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**Name of Journal:** *World Journal of Methodology*

**Manuscript NO:** 86511

**Manuscript Type:** REVIEW

**Telemedicine in inflammatory bowel diseases: A new brick in the medicine of the future?**

Telehealth in IBD

**Abstract**

Inflammatory bowel disease (IBD) is a chronic digestive disease that requires continuous monitoring by healthcare professionals to determine the appropriate therapy and monitor short- and long-term complications. The progressive development of information technology has enabled healthcare personnel to remotely deliver care services to patients remotely. Therefore, various applications of telemedicine in IBD management have evolved, including telemonitoring, teleconsulting, teleeducation, telenursing, telenutrition, and telepathology. While evidence has been provided for some telemedicine applications, targeted studies are still required. This Review summarises the major studies that have evaluated telemedicine and its application in the management of IBD.

**Key Words:** Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Telemedicine; Telemonitoring; Telenutrition; Telepathology; Tele-education; Telepsychology

Gravina AG, Pellegrino R, Durante T, Palladino G, D'Onofrio R, Mammone S, Arboreto G, Auletta S, Imperio G, Ventura A, Romeo M, Federico A. Telemedicine in inflammatory bowel diseases: A new brick in the medicine of the future? *World J Methodol* 2023; In press

**Core Tip:** The progressive development of technology has provided new telehealth tools for gastroenterologists to manage patients with inflammatory bowel disease. Through online platforms, simple e-mails, phone calls, and websites, physicians can monitor patients, adapt therapies, summon patients in case of alerts or red flags, and communicate with them. However, there is a need to scientifically test these methods by comparing them with the standard of care to determine whether these forms of care are superimposable, or at least comparable.

## **INTRODUCTION**

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Inflammatory bowel diseases (IBD) include ulcerative colitis (UC) and Crohn's disease (CD). They are characterised by chronic, self-sustained digestive inflammation with a relapsing and remitting course that leads to disability, reduced quality of life, and increased healthcare costs [1].

At present, the exact etiopathogenesis of IBD remains to a large extent, unclear. However, it is believed that it may be the product of a series of complex interactions between genetic (as well as genomic and epigenomic) factors related to the colic mucosal immune system and gut microbiota. This creates an imbalance in gastrointestinal inflammatory homeostasis by activating the inflammatory process and upregulating proinflammatory cytokines at the expense of anti-inflammatory cytokines [1]. IBD has a significant epidemiological burden. The incidence and prevalence of IBD are steadily increasing, with the highest incidence rates in Western and Northern Europe and North America. The most frequent age range at diagnosis is 16–35 years, and about 6–7% of newly diagnosed patients are children younger than 15 years [2].

The chronic and relapsing nature of IBD poses the problem of inducing and maintaining remission to avoid developing short- and long-term complications, disability, and the onset of neoplasia [3,4]. To this end, it is mandatory to continuously monitor various outcomes (e.g. clinical, biochemical, and endoscopic) to weigh the therapeutic efficacy in both the initiation and maintenance phases of treatment to reduce the recurrence rate and minimise complications [5]. Such monitoring is traditionally performed during regular

outpatient visits, determination of hematochemical indices, and instrumental investigations, mainly endoscopic exams [5].

However, there is an increasing need to initiate a digital transition in IBD medicine to achieve multiparametric clinical benefits, ranging from increased therapeutic adherence to close monitoring with feasibility in terms of economic sustainability and reduction in healthcare costs [6,7].

The gradual shift from symptom- to prevention-oriented approaches has promoted and accelerated the development of mobile health (mHealth) technologies with the potential to radically transform healthcare delivery [8].

Despite the availability of various digital health tools, there are still no specific codified recommendations regarding which telehealth tools are the best for patients with IBD, the precise indications and contraindications, or the outcomes they can weigh most effectively and safely.

This Narrative Review aims to provide primary evidence on telemedicine applications, specifically in the setting of IBD.

## **TELEMEDICINE: GENERAL CONSIDERATIONS**

### ***Telemedicine: Definitions and applications***

Telemedicine uses technological tools to provide medical care (from diagnosis to treatment) from a distance [9].

The need for a proper definition of telemedicine is challenging in the early stages of testing and implementation. More than fifteen years ago, a peer review of one hundred and four different definitions of telemedicine allowed telemedicine to be defined as *“Telemedicine being a subset of telehealth, uses communications networks for delivery of healthcare services and medical education from one geographical location to another, primarily to address challenges like uneven distribution and shortage of infrastructural and human resources”* [10].

Several aspects must be addressed when approaching the subject of telemedicine. First, while it offers the possibility of providing care with greater immediacy and constancy,

and at a potentially better cost-benefit ratio, there are several aspects to be considered. Specifically, those related to privacy, confidentiality, and the need to achieve adequate information transparency with prior informed consent well-stated by the patient have already been stigmatized [9].

Telemedicine is not a particularly recent technique, but pioneering examples were found even before the 2000s. The telepsychiatry system was established in 1959 at the University of Nebraska School of Medicine [11]. However, the modern era of telemedicine fell later in 1968 when a multispecialty telemedicine system was established at Massachusetts General Hospital and offered to workers and passengers at Logan International Airport [11].

Examples of national telehealth programs can be identified later, in the 1980s, by the Norwegian government to provide health services to isolated portions of the population in rural areas with difficult access to health care. Similar services were offered in Australia, Canada, Japan, and the United States of America [12]. Since the 1990s, telemedicine has undergone marked growth in the technologies used and territorial implementation [11].

Bashshur *et al* [13] presented a telemedicine taxonomy by identifying three dimensions (functionality, application, and technology). Functionality, in turn, is divided into consultation, diagnosis, mentoring, and monitoring applications, and into specialty, disease, site, and treatment. Finally, technology was divided into synchronicity, networks, and connectivity. This is called the "Three-dimensional model" [13].

Synchronicity is an important term in the telemedicine glossary in that telemedicine can be carried out as much in an "asynchronous" sense as in the case of diagnostic images or surveys as in a "synchronous" mind, for example, in remote medical examinations [14]. The need for greater connectivity has increased dramatically in recent decades. This can be partly explained by the extensive advances in digital technology, which have made it increasingly easy to connect patients and healthcare providers remotely [14]. Easy access to scientific sources also lays the foundation for continuing medical education at a

distance <sup>[12]</sup>. This could also be relevant in the field of IBD, given the continuous progress made in medical and surgical science in this field.

Telemedicine offers several benefits. The first is the possibility of improving access to health services and increasing the spread with which these are delivered <sup>[12]</sup>. Second, it is possible to enhance the degree to which patients and healthcare providers are informed while setting up systems for quality control and improving the feasibility of screening programs <sup>[12]</sup>.

As telemedicine should affect IBD, we need to consider that it is a chronic condition with a very often unpredictable course and epidemiology that deeply affects younger population segments <sup>[15]</sup>. Telemedicine can interject itself into these difficulties and provide support in monitoring the disease (telemonitoring), providing medical care and choices (teleconsulting), educating patients about IBD and its management (teleducation), and managing the nutritional aspects (telenutrition) (Figure 1).

Already two meta-analyses on telehealth in IBD have shown that current evidence may justify a role for it in the treatment of IBD <sup>[16,17]</sup>. This finding seems to be most evident for quality of life in adolescents and in the reduction in the number of outpatient visits <sup>[16]</sup>.

#### ***The patient's point of view: Perspectives and beliefs related to telehealth***

Regardless of the remote care technique employed, IBD patients must benefit and accept it. Several studies before and after the COroNaVirus Disease 19 (COVID-19) pandemic weighed the expectations and perspectives of IBD patients in this regard. However, while there are benefits of non-invasive and continuous healthcare, there is also a need to ensure equity in the delivery of telemedicine and assurance of confidentiality <sup>[18]</sup>. Therefore, the voice of the patient, the recipient of these services, must be carefully heard. A systematic review conducted by Al Khoury *et al* <sup>[19]</sup> identified that the highest expectations experienced by patients with IBD were pain control, endoscopic reporting in the normal range, and adequate QoL. Additionally, some patients wanted to be informed by gastroenterologists about their IBD. However, one of the most interesting

elements that emerged was the propensity of patients toward e-health tools that were deemed feasible and acceptable.

Beyond healthcare, e-health resources are also potential sources of information for patients with IBD. For example, an extensive survey involving more than 300 patients with IBD revealed that, while the healthcare team was the preferred source of medical information, the second favourite source was the Internet <sup>[20]</sup>. Approximately 80% of the participants had searched the Internet for information about IBD, and approximately 30% did so at least once a week. In this study, patients were given a website for consultation, as recommended by health professionals.

This survey provides a source of food for further research. First, there probably needs to be an effort by health professionals to alert patients to potential sources of misinformation on the Web. Indeed, the concept of "*infodemic*" to which patients are subjected has emerged with COVID-19 more and more strongly <sup>[21]</sup>.

Several surveys were conducted during the pandemic to weigh the beliefs and perceptions of physicians involved in managing IBD and patients suffering from healthcare consequences.

Patient beliefs regarding the relationship between IBD and COVID-19 are among the major issues to be addressed by busy gastroenterologists during the pandemic.

For example, a Portuguese survey recorded how patients believed they were at an increased risk of severe COVID-19 if they had active IBD or were taking corticosteroids within three months <sup>[22]</sup>. In addition, Pellegrino *et al* <sup>[23]</sup> reported a reduction in therapeutic adherence during outpatient follow-up during the COVID-19 pandemic at a referral IBD centre in southern Italy by employing a remote questionnaire-based interview.

Additionally, in an Indian survey, patients reported similar fears aimed at patients in remission in most or all-controlled clinical activities in which telemedicine methods had also been applied in most of the sample <sup>[24]</sup>. The authors reported reduced involuntary adherence (due to the unavailability of medication, financial constraints, and difficulty in reaching dedicated health facilities) with increased disease activity. In addition, the

authors recorded an involuntary need to switch therapies due to the unavailability of previous therapies.

In addition, a French survey examined how telemedicine met with some success in terms of preference by healthcare personnel and a sample of patients during the COVID-19 pandemic [25]. However, an element that emerged in this survey was the need for a filter because disease flare-ups require in-person consultation.

Indeed, one cannot analyse the changes forced by the restrictions of the pandemic on remote medicine systems without considering that not all age groups have overlapping adaptive capacities. Moum *et al* [26], for example, showed in an analysis of more than 500 patients with IBD that although the preferred follow-up method was outpatient visits, the under-50 age group preferred telephone follow-up more than the older age group. Unsurprisingly, another study showed that younger patients were more prone to use telemedicine [27]. However, other evidence has shown encouraging results regarding the involvement of older adults in telemedicine systems, especially with the advent of the COVID-19 pandemic [28].

Another system by which patients with IBD can receive remote healthcare is through social media (e.g. Facebook, Instagram, LinkedIn, Twitter). A survey conducted in 2020 on over 100 patients with IBD (with an average age of 47 years) showed that Facebook and Instagram were the social networks most frequently used by patients. Of these, approximately 30% used social media concerning their IBD (i.e. for information about IBD, for support and coping strategies, to improve their anxiety levels, and to connect with other IBD patients) [29]. In addition, most participants (72.3%) reported wanting to receive telemedicine through society.

The use of social services for this purpose was also evaluated in settings where healthcare became complex, that is, in rural locations. For example, an experience conducted in the rural community of West Virginia involving over 600 patients with IBD confirmed that book/Instagram was the preferred social platform, and over 90% of the sample desired to receive care from their physicians through these platforms [30].

Ultimately, different voices emerged in different geographical settings, with a common matrix of good acceptability/preference for telehealth tools by IBD patients.

*The COVID-19 pandemic helped accelerate the implementation of telemedicine in the management of IBD: From pandemic damage to the possibilities of remote medicine*

<sup>5</sup> In 2019, the outbreak of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), a beta-coronavirus, arose in the Wuhan district of China and gradually acquired characteristics defined as a pandemic by the World Health Organization [31]. Although the diction of SARS-Cov-2 emphasizes the primary pulmonary involvement of the disease, it has gradually emerged that the condition could also affect the gastrointestinal tract as much as nonspecific clinical manifestations (such as vomiting/nausea, abdominal pain, and diarrhoea), as with direct organ damage as in hepatitis [32]. Furthermore, gastrointestinal involvement is associated with a worse intrahospital prognosis and requires intensive care [32]. Nevertheless, severe gastrointestinal disorders related to COVID-19 have been reported [33–35]. Additionally, suspicions have been raised regarding the possible role of SARS-CoV-2 in triggering the onset of *de novo* IBD [36]. The gastroenterological world has been strongly advocating preserving patients with IBD and those who are chronic and require continuous care over time. Telemedicine has accelerated abruptly to address this need [37]. The COVID-19 pandemic has drastically occupied beds in hospital facilities, resulting in the closure of outpatient facilities for emergency management and the reshuffling of healthcare personnel by redirecting them to COVID-19 centres. Therefore, the need for telemedicine arose from an unquantifiable set of requirements for IBD patients, impacted by the priority that COVID-19 patients had acquired (such as management of moderate-severe cases, severe acute UC, complicated CD, chronic control of biologic therapy, and oncologic surveillance of patients with long-standing IBD) [38].

Telemonitoring during pandemics has often been mandated in territories affected by lockdowns. Nevertheless, an economic analysis has also suggested telemonitoring as a cost-effective strategy for improving quality-adjusted life-years and costs of care [39].

All these events have, in the gastroenterology research landscape, resulted in substantial growth of studies examining the potential of telehealth in the IBD patient (Figure 2).

### **TELEMONITORING IN IBD**

Medical telemonitoring is a continuous or non-continuous monitoring process generally applied to chronic diseases, allowing healthcare providers to monitor and interpret patient data to make decisions about the health of the monitored patient [40]. Over time, several modalities have been outlined for applying information technology to telemonitoring for IBD. For example, some studies have examined home tele management systems and website-based systems as the most straightforward systems for the exchange of emails or phone calls between physicians and patients [41].

Many studies conducted on telemonitoring also included telemonitoring components because they provided information and educational content to patients about their IBD [42,43].

#### ***Cross group's experiences with the Home Automated Tele management (HAT) system***

The U.S. Cross Group evaluated several applications of the HAT system for IBDs in subsequent studies. The HAT system consists of three elements: a patient unit, a server supporting decision-making, and a web portal for physicians [44]. However, this system has not been applied to many patients with IBD. The first component was a laptop that served patients for self-testing. This concept is based on the genesis of alerts exhibited to clinicians (i.e. alert systems) from a dedicated web system when the patient's self-reported values exceed certain predetermined thresholds. The main variables collected by the authors were based on a numerical scale to weigh symptoms, compliance with medical therapy, body weight, and adverse events related to treatment.

In 2006, the first uncontrolled and nonrandomised pilot study enrolled five patients with CD and five with UC (almost all Caucasians) with a mean age of approximately 48 years. None of the patients exhibited severe disease activity. Several interesting findings emerged from the study, including the fact that 20% of the participants had not been

previously educated about computer use. All patients found HAT feasible and easy to use without a special commitment to their daily lives by ensuring weekly completion [44]. The same group conducted a subsequent HAT-based study in 2007 on 25 patients with IBD, with a mean age of 43 years. In this study, the feasibility and patient acceptance of HAT re-emerged. During the study, which took place over six months of follow-up, there was a reduction in disease activity and indices of inflammation (i.e., C-reactive protein and erythrocyte sedimentation rate). This was also accompanied by an increased QoL and patient self-awareness of IBD [45].

The authors also evaluated patients' preferences for HAT by confirming their acceptability in a survey of patients included in HAT studies [46].

Finally, the cross-group conducted a randomised controlled trial on HAT targeting 25 UC patients on HAT *vs* 22 on the standard of care with a follow-up in both groups of one year [47]. However, during the study, 11 patients dropped out of the HAT group, and at the end of the follow-up, the authors concluded that there was a lack of reduction in disease activity as well as a failure to increase therapeutic adherence. Nevertheless, corrective analyses revealed a modest increase in QoL. However, this study was limited by its small sample size, which might have revealed only gross differences between the groups; the fact that there was a significant proportion of patients in long-term remission; and the dropout rate in the intervention group.

Ultimately, this system showed excellent patient acceptability and feasibility in all studies. However, as described, the data on QoL and impact on therapeutic compliance and disease activity were discordant and inconclusive, probably because of the small sample size common to all three studies.

However, these experiences, while home-based, have been among the starting points for more modern expressions of telehealth and do not require special hardware devices to be placed in patients' homes.

*The gradual evolution toward more immediate systems: The “Constant-Care” web-based telemonitoring*

The rapid and recent evolution of the internet has resulted in the development of numerous online computer platforms, from real-time chat systems and emails to online portals dedicated to health. Thus, the concept of eHealth (the use of telecommunications and information technology in healthcare services) emerged. The concept of eHealth has been introduced for the development of portable medical devices.

A Danish group employed a web-based telemonitoring system called Constant-Care embedded explicitly in a dedicated website ([www.constant-care.dk](http://www.constant-care.dk)), validated in an initial study conducted over a decade ago in 21 patients with mild-to-moderate UC [48]. The authors assessed various outcomes from education (i.e. knowledge of IBD), QoL, anxiety, and depression levels. While no particular impact was recorded on the QoL and mood (i.e. anxiety and depression), the systems showed excellent feasibility and acceptance by patients and increased knowledge of their disease. The same group later conducted a randomised controlled trial on the same platform, including over 300 patients with mild-to-moderate UC on first-line therapy with 5-aminosalicylate acid derivatives, randomised into two groups (constant care *versus* usual care) for one year [49]. In contrast to the first study, in addition to the confirmation of feasibility/acceptance by patients, there was an increase in therapeutic adherence and QoL compared to the control and a decrease in the number of outpatient visits and the average patient/year costs. However, there was no impact on the frequency of IBD flare-ups, hospitalisation, or surgical outcomes.

Moreover, the Constant-Care platform has been used to optimise infusion sessions in patients with CD undergoing intravenous therapy with infliximab. In detail, in an initial pilot study, Pedersen *et al* [50] in an initial pilot study involved 27 patients with CD on maintenance infliximab therapy for 52 wk of follow-up (reached in the majority of the sample). The authors recorded the platform data regarding symptomatology and CD activity of the patients weekly, and faecal calprotectin levels were recorded weekly. All these parameters were computed into a score (i.e. inflammatory burden score) adopted by the authors to classify patients into a visual colour system (green, yellow, or red zones) to refer to yellow and red patients for medical consultation. An interesting element

emerging from this pilot study was the high rate of therapeutic change: 39% of the sample obtained therapeutic optimisation, while 50% obtained lengthening as opposed to infusion sessions. Pedersen *et al* <sup>[51]</sup> applied the same platform in a prospective open-label study targeting 95 patients with mild-to-moderate UC on mesalazine therapy for three months showing excellent results on the therapeutic adjustment of its dosages. Patients were required to complete the simple clinical colitis activity index each week and their faecal calprotectin values were recorded. Again, the authors, employing these variables, calculated an equal inflammatory burden score, similar to what was done in a previous study of CD patients, calculated an equal inflammatory burden score. There was a significant reduction in the simple clinical colitis activity index score and faecal calprotectin levels. Through this form of monitoring, the authors reduced the dosage of mesalazine in a quarter of the patients at week three to half of the subjects at week five and in almost all patients (88%) at week 12.

Subsequently, Carlsen *et al* <sup>[52]</sup> applied a monthly Constant-Care web application ([www.young.constant-care.com](http://www.young.constant-care.com)) to paediatric patients with IBD, significantly reducing outpatient visits and school absences in the constant-care group compared to the control group, which followed classic quarterly outpatient monitoring. There were no significant differences in therapeutic adherence or QoL between the intervention and control groups. An interesting finding was the excellent acceptability (81% adherence) in a complex setting, such as paediatrics.

#### ***Other experiences based on telemonitoring systems using web-based systems***

Other web-based portals have been implemented to establish telemonitoring for patients with IBD. For example, de Jong *et al* <sup>[53]</sup>, in 2017, examined a telemonitoring system (myIBD Coach) in a randomised trial. This system is a webpage accessible from tablets and smartphones for the monthly monitoring of disease activity levels, therapeutic adherence, adverse drug events, nutritional status, anxiety and depression levels, and other outcomes (such as physical activity and patients' ability to self-manage). Physicians can monitor these parameters, communicate with patients, and use the e-learning

modules. The authors assigned more than 450 patients to the myIBD coach group and 444 to the usual care group. The study's primary results were a significant reduction in hospital access for outpatient visits and the number of hospitalisations by the myIBD coach.

A further randomised trial compared the web-based system on the platform "Telemonitorización de la Enfermedad de Crohn's Disease y Colitis Ulcerosa or Telemonitoring of Crohn's Disease and Ulcerative Colitis" (TECCU) *vs* usual care and telemedicine by phone calls by examining clinical outcomes (i.e., clinical remission at week 24, QoL, therapeutic adherence, adverse events to therapies, social activities, hospitalisations, IBD surgery, number of outpatient visits) [54]. In these three study arms (21 patients per group) consisting of patients on immunosuppressive therapy, the TECCU group had the highest remission rate, the best disease activity scores, and reduced faecal calprotectin values.

Cross *et al* [55], to overcome the limitations of the HAT system, also evaluated another web-based telemedicine system (i.e., TELE-IBD) based on text messages. A three-arm randomised trial (TELE-IBD administered every week, TELE-IBD every two weeks, and a standard care group) involved more than 300 patients with IBD with at least one disease flare-up tracked in the previous two years. The trial showed improved disease activity and QoL, and reduced hospitalisations in the TELE-IBD group; however, no clear superiority of TELE-IBD over the standard of care was demonstrated. Schliep *et al* [56] conducted a follow-up analysis of the data from the already mentioned TELE-IBD trial by Cross *et al*, who conducted a specific analysis on the levels of depressive symptoms (assessed with the Mental Health Inventory 5) and QoL (set using the Short Form 12) and showed that text message-based monitoring did not increase depressive symptoms and QoL.

A trial based on web-based telemonitoring with text messages was conducted by Bilgrami *et al* [57] in 222 IBD patients with at least one exacerbation in the previous two years compared with usual care. Again, no particular difference emerged in the outcomes

assessed between the telemonitoring and standard of care groups (i.e. self-efficacy and patient activation).

An additional platform weighed in this context is the EasyMICI-MaMICI® studied in a randomised controlled trial directed at patients with active IBD *vs* standard of care and determining the improved QoL and satisfaction in the included patients (i.e., 54 IBD patients) and reduced outpatient visits [58]. EasyMICI-MaMICI® contemplates a smartphone-accessible app (EasyMICI) and online portal system (MaMICI). This platform provides a method for data collection and enables communication between users and caregivers.

Ghoshal *et al* [59], in 2021, employed a web-based platform video/audio consultation during the COVID-19 pandemic in 50 IBD patients reviewing IBD activity, anxiety levels, QoL, and probable COVID-19 symptoms, and recorded a comparable SARS-Cov-2 infection rate in IBD *vs.* non-IBD controls, QoL comparable or better than before the pandemic.

Ultimately, web-based systems have been among the most abundantly tested and have provided interesting results, as described above, about first-level outcomes in IBD (i.e., clinical remission rates and hospitalizations).

#### ***More accessible telemonitoring systems: Use of phone calls, text messages, emails or apps***

Telehealth strategies that do not use complex online platforms or home-based telemonitoring systems should certainly be included in the analysis of telemonitoring, as well as in systems that have tools within everyone's reach, such as simple SMS messages, emails, or even simpler phone calls between healthcare caregivers and patients with IBD. Examples of such methodologies can already be found several years ago, in 2009, in a retrospective study conducted by Herrera *et al* [54], who aimed to collect care data from the Crohn's Colitis Care Unit at Vall d'Hebron University Hospital in Spain over nine years (i.e. 1999 to 2007). They collected data from 1784 patients and observed how remote tools (telephone and fax) were employed more often than presential activities. The

Crohn's Colitis Care Unit also used a web-based system (which recorded over 3500 registered IBD users and over 150000 visits).

Other examples can be traced to the paediatric population. For instance, Heida *et al* <sup>[60]</sup> telemonitored 160 patients aged 10 to 19 years through the use of even e-mail and phone calls. They found an increase in the patients' self-efficacy and acceptance of telemedicine. The authors also recorded significant economic gains and reduced the number of in-person visits in the telemonitoring group.

Pinto *et al* <sup>[61]</sup> telemonitored 21 patients with CD and 56 patients with UC *via* telephone calls during the COVID-19 pandemic through a collection of patient-reported outcomes to assess disease activity and adopt treatment adjustments.

Few studies have examined cell phone applications as tools for IBD settings. Among them, a study conducted by Echarri *et al* <sup>[62]</sup> evaluated the Harvey-Bradshaw index self-administered *via* an app (i.e., the MediCrohn Study) by patients to determine if their results agreed with the same index calculated in the hospital by a physician. The study found a high percentage of concordance between the HBI assessed by the app and that assessed by the physician. Another study by McCombie *et al* <sup>[63]</sup> using a telemonitoring system for outpatients employing two smartphone apps (i.e., "IBDsmart" for symptoms and "IBDoc" for faecal calprotectin monitoring) and comparing it with usual care leaned toward the efficacy and acceptability of the telemonitoring system finding it particularly effective when used in patients with mild to moderate disease not recently diagnosed with a reduction in outpatient visits. Similar results were reported in a randomised trial by Östlund *et al* <sup>[64]</sup>. Again, participants found self-monitoring using a home faecal calprotectin assay and a digital application feasible and appreciated.

Finally, the study conducted by Zhen *et al* <sup>[65]</sup> involved the use of an app (i.e., "HealthPROMISE") by patients with IBD to monitor the condition after one year of data collection showed no improvements in QoL between patients followed through the app and those undergoing standard care; however, patients reported an increase in their understanding of the nature/causes of their condition after the period of using the app,

a statistically significant decrease in IBD-related hospitalisations and emergency room visits was also found.

### **TELECONSULTING IN IBD**

Teleconsulting provides healthcare consultation *via* telecommunications, directed by healthcare personnel to patients. Therefore, many of the aforementioned studies on telemonitoring inevitably have a teleconsulting component. In addition, many of the telemonitoring systems and platforms studied are aimed at providing consultations to patients to make diagnostic or therapeutic choices. However, over time, experiences aimed at studying teleconsulting (in isolation), its impact on clinical practice, and the significant outcomes of IBD have emerged.

A preliminary study conducted by Krier *et al* <sup>[66]</sup> used a real-time imaging-based system (i.e., Solar Digital Unity software, San Diego, CA) capable of integrating audio-visual communication between physicians and patients as well as the ability to share digital content (such as diagnostic images) to care for 34 veterans with IBD. The authors demonstrated that, through this follow-up system of telemedicine outpatient consultation *via* video calls, a similar level of patient satisfaction was achieved as that obtained from in-person encounters concerning indices such as attention to patient concerns and the physician's perceived skill level. The interviewed physicians welcomed the technical and informational qualities of the telemedicine sessions.

In addition, in the retrospective experience of the Crohn's Colitis Care Unit at Vall d'Hebron University Hospital in Spain by Herrera *et al* <sup>[54]</sup>, much of the care provided to patients over the nine years of reviewed care was *via* teleconsulting.

In the Highlands and Scottish Isles, the study conducted by Ruf *et al* <sup>[67]</sup> showed that Virtual Care clinics can be a safe and effective model of patient-centred care for patients with IBD living in remote areas, allowing enormous potential for time and cost savings.

<sup>2</sup> Li *et al* <sup>[68]</sup> evaluated whether a telemedicine-based IBD clinic could provide a high-quality, low-cost alternative to traditional care. Telemedicine clinics are based on virtual appointments with IBD specialists using an Internet-connected device. <sup>2</sup> Patients

completed a pre-visit survey reporting information about their disease activity, a post-visit study about their experience during the web appointment with the specialist, the time and money saved by not having to travel to the visit, and their preferences for future visits. At the end of the study, 77% of the patients reported that they preferred web appointments, again demonstrating the applicability of web monitoring systems as an alternative to outpatient visits to save time and money without compromising quality of care.

<sup>1</sup> Gastroenterologists and IBD specialists can also benefit from the educational potential of telemedicine as it provides a forum to discuss patient cases with complex diagnostic or treatment dilemmas. <sup>1</sup> Live inter-institutional interdisciplinary videoconference education (IBD LIVE) is an example of a multisite, multidisciplinary videoconference platform. The participating members included <sup>1</sup> gastroenterologists, surgeons, pathologists, radiologists, and other medical specialists. The objectives of each session included a review of evidence-based data and exchange of inputs for managing patients with IBD [69].

### **TELENUTRITION IN IBD**

IBD causes significant digestive changes that require careful evaluation and monitoring by clinical nutritional specialists. Therefore, attention has also been paid to telemedicine (although few studies are available) for the possibility of providing nutritional care to patients with IBD remotely (telenutrition).

In addition, the nutrition of patients with IBD must be adapted not only to the patient's clinical-demographic and anthropometric characteristics, but also to changes in disease activity in situations in which therapeutic fasting and parenteral nutrition may be necessary [70].

While many of the studies conducted in telemedicine have primarily focused on modifying medical-therapeutic parameters for outcomes directly related to IBD disease activity, another concept is also emerging. Given the lack of need for a physical examination in many dietitian encounters, telenutrition could fit into this context and address the nutritional needs of IBD patients [71].

Similar to the previously discussed telemedicine applications, the nutritional aspect has also been dramatically affected by the COVID-19 pandemic, and there have been many efforts to provide chronic patients with remote nutritional care [72,73].

Thus, telenutrition can investigate various aspects such as weight history, food intolerance, diet setting, evaluation of diet response, hunger assessment, monitoring, and therapeutic adjustments of enteral and parenteral nutrition therapy [74]. However, in the available studies, the study design was not always explicitly outlined for the remote assessment of nutritional status. This outcome is often one of the other outcomes examined (e.g. disease activity and therapeutic adherence).

For example, Ehrlich *et al* [75], in 2012, proposed an app (i.e., "GI Buddy") available for iPhones or also *via* a dedicated website in which patients 13 years of age and older entered data related to patient-reported medical outcomes but also dietary logs. In other words, there was a categorisation of data that the patients could input: symptoms, treatment, diet, and lifestyle.

Later, there was a nutritional component in a previously described study by De Jong *et al* [53] employing the myIBDcoach app. A tel-education service also provides educational modules for nutrition and IBD.

Other teleconsulting experiences (e.g. the PACE telemedicine program) included the nutritionist experience in IBD as part of the team and consultation [76].

An Indian congressional communication at the 17th Congress of the European Crohn's and Colitis Organization presented a digital health platform designed explicitly for telenutrition (i.e. IBD NutriCare) [77]. This application, available for both Android and iOS, allows the recording of dietary variables based on over 600 Indian recipes, as well as other clinical parameters of disease activity. These data were then used to analyse the nutrients consumed by patients to provide real-time tracking of the diet of the monitored IBD patients.

In conclusion, evidence for telenutrition in patients with IBD is particularly scarce and has not increased, even during the COVID-19 pandemic. Therefore, more efforts from the research community on IBD and nutrition are undoubtedly desirable to test new tools

and further validate those already available to improve chronic nutritional care and properly manage patients with IBD.

### **TELEDUCATION IN IBD**

There are not many studies conducted exclusively on teleducation. Instead, many of the studies conducted in other branches of telehealth have included teleducation components. Some examples are the telenutrition platforms exposed above. As stated, de Jong *et al* [42,53] included in the “MyIBDcoach” platform specific e-learning modules delivered to patients with IBD. Central among these modules was the discussion of IBD in general and the importance of immunosuppressive and biological therapies and traditional treatments (i.e., mesalamine). In addition, the authors educated patients on "self-management", that is, adopting strategies to prevent/reduce symptoms. Also completing these modules were sections on influenza vaccination, anxiety and depression. Also, as mentioned above, an authentic "educational curriculum" was provided in the TELE-IBD platform [43]. In this system, each participant received educational advice once or twice a week (depending on which intervention arm they belonged to). In addition, healthcare providers could also send educational messages exempt from this temporal logic concerning, for example, advice during flu seasons. Similarly, the web-based platform "Constant-Care" also hosted an educational training on the website [48].

### **SPECIAL APPLICATIONS**

#### ***Telepathology***

Care for patients with IBD is also achieved through accurate diagnosis of histologic specimens both at the time of the first diagnosis, where differential diagnosis between CD and UC becomes crucial, and during follow-up endoscopic investigations and colorectal cancer surveillance.

In telepathology, a remote consultation with a pathologist is achieved by transmitting digital images. The main telepathology experiments conducted in the field of IBD have

primarily targeted the burden of interobserver variability in diagnosing IBD-associated dysplasia/cancer, which often requires evaluation by multiple pathologists.

In the early 2000s, Odze *et al* [78] weighed the utility of telepathology and interobserver variability in detecting UC-associated dysplasia in approximately forty cases of UC. Four pathologists reviewed the slides of the haematoxylin-eosin images of the UC. The degree of concordance among the pathologists was fair, with a kappa ( $\kappa$ ) of 0.4 and worse results were observed for low-grade or indefinite dysplasia. However, the resolution of the images had not yet reached the current quality levels, so much so that, in this study, the same pathologists had generally given an upgrade in the degree of dysplasia on direct evaluation of the slides, but not in telepathology. The method used to obtain images was a Twin Cam MX-700 digital camera (Fuji film) provided with a dedicated (for use with a microscope) ocular device (I. Miller Precision Optical Instruments Inc., Philadelphia, PA). Later, Odze *et al* [79] recorded telepathology in the same setting involving seven pathologists (of whom only one was an expert in digestive pathology). A dynamic Apollo Telepath system (Apollo Telemedicine, Falls Church, VA, USA) was deployed for image transmission. However, the  $\kappa$  was poor ( $\kappa=0.32$ ), with a worse level for low-grade and indefinite dysplasia.

However, subsequent studies have shown more encouraging results. For example, Wu *et al* [80] involved four Chinese pathologists in examining fifty IBD colonic biopsies digitized using the Aperio system (Leica Biosystems). The degree of agreement among the pathologists was much higher ( $\kappa=0.68$ ) for interpreting IBD-associated neoplasms. Moreover, an interesting aspect of the study was the comparison of this agreement with that of four pathologists in the U.S. In this case, the  $\kappa$  was greater than 0.74.

Further experience was provided by the Italian Group for the study of the Inflammatory Bowel Disease (i.e., IG-IBD) pathology group [81]. In this study, 20 pathologists with experience in digestive pathology evaluated 54 diagnostic blocks from 30 colonoscopies in patients with IBD. Dysplasia detection showed a moderate degree of agreement ( $\kappa = 0.48$ ).

Ultimately, telepathology could be of great help in the management of patients with IBD. Guidelines recommend that the evaluation of dysplasia in patients with IBD, given the increased risk of colorectal cancer compared to the general population, should be performed by pathologists experienced in IBD [82]. However, IBD referral centres are not always available in all geographic regions; therefore, telepathology could provide valuable support in such settings.

### *Telenursing*

IBD nurse practitioners are increasingly gaining importance in clinical life [83–86], even in post-surgical stoma management but little evidence is available on telenursing (i.e. remote nursing care provided to patients with IBD) [87].

Cook *et al* [88] reported in 2010 on the application of telenursing to address cognitive and emotional barriers to therapeutic adherence of mesalazine in patients with UC. A large sample of > 200 patients was included in a nurse-managed telephone follow-up program to increase therapeutic adherence through cognitive-behavioural and motivational techniques. Ultimately, the authors recorded a significant increase in therapeutic adherence after the telenursing programme.

In a study by Del Hoyo *et al* [89], nurses played a role in telemonitoring IBD patients *via* telephone assistance, showing encouraging results from a cost-effective perspective. Specifically, telenursing experience showed a 67% probability of producing economic savings per additional quality-adjusted life-year compared with standard care.

Squires *et al* [90] found that a nurse-operated telephone advice line is a cost-effective intervention that allows patients to avoid going to the hospital when unnecessary and saves money in primary and secondary care.

A similar study by Alvarez *et al* [91] found increased telephone consultation requests by nurses and a decreased need for medical consultations, with savings on care amounting to 73.603 euros from 2009 to 2011.

Ultimately, the role of IBD nurses in telehealth has yet to be well evaluated in the literature and could show strong potential in managing chronic patients such as IBD

patients and providing relevant support to medical staff. In addition, a large proportion of these studies employed nurses as ancillary elements through phone calls. Studies in which IBD nurses could play a more primary role would perhaps be desirable since they often spend the most time with patients with IBD.

*Telehealth as a tool to weigh anxiety-depressive disorders in the IBD patient and the initial experiences on telepsychology*

It is increasingly emerging that the gut-brain axis plays a role in the pathogenesis of IBD as it affects the course of the disease, such that bidirectional communication with a mutual influence between the brain and gut is realised [92]. The bidirectionality in the gut-brain axis is one of its gnoseological pillars, in that the prevalence of anxiety-depressive disorders reaches about 30% in patients in remission and increases to about 70% in patients with active IBD [93]. During the COVID-19 pandemic, it was also observed in Italy that, during the first lockdown, there were particularly high rates of anxiety, depression, and poor sleep quality in patients with IBD in remission [94]. Nonetheless, anxiety-depressive disorders may also influence the frequency of disease flare-ups in patients with IBD, potentially leading to an increased frequency of flare-ups, an often more aggressive presentation, increased rates of hospital readmission, and an increased risk of surgical intervention [93]. However, this issue is not always adequately addressed in managing IBD and often takes a back seat. Unsurprisingly, some studies have reported that, in some settings, up to 70% of patients with anxiety-depressive disorders (even severe ones) are not treated by a dedicated specialist [95-97].

The different psychological techniques applied to IBD include cognitive behavioural therapy (CCBT), social support, stress management, and targeted techniques [97,98]. Many studies that have weighed the impact of psychology on managing IBD have also included remotely performed treatments.

Therefore, telemedicine and telepsychology interventions could be promising alternatives for patients with IBD who need them. In addition, web-based psychological

interventions have proven effective in other situations, such as treating depression and anxiety [99,100], insomnia [101], and irritable bowel syndrome [102,103].

Some of these projects are currently underway. One example is the randomised trial by Evans *et al* [93] designed the "ACTforIBD" program. The latter is based on acceptance-commitment therapy (i.e. a technique specifically for patients with IBD and concomitant psychopathological comorbidities) to address unresolved problems related to chronic IBD. This technique will be administered to patients by dedicated psychological therapists in one-hour sessions for eight weeks.

Schliep *et al* [56] additionally conducted a posthoc analysis of data from the TELE-IBD trial [55]. They extrapolated the variables of mental health (assessed using the Mental Health Inventory 5) and QoL (assessed with the Short Form 12 questionnaire). They compared a group that received telemedicine with a control group (i.e. the standard of care). The TELE-IBD method, which is mainly based on text messages, did not positively affect depressive symptoms or the QoL.

Other studies have attempted to provide CCBT psychotherapy to remote patients with IBD by comparing it with the in-person standard of care. For example, McCombie *et al* [104] showed that CCBT is associated with improved disease activity and QoL, including anxiety and depressive symptoms, in the first 12 wk. However, these results were not confirmed at six months. However, patients with less than 50% adherence to the CCBT program had many outcomes at six months. Therefore, future research should focus on adherence to psychological therapies.

Telepsychology has also provided interesting results regarding adherence to conventional therapy for IBD. For example, Hommel *et al* [105] offered behavioural therapy with four 60–90-minute sessions to patients with IBD and measured therapeutic adherence with the pill count strategy; they reported interesting results, although not significant, about a 29% increase in adherence to mesalazine.

### ***Tele-endoscopy***

Patients with IBD require recurrent assessment with quality endoscopic methods <sup>[106]</sup> as much in initial diagnosis as in monitoring and oncologic surveillance, so much so that endoscopic outcome is the focus of the most up-to-date "Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE-II)" consensus <sup>[107]</sup>.

To consider the application of telemedicine in endoscopic evaluations, one can turn to the concept of "tele-endoscopy".

Tele-endoscopy has already been generally proposed for digestive diseases and, in particular, for geographically remote regions <sup>[108-111]</sup>.

However, to the best of our knowledge, no study has been explicitly designed for IBD.

### ***Telepharmacy***

Telehealth can also be applied to dispense drugs to patients with IBD through remote contact between the patient and the pharmacist. However, no *ad hoc* studies have been designed for such applications in the treatment of IBD.

However, there are some initial data on home delivery services set up during the COVID-19 pandemic. For example, in one communication by Ruiz Garcia *et al* <sup>[112]</sup>, they addressed patients with immune-mediated diseases receiving home medication delivery. Among them there were seven IBD patients corresponding to 6.03% of the sample.

### **CONCLUSION**

In conclusion, IBD is a complex disease with many variables in its management, and a disease course that is rarely predictable. Close monitoring of this type of patient is necessary, as they require constant and continuous care, especially when the disease flares. Regular follow-up is also needed to determine whether the therapy is achieving its target. As highlighted by the STRIDE-II consensus, the goal is to ensure a QoL that overlaps that of the general population with the help of medicine. Telemedicine can intervene by meeting the needs of these patients (Figure 3). Many telehealth applications have been studied; however, other applications require considerable attention and new evidence. It is still well needed to study tele-endoscopy, telepharmacy, telesurgery or

telerehabilitation in the context of IBD and studies are still awaited. In addition, telehealth has several limitations to consider. That is, it is not clear, first, under what precise conditions the telehealth medical examination can be superimposed on the in-person examination. It is not yet defined what spectrum of patients may or may not be followed with such remote modalities, although much of the literature addresses patients with mild-to-moderate IBD and not necessarily in advanced therapy. The absence of an objective examination that can be done in attendance is certainly another limitation to consider. Indeed, to achieve these goals, one needs systems that integrate patient-reported symptom data with objective data (i.e., laboratory tests and instrumental examinations) so that the telehealth visit can be as reliable as possible.

Conversely, there is a need to evaluate which patients may be compliant with such systems and can use them fully. There are, however, exciting perspectives and evidence, as outlined in this review on telemonitoring, that make, in any case, telehealth a tool certainly to be considered in the management of chronic patients such as those with IBD. In addition, psychological monitoring tools (considering how much these patients suffer from anxiety-depressive disorders compared to the general population) should be encouraged.

In addition, in many realities, the COVID-19 pandemic was, in its contemporary having been, an unexpected and dramatic event, an opportunity for telemedicine systems to be an obligatory and ready solution to solving the medical care shortage. In this context, these efforts, as the pandemic epidemiological situation improves, should not be thwarted and represent an important starting point for the continued implementation of telehealth systems. In addition, the robust research growth that there has been with COVID-19 should similarly not come to a halt. All of these would enable the collection of additional evidence, as much real-life as the result of clinical trials, that could hopefully stimulate precise recommendations from the world's major IBD guidelines.

## **Figure Legends**

**Figure 1. Telehealth modality proposed in the management of Inflammatory Bowel Diseases (IBD).** Various data-obtaining and telecommunication systems can be established between patients and physicians engaged in the direction of IBD management. Combining these data and interactions leads to the genesis of various telemedicine applications in the IBD setting to ensure a range of outcomes (i.e., clinical, therapeutic, diagnostic, nutritional, psychological, *etc.*).

**Figure 2. Trends in telehealth research before and after the COronaVirus 19 (COVID-19) outbreak.** Conducting a simple search in papers indexed in MEDLINE, it is glaring how since 2019 (the year in which the onset of today's COVID-19 pandemic falls), there has been significant growth in papers produced combining telehealth with Inflammatory Bowel Diseases (IBD). We also note, predictably, that before 2019 the mass of papers on IBD gradually showed a gradual growth trend in the period 1992-2008. The search for such data in this figure stopped on April 2, 2023.

**Figure 3. Inflammatory Bowel Disease (IBD) patient telemedicine pathway.** Based on the current evidence, various telemedicine applications are across the entire IBD management, from diagnosis to treatment setting and short- and long-term monitoring of its effectiveness. Nevertheless, such telehealth applications are bidirectional. That is, they may have the potential to be both active (provided by the physician, psychologist, nurse or nutritionist, *etc.*) and passively requested by the patient from their healthcare managers on needs.

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SIMILARITY INDEX

### PRIMARY SOURCES

- |   |  |                 |
|---|--|-----------------|
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