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Practical Strategies for Enhancing Adherence to Treatment Regimen in Inflammatory Bowel Disease

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Abstract

Promoting adherence to treatment among pediatric and adult patients with inflammatory bowel disease (IBD) is a critical yet challenging task for health care providers. Several existing interventions to enhance adherence among individuals with IBD offer useful information about practical strategies to enhance adherence. The current review article has 3 goals. First, the review provides a context for understanding treatment regimen adherence in IBD by reviewing key definitional, measurement, and conceptual challenges in this area. Next, published studies focused on interventions to enhance adherence in IBD are briefly summarized, followed by a synthesis of practical adherence promotion strategies for use in IBD by health care providers. Strategies are distinguished by the level of evidence supporting their utility as well as by age group. Finally, recommendations for future research to facilitate the development and implementation of practical, evidence-based strategies for adherence promotion in IBD are provided. Findings from the literature review suggest that strategies including education, regimen simplification, and use of reminder systems and organizational strategies (e.g., pill boxes) are likely to be best suited for addressing accidental nonadherence. In contrast, addressing motivational issues, teaching problem-solving skills, and addressing problematic patterns of family functioning are more likely to benefit individuals displaying intentional nonadherence.

Keywords

inflammatory bowel disease; adherence; intervention; review

Promoting adherence to treatment among individuals affected by inflammatory bowel disease (IBD) is a challenge for health care providers in both pediatric and adult settings. Although interventions to enhance adherence in IBD are still largely in their infancy, some important information about practical strategies to enhance adherence can be gleaned from this literature. The purpose of the current review is threefold. First, the review aims to provide a context for understanding treatment regimen adherence in IBD by briefly reviewing key definitional, measurement, and conceptual challenges in this area. Next, the literature on interventions to enhance adherence is briefly reviewed, followed by a synthesis

of practical adherence promotion strategies for use in IBD by health care providers. Strategies are distinguished by the level of evidence supporting their utility as well as by age group. The review concludes with recommendations for future research to facilitate the development and implementation of practical evidence-based strategies for adherence promotion in IBD, with an emphasis on illustration of next steps using examples from ongoing research or clinical practice.

DEFINING ADHERENCE

Over the past several decades, terminology regarding patient management of chronic conditions has evolved considerably. “Compliance” is now used less often in reference to the patient’s success in following the treatment regimen due to the connotation of patient obedience and blame (i.e., the patient did or did not follow directions) associated with the term. Instead, the term “adherence” is now more commonly used as it connotes a more positive interpretation of patient behavior, reflects the ideal collaboration between patients and providers in treatment planning, and implies a continuum of behavior related to treatment completion. Various definitions of adherence have been proposed; however, the vast majority of these are derivations of the Haynes¹ definition: “The extent to which a person’s behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice.” There were distinctions drawn between intentional or volitional nonadherence, in which patients/families make an informed decision to not adhere to a particular regimen versus accidental nonadherence, in which the intention to adhere to the regimen is present, but practical issues interfere with adherence, such as forgetting.² Importantly, these definitions conceptualize adherence as an outcome or mediator of disease outcomes, as adherence essentially refers to a quantification of self-management behaviors. The term “self-management,” then, is defined as “the interaction of health behaviors and related processes that patients and families engage in to care for a chronic disease.”³ This definition accounts for the interaction of cognitive and behavioral processes in patients and their families as well. Thus, patient self-management behavior results in the extent to which he/she is adherent, which may consequently have implications for clinical/disease outcomes. Notably, these definitions take into account both the patient and his/her family environment. This is particularly important in pediatrics, as parents often have a substantial role in self-management behavior. However, it may also be a relevant consideration in adult health care because adult patients also often benefit from family support for illness management and self care.

THE NEED FOR ADHERENCE PROMOTION INTERVENTIONS IN IBD

Interventions to enhance oral medication adherence in IBD are warranted given the pervasive nature of nonadherence in both adult and pediatric IBD populations. Between 43% and 60% adults with IBD are nonadherent to their prescribed oral medication regimen.^{4,5} Furthermore, nonadherent adults are 5.5 times more likely to experience a disease flare than are their adherent counterparts.⁴ Nonadherence estimates vary across pediatric IBD studies, depending upon medication type, complexity of regimen, and method of adherence assessment, with objective approaches typically yielding higher nonadherence estimates than subjective approaches.^{6,7} Among studies using self-report methodology, prevalence of oral medication nonadherence as low as 2% has been reported,⁸ whereas studies using objective methods report nonadherence ranging from 38% to 66%.^{8–10} Despite this variability, the pediatric IBD literature is similar to the adult literature in supporting that nonadherence has noteworthy consequences for disease activity,¹¹ greater health care utilization,¹⁰ and poorer health-related quality of life.⁷ In addition to the negative impact of nonadherence on disease outcomes, it also has implications for rising health care costs and clinical trial research.^{5–12}

CHALLENGES IN PROMOTING ADHERENCE IN IBD

Several barriers to enhancing adherence in IBD exist. Because adherence is a multifaceted construct, determining the most appropriate time frame and assessment approach poses challenges to clinical researchers seeking to obtain accurate measurements of adherence.

Cognitive and physical developmental issues must be considered when assessing adherence and providing treatment for nonadherence. Our clinical and research experience with the IBD population has provided some insight into these developmental issues across age groups. Young children may not understand why they must take daily medication, which has the potential to result in oppositional behavior related to the medication regimen. Adolescents generally have the cognitive capacity to understand the rationale for long-term medication use, but often desire to be “normal” and not burdened by the demands of their treatment regimens, which may interfere with medication taking particularly when around peers or when taking the medication may interfere with other activities. The expectation for transition-aged youth to take on more independence for medication taking assumes adequate skill in this area. However, when youth have not had an adequate opportunity to learn about their regimen or to develop an organization system to support adherence during early adolescence and midadolescence, they may struggle to successfully adhere to their regimen when expected to do so autonomously at a later point. Both young and middle-age adults may have multiple responsibilities that present barriers to adherence including work responsibilities and child-rearing responsibilities, whereas older adults may experience cognitive declines that may interfere with treatment adherence.¹³ Thus, assessment and treatment for youth should consist of obtaining estimates of adherence from multiple reporters (e.g., patients and parents) to supplement objective measures; intervention would involve both the patient and his/her parents to focus on the impact of shared responsibility of treatment adherence and increasing autonomy of patient self care. In adults, assessment and treatment may be more or less patient-focused depending on the individual’s particular circumstances. Assessment and treatment for young and middle-age adults may involve only the patient or patient and spouse, whereas the inclusion of adult children or other caregivers may be an important component of adherence promotion of older adults. Regardless of patient age, a comprehensive understanding of how the patient manages his/her regimen and who provides support is critical for determining what type of intervention strategies to employ.

Objective methodology such as electronic monitoring, pill counts, analysis of drug metabolites, and the use of pharmacy refill data is commonly preferred over subjective approaches to measuring assessment within the adult^{14,15} and pediatric IBD literature,^{6,8} given that it is less prone to social desirability and recall bias. In fact, a recent study comparing teen self-reported adherence to electronic monitoring of adherence found that nonadherent youth are at risk of overestimating oral medication adherence by 23%.⁶ In addition to providing a more precise adherence estimate in contrast to self-report data, electronic monitoring allows researchers to acquire continuous and long-term data in real time.^{12,16} This is essential to adherence assessment among individuals with chronic conditions given the data to suggest that adherence is lower overall among those with chronic illness in contrast to individuals with acute conditions and because adherence is not static across time.¹⁷ Adherence tends to diminish over time among adult populations, with pronounced declines after the first 6 months,¹⁷ and similar rates of decline are observed among youths as they approach adolescence.¹² Moreover, diseases such as IBD pose added obstacles to accurate adherence measurement, given that medication must be administered during both active and quiescent phases of the disease.¹⁸ However, electronic monitoring is not free of limitations, as device malfunctions can occur and, similar to pill count or pharmacy data assessment methods, it cannot assure that medication was ingested by the

patient.^{12,16} Moreover, concerns related to reactive measurement effects necessitate that researchers take precautions (e.g. building a time frame into the early measurement period during which electronic data will be excluded) when electronic monitoring methodology is used.¹⁹ Finally, given the cost associated with electronic monitoring devices, clinical application of this methodology is limited. Thus, as a result of the lack of a gold standard for assessing oral medication adherence, researchers have suggested the use of at least 2 methods of adherence assessment.¹⁶ This has the potential to be applied in clinical contexts in which both patient and collateral reports of adherence are obtained, or through the use of pill counts, pharmacy refill data, or bioassays as available to supplement patient self-report.

INTERVENTIONS TO ENHANCE ADHERENCE IN IBD

Interventions to enhance adherence is complicated by the aforementioned conceptual and methodological challenges in adherence assessment. Nonetheless, systematic examination of strategies to enhance adherence is imperative given the high rates of nonadherence in IBD and the significant individual and societal costs associated with nonadherence. The literature on interventions to enhance adherence in IBD is small. Table 1 summarizes key components of each of these studies. Existing adherence interventions have disproportionately focused on adults with ulcerative colitis (UC) and on enhancing adherence to oral IBD maintenance medications. Moreover, existing interventions have primarily focused on demonstrating intervention efficacy rather than effectiveness. Efficacy studies seek to demonstrate that an intervention works under highly controlled circumstances, whereas effectiveness studies examine the impact of interventions under conditions that more closely approximate real life. Given the focus on efficacy trials, issues related to intervention cost-effectiveness, time commitment required of the provider, and training level required of interventionists have been considered less frequently, making the practical application of such approaches challenging to evaluate.

Existing intervention approaches to enhance adherence in IBD can be broadly grouped into 4 categories: educational, behavioral, cognitive behavioral, and multicomponent interventions. Within each domain, interventions vary with respect to the extent to which technology is used in the delivery of the intervention, whether the intervention is delivered individually or in a group setting, and the intensity and duration of the intervention.

EDUCATIONAL INTERVENTIONS

Educational interventions aim to enhance patient knowledge of IBD and symptoms, the benefits and mechanisms of action of the medication regimen, the consequences of nonadherence, and potential side effects of treatment. Furthermore, educational interventions typically involve provision of information on the medication dosing schedule.

One educational intervention to enhance adherence in IBD were developed and evaluated in adult populations. Waters et al²⁰ evaluated the efficacy of a 4-session group educational intervention delivered by a gastroenterology (GI) nurse practitioner. Results demonstrated a statistically nonsignificant trend toward lower rates of missed medication in the intervention group compared with a standard care comparison group over time. No interventions that focus exclusively on education as a mechanism of adherence promotion in pediatric IBD have been published.

BEHAVIORAL INTERVENTIONS

Behavioral interventions promote the act of medication taking and/or reinforce adherence by providing incentives for medication taking or altering environmental antecedents and contingencies associated with medication taking. Examples of behavioral interventions

include simplification of the regimen, use of visual or auditory reminder systems, and use of behavioral contracting or reward systems for taking medication as prescribed.

Regimen simplification interventions were evaluated in 2 studies of adult IBD populations.^{21,22} Kane et al²¹ randomized adults with UC to either once daily dosing (QD) or a conventional regimen (2 or 3 times daily dosing). At 3 months after initiation of the trial, all patients in the QD group were adherent, whereas only 70% of patients in the conventional dosing group were adherent. Although the benefit of once daily dosing decreased by 6-month follow-up, consumption remained significantly higher in the QD group. Additionally, Dignass et al²² found that the remission rate was significantly higher among adults given a QD dose of mesalazine compared with those dosed twice daily. Patient report suggested higher adherence in the QD group, likely contributing, in part, to the difference in remission rates. No interventions that focus exclusively on behavioral strategies to improve adherence in pediatric IBD have been published.

COGNITIVE BEHAVIORAL INTERVENTIONS

Cognitive behavioral interventions enhance adherence by altering thinking patterns that contribute to nonadherence while also establishing behavioral patterns that support adherence using aforementioned behavioral strategies. Problem-solving skills training is a cognitive behavioral modality that aims to enhance adherence via teaching individuals a structured framework for identifying barriers to adherence, generating and evaluating the likely impact of solutions, and implementing the solution that is most likely to resolve the adherence barrier.²³

Although cognitive behavioral interventions have not been evaluated among adult IBD populations, 1 recent study used problem-solving skill training among a sample of youth with IBD (Table 1). Specifically, Greenley et al²⁴ evaluated a 2-session phone-delivered family problem-solving skills training intervention among a group of 31 youths. Results suggested adherence improved by 10% for the full sample and by 18% among those with imperfect baseline adherence.

MULTICOMPONENT INTERVENTIONS

Multicomponent interventions use multiple strategies to enhance adherence including educational, behavioral, cognitive behavioral, motivational, and/or support provision strategies. Multicomponent interventions are advantageous insofar as they maximize the likelihood of an intervention effect by using a variety of theoretically or empirically based approaches to enhancing adherence. However, they do not allow for isolation of which specific intervention components are necessary to enhance adherence.

Evidence exists to support that multicomponent interventions can enhance adherence in adults with UC on 5-ASAs^{25–27} and in youth with IBD on thiopurines and aminosalicylates.^{28,29}

Four studies support the efficacy of multicomponent interventions for adults with IBD. First, Elkjaer et al²⁵ documented higher levels of adherence to a 4-week acute 5-ASA treatment protocol in adult patients with UC participating in the intervention compared with those in the comparison group. Intervention components included web-based education, individualized feedback on symptom severity, and suggested medication regimen adjustments through an automated system, and opportunities for interaction with a physician via electronic means (e.g. e-mail, text message, or through the study Website). Additionally, Cross and colleagues developed the UC HAT program for adults with UC.^{26,27} Their results documented higher adherence to those in the intervention group at 12 months after

intervention relative to a control group; however, there were no differences between intervention and control groups at 4 or 8 months after intervention. Intervention components included patient education, individualized and automated feedback on patient symptoms, and follow-up phone contact with nurses to alter the medication regimen when clinically indicated based on symptom profiles. Third, Cook et al¹⁸ evaluated a telephone nurse counseling intervention for patients with UC and found that rates of adherence over the 6 months following the intervention were higher than published rates of adherence in this population, supporting the intervention's efficacy. Intervention components included education, motivational interviewing strategies, and cognitive behavioral techniques. Finally, Moshkovska et al³⁰ examined the impact of a tailored patient preference intervention on adherence to 5-ASAs among adults with UC. Significantly higher rates of adherence were documented after intervention in the intervention group compared with the control group. Intervention components were tailored to each individual's preferences. All participants were provided with education and motivational enhancement training during an initial call and 2 follow-up calls. Additionally, participants chose up to 3 additional intervention components including a simplified dosing regimen, a medication reminder chart, visual medication reminders for refrigerator or bedside cabinet, daily pill box organizers with alarms, weekly pill box organizers, weekly nonelectric pill box organizer, or cell phone alarm set up.

Two pediatric studies support the utility of multicomponent interventions for adherence promotion. First, Hommel et al²⁸ evaluated a family-based individually tailored treatment among a group of 14 adolescents. The intervention consisted of four 60- to 75-minute sessions focused on educational and organizational interventions, behavior modification, problem solving, monitoring of adherence, and promoting adaptive family functioning. Youth demonstrated thiopurine adherence increases of 4% and mesalamine adherence increases of 25% from before to after intervention. Second, Hommel et al²⁹ also evaluated a group-based multicomponent intervention among a group of 40 youths aged 11 to 18 years. The intervention consisted of educational/organizational components, behavior modification, problem-solving skills training, monitoring of adherence, and addressing problematic family functioning (i.e., reducing conflict and improving communication). Compared with the no treatment control group, those in the intervention group demonstrated a statistically significant improvement in mesalamine adherence; however, no differences in thiopurine adherence were documented.

PRACTICAL STRATEGIES TO ENHANCE ADHERENCE

In the sections that follow, recommendations for practical strategies to enhance adherence in IBD are provided. Strategies are divided into evidence-based and promising strategies. Evidence-based strategies refer to those that are supported by research as effective intervention approaches in IBD populations. Promising strategies are those supported as useful in multicomponent trials with IBD populations. Recommendations are tailored by age, as appropriate, to highlight relevant developmental considerations in promoting adherence.

EVIDENCE-BASED STRATEGIES

Adult Populations

Education—Educational interventions focused on providing information about IBD, symptoms, and the medication regimen have a beneficial impact on adherence in adults with UC.²⁰ However, enhancing knowledge is likely best conceptualized as a necessary but not sufficient condition for medication adherence, and the combination of behavioral and educational interventions is likely superior to either one alone in enhancing adherence.³¹

Furthermore, educational interventions are probably most beneficial in addressing accidental nonadherence, which results from misunderstanding of the regimen requirements or organizational difficulty rather than volitional nonadherence.

Dose Simplification—Simplification of the regimen dosing schedule to once per day has improved adherence among adult patients with UC.^{21,22} This approach is likely most beneficial in addressing accidental nonadherence related to regimen complexity.

Pediatric Populations

Problem-Solving Training—Family-based problem-solving skills training seem to enhance oral medication adherence in youth with IBD.²⁴ Teaching patients how to systematically identify barriers to adherence, develop solutions, and implement these solutions can effectively be done through telephone and thus, have the potential to be integrated into clinical care in this manner. Recent efforts in other pediatric chronic disease populations add additional support for the practical applicability of this approach in documenting that problem-solving skills training can be delivered by health care providers during routine outpatient appointments.³²

PROMISING STRATEGIES

All Age Groups

Behavioral Strategies—Behavioral strategies such as visual reminder systems, auditory reminder systems, or use of a weekly or daily pill box are often included in multicomponent adherence promotion interventions in IBD³⁰ and are likely of practical value in enhancing adherence. Reminder systems have been documented to increase adherence between 6% to 25% across other chronic illness groups.^{33,34} Type of reminder system (phone or pager text message, phone call, video call, interactive voice response system, or electronic monitoring device with integrated reminder alarm) appears to not significantly impact adherence rates.³⁴

Reminder systems are likely most beneficial in addressing accidental nonadherence and may take several forms including visual reminders (e.g., posted notes, placement of pill bottles in conspicuous locations) or auditory reminders (e.g., automated text messages, alarms). Specific reminder systems, which provide specific information about which medication is to be taken at a given time, along with dosing instructions, are likely to be most helpful.

Enhancing Patient–Provider Communication—Enhancing the quality of the patient–provider relationship has the potential to enhance adherence in IBD. Interventions in adults with UC that have included individual interaction with health care professionals as 1 part of a multicomponent intervention suggest this as a promising approach.^{25–27} Additionally, descriptive research corroborates the importance of the patient–provider relationship in suggesting that nonadherence is more frequent when there is discordance between patient and physician, a phenomenon documented among adults with IBD³⁵ and other illness groups.^{36,37} In contrast, specific provider behaviors that may enhance adherence include a collaborative style of interaction, open discussion of the patient’s level of knowledge about their regimen, and discussion about the patient’s beliefs about the acceptability and necessity of the medication, concerns related to taking medication, and perceived impact of IBD on their functioning.^{38–40}

Adult Populations

Individualized Feedback on Symptoms—Results from several multicomponent adult intervention trials support the value of providing patients with recommendations for medication adjustments tailored to their symptom profiles.^{25–27} Although in the context of

extant studies feedback was delivered through automated systems, it seems reasonable to expect that specific feedback about benefits of adjusting medication dosing schedules based on current symptoms and the importance of adherence to the schedules could be done during routine clinic appointments or phone follow-ups with patients as well. Providing patients with feedback on symptoms and necessary medication adjustments between appointments is likely to be of benefit to individuals who experience volitional nonadherence related to misinterpretation of symptoms as medication side effects or for those who view medications as unlikely to benefit their disease functioning in a specific way. Additionally, feedback may also serve to improve accidental nonadherence insofar as it offers an opportunity for providers to provide clarification about the expected medication dosing regimen.

Motivational Enhancement—Several adult adherence promotion trials in IBD have incorporated motivational interviewing techniques to enhance adherence as one of multiple intervention components.^{18,30} Motivational interviewing strategies seek to help an individual identify their core values/goals and to increase the patient's insight regarding the role of medication adherence in achieving their goals. Motivational interviewing is effective in promoting behavior change in multiple areas including substance use/abuse, HIV-risk prevention, diet, and exercise, as well as medication adherence in other chronic illness groups.^{41–43} Specific techniques used to enhance motivation include the following: (1) conveying a nonjudgmental understanding of the patient's perspective, (2) working with the patient to see a discrepancy between their personal goals (e.g., returning to work, being socially active) and their present behavior (e.g., not taking medication as prescribed), (3) treating resistance to change as normal, and (4) supporting patient self efficacy development. Motivational enhancement may be particularly useful in addressing volitional nonadherence. In contrast, patients who are already invested in being adherent but experience barriers to adherence that are contextual in nature (e.g., lack of organized system and financial barriers to getting medication refilled consistently) may be less likely to benefit from motivational enhancement strategies.

Problem-Solving Training—As previously indicated, problem-solving skills training, has some support for effectiveness in pediatric trials.^{24,28,29} Problem solving has also been a component of several adult IBD adherence promotion interventions.¹⁸ Problem-solving training is a strategy that has the potential to address both volitional and accidental nonadherence given that the process of problem solving involves identifying barriers specific to an individual.

Pediatric Populations

Enhancing Knowledge—Enhancing knowledge is a useful stand-alone intervention to improve adherence among adults with IBD²⁰ and educational interventions are often used in conjunction with other methods of intervention in both adult and pediatric adherence promotion trials.^{25–29} As such, enhancing knowledge may help to improve adherence in pediatric IBD. One recent descriptive study in pediatric IBD offers some support for this supposition. Specifically, Greenley et al found that higher levels of youth knowledge about the reason for nutritional supplementation in IBD were associated with higher supplement adherence rates (Greenley, Stephens, Nguyen, et al., unpublished data, 2012). Whereas in adult populations, patient education may be sufficient, given that treatment management regimen responsibilities for youth often fall on parents and children, family-based education approaches are important to maximize the likelihood of adherence and should focus on providing information in written and verbal formats. Knowledge about the names of medications, dosing schedules, mechanisms of action, and potential side effects is imperative, as is provision of information about likely benefits of medication even during times of disease remission (for maintenance medications). Educational interventions are

likely to be most beneficial in addressing accidental nonadherence that results from misunderstandings of dosing schedules or regimen components or in addressing volitional nonadherence related to a lack of perceived benefit of taking medication during times of symptom remission.

Dose Simplification—Simplification of dosing regimen may be another useful intervention in pediatric populations, given this strategy has been associated with improved adherence in adult IBD populations and in other chronic illness groups.^{21,22,33,44,45} Across chronic illness groups, once or twice daily dosing has been associated with significantly higher regimen adherence than 3 or 4 time daily dosing.^{22,44,45} Dose simplification is likely to be most beneficial in the context of accidental nonadherence, as it assumes the patient is motivated to take the medication as prescribed.

Behavioral Management—Behavior management strategies such as development of reward systems for taking medication as prescribed, or behavioral contracting in which privileges are awarded or rescinded based on medication taking behavior is a promising intervention approach in pediatric populations that has been included in multicomponent pediatric IBD adherence enhancement trials.^{28,29} These strategies also have been shown to be efficacious in other pediatric disease populations.⁴⁶ Reward systems or behavioral contracting may be particularly useful for addressing oppositional youth behavior, in counteracting the impact of negative medication side effects on adherence and in addressing low motivation to adhere to maintenance medications in which symptom prevention rather than symptom amelioration is the goal. Rewards for taking medication can take the form of objects (e.g. stickers) or privileges (e.g. having a friend spend the night), and they provide concrete reinforcement for engaging in a task that is otherwise nonrewarding or possibly mildly aversive.¹² In general, positive reinforcement is preferred over loss of privileges; however, in cases where positive reinforcement is not sufficient to promote behavior change, loss of privileges can be a useful strategy.¹² Rewards should be tied to attainable goals (e.g., earning a reward after taking medication 10 times), rather than less attainable ones (e.g. not missing medication at all for the whole month) and should be developed with youth input to enhance their motivating value.

Increasing the Frequency of Contact with GI Provider—Increasing frequency of contact with provider is another possibly efficacious strategy to promote adherence in pediatric populations. In 1 study, adherence to oral thiopurine medications was significantly higher in the 3 days before, the day of, and the 3 days after a pediatric GI specialty appointment among youths aged 11 to 18 years with IBD (Nguyen et al, unpublished data, 2012).

Promoting Adaptive Family Functioning—Several multicomponent adherence promotion interventions in pediatric IBD address family communication deficiencies and teach family conflict resolution skills as methods of enhancing adherence.^{28,29} Additionally, high levels of family involvement in condition management may serve to enhance adherence in pediatric IBD. In 1 study, youth who reported being “involved almost all the time” in taking their daily medication were significantly less likely to be nonadherent.⁶ However, a high level of youth involvement in the absence of high levels of parent involvement is not expected to enhance adherence. Rather, high levels of both youth and parent involvement in disease management have been supported as advantageous for adherence in other pediatric populations.^{47–49} Similarly, in a recent study, families of youth with IBD categorized as having both high youth and paternal involvement had significantly higher aggregate adherence ratings over time than did families with high involvement of just 1 person or low involvement of both (Greenley, Thomason, Kunz, unpublished data, 2012).

FUTURE DIRECTIONS

Target Interventions to At-Risk Groups

One important direction for future research involves targeting adherence interventions to at-risk populations. A movement away from universal interventions (i.e., those in which the entire population of individuals with IBD are potentially targeted) toward more focused interventions acknowledges the limited resources available for intervention and ensures that those most in need of intervention are most likely to receive it. Several risk factors for nonadherence have been identified in demographic, disease-related, and individual functioning domains. Attention to these risk factors may elucidate subgroups that may benefit from more targeted intervention approaches.

Demographic risk factors for nonadherence from the adult literature include being male, single, being employed full time, and having a higher education level.^{15,50-55} Demographic factors have not consistently emerged as risk factors for nonadherence in pediatric populations.

Disease-related risk factors for nonadherence across both adult and pediatric populations include quiescent disease.^{10,18,21,26,51} Adult patients with longer standing disease are also less likely to be adherent.^{51,56} Additionally, aspects of the disease management regimen have been documented as risk factors for nonadherence. Understandably, patients have more difficulty with adherence when they are on multiple medications and are required to take medication more than once per day.^{51,55,56} Unknown or known side effects of the medications, such as headaches or nausea can also negatively affect adherence.^{18,56} However, it is important to note that those patients actually experiencing adverse drug events tend to be adherent if they believe their treatment is beneficial.¹⁸

Individual psychological dysfunction has also been documented as a risk factor for nonadherence in pediatric and adult groups. Depressive symptoms have been associated with nonadherence in youths and adults with IBD.^{18,51,57,58} Additionally, anxiety symptoms, anxiety disorders, somatoform disorders, and certain personality disorders have been related to nonadherence in adult populations.^{30,35,55,57} Among pediatric populations, oppositional and avoidant behaviors have been correlated with nonadherence, as has impaired health-related quality of life.^{2,7,9,59,60}

Research that targets adherence promotion in at-risk groups is an emerging area. To maximize efficient use of clinical resources, it is necessary to identify the patients who are at greatest risk for poor self-management and associated psychosocial dysfunction. Current efforts to examine the psychosocial risk factors that predict poor self-management in a clinical population are underway. The benefit of this research is that we will ultimately know the most salient psychosocial predictors of self-management and disease outcomes so that we can screen for these issues in clinical settings and address them more proactively.

Deconstruct Multicomponent Interventions

Across both adult and pediatric populations, support for the efficacy of several multicomponent interventions exists.^{18,25-30} Future research, which focuses on deconstructing these multicomponent interventions, would aide in the identification of the intervention component or components that are critical for enhancing adherence. In the context of deconstructing such multicomponent interventions, attention to evaluating the individual impact of low-cost strategies and those that have the potential to be integrated in regular care (e.g., use of pill boxes) would substantially contribute to our understanding of practical strategies.

Determine Which Interventions can be Delivered by Regular Providers or in Real Life Settings

A parallel line of research that would be informative is to examine the extent to which current evidence-based methods of intervention could be delivered by a regular health care provider or could be integrated into routine clinical practice. For example, problem-solving skills training can improve adherence in pediatric IBD populations when delivered through telephone by individuals with backgrounds in behavioral health psychology.²⁴ A logical next step would be to examine the extent to which this intervention remains useful when administered by nurses over the telephone or when integrated into regular clinic appointments. Because behavioral health services may be limited in certain settings, understanding the extent to which medical providers may be effective in implementing certain interventions may extend availability of adherence promotion resources to a broader range of patients.

As an example, there is a current effort to dismantle the treatment protocol used by Hommel et al²⁸ in a clinical setting. This involves testing individual components of the protocol across multiple patients to determine which components have the greatest impact on medication adherence. This is an excellent example of the type of translational research that needs to occur to make research clinical trials clinically relevant (applicable to patients who present with multiple comorbidities, greater complexity of behavioral difficulties, etc.).

Use Existing Technology

Similarly, interventions that incorporate freely available technology (e.g. smart phone application medication reminder systems) have the potential to be incorporated into routine clinical care and/or to reach a population of patients for whom it would be difficult to participate in face-to-face interventions. For example, in an ongoing multisite trial, Hommel and colleagues are applying their in-person intervention to promote medication adherence through virtual face-to-face technology. They will evaluate the impact of this treatment, being delivered through Skype, on medication adherence and disease outcomes. The benefit of this telehealth approach is that the treatment can be delivered to anyone in the world without requiring the patient and provider to be physically at the same location, which is a clear benefit to a large number of patients and clinicians who do not have access to this type of clinical intervention at their treatment facility.

Expand Focus Beyond Oral Medication Adherence

Expanding interventions to focus on more than just oral medication adherence is an imperative next step. Some preliminary data from pediatric populations suggest that nonadherence to nutritional supplements is poor among youths with IBD, with rates below 50% (Greenley, Stephens, Nguyen, et al., unpublished data, 2012). Additionally, recent data from the adult IBD literature suggest that adherence to infusion treatment is suboptimal.⁶¹ Attention to enhancing adherence to all aspects of IBD management is important in promoting optimal disease functioning broadly.

CONCLUSIONS

Promoting adherence to treatment among patients with IBD is a challenging yet important task. Health professionals are in a unique role to facilitate optimal adherence given their ongoing interactions with patients. Effective intervention starts with an accurate assessment of adherence, which we recommend include collateral reports, pill counts, and bioassay measures to the extent possible. Once baseline levels of adherence are ascertained, exploration of barriers to adherence is critical to identify volitional and accidental reasons for nonadherence, as each may benefit from different intervention approaches. Interventions

should be tailored to the specific barriers to adherence for the individual patient, and developmental factors should be considered in the choice of intervention approach. Strategies including education, regimen simplification, and use of reminder systems or organizational strategies (e.g. pill boxes) are likely to be best suited for addressing accidental nonadherence. In contrast, addressing motivational issues, teaching problem-solving skills, and addressing problematic patterns of family functioning are more likely to benefit individuals displaying intentional non-adherence. Although these strategies appear promising in promoting adherence in IBD, much more work is needed to translate existing interventions into clinical practice and to develop additional practical strategies to enhance adherence in IBD.

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TABLE 1

Summary of Intervention Studies to Enhance Adherence in IBD

Study	Sample Characteristics	Adherence Intervention	Method of Adherence Assessment	Adherence Outcomes	Considerations in Practical Implementation
Cook et al (2010)	N = 278 Diagnosis: UC Age range: adults	Multicomponent telephone nurse counseling intervention. Pre-/postdesign with no control group. Nurses conducted an initial call and used motivational interviewing and cognitive behavioral strategies. Written follow-up materials to reinforce call content were sent at the nurses' discretion. High-risk patients received additional calls over 6 mo	Patient report of mesalazine adherence, with adherence defined as months of mesalazine treatment completed	4 participants did not start treatment. 3 agreed to start after speaking with nurses, of which 2 did. 19 (7%) reported stopping mesalazine at any point. 10 (53%) agreed to resume treatment, with confirmatory follow-up in 7 (37%) cases	<i>Strengths:</i> Brief phone format reduced patient burden and enhances feasibility of use in routine clinical care <i>Weaknesses:</i> Would significantly increase work load for nurses if implemented as a part of routine care; multicomponent nature precludes isolation of critical intervention components
Cross, et al (2007, 2012)	N = 47 Diagnosis: UC Age range: adults	Multicomponent intervention. RCT compared home TMI to SC. TMI consisted of a home unit (laptop computer, weight scale), a decision support server, and a web-based clinician portal. Participants answered questions about symptoms, side effects, adherence, and received disease-specific education using the home unit. Participants also received a self-management action plan based on symptom report responses	Patient report of unspecified medication adherence	At 12-mo follow-up, 68% of those in the SC group were adherent compared with 45% of those in the TMI group. No differences between groups in adherence at months 4 and 8 were documented	<i>Strengths:</i> Delivered through telephone so reduced travel burden for participants <i>Weaknesses:</i> Significant cost associated with use of home unit and development/maintenance of server; required home internet access
Dignass & Veerman (2008)	N = 362 Diagnosis: UC Age range: adults	Behavioral RCT in which patients were randomized to QD or BD regimen	Patient report of mesalazine maintenance therapy adherence, defined as noninferiority (not more than 10% less efficacy below the QD treatment)	Adherence was significantly higher in the QD group following dosing change. After 1 yr, the difference between the 2 groups was significantly above the noninferiority limit with a treatment difference of 11.9% favoring QD. At end-of-study, 73.8% and 63.6% of patients in the QD and BD groups, respectively, were in clinical and endoscopic remission	<i>Strengths:</i> High feasibility for implementation into routine clinical care; Low provider burden; No additional staff or equipment costs <i>Weaknesses:</i> Focused solely on mesalazine maintenance therapy. Unclear if would generalize to other regimens
Elkjaer et al (2010)	N = 333 Diagnosis: UC Age range: 18–69 yr	Multicomponent, multisite RCT evaluating EDUC + SC versus SC. The EDUC + SC group received 3 h of education and feedback on IBD symptoms using an automated system, which prompted the patients to make adjustments in the medication regimen when clinically indicated. Opportunities to interact with a physician through e-mail, text message or phone also existed	E-prescription pharmacy database for 5-ASA maintenance therapy	At site 1, adherence to 4 wk of acute treatment was 73% in the EDUC + SC group compared with 42% in SC patients At site 2, adherence to 4 wk of acute treatment was 73% in the EDUC + SC group compared with 29% in the SC group	<i>Strengths:</i> Wide age range and large sample size; automated system reduced provider burden <i>Weaknesses:</i> Multicomponent nature precludes isolation of critical intervention components; significant cost associated with use of automated symptom tracking system
Greenley, et al (2012)	N = 31 Diagnosis: IBD Age range: 11–18 yr	Cognitive behavioral problem-solving skills training (PSST) family intervention delivered through telephone. RCT	Electronic monitoring of IBD thiopurine or 5-ASA maintenance medication adherence	From pre- to postintervention, adherence improved 10% for the full sample (from 74% to 84%)	<i>Strengths:</i> Delivered through telephone so reduced travel burden for participants; brief intervention

Study	Sample Characteristics	Adherence Intervention	Method of Adherence Assessment	Adherence Outcomes	Considerations in Practical Implementation
Hommel, et al (2012)	N = 40 Diagnosis: IBD Age range: 11–18 yr	evaluating 2 PSST interventions compared to a WLCC Multicomponent RCT comparing 4-session family-based group behavioral treatment or SC over a 6-wk period. The intervention consisted of educational/organizational components, behavior modification, problem-solving skills, monitoring of adherence, and enhancing family functioning	Pill count, patient report, and electronic monitoring of thiopurine or mesalamine maintenance therapy	Among those with less than perfect adherence at baseline, adherence from pre- to postintervention improved by 18% Statistically significant improvement in patient-reported mesalamine adherence over time and compared with comparison group from baseline to posttreatment assessments	<i>Weaknesses:</i> Small sample size limits generalizability; interventionists had psychology background <i>Strengths:</i> Relatively brief intervention <i>Weaknesses:</i> Required travel to center; interventionists had graduate-level training in psychology <i>Strengths:</i> multicomponent nature precludes isolation of critical intervention components
Hommel, et al (2011)	N = 14 Diagnosis: IBD Age range: 11–18 yr	Multicomponent RCT examined 4-session family-based individually tailored treatment compared to a WLCC. Sessions focused on educational and organizational interventions, behavioral modification, problem solving, adherence monitoring, and promotion of adaptive family functioning	Pill count of thiopurine or mesalamine maintenance therapy	Youth demonstrated thiopurine adherence increases of 4% and mesalamine adherence increases of 25% from pre- to postintervention in both groups	<i>Strengths:</i> Relatively brief intervention <i>Weaknesses:</i> Small sample size; interventionists had graduate-level training in psychology; required travel to center; multicomponent nature precludes isolation of critical intervention components
Kane et al (2003)	N = 22 Diagnosis: UC Age range: adults	Behavioral intervention in which participants were randomized to QD or CD	Pharmacy refill data for mesalamine. Adherence was defined as >80% of expected doses	QD group adherence at 3-mo postintervention was significantly higher than CD group (100% versus 70%) At 6-mo postintervention, a nonsignificant trend favoring QD group remained (75% adherent versus 70% adherent)	<i>Strengths:</i> High feasibility for implementation into routine care; Low provider burden; No additional staff or equipment costs <i>Weaknesses:</i> Small sample size; Treatment effects may dissipate over time and as such, additional intervention strategies may be needed
Moshkovska et al (2011)	N = 71 Diagnosis: UC Age range: 18–80 yr	Multicomponent RCT comparing individual EDUC + MOT to SC. EDUC + MOT session aimed to enhance motivation to adhere, identify barriers to adherence, and allowed patients to choose three practical adherence interventions (simplifying of dosing regimen, medication reminder charts, visual medication reminders, pill box organizers, or mobile telephone alarm set up)	High-performance liquid chromatography for 5-ASA concentration in the urine	At 48-wk follow-up, adherence in the EDUC + MOT was 44% higher than in the SC group. There was a nonsignificant difference in adherence of 71% in the SC group compared to 81% in the EDUC + MOT group	<i>Strengths:</i> Brief intervention; customized to patient preferences; emphasized use of practical strategies in home context <i>Weaknesses:</i> Multicomponent nature precludes isolation of critical intervention components
Waters et al. (2005)	N = 69 Diagnosis: UC or CD Age range: 18–74 yr	Educational intervention delivered by a GI nurse practitioner in a group format. This 2 group RCT compared formal IBD EDUC + SC to SC. The EDUC + SC group attended an education program provided in 3-h blocks over 4 consecutive weeks. The SC group received educational pamphlets and ad hoc physician education	Patient diary entry of missed medication event	The EDUC + SC group demonstrated a nonsignificant trend for lower rates of medication nonadherence at post intervention than the SC group (M = 0.91 versus M = 3.43)	<i>Strengths:</i> Intervention delivered by member of health care team <i>Weaknesses:</i> Required participants to travel to center; required significant time commitment on part of patient; significant provider burden

Study	Sample Characteristics	Adherence Intervention	Method of Adherence Assessment	Adherence Outcomes	Considerations in Practical Implementation
BD, twice daily dosing; CD, Crohn's disease; EDUC + SC, education plus standard care; EDUC + MOT, education and motivation intervention; M, average; RCT, randomized control trial; TMI, tele-management intervention; UC, ulcerative colitis; SC, standard care; WLCCG, wait list comparison group.					associated with intervention implementation