

Adherence improvement in patients with ulcerative colitis: a multidisciplinary consensus document

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Received: 03/06/2021 · Accepted: 08/07/2021

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ABSTRACT

Objectives: a) to analyze the evidence available about poor adherence/non-adherence, including prevalences, associated factors, and interventions in ulcerative colitis (UC) patients; b) to provide a framework to improve poor adherence/non-adherence.

Methods: a qualitative approach was used. A literature review was performed using Medline. Primary searches were performed with Mesh and free texts to identify articles that analyzed prevalence, causes, associated factors, and interventions designed to improve poor adherence/non-adherence in UC patients. Study quality was evaluated using the Oxford scale. The results were presented and discussed in a nominal group meeting comprising a multidisciplinary committee of six gastroenterologists, one psychologist, one nurse, and one patient. Several overarching principles and recommendations were generated. A consensus procedure was implemented via a Delphi

process, during which each committee member produced a score ranging from 0 = totally disagree to 10 = totally agree. Agreement was considered when at least 70 % of participants had voted ≥ 7 .

Results: the literature review included 75 articles. Non-adherence rates ranged from 7 % to 72 %. We found a great variability in the methods employed to assess adherence, associated factors, and interventions designed to improve adherence. Overall, eight overarching principles and six recommendations were generated, all of them achieving the pre-established agreement level, including, among others, the identification, classification, and management of non-adherence.

Conclusions: Poor adherence/non-adherence are common in UC patients, this being a relevant clinical concern. Health professionals should address this issue and actively involve their patients in implementing effective, individualized interventions to improve adherence.

Keywords: Ulcerative colitis. Adherence. Prevalence. Associated factors. Interventions. Delphi.

Funding: this work was supported by Pfizer. Estíbaliz Loza, who works at the Institute of Musculoskeletal Health (Instituto de Salud Musculoesquelética, INMUSC), which in turn was funded by Pfizer, provided assistance in methodological coordination.

Conflicts of interest: FC has received research funding from AbbVie, Ferring, MSD, Shire, Takeda, and Zambon; speaker fees from AbbVie, Chiesi, Ferring, Gebro, MSD, Shire, Takeda, and Zambon. PF, AC and SG are employees of Pfizer (Spain). FC, YG, FM, LM, LC, DG, SG and MB have received consultancy fees from Pfizer S.L.U. for their work in this project but have no other relevant financial relationships to disclose. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in, or a financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Casellas F, González-Lama Y, Ginard Vicens D, García-López S, Muñoz F, Marín Sánchez L, Camacho L, Cabez A, Fortes P, Gómez S, Bella Castillo P, Barreiro-de Acosta M. Adherence improvement in patients with ulcerative colitis: a multidisciplinary consensus document. *Rev Esp Enferm Dig* 2022;114(3):156-165

DOI: 10.17235/reed.2021.8130/2021

INTRODUCTION

Ulcerative colitis (UC) is a relapsing inflammatory bowel disease (IBD) that often requires medical treatment to ensure remission (1). As the spectrum of IBD treatments continues to expand, choosing the most appropriate therapy for a patient becomes more challenging (2).

Adherence is generally optimal in short-term diseases, which are characterized by one or several symptoms whose appearance is predictable and continuous. The opposite is encountered in diseases that run an unpredictable course, with long periods of low activity, during which the advantages of taking drugs are at times difficult to appreciate. These are situations in which therapeutic adherence must be ensured, and an optimal patient-doctor relationship is most likely the cornerstone of any strategy designed to improve or ensure adherence (3).

According to the World Health Organization (WHO), adherence is defined as: "The extent to which a person's behavior, such as taking a medication, following a diet, and executing lifestyle changes, aligns with agreed recommendations from a health care provider". However, there are different methods to define and measure adherence (4).

Treatment adherence in UC patients, regardless of the definition and method applied to measure it, has been associated with better health outcomes by lowering the risks of flares, surgery requirements, hospitalizations, and colorectal cancer occurrence (5). When maintained, disease remission is associated with lower healthcare costs and quality of life improvements (5,6). Non-adherence is common in UC patients, with rates up to 50 % (7). In a review to analyze the factors influencing patient adherence, patients' own beliefs about medications and doctor-patient disagreement emerged as the most relevant ones (7). On the other hand, non-adherence was revealed to increase the probability of relapse by a factor of four, and was associated with poor quality of life (QoL), loss of response to tumor necrosis factor (TNF) inhibitors, and higher disability, morbidity, mortality, and costs (8,9).

Improving medication adherence is a major challenge for physicians involved in UC care. Understanding patients in terms of their sociodemographic profiles, disease profiles, personal habits, and medication-taking behaviors could be a first step towards improving medication adherence. Indeed, by adopting patient-tailored interventions, physicians can ensure that their patients receive the full benefits of their medication, thereby achieving disease remission (10).

Taking all the above into consideration, our project primarily sought to analyze adherence issues in UC patients, and secondarily to search for improved opportunities to further promote adherence.

METHODS

Design

This was a qualitative work based on a literature review, the consensus of a multidisciplinary committee of health professionals, and the opinion of an UC patient. The proj-

ect was carried out in accordance with the Good Clinical Practice regulations.

Selection of expert health professionals and patient

A multidisciplinary committee comprised of six gastroenterologists with broad experience in IBD, one nurse, one psychologist, and one patient was established. Selection criteria for health professionals included: a) proven experience in UC; b) interest in UC; c) representativeness of hospital type and care level. On the other hand, concerning patient selection, we contacted the Association of Patients with Crohn's Disease and Ulcerative Colitis (ACCU), requesting their participation. The association designated the expert patient.

Literature review

With the help of an expert documentalist, a narrative literature review in Medline was performed using PubMed's Clinical Queries tool, along with individual searches using Mesh and free-text terms up to September 2020, which was then updated for publishing purposes in February 2021. Our aim was to identify articles describing adherence levels to UC treatment, recommendations, and other care processes like follow-up visits, assessment methods including definitions, criteria, and thresholds, as well as determinants of nonadherence, in addition to interventions to improve adherence. Only meta-analyses, systematic literature reviews (SLRs), randomized clinical trials, observational and qualitative studies were accepted. Two reviewers independently selected articles and collected the data. Evidence and result tables were generated. Study quality was assessed using the 2011 Oxford Scale.

Nominal group meeting

The results of the literature review were presented and discussed in a nominal group meeting. Thereafter, the participant health professionals and patient proposed several overarching principles and recommendations to further increase therapeutic adherence in UC patients.

Delphi

The overarching principles and recommendations were submitted to a Delphi process, during which the expert health professionals and patient produced each a score ranging from 0 = totally disagree to 10 = totally agree. Agreement was considered when at least 70 % of participants voted ≥ 7 . When agreement level was < 70 %, we re-evaluated the principle and, if appropriate, re-edited and voted in a second Delphi round.

Statistical analysis and final document edition

Delphi results were expressed as percentages. The results of the narrative literature review, decisions of the nominal group, and Delphi outcomes were integrated into a draft document that was circulated among the experts for final assessment and comments.

RESULTS

Prevalence of poor adherence/non-adherence in UC

We found several SLRs and meta-analyses that highlighted a relevant non-adherence rate in UC patients, which may differ depending on study design, follow-up time, methodology applied to assess adherence, data sources, treatment types, and individual patients (7,11,12). Non-adherence rates ranged from 7 % to 72 %, with most studies reporting a 30 %-45 % of patients being non-adherent to treatment (7,11,12). While most of the studies analyzed adherence to pharmacological drugs (4,13), there were others that assessed adherence to diet (14), exercise, or follow-up visits (15).

Methods to measure adherence

No standardized adherence definition has so far been accepted. Several methods to measure adherence exist (Table 1), based on different definitions, items, thresholds, and intervals (4). They include direct observation, self-re-

ported methods like scales or questionnaires, and biological sample monitoring (4,16). Most methods are generic, while some others have been specifically designed for UC patients, using specific tools or adaptations (17).

Concerning generic methods to evaluate adherence in UC patients (Table 2), some of them are based on medicine counts, like the medication possession ratio (12), percentage of days covered (12), or medication refill adherence. There are also scales, including the Medication Adherence Report Scale (4), Visual Analogue Scale (4) or Forget Medicine Scale (4). For evaluating adherence, one of the most widely used scales is the 4-item and, particularly, 8-item Morisky Medication Adherence Scale (4,18,19). Other methods include questionnaires like the Beliefs about Medication Questionnaire (20) and, as previously discussed, structured interviews, mostly administered by a trained nurse (21), as well as patient medication diaries.

There are specific, designed *ad-hoc*, methods to measure adherence in UC patients, mainly involving questionnaires. It should be noted that many questionnaires were

Table 1. Main methods to measure adherence — their strengths and weaknesses

#	Method	Strengths	Weaknesses
1	Direct observation	<ul style="list-style-type: none"> • Most accurate, best method for intravenous infusions or other injections given at hospital 	<ul style="list-style-type: none"> • Cannot be used in real life for any medications taken at home
2	Unstructured and structured interview	<ul style="list-style-type: none"> • Allows qualitative questions • It is a fundamental part of the doctor-patient relationship • Allows a measurement of adherence (at least provides a general idea) 	<ul style="list-style-type: none"> • Recall bias • Time-consuming • Dependent on good communication skills • “White coat” adherence effect • No guarantee that medication has been taken
3	Questionnaires Scales	<ul style="list-style-type: none"> • Useful for large cohorts • Validated tools available • Allows a partial measurement of adherence 	<ul style="list-style-type: none"> • Recall bias • Highly dependent on patient interpretation and skills • No guarantee that medication has been taken
4	Patient diary	<ul style="list-style-type: none"> • Simple • Cheap • Useful for unintentional factors associated to non-adherence 	<ul style="list-style-type: none"> • Strongly influenced by personal opinion and patient commitment • No guarantee that medication has been taken
5	Tablet counts Pharmacy refills	<ul style="list-style-type: none"> • Measurable • Allows a partial measurement of adherence 	<ul style="list-style-type: none"> • Time-consuming • No guarantee that medication has been taken
6	Biological samples (measurement of drug or metabolite levels)	<ul style="list-style-type: none"> • Accurate record • Reproducible 	<ul style="list-style-type: none"> • Expensive • Partially invasive • Inter-patient variability • “White coat” adherence effect
7	Electronic-health technologies	<ul style="list-style-type: none"> • Allow continuous remote monitoring • Rapid access to healthcare providers • Attractive for younger patients 	<ul style="list-style-type: none"> • Expensive • Difficult to use for some patients • Less feasible for elderly patients • Little evidence • No guarantee that medication has been taken
8	Electronic drug bottles	<ul style="list-style-type: none"> • Measurable • Accurate registration 	<ul style="list-style-type: none"> • Expensive • No guarantee that medication has been taken • No evidence in clinical practice

Table 2. Generic methods to measure adherence usually applied in IBD patients

Method	Features and common thresholds	References
Medication Possession Ratio (MPR)	<ul style="list-style-type: none"> Calculated by adding up the total days supply of a drug administered during a defined follow-up period, which can be fixed (e.g., 365 days) or variable (start to end of therapy), and dividing by the total number of days in that period MPR \geq 80 % to define adherence 	(12)
Proportion of days covered (PDC)	<ul style="list-style-type: none"> A measure similar to MPR but curtails medication oversupply when present and uses a fixed period for assessment A patient's mean MRA score provides an overall assessment of adherence 	(12)
Medication Refill Adherence (MRA)	<ul style="list-style-type: none"> Total days supply divided by number of days in observation period and multiplied by 100 to obtain a percentage A patient's mean MRA score provides an overall assessment of adherence 	(11)
Medication Adherence Report Scale (MARS)	<ul style="list-style-type: none"> 5-point Likert scale to assess adherence with individual statements such as "I decided to miss a dose of these medicines"; score ranging from 4 to 20 Scores below 20 are considered non-adherence 	(4)
VAS	<ul style="list-style-type: none"> Scale of 0-100 cm: 0, total non-adherence; 100, complete adherence VAS \geq 80 usually defines adherence 	(4)
Forget Medicine Scale	<ul style="list-style-type: none"> One question with 6 possible answers that assesses how often patients forget to take their medicines, from no, never to \geq 3 times a week 	(4)
8-item Morisky Medication Adherence Scale (MMAS-8)	<ul style="list-style-type: none"> 8 questions covering various aspects of adherence behavior with "yes" and "no" as optional answers; score ranging from 0 to 8 A score below 6 is considered low adherence; of 6-7, medium adherence; of 8, high adherence 	(4,18,19)
Compliance questionnaire	<ul style="list-style-type: none"> 5 questions: easy access to prescription, ability to recognize relapse, following doctor's advice, ability to self-management in the acute phase, adherence to treatment with dichotomized answers 	(13)
Beliefs about Medication Questionnaire (BMQ)	<ul style="list-style-type: none"> 5-point Likert scale to assess adherence through 11 questions (5 necessity questions and 6 concern questions) 	(20)
<i>Ad-hoc</i> questionnaires and others		(13,17,22,23)

IBD: inflammatory bowel disease; VAS: visual analogue scale; MRA: medication adherence report; MPR: medication possession ratio.

not validated (13,17,22,23), like the compliance questionnaire, which is composed of five questions, including easy access to prescription, ability to recognize relapse, following doctor's advice, ability to self-manage in the acute phase, and adherence to 5-aminosalicylic acid treatment, with dichotomized answers (13). In another study, a trained interviewer asked open-ended questions designed to elicit patient adherence to their medications, and classified them as either total adherence or intermittent non-adherence (23). Other researchers used direct questions on adherence, which was defined as the completion of 80 % or more of the weekly or biweekly supplies (22). Formulas have been published to calculate adherence as well (24). We also identified one study that measured non-adherence based on medication interruption due to patient-driven circumstances (25).

Finally, there is little information about the proper frequency at which adherence should be assessed.

Determinants of poor adherence/nonadherence and interventions to improve adherence

Our review identified multiple factors associated with poor adherence/nonadherence. Some are non-modifiable, whereas others could be modified. Table 3 summarizes these factors and depicts improvement strategies.

These factors are related to patient characteristics, some of which generated conflicting results, like gender or age (4). Others were more steadily associated with non-adherence, such as psychological problems or personality issues like fears and forgetfulness (11,26). As in other chronic conditions, socio-economic aspects have also been associated with non-adherence (10,16). Besides, a patient's environment, i.e., social stigma, may be a strong factor favoring worse adherence outcomes (23), as are inequities in health systems and local organizations (4,23). As expected, adherence is likewise influenced by UC treatment characteristics (6,23,27).

Table 3. Risk factors for poor adherence and improvement strategies in IBD

Category	Factors	Improvement strategies
Patient-centered	<ul style="list-style-type: none"> • Sex (contradictory results) • Age (contradictory results) • Ethnicity (minorities) (4) • Family history (contradictory results) (4) • Marital status (contradictory results) (4) • Pregnancy or planning to get pregnant (4) • Full-time employment (47) • Educational level (contradictory results) (47) • Low socio-economic level (10) • Psychological problems (11,26) • Personality features (forgetfulness, disorganization), beliefs (fears), expectations (frustration), skepticism, attitudes (4,23) • Being busy or distracted by work or other activities, or a change in routine on weekends and vacations (23) • Insufficient knowledge/understanding of therapy benefits (23,29,48) 	<ul style="list-style-type: none"> • Implement health education • Improve primary prevention • The physician should address nonadherence factors • Economic support • Psychological and social support
Patient environment	<ul style="list-style-type: none"> • Stigma (23) • Embarrassment (23) • Peer pressure (23) 	<ul style="list-style-type: none"> • Psychological and social support
Health system	<ul style="list-style-type: none"> • Inequities (4) • Lack of accessibility (4) • Difficulties in pharmacy/long waiting lists (4,23) 	<ul style="list-style-type: none"> • Implement funds • Facilitate access
Treatment	<ul style="list-style-type: none"> • Safety (adverse events) (6,23,27) • Several daily doses • Complexity of therapeutic regimen (6) • Treatment formulation (rectal vs. oral) • Concomitant prescription of other treatments (47) • Lack of confidence in treatment (6) • Cost of medications (23) • Long time to response (23) • Large pill size (mesalazine) (23) 	<ul style="list-style-type: none"> • Provide more information about treatment features and objectives • Discuss with patient the most suitable route of administration • Implement drug monitoring • Simplify regimens as best as possible (long-acting drugs, once-a-day regimen)
Disease	<ul style="list-style-type: none"> • Longer disease duration • Higher disease severity and disability (4) • Disease activity and remission (27) • Recent diagnosis (6) 	<ul style="list-style-type: none"> • Early diagnosis • Early assessment and complications identification • Early treatment • Provide more information about the disease features
Physician	<ul style="list-style-type: none"> • Lack of communication skills (4) • Low on ability to empathize (4) • No recognition of poor adherence/nonadherence (30) 	<ul style="list-style-type: none"> • Spend more time with the patient • Address patient preferences, expectations • Practice empathy • Implement a method to measure adherence
Patient-physician relationship	<ul style="list-style-type: none"> • Unsatisfactory relationship (26) • Disagreements (29) • Low trust in physician (4) • Lack of shared decision-making (42) 	<ul style="list-style-type: none"> • Spend more time with the patient • More dialogue • Implement shared decision-making

IBD: inflammatory bowel disease.

Many articles observed lower adherence rates when using complex therapeutic regimens (6), depending on formulation (rectal vs oral) (28), long delay to response (23), or other concomitant medications. Similarly, some UC characteristics, such as disease activity or severity, have definitely been associated with non-adherence. Finally, other factors linked to physician characteristics and physician-patient relationship have been addressed in poor adherence cases, such as lack of shared decision-making (4,29,30).

On the other hand, different interventions have been described in the literature that were designed to improve adherence to treatments and other aspects like follow-up visits for UC patients. Interventional approaches are usually classified into four categories, including educational, behavioral, cognitive-behavioral, and multicomponent interventions. Besides, some interventions require an active involvement of health professionals (IBD nurses, gastroenterologists, others) (17,31-33), while others are more patient-centered and employ digital health technologies like websites or mobile applications (34-36). The quality of these studies is highly variable, yet generally poor to moderate; although no direct and valid comparisons of these studies have been performed, multicomponent interventions have provided the strongest evidence for further promoting adherence. Notably, not all of the published interventions demonstrated efficacy (37); as such, clinic visit frequency was not associated with better patient adherence to medications or blood sampling (15).

The efficacy of skilled IBD nurse interventions, with most of them using multicomponent interventions, in the overall management of this disease has been extensively described, yet including several methodological limitations (17,21,32,33). Different studies have demonstrated a decrease in health care utilization, such as emergency room and unscheduled visits, or an improvement in quality of life and self-management skills. We found a wide variety of skilled IBD nurse interventions that were designed to improve UC outcome and treatment adherence, including telephone calls, dedicated email messages, face-to-face interviews, educational activities, or specific programs for the transition from pediatric to adult consultations (17,21,31).

Another essential intervention source is the e-Health domain. E-Health refers to the use of novel information and communication technologies for health. The improvement in medication adherence based on these interventions in UC patients is somewhat controversial. Some studies have failed to depict any effect on adherence (34), whereas many others have revealed significant improvements (22,34,35). For UC patients, e-Health interventions, which usually consist of multicomponent interventions, are set up through different digital technologies, including websites. However, some experiences have been made in the context of telemedicine or through mobile applications (apps) (36). They include specific training modules focused on adherence, information about treatments, or strategies to enhance medication adherence (13,35). On the other hand, in recent years, there has been an increased and specific interest in telemedicine, especially due to the COVID-19 pandemic. In many studies involving UC patients, telemedicine has been implemented as a complement to regular clinical con-

sultation in order to facilitate self-management and disease management (22,34). Similarly to websites or apps, great variability exists in the contents and characteristics of the interventions designed to improve adherence, which also include telemedicine, where promising results have been obtained (22,35).

Along with e-Health interventions, motivational interviews (MIs) have emerged as an effective tool to increase adherence in UC patients (21,38). These interviews consist of providers communicating in supportive, caring, and empathic ways to resolve patient ambivalence to change health behaviors (39). A comprehensive SLR published in 2017 revealed that MI interventions were related to positive outcomes in terms of therapeutic adherence. In line with MIs, psychotherapy as an intervention to promote medication adherence has shown promising results that, however, remain to be validated in further trials (40).

Overarching principles and recommendations

The panel generated a framework for the adherence approach consisting of eight overarching principles and six recommendations (Table 4), all of them reaching the predefined agreement level in the first Delphi round.

The committee totally agreed on recognizing nonadherence as a common and relevant issue in UC, concerning above all medications but also follow-up visits, screenings, and lifestyle recommendations as well. Therefore, it must be addressed in daily practice and involve both health professionals and patients in order to improve adherence. In the view of the committee members, adherence should also be sought when prescribing medicines or planning medical visits (30). If health professionals do not take into account patient features, preferences, and opinions, the risk of non-adherence is likely to increase. Patient preferences is a key aspect of shared decision-making between patients and physicians (41), while patient preferences for treatments often relate to dosing frequency. Therefore, incorporating patient preferences by offering different formulations like the option of once-daily or twice-daily dosing may effectively improve adherence.

In order to identify nonadherence, it is vital to know its causes and associated factors, as well as effective interventions to improve this condition. Given this context, the committee members have especially focused on patients in clinical remission. These patients may stop taking any medication and even attending follow-up visits, as they feel in good shape. However, if patients stop taking their medications a disease flare may occur; restarting the same therapy does not necessarily translate into prompt clinical remission. Therefore, it is strongly recommended to systematically evaluate adherence in daily practice. Taking into account that different methods enable assessing adherence, while there is no evidence demonstrating that one is better than the others, the committee members reached a consensus in recommending using any of the methods reported in the literature. Although the evaluation of adherence to medications appears very relevant, UC management also comprises other issues such as follow-up visits, undergoing tests, or lifestyle recommendations.

Table 4. Level of agreement with overarching principles and recommendations

#	Overarching principles	Level of agreement %
1	Nonadherence is frequent in UC	100
2	Nonadherence is an important clinical problem	100
3	Adherence to treatment is the responsibility of both health professionals and patients	100
4	Health professionals involved in the care of patients with UC should be aware of nonadherence causes and associated factors, and know effective interventions to improve it	100
5	Adherence assessment should be a part of clinical practice	100
6	Health professionals should pay particular attention to nonadherence in patients with UC in remission	100
7	Shared decision making is crucial to improve patient adherence	100
8	Patient motivation is vital to improve adherence	100
#	Recommendations	Level of agreement %
1	<p>It is recommended to systematically evaluate adherence in daily practice, during all clinical visits, through the medical interview</p> <ul style="list-style-type: none"> • In a climate of trust • Adapted to patient characteristics • Using any method to measure adherence, including: <ul style="list-style-type: none"> – Direct observation/questions – Validated questionnaires – Patient diary – Drug counts, etc. 	100
2	<ul style="list-style-type: none"> • The evaluation of adherence includes the following: <ul style="list-style-type: none"> • Medications: doses, frequency, route of administration, and other specific indications • Recommendations on prevention and health promotion, and advice on such things as diet, exercise, lifestyle changes, smoking cessation, vaccines, sun protection, dental checks, stress management, and sleep hygiene techniques • Medical visits: frequency of scheduled visits • Tests: frequency of scheduled tests 	100
3	It is recommended to identify the causes of, and potential factors associated with poor adherence, especially when they may be modified	100
4	It is recommended to classify nonadherence according to intention and nonadherence type (partial, sporadic, sequential, white coat compliance, permanent nonadherence)	86
5	In cases of nonadherence, it is recommended that interventions of proven efficacy be selected and implemented, as adapted to patient characteristics	100
6	It is recommended to include adherence in nursing protocols	100

UC: ulcerative colitis.

According to the committee, if nonadherence is detected, healthcare professionals should attempt to identify its possible causes and associated factors, especially those that are modifiable. This is likely to be instrumental in selecting proper interventions. Similarly, it might be helpful to classify non-adherence, according to patient intention, as intentional or non-intentional, and according to type as partial, sporadic, sequential, white-coat compliance, or permanent. This should be done to further involve and motivate patients. More specifically, when internality is present, a careful, empathetic and detailed approach directed to the problem's origin is recommended. If this is impossible, different strat-

egies have been reported to avoid forgetfulness. Similarly, by assessing nonadherence type, health professionals may be in a position to select more appropriate interventions. In this context, the committee would like to emphasize that the frequency of clinic visits is not directly associated with improved patient adherence to medication intake or blood sampling (15); it may even cause the opposite of the desired effect. The active implication of patients in UC management is actually the key point to improve adherence (4,29,30,42). This is a key point, given that in the current care model for chronic illnesses a holistic and personalized attention should be provided. As reported in a previous publication,

some issues concerning patient empowerment or active involvement in disease management, such as considering the patient's opinion in decision-making, appear to be vital, especially when different therapies are available or flexible clinical care is rendered possible (41).

The committee highlighted the increased risk of nonadherence in UC patients during disease remission. In these cases, health professionals must reassure patients and provide structured education on the relevance of continuous therapy, even in periods of well-being. Notably, such continuous therapy is aimed to prevent disease exacerbations.

Finally, the committee recognized the valuable role of IBD-skilled nurses in overall UC management, especially in terms of adherence issues. As a result, and based on available evidence, this adherence concept should be included in nursing protocols.

DISCUSSION

We have first critically reviewed different aspects relating to poor adherence/nonadherence in UC patients, including their prevalence, associated factors, and interventions. Then, we have proposed a framework in order to identify and manage poor adherence/nonadherence. For this purpose a multidisciplinary committee analyzed the evidence available and generated a set of overarching principles and recommendations. The high agreement level depicted in the Delphi rounds reinforces the validity of the results.

One of the project's highlights is the high prevalence of poor adherence/nonadherence in UC patients, particularly concerning patients in remission (7,11,43). This is a relevant clinical problem, as poor adherence/nonadherence is associated with poor outcomes in UC (8). Therefore, non-adherence should be addressed in daily practice and managed appropriately (14,15). We would also like to emphasize that some methods to assess adherence may be too intrusive, like metabolite determination, while others are not sufficiently reliable, like visual analog scales.

However, improving adherence is a challenging task. The committee proposed several steps to successfully address and manage poor adherence/nonadherence. The first one is to be aware of and recognize that poor adherence/nonadherence is common in daily practice. Several methods have been proposed to measure adherence (4,17). As no standardized or globally accepted method exists, based on their experience and resources, the committee members simply recommended health professionals to select one method and implement it consistently. Likewise, in order to select the most appropriate intervention to improve this issue, health professionals involved in UC care must also identify the factors associated with poor adherence/nonadherence. These factors are often related to patient characteristics, their environment, or disease and treatment features, but they may also be linked to the health system, health professionals, and physician-patient relationship (4,6,10,11,23,26,27,29,42,44).

On the other hand, considering the interventions designed to improve adherence, the evidence collected so far has shown that most of them have proven effective in UC, specially

multicomponent interventions (17,19,21,22,31,34,35,38-40). As a consequence, it is impossible to recommend one single or specific intervention; therefore, health professionals should always carefully analyze their given context as well as patient characteristics and resources. To achieve their goal, they should always involve patients in the discussion when selecting and implementing interventions to improve adherence. Here, the committee would like to highlight some of the published interventions that have demonstrated efficacy or brought about promising results, which can easily be implemented in daily practice. The efficacy of skilled IBD-nurse interventions is clear, with most of them employing multicomponent interventions (17,31,32). The IBD nurse is the patient's most trusted person; these nurses also act as intermediates between patients, their families, and healthcare providers. Therefore, the committee members strongly recommend that adherence concepts be included in nursing protocols, and to further promote their role in this context. However, skilled IBD nurses are lacking in many centers (45).

Currently, there is a growing body of evidence to support the use of e-Health for UC patients, based on the promising results of these new technologies (19,22,34,35). However, although digital health technologies (websites, apps) or even telemedicine have shown an ability to fit into, complement, and improve the standard clinical care of UC patients, more research is needed to validate these findings. Likewise, it is unclear whether existing health systems are already prepared to implement these new technologies. Even with this limitation, the committee members encourage health providers to implement any of the interventions that are offered via e-Health technology. In recent years, MIs have also attracted interest among health care providers for UC patients, and the outcomes observed in different trials support MI implementation in daily practice as well (21,38,39). The committee members consider MI to be a valuable tool to improve adherence; they thus encourage health professionals to implement it in their daily practice.

This work presents some limitations. The main one is the great variability found in study designs, methods to measure adherence, and intervention types to improve adherence. This limits comparability of studies, generalization of results, and generation of robust and specific recommendations. However, we are confident that our multidisciplinary approach, which has been based on the best available evidence and experience, has succeeded to overcome these limitations. Moreover, only the committee members took part in the Delphi rounds. Nonetheless, we have provided a general framework for this project, in addition to a comprehensive review of the available evidence. We thus consider that, for this purpose, it was not absolutely necessary to test the Delphi in more health professionals.

In summary, as increasing adherence to UC therapies may lead to better health outcomes in UC patients (5,6), we are confident that our proposed framework will provide health professionals with a general guide to improve patient adherence to therapeutic plans and other aspects of care. Moreover, in order to achieve this goal, patients should always be actively involved in selecting the interventions designed to improve their outcomes.

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