 2017/2018, the trust migrated MyMR into the managed Cloud (Microsoft Azure®). This allowed expansion of the site and meant that UHS was able to hand over management of the security arrangements for patient data to a more experienced and secure professional organisation. This did however mean that progress with VC developments slowed down for this period as IT resources were diverted elsewhere.

4. <u>Reflexive monitoring</u>

a. Systematization

How did we determine how effective and useful MyMR is for staff and patients?

Systematization took place largely informally through personal reflection from staff whilst using the website. Once fully underway, the effects of MyMR and the virtual clinic on telephone flareline rates, outpatient clinic attendance, hospital admissions will be examined, as well as

patient and staff satisfaction. The NoMAD tool provided early insight into staff opinions on the effects of MyMR and the VC on their working and patient care (section 6.3.3.2).

b. Communal appraisal

How did we work together to evaluate the worth of MyMR?

Regular discussions took place informally between members of staff and in the context of the IBD focus group, where frustrations were voiced about any areas of the service that did not run smoothly. This was usually mitigated by acknowledgement of the potential worth of MyMR in improving patient care and efficiency and these discussions usually generated ideas that ultimately helped to improve service. The development of a MyMR steering group will provide a formal platform for communal appraisal and will allow sharing of ideas between medical specialties.

c. Individual appraisal

What work did we do to appraise the effects of the virtual clinic/MyMR on our own working?

Individuals continuously reflected upon the effects of the MyMR virtual clinic on their personal practice. Where issues led to a perceived increase in workload (for example delays in completing VC review due to slow loading of the patient dashboard), the MyMR project manager liaised with the IT team to rectify the problem. When improvements were slow to occur, this led to decreased individual engagement with the virtual clinic and subsequent delay in going live. Repetition of the nurse diary monitoring exercise once the virtual clinic is fully established will explore any effects on working patterns.

d. Reconfiguration

What attempts were made to redefine procedures and modify practice to make it workable?

Whilst most reconfiguration took place during the developmental phase using a demo version of MyMR, many workability issues came to light when putting the digital VC into practice due to the complexity of the intervention and the number of different people involved. Compromises had to be made within the limitations of the software available.

Registration of patients proved challenging due to time constraints on clinical staff. The initial method for registration was for the IBD secretary to post a letter inviting patients to use the digital VC and follow up with a phone call, however it was difficult to contact patients, particularly during the working day. This was addressed by utilising hospital switchboard staff between 3-8pm to contact virtual clinic patients via telephone using a scripted registration dialogue. This required significant input by way of prompting from the MyMR project manager and would unlikely be a long-term option.

Not all patients approached could be registered for VC, largely due to failed contact attempts or not using email. These patients could still be managed via MyMR as a 'non-IT user' and assigned a random email containing their UHS patient number generated by code within MyMR. Consent to store patient information outside of UHS was addressed at the time of inviting patients via post to participate by explaining MyMR and its security arrangements.

Time to provision of blood results to patients has been an area of debate and reconfiguration. The current trust standard is to release blood results to MyMR after 5 days to allow time for the requesting/overseeing clinician to review and sign off ('acknowledge') results, ensuring any abnormalities can be addressed. This did not fit with the concept of self-management as patients were not provided with information that may help decision-making in a timely fashion. In IBD, a delay of 5 days to accessing a result could lead to a significant delay in important treatment, particularly in the context of a disease flare up of medication side effect. The IBD MyMR website was therefore reconfigured to allow the release of selected appropriate blood results on the same day, but with clear explanations of results to aid patient understanding. This will need to be monitored closely to ensure no increase in patient anxiety, and this could be a future area of study when the VC is fully established.

To establish a fully digital VC, blood forms will need to be provided electronically. Whilst this process is now fully functional within the wider hospital for inpatient care, this practice has not yet spread to outpatient and primary care. This would involve numerous primary care providers switching to electronic test requesting and is a considerable piece of IT work which will take time to develop and coordinate with GPs.

Reconfiguration, as with all the NPT constructs, is an iterative process. The normalisation of MyMR and the Virtual Clinic is ongoing and is expected to continue to evolve over many years with continuing development of the service.

7.3.3.2 NoMAD survey results

5 out of 6 members of the clinical and administrative team (2 clerical, 3 nursing) most closely involved in running the MyMR virtual clinic responded to invitation to complete the NoMAD survey (Figure 57). Questions 1-3 generated a score out of 10 via a visual analogue scale, whereas the remaining questions could be answered with strongly agree/agree/neither agree nor disagree/disagree/strongly disagree/not relevant. There was wide variability in some responses, however in other areas, responses were more consistent.

Figure 57: NoMAD survey

1. When you use MyMR VC how familiar does it feel?
2. Do you feel MyMR VC is currently a normal part of your work
3. Do you feel MyMR VC will become a normal part of your work
4. I can see how MyMR VC differs from usual ways of working
5. Staff in this organisation have a shared understanding of the purpose of MyMR VC
6. I understand how MyMR VC affects the nature of my own work
7. I can see the potential value of MyMR VC for my work
8. There are key people who drive MyMR VC forward and get others involved
9. I believe that participating in MyMR VC is a legitimate part of my role
10. I'm open to working with colleagues in new ways to use MyMR VC
11. I will continue to support MyMR VC
12. I can easily integrate MyMR VC into my existing work
13. MyMR VC disrupts working relationships
14. I have confidence in other people's ability to use MyMR VC
15. Work in assigned to those with skills appropriate to MyMR VC
16. Sufficient training is provided to enable staff to implement MyMR VC
17. Sufficient resources are available to support MyMR VC
18. Management adequately supports MyMR VC
19. I am aware of reports about the effects of MyMR VC
20. The staff agree that MyMR VC is worthwhile
21. I value the effects that MyMR has had on my work VC
22. Feedback about MyMR can be used to improve it in the future VC
23. I can modify how I work with MyMR VC

When asked about the familiarity of the MyMR VC (0: Still feels very new, 10: feels completely familiar), respondents suggested it was still unfamiliar with a mean score of 3.4/10 (median 4, range 1-5). When asked if they felt the MyMR VC was currently a normal part of their work (0: not at all, 10: completely), respondents gave a mean score of 4.2 (median 4, range 3-5). When asked if they felt the MyMR VC would become a normal part of their work, responses were more positive with a mean score of 7.4 (median 7, range 7-8).

Questions relating to coherence and cognitive participation with MyMR VC largely generated positive responses. Respondents all answered “agree” or “strongly agree” to coherence of the effects of the VC on the nature of their own work (Qu. 6). All agreed or strongly agreed that they could see the potential value of the MyMR VC for their work (Qu.7). All agreed there were key people driving MyMR VC forward and getting others involved (Qu.8), that participating in MyMR VC was a legitimate part of their role (Qu.9), that they were open to working with colleagues in new ways to use MyMR VC (Qu.10) and that they would continue to support MyMR VC(Qu.11).

Questions relating to support and training for staff showed the challenges encountered in collective action. All respondents disagreed that sufficient training (Qu.16) or resources (Qu.17) were provided to enable staff to implement the digital VC, and all also disagreed with the statement that management adequately supported MyMR VC (Qu. 18).

7.3.4 *Initial findings*

This section presents quantitative data on patient registration as well as website, e-messaging, and telephone flareline usage. I did not examine patient outcomes at this early stage, but this will be studied in future as the digital VC becomes established.

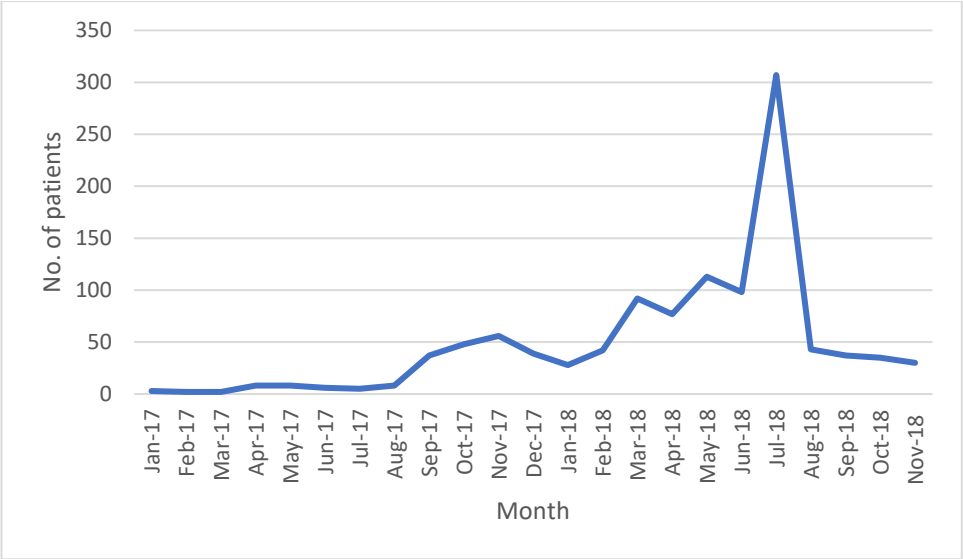
7.3.4.1 MyMR Registration

75 IBD patients were registered to MyMR between 2012 and 2016, but by November 2018 there were 1199 IBD patients registered to MyMR for IBD (both virtual clinic and non-virtual clinic users) which represents over a third of IBD patients at UHS. There was a surge in registrations in May, June and July 2018 (Figure 58) which corresponded with dedicated time spent by the MyMR project manager registering patients and a push for clinical staff to register patients in clinic. Since then, registration has fallen to a steadier rate of around 30 patients per month.

7.3.4.2 Digital VC registration

The first fully digital VC was conducted in November 2018. 35 patients were signed up for the November 2018 VC, of which 18 were IT users and 17 were non-IT users (declined to participate or not possible to contact).

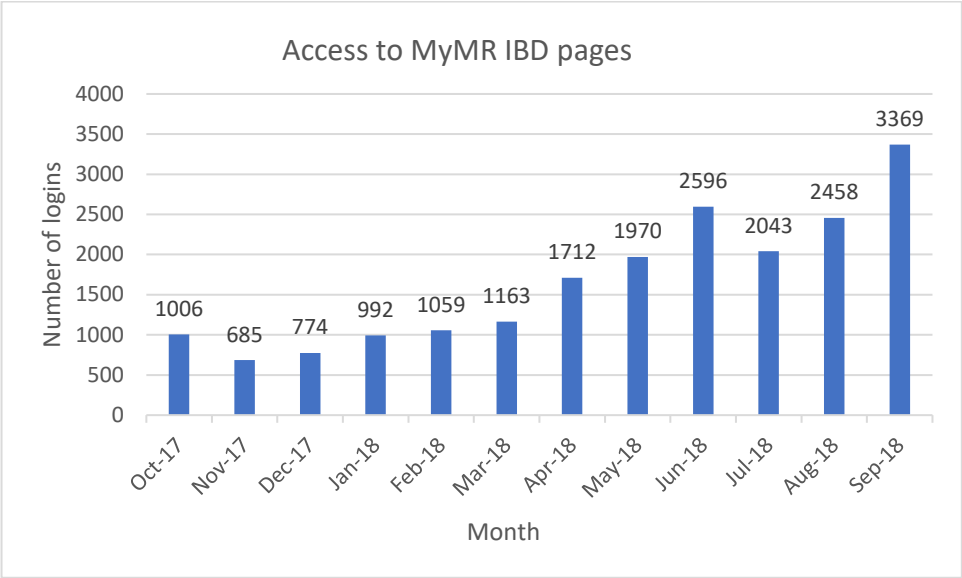
Figure 58: Monthly MyMR IBD patient registration



7.3.4.3 Website usage

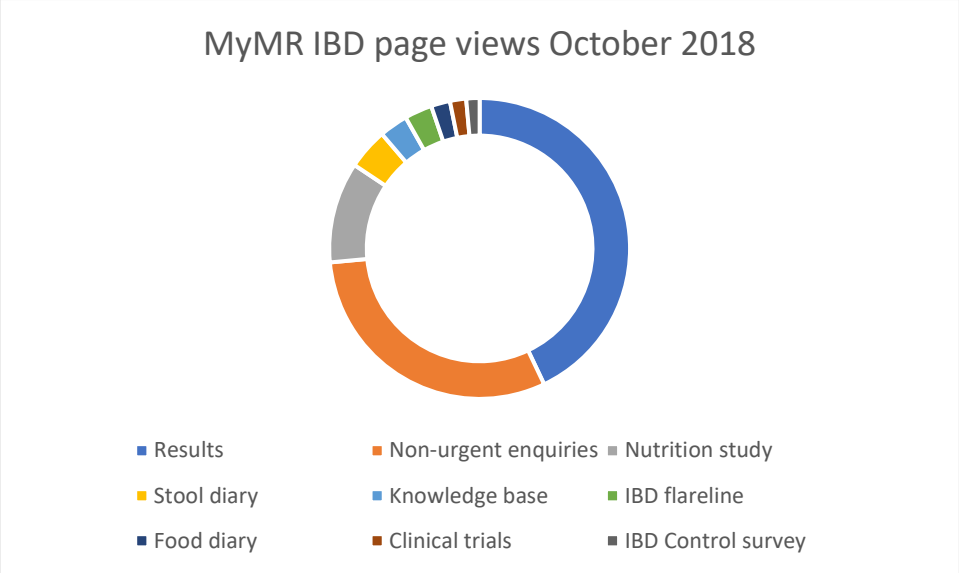
MyMR website usage (using login data for all IBD pages) climbed steadily over 2018 as registration increased (Figure 59). There was a drop off in usage in the summer months of July and August.

Figure 59: Monthly login to MyMR IBD pages



The most accessed pages (Figure 60) were results and non-urgent enquiries (e-messaging), followed by pages for a local nutrition study utilising MyMR as a platform for administering nutrition questionnaires.

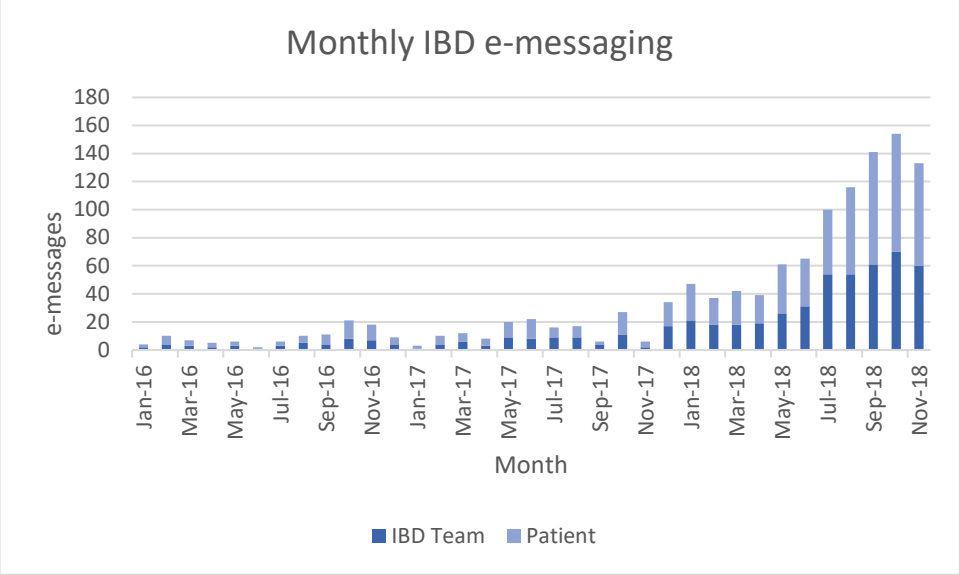
Figure 60: Breakdown of IBD page views



7.3.4.4 Messaging utilisation

Messaging utilisation (Figure 61) increased rapidly as more patients were registered to MyMR. Mean monthly messages over 6 months (June-November 2018; patient and IBD team combined) were 118 per month with 133 messages in November 2018. 100% of messages were responded to by the nursing team the 3 months from September-November 2018. The revenue from messaging in November 2018 (35 individual patient messaging threads, £25 tariff per patient) was £875.

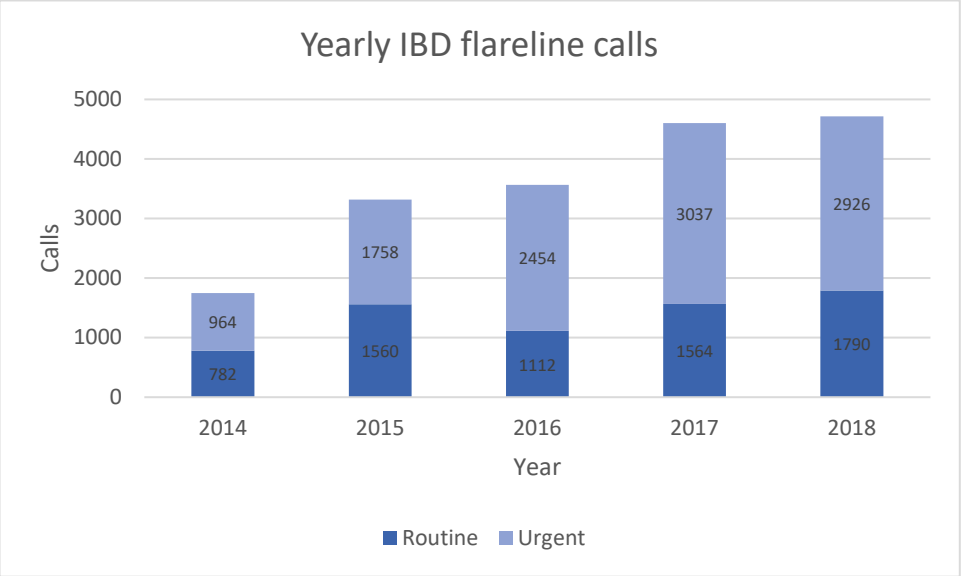
Figure 61: Monthly IBD e-messaging



7.3.4.5 Telephone flareline usage

Yearly data from the IBD flareline show that call volume has also grown year on year (Figure 62), with a total of 4716 calls in 2018. There was a slight slowing of growth compared with previous years, but it is too early to comment on whether the recent drive towards MyMR patient registration may be associated with this. Yearly 'urgent' calls consistently outnumbered 'routine' calls.

Figure 62: Yearly IBD flareline calls



7.4 Discussion

7.4.1 *Interpretation*

7.4.1.1 Preliminary work

The preliminary work provided useful insight into the current working environment of the IBD team and provided rationale for implementing the digital VC from a health professional perspective. Nurses cited areas that they did not enjoy about their work, particularly an unmanageable workload and the backlog of outstanding existing virtual clinic reviews. There was repeated reference to the need for increased resources, both in staffing and IT provision, reflecting chronic pressures across the NHS. Communication and team-working were felt to be important to the CNS role, apparent when dissecting the processes involved in implementing a new service via NPT.

The diary monitoring and administrative pathway-mapping exercises highlighted the high administrative burden faced by nursing and clerical teams both in their day to day job and the existing virtual clinic. Excessive requirements for paperwork and data entry have been cited as worrying consequences of changes to NHS structure (267). By implementing our new system of working, there was an initial increase in burden for nurses and clerical staff, for example in registering patients to MyMR and uploading data and patient protocols for VC reviews. It is hoped that this initial outlay will be mitigated by future benefits when the VC is more firmly established, when patient protocols recur automatically, and VC patients start to take a greater role in entering data and managing their health.

7.4.1.2 Implementation

The implementation of the MyMR patient-facing site had several successes. The messaging service has been beneficial to both patients and staff, and the progressive uptake of this service is testament to its popularity. The securement of a fixed tariff for messaging threads recognises the clinical work undertaken although a reduction in flareline calls although this has not yet been observed. This rate does appear to be slowing and the figures must also be interpreted in the context of increasing numbers of IBD patients each year. The latter is hard to quantify due to difficulty in tracking IBD patients (currently all IBD outpatient visits are coded under 'gastroenterology' as a whole). The goal of registering all current and future IBD patients to MyMR will hopefully lead to better data regarding the number of patients using the service.

Electronic messaging has been in use since the 1990s. Patients across disease specialties have found electronic messaging systems to be convenient, time-saving and useful, and clinicians do not appear to report any significant adverse effects from their use(268). Jeong da et al(269) examined the clinical usefulness of electronic messaging between IBD patients and clinicians as part of a wider study of the use of a web-based self-reporting Crohn's symptom diary. The study authors retrospectively reviewed 686 messages sent by 152 patients from July 2012 to July 2014. Most messages regarded symptoms (55.5%), followed by self-reports about general health (28.4%) and treatment queries (10.3%). The doctor response rate to messages was low at 56.3% (our nursing team responded to 100% of enquiries using MyMR messaging). The popularity of this function of MyMR, as well as the potential cost and time-saving benefits, is an encouraging outcome of the service development.

A 2011 review of the impact of eHealth on care quality and safety(270) highlighted a need for two major areas for research. Firstly, there has been a gap between the proposed and demonstrated

cost benefits of eHealth technologies and thus a full economic analysis in any further larger study of the MyMR technology would be crucial to establishing its value. The authors also recommended rigorous evaluation of efficacy and cost-effectiveness throughout all stages of the technology's life cycle and careful attention to social and technical factors that might maximise the likelihood of successful implementation and adoption.

It is recognised that electronic health initiatives often place initial burdens on staffing and infrastructure when integrating the new technology(271) and workflow may be affected. Clinical and administrative engagement proved challenging due to the already overstretched resources amongst the team. Staff workload meant it was difficult to set aside the time required to develop and test MyMR and virtual clinic procedures fully. It became apparent that earlier engagement of administrative staff would have been particularly beneficial when the mapping exercise highlighted the complexity if procedures involved in running the virtual clinic, duplication of tasks, and excessive paperwork and postage. It was only once the live virtual clinic was attempted that logistical problems came to light. More rigorous testing of procedures may have ensured a smoother transition to the new way of working however this must be countered by the need to appreciate that such systems may never be 'perfect' and there is a practical limit to testing of processes before the need to transition in to practice where it can continue to be refined.

Reflection on the processes of implementing the digital VC highlighted the importance of connecting users of the virtual clinic (clerical and nursing) with IT developers. A disconnect between users and developers has previously been cited as a barrier to innovation in health IT(272). Most digital health records are developed by either established IT companies, internet start-ups, or academic research departments(272) and a strength of this project is the close working relationship between our IT and clinical departments.

Normalisation process theory provided a helpful framework to focus observations and reflect upon the process involved in normalising the digital VC into routine practice for staff. The NoMAD tool gave insight into the thoughts of the nursing and administrative staff who appeared to feel that whilst MyMR and the VC would become a normal part of their work, they didn't feel familiar with it yet and needed more support and training. Whilst they understood the potential, only some valued its effects on their working. NPT and the NoMAD tool also revealed that although staff were willing and understood the benefits of the MyMR VC, shortcomings in training, support and the website itself led to a loss of confidence in the tool. This was illustrated by the more negative responses to questions about how well the intervention would integrate into their usual work.

NPT predominantly appears to be used as a tool to analyse qualitative data and is often used as a coding framework when conducting thematic analyses(273). Godden et al examined healthcare professional attitudes to implementing telemedicine for chronic lung disease in a rural area of Scotland(274). They noted similar concerns to those experienced in our project, namely skill set workability and allocation of tasks and resources, with concerns about potential extra work being generated by facilitating easier communication between patients and staff. Concerns were also raised about adequacy of training for staff. Users queried adequacy of resources and the costs involved in setting up new IT initiatives, and the authors acknowledge that new telehealth systems often have high start-up costs, with benefits often seeing several years to realise(275).

Barriers and facilitators to implementing new e-health initiatives have been studied previously by Mair et al (276) who conducted a systematic review of factors that promote or inhibit the implementation of e-health initiatives , using NPT as a conceptual framework with which to analyse the literature. This revealed a growing emphasis on problems related to e-health systems' workability. Many of the included studies focused on the "ease of use" of the new systems for clinicians, with the underlying assumption that clinicians would be deterred from or resistant to using systems that added complexity or required additional effort or time. They also highlighted a need for more research into ways in which ways to engage with professionals to facilitate implementation of new health technologies. Facilitators to cognitive participation included the recruitment of local "champions" to legitimize participation in the implementation process. This was particularly helpful in the implementation of MyMR through the project manager and key patient panel member, as well as motivated nursing and medical colleagues. I found that it was important to have champions outside of the direct clinical team, ideally with dedicated time to commit to the project as given then current stresses our clinical team were under already it was difficult to devote time to furthering the project.

7.4.2 *Strengths and limitations*

The preliminary work for this service development was limited by both time and staff-working patterns and it was difficult to access nurses and clerical staff during very busy working days. In the workshop, the use of post-it notes to collate feedback meant that data was very high level and did not allow for in-depth exploration of nurses' views on their role. This exercise could have been improved by recording it and doing a more detailed qualitative analysis of the discussions. I felt that conducting the workshop as a group generated good discussion which helped me to understand the nurses' roles and needs better, but there is a risk that participants may not have felt able to speak so freely in front of colleagues and myself, having previously worked closely

with them. The workshop was not recorded and analysed in detail and this is a limitation of the service development. On reflection, a valuable learning opportunity may have been missed to explore early barriers and facilitators in more detail as opposed to recording more 'high-level' feedback.

The design of the service development could have been improved by earlier involvement of key stakeholders, more notably patients and administrative staff. I did gain feedback which helped the development of the site from the patient focus group (Chapter 5), but to be truly effective PPI, this should have been more of an iterative process and would ideally involve the participation of an active virtual clinic user to test-run the new electronic version before going live. It will be important to conduct further PPI by surveying users from the first months of virtual clinic follow-up to gain early feedback that will allow improvements to be made for subsequent users, as well as gaining early feedback from the healthcare team regularly using the service.

For the November 2018 virtual clinic, only 18/35 (51%) patients were registered MyMR users. The number of patients participating in the first digital VC was disappointing. This may not necessary fully reflect patient preference as it includes patients whom it was not possible to contact, as well as those who were contacted but declined. Although the views of patients who did not wish to register with MyMR and the digital VC were sought informally by staff when inviting patients, this should be documented in a more structured manner in future evaluation. Sanders et al examined patient reasons for non-adoption of digital patient records during qualitative work as part of a larger RCT(277) and cited respondent concerns of requirements for technical competence and operation of equipment; threats to identity associated with online records, independence and self-care; expectations and reluctance to risk potentially disruptive changes to existing services that were already highly valued. It is therefore important that future work we do with the virtual clinic involves careful patient education to provide explanation and reassurance to maximise adoption. For any new patients referred to the virtual clinic, the digital version will be offered primarily (over the paper version) with the aim of normalising this method to both patients and staff over time.

The creators of NPT support its use within a wide scope of applications. Whilst NPT was a useful tool to aid reflection, it proved confusing at times as there was often overlap of actions between the different constructs. I used it as a tool to document the actions of implementing the virtual clinic, but being a relatively new concept, was unable to find any comparable literature or experiences of its use in this context. It was however a very useful tool to aid reflection. Going forward with the experience I have gained from this service development, I would be interested

to use it as a tool in the planning stages of subsequent developments, to help anticipate and overcome any potential barriers to change early in the process.

It may be difficult to generalise the findings from this VC development to other centres due to potential inequalities in structure and resources. UHS is a large teaching hospital with a team of IBD nurses overseeing the care of many IBD patients. It has benefitted from funding from both the Health Foundation and as part of a Global Digital Exemplar award which has enabled significant expansion of its IT services. Sufficient staffing and a high level of IT would be required to support MyMR and the virtual clinic. We frequently experienced difficulties in releasing staff from clinical duties to help with developmental work and this problem will be seen throughout the health service. Lessons learned from the implementation of MyMR and the VC could still be of benefit to users of other health records (and more generally in implementing new IT services) in terms of potential hurdles and the importance of staff engagement.

7.5 Conclusion

Several self-management websites and digital records such MyMR have been described in the IBD literature in recent years(278). Whilst the concept of telemedicine in the management of IBD is not a new one, the majority are reliant on patients entering data which either prompts guidance on treatment or contact with the IBD team. Whilst MyMR utilises these aspects, the development of our clinical dashboard and protocol-based VC system appears to be a novel approach to administering and managing stable IBD patients. The service provides a truly interactive digital management system for both patients and healthcare staff.

I described the development of the interactive digital patient health record MyMR and the implementation of a digital virtual IBD clinic using MyMR as a platform. This was a team project in which I played a key role in the development and implementation. The project took place over several years and whilst the virtual clinic has now been implemented and over a thousand patients registered to MyMR, it is a work in progress, and will hopefully continue to develop and improve over time. Successes from the perspective of staff and patients were the access to test results and e-messaging on MyMR and achieving a better understanding of the processes involved in the running of the virtual clinic. This in turn has resulted in a clearer audit trail which has meant that the work that clinical and administrative staff perform can be fully recognised and appropriately reimbursed.

The process of implementation has been challenging and would benefit from enhanced attempts to engage key staff and patients early on in development processes. This project was primarily

focused on implementation for which normalisation process theory provided a structured theory-based means of reflecting on process. Whilst it is too early to examine outcomes from patient-users of MyMR and the virtual clinic, this will be an important area of focus in the future.

7.6 Other Information

7.6.1 *Funding*

This service development was partially funded by a grant from the Health Foundation as part of its Innovating for Improvement programme(266), and continues to be supported as part of the continuing development of MyMR under the Global Digital Exemplar award(136).

8 Discussion

8.1 Introduction

IBD is a challenging condition to manage. The chronicity of the disease means that patients will have lifelong contact with health services. The IBD Standards for the care of people with IBD(2) recommend different approaches (from diagnosis through to ongoing care) which include the use of diagnostic tools such as faecal calprotectin and self-management to improve patient care. New technologies are increasingly being used in healthcare and have the potential to transform how we deliver this. This thesis explores how these technologies can be used to augment the patient pathway from diagnosis and referral from primary care, to specialist management in secondary care, and then finally by providing patients with the tools to take ownership of managing their illness through supported remote monitoring.

This chapter summarises the contents of this thesis, pertinent findings of the research compared with existing literature, strengths/limitations, ideas for future research and development, as well as my own personal reflections on my research and thesis.

8.2 Overview of thesis

Chapter 1 provides background to the research presented in this thesis by describing the burden of IBD, how it may be diagnosed (including the use of FC in diagnosis and monitoring), traditional outpatient management and the challenges this poses to care providers, before outlining the aims of the research.

Chapter 2 presents a systematic review of the effects of digital self-management interventions (which provide a two-way interaction between patients and healthcare providers) on IBD patient outcomes.

Chapter 3 presents the methodology used in this thesis. I introduced the different research paradigms and reflected upon my own research paradigm. I describe the importance of developmental work as directed by the MRC framework for complex interventions, the methodology of systematic review, qualitative data analytical strategies, PPI and qualitative research, and the uses of Normalisation Process Theory in research and development.

Chapter 4 presents a pilot study of FC testing in primary care as part of a local service evaluation. This chapter describes FC and its utility in both diagnosis and monitoring of IBD in more detail. Although not directly a self-management focused project, the study was relevant to the thesis and introduces the first step of the IBD patient pathway and FC testing.

My Medical Record forms the basis for much of the research conducted in this thesis. Chapter 5 summarises my contributions to the developmental work involved in refining the patient-facing version of the website and linking home FC testing to facilitate the feasibility study described in Chapter 6.

Chapter 6 presents the main research project in my thesis: a study of the feasibility and acceptability of the combination of a supported self-management website and home FC testing to monitor patients who had stopped a medication for IBD instead of usual outpatient care. I used a mixed method approach, collecting quantitative data and conducting qualitative interviews to establish patient-acceptability in greater depth, and reflected on my involvement as the sole researcher.

Moving on from the developmental work on MyMR conducted in Chapter 5, Chapter 7 describes a service development to create a clinical version of MyMR for members of the IBD team to digitally monitor more stable IBD and replace the existing paper-based Virtual IBD clinic. This chapter focuses on the learning and understanding derived from the development processes, rather than on outcomes from the service itself, but this will be an area for future work. I used Normalisation Process Theory(160) to provide structure when reflecting on the challenges and successes of implementing the service.

8.3 Comparison with existing literature

This section summarises how this thesis adds to current knowledge and to the existing literature on different aspects of IBD patient care.

The calprotectin testing in primary care pilot study supports current understanding of FC as a highly effective screening tool for differentiating symptoms of IBD from those of irritable bowel syndrome(36). The study used a cut-off of <50 µg/g as a 'negative' test, 50-100 µg/g as 'indeterminate' and >100 µg/g as a 'positive' test. Negative predicative values ranged from 100% to 93.5% based upon a range of FC from 50-250. There is no clear UK consensus on cut-off for FC testing as a screening tool(36). In our cohort the optimal cut-off could be argued as either 150 µg/g (sensitivity 95.8%, specificity of 52.3%) or 200 µg/g (sensitivity 91.7%, specificity rose to 85.3%). There are however significant compromises to both in terms of sensitivity and ensuring appropriateness of further investigation. Despite a negative (<50 µg/g) FC, a significant proportion of patients with negative FC were referred to secondary care (more than 1 in 10), but still lower than in a similar study quoting 30% (192). Almost half of this group underwent endoscopy, implying that at a significant proportion of these referrals were still considered appropriate by the

secondary care physician. No cases of IBD were identified in this group and this reinforces the utility of FC as a valuable screening tool. This message needs to be reinforced to minimise risk to patients in undergoing invasive investigations and to ensure appropriate use of outpatient resources. The utility of FC as a screening test in terms of patients being spared investigative procedures is further demonstrated by the observation that a negative FC appeared to influence GPs' plans to refer patients to secondary care. Reversal of plans to refer occurred 24/55 (43.6%) times when FC was negative, versus no decision changes when FC was positive. The influence of a negative test on GP decision-making and intention to refer has not been explored previously in the IBD literature.

Time to diagnosis in IBD is important to minimise treatment delay and longer-term complications. Although the mean time to specialist assessment in patients diagnosed with IBD was less than the overall mean for all diagnoses (39.9 vs 70.6 days for outpatient clinic review), this still falls short of the 30 day target for specialist assessment of suspected IBD cases proposed by NICE(4). Time from GP referral to endoscopy was even longer at a mean of 71.3 days for patients diagnosed with IBD. As part of a new suspected IBD pathway I proposed the use of a straight-to-test endoscopy which has been used successfully in younger patients unlikely to have significant contraindications to colonoscopy and bowel preparation(196). Straight-to-test has already been used to good effect locally through use of a direct access IBD-physician delivered flexible sigmoidoscopy in established IBD patients at UHS following call to an IBD flareline. A similar model for new referrals could provide prompt specialist investigation and treatment and would be an opportunity for future research and service improvement.

There are now several digital IBD platforms available for use, with more under development. They appear to acceptable to patients, and have potential benefits including improved quality of life and cost savings. The latter is predominantly realised through a reduction in outpatient and appointments and expensive drug treatments such as biologics through closer monitoring, allowing resources to be fed back into patients care. Development of digital portals requires significant resources (something I experienced first-hand) and this could present a barrier to future adoption. The literature on supported self-management websites for IBD is largely dominated by the Constant Care group(1, 127, 174, 208, 228) in Denmark. Their early research explored the use of a self-management website in more stable patients with UC, but over time they have developed to include more complex patients with UC or Crohn's and those receiving biological therapy(1) and thus a more severe disease subgroup. To build on and extend the current evidence base, I chose to conduct a feasibility study of self-management using monitoring

via MyMR and home FC in only those patients who had stopped a medication for IBD and thus were at an increased risk of a flare-up of their disease.

One of the most interesting outcomes of the feasibility study emerged from the qualitative interview data – with themes arising around stopping medication such as fear of a flare and the strong need for reassurance, which appeared to be provided by the portal and FC testing. The key discussions regarding home-monitoring revolved around the themes of usability and fitting it into daily life (and how these aspects could be improved). In terms of feasibility, recruitment was a challenge (discussed in section 5.5 and below in 7.4). This did not appear to be such a problem in less selective studies with broader inclusion criteria. Smaller recruitment figures were seen in studies with more limited criteria, for example Pedersen et al(1) who recruited patients who had lost response to infliximab therapy. The study ran for just under 2 years, but was a pilot study, so numbers were not expected to be high, but the authors did not provide a target sample size nor define recruitment time-frames therefore it is difficult to draw comparisons. I defined feasibility for the study using different outcome measures, including study retention: 80% successful completion of at least 5 out of 7 home FC tests, with no periods without login to MyMR of greater than 3 consecutive months, questionnaire completion 70%. Retention for the study was good with 80% (8/10) participants successfully completing a minimum of 5 FC tests and 7 of these patients completing all tests. 7/10 participants (70%) completed the minimum requirement for completion of both FC test and MyMR log in, falling just short of the 80% target for retention. This compares to 86% (1) in a small pilot study which required weekly log in and data entry to a self-management website and laboratory FC. Walsh et al(130) demonstrated high retention rates of 90% however retention in this study was simply defined as “ongoing completion of questionnaires” in a similar pilot study of monthly home FC smartphone testing and UC True Colours self-management site. I found that most feasibility study patients required repeat prompting to conduct their home calprotectin testing and monthly IBD Control surveys. There is little in the current literature as to what extent patients were reminded to complete study requirements and it does call into question the feasibility of a larger scale study. Automated reminders would be an important step to reduce researcher workload as well as providing a more robust reminder method. Although small, my study provided useful insight into the logistics of running a larger study and the resources that might be required.

The integration of faecal calprotectin testing into routine monitoring using digital platforms has been increasingly used in recent years. In previously studied digital platforms, FC monitoring has taken place either through postal laboratory specimens, point of care FC testing (conducted by a practitioner), and increasingly using smartphone technology such as QuantOn Cal® or IBDoc®.

Only one study in the systematic review (Chapter 2) utilised home FC testing – Walsh et al(130) successfully integrated IBDoc® into their True Colours electronic platform which was reportedly successful but the level of IT input required for the integration was not reported. The IT team at UHS were able to set up an interface between QuantOn Cal® and MyMR rapidly (one IT specialist wrote the code required in less than one day). The integration did not appear to be a significant barrier in our UK-based studies, but both were developed at large teaching hospitals with significant IT infrastructure, with UHS benefitting from significant IT investment through the GDE award. Pulling all the patient data into a single portal such as MyMR can be advantageous as all the information needed to guide treatment decisions (such as initiating or stopping medications) is readily available to both patients and healthcare providers.

I presented the development of MyMR in 2 parts. The refinement of the patient-facing version of MyMR (Chapter 5) required to conduct the feasibility study was largely descriptive. I was more closely involved in the further development of the clinical MyMR site and dashboard (Chapter 7) required for the implementation of a digital virtual IBD clinic. I used Normalisation Process Theory(160) as a novel way to frame this development work and reflect upon it. Whilst NPT has not been used previously in the field of IBD, it has been used in e-medicine to study barriers and facilitators to implementing digital interventions for other long-term conditions. This chapter contributes to current understanding of e-health initiatives in chronic disease by reflecting on barriers and facilitators to change through novel use of the NPT tool. Adequacy of training for staff has previously been identified as a significant barrier to change and this was certainly a concern of our staff reported using the NoMAD toolkit. Mair et al (276) conducted a systematic review of factors that promote or inhibit the implementation of e-health initiatives , using NPT as a conceptual framework with which to analyse the literature. Inhibitors included potential problems relating to e-health systems' workability. Many of the included studies focused on the "ease of use" of the new systems, with the underlying assumption that clinicians would be deterred from using systems that added complexity or required additional time. My service evaluation supports these findings as illustrated by the feedback gained from staff using the NoMAD toolkit with frequent comment on difficulties on using the new system and the time taken to initiate this new way of working. One of the major facilitators to cognitive participation included the recruitment of local "champions" to legitimize participation in the implementation process. It was difficult for clinical team members to devote time to furthering the project and protected time will need to be made available for subsequent developments.

8.4 Strengths and limitations

One of the strengths of this thesis is that it provides a comprehensive overview of three different aspects of the IBD patent pathway, from primary care referral and diagnosis, through active disease monitoring, to longer term follow-up of more stable patients. FC has been a hugely useful tool in the armoury of IBD management and it features across all 3 projects, particularly now it is an integral part of the MyMR site. For each project, I tried to take a systematic approach to the write-up, for example using the CONSORT checklist(149) when reviewing papers for the systematic review, using the Squire 2.0 guidelines(259) to present the service development, or using NPT(160) as a tool to reflect on the challenges of implementation.

Chapter 4, pilot FC testing in primary care, whilst not a self-management intervention, helps to build understanding of the ways in which patients arrive at a diagnosis of IBD and introduces FC, a valuable tool in both diagnosis and disease monitoring. One of the strengths of this study was its relatively large sample size compared to similar literature(189, 279), with over 400 FC samples processed. One of the more unique features of the pilot study was asking GPs to state their intention to refer or not and to examine whether the FC results appeared to influence this, and this would prove an interesting avenue for further qualitative study to determine if there were other influences.

The feasibility study of home-monitoring with FC and MyMR website clearly had a very small sample size therefore it is very difficult to draw significant conclusions from the quantitative data available. It was however still a very useful exercise in gaining information that could inform further larger scale study. The technologies of QuantOn Cal® and MyMR appeared to work well together. Further larger scale study would not be feasible without making some changes to extend inclusion criteria, as well as ensuring a more robust automated means of following up study patients via MyMR. Adaptations to inclusion criteria, for example lengthening the time since treatment cessation and/or changing the criteria to include treatment de-escalation as well as cessation could potentially increase the available pool. Study procedures such as monitoring of patient-entered data and reminding patients to complete study questionnaires, whilst feasible for a small number, are unlikely to be manageable for a larger cohort, and MyMR would need to undergo further developments to ensure robustness on a larger scale.

The integration of the two technologies of MyMR and home FC testing was relatively straightforward for our experienced IT team working with a sophisticated digital platform. Although applicability may be reduced at other centres without similar IT platforms, the Doctor's Portal website supported by QuantOn Cal® (which displays results to healthcare providers almost

instantly and sends automated emails) means that home monitoring is not dependent on platforms such as MyMR and be accessed immediately by any provider, making this aspect of the study more accessible for future study or clinical use. Home FC testing provides rapid assessment of disease activity compared with laboratory testing (which can take over a week to obtain a result locally). It is a convenient test for patients, reducing the need to travel to healthcare providers to deliver specimens, and appeared to be well-liked by our small study population, providing reassurance to most.

Another of the intentions of home monitoring would be to improve resource utilisation by moving more care into patients own homes, thereby reducing the need for hospital appointments, travel etc. There is also a potential to improve disease outcomes through monitoring, with a reduction in IBD-related complications such as surgery and hospitalisation. Although the costs of home versus laboratory testing are known (around £40 versus £22.79) and tests such as FC have the potential to replace the need for colonoscopy (which costs around £480 per procedure(36)), the study lacked an economic analysis and this (from both a health services and societal perspective) should form an important part of any subsequent larger study. Another financial aspect to consider is the cost (and convenience) of training of users. The manufacturers provide a very instructional how-to video and there may be work to be done exploring whether patients require face to face training such as in my study or if the educational video is sufficient to establish testing. Testing is also dependent on patient motivation, with some users requiring frequent prompting, but this may the case across many different self-management interventions, and as discussed early in this thesis, self-management may not be for everyone and patient selection needs to be explored through qualitative research.

The qualitative interviews provided insight into patient experience of both stopping medication and on the acceptability of home monitoring via MyMR and calprotectin but were obviously limited by the small numbers. Although I observed themes emerging, I do not feel that I reached data saturation and more participants would have made the data more robust. Whilst most patients provided positive feedback for the home stool testing, there were some software limitations within the QuantOn Cal® app that meant testing was not possible for all participants.

Whilst early MyMR developmental work was guided by patient feedback from the IBD open day, this could have been a more iterative process to be effective PPI. It was helpful to have more informal feedback on design issues relating to MyMR via an interested member of the IBD patient panel however as a member of staff, this feedback may not be truly reflective of lay patients. Similarly, for the clinical version of the site, although I engaged with nursing and medical staff via

a workshop, regular meetings and feedback sessions, the NPT reflective work highlighted that early involvement of clerical staff, key stakeholders in implementing a new way of working, will be key to any future successes. Whilst UHS has benefitted from recent investment in IT services which has allowed the further development of both MyMR and home FC testing, not all centres will have the capabilities to support similar projects and most centres use different software which may not be compatible with those developed in these projects. However, lessons were learned in terms of how to develop digital interventions such as these, and more generally how to better engage key stakeholders. As the NHS becomes increasingly digitalised it is important to refine and move these technologies forward.

8.5 Future research, development and dissemination

All three projects have potential to be developed further. The GP calprotectin project led to the development of a protocol to run a positive FC clinic and it would be valuable to assess the effects on both patient outcomes (for example time to diagnosis versus usual care pathways) and financial implications through a formal service and financial evaluation. The exploratory feasibility study highlighted difficulties in recruiting from a more limited pool of potential patients. Future study could take the form of a randomised controlled trial of MyMR and home FC testing versus usual care, but in view of the small numbers studied and the relatively new technology of MyMR, it may be more prudent to conduct a larger scale feasibility study prior to RCT, perhaps with revised inclusion criteria and a more developed version of MyMR. Finally, the development of the digital MyMR virtual clinic provided valuable insight into barriers and facilitators to implementation of a new technology within the NHS, but the next step will be to conduct a full-service evaluation, assessing the impact upon key stakeholders such as nursing and clerical staff. All three projects could benefit from increased patient and public involvement throughout the developmental stages and through further qualitative work.

The primary care faecal calprotectin pilot study has been presented at the British Society of Gastroenterology (BSG) annual meeting and is being prepared for submission to a primary care journal to increase awareness in primary care. The feasibility study has been presented to colleagues at a meeting of Wessex gastroenterologists, has been submitted to the BSG and is being prepared for journal publication. A successful business case has now been accepted at UHS for the use of home faecal calprotectin monitoring in selected cases of IBD because of this research. When more data and experience of the digital virtual clinic has been collected this will be submitted for publication as a service development.

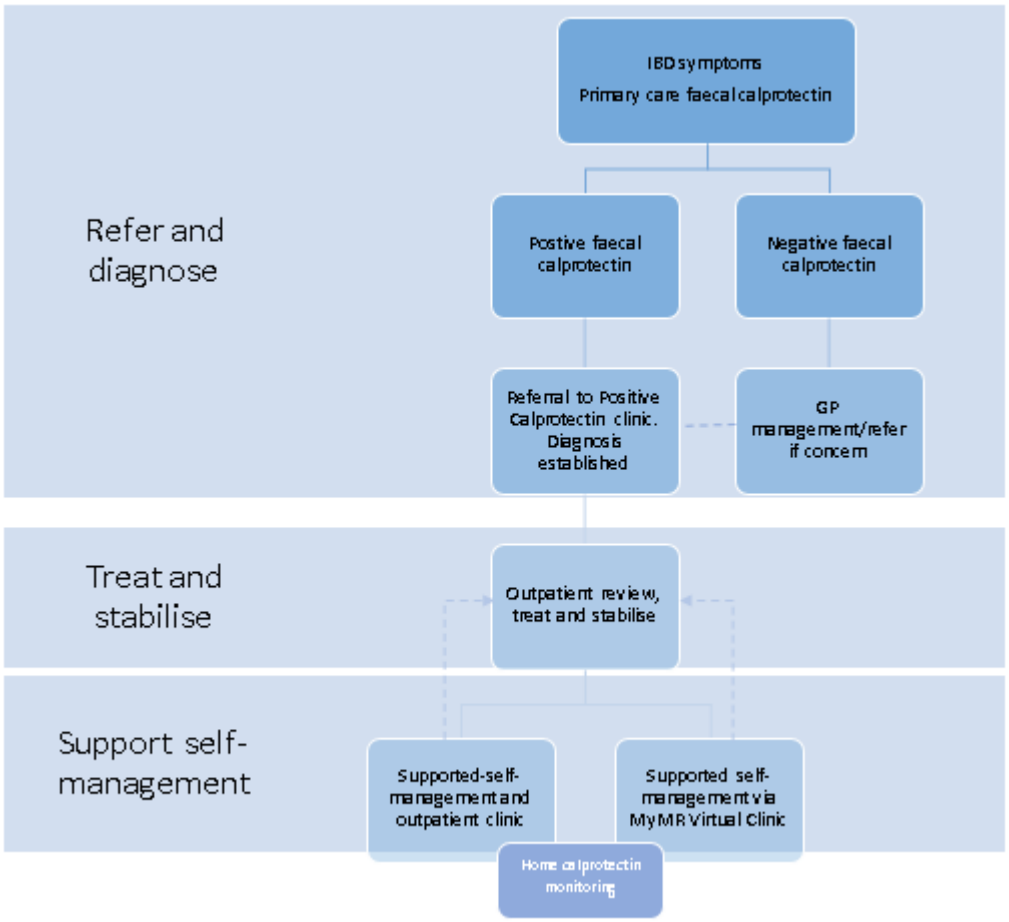
8.6 Personal reflections

My part-time DM spanned 3 years between September 2014 to 2019, with 2 years out for periods of maternity leave. I conducted the research on a 60% full-time equivalent basis and conducted medical registrar on call shifts for 2 out of 6 weeks before returning to clinical training in January 2019. Managing family life, work and research has been challenging at times but has provided me with increased resilience and time management skills which will be valuable in my future career. My DM has allowed me to develop a whole new set of research skills, conducting a systematic review, service evaluation, applying for ethical approval and funding grants and designing and conducting a feasibility study. One of the most enjoyable aspects was the opportunity to develop and refine my qualitative research skills. I received training in qualitative research methods, including qualitative interviewing and thematic analysis which helped with the design and implementation of the qualitative elements of my feasibility study. Being able to talk to IBD patients about dealing with the impact of IBD was extremely enlightening and has reinforced my desire to further a subspecialty interest in IBD and support local research.

8.7 Conclusion

This thesis comprises developmental and research work exploring the role of new technologies in three key parts of the IBD patient journey: referral from primary care and diagnosis, supported self-management in established IBD, and remote management in stable IBD. Figure 63 illustrates how these technologies can be delivered.

Figure 63: The IBD Patient Journey



There are many areas in which we can improve the care we provide for patients with IBD. FC is a reliable tool which may give GPs greater confidence when differentiating between IBD and IBS. The pilot study suggested that using FC can alter GP decision-making and guide appropriate referrals to secondary care clinics. Once the diagnosis of IBD is established, most patients remain under outpatient follow-up which is not always responsive to the needs of patients with this unpredictable disease. The exploratory feasibility study suggests that home calprotectin testing and use of a self-management website, whilst acceptable to patients, was difficult to recruit to and numbers were very small. Any subsequent study would need careful consideration and a review of the inclusion criteria. Providing patients with self-management tools can provide significant reassurance to patients vulnerable to the risk of disease flares, as illustrated by the qualitative interviews. Establishing a digital virtual clinic for patients with stable IBD has provided better understanding of the processes behind our current IBD service provision and how to facilitate the implementation of new services. Whilst there have been several implementation challenges, the service is now up and running, with over a third of patients registered to the MyMR site, appropriate financial tariffs in place, and staff can envisage its place in the routine

care of IBD patients. Continued improvement will require full engagement with all stakeholders, with a focus on patients, administrative staff, and nursing colleagues.

IBD is a life-changing disease, and early diagnosis, recognition and treatment of disease flares is crucial to establishing control. Patients with IBD require ongoing treatment and support throughout their lives and exploring ways of using new technologies to improve the patient pathway from diagnosis through to long-term follow-up should be a priority for future IBD research.

9 Appendix

Appendix A

Appendix A.1 IBD Standards – pre—diagnosis and ongoing care

Statement 2.1

Clear pathways and protocols for investigating children and adults with persistent lower gastrointestinal symptoms should be agreed between primary and secondary care and should include guidance on the use of faecal biomarker tests in primary care to aid rapid diagnosis.

Statement 2.2

Patients who are referred with suspected IBD should be seen within four weeks, or more rapidly if clinically necessary.

Statement 2.3

Patients presenting with acute severe colitis should be admitted to a centre with medical and surgical expertise in managing IBD that is available at all times.

Statement 2.4

All patients should be provided with a point of contact and clear information about pathways and timescales while awaiting the outcome of tests and investigations.

Section 7: Ongoing Care

Statement 7.1

A personalised care plan should be in place for every IBD patient, with access to an IBD nurse specialist and telephone/email advice line

Statement 7.2

Patients should be supported in self-management, as appropriate, through referral or signposting to education, groups and support.

Statement 7.3

Clear protocols should be in place for the supply, monitoring and review of medication across primary and secondary care settings.

Statement 7.4

Pain and fatigue are common symptoms for IBD patients and should be investigated and managed using a multidisciplinary approach including pharmacological, non-pharmacological and psychological interventions where appropriate.

Statement 7.5

Any reviews and changes of treatment in primary or secondary care should be clearly recorded and communicated to all relevant parties within 48 hours.

Appendix B

Appendix B.1 CONSORT checklists for systematic review papers

Elkjaer, M., et al., *E-health empowers patients with ulcerative colitis: a randomised controlled trial of the web-guided 'Constant-care' approach.* Gut, 2010. 59(12): p. 1652-61

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1652
	1b	Structured summary of trial design, methods, results, and conclusions	1652
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	1653
	2b	Specific objectives or hypotheses	1653
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	1653
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	x
Participants	4a	Eligibility criteria for participants	1653
	4b	Settings and locations where the data were collected	1653-4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	1653-4
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	1654
	6b	Any changes to trial outcomes after the trial commenced, with reasons	x
Sample size	7a	How sample size was determined	x
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			1653
Sequence	8a	Method used to generate the random allocation sequence	

generation	8b	Type of randomisation; details of any restriction (such as blocking and block size)	1653
Allocation Concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	1653
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	1653
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	n/a
	11b	If relevant, description of the similarity of interventions	1654
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	1654
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n/a
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	1655
	13b	For each group, losses and exclusions after randomisation, together with reasons	1655
Recruitment	14a	Dates defining the periods of recruitment and follow-up	x
	14b	Why the trial ended or was stopped	x
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	1656-7
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	1654
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	1657-9
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All-important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	1658
Discussion			

Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	X minimal 1660
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to more severe IBD but not outside centre 1660
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	1660 minimal, other evidence not considered
Other information			
Registration	23	Registration number and name of trial registry	x
Protocol	24	Where the full trial protocol can be accessed, if available	x
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	1660 (brief)

A Randomized, Controlled Trial of Home Telemanagement in Patients with Ulcerative Colitis (UC HAT)

Cross et al, USA 2012

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2
	2b	Specific objectives or hypotheses	2
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	2
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	2(brief, adults with UC)
	4b	Settings and locations where the data were collected	3 (brief)

Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	3
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	4
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	4
	7b	When applicable, explanation of any interim analyses and stopping guidelines	4
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	3
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	3
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	x
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	3
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	3
	11b	If relevant, description of the similarity of interventions	3
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	4
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	5
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	11
	13b	For each group, losses and exclusions after randomisation, together with reasons	11, no reasons
Recruitment	14a	Dates defining the periods of recruitment and follow-up	2
	14b	Why the trial ended or was stopped	x
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	14
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	14, not clear

Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	5-6
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All-important harms or unintended effects in each group	x
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	6-7
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	7
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	7
Other information			
Registration	23	Registration number and name of trial registry	x
Protocol	24	Where the full trial protocol can be accessed, if available	x
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	8

eHealth: individualisation of infliximab treatment and disease course via a self-managed web-based solution in Crohn's disease

Pedersen et al, Denmark 2012(1)

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	x
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	840
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	841
	2b	Specific objectives or research questions for pilot trial	841
Methods			

Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	841
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	846
Participants	4a	Eligibility criteria for participants	841
	4b	Settings and locations where the data were collected	841
	4c	How participants were identified and consented	x
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	842, 843
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	845, 846
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	846
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	x
Sample size	7a	Rationale for numbers in the pilot trial	x
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	n/a
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	n/a
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	n/a
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	n/a
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	n/a
	11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	843
Results			
	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly	844

Participant flow (a diagram is strongly recommended)		assigned, received intended treatment, and were assessed for each objective	
	13b	For each group, losses and exclusions after randomisation, together with reasons	844
Recruitment	14a	Dates defining the periods of recruitment and follow-up	x
	14b	Why the pilot trial ended or was stopped	x
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	844
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	843-846
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	843-845
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	n/a
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	845,846
	19a	If relevant, other important unintended consequences	846
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	848
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	x
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	847,848
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	848
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	x
Protocol	24	Where the pilot trial protocol can be accessed, if available	x
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	x
	26	Ethical approval or approval by research review committee, confirmed with reference number	843

eHealth: Individualization of Mesalazine Treatment Through a Self-Managed Web-based Solution in Mild-to-moderate Ulcerative Colitis Pedersen et al, Denmark 2014				
Section	Item	Standard CONSORT description	Extension for pragmatic trials	Page
Title and abstract	1	How participants were allocated to interventions (e.g., “random allocation,” “randomised,” or “randomly assigned”)		n/a
Introduction				
Background	2	Scientific background and explanation of rationale	Describe the health or health service problem that the intervention is intended to address and other interventions that may commonly be aimed at this problem	2277
Methods				
Participants	3	Eligibility criteria for participants; settings and locations where the data were collected	Eligibility criteria should be explicitly framed to show the degree to which they include typical participants and/or, where applicable, typical providers (e.g., nurses), institutions (e.g., hospitals), communities (or localities e.g., towns) and settings of care (e.g., different healthcare financing systems)	2277
Interventions	4	Precise details of the interventions intended for each group and how and when they were actually administered	Describe extra resources added to (or resources removed from) usual settings in order to implement intervention. Indicate if efforts were made to standardise the intervention or if the intervention and its delivery were allowed to vary between participants, practitioners, or study sites	2277-8
			Describe the comparator in similar detail to the intervention	n/a
Objectives	5	Specific objectives and hypotheses		2277

Outcomes	6	Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors)	Explain why the chosen outcomes and, when relevant, the length of follow-up are considered important to those who will use the results of the trial	2277 No discussion on length of follow up
Sample size	7	How sample size was determined; explanation of any interim analyses and stopping rules when applicable	If calculated using the smallest difference considered important by the target decision maker audience (the minimally important difference) then report where this difference was obtained	x
Randomisation—sequence generation	8	Method used to generate the random allocation sequence, including details of any restriction (e.g., blocking, stratification)		n/a
Randomisation—allocation concealment	9	Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned		n/a
Randomisation—implementation	10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups		n/a
Blinding (masking)	11	Whether participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment	If blinding was not done, or was not possible, explain why	n/a
Statistical methods	12	Statistical methods used to compare groups for primary outcomes; methods for additional analyses, such as subgroup analyses and adjusted analyses		2278-9
Results				
Participant flow	13	Flow of participants through each stage (a diagram is strongly recommended)—specifically, for each group, report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analysed for the primary outcome;	The number of participants or units approached to take part in the trial, the number which were eligible, and reasons for non-participation should be reported	2279 No discussion on number approached

		describe deviations from planned study protocol, together with reasons		
Recruitment	14	Dates defining the periods of recruitment and follow-up		2277 Brief
Baseline data	15	Baseline demographic and clinical characteristics of each group		2280
Numbers analysed	16	Number of participants (denominator) in each group included in each analysis and whether analysis was by "intention-to-treat"; state the results in absolute numbers when feasible (e.g., 10/20, not 50%)		2279-82 Mostly
Outcomes and estimation	17	For each primary and secondary outcome, a summary of results for each group and the estimated effect size and its precision (e.g., 95% CI)		2279-82
Ancillary analyses	18	Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating which are prespecified and which are exploratory		n/a
Adverse events	19	All important adverse events or side effects in each intervention group		2282
Discussion				
Interpretation	20	Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes		2282-3
Generalisability	21	Generalisability (external validity) of the trial findings	Describe key aspects of the setting which determined the trial results. Discuss possible differences in other settings where clinical traditions, health service organisation, staffing, or resources may vary from those of the trial	X No discussion of generalizability
Overall evidence	22	General interpretation of the results in the context of current evidence		2282-4

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

De Jonge et al, Netherlands 2017

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	959
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	959
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	959-60
	2b	Specific objectives or hypotheses	962
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	961
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	961
	4b	Settings and locations where the data were collected	961
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	961-2
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	962-3
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	963
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	961
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	961
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	961
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	961

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	961
	11b	If relevant, description of the similarity of interventions	962
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	963
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	963
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	963
	13b	For each group, losses and exclusions after randomisation, together with reasons	963
Recruitment	14a	Dates defining the periods of recruitment and follow-up	964
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	964
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	964
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	964-5
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	965
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	959 – safety endpoints of flares, steroids, admissions etc but no formal section on safety. Brief mention of one pt developing cancer.
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	966

Generalisability	21	Generalisability (external validity, applicability) of the trial findings	966-7
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	966
Other information			
Registration	23	Registration number and name of trial registry	963
Protocol	24	Where the full trial protocol can be accessed, if available	x
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	963

Feasibility of TrueColours Ulcerative Colitis **Walsh et al, UK 2017**			
Section/Topic	**Item No**	**Checklist item**	**Reported on page No**
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	51
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	n/a - thesis
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	52-3 and preceding chapters of thesis
	2b	Specific objectives or research questions for pilot trial	53,55
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	x
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	58
	4b	Settings and locations where the data were collected	60, and elsewhere in thesis
	4c	How participants were identified and consented	55,58
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	59-61
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	61-2

	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	n/a
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	x
Sample size	7a	Rationale for numbers in the pilot trial	54, brief
	7b	When applicable, explanation of any interim analyses and stopping guidelines	x
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	n/a
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	n/a
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	n/a
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	n/a
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	n/a
	11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	x
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	64-6, no diagram
	13b	For each group, losses and exclusions after randomisation, together with reasons	n/a
Recruitment	14a	Dates defining the periods of recruitment and follow-up	64
	14b	Why the pilot trial ended or was stopped	x
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	x
Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	64-70
Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	64-70, no CIs
Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	x

Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	x
	19a	If relevant, other important unintended consequences	x
Discussion			
Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	73-5
Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	73-5
Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	x
	22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	72-5
Other information			
Registration	23	Registration number for pilot trial and name of trial registry	x
Protocol	24	Where the pilot trial protocol can be accessed, if available	54
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	iii, brief
	26	Ethical approval or approval by research review committee, confirmed with reference number	56

A Randomized Controlled Trial of TELEmedicine for Patients with Inflammatory Bowel Disease (TELE-IBD)

Cross et al, USA 2019

Section/Topic	**Item No**	**Checklist item**	**Reported on page No**
Title and abstract			
	1a	Identification as a randomised trial in the title	472
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	472-3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	473
	2b	Specific objectives or hypotheses	473
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	473

	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n/a
Participants	4a	Eligibility criteria for participants	473
	4b	Settings and locations where the data were collected	473
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	473-4
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	474
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	474
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	473
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	473
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	473
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	x
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	n/a
	11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	474
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	474
Results			

Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	474
	13b	For each group, losses and exclusions after randomisation, together with reasons	474-5
Recruitment	14a	Dates defining the periods of recruitment and follow-up	x
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	476-7
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	474-5
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	477-480
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	n/a
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n/a
Harms	19	All important harms or unintended effects in each group	x
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	480
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	x
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	480
Other information			
Registration	23	Registration number and name of trial registry	474
Protocol	24	Where the full trial protocol can be accessed, if available	x
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	481

Appendix B.2 Standards for Reporting Qualitative Research (SRQR)

Feasibility and acceptability of an IBD supported self- management website and home faecal calprotectin-testing in treatment cessation

http://www.equator-network.org/reporting-guidelines/srqr/

Page/line no(s).

Title and abstract

Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	n/a – Chapter part of wider thesis
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	n/a - Chapter part of wider thesis, but would include in standalone publication

Introduction

Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	73
Purpose or research question - Purpose of the study and specific objectives or questions	74

Methods

Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	33-5, 38, 115-6
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	107, 161-2
Context - Setting/site and salient contextual factors; rationale**	107
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	107-9

Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	106-7
Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	115-116
Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection, if/how the instrument(s) changed over the course of the study	116
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	120-1
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	116
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	116
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	-

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	138-152
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	138-152

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	153-160
Limitations - Trustworthiness and limitations of findings	160-162

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	107
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	107

Appendix C

Appendix C.1 GP invitation letter to supply further information

University Hospital Southampton NHS
NHS Foundation Trust

Gastroenterology
CE145 Level E, Mailpoint 134
Southampton General Hospital
Tremona Road
Southampton
SO16 6YD

Telephone: 023 8120 8462
Fax: 023 8120 5203

Date:

Service evaluation: Pilot faecal calprotectin testing for suspected inflammatory bowel disease in primary care

R.e. Patient: *Insert Patient's name and address, NHS number*

Dear *Dr's name and title*

You recently took part in a pilot testing programme of faecal calprotectin for the above named patient with suspected inflammatory bowel disease.

We have been undertaking an evaluation of the service and have found that your patient had a positive faecal calprotectin on ..... but cannot find record of them having been referred to University Hospital Southampton for further investigation.

We appreciate that this may be due to a number of reasons such as referral elsewhere, resolution of symptoms etc., or perhaps an administrative error has occurred on our part.

We are keen to ensure that all patients are followed up appropriately and would therefore be very grateful if you could review your patient records and return the enclosed reply slip with further details. We will endeavour to arrange any outstanding IBD outpatient appointments as appropriate.

Many thanks for your kind assistance.

With best wishes,

Yours sincerely,

Dr Nicola Taylor
IBD Research Fellow

Dr Fraser Cummings
IBD Consultant and Clinical Lead

University Hospital Southampton NHS
NHS Foundation Trust

Reply slip:

Please complete and return to:

Dr Nicola Taylor
IBD Research Fellow
Gastroenterology
CE146 Level E, Mailpoint134
Southampton General Hospital
Tremona Road
Southampton
SO16 6YD

Telephone: 023 8120 8462
Fax: 023 8120 5203

Service evaluation: Pilot faecal calprotectin testing for suspected inflammatory bowel disease in primary care

We would be very grateful if you could let us know of any reason(s) why your patient may not have been referred to UHS for further investigation of a raised faecal calprotectin (please tick as appropriate and provide further details if available).

Reason	Please tick	Further details
Resolution of symptoms		
Alternative diagnosis reached		
Patient declined referral		
Patient moved out of area		
Referred to another hospital		
Referral made, no UHS appointment received		
Other		

Do you feel your patient still needs to be seen in gastroenterology outpatients? Yes ☐ No ☐

Many thanks for your time in completing this form.

Appendix D

Appendix D.1 QuantOn Cal® EC certificate

EC Certificate

mdc medical device certification GmbH
Notified Body 0483
herewith grants

Immundiagnostik AG
Stubenwald-Allee 8a
64625 Bensheim
Germany

for the scope

QuantOn Cal - immunological rapid test for the determination of fecal Calprotectin in combination with evaluation by smartphone app

the

EC Design Examination Certificate

The examination of the design of the product by mdc has proven that the design meets the requirements according to

Annex III – Section 6
of the Council Directive 98/79/EC

of the European Parliament and of the Council of
27 October 1998 on in vitro diagnostic medical devices.

Valid from	2016-02-10
Valid until	2021-02-09
Registration no.	D1371500004
Report no.	P15-01752-60953
Stuttgart	2016-02-10

Head of Certification Body

mdc medical device certification GmbH
Kriegerstraße 6

Appendix D.2 Semi structured topic guide

- Introduction
- About the session
    - Interactive, feedback session on experiences so far and future developments.
- Agenda: Recent updates, updates under development, demo site
- Check usage/experience
    - Do all the group have access to MyMR?
    - How often do you use it?

    What do you mainly use it for?
    - Recent updates to IBD site:
- New layout
- Accessing blood tests – has anyone had opportunity to use this function yet? (show results section). How can we make this more meaningful – colour coding? Normal ranges etc?
- IBD Control survey (demo) – quick new survey that measures disease activity from patients' perspective.
    - Is this something you as a patient might be prepared to fill out once in a while?
    - How often do think you would mind doing it? Fortnightly, monthly etc? If something has changed?
- FC (show in results section)
    - New rapid measure of disease activity
    - home testing vs hospital testing – pros of at home
    - plan for study – frequency – monthly likely reasonable?
    - Is this something you would find a useful addition to the site? Why?
- Pathology requests
    - Do you think it is useful to see your blood tests?
    - If you need a blood test, how do you usually access the test form?
    - Would you find it useful to be able to print it off/have electronically?
- Virtual clinic
    - Plans for VC project –stable patients, f/u using MyMR – blood tests, colonoscopy reminders, IBD Control survey.
    - Thoughts on monitoring requirements, frequency of monitoring.

  Any other feedback/suggestions?

Appendix D.3 IBD Control Questionnaire

(To each question there is a tick box for "yes", "no" and "not sure", except for number 2 where the responses are "better", "no change" or "worse")

1. Do you believe that:
    a. Your IBD has been well controlled in the past 2 weeks?
    b. Your current treatment is useful in controlling your IBD

2. Over the past 2 weeks, have your bowel symptoms been getting worse, getting better or not changed?

3. In the past 2 weeks, did you:
    a. Miss any planned activities because of IBD? (e.g. attending school/college, going to work or a social event)
    b. Wake up at night because of symptoms of IBD?
    c. Suffer from significant pain or discomfort?
    d. Often feel lacking in energy (fatigued)? (often meaning more than half of the time)
    e. Feel anxious or depressed because of your IBD?
    f. Think you needed a change to your treatment?

4. At your next consultation, would you like to discuss:
    a. Alternative types of drug for controlling IBD?
    b. Ways to adjust your own treatment.
    c. Side effects or difficulties with using your medicines?
    d. New symptoms that have developed since your last consultation?

5. How would you rate the OVERALL control of your IBD in the past 2 weeks?

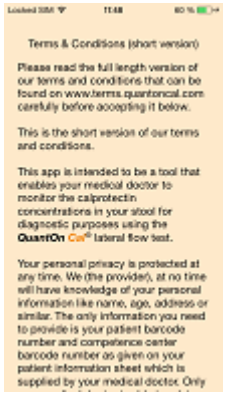
6. Visual analogue scale:

Worst possible control Best possible control

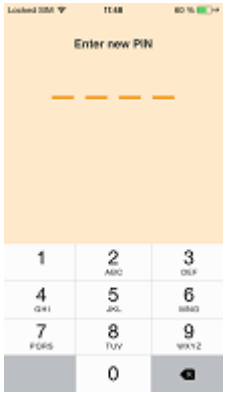
Appendix D.4 QuantOn Cal® test procedures

Setting up the QuantOn Cal® app

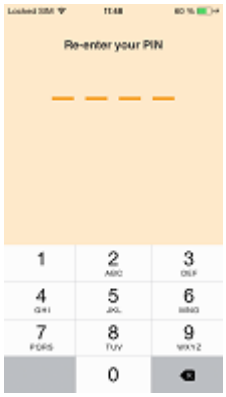
Each time you start the app, you first see the ***QuantOn Cal®*** welcome screen.



When you first start the app, a short version of our general terms and conditions is displayed after the welcome screen. The full version of our terms and conditions is available at www.terms.quantoncal.com. You can read our data privacy policy at www.privacy.quantoncal.com. Please read our terms and conditions and data privacy policy carefully and confirm your acceptance by clicking the "**Accept**" button at the end of the terms. If you have reservations about our terms and conditions or data privacy policy, your doctor will advise you about alternatives to ***QuantOn Cal®***.

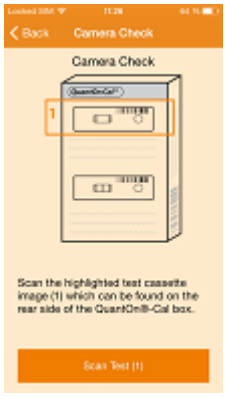


Once you have accepted the terms, you will be asked to enter a **P**ersonal **I**dentification **N**umber (**PIN**) to protect your test results from unauthorised access. Please take a note of this PIN as you will have no access to your data without it and will have to reinstall the app. You can find more information here.



On the next screen you will be asked to re-enter your PIN. You can only proceed to the next screen if the PIN you re-enter matches the first PIN you entered.

If the PIN you enter does not match the first one you entered, you can re-enter the PIN again. If you make an error the first time you enter your PIN, you can simply close the app and restart it. You will then reach the first PIN input screen again and can re-enter your PIN.

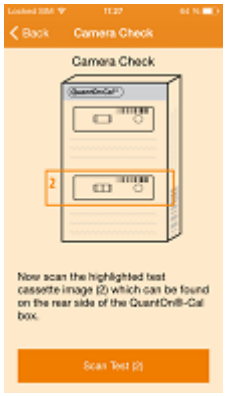


The next step is the camera test. For this purpose, on the inside of the *QuantOn Cal®* product packaging you will find two different schematic diagrams of test devices, marked number 1 and number 2. Now click the "**Scan Test (1)**" button.

The camera and the flash on your smartphone are activated. On your smartphone screen you will see the camera image as well as the outline of a test device, displayed as an orange-coloured frame.

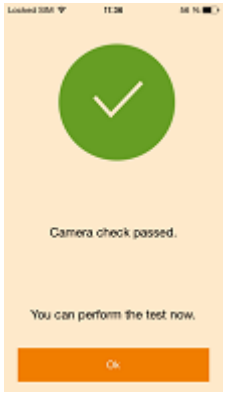
Now line up the schematic diagram of test device 1 on the ***QuantOn Cal®*** product packaging with the outline on the screen. Make sure that the size, position and rotation of test device and outline match.

As soon as the camera is correctly aligned, the ***QuantOn Cal®*** app takes the photo automatically and switches to the analysis screen.



Press "**Scan Test (2)**" to repeat the procedure with diagram 2.

Line up the diagram of test device 2 on the inside of the ***QuantOn Cal®*** product packaging with the orange-coloured outline on the screen.

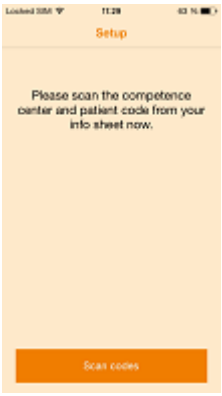


When the second photo has been taken, the result of the camera test is displayed.

If the camera test was successful, you can proceed to the next step immediately by clicking the "**OK**" button. If the camera test was unsuccessful, you can find help in the "**FAQ**" section of this homepage. Your phone may not be supported by the *QuantOn Cal®* app or the camera lens may be dirty.

You can repeat the camera test at any time as often as you like, for example to practice scanning test devices, if you wish to.

Please note that your results are invalid if your smartphone has not passed the camera test. Find out why your smartphone has not passed the test and rectify this before performing the test.



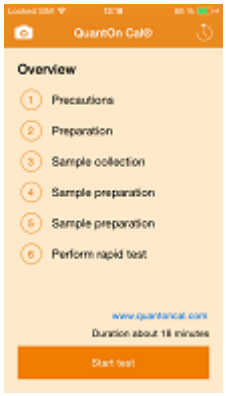
In order to register the app for the ***QuantOn Cal®*** program you require the patient information sheet which your doctor gave you during the consultation. Press the "**Scan Codes**" button to activate the camera on your smartphone.

The screen of your smartphone will appear dark, leaving a rectangular section clear. Align the camera so that both barcodes on the patient information sheet can be seen in the clear section. If the barcodes look blurred in the display, you can focus the camera by tapping on the barcodes on the screen with your finger. The app will take the picture automatically as soon as both barcodes are recognised.

The *QuantOn Cal®* app matches the scanned barcodes with the registered competence centres and patients. Compare the numbers displayed with those on your patient information sheet. If the numbers match, you can finish the set-up of the app by pressing "**OK**".

Your app has now been set up and can be used immediately for testing. You will be taken to the main menu of the app automatically.

Main menu and running the test

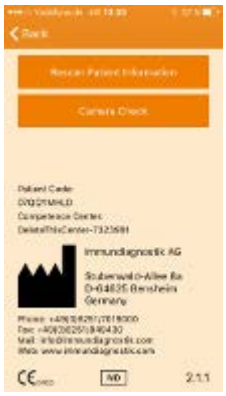


Once you have set up the *QuantOn Cal®* app, you will be automatically redirected to the main menu every time after you have started the app and entered your PIN.

In the main menu you have the following options:

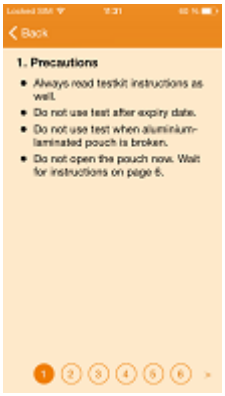
- Scan the patient sheet or add new information about the patient or competence centre **(cogwheel icon at top left)**
- View your test history **(clock icon at top right)**
- Overview of the Quick Start Guide for testing (pages 1-6)
- Perform new test ("**Run Rapid Test**" button).

When you click on the "**Run Rapid Test**" button, you will be guided through the Quick Start Guide before you can perform the rapid test.



By clicking on the respective command, you can

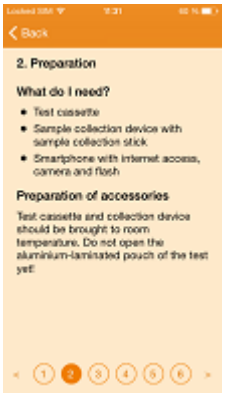
- Go back to the main menu
- Scan the patient sheet again
- Repeat the Camera Test



Page 1 "**Precautions**"

- Only use the printed instructions enclosed with the test kit to run the test.
- Do not use the test after the expiry date has passed.
- Do not use the test if the aluminium pouch is damaged.
- The aluminium pouch must not be opened until you are instructed to do so on page 6 of the instructions.

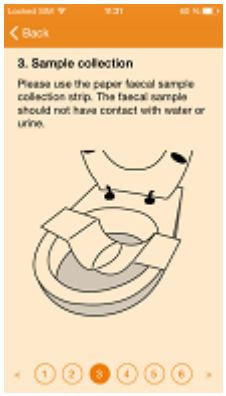
You can skip to the next page by swiping across the screen from right to left or tapping the next page number or the small arrow at the bottom of the screen.



Page 2 "**Preparation**"

You will need the following components for the test:

- Test device in aluminium pouch
- Sample collection tube
- Smartphone with internet connection, functional camera and flash



Page 3 "**Sampling**"

Unfold the paper stool catcher and use the adhesive surfaces to stick it to the two opposite sides of the toilet bowl. The paper stool catcher should hang down in the middle, without coming into contact with the toilet water.

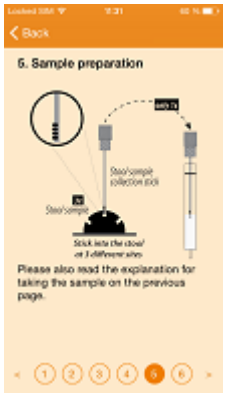
Catch your stool sample using the paper stool catcher.

Page 4 "**Prep sample**"

Unscrew the cap of the stool sample collection tube and remove the sample collection stick. Then, in one go, insert the sample collection stick into the stool sample at **3 different points** and ensure that the **grooves** at the bottom of the sample collection stick are **completely covered in faeces**.

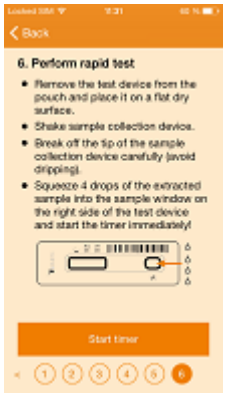
Return the sample collection stick with the adhering faecal sample into the sample collection tube containing an extraction buffer solution. **Do this only once.** Do not repeat this step as the functionality of the test will otherwise be impaired!

Screw the cap on the sample collection tube and shake well, **until the entire faecal sample** has shifted from the grooves to the liquid.



Page 5 "**Prep sample**"

This page shows a pictorial representation of the instructions described on page 4 for sample preparation.



Page 6 "**Run Rapid Test**"

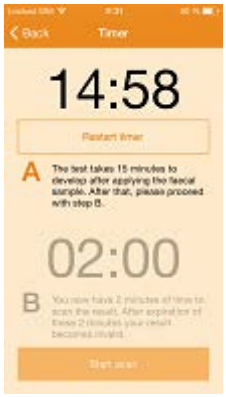
Open the aluminium pouch containing the test device and place the test device on a flat, dry, light surface.

Shake the sample collection tube once more to mix the sample quickly.

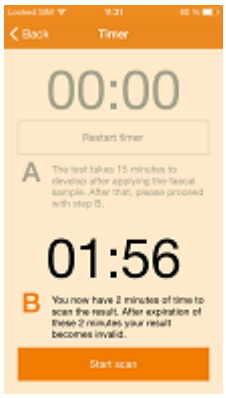
Carefully break off the tip of the sample collection tube. Avoid splashing.

Squeeze 4 drops from the sample collection tube onto the round sample application window of the test device. Start the timer of the *QuantOn Cal®* app immediately by pressing the "**Start Timer**" button.

You will now be taken automatically to the next screen, where a timer counts down the incubation time.



The timer in the upper half of the screen displays the incubation time required to successfully measure calprotectin in faeces. During the incubation time, a red fluid runs across the results window of the rapid test. This fluid forms the measuring signal, which is later evaluated by your ***QuantOn Cal®*** app and sent to your doctor.



After the incubation period has finished, the second timer starts in the bottom half of the screen. This timer shows how much time you have to evaluate your test.

When evaluating the test avoid shadows, strong light from the side and direct sunlight. Press "**Start scan**" before the timer runs out. If you wait any longer, your test result may be invalid.

The camera on your smartphone is activated. As in the camera test, you will see the camera image on your screen, as well as the orange-coloured outline of a test device.

Align your smartphone so that the outline is aligned with the test device. Pay particular attention to the position, rotation and size of the outline and test device.

If the test device appears blurred on the screen, you can focus the camera by tapping the test device on the screen.

Hold the camera steady in this position, until the *QuantOn Cal®* app takes the photo automatically and switches to the analysis screen.

When the analysis screen appears, the *QuantOn Cal®* app is evaluating the image of your rapid test.

If the app finds that the image is not suitable for evaluation, you will be asked to repeat the scan.

The test value will only be calculated when the image is suitable for evaluation beyond a doubt.

This test value is then automatically sent to your doctor.

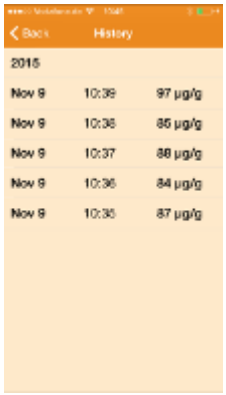
The progress of the test value transmission is displayed on your screen. **Please wait until the test value has been sent successfully.**

If a connection error occurs during transmission, the *QuantOn Cal®* app informs you of this and gives you the option to re-start the test value transmission. Please repeat this until transmission is successful.

After successful transmission, the *QuantOn Cal®* app displays your test value and the notification "**Result sent!**".

Your test is now finished and you can press the "**Exit**" button to return to the main menu. You can view your test values at any time in your history, which you can access from the main menu.

Your doctor can see your test value on his/her PC and can contact you using conventional methods for a consultation or to discuss therapy recommendations.



Appendix E

Appendix E.1 BioHit® letter of confirmation

BIOHIT HealthCare
Innovating for Health

20th December 2016

Dr N Taylor
IBD Research Fellow
c/o Deprtment of Gastroenterology
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust
Tremona Road
Southampton
Hampshire
SO16 6YD

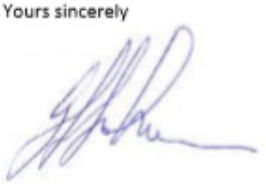
Dear Dr Taylor

Provision of Faecal Calprotectin test kits for QuantOn Cal home faecal calprotectin monitoring

This is to confirm that BIOHIT HealthCare Ltd shall provide a total of 250 Faecal Calprotectin tests to the Feasibility of SSM website and FC in IBD study (reference IRAS 214907) free of charge.

I wish you every success with your study.

Yours sincerely



Graham Johnson
Managing Director

Appendix E.2 HRA approval

NHS
Health Research Authority

Dr Nicola Taylor
7 Nelson Road
Winchester
S023 0QF

Email: hra.approval@nhs.net

07 February 2017

Dear Dr Taylor,

Letter of HRA Approval

Study title:	**Feasibility and acceptability of an inflammatory bowel disease self-management website and home faecal calprotectin monitoring**
IRAS project ID:	**214907**
Protocol number:	**MED1269**
REC reference:	**17/SC/0002**
Sponsor	**University Hospital Southampton NHS Foundation Trust**

I am pleased to confirm that **HRA Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

The document *"After Ethical Review – guidance for sponsors and investigators"*, issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application

procedure. If you wish to make your views known please email the HRA at hra.approval@nhs.net. Additionally, one of our staff would be happy to call and discuss your experience of HRA Approval.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **214907**. Please quote this on all correspondence.

Yours sincerely

Rekha Keshvara
Assessor

Email: hra.approval@nhs.net

Copy to: *Ms Jennifer Peach, University Hospital Southampton NHS Foundation Trust*

IRAS project ID	214907

Appendix A - List of Documents

The final document set assessed and approved by HRA Approval is listed below.

Document	*Version*	*Date*
Copies of advertisement materials for research participants [Recruitment poster]	1	01 November 2016
Covering letter on headed paper [Cover letter]	1	02 December 2016
GP/consultant information sheets or letters [GP letter]	2	24 January 2017
Instructions for use of medical device [QuantonCal instructions]	1	24 January 2017
Interview schedules or topic guides for participants [Interview guide]	1	15 November 2016
IRAS Application Form [IRAS_Form_02122016]		02 December 2016
IRAS Application Form XML file [IRAS_Form_02122016]		02 December 2016
IRAS Checklist XML [Checklist_10012017]		10 January 2017
IRAS Checklist XML [Checklist_02122016]		02 December 2016
Letter from funder [BioHit confirmation of FC kit provision]		20 December 2016
Letter from sponsor [Letter from sponsor]	1	24 July 2015
Letters of invitation to participant [Patient invitation]	1	01 November 2016
Letters of invitation to participant [Nurse invitation]	1	01 November 2016
Non-validated questionnaire [End of study questionnaire]	1	15 November 2016
Other [EC Certificate]		10 February 2016
Other [Confirmation of GCP]	1	24 January 2017
Participant consent form [Patient consent]	2	24 January 2017
Participant consent form [Nurse consent]	2	24 January 2017
Participant information sheet (PIS) [Patient information]	1	01 November 2016
Participant information sheet (PIS) [Nurse information]	1	01 November 2016
Research protocol or project proposal [Protocol]	1	01 November 2016
Summary CV for Chief Investigator (CI) [CV Nicola Taylor (student)]	1	14 November 2016
Summary CV for student [CV Nicola Taylor]	1	14 November 2016
Summary CV for supervisor (student research) [CV Fraser Cummings]	1	19 April 2016
Summary CV for supervisor (student research) [CV Hazel Everitt]	1	07 November 2016
Summary CV for supervisor (student research) [CV Sue Latter]	1	08 November 2016
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Summary protocol]	1	01 November 2016
Validated questionnaire [IBD Control questionnaire]	1	01 November 2016
Validated questionnaire [CCKNOW questionnaire]	1	01 November 2016
Validated questionnaire [SIBDQuestionnaire]	1	01 November 2016

IRAS project ID	214957

Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed for HRA Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England to assist in assessing and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the *participating NHS organisations, capacity and capability* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Ms Jennifer Peach
Email: jennifer.peach@uhs.nhs.uk
Tel: 02381203920

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
1.1	IRAS application completed correctly	Yes	No comments
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	This is a non-commercial single site study taking place in the NHS where the single NHS organisation is also the study sponsor. Therefore no study agreements are required.
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the

IRAS project ID	214907

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
			activities expected of them for this research study
4.3	Financial arrangements assessed	Yes	The study is funded by AbbVie Ltd.
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	The applicant has submitted EC certificate for the QuantonCal faecal calprotectin test.
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

IRAS project ID	214907

Participating NHS Organisations in England

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.
This is a non-commercial single site study taking place in the NHS where that single NHS organisation is also the study sponsor. Therefore there is only one site type involved in the research. If this study is subsequently extended to other NHS organisation(s) in England, an amendment should be submitted to the HRA, with a Statement of Activities and Schedule of Events for the newly participating NHS organisation(s) in England. The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website. If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA will work with these organisations to achieve a consistent approach to information provision.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.
This is a single site study sponsored by the site. The R&D office will confirm to the CI when the study can start.

Principal Investigator Suitability

This confirms whether the sponsor's position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England, and the minimum expectations for education, training and experience that PIs should meet (where applicable).
A Principal Investigator to be allocated at the participating NHS site. GCP training is not a generic training expectation, in line with the HRA statement on training expectations.

IRAS project ID	214907

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken.
It is expected that all study activities will be undertaken by local staff employed by the participating NHS organisation. Honorary Research Contracts to be in place for any research team member that does not have an existing contractual arrangement with the research sites. The pre-engagement checks should include an enhanced DBS check (including a check against the DBS 'barred list' for adults), and Occupational Health Clearance.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England in study set-up.
• The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

Appendix E.3 University of Southampton ERGO ethics committee approval

University of
Southampton

Dr Nicola Taylor
Department of Gastroenterology,
University Hospital Southampton
Tremona Road
Southampton
SO16 6YD

Date: 6th March 2017

Dear Dr Taylor,

Professional Indemnity and Clinical Trials Insurance

Project Title: Feasibility and acceptability of an inflammatory bowel disease self-management website and home faecal calprotectin monitoring

ERGO Ref: 25830

Participant Type	Number of participants	Participant age group
Patients	30	Adult

Thank you for submitting the completed questionnaire and attached papers.

Having taken note of the information provided, I can confirm that this project will be covered under the terms and conditions of the above policy, subject to written informed consent being obtained from the participating volunteers .

I would also advise that it is a condition of the University's insurance that any incidents that could eventually result in a claim are reported immediately. Serious adverse events, suspected unexpected serious adverse reactions and similar fall into this category. For studies hosted by or sponsored by UHS the Research and Development Office will copy the SAE and SUSAR reports they receive to the University Insurance Office. For all other studies such events must be reported to me at the same time as they are reported under the Protocol. Failure to do this could invalidate the insurance.

If there are any changes to the above details, please advise us as failure to do so may invalidate the insurance.
Yours sincerely

Mrs Jenny King
Senior Insurance Services Assistant

Tel: 023 8059 2417
email: jsk1n08@soton.ac.uk
Finance Department, University of Southampton, Highfield Campus, Southampton SO17 1BJ U.K.
Tel: +44(0)23 8059 5000 Fax: +44(0)23 8059 2195 www.southampton.ac.uk

Appendix E.4 Recruitment poster

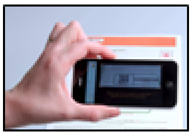
University Hospital Southampton NHS
NHS Foundation Trust

Do you have inflammatory bowel disease (ulcerative colitis or Crohn's disease)?
Have you recently stopped/are planning to stop one of your IBD treatments?
Do you have access to a smartphone?

Would you like to help with a research study?

We understand the importance of helping patients to take more control over managing their inflammatory bowel disease. Patients who are risk of disease relapse (such as those stopping a treatment) may wish to keep a closer eye on their illness.

We are looking for volunteers aged 18 and over to try out our **new website, home stool test** and **smartphone app** as part of a research study.



If you would like more information, please contact us on the details below:

Appendix E.5 Patient Invitation letter

Date:

Dear [Patient],

Research study: Feasibility and acceptability of an IBD self-management website and home FC monitoring

On behalf of the IBD Research Team, I am writing to invite you to take part in the above research study.

This study has been funded by [insert details] and has been given NHS Research Ethics Committee approval [Insert details].

Your clinical team have identified you as having stopped or planning to stop a treatment for your IBD (IBD). We are asking IBD patients in this situation if they might be interested in taking part in a research study to test whether our website: 'My Medical Record (MyMR)' can be used together with a home stool test to help patients to monitor their IBD and detect disease relapses. We are particularly looking at patients who have stopped a treatment for their IBD for any reason.

Full details of what the research would involve are provided in the attached Participant Information Sheet. We would be grateful if you could take the time to read this to help you decide whether you wish to take part in the study. You may like to consider talking about participation with others, including healthcare professionals, before deciding to take part.

If you wish to take part, provide feedback, or discuss the study further, please contact the research team via telephone or email (details below).

We look forward to hearing from you.

Yours sincerely,

(Insert researcher name, job title, address, e mail and telephone contact for researcher)

Appendix E.6 Patient information leaflet

PARTICIPANT INFORMATION SHEET

WP1+2

PATIENTS

Research study: Feasibility and acceptability of an IBD self-management website and home FC monitoring

You have been invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully.

What is the research about?
We have developed a website called My Medical Record (MyMR) to help patients to take greater control over managing their IBD (IBD). The website includes a secure messaging service to contact the IBD team, useful information about IBD, diaries to help monitor symptoms, and access to clinic letters and test results.

We are also exploring the use of a new stool test that can be used by patients at home to help detect a disease relapse (flare-up) using a smartphone application ('app'). The test is called FC (FC) and is useful because FC levels can rise well before you get any symptoms, allowing early diagnosis and treatment of a flare-up. FC tests are usually carried out in a hospital laboratory and there can be a delay of several days before getting a result. The home FC testing kit provides a result in less than 10 minutes using an app on your smartphone. The result can be uploaded to the MyMR website for you and your IBD team to monitor.

We wish to investigate the impact of the website/FC test on patients and whether it might be an acceptable alternative to attending routine outpatient clinic appointments.

Who is conducting the research?
A team of researchers from University Hospital Southampton and Southampton University (Faculties of Medicine and Health Science) are conducting the project. The project will be overseen by Dr Fraser Cummings and the researcher conducting data collection is Dr Nicola Taylor. The project is funded by (insert details). The sponsor for the study is the University Hospitals Southampton NHS Foundation Trust.

Who has reviewed the study?
This study has been reviewed and approved by [REC approval details] and the University Hospital Southampton NHS Foundation Trust Research and Development Office.

Why have I been chosen?
We are interested in recruiting patients into the study who have IBD (ulcerative colitis or Crohn's disease) and who have recently stopped (within the last 8 weeks) or are planning to stop a treatment for IBD in the near future. Treatments for IBD are usually stopped with good reason, for example side effects or disease remission. However, patients who have stopped a treatment need to be monitored closely for signs that their IBD is becoming more active again, so that treatment can be changed or restarted if necessary.

Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do, you will be asked to sign a consent form. You are still free to withdraw your consent at any time and without giving a reason. If you decide not to take part, this will not affect your usual care in any way.

What will happen to me if I take part?
If you think you might like to take part, a member of the research team will discuss the trial in further detail with you, either in person or on the telephone.

If you agree to participate, we would like you to use a combination of the MyMR website and home FC- testing to monitor your disease for 6 months, instead of attending routine outpatient appointments.

You will be asked to take part in the following:

1. Initial study visit
   A member of the research team will arrange an initial visit at a time convenient to you. This will take place either at UHS (in which case you will be reimbursed for travel and parking), or in your own home – whichever you prefer. They will go through the study with you in detail and if you are happy to proceed you will be asked to sign a consent form. (You are free to withdraw your consent at any time and this will not affect any future care you receive.) During this visit, you will be given login details and shown how to use the MyMR website. The researcher will teach you how to do your first FC test and will provide you with further test kits. You will be asked to fill out an online questionnaire about your IBD.

2. Website
   You will be asked to log in to and use the website at least once per month to monitor your IBD symptoms, but you are encouraged to use the website as often as you feel is helpful to you. When the study is finished, you will be able to continue to use the website if you wish.

3. FC (FC) tests
   You will be asked to do a home FC test once per month and to contact the IBD team using the MyMR messaging service for treatment advice if the result is abnormal. The IBD team will also monitor the results and get in touch with you if they haven't heard from you after a week.

4. Blood tests
   You will be asked to have one routine blood test at the start of the study (you may already have had this) and one after 6 months at the end of the monitoring period. If you take medications that usually require more frequent blood tests for monitoring, you should continue to do this, and will be asked to contact the IBD team for advice if any of these become abnormal. To ensure your safety during the study, the IBD team will keep an eye on these results and will get in touch with you if they haven't heard from you within a week to make sure you are okay. The researcher will provide you with all the blood test forms you need during your initial visit.

5. Messaging the IBD team

If you have any worries about your IBD at any time during the study, you can contact the IBD team for advice and support using the secure messaging service available through the MyMR website.

6. Clinic appointments
   During the study, you won't need to come to hospital for any routine outpatient appointments for your IBD. If you become unwell during the study and need to talk to your IBD doctor/nurse on the telephone/in person, this can be arranged using the website messaging service. You will be sent an outpatient appointment to see your IBD doctor or nurse at the hospital once you have completed the study, to review your IBD and ensure you are well.

7. End of study
   At the end of the study, we will send you a link to an online questionnaire to find out how you found using the website and home FC testing. We will also invite around half of participants to an interview with a member of the research team to explore your thoughts in more detail. This interview can take place either in your own home if convenient or via telephone. With your permission, we would like to tape record these interviews.

Are there any benefits in my taking part?
By participating in the research, you may find that using a website to help manage your disease is more convenient than coming to an appointment at hospital. You will have access to more information and tools that may help you to manage your IBD, including your test results. The FC stool test may help you to detect disease flare-ups. You may find there is no benefit in taking part, however the information gathered from your experience may help improve the care of IBD patients in the future.

Are there any risks involved?
We do not anticipate there will be any significant risks involved in taking part in the study. Participants will have access to telephone and/or email advice from the IBD team as needed. If your illness should worsen during the study and you and/or your doctor feel you need to be seen in the IBD clinic, this can be arranged.

Will my participation be confidential?
Yes. You will not be identifiable in any written report associated with the research. All person identifiable data will be stored in a locked filing cabinet. Access will be available to the study researchers and auditors (for example, from NHS Research and Development Offices) only. Interview data stored on computers will be password protected and will be stored according to University Hospital Southampton NHS Foundation Trust regulations. Audio recordings will be downloaded onto the University Hospital Southampton system, and will then be immediately wiped from the recording device. All transcriptions from interviews will be anonymised to ensure they contain no personally identifiable information.

In order to find out how taking part in the research study has affected your IBD and treatment, the researchers may need to access medical records relating to your IBD.

With your permission, we would like to inform your General Practitioner if you agree to take part in the study.

What happens if I change my mind?

If you change your mind about taking part in the study, you have the right to withdraw at any time. If you change your mind about your involvement in the study, then, with your consent, we would like to use the data collected up to that point for the purpose of the research.

What will happen to the results of the research study?
The results will be analysed and findings may be presented at scientific meetings or published in scientific journals. You will not be identified in any publication. You are very welcome to a copy of any publication resulting from this work, which can be obtained by giving us your email address or postal address.

What happens if something goes wrong?
If you have a concern or a complaint about this study you should contact Mikayala King, Research Governance Lead, University Hospitals Southampton NHS Foundation Trust, Tremona Road, Southampton, SO16 6YD. Tel: 023 8120 8689 Email: Mikayala.king@uhs.nhs.uk.

Where can I get more information?
If you would like to discuss any aspect of the study and your participation further after reading this information sheet, please contact the research team on the details below.

What do I do now?
If you would like to take part in the study, discuss any aspects further, or provide us with feedback, please get in touch using the contact details below.

THANK YOU FOR TAKING THE TIME TO READ THIS INFORMATION SHEET.

We look forward to hearing from you,

Yours sincerely,

[Researcher contact details: name, job title, address, e mail and telephone]

Appendix E.7 Patient consent form

CONSENT FORM

WP1+2

PATIENTS

Research study: Feasibility and acceptability of an IBD self-management website and home FC monitoring

PARTICIPANT STUDY ID _____

Please initial the boxes if you agree with the statement.

1. I confirm that I have read and understood the information sheet (insert date /version no. of participant information sheet) for the above study and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.

3. I give consent for data from my questionnaires and collected on the MyMR website to be used in the research study.

4. If selected, I give consent to participate in an interview with the researcher.

5. If selected, I give consent for the interview to be audio-recorded.

6. I give consent for the researchers to use anonymised quotes from my interview in reports or publications.

7. If I withdraw from the study, I give consent for the data collected from me up until that point to be used in the research study.

8. I agree that the anonymised data I give for this study can be used for teaching students.

9. I give consent for my GP to be informed about my participation in the study.

10. I give consent for the researchers to access electronic hospital medical records relating to my IBD.

11. I agree to take part in the above study.

Name of Participant	Date	Signature
_____	_____	_____

Name of Researcher	Date	Signature
_____	_____	_____

Appendix E.8 GP information letter

Research study: Feasibility and acceptability of an IBD self-management website and home FC monitoring

Re. Patient: *Insert Patient's name and address, study number, NHS number*

Dear *Dr's name and title*

Your patient has kindly agreed to participate in the above-named trial at Southampton General Hospital.

IBD can be challenging to manage as disease flares are often unpredictable and rarely coincide with scheduled outpatient appointments. Websites are a novel way of assisting patients to take more control over monitoring and managing symptoms and have been shown to improve outcomes in some chronic diseases. We have developed a website called My Medical Record (MyMR) to help patients learn about IBD, access test results, monitor symptoms, and manage their medications, with email support from our IBD team.

We are also exploring the use of home FC monitoring. This marker of IBD activity is normally performed in hospital laboratories and becomes elevated before the onset of clinical symptoms of an IBD flare. New technologies enable patients to perform the test at home with the aid of a smartphone application.

We plan to conduct a 6-month exploratory feasibility study to assess if a combination of MyMR and a home faecal testing kit is a feasible and acceptable means for patients to monitor their illness. We are particularly interested in their use in patients who have recently stopped a treatment for IBD, as up to 50% of these patients will have a disease flare within a year.

Interventions

- **Clinic appointments**
  Study participants will not be required to attend any routine outpatient follow up appointments for the 6-month study period, after which they will be reviewed by a member of the IBD team.

- **Questionnaires and interviews**
  Patients will receive questionnaires and a sample of patients will also undergo interviews to explore their views regarding the website and stool test.

- **Website**
  Participants will be encouraged to use all functions of the website at least monthly:

1. Secure email messaging service
2. IBD educational material
3. Stool, nutritional and flare journals
4. Blood and test results
5. FC monitoring – monthly testing (or sooner if symptoms of a flare-up). Patients will test and monitor their FC levels monthly. The results will be overseen by the IBD team who will make contact within a week in the event of abnormal results if the patient has not already done so.

- **Blood tests**
  All patients will have a routine blood test at 0 and 6 months. Patients taking azathioprine, mercaptopurine and methotrexate should continue regular blood monitoring (minimum of 3 monthly FBC, U&E, LFT and CRP) as usual practice. Patients will be provided with blood forms. We would be very grateful if you can continue to facilitate these blood tests where necessary as part of the ongoing shared care agreement between primary and secondary care. Patients will be provided with blood test results and explanations of their significance via MyMR. The results will be overseen by the IBD team who will make contact within a week in the event of abnormal results if the patient has not already done so.

- **Safety**
  Patients can contact the IBD team the email messaging service at any time for advice and support. The IBD flare telephone messaging service (02381 205362 routine; 02381 205363 urgent) is available during the study as an additional means for patients/GPs to communicate with the team.

  Participants will be advised to contact the IBD team via email/phone if they experience any of the following symptoms for concern:

  - Losing weight without dieting.
  - Severe abdominal pain
  - Fevers
  - Any anxieties or concerns about their IBD that they do not feel confident to self-manage

If you feel you have any information which might be important with regard to your patient being enrolled in this study, or you require any additional information, please do not hesitate to contact me.

Many thanks for your assistance,

With best wishes

Yours sincerely

Appendix E.9 CCKNOW questionnaire

(Please tick only one answer for each question)

1. The intestines play an important role in the body but they only work during mealtimes:
a) True
b) False
c) Don't know

2. People with IBD are never allowed to eat dairy products:
a) True
b) False
c) Don't know

3. Elemental feeds are sometimes used to treat Crohn's disease and ulcerative colitis. They:
a) Always contain a lot of fibre
b) Are very easy to digest
c) Come in the form of tablets
d) Don't know

4. Proctitis:
a) Is a form of colitis that affects the rectum or back passage only
b) Is a form of colitis that affects the whole of the large bowel
c) Don't know

5. When a patient with IBD passes blood in their stool it means:
a) They definitely have bowel cancer
b) They are having a flare up of their disease
c) Don't know

6. Patients with IBD are probably cured if they have been symptom free for 3 years:
a) True
b) False
c) Don't know

7. IBD runs in families:
a) True
b) False
c) Don't know

8. If patients with IBD are not careful with their personal hygiene they can pass on their disease to friends and members of the family:
a) True
b) False
c) Don't know

9. Patients with IBD can get inflammation in other parts of the body as well as the bowel:
a) True
b) False
c) Don't know

10. A fistula:
a) Is an abnormal track between 2 pieces of bowel or between the bowel and skin
b) Is a narrowing of the bowel which may obstruct the passage of the contents
c) Don't know

11. The terminal ileum:
a) Is a section of the bowel just before the anus
b) Is a section of the bowel just before the large intestine
c) Don't know

12. During a flare up of IBD:
a) The platelet count in the blood rises
b) The albumin level in the blood rises
c) The white cell count in the blood falls
d) Don't know

13. Steroids (such as prednisolone/prednisone/budesonide/hydrocortisone):
a) Can only be taken by mouth
b) Can be given in the form of an enema into the back passage
c) Cannot be given directly into the vein
d) Don't know

14. Steroids usually cause side effects:
a) Only after they have been taken for a long time and in high doses
b) Immediately and even after small doses
c) Which are not permanent, and all disappear after treatment is stopped
d) Don't know

15. Immunosuppressive drugs are given to IBD patients to:
a) Prevent infection in the bowel by bacteria
b) Reduce inflammation in the bowel
c) Don't know

16. Sulphasalazine:
a) Controls the level of sulphur in the bloodstream
b) Can be used to reduce the frequency of flare ups
c) Cannot be used to prevent flare ups
d) Don't know

17. An example of an immunosuppressive drug used in IBD is:
a) Sulphasalazine
b) Mesalazine
c) Azathioprine
d) Don't know

18. If a woman has Crohn's disease:
a) She may find it more difficult to become pregnant
b) She should not have children
c) Her pregnancy will always have complications
d) She should stop all medication during her pregnancy
e) Don't know

19. Patients who smoke are more likely to have:
a) Ulcerative colitis
b) Crohn's disease
c) Don't know

20. Which one of the following statements is false?
a) Ulcerative colitis can occur at any age
b) Stress and emotional events are linked with the onset of ulcerative colitis
c) Ulcerative colitis is least common in Europeans and North Americans
d) Patients with ulcerative colitis have an increased risk of developing bowel cancer
e) Don't know

21. The examination of the large bowel with a flexible camera is called a:
a) Barium enema
b) Biopsy
c) Colonoscopy
d) Don't know

22. Male patients who take sulphasalazine:
a) Have reduced fertility levels that are reversible
b) Have reduced fertility levels that are not reversible
c) The drug does not have any effect on male fertility
d) Don't know

23. The length of the small bowel is approximately:
a) 2 feet
b) 12 feet
c) 20 feet
d) Don't know

24. The function of the large bowel is to absorb:
a) Vitamins
b) Minerals
c) Water
d) Don't know

25. Another name for an ileorectal anastomosis operation with formation of a reservoir is:
a) Purse
b) Pouch
c) Stoma
d) Don't know

26. If a part of the bowel called the terminal ileum is removed during surgery the patient will have impaired absorption of:
a) Vitamin C
b) Vitamin A
c) Vitamin B12
d) Don't know

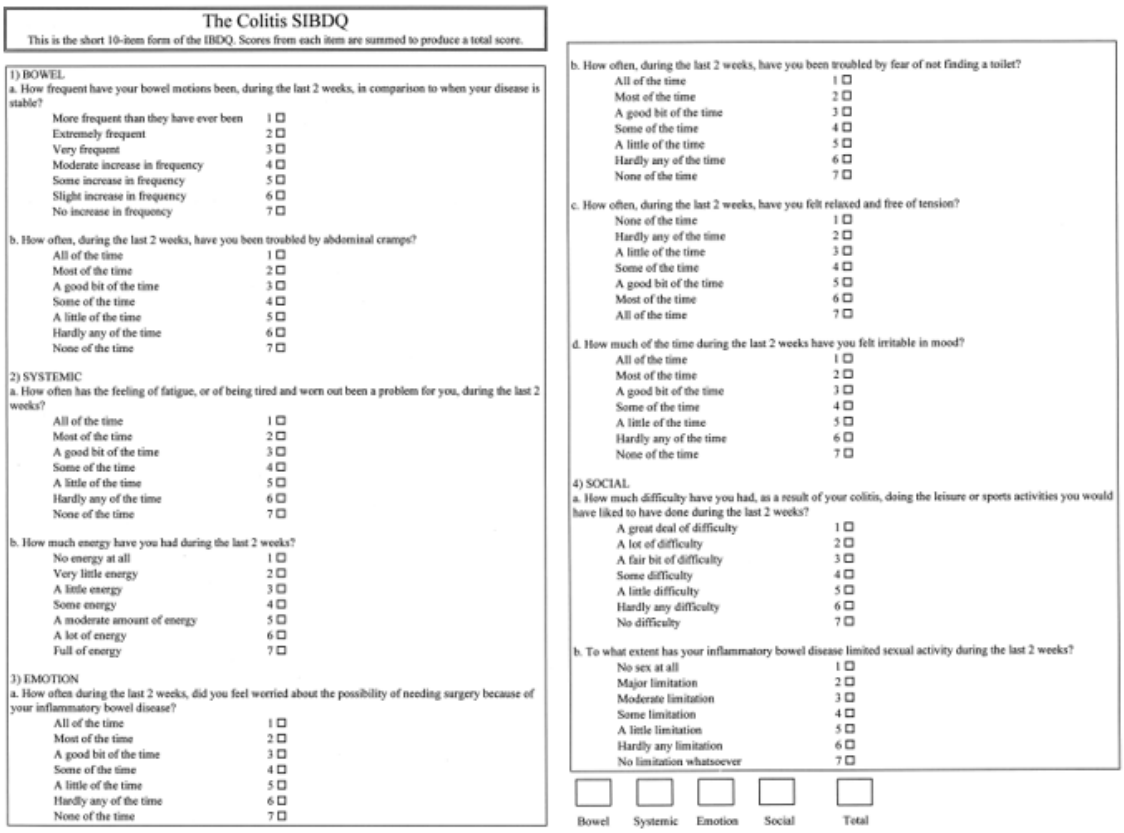
27. Patients with IBD need to be screened for cancer of the colon. Which one of the following statements about screening is false?
Screening should be offered to all patients with ulcerative colitis:
a) Which affects only the rectum
b) Which has lasted for 8–10 years
c) Which started before the age of 50
d) Don't know

28. There are millions of tiny "hairs" in the small bowel to increase the absorptive surface. They are called:
a) Villi
b) Enzymes
c) Bile salts
d) Crypts
e) Don't know

29. Which one of the following is not a common symptom of IBD?
a) Abdominal pain
b) Change in bowel habit
c) Headache
d) Fever
e) Don't know

30. If a child has IBD; he/she probably will not:
a) live beyond the age of 45
b) be as tall as his or her friends
c) be as intelligent as his or her friends
d) Don't know

Appendix E.10 S-IBDQ questionnaire



The Colitis SIBDQ

This is the short 10-item form of the IBDQ. Scores from each item are summed to produce a total score.

1) BOWEL

a. How frequent have your bowel motions been, during the last 2 weeks, in comparison to when your disease is stable?

More frequent than they have ever been	1 ☐
Extremely frequent	2 ☐
Very frequent	3 ☐
Moderate increase in frequency	4 ☐
Some increase in frequency	5 ☐
Slight increase in frequency	6 ☐
No increase in frequency	7 ☐

b. How often, during the last 2 weeks, have you been troubled by abdominal cramps?

All of the time	1 ☐
Most of the time	2 ☐
A good bit of the time	3 ☐
Some of the time	4 ☐
A little of the time	5 ☐
Hardly any of the time	6 ☐
None of the time	7 ☐

2) SYSTEMIC

a. How often has the feeling of fatigue, or of being tired and worn out been a problem for you, during the last 2 weeks?

All of the time	1 ☐
Most of the time	2 ☐
A good bit of the time	3 ☐
Some of the time	4 ☐
A little of the time	5 ☐
Hardly any of the time	6 ☐
None of the time	7 ☐

b. How much energy have you had during the last 2 weeks?

No energy at all	1 ☐
Very little energy	2 ☐
A little energy	3 ☐
Some energy	4 ☐
A moderate amount of energy	5 ☐
A lot of energy	6 ☐
Full of energy	7 ☐

3) EMOTION

a. How often during the last 2 weeks, did you feel worried about the possibility of needing surgery because of your inflammatory bowel disease?

All of the time	1 ☐
Most of the time	2 ☐
A good bit of the time	3 ☐
Some of the time	4 ☐
A little of the time	5 ☐
Hardly any of the time	6 ☐
None of the time	7 ☐

b. How often, during the last 2 weeks, have you been troubled by fear of not finding a toilet?

All of the time	1 ☐
Most of the time	2 ☐
A good bit of the time	3 ☐
Some of the time	4 ☐
A little of the time	5 ☐
Hardly any of the time	6 ☐
None of the time	7 ☐

c. How often, during the last 2 weeks, have you felt relaxed and free of tension?

None of the time	1 ☐
Hardly any of the time	2 ☐
A little of the time	3 ☐
Some of the time	4 ☐
A good bit of the time	5 ☐
Most of the time	6 ☐
All of the time	7 ☐

d. How much of the time during the last 2 weeks have you felt irritable in mood?

All of the time	1 ☐
Most of the time	2 ☐
A good bit of the time	3 ☐
Some of the time	4 ☐
A little of the time	5 ☐
Hardly any of the time	6 ☐
None of the time	7 ☐

4) SOCIAL

a. How much difficulty have you had, as a result of your colitis, doing the leisure or sports activities you would have liked to have done during the last 2 weeks?

A great deal of difficulty	1 ☐
A lot of difficulty	2 ☐
A fair bit of difficulty	3 ☐
Some difficulty	4 ☐
A little difficulty	5 ☐
Hardly any difficulty	6 ☐
No difficulty	7 ☐

b. To what extent has your inflammatory bowel disease limited sexual activity during the last 2 weeks?

No sex at all	1 ☐
Major limitation	2 ☐
Moderate limitation	3 ☐
Some limitation	4 ☐
A little limitation	5 ☐
Hardly any limitation	6 ☐
No limitation whatsoever	7 ☐

☐ Bowel ☐ Systemic ☐ Emotion ☐ Social ☐ Total

Appendix E.11 End of study questionnaire

Q1. When it comes to managing your IBD, how helpful did you find viewing your test results on the MyMR website?

Q2. When it comes to managing your IBD, how helpful did you find looking at your clinic letters on the MyMR website?

Q3. When it comes to managing your IBD, how helpful did you find using the email messaging service on the MyMR website?

Q4. When it comes to managing your IBD, how helpful did you find reading the IBD educational material on the MyMR website

Q5. When using the email messaging service on the MyMR website, how satisfied were you with the speed of response from the IBD team?

Q6. How easy or difficult was the home faecal calprotectin test to use?

Q7. Was monthly faecal calprotectin-testing appropriate?

Q8. Did home faecal calprotectin monitoring improve your confidence in stopping a medication for your IBD?

Q9. Which (if any) self-management tools would you consider continuing to use after the study ends?

Appendix E.12 Interview guide

University Hospital Southampton NHS
NHS Foundation Trust

DRAFT INTERVIEW SCHEDULE

PATIENT INTERVIEWS

WP2

Research study: Feasibility and acceptability of an IBD self-management website and home FC monitoring

The interviews will explore areas addressed in the end-of-study questionnaire in greater depth. It is expected that interview questions will evolve and develop over time. This is normal practice in qualitative research and is necessary to explore emerging themes that develop as the study progresses.

- Tell me about your experience of using a) the website b) the stool testing kit.
- What, if anything, worked well?
- What didn't work so well for you?
- How have your experiences of using the a) website b) stool test influenced or not influenced how you manage your IBD?
- How did you find doing a regular stool test yourself at home?
- Is there anything you would like to change about the a) website b) stool test?
- How did having the regular home stool testing influence or not influence your confidence in stopping a medication?
- What, if anything, would give you greater confidence in managing your IBD?
- Is there anything in particular that you have thought of that you would like to share?

Appendix E.13 S-IBDQ 1 results

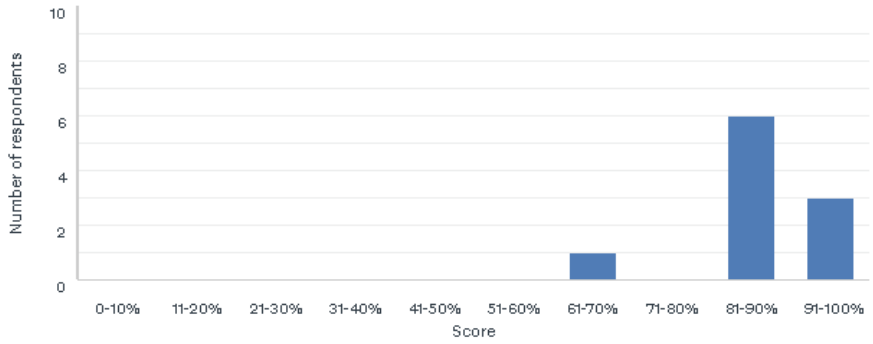
Short IBDQ

Sunday, August 25, 2019

Quiz Summary

AVERAGE SCORE

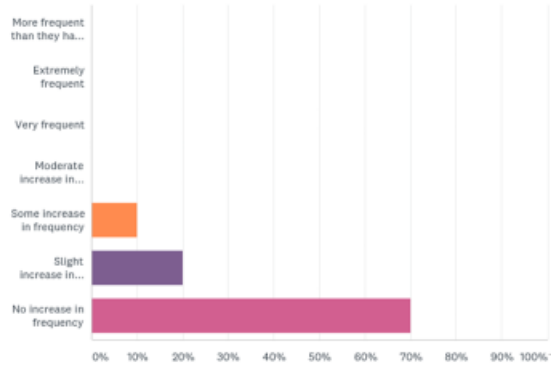
86% • **60**/70 PTS



STATISTICS		
Lowest Score	Median	Highest Score
70%	86%	93%
Mean: 86%		
Standard Deviation: 7%		

Q1: How frequent have your bowel motions been in the last 2 weeks in comparison with when your disease is stable?

Answered: 10 Skipped: 0



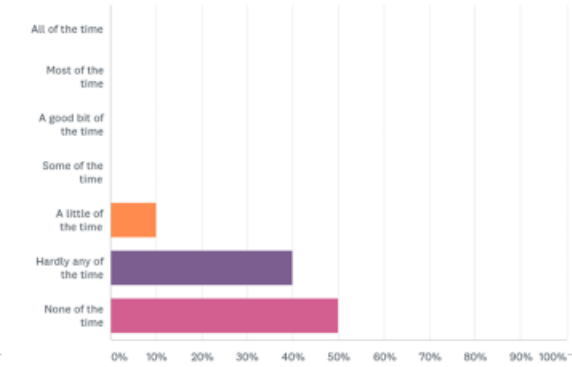
Q1: How frequent have your bowel motions been in the last 2 weeks in comparison with when your disease is stable?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
More frequent than they have ever been	0.00%	0
Extremely frequent	0.00%	0
Very frequent	0.00%	0
Moderate increase in frequency	0.00%	0
Some increase in frequency	10.00%	1
Slight increase in frequency	20.00%	2
No increase in frequency	70.00%	7
TOTAL		10

Q2: How often during the last 2 weeks have you been troubled by abdominal cramps?

Answered: 10 Skipped: 0



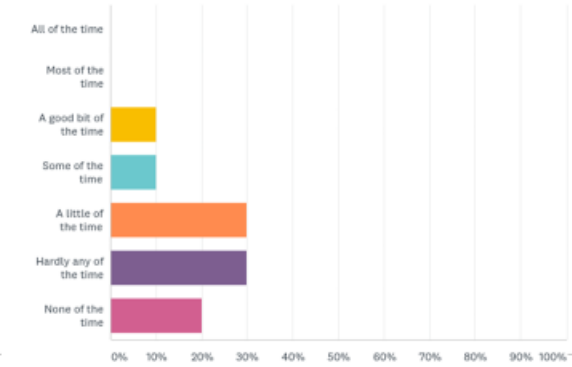
Q2: How often during the last 2 weeks have you been troubled by abdominal cramps?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	0.00%	0
A little of the time	10.00%	1
Hardly any of the time	40.00%	4
None of the time	50.00%	5
TOTAL		10

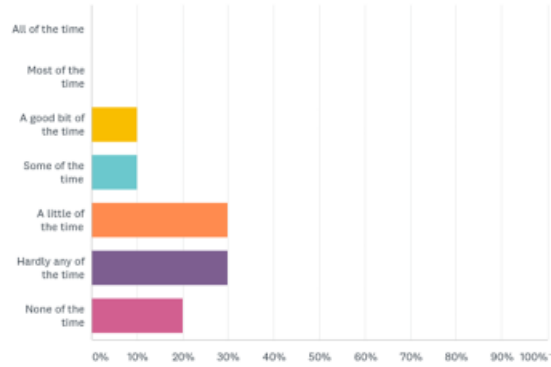
Q3: How often has the feeling of fatigue, or of being tired and worn out been a problem for you in the last 2 weeks?

Answered: 10 Skipped: 0



Q3: How often has the feeling of fatigue, or of being tired and worn out been a problem for you in the last 2 weeks?

Answered: 10 Skipped: 0



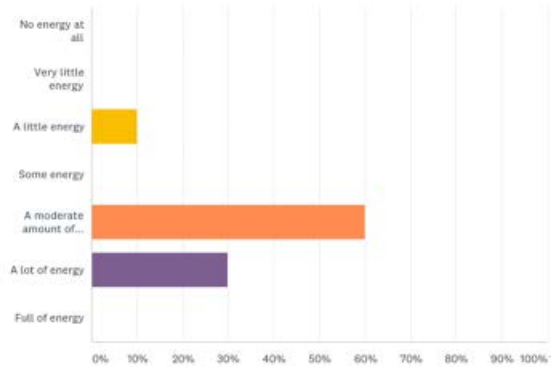
Q3: How often has the feeling of fatigue, or of being tired and worn out been a problem for you in the last 2 weeks?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	10.00%	1
Some of the time	10.00%	1
A little of the time	30.00%	3
Hardly any of the time	30.00%	3
None of the time	20.00%	2
TOTAL		10

Q4: How much energy have you had in the last 2 weeks?

Answered: 10 Skipped: 0



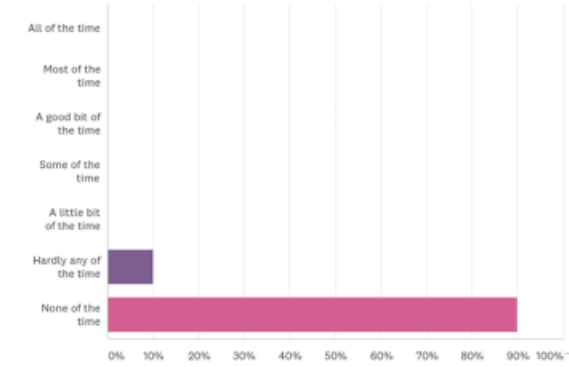
Q4: How much energy have you had in the last 2 weeks?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
No energy at all	0.00%	0
Very little energy	0.00%	0
A little energy	10.00%	1
Some energy	0.00%	0
A moderate amount of energy	60.00%	6
A lot of energy	30.00%	3
Full of energy	0.00%	0
TOTAL		10

Q5: How often during the last 2 weeks did you feel worried about the possibility of needing surgery for your inflammatory bowel disease?

Answered: 10 Skipped: 0



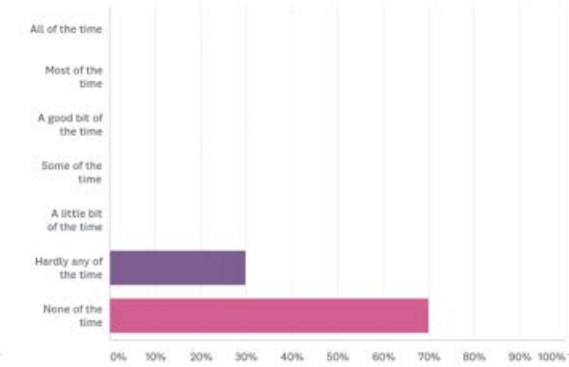
Q5: How often during the last 2 weeks did you feel worried about the possibility of needing surgery for your inflammatory bowel disease?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	0.00%	0
A little bit of the time	0.00%	0
Hardly any of the time	10.00%	1
None of the time	90.00%	9
TOTAL		10

Q6: How often during the last 2 weeks have you been troubled by fear of not finding a toilet?

Answered: 10 Skipped: 0



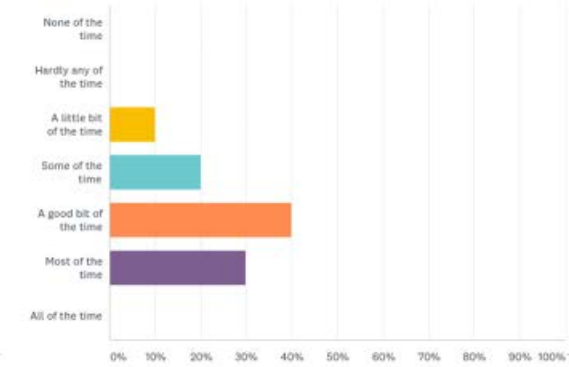
Q6: How often during the last 2 weeks have you been troubled by fear of not finding a toilet?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	0.00%	0
A little bit of the time	0.00%	0
Hardly any of the time	30.00%	3
None of the time	70.00%	7
TOTAL		10

Q7: How often during the last 2 weeks have you felt relaxed and free of tension?

Answered: 10 Skipped: 0



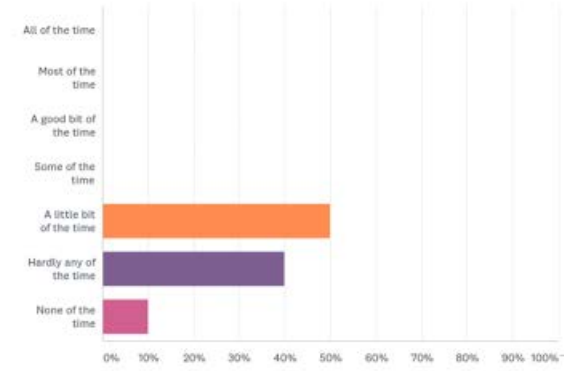
Q7: How often during the last 2 weeks have you felt relaxed and free of tension?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
None of the time	0.00%	0
Hardly any of the time	0.00%	0
A little bit of the time	10.00%	1
Some of the time	20.00%	2
A good bit of the time	40.00%	4
Most of the time	30.00%	3
All of the time	0.00%	0
TOTAL		10

Q8: How much of the time during the last 2 weeks have you felt irritable in mood?

Answered: 10 Skipped: 0



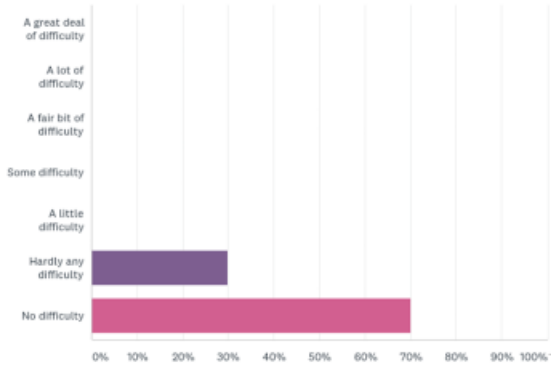
Q8: How much of the time during the last 2 weeks have you felt irritable in mood?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	0.00%	0
A little bit of the time	50.00%	5
Hardly any of the time	40.00%	4
None of the time	10.00%	1
TOTAL		10

Q9: How much difficulty have you had (as a result of your inflammatory bowel disease)doing the leisure or sports activities that you would like to have done in the last 2 weeks?

Answered: 10 Skipped: 0



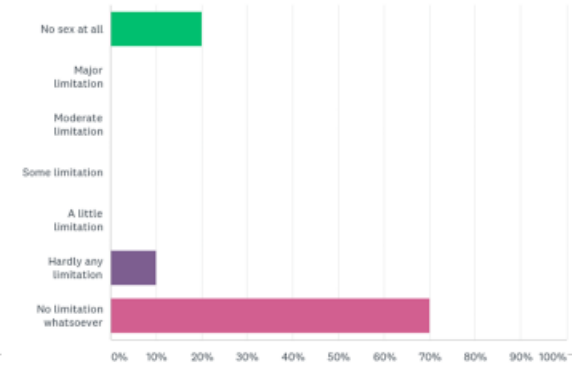
Q9: How much difficulty have you had (as a result of your inflammatory bowel disease)doing the leisure or sports activities that you would like to have done in the last 2 weeks?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
A great deal of difficulty	0.00%	0
A lot of difficulty	0.00%	0
A fair bit of difficulty	0.00%	0
Some difficulty	0.00%	0
A little difficulty	0.00%	0
Hardly any difficulty	30.00%	3
No difficulty	70.00%	7
TOTAL		10

Q10: To what extent has your inflammatory bowel disease limited sexual activity in the last 2 weeks?

Answered: 10 Skipped: 0



Q10: To what extent has your inflammatory bowel disease limited sexual activity in the last 2 weeks?

Answered: 10 Skipped: 0

ANSWER CHOICES	RESPONSES	
No sex at all	20.00%	2
Major limitation	0.00%	0
Moderate limitation	0.00%	0
Some limitation	0.00%	0
A little limitation	0.00%	0
Hardly any limitation	10.00%	1
No limitation whatsoever	70.00%	7
TOTAL		10

Appendix E.14 S-IBDQ 2 results

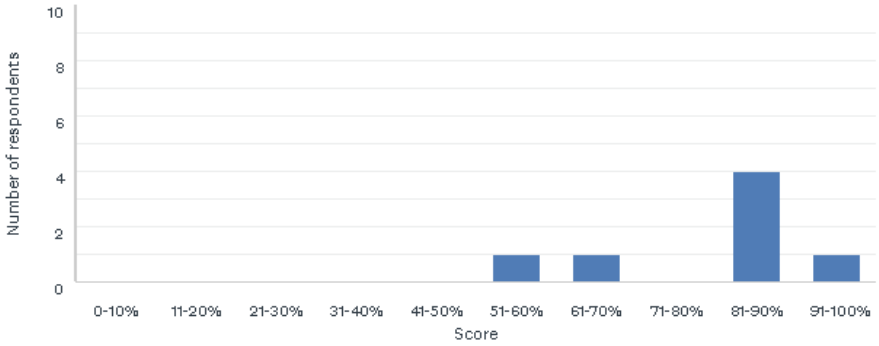
Short IBDQ (2)

Sunday, August 25, 2019

Quiz Summary

AVERAGE SCORE

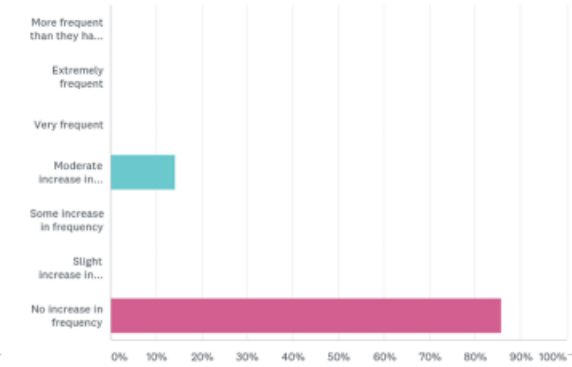
80% • **56**/70 PTS



STATISTICS		
Lowest Score	Median	Highest Score
54%	86%	94%
Mean: 80%		
Standard Deviation: 15%		

Q1: How frequent have your bowel motions been in the last 2 weeks in comparison with when your disease is stable?

Answered: 7 Skipped: 0



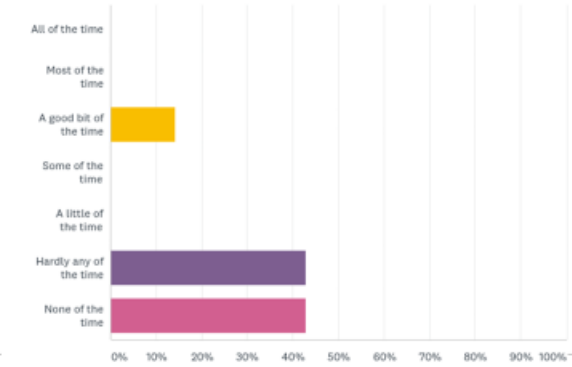
Q1: How frequent have your bowel motions been in the last 2 weeks in comparison with when your disease is stable?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
More frequent than they have ever been	0.00%	0
Extremely frequent	0.00%	0
Very frequent	0.00%	0
Moderate increase in frequency	14.29%	1
Some increase in frequency	0.00%	0
Slight increase in frequency	0.00%	0
No increase in frequency	85.71%	6
TOTAL		7

Q2: How often during the last 2 weeks have you been troubled by abdominal cramps?

Answered: 7 Skipped: 0



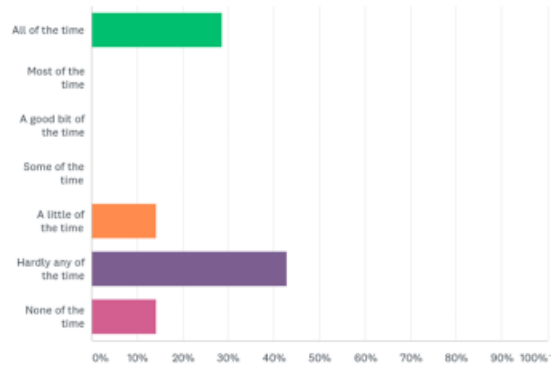
Q2: How often during the last 2 weeks have you been troubled by abdominal cramps?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	14.29%	1
Some of the time	0.00%	0
A little of the time	0.00%	0
Hardly any of the time	42.86%	3
None of the time	42.86%	3
TOTAL		7

Q3: How often has the feeling of fatigue, or of being tired and worn out been a problem for you in the last 2 weeks?

Answered: 7 Skipped: 0



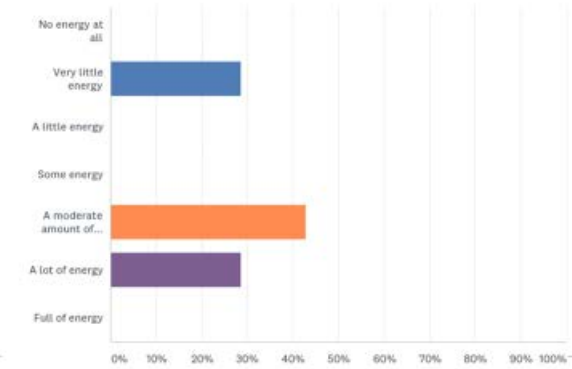
Q3: How often has the feeling of fatigue, or of being tired and worn out been a problem for you in the last 2 weeks?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	28.57%	2
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	0.00%	0
A little of the time	14.29%	1
Hardly any of the time	42.86%	3
None of the time	14.29%	1
TOTAL		7

Q4: How much energy have you had in the last 2 weeks?

Answered: 7 Skipped: 0



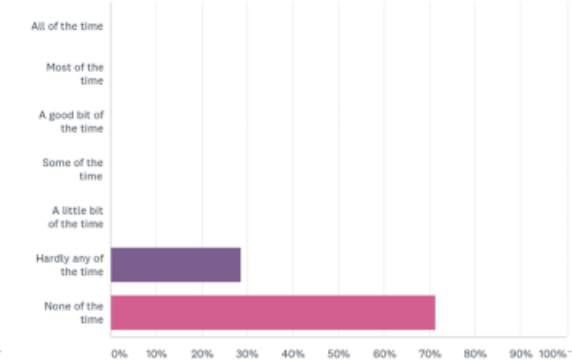
Q4: How much energy have you had in the last 2 weeks?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
No energy at all	0.00%	0
Very little energy	28.57%	2
A little energy	0.00%	0
Some energy	0.00%	0
A moderate amount of energy	42.86%	3
A lot of energy	28.57%	2
Full of energy	0.00%	0
TOTAL		7

Q5: How often during the last 2 weeks did you feel worried about the possibility of needing surgery for your inflammatory bowel disease?

Answered: 7 Skipped: 0



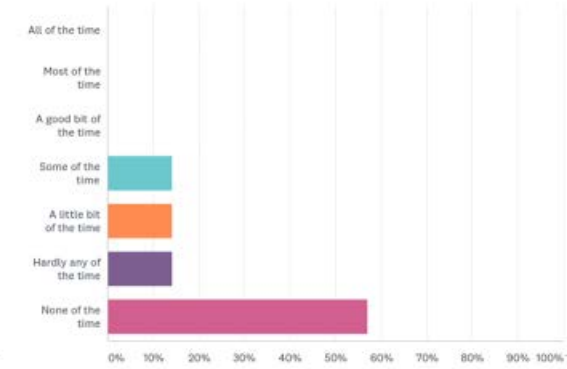
Q5: How often during the last 2 weeks did you feel worried about the possibility of needing surgery for your inflammatory bowel disease?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	0.00%	0
A little bit of the time	0.00%	0
Hardly any of the time	28.57%	2
None of the time	71.43%	5
TOTAL		7

Q6: How often during the last 2 weeks have you been troubled by fear of not finding a toilet?

Answered: 7 Skipped: 0



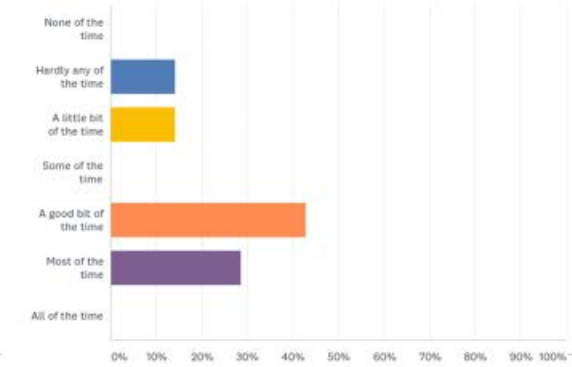
Q6: How often during the last 2 weeks have you been troubled by fear of not finding a toilet?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	0.00%	0
A good bit of the time	0.00%	0
Some of the time	14.29%	1
A little bit of the time	14.29%	1
Hardly any of the time	14.29%	1
None of the time	57.14%	4
TOTAL		7

Q7: How often during the last 2 weeks have you felt relaxed and free of tension?

Answered: 7 Skipped: 0



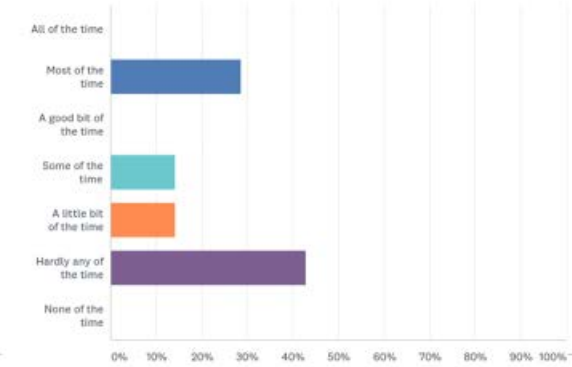
Q7: How often during the last 2 weeks have you felt relaxed and free of tension?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
None of the time	0.00%	0
Hardly any of the time	14.29%	1
A little bit of the time	14.29%	1
Some of the time	0.00%	0
A good bit of the time	42.86%	3
Most of the time	28.57%	2
All of the time	0.00%	0
TOTAL		7

Q8: How much of the time during the last 2 weeks have you felt irritable in mood?

Answered: 7 Skipped: 0



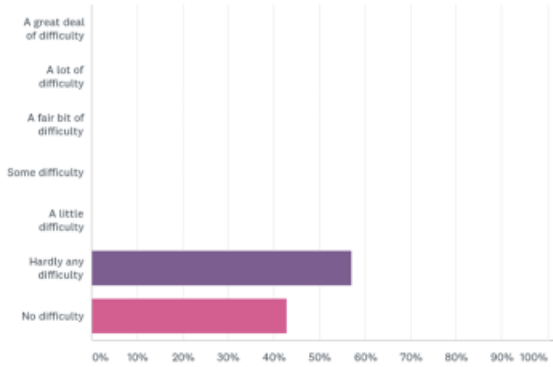
Q8: How much of the time during the last 2 weeks have you felt irritable in mood?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
All of the time	0.00%	0
Most of the time	28.57%	2
A good bit of the time	0.00%	0
Some of the time	14.29%	1
A little bit of the time	14.29%	1
Hardly any of the time	42.86%	3
None of the time	0.00%	0
TOTAL		7

Q9: How much difficulty have you had (as a result of your inflammatory bowel disease)doing the leisure or sports activities that you would like to have done in the last 2 weeks?

Answered: 7 Skipped: 0



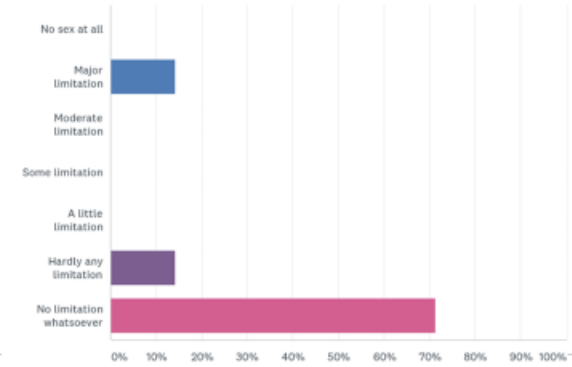
Q9: How much difficulty have you had (as a result of your inflammatory bowel disease)doing the leisure or sports activities that you would like to have done in the last 2 weeks?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
A great deal of difficulty	0.00%	0
A lot of difficulty	0.00%	0
A fair bit of difficulty	0.00%	0
Some difficulty	0.00%	0
A little difficulty	0.00%	0
Hardly any difficulty	57.14%	4
No difficulty	42.86%	3
TOTAL		7

Q10: To what extent has your inflammatory bowel disease limited sexual activity in the last 2 weeks?

Answered: 7 Skipped: 0



Q10: To what extent has your inflammatory bowel disease limited sexual activity in the last 2 weeks?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
No sex at all	0.00%	0
Major limitation	14.29%	1
Moderate limitation	0.00%	0
Some limitation	0.00%	0
A little limitation	0.00%	0
Hardly any limitation	14.29%	1
No limitation whatsoever	71.43%	5
TOTAL		7

Appendix E.15 CCKNOW 1 results

Crohn's and Colitis Knowledge Questionnaire 1

Sunday, August 25, 2019

11

Total Responses

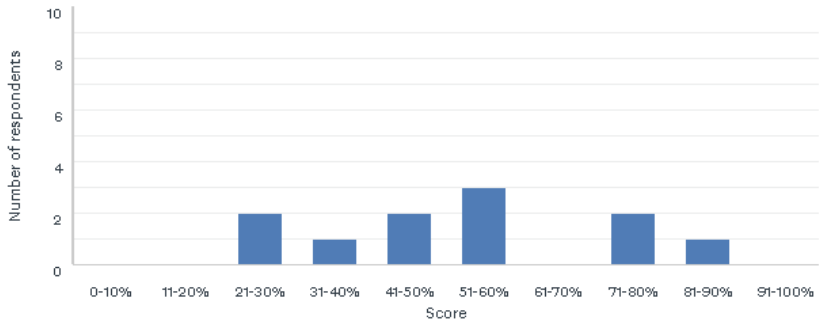
Date Created: Tuesday, April 04, 2017

Complete Responses: 11

Quiz Summary

AVERAGE SCORE

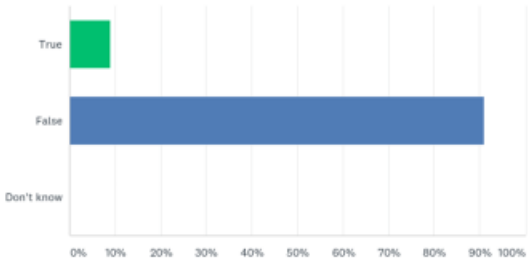
55% • **16**/30 PTS



STATISTICS		
Lowest Score	Median	Highest Score
27%	57%	83%
Mean: 55%		
Standard Deviation: 20%		

Q1: The intestines play an important role in the body but they only work during meal times

Answered: 11 Skipped: 0



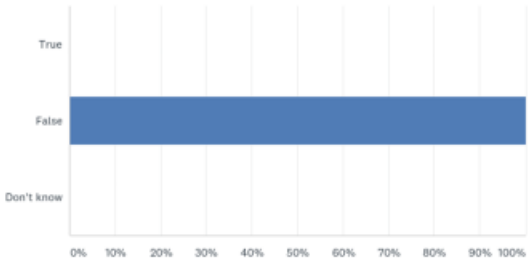
Q1: The intestines play an important role in the body but they only work during meal times

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	9.09%	1
False	90.91%	10
Don't know	0.00%	0
TOTAL		11

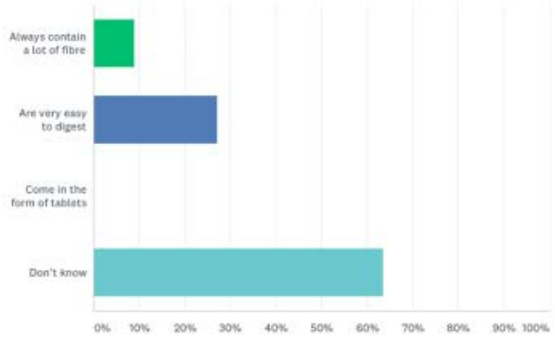
Q2: People with inflammatory bowel disease are never allowed to eat dairy products:

Answered: 11 Skipped: 0



Q3: Elemental feeds are sometimes used to treat Crohn's disease and ulcerative colitis. They:

Answered: 11 Skipped: 0



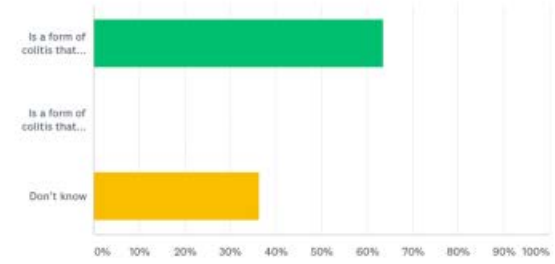
Q3: Elemental feeds are sometimes used to treat Crohn's disease and ulcerative colitis. They:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Always contain a lot of fibre	9.09%	1
Are very easy to digest	27.27%	3
Come in the form of tablets	0.00%	0
Don't know	63.64%	7
TOTAL		11

Q4: Proctitis:

Answered: 11 Skipped: 0



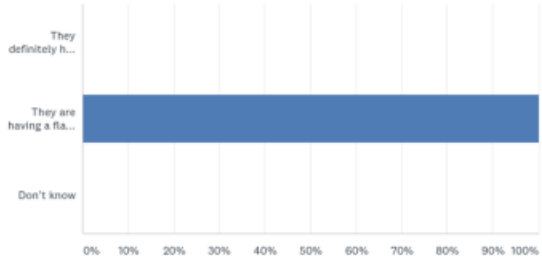
Q4: Proctitis:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Is a form of colitis that affects the rectum or back passage only	63.64%	7
Is a form of colitis that affects the whole of the large bowel	0.00%	0
Don't know	36.36%	4
TOTAL		11

Q5: When a patient with inflammatory bowel disease passes blood in their stool it means:

Answered: 11 Skipped: 0



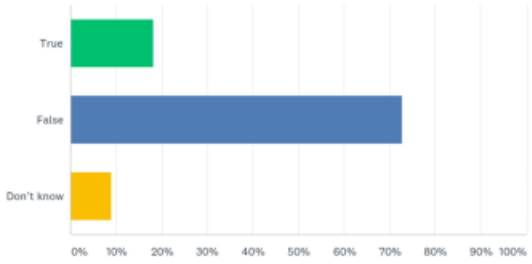
Q5: When a patient with inflammatory bowel disease passes blood in their stool it means:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
They definitely have bowel cancer	0.00%	0
They are having a flare up of their disease	100.00%	11
Don't know	0.00%	0
TOTAL		11

Q6: Patients with inflammatory bowel disease are probably cured if they have been symptom free for 3 years:

Answered: 11 Skipped: 0



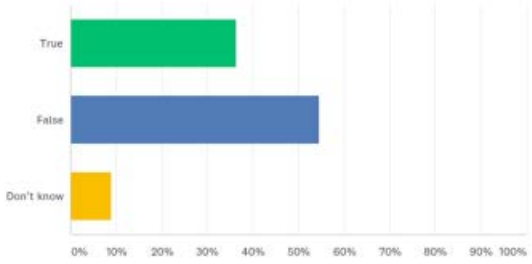
Q6: Patients with inflammatory bowel disease are probably cured if they have been symptom free for 3 years:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	18.18%	2
False	72.73%	8
Don't know	9.09%	1
TOTAL		11

Q7: Inflammatory bowel disease runs in families:

Answered: 11 Skipped: 0



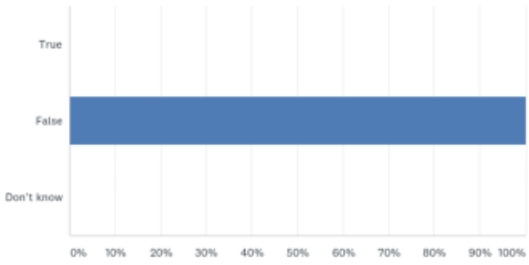
Q7: Inflammatory bowel disease runs in families:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	36.36%	4
False	54.55%	6
Don't know	9.09%	1
TOTAL		11

Q8: If patients with inflammatory bowel disease are not careful with their personal hygiene they can pass on their disease to friends and members of the family:

Answered: 11 Skipped: 0



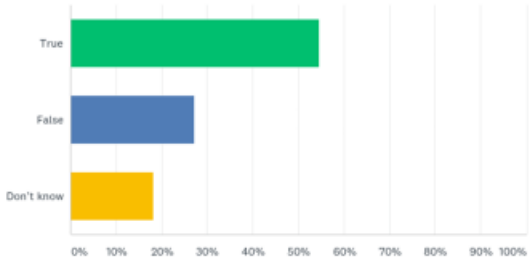
Q8: If patients with inflammatory bowel disease are not careful with their personal hygiene they can pass on their disease to friends and members of the family:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	0.00%	0
False	100.00%	11
Don't know	0.00%	0
TOTAL		11

Q9: Patients with inflammatory bowel disease can get inflammation in other parts of the body as well as the bowel:

Answered: 11 Skipped: 0



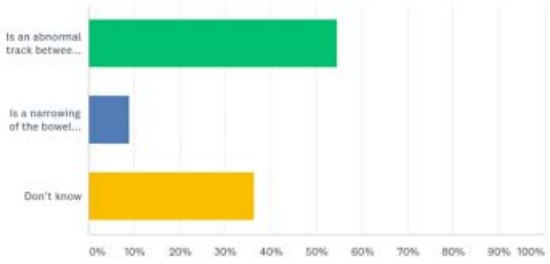
Q9: Patients with inflammatory bowel disease can get inflammation in other parts of the body as well as the bowel:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	54.55%	6
False	27.27%	3
Don't know	18.18%	2
TOTAL		11

Q10: A fistula:

Answered: 11 Skipped: 0



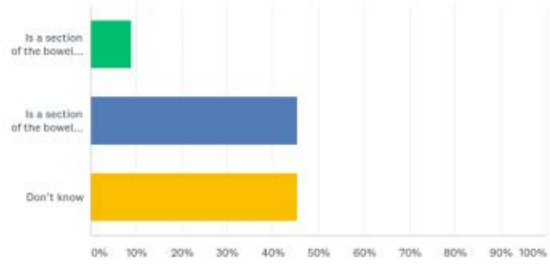
Q10: A fistula:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Is an abnormal track between 2 pieces of bowel or between the bowel and skin	54.55%	6
Is a narrowing of the bowel which may obstruct the passage of the contents	9.09%	1
Don't know	36.36%	4
TOTAL		11

Q11: The terminal ileum:

Answered: 11 Skipped: 0



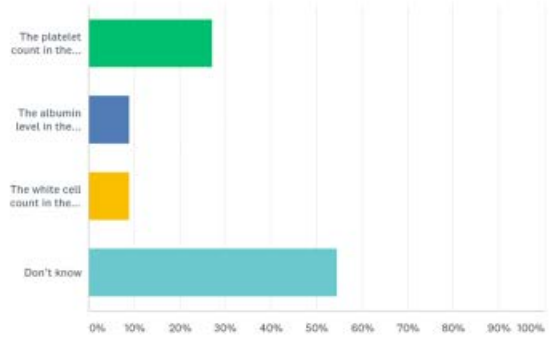
Q11: The terminal ileum:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Is a section of the bowel just before the anus	9.09%	1
Is a section of the bowel just before the large intestine	45.45%	5
Don't know	45.45%	5
TOTAL		11

Q12: During a flare up of inflammatory bowel disease:

Answered: 11 Skipped: 0



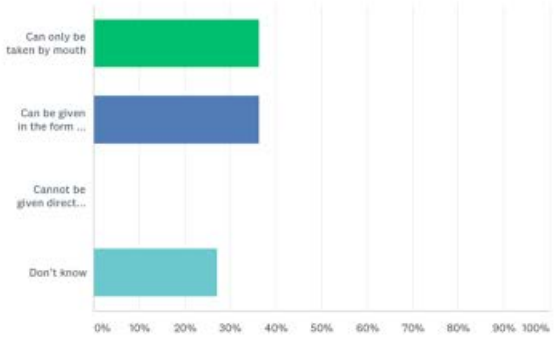
Q12: During a flare up of inflammatory bowel disease:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
The platelet count in the blood rises	27.27%	3
The albumin level in the blood rises	9.09%	1
The white cell count in the blood falls	9.09%	1
Don't know	54.55%	6
TOTAL		11

Q13: Steroids (such as prednisolone/prednisone/budesonide/hydrocortisone):

Answered: 11 Skipped: 0



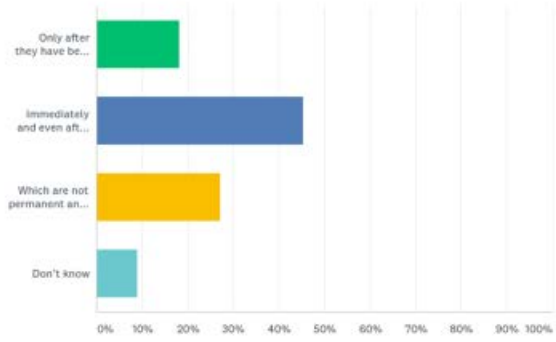
Q13: Steroids (such as prednisolone/prednisone/budesonide/hydrocortisone):

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Can only be taken by mouth	36.36%	4
Can be given in the form of an enema into the back passage	36.36%	4
Cannot be given directly into the vein	0.00%	0
Don't know	27.27%	3
TOTAL		11

Q14: Steroids usually cause side effects:

Answered: 11 Skipped: 0



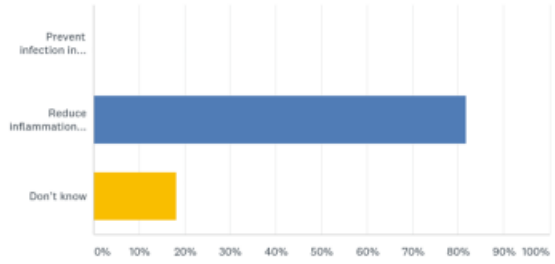
Q14: Steroids usually cause side effects:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Only after they have been taken for a long time and in high doses	18.18%	2
Immediately and even after small doses	45.45%	5
Which are not permanent and all disappear after treatment is stopped	27.27%	3
Don't know	9.09%	1
TOTAL		11

Q15: Immunosuppressive drugs are given to inflammatory bowel disease patients to:

Answered: 11 Skipped: 0



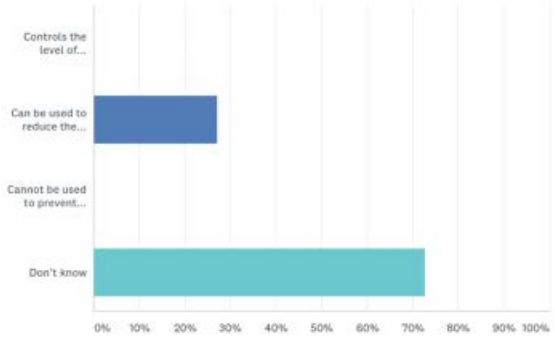
Q15: Immunosuppressive drugs are given to inflammatory bowel disease patients to:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Prevent infection in the bowel by bacteria	0.00%	0
Reduce inflammation in the bowel	81.82%	9
Don't know	18.18%	2
TOTAL		11

Q16: Sulphasalazine:

Answered: 11 Skipped: 0



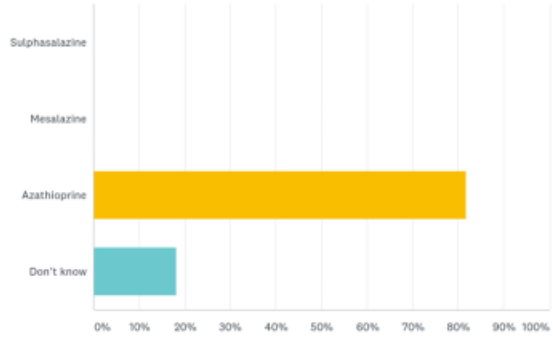
Q16: Sulphasalazine:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Controls the level of sulphur in the bloodstream	0.00%	0
Can be used to reduce the frequency of flare ups	27.27%	3
Cannot be used to prevent flare ups	0.00%	0
Don't know	72.73%	8
TOTAL		11

Q17: An example of an immunosuppressive drug used in inflammatory bowel disease is:

Answered: 11 Skipped: 0



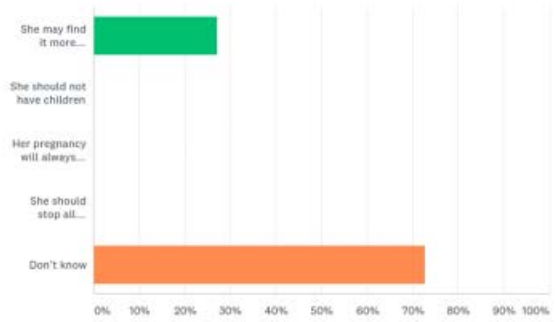
Q17: An example of an immunosuppressive drug used in inflammatory bowel disease is:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Sulphasalazine	0.00%	0
Mesalazine	0.00%	0
Azathioprine	81.82%	9
Don't know	18.18%	2
TOTAL		11

Q18: If a woman has Crohn's disease:

Answered: 11 Skipped: 0



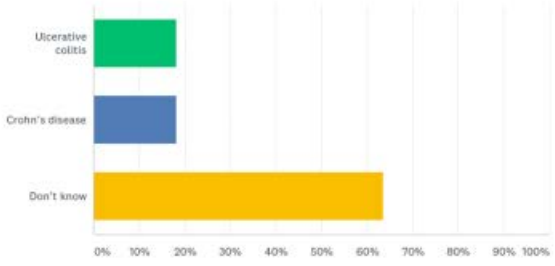
Q18: If a woman has Crohn's disease:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
She may find it more difficult to become pregnant	27.27%	3
She should not have children	0.00%	0
Her pregnancy will always have complications	0.00%	0
She should stop all medication during her pregnancy	0.00%	0
Don't know	72.73%	8
TOTAL		11

Q19: Patients who smoke are more likely to have:

Answered: 11 Skipped: 0



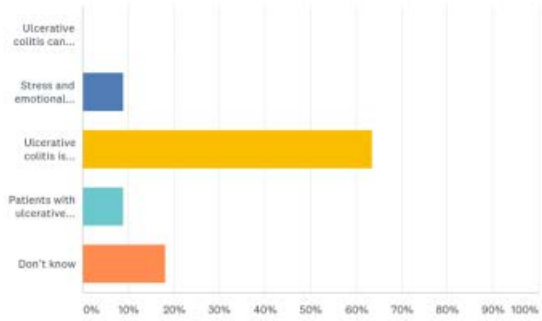
Q19: Patients who smoke are more likely to have:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Ulcerative colitis	18.18%	2
Crohn's disease	18.18%	2
Don't know	63.64%	7
TOTAL		11

Q20: Which one of the following statements is false?

Answered: 11 Skipped: 0



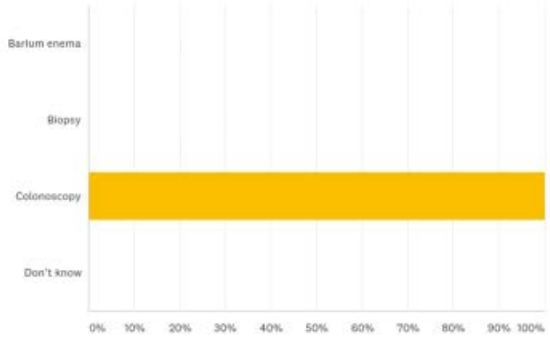
Q20: Which one of the following statements is false?

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Ulcerative colitis can occur at any age	0.00%	0
Stress and emotional events are linked with the onset of ulcerative colitis	9.09%	1
Ulcerative colitis is least common in Europeans and North Americans	63.64%	7
Patients with ulcerative colitis have an increased risk of developing bowel cancer	9.09%	1
Don't know	18.18%	2
TOTAL		11

Q21: The examination of the large bowel with a flexible camera is called a:

Answered: 11 Skipped: 0



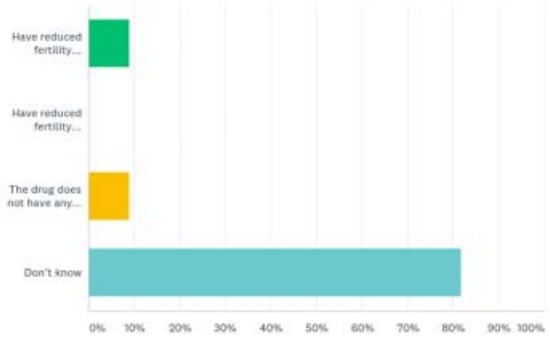
Q21: The examination of the large bowel with a flexible camera is called a:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Barium enema	0.00%	0
Biopsy	0.00%	0
Colonoscopy	100.00%	11
Don't know	0.00%	0
TOTAL		11

Q22: Male patients who take sulphasalazine:

Answered: 11 Skipped: 0



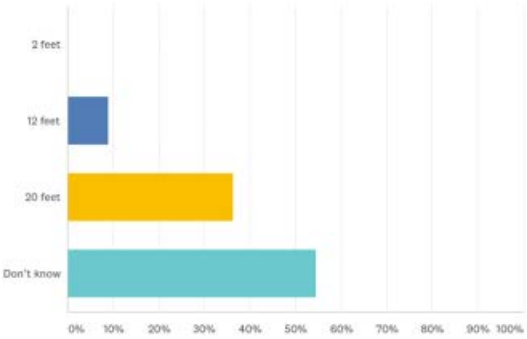
Q22: Male patients who take sulphasalazine:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Have reduced fertility levels that are reversible	9.09%	1
Have reduced fertility levels that are not reversible	0.00%	0
The drug does not have any effect on male fertility	9.09%	1
Don't know	81.82%	9
TOTAL		11

Q23: The length of the small bowel is approximately:

Answered: 11 Skipped: 0



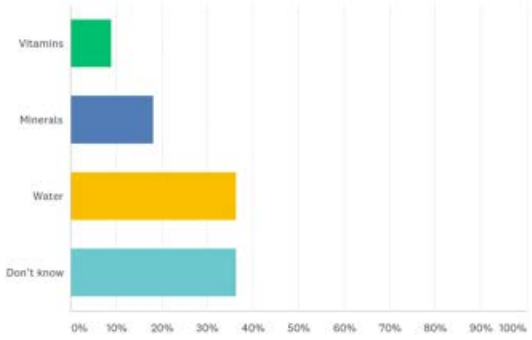
Q23: The length of the small bowel is approximately:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
2 feet	0.00%	0
12 feet	9.09%	1
20 feet	36.36%	4
Don't know	54.55%	6
TOTAL		11

Q24: The function of the large bowel is to absorb:

Answered: 11 Skipped: 0



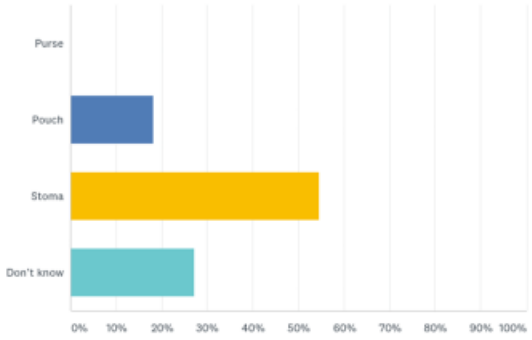
Q24: The function of the large bowel is to absorb:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Vitamins	9.09%	1
Minerals	18.18%	2
Water	36.36%	4
Don't know	36.36%	4
TOTAL		11

Q25: Another name for an ileorectal anastomosis operation with formation of a reservoir is:

Answered: 11 Skipped: 0



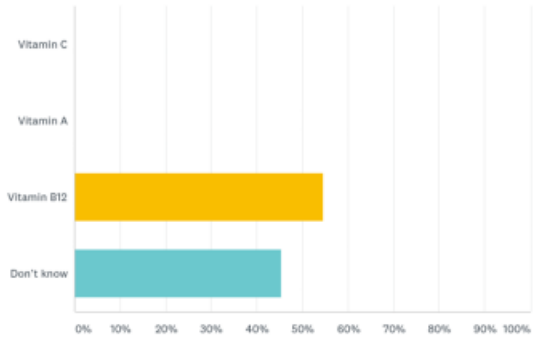
Q25: Another name for an ileorectal anastomosis operation with formation of a reservoir is:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Purse	0.00%	0
Pouch	18.18%	2
Stoma	54.55%	6
Don't know	27.27%	3
TOTAL		11

Q26: If a part of the bowel called the terminal ileum is removed during surgery the patient will have impaired absorption of:

Answered: 11 Skipped: 0



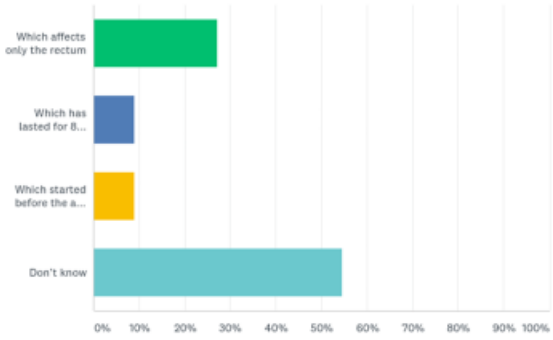
Q26: If a part of the bowel called the terminal ileum is removed during surgery the patient will have impaired absorption of:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Vitamin C	0.00%	0
Vitamin A	0.00%	0
Vitamin B12	54.55%	6
Don't know	45.45%	5
TOTAL		11

Q27: Patients with IBD need to be screened for cancer of the colon. Which one of the following statements about screening is false? Screening should be offered to all patients with ulcerative colitis:

Answered: 11 Skipped: 0



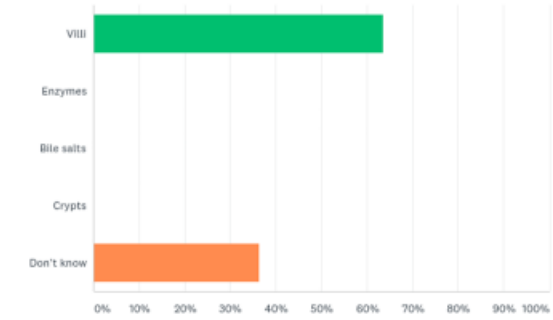
Q27: Patients with IBD need to be screened for cancer of the colon. Which one of the following statements about screening is false? Screening should be offered to all patients with ulcerative colitis:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Which affects only the rectum	27.27%	3
Which has lasted for 8–10 years	9.09%	1
Which started before the age of 50	9.09%	1
Don't know	54.55%	6
TOTAL		11

Q28: There are millions of tiny "hairs" in the small bowel to increase the absorptive surface. They are called:

Answered: 11 Skipped: 0



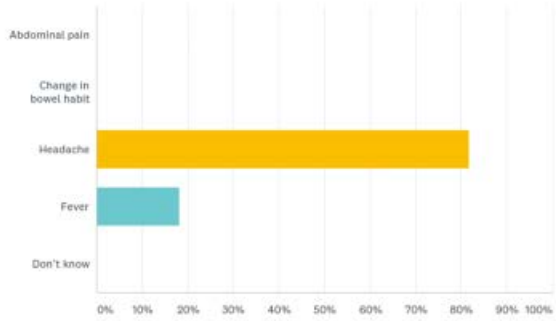
Q28: There are millions of tiny “hairs” in the small bowel to increase the absorptive surface. They are called:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Villi	63.64%	7
Enzymes	0.00%	0
Bile salts	0.00%	0
Crypts	0.00%	0
Don't know	36.36%	4
TOTAL		11

Q29: Which one of the following is not a common symptom of inflammatory bowel disease?

Answered: 11 Skipped: 0



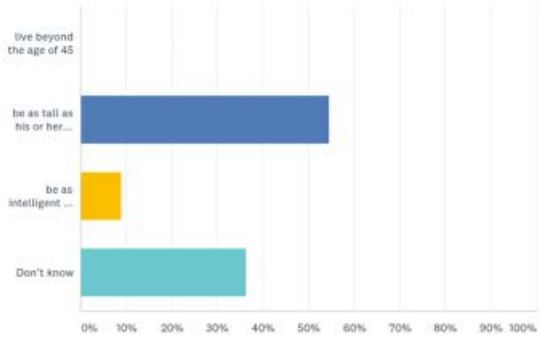
Q29: Which one of the following is not a common symptom of inflammatory bowel disease?

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
Abdominal pain	0.00%	0
Change in bowel habit	0.00%	0
Headache	81.82%	9
Fever	18.18%	2
Don't know	0.00%	0
TOTAL		11

Q30: If a child has inflammatory bowel disease; he/she probably will not:

Answered: 11 Skipped: 0



Q30: If a child has inflammatory bowel disease; he/she probably will not:

Answered: 11 Skipped: 0

ANSWER CHOICES	RESPONSES	
live beyond the age of 45	0.00%	0
be as tall as his or her friends	54.55%	6
be as intelligent as his or her friends	9.09%	1
Don't know	36.36%	4
TOTAL		11

Appendix E.16 CCKNOW 2 results

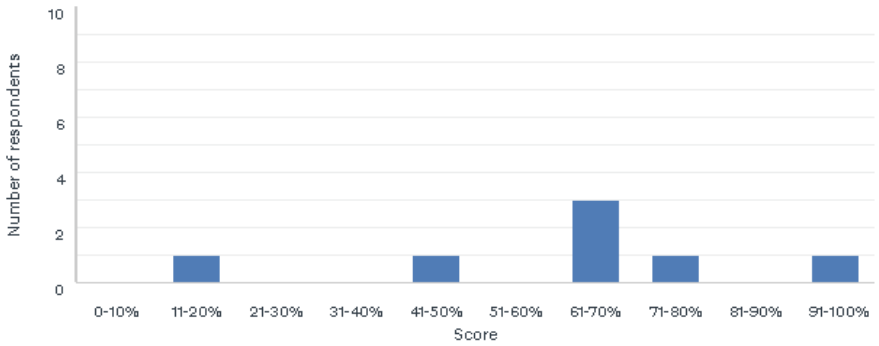
Crohn's and Colitis Knowledge Questionnaire 2

Sunday, August 25, 2019

Quiz Summary

AVERAGE SCORE

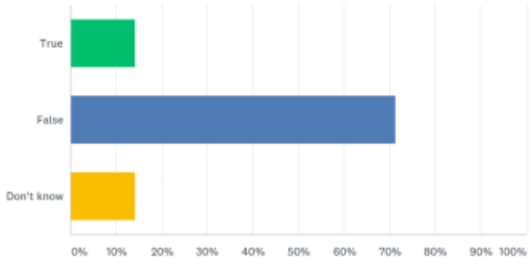
60% • **18**/30 PTS



STATISTICS		
Lowest Score	Median	Highest Score
17%	63%	93%
Mean: 60%		
Standard Deviation: 23%		

Q1: The intestines play an important role in the body but they only work during meal times

Answered: 7 Skipped: 0



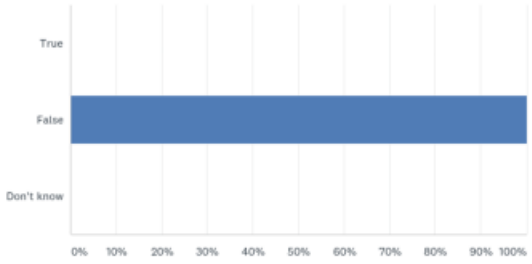
Q1: The intestines play an important role in the body but they only work during meal times

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	14.29%	1
False	71.43%	5
Don't know	14.29%	1
TOTAL		7

Q2: People with inflammatory bowel disease are never allowed to eat dairy products:

Answered: 7 Skipped: 0



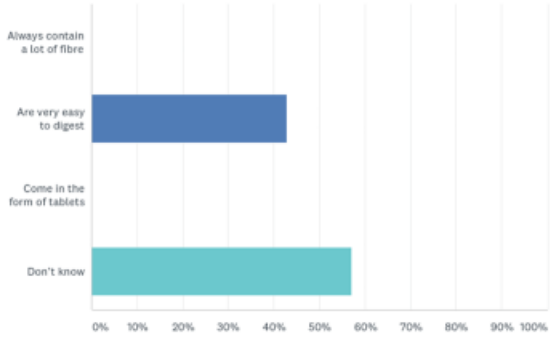
Q2: People with inflammatory bowel disease are never allowed to eat dairy products:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	0.00%	0
False	100.00%	7
Don't know	0.00%	0
TOTAL		7

Q3: Elemental feeds are sometimes used to treat Crohn's disease and ulcerative colitis. They:

Answered: 7 Skipped: 0



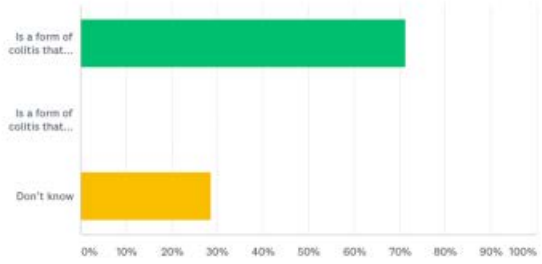
Q3: Elemental feeds are sometimes used to treat Crohn's disease and ulcerative colitis. They:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Always contain a lot of fibre	0.00%	0
Are very easy to digest	42.86%	3
Come in the form of tablets	0.00%	0
Don't know	57.14%	4
TOTAL		7

Q4: Proctitis:

Answered: 7 Skipped: 0



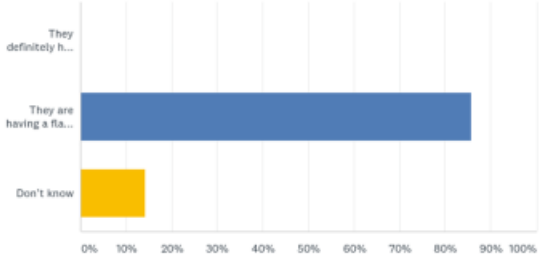
Q4: Proctitis:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Is a form of colitis that affects the rectum or back passage only	71.43%	5
Is a form of colitis that affects the whole of the large bowel	0.00%	0
Don't know	28.57%	2
TOTAL		7

Q5: When a patient with inflammatory bowel disease passes blood in their stool it means:

Answered: 7 Skipped: 0



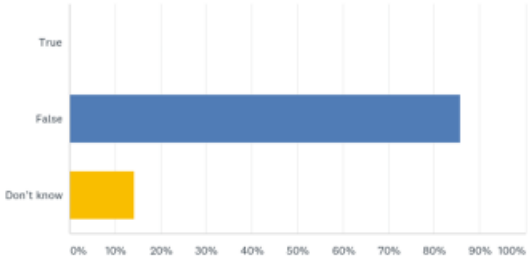
Q5: When a patient with inflammatory bowel disease passes blood in their stool it means:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
They definitely have bowel cancer	0.00%	0
They are having a flare up of their disease	85.71%	6
Don't know	14.29%	1
TOTAL		7

Q6: Patients with inflammatory bowel disease are probably cured if they have been symptom free for 3 years:

Answered: 7 Skipped: 0



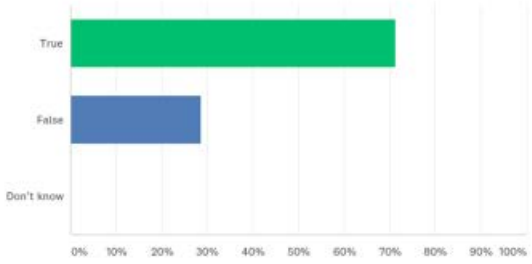
Q6: Patients with inflammatory bowel disease are probably cured if they have been symptom free for 3 years:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	0.00%	0
False	85.71%	6
Don't know	14.29%	1
TOTAL		7

Q7: Inflammatory bowel disease runs in families:

Answered: 7 Skipped: 0



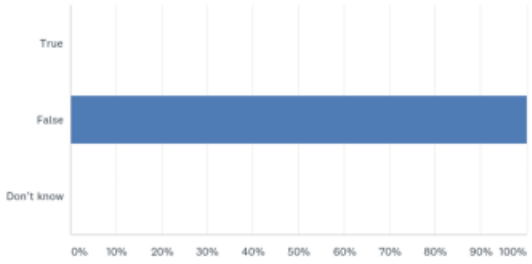
Q7: Inflammatory bowel disease runs in families:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	71.43%	5
False	28.57%	2
Don't know	0.00%	0
TOTAL		7

Q8: If patients with inflammatory bowel disease are not careful with their personal hygiene they can pass on their disease to friends and members of the family:

Answered: 7 Skipped: 0



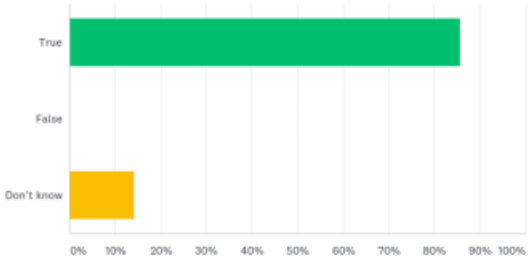
Q8: If patients with inflammatory bowel disease are not careful with their personal hygiene they can pass on their disease to friends and members of the family:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	0.00%	0
False	100.00%	7
Don't know	0.00%	0
TOTAL		7

Q9: Patients with inflammatory bowel disease can get inflammation in other parts of the body as well as the bowel:

Answered: 7 Skipped: 0



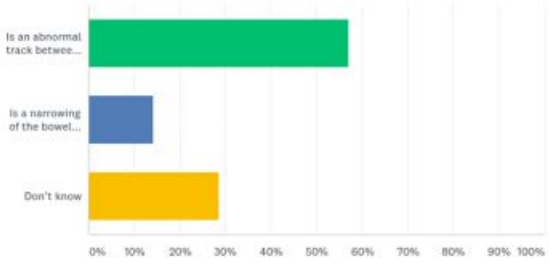
Q9: Patients with inflammatory bowel disease can get inflammation in other parts of the body as well as the bowel:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
True	85.71%	6
False	0.00%	0
Don't know	14.29%	1
TOTAL		7

Q10: A fistula:

Answered: 7 Skipped: 0



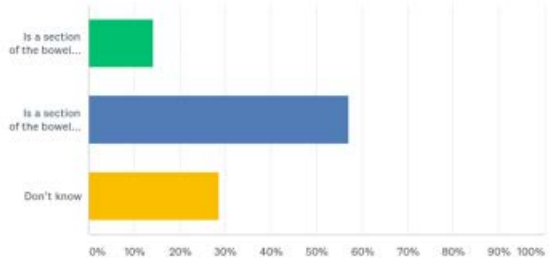
Q10: A fistula:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Is an abnormal track between 2 pieces of bowel or between the bowel and skin	57.14%	4
Is a narrowing of the bowel which may obstruct the passage of the contents	14.29%	1
Don't know	28.57%	2
TOTAL		7

Q11: The terminal ileum:

Answered: 7 Skipped: 0



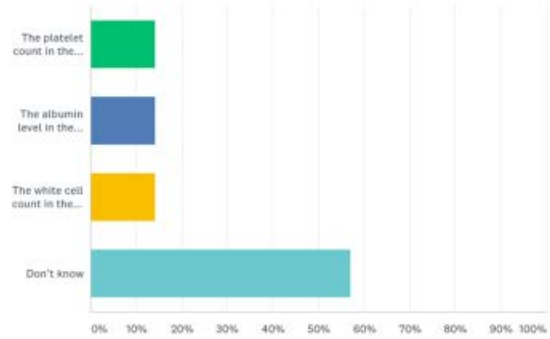
Q11: The terminal ileum:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Is a section of the bowel just before the anus	14.29%	1
Is a section of the bowel just before the large intestine	57.14%	4
Don't know	28.57%	2
TOTAL		7

Q12: During a flare up of inflammatory bowel disease:

Answered: 7 Skipped: 0



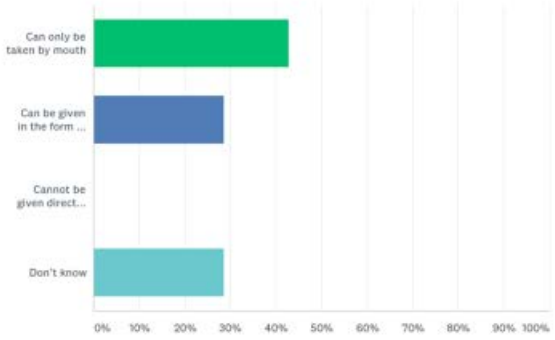
Q12: During a flare up of inflammatory bowel disease:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
The platelet count in the blood rises	14.29%	1
The albumin level in the blood rises	14.29%	1
The white cell count in the blood falls	14.29%	1
Don't know	57.14%	4
TOTAL		7

Q13: Steroids (such as prednisolone/prednisone/budesonide/hydrocortisone):

Answered: 7 Skipped: 0



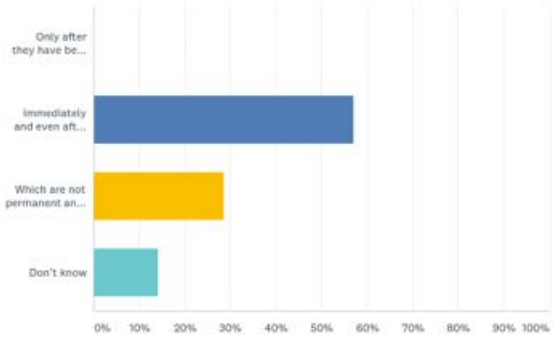
Q13: Steroids (such as prednisolone/prednisone/budesonide/hydrocortisone):

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Can only be taken by mouth	42.86%	3
Can be given in the form of an enema into the back passage	28.57%	2
Cannot be given directly into the vein	0.00%	0
Don't know	28.57%	2
TOTAL		7

Q14: Steroids usually cause side effects:

Answered: 7 Skipped: 0



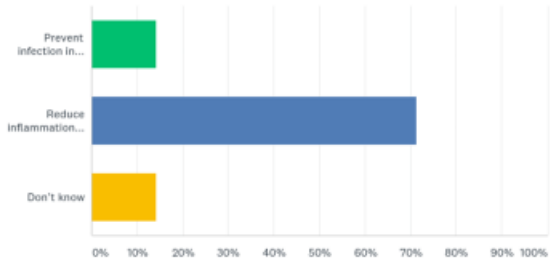
Q14: Steroids usually cause side effects:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Only after they have been taken for a long time and in high doses	0.00%	0
Immediately and even after small doses	57.14%	4
Which are not permanent and all disappear after treatment is stopped	28.57%	2
Don't know	14.29%	1
TOTAL		7

Q15: Immunosuppressive drugs are given to inflammatory bowel disease patients to:

Answered: 7 Skipped: 0



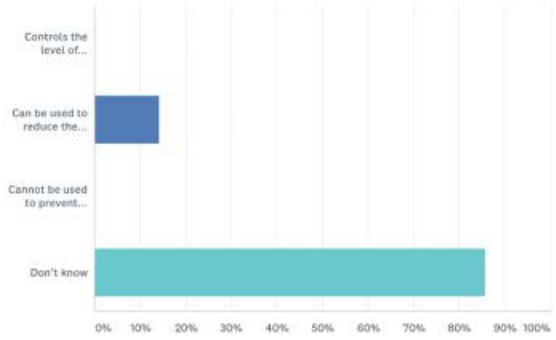
Q15: Immunosuppressive drugs are given to inflammatory bowel disease patients to:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Prevent infection in the bowel by bacteria	14.29%	1
Reduce inflammation in the bowel	71.43%	5
Don't know	14.29%	1
TOTAL		7

Q16: Sulphasalazine:

Answered: 7 Skipped: 0



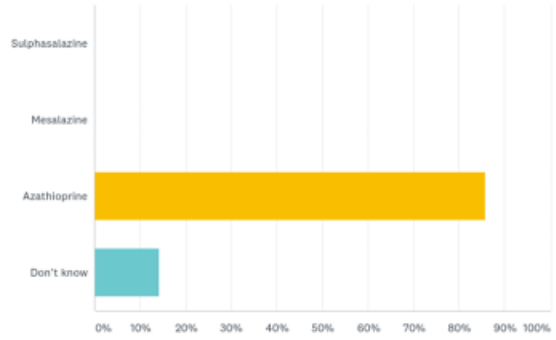
Q16: Sulphasalazine:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Controls the level of sulphur in the bloodstream	0.00%	0
Can be used to reduce the frequency of flare ups	14.29%	1
Cannot be used to prevent flare ups	0.00%	0
Don't know	85.71%	6
TOTAL		7

Q17: An example of an immunosuppressive drug used in inflammatory bowel disease is:

Answered: 7 Skipped: 0



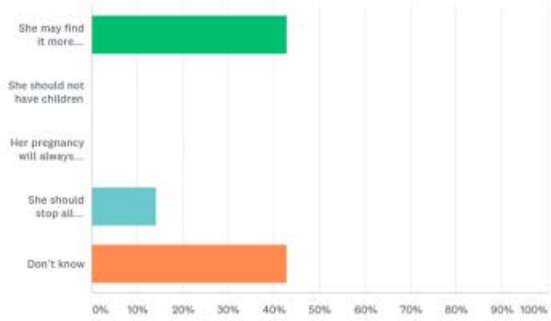
Q17: An example of an immunosuppressive drug used in inflammatory bowel disease is:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Sulphasalazine	0.00%	0
Mesalazine	0.00%	0
Azathioprine	85.71%	6
Don't know	14.29%	1
TOTAL		7

Q18: If a woman has Crohn's disease:

Answered: 7 Skipped: 0



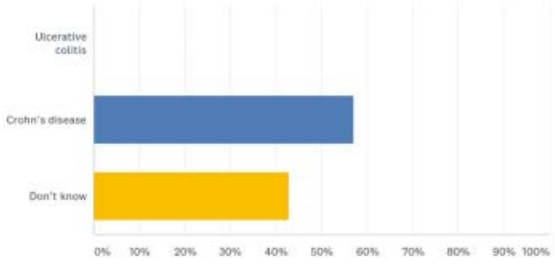
Q18: If a woman has Crohn's disease:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
She may find it more difficult to become pregnant	42.86%	3
She should not have children	0.00%	0
Her pregnancy will always have complications	0.00%	0
She should stop all medication during her pregnancy	14.29%	1
Don't know	42.86%	3
TOTAL		7

Q19: Patients who smoke are more likely to have:

Answered: 7 Skipped: 0



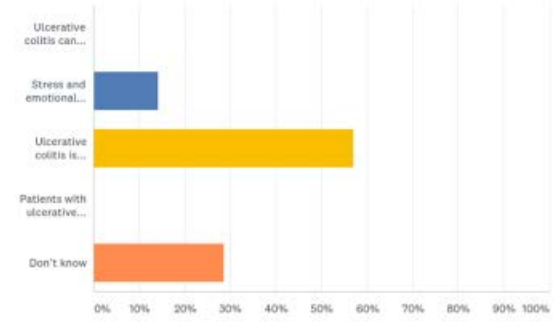
Q19: Patients who smoke are more likely to have:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Ulcerative colitis	0.00%	0
Crohn's disease	57.14%	4
Don't know	42.86%	3
TOTAL		7

Q20: Which one of the following statements is false?

Answered: 7 Skipped: 0



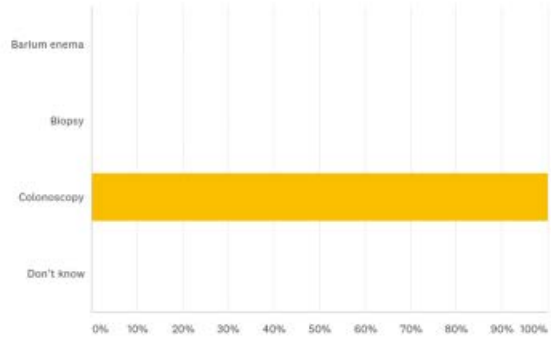
Q20: Which one of the following statements is false?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Ulcerative colitis can occur at any age	0.00%	0
Stress and emotional events are linked with the onset of ulcerative colitis	14.29%	1
Ulcerative colitis is least common in Europeans and North Americans	57.14%	4
Patients with ulcerative colitis have an increased risk of developing bowel cancer	0.00%	0
Don't know	28.57%	2
TOTAL		7

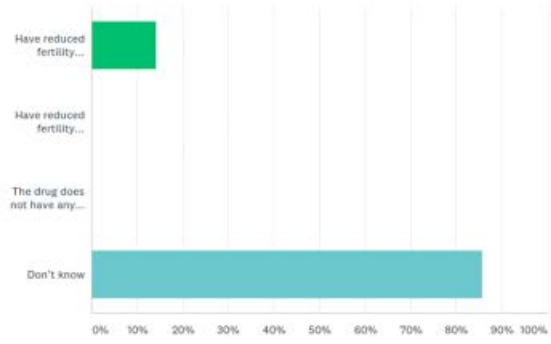
Q21: The examination of the large bowel with a flexible camera is called a:

Answered: 7 Skipped: 0



Q22: Male patients who take sulphasalazine:

Answered: 7 Skipped: 0



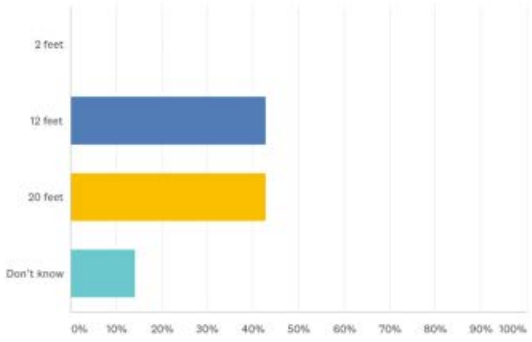
Q22: Male patients who take sulphasalazine:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Have reduced fertility levels that are reversible	14.29%	1
Have reduced fertility levels that are not reversible	0.00%	0
The drug does not have any effect on male fertility	0.00%	0
Don't know	85.71%	6
TOTAL		7

Q23: The length of the small bowel is approximately:

Answered: 7 Skipped: 0



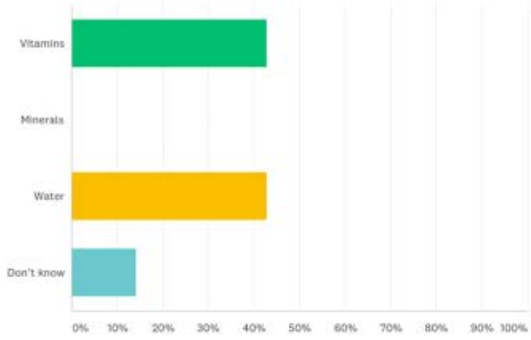
Q23: The length of the small bowel is approximately:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
2 feet	0.00%	0
12 feet	42.86%	3
20 feet	42.86%	3
Don't know	14.29%	1
TOTAL		7

Q24: The function of the large bowel is to absorb:

Answered: 7 Skipped: 0



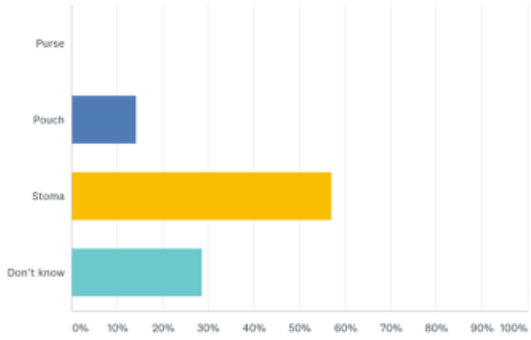
Q24: The function of the large bowel is to absorb:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Vitamins	42.86%	3
Minerals	0.00%	0
Water	42.86%	3
Don't know	14.29%	1
TOTAL		7

Q25: Another name for an ileorectal anastomosis operation with formation of a reservoir is:

Answered: 7 Skipped: 0



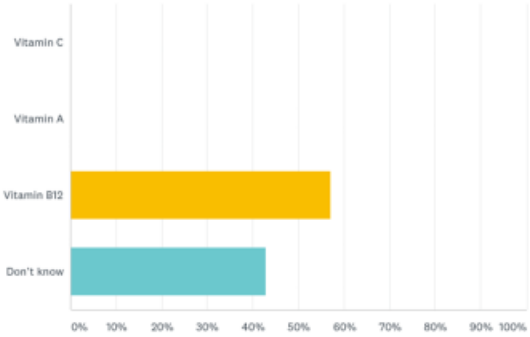
Q25: Another name for an ileorectal anastomosis operation with formation of a reservoir is:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Purse	0.00%	0
Pouch	14.29%	1
Stoma	57.14%	4
Don't know	28.57%	2
TOTAL		7

Q26: If a part of the bowel called the terminal ileum is removed during surgery the patient will have impaired absorption of:

Answered: 7 Skipped: 0



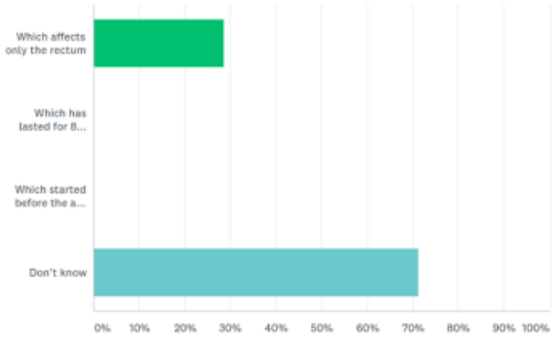
Q26: If a part of the bowel called the terminal ileum is removed during surgery the patient will have impaired absorption of:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Vitamin C	0.00%	0
Vitamin A	0.00%	0
Vitamin B12	57.14%	4
Don't know	42.86%	3
TOTAL		7

Q27: Patients with IBD need to be screened for cancer of the colon. Which one of the following statements about screening is false? Screening should be offered to all patients with ulcerative colitis:

Answered: 7 Skipped: 0



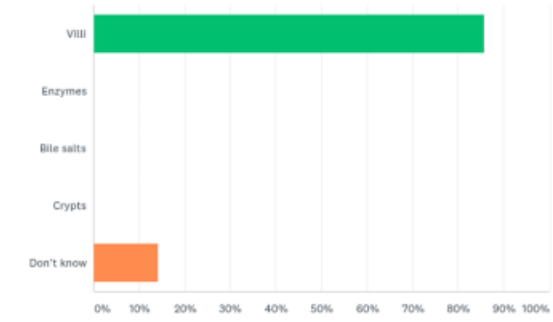
Q27: Patients with IBD need to be screened for cancer of the colon. Which one of the following statements about screening is false? Screening should be offered to all patients with ulcerative colitis:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Which affects only the rectum	28.57%	2
Which has lasted for 8–10 years	0.00%	0
Which started before the age of 50	0.00%	0
Don't know	71.43%	5
TOTAL		7

Q28: There are millions of tiny "hairs" in the small bowel to increase the absorptive surface. They are called:

Answered: 7 Skipped: 0



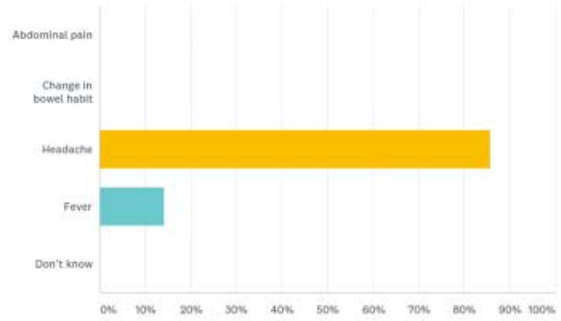
Q28: There are millions of tiny “hairs” in the small bowel to increase the absorptive surface. They are called:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Villi	85.71%	6
Enzymes	0.00%	0
Bile salts	0.00%	0
Crypts	0.00%	0
Don't know	14.29%	1
TOTAL		7

Q29: Which one of the following is not a common symptom of inflammatory bowel disease?

Answered: 7 Skipped: 0



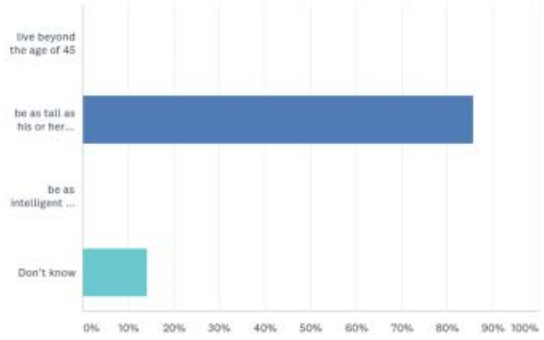
Q29: Which one of the following is not a common symptom of inflammatory bowel disease?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Abdominal pain	0.00%	0
Change in bowel habit	0.00%	0
Headache	85.71%	6
Fever	14.29%	1
Don't know	0.00%	0
TOTAL		7

Q30: If a child has inflammatory bowel disease; he/she probably will not:

Answered: 7 Skipped: 0



Q30: If a child has inflammatory bowel disease; he/she probably will not:

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
live beyond the age of 45	0.00%	0
be as tall as his or her friends	85.71%	6
be as intelligent as his or her friends	0.00%	0
Don't know	14.29%	1
TOTAL		7

Appendix E.17 End of study questionnaire results

Home faecal calprotectin monitoring study

Sunday, August 25, 2019

7

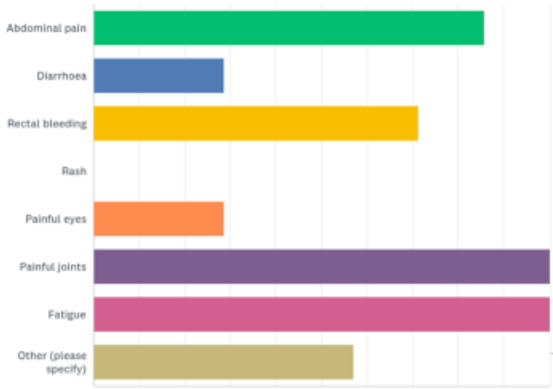
Total Responses

Date Created: Tuesday, January 30, 2018

Complete Responses: 7

Q1: What are the typical symptoms you experience during a flare-up of your IBD? Please tick all that apply.

Answered: 7 Skipped: 0



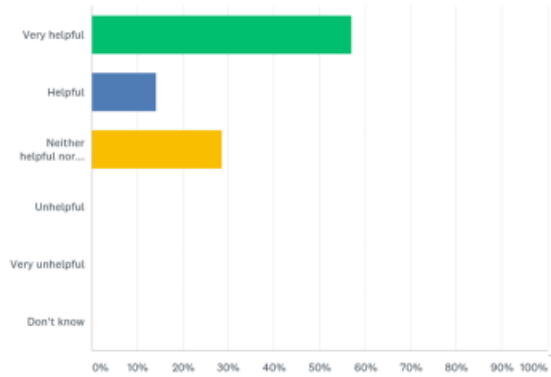
Q1: What are the typical symptoms you experience during a flare-up of your IBD? Please tick all that apply.

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Abdominal pain	85.71%	6
Diarrhoea	28.57%	2
Rectal bleeding	71.43%	5
Rash	0.00%	0
Painful eyes	28.57%	2
Painful joints	100.00%	7
Fatigue	100.00%	7
Other (please specify)	57.14%	4
Total Respondents: 7		

Q2: When it comes to managing your IBD, how helpful did you find viewing your tests results on the MyMR website?

Answered: 7 Skipped: 0



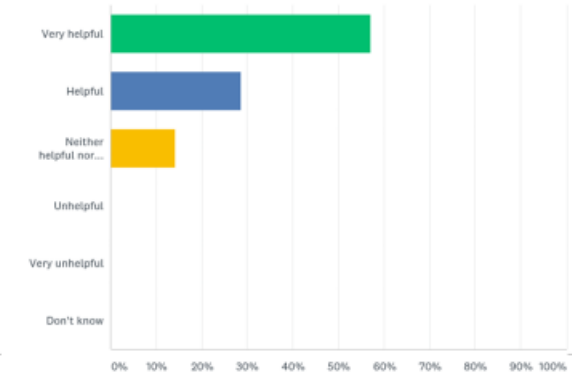
Q2: When it comes to managing your IBD, how helpful did you find viewing your tests results on the MyMR website?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Very helpful	57.14%	4
Helpful	14.29%	1
Neither helpful nor unhelpful	28.57%	2
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	0.00%	0
TOTAL		7

Q3: When it comes to managing your IBD, how helpful did you find looking at your clinic letters on the MyMR website?

Answered: 7 Skipped: 0



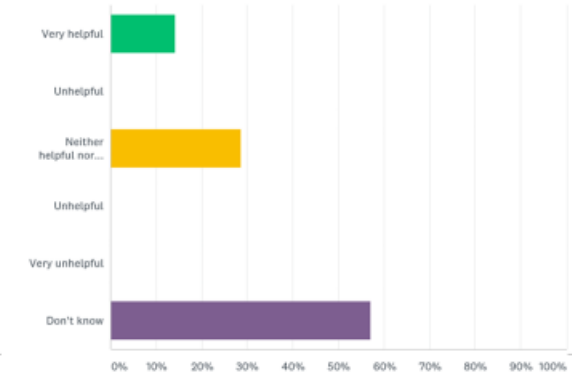
Q3: When it comes to managing your IBD, how helpful did you find looking at your clinic letters on the MyMR website?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Very helpful	57.14%	4
Helpful	28.57%	2
Neither helpful nor unhelpful	14.29%	1
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	0.00%	0
TOTAL		7

Q4: When it comes to managing your IBD, how helpful did you find using the email messaging service on the MyMR website?

Answered: 7 Skipped: 0



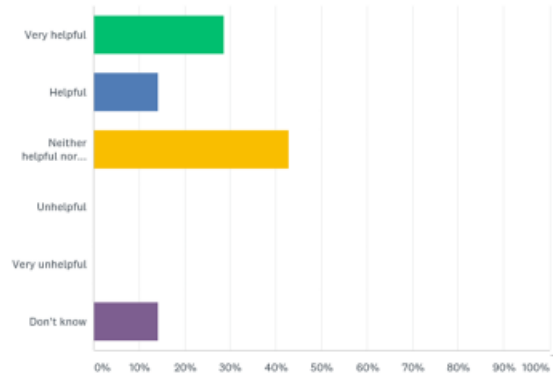
Q4: When it comes to managing your IBD, how helpful did you find using the email messaging service on the MyMR website?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Very helpful	14.29%	1
Unhelpful	0.00%	0
Neither helpful nor unhelpful	28.57%	2
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	57.14%	4
TOTAL		7

Q5: When it comes to managing your IBD, how helpful did you find reading the IBD educational material on the MyMR website?

Answered: 7 Skipped: 0



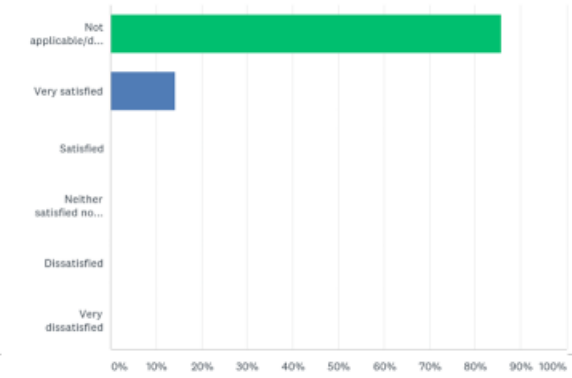
Q5: When it comes to managing your IBD, how helpful did you find reading the IBD educational material on the MyMR website?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Very helpful	28.57%	2
Helpful	14.29%	1
Neither helpful nor unhelpful	42.86%	3
Unhelpful	0.00%	0
Very unhelpful	0.00%	0
Don't know	14.29%	1
TOTAL		7

Q6: When using the email messaging service on the MyMR website, how satisfied where you with the speed of response from the IBD team?

Answered: 7 Skipped: 0



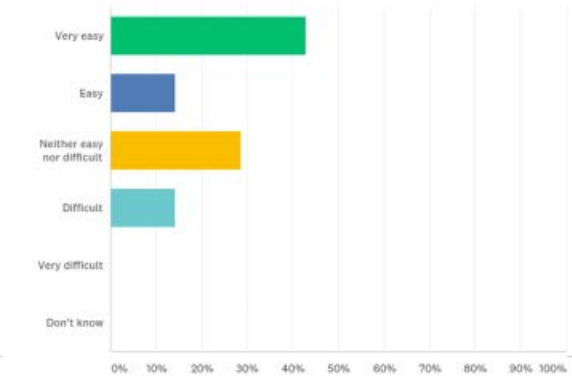
Q6: When using the email messaging service on the MyMR website, how satisfied where you with the speed of response from the IBD team?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Not applicable/didn't use this service	85.71%	6
Very satisfied	14.29%	1
Satisfied	0.00%	0
Neither satisfied nor dissatisfied	0.00%	0
Dissatisfied	0.00%	0
Very dissatisfied	0.00%	0
TOTAL		7

Q7: How easy or difficult was the home faecal calprotectin test to use?

Answered: 7 Skipped: 0



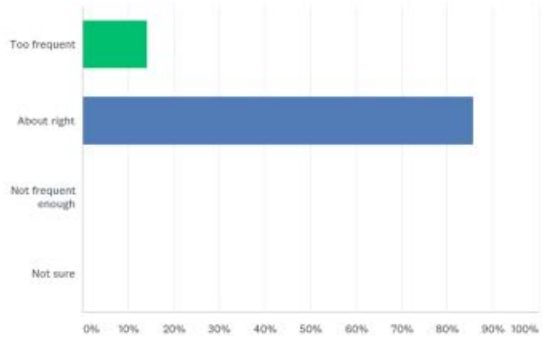
Q7: How easy or difficult was the home faecal calprotectin test to use?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Very easy	42.86%	3
Easy	14.29%	1
Neither easy nor difficult	28.57%	2
Difficult	14.29%	1
Very difficult	0.00%	0
Don't know	0.00%	0
TOTAL		7

Q8: Was monthly faecal calprotectin-testing appropriate?

Answered: 7 Skipped: 0



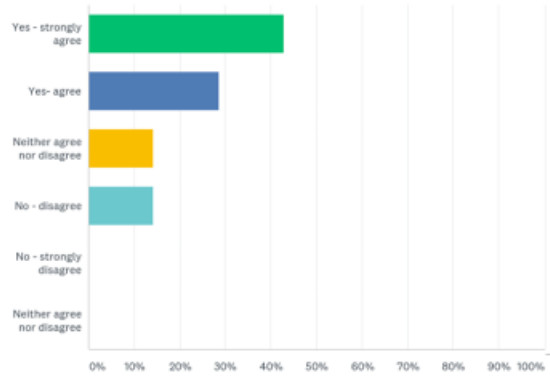
Q8: Was monthly faecal calprotectin-testing appropriate?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Too frequent	14.29%	1
About right	85.71%	6
Not frequent enough	0.00%	0
Not sure	0.00%	0
TOTAL		7

Q9: Did home faecal calprotectin monitoring improve your confidence in stopping a medication for your IBD?

Answered: 7 Skipped: 0



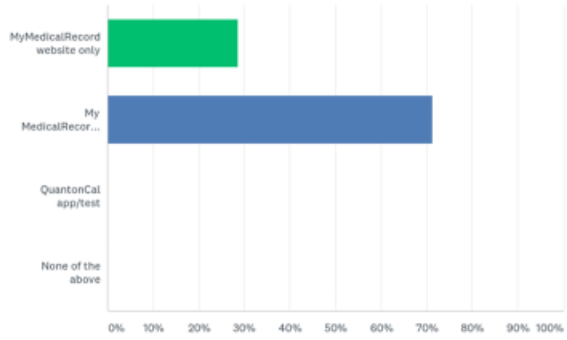
Q9: Did home faecal calprotectin monitoring improve your confidence in stopping a medication for your IBD?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
Yes - strongly agree	42.86%	3
Yes- agree	28.57%	2
Neither agree nor disagree	14.29%	1
No - disagree	14.29%	1
No - strongly disagree	0.00%	0
Neither agree nor disagree	0.00%	0
TOTAL		7

Q10: Which (if any) self-management tools would you consider continuing to use after the study ends?

Answered: 7 Skipped: 0



Q10: Which (if any) self-management tools would you consider continuing to use after the study ends?

Answered: 7 Skipped: 0

ANSWER CHOICES	RESPONSES	
MyMedicalRecord website only	28.57%	2
My MedicalRecord website plus QuantonCal app/test	71.43%	5
QuantonCal app/test	0.00%	0
None of the above	0.00%	0
TOTAL		7

Appendix E.18 Compatible smartphones - QuantOn Cal® 2019

Smartphones supporting QuantOn Cal® app	Operating systems supporting QuantOn Cal® app
iPhone 4	iOS 7.x
iPhone 5	iOS 9.0 - 9.3
iPhone 5c	iOS 11.0 - 11.2
iPhone 6s	Android 5.0 - 5.1
iPhone 6s+	Android 7.0 - 7.1
iPhone 7	iOS 8.x
iPhone 8	iOS 10.0 - 10.3
Samsung Galaxy Grand Prime	Android 4.4
Samsung Galaxy A5 (2016 / 2017)	Android 6.0
Samsung Galaxy J5 (2016 / 2017)	Android 8.0
Samsung Galaxy Note 3	iOS 8.x
Samsung Galaxy S4 mini	iOS 10.0 - 10.3
Samsung Galaxy S5 mini	Android 4.4
Samsung Galaxy S7	Android 6.0
Samsung Galaxy S8	Android 8.0
LG Nexus 5	
LG G4	
LG K8	
Motorola G5 Plus	
Homtom HT16	
Huawei P9	
Huawei Honor 8	
HTC 10	
iPhone 4s	
iPhone 5s	
iPhone 6	
iPhone 6+	
iPhone SE	
iPhone 7+	
iPhone X	
Samsung Galaxy A3	
Samsung Galaxy J3 (2016)	
Samsung Galaxy J7 (2016 / 2017)	
Samsung Galaxy S4	
Samsung Galaxy S5	
Samsung Galaxy S6	
Samsung Galaxy S7 Edge	
Samsung Galaxy S8+	
LG Nexus 5X	
LG G5	
Motorola Moto G3	
Motorola Nexus 6	
Huawei P8	
Huawei Honor 7	
Huawei Nexus 6P	
Krüger&Matz MOVE 6	

Appendix F

Appendix F.1 Revised Standards for Quality Improvement Reporting Excellence, SQUIRE 2.0

Notes to Authors	
The SQUIRE guidelines provide a framework for reporting new knowledge about how to improve healthcare. The SQUIRE guidelines are intended for reports that describe system level work to improve the quality, safety, and value of healthcare, and used methods to establish that observed outcomes were due to the intervention(s). A range of approaches exists for improving healthcare. SQUIRE may be adapted for reporting any of these. Authors should consider every SQUIRE item, but it may be inappropriate or unnecessary to include every SQUIRE element in a particular manuscript. The SQUIRE Glossary contains definitions of many of the key words in SQUIRE. The Explanation and Elaboration document provides specific examples of well-written SQUIRE items, and an in-depth explanation of each item. Please cite SQUIRE when it is used to write a manuscript.	
Title and Abstract	
1. Title	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patient-centeredness, timeliness, cost, efficiency, and equity of healthcare)
2. Abstract	a. Provide adequate information to aid in searching and indexing b. Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions
Introduction	*Why did you start?*
3. Problem Description	Nature and significance of the local problem

4. Available Knowledge	Summary of what is currently known about the problem, including relevant previous studies
5. Rationale	Informal or formal frameworks, models, concepts, and/or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work
6. Specific Aims	Purpose of the project and of this report
Methods	*What did you do?*
7. Context	Contextual elements considered important at the outset of introducing the intervention(s)
8. Intervention(s)	a. Description of the intervention(s) in sufficient detail that others could reproduce it b. Specifics of the team involved in the work
9. Study of the Intervention(s)	a. Approach chosen for assessing the impact of the intervention(s) b. Approach used to establish whether the observed outcomes were due to the intervention(s)
10. Measures	a. Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability b. Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost c. Methods employed for assessing completeness and accuracy of data
11. Analysis	a. Qualitative and quantitative methods used to draw inferences from the data b. Methods for understanding variation within the data, including the effects of time as a variable

12. Ethical Considerations	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest
Results	*What did you find?*
13. Results	a. Initial steps of the intervention(s) and their evolution over time (e.g., time-line diagram, flow chart, or table), including modifications made to the intervention during the project b. Details of the process measures and outcome c. Contextual elements that interacted with the intervention(s) d. Observed associations between outcomes, interventions, and relevant contextual elements e. Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s). f. Details about missing data
Discussion	*What does it mean?*
14. Summary	a. Key findings, including relevance to the rationale and specific aims b. Particular strengths of the project
15. Interpretation	a. Nature of the association between the intervention(s) and the outcomes b. Comparison of results with findings from other publications c. Impact of the project on people and systems d. Reasons for any differences between observed and anticipated outcomes, including the influence of context e. Costs and strategic trade-offs, including opportunity costs
16. Limitations	a. Limits to the generalizability of the work b. Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis

	c. Efforts made to minimize and adjust for limitations
17. Conclusions	a. Usefulness of the work b. Sustainability c. Potential for spread to other contexts d. Implications for practice and for further study in the field e. Suggested next steps
Other Information	
18. Funding	Sources of funding that supported this work. Role, if any, of the funding organization in the design, implementation, interpretation, and reporting

Appendix F.2 Nurse diary-monitoring key

key to codes:

C Clinic
FL flareline duties
E email queries
VC VC duties (checking blds, telephone calls etc)
P Prescribing
D Dictation/letters
B Break
A - Clinical Admin tasks (checking results etc)
M Meeting
O Other
VH Victoria House patient review
IP Inpatient reviews
PP Patient Panel
Off
Uni University course
AU Audit/Database
T Telephone calls
FU follow up
Aa - Admin that could be undertaken by an admin person

Key

clinical
Admin
Non-working

Appendix F.3 Patient protocols for clinical tracker

Example protocol 1: Non-immunomodulator, Crohn's

Month	Interval (mths)	CRP	FBC	U&E	LFTs	Ferritin	B12	Folate	Vit D	IBD Control Survey	Colonoscopy (1,3,5 yr interval)	DEXA scan
0	0	+	+	+	+	+	+	+	+	+		(+)
12	12	+	+	+	+	+	+	+	+	+	(+)	
24	12	+	+	+	+	+	+	+	+	+		
36	12	+	+	+	+	+	+	+	+	+	(+)	
48	12	+	+	+	+	+	+	+	+	+		
60	12	+	+	+	+	+	+	+	+	+	(+)	

Protocol 2: Non-immunomodulator, UC

Month	Interval (mths)	CRP	FBC	U&E	LFTs	Ferritin	B12	Folate	Vit D	IBD Control Survey	Colonoscopy (1,3,5 yr interval)	DEXA scan
0	0	+	+	+	+	+			+	+		(+)
12	12	+	+	+	+	+			+	+	(+)	
24	12	+	+	+	+	+			+	+		
36	12	+	+	+	+	+			+	+	(+)	
48	12	+	+	+	+	+			+	+		
60	12	+	+	+	+	+			+	+	(+)	

Protocol 3: Immunomodulator, Crohn's

Month	Interval (mths)	CRP	FBC	U&E	LFTs	Ferritin	B12	Folate	Vit D	IBD Control Survey	Colonoscopy (1,3,5 yr interval)	DEXA scan	Outpatient review
0	0	+	+	+	+	+	+	+	+	+		(+)	
12	12	+	+	+	+	+	+	+	+	+	(+)		
24	12	+	+	+	+	+	+	+	+	+			
36	12	+	+	+	+	+	+	+	+	+	(+)		+
48	12	+	+	+	+	+	+	+	+	+			
60	12	+	+	+	+	+	+	+	+	+	(+)		

Protocol 4: Immunomodulator, UC

Month	Interval (mths)	CRP	FBC	U&E	LFTs	Ferritin	B12	Folate	Vit D	IBD Control Survey	Colonoscopy (1,3,5 yr interval)	DEXA scan	Outpatient review
0	0	+	+	+	+	+			+	+		(+)	
12	12	+	+	+	+	+			+	+	(+)		
24	12	+	+	+	+	+			+	+			
36	12	+	+	+	+	+			+	+	(+)		+
48	12	+	+	+	+	+			+	+			
60	12	+	+	+	+	+			+	+	(+)		

Appendix F.4 Principles of normalisation process theory

Coherence is the **sense-making work** that people do individually and collectively when they are faced with the problem of operationalizing some set of practices. Like all NPT constructs it has four components.

1.1 Differentiation: An important element of sense-making work is to understand how a set of practices and their objects are different from each other. For example, when doctors use a videoconferencing system to consult with patients, what do they do to understand and organize the differences between face-to-face consultations and videoconferencing.

1.2 Communal specification: Sense-making relies on people working together to build a shared understanding of the aims, objectives, and expected benefits of a set of practices. A great example is the team of investigators leading a clinical trial, as they work out how to integrate a complex clinical experiment into a healthcare setting, and as they try to identify and anticipate the relationship between elements of the trial and everyday clinical practice.

1.3 Individual specification: Sense-making has an individual component too. Here participants in coherence work need to do things that will help them understand their specific tasks and responsibilities around a set of practices. For example, nurses recruiting patients into a trial need to have a strong understanding of the work they must do to secure informed consent from patients, and how they will go about this.

1.4 Internalization: Finally, sense-making involves people in work that is about understanding the value, benefits and importance of a set of practices. So, returning to the example of doctors using a videoconferencing system to consult with their patients, it's about the work that they do to attribute worth to a new way of working.

Cognitive Participation is the **relational work** that people do to build and sustain a community of practice around a new technology or complex intervention. Like all NPT constructs, it has four components.

2.1 Initiation: When a set of practices is new or modified, a core problem is whether or not key participants are working to drive them forward. For example, the work of setting up a clinical service is often delegated to a small group of managers and professionals who are charged with the work of setting up systems, procedures, and protocols and engaging with others to make things happen.

2.2 Enrolment: Participants may need to organize or reorganize themselves and others in order to collectively contribute to the work involved in new practices. This is complex work that may involve rethinking individual and group relationships between people and things. For example, getting nurses to 'buying in' to a falls prevention strategy is vital to its success, but the work of buying in to the strategy is not simply about individual commitment, but is about building communal engagement.

2.3 Legitimation: An important component of relational work around participation is the work of ensuring that other participants believe it is right for them to be involved, and that they can make a valid contribution to it. New service interventions often founder because of a lack of investment in ensuring that they fit with the ways that different groups of professionals - and sometimes patients - define their possible contribution to them.

2.4 Activation: Once it is underway, participants need to collectively define the actions and procedures needed to sustain a practice and to stay involved. In fact, staying on the case is vital to sustaining clinical interventions. This is the work of keeping the new practices in view and connecting them with the people who need to be doing them

Collective Action is the **operational work** that people do to enact a set of practices, whether these represent a new technology or complex healthcare intervention. Like all NPT constructs, it has four components. These were the first NPT constructs to be developed and their names reflect qualities of technologies or complex interventions, rather than the character of the work that these involve.

3.1 Interactional Workability: This refers to the interactional work that people do with each other, with artefacts, and with other elements of a set of practices, when they seek to operationalize them in everyday settings. For example, a key problem of telemedicine systems has been shown to be their negotiation by doctors and patients as they try to communicate complex clinical information each other over a videoconferencing link.

3.2 **Relational Integration**: This refers to the knowledge work that people do to build accountability and maintain confidence in a set of practices and in each other as they use them. A telemedicine system that transmitted clinical images of skin lesions ran into trouble when individual doctors began to lose confidence in what these images actually represented and started to examine patients in parallel to digitized images - thus doubling their workload and putting their clinical department under pressure.

3.3 Skill set Workability: This refers to the allocation work that underpins the division of labour that is built up around a set of practices as they are operationalized in the real world. Who gets to do the work is an important element of any set of practices? For example, a core problem for a research group investigating the effectiveness of a decision aid for medication choice after a serious illness event was whether the decision aid should be administered by trial managers with no clinical responsibility for the patient, or nurse practitioners actively involved in their care. Allocating the work to the former meant that the decision aid was more easily delivered, but trial managers lacked the clinical expertise of the nurse practitioners which meant that it was hard for them to answer patients' questions.

3.4 Contextual Integration: This refers to the resource work - managing a set of practices through the allocation of different kinds of resources and the execution of protocols, policies and procedures. Typically, the implementation of a new set of practices is seen as a management problem, and it's true that the power to allocate resources and define the processes by which new technologies or complex interventions are executed in practice. The work that is involved in this is about resourcing the ways that others enact a new set of practice

Reflexive Monitoring is the **appraisal work** that people do to assess and understand the ways that a new set of practices affect them and others around them. Like all NPT constructs, it has four components:

4.1 Systematization: participants in any set of practices may seek to determine how effective and useful it is for them and for others, and this involves the work of collecting information in a variety of ways. The work of systematization may be highly formal - the Randomized Controlled Clinical Trial is a prime example of formal systematization. But it may also be very informal, the collection of anecdotal examples of problems in practice around a set of common themes by an unqualified care assistant is every bit as much an example of the systematization of information.

4.2 Communal appraisal: participants work together - sometimes in formal collaboratives, sometimes in informal groups to evaluate the worth of a set of practices. They may use many different means to do this drawing on a variety of experiential and systematized information. These events happen continuously in almost every setting where people interact around a piece of hardware or new way of organizing work and ask each other 'is it working?' How they put the answers to these questions and negotiate the difficulties that stem from conflicts about what sort of information counts, and how it counts for different groups, are central to the future of any set of practices. Acts of communal appraisal - like data analysis meetings in clinical trials, or quality circles in lean healthcare organizations - are common and may be highly formalized as well as casual and informal.

4.3 Individual appraisal: Participants in a new set of practices also work experientially as individuals to appraise its effects on them and the contexts in which they are set. From this work stem actions through which individuals express their personal relationships to new technologies or complex interventions. For example, a nurse working in a falls prevention program will work to appraise not only the worth of the program, but also its impact on her other tasks. So, a falls program that complicates and adds to an already complicated and demanding workload may well be have a low value attributed to it in practice irrespective of its effects on falls within the hospital.

4.4 Reconfiguration: appraisal work by individuals or groups may lead to attempts to redefine procedures or modify practices - and even to change the shape of a new technology itself. For example, a nurse leading a falls prevention program might look again at the ways in which risk of falling was calculated in practice and the demands that this risk placed on the delivery of nursing care elsewhere on the ward. If the work of calculating risk of falling was disproportionate to the work involved in dealing with other kinds of risks on the ward, then there would be pressure to modify the falls prevention program to make it workable in practice.

Appendix F.5 NoMAD survey

Please cite as: Finch, T.L., Girling, M., May, C.R., Mair, F.S., Murray, E., Treweek S., Steen, I.N., McColl, E.M., Dickinson, C., Rapley, T. (2015). NoMad: Implementation measure based on Normalization Process Theory. [Measurement instrument]. Retrieved from http://www.normalizationprocess.org.

Survey Instructions

This survey is designed to help get a better understanding of how to apply and integrate new technologies and complex interventions in healthcare.

This survey asks questions about the implementation of **MyMedicalRecord**. We understand that people involved with MyMedicalRecord have different roles, and that people may have more than one role.

From the statements below please choose an option that best describes ***your main role*** in relation to **[the intervention]:**

- **I am involved in managing or overseeing [the intervention]** ☐
- **I am involved in delivering [the intervention]** ☐

The survey is in 3 parts. Part A asks some brief questions about yourself and your role. Part B includes three general questions about **MyMedicalRecord.** Part C contains a set of more detailed questions about MyMR. For each statement in Part C, there is the option to agree or disagree with what is being asked **(OPTION A).** However, if you feel that the statement is not relevant to you, there are also options to tell us why **(OPTION B).**

Please take the time to decide which answer **best suits your experience for each statement and tick the appropriate circle**

Development of this survey was funded by the Economic and Social Research Council; Study Grant RES-062-23-3274.

Part A: About yourself

1. How many years have you worked for the IBD Team?

○ Less than one year ○ 1-2 years ○ 3-5 years ○ 6-10 years ○ 11-15 years ○ More than 15 years

2. How would you describe your professional job category?

2

Part B: General questions about the intervention [THESE CAN BE ADAPTED, DROPPED AND/OR ADDED TO AS APPROPRIATE]

When you use MyMR, how familiar does it feel?

Still feels very new — **Feels completely familiar**

0 1 2 3 4 5 6 7 8 9 10

Do you feel MyMR is currently a normal part of your work?

Not at all — **Somewhat** — **Completely**

0 1 2 3 4 5 6 7 8 9 10

Do you feel MyMR will become a normal part of your work?

Not at all — **Somewhat** — **Completely**

0 1 2 3 4 5 6 7 8 9 10

3

Part C: Detailed questions about MyMR

For each statement please select an answer that best suits your experience using Option A. If the statement is not relevant to you please select an answer from Option B.

Section C1		Option A					Option B		
		Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Not relevant to my role	Not relevant at this stage	Not relevant to the intervention
1.	I can see how MyMR differs from usual ways of working	○	○	○	○	○	○	○	○
2.	Staff in this organisation have a shared understanding of the purpose of MyMR	○	○	○	○	○	○	○	○
3.	I understand how MyMR affects the nature of my own work	○	○	○	○	○	○	○	○
4.	I can see the potential value of MyMR for my work	○	○	○	○	○	○	○	○

For each statement please select an answer that best suits your experience using Option A. If the statement is not relevant to you, please select an answer from Option B.

Section C2		Option A					Option B		
		Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Not relevant to my role	Not relevant at this stage	Not relevant to the intervention
1.	There are key people who drive MyMR forward and get others involved	○	○	○	○	○	○	○	○
2.	I believe that participating in MyMR is a legitimate part of my role	○	○	○	○	○	○	○	○
3.	I'm open to working with colleagues in new ways to use MyMR	○	○	○	○	○	○	○	○
4.	I will continue to support MyMR	○	○	○	○	○	○	○	○

For each statement please select an answer that best suits your experience using Option A. If the statement is not relevant to you please select an answer from Option B.

Section C3		Option A					Option B		
		Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Not relevant to my role	Not relevant at this stage	Not relevant to the intervention
1.	I can easily integrate MyMR into my existing work	○	○	○	○	○	○	○	○
2.	MyMR disrupts working relationships	○	○	○	○	○	○	○	○
3.	I have confidence in other people's ability to use MyMR	○	○	○	○	○	○	○	○
4.	Work is assigned to those with skills appropriate to MyMR	○	○	○	○	○	○	○	○
5.	Sufficient training is provided to enable staff to implement MyMR	○	○	○	○	○	○	○	○
6.	Sufficient resources are available to support MyMR	○	○	○	○	○	○	○	○
7.	Management adequately supports MyMR	○	○	○	○	○	○	○	○

For each statement please select an answer that best suits your experience using Option A. If the statement is not relevant to you please select an answer from Option B.

Section C4		Option A					Option B		
		Strongly Agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Not relevant to my role	Not relevant at this stage	Not relevant to the intervention
1.	I am aware of reports about the effects of MyMR	○	○	○	○	○	○	○	○
2.	The staff agree that MyMR is worthwhile	○	○	○	○	○	○	○	○
3.	I value the effects that MyMR has had on my work	○	○	○	○	○	○	○	○
4.	Feedback about MyMR can be used to improve it in the future	○	○	○	○	○	○	○	○
5.	I can modify how I work with MyMR	○	○	○	○	○	○	○	○

Any additional comments about MyMR?

Thank you for completing our survey.

Appendix F.6 NoMAD results

Respondent	1	2	3	4	5	mean
When you use MyMR how familiar does it feel?	5	1	4	3	4	3.4
Do you feel MyMR is currently a normal part of your work	4	3	5	4	5	4.2
Do you feel MyMR will become a normal part of your work	8	7	7	7	8	7.4
I can see how MyMR differs from usual ways of working	neither	agree	neither	agree	agree	
Staff in this organisation have a shared understanding of the purpose of MyMR	disagree	agree	not relevant	neither	agree	
I understand how MyMR affects the nature of my own work	agree	agree	not relevant	agree	agree	
I can see the potential value of MyMR for my work	strongly agree	agree	agree	agree	strongly agree	
There are key people who drive MyMR forward and get others involved	agree	agree	agree	agree	agree	
I believe that participating in MyMR is a legitimate part of my role	agree	agree	agree	agree	agree	
I'm open to working with colleagues in new ways to use MyMR	agree	agree	agree	agree	agree	
I will continue to support MyMR	agree	agree	agree	agree	agree	
I can easily integrate MyMR into my existing work	disagree	disagree	agree	disagree	neither	
MyMR disrupts working relationships	agree	disagree	disagree	disagree	disagree	
I have confidence in other people's ability to use MyMR	neither	neither	neither	disagree	neither	
Work in assigned to those with skills appropriate to MyMR	agree	neither	not relevant	agree	agree	
Sufficient training is provided to enable staff to implement MyMR	disagree	strongly disagree	neither	disagree	neither	
Sufficient resources are available to support MyMR	disagree	strongly disagree	not relevant	strongly disagree	disagree	
Management adequately supports MyMR	neither	neither	neither	disagree	neither	
I am aware of reports about the effects of MyMR	strongly disagree	disagree	disagree	neither	neither	
The staff agree that MyMR is worthwhile	disagree	disagree	disagree	neither	agree	
I value the effects that MyMR has had on my work	agree	disagree	disagree	neither	agree	
Feedback about MyMR can be used to improve it in the future	agree	agree	agree	agree	agree	
I can modify how I work with MyMR	neither	disagree	agree	agree	agree	

List of References

1. Pedersen N, Elkjaer M, Duricova D, Burisch J, Dobrzanski C, Andersen NN, 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(9):840-9.
2. The IBD Standards 2018 [IBD standards]. Available from: http://www.ibdstandards.org.uk/default.asp.
3. Fourie S, Jackson D, Aveyard H. Living with Inflammatory Bowel Disease: A review of qualitative research studies. Int J Nurs Stud. 2018;87:149-56.
4. NICE. NICE Quality Standard QS81 2015 [Available from: https://www.nice.org.uk/guidance/qs81.
5. Ghosh S, Mitchell R. Impact of inflammatory bowel disease on quality of life: Results of the European Federation of Crohn's and Ulcerative Colitis Associations (EFCCA) patient survey. J Crohns Colitis. 2007;1(1):10-20.
6. Vavricka SR, Spigaglia SM, Rogler G, Pittet V, Michetti P, Felley C, et al. Systematic evaluation of risk factors for diagnostic delay in inflammatory bowel disease. Inflamm Bowel Dis. 2012;18(3):496-505.
7. Schoepfer AM, Dehlavi MA, Fournier N, Safroneeva E, Straumann A, Pittet V, et al. Diagnostic delay in Crohn's disease is associated with a complicated disease course and increased operation rate. Am J Gastroenterol. 2013;108(11):1744-53; quiz 54.
8. Abdalla M, Herfarth H. Rethinking Colorectal Cancer Screening in IBD, Is It Time to Revisit the Guidelines? J Crohns Colitis. 2018;12(7):757-9.
9. Colombel JF, Rutgeerts P, Reinisch W, Esser D, Wang Y, Lang Y, et al. Early mucosal healing with infliximab is associated with improved long-term clinical outcomes in ulcerative colitis. Gastroenterology. 2011;141(4):1194-201.
10. D'Haens G, Baert F, van Assche G, Caenepeel P, Vergauwe P, Tuynman H, et al. Early combined immunosuppression or conventional management in patients with newly diagnosed Crohn's disease: an open randomised trial. Lancet. 2008;371(9613):660-7.
11. Park SH, Yang SK, Park SK, Kim JW, Yang DH, Jung KW, et al. Atypical distribution of inflammation in newly diagnosed ulcerative colitis is not rare. Can J Gastroenterol Hepatol. 2014;28(3):125-30.
12. Abdelrazeq AS, Wilson TR, Leitch DL, Lund JN, Leveson SH. Ileitis in ulcerative colitis: is it a backwash? Dis Colon Rectum. 2005;48(11):2038-46.
13. Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut. 2019;68(Suppl 3):s1-s106.
14. Feakins RM, British Society of G. Inflammatory bowel disease biopsies: updated British Society of Gastroenterology reporting guidelines. J Clin Pathol. 2013;66(12):1005-26.
15. Tremaine WJ. Review article: Indeterminate colitis--definition, diagnosis and management. Aliment Pharmacol Ther. 2007;25(1):13-7.
16. Satsangi J, Silverberg MS, Vermeire S, Colombel JF. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. Gut. 2006;55(6):749-53.
17. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. N Engl J Med. 1987;317(26):1625-9.
18. Lewis JD, Chuai S, Nessel L, Lichtenstein GR, Aberra FN, Ellenberg JH. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. Inflamm Bowel Dis. 2008;14(12):1660-6.

19. Lobaton T, Bessissow T, De Hertogh G, Lemmens B, Maedler C, Van Assche G, et al. The Modified Mayo Endoscopic Score (MMES): A New Index for the Assessment of Extension and Severity of Endoscopic Activity in Ulcerative Colitis Patients. J Crohns Colitis. 2015;9(10):846-52.
20. Silverberg M S SJ, Ahmad T.et al. Toward an integrated clinical, molecular and serological classification of inflammatory bowel disease: Report of a Working Party of the 2005 Montreal World Congress of Gastroenterology. Can J Gastroenterol. 2005;19:5-36.
21. Best WR, Becktel JM, Singleton JW, Kern F, Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology. 1976;70(3):439-44.
22. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet. 1980;1(8167):514.
23. Mary JY, Modigliani R. Development and validation of an endoscopic index of the severity for Crohn's disease: a prospective multicentre study. Groupe d'Etudes Therapeutiques des Affections Inflammatoires du Tube Digestif (GETAID). Gut. 1989;30(7):983-9.
24. Daperno M, D'Haens G, Van Assche G, Baert F, Bulois P, Maunoury V, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: the SES-CD. Gastrointest Endosc. 2004;60(4):505-12.
25. Rutgeerts P, Geboes K, Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. Gastroenterology. 1990;99(4):956-63.
26. Samuel S, Bruining DH, Loftus EV, Jr., Becker B, Fletcher JG, Mandrekar JN, et al. Endoscopic skipping of the distal terminal ileum in Crohn's disease can lead to negative results from ileocolonoscopy. Clin Gastroenterol Hepatol. 2012;10(11):1253-9.
27. Panes J, Bouzas R, Chaparro M, Garcia-Sanchez V, Gisbert JP, Martinez de Guerenu B, et al. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal complications of Crohn's disease. Aliment Pharmacol Ther. 2011;34(2):125-45.
28. Rutgeerts P, Onette E, Vantrappen G, Geboes K, Broeckaert L, Talloen L. Crohn's disease of the stomach and duodenum: A clinical study with emphasis on the value of endoscopy and endoscopic biopsies. Endoscopy. 1980;12(6):288-94.
29. Annunziata ML, Caviglia R, Papparella LG, Cicala M. Upper gastrointestinal involvement of Crohn's disease: a prospective study on the role of upper endoscopy in the diagnostic work-up. Dig Dis Sci. 2012;57(6):1618-23.
30. Bourreille A, Ignjatovic A, Aabakken L, Loftus EV, Jr., Eliakim R, Pennazio M, et al. Role of small-bowel endoscopy in the management of patients with inflammatory bowel disease: an international OMED-ECCO consensus. Endoscopy. 2009;41(7):618-37.
31. Choi M, Lim S, Choi MG, Shim KN, Lee SH. Effectiveness of Capsule Endoscopy Compared with Other Diagnostic Modalities in Patients with Small Bowel Crohn's Disease: A Meta-Analysis. Gut Liver. 2017;11(1):62-72.
32. Kopylov U, Yung DE, Engel T, Vijayan S, Har-Noy O, Katz L, et al. Diagnostic yield of capsule endoscopy versus magnetic resonance enterography and small bowel contrast ultrasound in the evaluation of small bowel Crohn's disease: Systematic review and meta-analysis. Dig Liver Dis. 2017;49(8):854-63.
33. NICE. Irritable bowel syndrome in adults: diagnosis and management 2008 [Available from: https://www.nice.org.uk/guidance/cg61.
34. Vermeire S, Van Assche G, Rutgeerts P. Laboratory markers in IBD: useful, magic, or unnecessary toys? Gut. 2006;55(3):426-31.
35. Mitsuyama K, Niwa M, Takedatsu H, Yamasaki H, Kuwaki K, Yoshioka S, et al. Antibody markers in the diagnosis of inflammatory bowel disease. World J Gastroenterol. 2016;22(3):1304-10.
36. NICE. Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel2013. Available from: https://www.nice.org.uk/guidance/dg11/chapter/1-Recommendations.

37. van Rheenen PF, Van de Vijver E, Fidler V. Faecal calprotectin for screening of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. BMJ. 2010;341:c3369.
38. Benitez JM, Garcia-Sanchez V. Faecal calprotectin: Management in inflammatory bowel disease. World J Gastrointest Pathophysiol. 2015;6(4):203-9.
39. Seenan JP, Thomson F, Rankin K, Smith K, Gaya DR. Are we exposing patients with a mildly elevated faecal calprotectin to unnecessary investigations? Frontline Gastroenterol. 2015;6(3):156-60.
40. Waugh N, Cummins E, Royle P, Kandala NB, Shyangdan D, Arasaradnam R, et al. Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. Health Technol Assess. 2013;17(55):xv-xix, 1-211.
41. Manolakis AC, Kapsoritakis AN, Tiaka EK, Potamianos SP. Calprotectin, calgranulin C, and other members of the s100 protein family in inflammatory bowel disease. Dig Dis Sci. 2011;56(6):1601-11.
42. Sipponen T, Haapamaki J, Savilahti E, Alfthan H, Hamalainen E, Rautiainen H, et al. Fecal calprotectin and S100A12 have low utility in prediction of small bowel Crohn's disease detected by wireless capsule endoscopy. Scand J Gastroenterol. 2012;47(7):778-84.
43. Masson PL, Heremans JF, Schonne E. Lactoferrin, an iron-binding protein in neutrophilic leukocytes. J Exp Med. 1969;130(3):643-58.
44. Langhorst J, Boone J. Fecal lactoferrin as a noninvasive biomarker in inflammatory bowel diseases. Drugs Today (Barc). 2012;48(2):149-61.
45. Gisbert JP, McNicholl AG, Gomollon F. Questions and answers on the role of fecal lactoferrin as a biological marker in inflammatory bowel disease. Inflamm Bowel Dis. 2009;15(11):1746-54.
46. Parsi MA, Shen B, Achkar JP, Remzi FF, Goldblum JR, Boone J, et al. Fecal lactoferrin for diagnosis of symptomatic patients with ileal pouch-anal anastomosis. Gastroenterology. 2004;126(5):1280-6.
47. Lewis JD. The utility of biomarkers in the diagnosis and therapy of inflammatory bowel disease. Gastroenterology. 2011;140(6):1817-26 e2.
48. Chung-Faye G, Hayee B, Maestranzi S, Donaldson N, Forgacs I, Sherwood R. Fecal M2-pyruvate kinase (M2-PK): a novel marker of intestinal inflammation. Inflamm Bowel Dis. 2007;13(11):1374-8.
49. Czub E, Herzig KH, Szaflarska-Popawska A, Kiehne K, Socha P, Wos H, et al. Fecal pyruvate kinase: a potential new marker for intestinal inflammation in children with inflammatory bowel disease. Scand J Gastroenterol. 2007;42(10):1147-50.
50. Kato J, Hiraoka S, Nakarai A, Takashima S, Inokuchi T, Ichinose M. Fecal immunochemical test as a biomarker for inflammatory bowel diseases: can it rival fecal calprotectin? Intest Res. 2016;14(1):5-14.
51. Saitoh O, Sugi K, Matsuse R, Uchida K, Matsumoto H, Nakagawa K, et al. The forms and the levels of fecal PMN-elastase in patients with colorectal diseases. Am J Gastroenterol. 1995;90(3):388-93.
52. Nakarai A, Kato J, Hiraoka S, Kuriyama M, Akita M, Hirakawa T, et al. Evaluation of mucosal healing of ulcerative colitis by a quantitative fecal immunochemical test. Am J Gastroenterol. 2013;108(1):83-9.
53. Inokuchi T, Kato J, Hiraoka S, Takashima S, Nakarai A, Takei D, et al. Fecal Immunochemical Test Versus Fecal Calprotectin for Prediction of Mucosal Healing in Crohn's Disease. Inflamm Bowel Dis. 2016;22(5):1078-85.
54. Kuriyama M, Kato J, Takemoto K, Hiraoka S, Okada H, Yamamoto K. Prediction of flare-ups of ulcerative colitis using quantitative immunochemical fecal occult blood test. World J Gastroenterol. 2010;16(9):1110-4.

55. Sandborn WJ, Hanauer SB. Systematic review: the pharmacokinetic profiles of oral mesalazine formulations and mesalazine pro-drugs used in the management of ulcerative colitis. Aliment Pharmacol Ther. 2003;17(1):29-42.
56. Muller AF, Stevens PE, McIntyre AS, Ellison H, Logan RF. Experience of 5-aminosalicylate nephrotoxicity in the United Kingdom. Aliment Pharmacol Ther. 2005;21(10):1217-24.
57. Tiede I, Fritz G, Strand S, Poppe D, Dvorsky R, Strand D, et al. CD28-dependent Rac1 activation is the molecular target of azathioprine in primary human CD4+ T lymphocytes. J Clin Invest. 2003;111(8):1133-45.
58. Fraser AG. Methotrexate: first-line or second-line immunomodulator? Eur J Gastroenterol Hepatol. 2003;15(3):225-31.
59. Peyrin-Biroulet L, Loftus EV, Jr., Colombel JF, Sandborn WJ. Long-term complications, extraintestinal manifestations, and mortality in adult Crohn's disease in population-based cohorts. Inflamm Bowel Dis. 2011;17(1):471-8.
60. Taylor N BM, Wright J, et al. The impact of an inflammatory bowel disease nurse-led biologics service. Frontline Gastroenterology. 2016;7:283-8.
61. Clarke K, Regueiro M. Stopping immunomodulators and biologics in inflammatory bowel disease patients in remission. Inflamm Bowel Dis. 2012;18(1):174-9.
62. Louis E, Mary JY, Vernier-Massouille G, Grimaud JC, Bouhnik Y, Laharie D, et al. Maintenance of remission among patients with Crohn's disease on antimetabolite therapy after infliximab therapy is stopped. Gastroenterology. 2012;142(1):63-70 e5; quiz e31.
63. Mowat C, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, et al. Guidelines for the management of inflammatory bowel disease in adults. Gut. 2011;60(5):571-607.
64. Roberts SE, Williams JG, Yeates D, Goldacre MJ. Mortality in patients with and without colectomy admitted to hospital for ulcerative colitis and Crohn's disease: record linkage studies. BMJ. 2007;335(7628):1033.
65. Hwang JM, Varma MG. Surgery for inflammatory bowel disease. World J Gastroenterol. 2008;14(17):2678-90.
66. Makkar R, Bo S. Colonoscopic perforation in inflammatory bowel disease. Gastroenterol Hepatol (N Y). 2013;9(9):573-83.
67. Louis E, Belaiche J, Reenaers C. Anti-TNF and Crohn's disease: when should we stop? Curr Drug Targets. 2010;11(2):148-51.
68. Hunter J, Claridge A, James S, Chan D, Stacey B, Stroud M, et al. Improving outpatient services: the Southampton IBD virtual clinic. Frontline Gastroenterol. 2012;3(2):76-80.
69. Harris R MM, Downey ML, et al. OTH-03 Impact of direct access IBD physician delivered sigmoidoscopy from acute IBD flare line call service. Gut. 2019;68.
70. NICE. Point-of-care and home faecal calprotectin tests for monitoring treatment response in inflammatory bowel disease 2017 [Available from: https://www.nice.org.uk/advice/mib132.
71. Parr H PP, Liew I, et al. PTH-054 Home-Testing of Faecal Calprotectin Using the IBDoc®™ System: A Comparative Pilot Study. Gut. 2016;65:A245-A6.
72. Vinding KK, Elsberg H, Thorkilgaard T, Belard E, Pedersen N, Elkjaer M, et al. Fecal Calprotectin Measured By Patients at Home Using Smartphones--A New Clinical Tool in Monitoring Patients with Inflammatory Bowel Disease. Inflamm Bowel Dis. 2016;22(2):336-44.
73. El-Matary W, Abej E, Deora V, Singh H, Bernstein CN. Impact of Fecal Calprotectin Measurement on Decision-making in Children with Inflammatory Bowel Disease. Front Pediatr. 2017;5:7.
74. Heida A, Knol M, Kobold AM, Bootsman J, Dijkstra G, van Rheenen PF. Agreement Between Home-Based Measurement of Stool Calprotectin and ELISA Results for Monitoring Inflammatory Bowel Disease Activity. Clin Gastroenterol Hepatol. 2017;15(11):1742-9 e2.
75. Ungar B. LA, Selinger L, et al. P181 Home smart-phone based measurement of fecal calprotectin by IBD patients: correlation with laboratory assay and applicability as patient-friendly monitoring tool. Journal of Crohn's and Colitis. 2017;11:S167–S8.

76. Haisma SM, Galaurchi A, Almahwzi S, Adekanmi Balogun JA, Muller Kobold AC, van Rheenen PF. Head-to-head comparison of three stool calprotectin tests for home use. PLoS One. 2019;14(4):e0214751.
77. Puolanne AM, Kolho KL, Alfthan H, Farkkila M. Is home monitoring of inflammatory bowel disease feasible? A randomized controlled study. Scand J Gastroenterol. 2019;54(7):849-54.
78. Bello C, Roseth A, Guardiola J, Reenaers C, Ruiz-Cerulla A, Van Kemseke C, et al. Usability of a home-based test for the measurement of fecal calprotectin in asymptomatic IBD patients. Dig Liver Dis. 2017;49(9):991-6.
79. Wei SC, Tung CC, Weng MT, Wong JM. Experience of patients with inflammatory bowel disease in using a home fecal calprotectin test as an objective reported outcome for self-monitoring. Intest Res. 2018;16(4):546-53.
80. Ankersen DV, Weimers P, Marker D, Bennedsen M, Saboori S, Paridaens K, et al. Individualized home-monitoring of disease activity in adult patients with inflammatory bowel disease can be recommended in clinical practice: A randomized-clinical trial. World J Gastroenterol. 2019;25(40):6158-71.
81. Battersby M LS, Pols R. . Conceptualisation of self-management. Translating Chronic Illness Research into Practice. In: Kralik D PB, Coares V, editor. West Sussex: John Wiley and Sons Ltd.; 2010. p. 85-105.
82. Barlow J, Wright C, Sheasby J, Turner A, Hainsworth J. Self-management approaches for people with chronic conditions: a review. Patient Educ Couns. 2002;48(2):177-87.
83. Audulv A. The over time development of chronic illness self-management patterns: a longitudinal qualitative study. BMC Public Health. 2013;13:452.
84. Barlow C, Cooke D, Mulligan K, Beck E, Newman S. A critical review of self-management and educational interventions in inflammatory bowel disease. Gastroenterol Nurs. 2010;33(1):11-8.
85. Corbin JM. The Corbin and Strauss Chronic Illness Trajectory model: an update. Sch Inq Nurs Pract. 1998;12(1):33-41.
86. Salisbury C, Montgomery AA, Simons L, Sampson F, Edwards S, Baxter H, et al. Impact of Advanced Access on access, workload, and continuity: controlled before-and-after and simulated-patient study. Br J Gen Pract. 2007;57(541):608-14.
87. Rose KD, Ross JS, Horwitz LI. Advanced access scheduling outcomes: a systematic review. Arch Intern Med. 2011;171(13):1150-9.
88. Hewlett S, Kirwan J, Pollock J, Mitchell K, Hehir M, Blair PS, et al. Patient initiated outpatient follow up in rheumatoid arthritis: six year randomised controlled trial. BMJ. 2005;330(7484):171.
89. Williams JG, Cheung WY, Russell IT, Cohen DR, Longo M, Lervy B. Open access follow up for inflammatory bowel disease: pragmatic randomised trial and cost effectiveness study. BMJ. 2000;320(7234):544-8.
90. Robinson A, Thompson DG, Wilkin D, Roberts C, Northwest Gastrointestinal Research G. Guided self-management and patient-directed follow-up of ulcerative colitis: a randomised trial. Lancet. 2001;358(9286):976-81.
91. Kennedy A, Nelson E, Reeves D, Richardson G, Roberts C, Robinson A, et al. A randomised controlled trial to assess the impact of a package comprising a patient-orientated, evidence-based self-help guidebook and patient-centred consultations on disease management and satisfaction in inflammatory bowel disease. Health Technol Assess. 2003;7(28):iii, 1-113.
92. Vinicor F, Cohen SJ, Mazzuca SA, Moorman N, Wheeler M, Kuebler T, et al. DIABEDS: a randomized trial of the effects of physician and/or patient education on diabetes patient outcomes. J Chronic Dis. 1987;40(4):345-56.
93. Liu C, Feekery C. Can asthma education improve clinical outcomes? An evaluation of a pediatric asthma education program. J Asthma. 2001;38(3):269-78.

94. Morisky DE, Levine DM, Green LW, Russell RP, Smith C, Benson P, et al. The relative impact of health education for low- and high-risk patients with hypertension. Prev Med. 1980;9(4):550-8.
95. Drossman DA, Patrick DL, Mitchell CM, Zagami EA, Appelbaum MI. Health-related quality of life in inflammatory bowel disease. Functional status and patient worries and concerns. Dig Dis Sci. 1989;34(9):1379-86.
96. Bernstein KI, Promislow S, Carr R, Rawsthorne P, Walker JR, Bernstein CN. Information needs and preferences of recently diagnosed patients with inflammatory bowel disease. Inflamm Bowel Dis. 2011;17(2):590-8.
97. Ringstrom G, Storsrud S, Posserud I, Lundqvist S, Westman B, Simren M. Structured patient education is superior to written information in the management of patients with irritable bowel syndrome: a randomized controlled study. Eur J Gastroenterol Hepatol. 2010;22(4):420-8.
98. Saito YA, Prather CM, Van Dyke CT, Fett S, Zinsmeister AR, Locke GR, 3rd. Effects of multidisciplinary education on outcomes in patients with irritable bowel syndrome. Clin Gastroenterol Hepatol. 2004;2(7):576-84.
99. Robinson A, Lee V, Kennedy A, Middleton L, Rogers A, Thompson DG, et al. A randomised controlled trial of self-help interventions in patients with a primary care diagnosis of irritable bowel syndrome. Gut. 2006;55(5):643-8.
100. Coulter A, Entwistle V, Gilbert D. Sharing decisions with patients: is the information good enough? BMJ. 1999;318(7179):318-22.
101. Probert CS, Jayanthi V, Mayberry JF. British gastroenterologists' care profile for patients with inflammatory bowel disease: the need for a patients' charter. J R Soc Med. 1993;86(5):271-2.
102. Cerveny P, Bortlik M, Kubena A, Vlcek J, Lakatos PL, Lukas M. Nonadherence in inflammatory bowel disease: results of factor analysis. Inflamm Bowel Dis. 2007;13(10):1244-9.
103. Hawthorne AB, Rubin G, Ghosh S. Review article: medication non-adherence in ulcerative colitis--strategies to improve adherence with mesalazine and other maintenance therapies. Aliment Pharmacol Ther. 2008;27(12):1157-66.
104. Waters BM, Jensen L, Fedorak RN. Effects of formal education for patients with inflammatory bowel disease: a randomized controlled trial. Can J Gastroenterol. 2005;19(4):235-44.
105. Kennedy A, Robinson A, Hann M, Thompson D, Wilkin D, North-West Region Gastrointestinal Research G. A cluster-randomised controlled trial of a patient-centred guidebook for patients with ulcerative colitis: effect on knowledge, anxiety and quality of life. Health Soc Care Community. 2003;11(1):64-72.
106. Araujo-Soares V, Hankonen N, Presseau J, Rodrigues A, Sniehotta FF. Developing Behavior Change Interventions for Self-Management in Chronic Illness: An Integrative Overview. Eur Psychol. 2019;24(1):7-25.
107. Ramos-Rivers C, Regueiro M, Vargas EJ, Szigethy E, Schoen RE, Dunn M, et al. Association between telephone activity and features of patients with inflammatory bowel disease. Clin Gastroenterol Hepatol. 2014;12(6):986-94 e1.
108. Clark RA, Inglis SC, McAlister FA, Cleland JG, Stewart S. Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis. BMJ. 2007;334(7600):942.
109. Wennberg DE, Marr A, Lang L, O'Malley S, Bennett G. A randomized trial of a telephone care-management strategy. N Engl J Med. 2010;363(13):1245-55.
110. Plener I, Hayward A, Saibil F. E-mail communication in the management of gastroenterology patients: a review. Can J Gastroenterol Hepatol. 2014;28(3):161-5.
111. Angelucci E, Orlando A, Ardizzone S, Guidi L, Sorrentino D, Fries W, et al. Internet use among inflammatory bowel disease patients: an Italian multicenter survey. Eur J Gastroenterol Hepatol. 2009;21(9):1036-41.

112. Crabb RM, Rafie S, Weingardt KR. Health-related internet use in older primary care patients. Gerontology. 2012;58(2):164-70.
113. Promislow S, Walker JR, Taheri M, Bernstein CN. How well does the Internet answer patients' questions about inflammatory bowel disease? Can J Gastroenterol. 2010;24(11):671-7.
114. CCUK. Crohn's and Colitis UK 2019 [Available from: https://www.crohnsandcolitis.org.uk/.
115. Oh H, Rizo C, Enkin M, Jadad A. What is eHealth?: a systematic review of published definitions. World Hosp Health Serv. 2005;41(1):32-40.
116. O'Neill S, Brady RR. Colorectal smartphone apps: opportunities and risks. Colorectal Dis. 2012;14(9):e530-4.
117. Free C, Phillips G, Galli L, Watson L, Felix L, Edwards P, et al. The effectiveness of mobile-health technology-based health behaviour change or disease management interventions for health care consumers: a systematic review. PLoS Med. 2013;10(1):e1001362.
118. Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, de Walque D, et al. Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS. 2011;25(6):825-34.
119. <Currell 2010. Cochrane review telemedicine.pdf>.
120. Dack C, Ross J, Stevenson F, Pal K, Gubert E, Michie S, et al. A digital self-management intervention for adults with type 2 diabetes: Combining theory, data and participatory design to develop HeLP-Diabetes. Internet Interv. 2019;17:100241.
121. Murray E, Burns J, See TS, Lai R, Nazareth I. Interactive Health Communication Applications for people with chronic disease. Cochrane Database Syst Rev. 2005(4):CD004274.
122. Osborn CY, Mayberry LS, Mulvaney SA, Hess R. Patient web portals to improve diabetes outcomes: a systematic review. Curr Diab Rep. 2010;10(6):422-35.
123. Pal K, Eastwood SV, Michie S, Farmer AJ, Barnard ML, Peacock R, et al. Computer-based diabetes self-management interventions for adults with type 2 diabetes mellitus. Cochrane Database Syst Rev. 2013(3):CD008776.
124. Lorig K, Ritter PL, Laurent DD, Plant K, Green M, Jernigan VB, et al. Online diabetes self-management program: a randomized study. Diabetes Care. 2010;33(6):1275-81.
125. Kruger JM, Helmick CG, Callahan LF, Haddix AC. Cost-effectiveness of the arthritis self-help course. Arch Intern Med. 1998;158(11):1245-9.
126. Krier M, Kaltenbach T, McQuaid K, Soetikno R. Potential use of telemedicine to provide outpatient care for inflammatory bowel disease. Am J Gastroenterol. 2011;106(12):2063-7.
127. Elkjaer M, Shuhaibar M, Burisch J, Bailey Y, Scherfig H, Laugesen B, et al. E-health empowers patients with ulcerative colitis: a randomised controlled trial of the web-guided 'Constant-care' approach. Gut. 2010;59(12):1652-61.
128. 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(6):1018-25.
129. Cross RK, Langenberg P, Regueiro M, Schwartz DA, Tracy JK, Collins JF, et al. A Randomized Controlled Trial of TELEmedicine for Patients with Inflammatory Bowel Disease (TELE-IBD). Am J Gastroenterol. 2019;114(3):472-82.
130. Walsh A. TrueColours: real time data collection in patients with ulcerative colitis [Doctoral dissertation]. Oxford University: Oxford; 2017.
131. Del Hoyo J, Nos P, Faubel R, Munoz D, Dominguez D, Bastida G, et al. A Web-Based Telemanagement System for Improving Disease Activity and Quality of Life in Patients With Complex Inflammatory Bowel Disease: Pilot Randomized Controlled Trial. J Med Internet Res. 2018;20(11):e11602.
132. Atreja A, Khan S, Rogers JD, Otobo E, Patel NP, Ullman T, et al. Impact of the Mobile HealthPROMISE Platform on the Quality of Care and Quality of Life in Patients With Inflammatory Bowel Disease: Study Protocol of a Pragmatic Randomized Controlled Trial. JMIR Res Protoc. 2015;4(1):e23.

133. de Jong MJ, van der Meulen-de Jong AE, Romberg-Camps MJ, Becx MC, Maljaars JP, Cilissen M, et al. Telemedicine for management of inflammatory bowel disease (myIBDcoach): a pragmatic, multicentre, randomised controlled trial. Lancet. 2017;390(10098):959-68.
134. MRC. A framework for the development and evaluation of RCTs for complex interventions to improve health. . London: The Medical Research Council; 2000.
135. Cross RK, Finkelstein J. Feasibility and acceptance of a home telemanagement system in patients with inflammatory bowel disease: a 6-month pilot study. Dig Dis Sci. 2007;52(2):357-64.
136. Trust UHSNF. UHS Digital 2016 [Available from: https://www.uhs.nhs.uk/AboutTheTrust/UHS-Digital/UHS-Digital.aspx.
137. England N. Global Digital Exemplars 2020 [Available from: https://www.england.nhs.uk/digitaltechnology/connecteddigitalsystems/exemplars/.
138. Crotty M. The foundations of social research: Meaning and perspective in the research process: Sage; 1998.
139. Handbook of mixed-methods in social and behavioral research. Tashakkori A. TC, editor. Thousand Oaks, CA: BMJ Publishing Group; 2003.
140. Hiles D CI. Qualitative Research: Transparency and Narrative Oriented Inquiry. 10th ECP; July 3-7, 2007; Prague, CZ2007.
141. Kuhn TS. The Structure of Scientific Revolutions. 1 ed. Chicago, IL: The University of Chicago Press; 1962.
142. Guba EG LY. Competing paradigms in qualitative research. . In: Denzin NK LY, editor. Handbook of qualitative research. 2: SAGE; 1994. p. 163-94.
143. Blaikie N. Approaches to social enquiry. 1st ed. Cambridge: Polity Press; 1993.
144. Mason J. Qualitative Researching. 2nd ed. London: SAGE; 2002.
145. Chia R. Essential Skills for Management Research. The Production of Management Knowledge: Philosophical Underpinnings of Research Design. 1st ed: SAGE; 2002.
146. Malterud K. Qualitative research: standards, challenges, and guidelines. Lancet. 2001;358(9280):483-8.
147. Gopalakrishnan S, Ganeshkumar P. Systematic Reviews and Meta-analysis: Understanding the Best Evidence in Primary Healthcare. J Family Med Prim Care. 2013;2(1):9-14.
148. PRISMA. http://www.prisma-statement.org/ 2015 [Available from: http://www.prisma-statement.org/.
149. CONSORT. CONSORT 2010 Checklist 2010 [Available from: http://www.consort-statement.org/.
150. Ryan R, . Cochrane Consumers and Communication Review Group.'Cochrane Consumers and Communication Review Group: data synthesis and analysis' 2013 [Available from: http://cccrg.cochrane.org.
151. Glaser B, Strauss AL. The Discovery of Grounded Theory: Strategies for Qualitative Research. Chicago: Aldine Publishing Company; 1967.
152. Pope C, van Royen P, Baker R. Qualitative methods in research on healthcare quality. Qual Saf Health Care. 2002;11(2):148-52.
153. Braun V. Using thematic analysis in psychology. Qualitative Research in Psycology. 2006;3:77-101.
154. Braun V CV. Teaching thematic analysis: Overcoming challenges and developing strategies for effective learning. The Psychologist. 2013;26(2):120-3.
155. Braun V, Clarke V. What can "thematic analysis" offer health and wellbeing researchers? Int J Qual Stud Health Well-being. 2014;9:26152.
156. Maguire M DB. Doing a Thematic Analysis: A Practical, Step-by-Step Guide for Learning and Teaching Scholars. AIHSE-J. 2017;8(3):3351-63.
157. Ritchie J LJ. Qualitative research practice: a guide for social science students and researchers. London: SAGE; 2003.
158. Pope M MN. Critical reflections on the rise of qualitative research. BMJ. 2009;339:737-9.

159. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. Acad Med. 2014;89(9):1245-51.
160. May C, Rapley, T., Mair, F.S et al. Normalization Process Theory On-line Users' Manual, Toolkit and NoMAD instrument 2015 [cited 2018 10/12/2018]. Available from: http://normalizationprocess.org/.
161. May CR, Cummings A, Girling M, Bracher M, Mair FS, May CM, et al. Using Normalization Process Theory in feasibility studies and process evaluations of complex healthcare interventions: a systematic review. Implement Sci. 2018;13(1):80.
162. Devlin AM, McGee-Lennon M, O'Donnell CA, Bouamrane MM, Agbakoba R, O'Connor S, et al. Delivering digital health and well-being at scale: lessons learned during the implementation of the dallas program in the United Kingdom. J Am Med Inform Assoc. 2016;23(1):48-59.
163. Ariens LF, Schussler-Raymakers FM, Frima C, Flinterman A, Hamminga E, Arents BW, et al. Barriers and Facilitators to eHealth Use in Daily Practice: Perspectives of Patients and Professionals in Dermatology. J Med Internet Res. 2017;19(9):e300.
164. French SD, McKenzie JE, O'Connor DA, Grimshaw JM, Mortimer D, Francis JJ, et al. Evaluation of a theory-informed implementation intervention for the management of acute low back pain in general medical practice: the IMPLEMENT cluster randomised trial. PLoS One. 2013;8(6):e65471.
165. Wilhelmsen M, Hoifodt RS, Kolstrup N, Waterloo K, Eisemann M, Chenhall R, et al. Norwegian general practitioners' perspectives on implementation of a guided web-based cognitive behavioral therapy for depression: a qualitative study. J Med Internet Res. 2014;16(9):e208.
166. Johnson MJ, May CR. Promoting professional behaviour change in healthcare: what interventions work, and why? A theory-led overview of systematic reviews. BMJ Open. 2015;5(9):e008592.
167. Morgan H, Thomson G, Crossland N, Dykes F, Hoddinott P, team Bs. Combining PPI with qualitative research to engage 'harder-to-reach' populations: service user groups as co-applicants on a platform study for a trial. Res Involv Engagem. 2016;2:7.
168. Muller I, Santer M, Morrison L, Morton K, Roberts A, Rice C, et al. Combining qualitative research with PPI: reflections on using the person-based approach for developing behavioural interventions. Res Involv Engagem. 2019;5:34.
169. The person-based approach 2020 [Available from: https://www.personbasedapproach.org/.
170. Yardley L, Ainsworth B, Arden-Close E, Muller I. The person-based approach to enhancing the acceptability and feasibility of interventions. Pilot Feasibility Stud. 2015;1:37.
171. Pedersen N, Thielsen P, Martinsen L, Bennedsen M, Haaber A, Langholz E, 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(12):2276-85.
172. Walmsley RS, Ayres RC, Pounder RE, Allan RN. A simple clinical colitis activity index. Gut. 1998;43(1):29-32.
173. 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(8):1571-8.
174. Elkjaer M, Burisch J, Voxen Hansen V, Deibjerg Kristensen B, Slott Jensen JK, Munkholm P. A new rapid home test for faecal calprotectin in ulcerative colitis. Aliment Pharmacol Ther. 2010;31(2):323-30.
175. Walsh A, Travis S. What's app? Electronic health technology in inflammatory bowel disease. Intest Res. 2018;16(3):366-73.
176. Kim A. RC, Feagan B., et al. P241 Defining patient-centered outcomes for Ibd-an international, cross-disciplinary consensus. Journal of Crohn's & colitis. 2017;11(suppl_1):S200.

177. Spiegel Bea. The IBD&me Randomized Controlled Trial 2018 [Available from: https://clinicaltrials.gov/ct2/show/NCT03695783?term=biologic&cond=IBD&draw=2&rank=17.
178. Patients Know Best 2020 [Available from: https://patientsknowbest.com/.
179. Bidmead E, Marshall A. A case study of stakeholder perceptions of patient held records: the Patients Know Best (PKB) solution. Digit Health. 2016;2:2055207616668431.
180. Calvert CR, Lal S, Stansfield C, McLaughlin J, Robinson A. OC-082 The Development of a Web-Based System to Enhance Care in Inflammatory Bowel Disease. Gut. 2013;62(Suppl 1):A35-A6.
181. Mclaughlin J SS, Lal S, et al. OTU-031 My–IBD portal: progress and impact update. Gut. 2018;67.
182. Van Deen WK, van der Meulen-de Jong AE, Parekh NK, Kane E, Zand A, DiNicola CA, et al. Development and Validation of an Inflammatory Bowel Diseases Monitoring Index for Use With Mobile Health Technologies. Clin Gastroenterol Hepatol. 2016;14(12):1742-50 e7.
183. CCUK. My IBD Care 2020 [Available from: https://www.ampersandhealth.co.uk/myibdcare/.
184. Soubieres A, Wilson P, Poullis A, et al. Burden of irritable bowel syndrome in an increasingly cost-aware National Health Service. Frontline gastroenterology. 2015(0):1-6.
185. Roseth AG, Schmidt PN, Fagerhol MK. Correlation between faecal excretion of indium-111-labelled granulocytes and calprotectin, a granulocyte marker protein, in patients with inflammatory bowel disease. Scand J Gastroenterol. 1999;34(1):50-4.
186. Roseth AG, Fagerhol MK, Aadland E, Schjonsby H. Assessment of the neutrophil dominating protein calprotectin in feces. A methodologic study. Scand J Gastroenterol. 1992;27(9):793-8.
187. Erbayrak M, Turkay C, Eraslan E, Cetinkaya H, Kasapoglu B, Bektas M. The role of fecal calprotectin in investigating inflammatory bowel diseases. Clinics (Sao Paulo). 2009;64(5):421-5.
188. Labaere D, Smismans A, Van Olmen A, Christiaens P, D'Haens G, Moons V, et al. Comparison of six different calprotectin assays for the assessment of inflammatory bowel disease. United European Gastroenterol J. 2014;2(1):30-7.
189. Dhar A, Borthwick HAD, Nair P, White C. Point-of-Contact Faecal Calprotectin (FC) Testing in Diarrhoea Helps Decision Making for Referral to Gastroenterologists: A Primary Care Pilot Study in North East England. Gastroenterology. 2013;144(5):S421-S.
190. dhar A. Faecal Calprotectin in County Durham – a decade of experience 2018 [Available from: http://www.ahsn-nenc.org.uk/wp-content/uploads/2018/06/Anjan-Dhar.pdf.
191. Williams M, Barclay Y, Benneyworth R, Gore S, Hamilton Z, Matull R, et al. Using best practice to create a pathway to improve management of irritable bowel syndrome: aiming for timely diagnosis, effective treatment and equitable care. Frontline Gastroenterol. 2016;7(4):323-30.
192. Turvill J, O'Connell S, Brooks A, Bradley-Wood K, Laing J, Thiagarajan S, et al. Evaluation of a faecal calprotectin care pathway for use in primary care. Prim Health Care Res Dev. 2016;17(5):428-36.
193. Turvill J. The new faecal calprotectin pathway 2018 [Available from: https://www.nice.org.uk/sharedlearning/the-new-faecal-calprotectin-care-pathway.
194. Authority NHR. HRA Decision Tool: Is my study reseach? 2019 [Available from: http://www.hra-decisiontools.org.uk/research/.
195. Prell C, Nagel D, Freudenberg F, Schwarzer A, Koletzko S. Comparison of three tests for faecal calprotectin in children and young adults: a retrospective monocentric study. BMJ Open. 2014;4(5):e004558.
196. Mowat C, Digby J, Strachan JA, Wilson R, Carey FA, Fraser CG, et al. Faecal haemoglobin and faecal calprotectin as indicators of bowel disease in patients presenting to primary care with bowel symptoms. Gut. 2016;65(9):1463-9.

197. Shivaji U CF, Ford AC. OC-059 Prevalence of Bile Acid Malabsorption as a Cause of Diarrhoea in Consecutive new Patient Referrals to a Gastroenterology Clinic. Gut. 2013;62.
198. Quintas Lorenzo P DRA, González MF, et al. Referrals to a gastroenterology outpatient clinic from primary care: evaluation of two programs. Gaceta Sanitaria. 2011;25(6):468-73.
199. Pelitari S, Hathaway C, Gritton D, Smith A, Bush D, Menon S, et al. Impact and cost-effectiveness of formal gastroenterology outpatient referral Clinical Assessment Service. Frontline Gastroenterol. 2018;9(2):159-65.
200. Hitchins CR, Lawn A, Whitehouse G, McFall MR. The straight to test endoscopy service for suspected colorectal cancer: meeting national targets but are we meeting our patients' expectations? Colorectal Dis. 2014;16(8):616-9.
201. Mukherjee S, Fountain G, Stalker M, Williams J, Porrett TR, Lunniss PJ, et al. The 'straight to test' initiative reduces both diagnostic and treatment waiting times for colorectal cancer: outcomes after 2 years. Colorectal Dis. 2010;12(10 Online):e250-4.
202. Bodger K, Ormerod C, Shackcloth D, Harrison M, Collaborative IBDC. Development and validation of a rapid, generic measure of disease control from the patient's perspective: the IBD-control questionnaire. Gut. 2014;63(7):1092-102.
203. Farrag K, Wintgens, K., Dignass A. et al. A92 analytical performance of a smartphone-based patient monitoring system compared to ELISA for the measurement of fecal calprotectin in IBD patients. Journal of the Canadian Association of Gastroenterology. 2019;2(S2):183-4.
204. Cheung WY, Garratt AM, Russell IT, Williams JG. The UK IBDQ-a British version of the inflammatory bowel disease questionnaire. development and validation. J Clin Epidemiol. 2000;53(3):297-306.
205. Turner D, Griffiths AM, Mack D, Otley AR, Seow CH, Steinhart AH, et al. Assessing disease activity in ulcerative colitis: patients or their physicians? Inflamm Bowel Dis. 2010;16(4):651-6.
206. Sutherland LR, Martin F, Greer S, Robinson M, Greenberger N, Saibil F, et al. 5-Aminosalicylic acid enema in the treatment of distal ulcerative colitis, proctosigmoiditis, and proctitis. Gastroenterology. 1987;92(6):1894-8.
207. Jowett SL, Seal CJ, Barton JR, Welfare MR. The short inflammatory bowel disease questionnaire is reliable and responsive to clinically important change in ulcerative colitis. Am J Gastroenterol. 2001;96(10):2921-8.
208. Elkjaer M, Burisch J, Avnstrom S, Lynge E, Munkholm P. Development of a Web-based concept for patients with ulcerative colitis and 5-aminosalicylic acid treatment. Eur J Gastroenterol Hepatol. 2010;22(6):695-704.
209. Hanauer S, Schwartz J, Robinson M, Roufail W, Arora S, Cello J, et al. Mesalamine capsules for treatment of active ulcerative colitis: results of a controlled trial. Pentasa Study Group. Am J Gastroenterol. 1993;88(8):1188-97.
210. Ribeiro PH, Gir E, Santos CB, Ribeiro RP, Hayashida M, Malaguti-Toffano SE, et al. Validation of an instrument to assess factors associated with adherence to standard precautions among dentists in primary healthcare. Acta Odontol Latinoam. 2014;27(1):9-15.
211. Gravis G, Protiere C, Eisinger F, Boher JM, Tarpin C, Coso D, et al. Full access to medical records does not modify anxiety in cancer patients: results of a randomized study. Cancer. 2011;117(20):4796-804.
212. Walker J, Meltsner M, Delbanco T. US experience with doctors and patients sharing clinical notes. BMJ. 2015;350:g7785.
213. Network UH. MyUHN patient portal: a patient and a doctor tell how it's made a difference 2016 [Available from: https://www.uhn.ca/corporate/News/Pages/myUHN_patient_portal_patient_and_doctor_tell_how_made_difference.aspx.
214. Dignass A, Van Assche G, Lindsay JO, Lemann M, Soderholm J, Colombel JF, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Current management. J Crohns Colitis. 2010;4(1):28-62.

215. Steenholdt C, Molazahi A, Ainsworth MA, Brynskov J, Ostergaard Thomsen O, Seidelin JB. Outcome after discontinuation of infliximab in patients with inflammatory bowel disease in clinical remission: an observational Danish single center study. Scand J Gastroenterol. 2012;47(5):518-27.
216. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ. 2015;350:h1258.
217. Bjarnason I. The Use of Fecal Calprotectin in Inflammatory Bowel Disease. Gastroenterol Hepatol (N Y). 2017;13(1):53-6.
218. Louis E. Fecal calprotectin: towards a standardized use for inflammatory bowel disease management in routine practice. J Crohns Colitis. 2015;9(1):1-3.
219. Rowan C, Alzubi, S., Healy, M., et al. Sa1794 - Utility of Faecal Calprotectin to Assess Crohn's Disease Activity in Patients with an Ileostomy. Gastroenterology. 2018;154(6):S-379.
220. Cross RK, Cheevers N, Finkelstein J. Home telemanagement for patients with ulcerative colitis (UC HAT). Dig Dis Sci. 2009;54(11):2463-72.
221. Eaden JA, Abrams K, Mayberry JF. The Crohn's and Colitis Knowledge Score: a test for measuring patient knowledge in inflammatory bowel disease. Am J Gastroenterol. 1999;94(12):3560-6.
222. Guyatt G, Mitchell A, Irvine EJ, Singer J, Williams N, Goodacre R, et al. A new measure of health status for clinical trials in inflammatory bowel disease. Gastroenterology. 1989;96(3):804-10.
223. Costa F, Mumolo MG, Ceccarelli L, Bellini M, Romano MR, Sterpi C, et al. Calprotectin is a stronger predictive marker of relapse in ulcerative colitis than in Crohn's disease. Gut. 2005;54(3):364-8.
224. BMJ. Selecting, designing, and developing your questionnaire. BMJ. 2004;328(1312).
225. DeJonckheere M, Vaughn, M. Semistructured interviewing in primary care research: a balance of relationship and rigour. Family Medicine and Community Health. 2019;7(2):e000057.
226. Fincham JE. Response rates and responsiveness for surveys, standards, and the Journal. Am J Pharm Educ. 2008;72(2):43.
227. Meling TR, Aabakken L, Roseth A, Osnes M. Faecal calprotectin shedding after short-term treatment with non-steroidal anti-inflammatory drugs. Scand J Gastroenterol. 1996;31(4):339-44.
228. Elkjaer M. E-health: Web-guided therapy and disease self-management in ulcerative colitis. Impact on disease outcome, quality of life and compliance. Dan Med J. 2012;59(7):B4478.
229. Julsgaard M, Hvas CL, Gearry RB, Vestergaard T, Fallingborg J, Svenningsen L, et al. Fecal Calprotectin Is Not Affected by Pregnancy: Clinical Implications for the Management of Pregnant Patients with Inflammatory Bowel Disease. Inflamm Bowel Dis. 2017;23(7):1240-6.
230. Bots S, Kuin S, Löwenberg M, Ponsioen C, van den Brink G, D'Haens GR. Mo1911 Relapse Risk and Predictors for Relapse in a Real-Life Cohort of IBD Patients After Discontinuation of Anti-TNF Therapy. Gastroenterology. 2016;150(4):S814.
231. Galea S, Tracy M. Participation rates in epidemiologic studies. Ann Epidemiol. 2007;17(9):643-53.
232. Pasternak B, Svanstrom H, Schmiegelow K, Jess T, Hviid A. Use of azathioprine and the risk of cancer in inflammatory bowel disease. Am J Epidemiol. 2013;177(11):1296-305.
233. Statista. Market share of smartphone manufacturers in the UK 2018 [Available from: https://www.statista.com/statistics/387227/market-share-of-smartphone-manufacturers-in-the-uk/
234. Telecoms. Average smartphone prices reach record high 2017 [Available from: http://telecoms.com/485636/average-smartphone-prices-reach-record-high-gfk/
235. Statistics OfN. Internet access – households and individuals, Great Britain: 2018 2018 [Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/householdcharacteristics/homeinternetandsocialmediausage/bulletins/internetaccesshouseholdsandindividuals/2018.

236. Dillman DA. Internet, Phone, Mail, and Mixed-Mode Surveys: The Tailored Design Method, 4th Edition. 4 ed: Wiley; 2014.
237. Casati J, Toner BB, de Rooy EC, Drossman DA, Maunder RG. Concerns of patients with inflammatory bowel disease: a review of emerging themes. Dig Dis Sci. 2000;45(1):26-31.
238. Lazarus R. Emotion and adaptation. London: Oxford University Press; 1991.
239. Schwarzer R SC. A critical survey of coping instruments Oxford, England: John Wiley & Sons 1996.
240. Smolen DM, Topp R. Coping methods of patients with inflammatory bowel disease and prediction of perceived health, functional status, and well-being. Gastroenterol Nurs. 1998;21(3):112-8.
241. Hall NJ, Rubin GP, Dougall A, Hungin AP, Neely J. The fight for 'health-related normality': a qualitative study of the experiences of individuals living with established inflammatory bowel disease (ibd). J Health Psychol. 2005;10(3):443-55.
242. Radley A. Making sense of illness—the social psychology of health and disease. . London: Sage publications; 1994.
243. Brown MM, Brown AA, Jason LA. Illness duration and coping style in chronic fatigue syndrome. Psychol Rep. 2010;106(2):383-93.
244. Nezlek JB DP. Use of humor as a coping mechanism, psychological adjustment, and social interaction. Humor. 2001;14(4):395-413.
245. Dixon-Woods M. Writing wrongs? An analysis of published discourses about the use of patient information leaflets. Soc Sci Med. 2001;52(9):1417-32.
246. Weingarten SR, Henning JM, Badamgarav E, Knight K, Hasselblad V, Gano A, Jr., et al. Interventions used in disease management programmes for patients with chronic illness-which ones work? Meta-analysis of published reports. BMJ. 2002;325(7370):925.
247. Health Do. DOH: The Expert Patient: A New Approach to Chronic Disease Management for the 21st Century. London; 2001.
248. Kemp K, Griffiths J, Lovell K. Understanding the health and social care needs of people living with IBD: a meta-synthesis of the evidence. World J Gastroenterol. 2012;18(43):6240-9.
249. Sammut J, Scerri J, Xuereb RB. The lived experience of adults with ulcerative colitis. J Clin Nurs. 2015;24(17-18):2659-67.
250. Sawicki PT. A structured teaching and self-management program for patients receiving oral anticoagulation: a randomized controlled trial. Working Group for the Study of Patient Self-Management of Oral Anticoagulation. JAMA. 1999;281(2):145-50.
251. Fairbrother P, Ure J, Hanley J, McCloughan L, Denvir M, Sheikh A, et al. Telemonitoring for chronic heart failure: the views of patients and healthcare professionals - a qualitative study. J Clin Nurs. 2014;23(1-2):132-44.
252. Fairbrother P, Pinnock H, Hanley J, McCloughan L, Sheikh A, Pagliari C, et al. Exploring telemonitoring and self-management by patients with chronic obstructive pulmonary disease: a qualitative study embedded in a randomized controlled trial. Patient Educ Couns. 2013;93(3):403-10.
253. Cooper JM, Collier J, James V, Hawkey CJ. Beliefs about personal control and self-management in 30-40 year olds living with Inflammatory Bowel Disease: a qualitative study. Int J Nurs Stud. 2010;47(12):1500-9.
254. Novick G. Is there a bias against telephone interviews in qualitative research? Res Nurs Health. 2008;31(4):391-8.
255. Aquilino W. Interview mode effects in surveys of drug and alcohol use: A field experiment. Public Opinion Quarterly. 1994;58:210-40.
256. Oltmann S. Qualitative Interviews: A Methodological Discussion of the Interviewer and Respondent Contexts Forum: Qualitative Social Research. 2016;17(2).
257. Pope M MN. Qualitative Research in Health: Blackwell Publishing; 2006.

258. Bailey J. First steps in qualitative data analysis: transcribing. Fam Pract. 2008;25(2):127-31.
259. SQUIRE. Revised Standards for Quality Improvement Reporting Excellence - SQUIRE 2.0 2015 [Available from: http://www.squire-statement.org/index.cfm?fuseaction=page.viewpage&pageid=471.
260. Hunter J, Claridge A, James S, Chan D, Stacey B, Stroud M, et al. Improving outpatient services: the Southampton IBD virtual clinic. Postgrad Med J. 2012;88(1042):487-91.
261. McGettigan N ea. Monitoring inflammatory Bowel disease activity in a virtual biologic clinic: The effects of proactive therapeutic drug monitoring on patient reported outcome measures. ECCO 2018; Vienna2018.
262. Selinger CP, Lenti MV, Clark T, Rafferty H, Gracie D, Ford AC, et al. Infliximab Therapeutic Drug Monitoring Changes Clinical Decisions in a Virtual Biologics Clinic for Inflammatory Bowel Disease. Inflamm Bowel Dis. 2017;23(12):2083-8.
263. Eaden JA, Mayberry JF, British Society for G, Association of Coloproctology for Great B, Ireland. Guidelines for screening and surveillance of asymptomatic colorectal cancer in patients with inflammatory bowel disease. Gut. 2002;51 Suppl 5:V10-2.
264. Caldicott F. Information: To Share Or Not To Share? The Information Governance Review 2013 [Available from: https://www.gov.uk/government/publications/the-information-governance-review.
265. Union TEPatCotE. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing directive 95/46/EC (General Data Protection Regulation) 2016 [cited 2018 11/12/2018]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32016R0679.
266. Foundation TH. Innovating for Improvement 2017 [Available from: https://www.health.org.uk/funding-and-partnerships/programmes/innovating-for-improvement.
267. Confederation N. Information overload: Tackling bureaucracy in the NHS. NHS Reform and Transition [Internet]. 2013; (13). Available from: https://www.nhsconfed.org/resources/2013/01/information-overload-tackling-bureaucracy-in-the-nhs.
268. Santana S, Lausen B, Bujnowska-Fedak M, Chronaki C, Kummervold PE, Rasmussen J, et al. Online communication between doctors and patients in Europe: status and perspectives. J Med Internet Res. 2010;12(2):e20.
269. Jeong da E, Kim KO, Jang BI, Kim EY, Jung JT, Jeon SW, et al. The clinical usefulness of a web-based messaging system between patients with Crohn disease and their physicians. Medicine (Baltimore). 2016;95(26):e4028.
270. Black AD, Car J, Pagliari C, Anandan C, Cresswell K, Bokun T, et al. The impact of eHealth on the quality and safety of health care: a systematic overview. PLoS Med. 2011;8(1):e1000387.
271. dePhillips H. Initiatives and barriers to adopting health information technology. Disease management and health outcomes. 2007;15(1):1-6.
272. Rudin RS, Bates DW, MacRae C. Accelerating Innovation in Health IT. N Engl J Med. 2016;375(9):815-7.
273. McEvoy R, Ballini L, Maltoni S, O'Donnell CA, Mair FS, Macfarlane A. A qualitative systematic review of studies using the normalization process theory to research implementation processes. Implement Sci. 2014;9:2.
274. Godden DJ, King G. Rational development of telehealth to support primary care respiratory medicine: patient distribution and organisational factors. Prim Care Respir J. 2011;20(4):415-20.
275. Seto E. Cost comparison between telemonitoring and usual care of heart failure: a systematic review. Telemed J E Health. 2008;14(7):679-86.

276. Mair FS, May C, O'Donnell C, Finch T, Sullivan F, Murray E. Factors that promote or inhibit the implementation of e-health systems: an explanatory systematic review. Bull World Health Organ. 2012;90(5):357-64.
277. Sanders C, Rogers A, Bowen R, Bower P, Hirani S, Cartwright M, et al. Exploring barriers to participation and adoption of telehealth and telecare within the Whole System Demonstrator trial: a qualitative study. BMC Health Serv Res. 2012;12:220.
278. Jackson BD, Gray K, Knowles SR, De Cruz P. EHealth Technologies in Inflammatory Bowel Disease: A Systematic Review. J Crohns Colitis. 2016;10(9):1103-21.
279. Lee S, Borthwick H, Dhar A. Faecal calprotectin testing in primary and secondary care Are the current manufacturer's cut-off values clinically useful? Journal of Crohns & Colitis. 2014;8:S155-S6.