Simon R. Knowles, PhD
George Alex, PhD, FRACP

CE
1.5
ANCC
Contact
Hours

Medication Adherence Across the Life Span in Inflammatory Bowel Disease

Implications and Recommendations for Nurses and Other Health Providers

ABSTRACT

This article reviews the differences and similarities in medication adherence between adolescent and adult cohorts with inflammatory bowel disease. The review covers the rates of medication adherence, as well as predictors, consequences, and related interventions. Rates of adherence were more favorable among adolescents (65%–90%) than among adults (55%–70%). Major risk factors for poor adherence in adolescents include low medication knowledge, not establishing good medication habits initially, and peer victimization with low social support. For adults, nonadherence is more frequently unintentional (e.g., forgetting) and occurs more often in the context of a poor-quality patient–physician relationship, low medication knowledge, infrequent/missed appointments, busy lifestyle, and concurrent mental health concerns. Nonadherence to medication is associated with worsening of symptoms and risk of relapse in adults and adolescents. Nurses can play a significant role in influencing adherence to medication in patients with inflammatory bowel disease. In particular, nurses can help to impart knowledge on the importance of medication and identify factors that may help or hinder an individual in terms of adherence. Based on the current review, implications for practice and recommendations for nurses to promote medication adherence across both adolescent and adult cohorts are provided. Limitations of the currently available evidence and suggestions for future research are discussed.

Inflammatory bowel disease (IBD) is a chronic relapsing and debilitating condition, and in many of the cases, there is no cure. It can first occur at any time from early childhood till late adulthood, with 20% occurring before the age of 20 years. The disease is potentially well controlled with patients experiencing a normal lifestyle with ongoing use of medical (pharmacological) therapy and, in select cases, surgical therapy. From adult studies, it has been reported that patients who are nonadherent to treatment are up to 5.5 times more likely to experience a relapse in symptoms (Kane, Huo, Aikens, & Hanauer, 2003). In addition, nonadherence to treatment generates a 12.5% greater annual healthcare cost than adherent patients (Higgins, Rubin, Kaulback, Schoenfield, & Kane, 2009).

Received November 11, 2018; accepted March 21, 2019.

About the authors: *Simon R. Knowles, PhD, is Senior Lecturer, Faculty of Health, Arts and Design, Swinburne University of Technology, Hawthorn, Australia; and Department of Colorectal Medicine and Genetics, The Royal Melbourne Hospital, Melbourne, Australia.*

George Alex, PhD, FRACP, is Head of IBD Services, Department of Gastroenterology, Royal Children's Hospital, Parkville, Victoria, Australia.

Funding for this study was provided from the corresponding author's personal funds. No other conflicts of interest are reported.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.gastroenterologynursing.com).

Correspondence to: *Simon R. Knowles, PhD, Department of Psychological Sciences, Faculty of Health, Arts and Design, Swinburne University of Technology, PO Box 218, Hawthorn, VIC 3122, Australia (sknowles@swin.edu.au).*

DOI: 10.1097/SGA.0000000000000467

Background

Adherence refers to the consistency between patient behavior and the medical advice given to them after collaboration regarding patient values and preferences (Sewitch et al., 2003). Good adherence involves taking medication at the correct dose and frequency, as well as following other lifestyle recommendations (e.g., diet, substance use) that also help promote good health (Bermejo et al., 2010). Medication nonadherence is associated with a threefold likelihood relapse in

symptom control (Feagins, Iqbal, & Spechler, 2014), underscoring the important preventive role that the medication offers. Nonadherence is not always intentional (i.e., a deliberate decision not to take medication as directed), and can occur unintentionally (i.e., forgetting, not fully understanding, financial barriers; Horne, Parham, Driscoll, & Robinson, 2009). Previous reviews identified convenient medication regimens and good patient–doctor relationship (Lakatos, 2009), as well as focusing on modifiable factors such as anxiety and medication attitudes, are considerations for intervention (Selinger, Robinson, & Leong, 2011).

Examining nonadherence in IBD cohorts is complicated by the drastic changes in treatment seen in recent years. A substantially greater number of patients are now treated with biological medications (e.g., infliximab, adalimumab; Yu et al., 2018). This change may reduce the burden associated with daily medication administration, as doses are administered every 2–8 weeks depending on the drug, rather than on a day-to-day basis, as is typically necessitated by oral medications (e.g., 5-ASA, azathioprine). Although some biological medications are self-administered via subcutaneous injections (e.g., adalimumab, certolizumab), others such as infliximab and vedolizumab require a switch to facility-administered intravenous infusions.

Several studies have highlighted the potential impact this change may have on medication adherence among IBD patients. As Bucci et al. (2017) recently found, patients undergoing biological therapies appear more likely to be adherent compared with those taking daily oral treatments. Rates of "low" adherence, according to the Morisky Adherence Scale (Morisky, Green, & Levine, 1986), were considerably less for intravenous (4.4%) and injectable biological medications (6.3%) compared with oral steroids (40%), oral 5-ASA (37.5%), and immunomodulators (28%). Along the same lines, facility-administered biological treatments are associated with greater adherence compared with self-administered biological medications (Selinger et al., 2013; Wentworth et al., 2018).

Despite the apparent adherence benefit of biological therapies, findings to date suggest that rates of nonadherence are still problematic among these patients. A review by Lopez, Billioud, Peyrin-Biroulet, and Peyrin-Biroulet (2013) across 13 studies revealed pooled adherence rates of 82.6% among infliximab and adalimumab cohorts. A more recent 24-month retrospective cohort study ($N = 365$) found pooled adherence rates across biologics to be 66%, with the highest rate for the facility-administered vedolizumab (83%) and the lowest for certolizumab pegol (50%; Wentworth et al., 2018). In comparison, another study examining infliximab adherence within a pediatric cohort found that 91.4% of patients were adherent (Vitale, Greenley, Lerner, Mavis, & Werlin, 2015).

As with conventional, nonbiological treatments, adherence is essential for achieving optimal patient outcomes. Nonadherence has been associated with a greater likelihood of acute infusion reactions, reduced efficacy due to greater antidrug antibody formation, and greater likelihood disease flare-ups (Baert et al., 2003; Fidder et al., 2009; Govani et al., 2018). While much of the extant literature is based on patients adhering to daily oral medication regimens, these findings are nonetheless relevant, given the use of concomitant immunomodulator therapy (e.g., daily azathioprine) among patients undergoing biological treatments (Khanna et al., 2015), and the low adherence rates associated with immunomodulator use in adult (Bucci et al., 2017; Mantzaris et al., 2006) and pediatric (Oliva-Hemker, Abadom, Cuffari, & Thompson, 2007) IBD cohorts alike.

In a recent comprehensive systematic review of the IBD adherence literature, Lenti and Selinger (2017) identified modifiable (e.g., psychological distress, doubts about medication, low trust in physician) and nonmodifiable (e.g., low socioeconomic status, minority patients, religion, pregnancy) predictors of nonadherence. However, Lenti and Selinger argued that little progress had been made with regard to interventions, and more rigorous methodology was needed. On the basis of their comprehensive review of the literature, Lenti and Selinger concluded that adherence is associated with a complex interaction of modifiable and nonmodifiable factors and that patient-tailored and multidimensional interventions are required. Recommendations in relating to adolescents versus adult IBD cohorts were not provided and hence are the basis for this paper.

Adolescence is commonly defined as the ages between 10 and 17 years, with adulthood beginning to emerge at the age of 18 years (Arnett, 2000). This article reviews the differences and similarities between adolescent and adult cohorts in relation to the rates, predictors, and consequences of nonadherence. Modifiable factors such as barriers, the social and medical setting, and interventions to improve adherence in IBD are also considered, with recommendations for healthcare professionals working in this area. Although this is the definition of adolescent and adult used in this paper, some studies reviewed may vary by ±2 years.

Methods of Adherence Measurement

Medication adherence can be measured by subjective (e.g., self-reported during interview), objective (e.g., pill counts), or biological (e.g., bioassay/blood draw) methods (Hommel, Davis, & Baldassano, 2009). Standardized subjective self-report scales have been

used such as the Medication Adherence Report Scale (e.g., Ediger et al., 2007) or the Morisky Medication Adherence Score (Morisky et al., 1986). However, it should be noted that the interpretation of scores vary, in that sometimes any items endorsed are classified as nonadherent (e.g., Cross, Cheevers, Rustgi, Langenberg, & Finkelstein, 2012) or there is a threshold such as 80% (e.g., Gifford et al., 2013). Objective pill counts have been undertaken involving manually monitoring prescription dates, dosing instructions, and remaining pills in bottles (e.g., Hommel, Hente, Herzer, Ingerski, & Denson, 2013), or using Medical Event Monitoring System pill bottles that electronically record the time and date of each time the bottle is opened (e.g., Greenley, Gumidyala, et al., 2015). Biological assays such as blood or urine tests can also objectively monitor adherence through medication levels in the body (Gifford et al., 2013; Hommel et al., 2009). See Lenti and Selinger (2017) for a detailed review of the advantages and disadvantages of adherence measure methods.

Rates of Adherence

Adult IBD Cohorts

Jackson, Clatworthy, Robinson, and Horne (2010) systematically reviewed medication adherence in IBD among adults and estimate that self-reported nonadherence rates (using self-reports, interviews) are between 55% and 70%. Younger adults have been found to be significantly less adherent (Červený, Bortlík, Kuběna, et al., 2007; Shale & Riley, 2003) and have significantly greater odds (1.04–1.5, 3.64 in women; Campos, Portela, Sousa, & Sofia, 2016; D'inca et al., 2008; Ediger et al., 2007; Moshkovska et al., 2009) of medication nonadherence. Lenti and Selinger (2017) argue that this finding is counterbalanced by studies that find no age difference among adults. However, many of these studies with nonsignificant age findings focused on individuals with IBD who are adults only (e.g., Bernal et al., 2006; Bokemeyer et al., 2007; López San Román, Bermejo, Carrera, Pérez-Abad, & Boixeda, 2005).

Adolescent IBD Cohorts

Adolescents report higher rates of adherence than the rate of adults described above, with 65%–90% of adolescents reporting perfect adherence (Greenley et al., 2012; Greenley, Stephens, Doughty, Raboin, & Kugathasan, 2010; LeLeiko, Lobato, Hagin, Hayes, et al., 2013; LeLeiko, Lobato, Hagin, McQuaid, et al., 2013; Reed-Knight, Lewis, & Blount, 2013). When comparing older adolescents with younger adolescents, younger adolescents report greater rates of >80% adherence (67%–84%) than older adolescents (15%–25%; LeLeiko, Lobato, Hagin, McQuaid, et al., 2013). Kamperidis et al. (2012) found in a sample of 138 patients that adolescents were over fourfold more likely to be nonadherent to thiopurines than adults. Individuals earlier in adolescence are more adherent than individuals later in adolescence (Kitney et al., 2009).

Comparing adults and adolescents with IBD, adolescents tend to be approximately 10%–20% more adherent, with this observation being more pronounced in early adolescence. This difference may be related to the fact that parents and caregivers have more of an influence in general on their children in all aspects of life when they are younger when compared with when they are older. As parental involvement and supervision are reduced, it is likely that adolescents lose a key protective factor with regard to nonadherence. Given that IBD may be diagnosed in middle age, it is also possible that these individuals do not have the same level of familiarity with long-term medication usage compared with adults who were diagnosed during adolescence, where parental involvement may help establish good medication-taking habits from an early age.

Risk Factors for Poor Adherence

Adult IBD Cohorts

Risk factors for nonadherence can be found in patient demographics and social surroundings, as well as the medical setting. Although largely not modifiable (Selinger et al., 2011), these influences are nonetheless illustrative of the range of challenges IBD patients must navigate in adhering to a medication regimen. Being busy with work (Kim et al., 2016; Shale & Riley, 2003) and higher perceived stress (Tabibian et al., 2015) have both been found to increase the risk of nonadherence. Further, a low education level has been found to nearly double the risk of nonadherence (Lakatos et al., 2010). Individuals with previous IBD surgeries are 48% less likely to be nonadherent (Pittet et al., 2014) and African Americans are less likely than White Americans to be adherent to medication, independent of employment, socioeconomic status, income, health insurance, and marital status (Nguyen et al., 2009).

With regard to social influences, Mountifield, Andrews, Mikocka-Walus, and Bampton (2014) found low social support doubles the risk of nonadherence, even after controlling for demographic correlates of nonadherence (i.e., age, gender, employment, pill burden, quality of life, and disease type). Another potential social factor in medication adherence may lie in the perceived social stigma experienced by IBD patients. This is evidenced by the findings of Taft, Keefer,

Leonhard, and Nealon-Woods (2009), which found social stigma to account for 5% of the variance in adherence to medication, after controlling for demographic variables and illness characteristics (e.g., remission status, flare ups, flare-up duration). Similarly, qualitative findings suggest the social embarrassment of taking multiple pills and fatigue of long-term medication use are potential barriers to adherence (Devlen et al., 2014). Research by Horne et al. (2009) examined IBD patient attitudes regarding maintenance therapy and found attitudes of skepticism (*low* perceived need, *high* concerns), indifference (*low* need, *low* concerns), and ambivalence (*high* perceived need, *high* concerns) to predict nonadherence, independent of clinical and demographic factors. Struggles with mental health, such as anxiety (Nahon et al., 2011) and depression (Goodhand et al., 2013; Long et al., 2014; Nahon et al., 2012; Shale & Riley, 2003) also impact adherence. However, it should be noted that adult IBD patients report a range of different strategies to aid with adherence, including using daily routine as cues (78%), a medication dispenser (17%), calendar or checklist (6%), reminder from a family member (6%), and blister pack from the pharmacy (3%; Ediger et al., 2007).

The relationship a patient has with medical professionals influences medication adherence. The patient–doctor relationship has been shown to be an important predictor of medication adherence. A study by Nguyen et al. (2009) of 235 IBD patients found that greater trust in their physician was associated with a decrease in nonadherence, and for each half a standard deviation increase of trust, there was a 41% increase in odds of being adherent. Similarly, having a negative relationship with medical professionals is associated with over a five-fold risk of low adherence (Mountifield et al., 2014). The frequency of clinical visits and absenteeism from IBD appointments has also been shown to be associated with nonadherence (Mountifield et al., 2014; Tae et al., 2016). Specifically, Tae et al. (2016) found that patients who visit 3 months apart are 30-fold less likely to be adherent than patients who attend monthly or less. With regard to appointment absenteeism, Mountifield et al. (2014) found that patients who missed IBD appointments were 4.4-fold more likely to be nonadherent. Experiencing visible bleeding as part of abdominal symptoms, being overburdened with nine or more tablets (Kawakami et al., 2014), three-times daily dosing (Shale & Riley, 2003), or four or more concomitant medications with mesalamine (Kane, Cohen, Aikens, & Hanauer, 2001) also predict nonadherence. Research also suggests that patient knowledge and information-seeking are related to medication nonadherence. Tae et al. (2016) found that low medication knowledge is associated with a 5.6-fold increased risk of nonadherence. After taking into account potential confounders and nonadherence risk factors, Pittet et al. (2014) found active information-seeking patients (i.e., seeking out information on IBD, treatments, research, and development) were 2.43 more likely to be nonadherent.

It is more common that individuals unintentionally (38%–81%) are nonadherent than intentionally (8%–39%; Bernal et al., 2006; Červený, Bortlik, Vlcek, Kubena, & Lukás, 2007; Sewitch et al., 2003). Unintentional nonadherence is self-reported as due to being the weekend (16%; Bernal et al., 2006), working days (10%; Bernal et al., 2006), not being home (10%; Bernal et al., 2006), forgetting (5%–60%; Ediger et al., 2007; Horne et al., 2009; López San Román et al., 2005; Sewitch et al., 2003), or just being careless at times about taking medication (12%–38%; López San Román et al., 2005; Sewitch et al., 2003). In contrast, intentional reduce-dose nonadherence is self-reported as being due to feeling well and no need to continue (11%–64%; Červený, Bortlík, Kuběna, et al., 2007; Červený, Bortlik, Vlcek, et al., 2007; Ediger et al., 2007; López San Román et al., 2005; Sewitch et al., 2003), adverse side effects (9%–33%; Červený, Bortlík, Kuběna, et al., 2007; Červený, Bortlik, Vlcek, et al., 2007; Ediger et al., 2007; López San Román et al., 2005; Sewitch et al., 2003), reducing dose by oneself without the doctor (11%–32%; Ediger et al., 2007; Horne et al., 2009), reducing the dose to avoid running out before appointment (18%–22%; Červený, Bortlík, Kuběna, et al., 2007; Červený, Bortlik, Vlcek, et al., 2007), reduce dose to reduce medication costs (25%; Ediger et al., 2007), deciding to skip doses (17%; Horne et al., 2009), not refilling their prescription in time (11%–15%; Červený, Bortlík, Kuběna, et al., 2007; Červený, Bortlik, Vlcek, et al., 2007), unpleasant associations with medication (13%; Ediger et al., 2007), uncertainties about the effectiveness of medication (12%; Ediger et al., 2007), or pregnancy or breastfeeding in women (4%–10%; Červený, Bortlik, Vlcek, et al., 2007). Regarding increase-dose intentional nonadherence (i.e., self-medicating), self-reported reasons include suspected worsening of disease (80%; Bernal et al., 2006), fear of hospitalization (12%; Bernal et al., 2006), and fear of being on sick leave (10%; Bernal et al., 2006).

Adolescent IBD Cohorts

Unintentional nonadherence in adolescents is often referred to as barriers to adherence (e.g., forgetting; Hommel & Baldassano, 2010). Semistructured clinical interviews (Medication Adherence Measure [MAM]; Zelikovsky & Schast, 2008), which assess perceived barriers to medication adherence (e.g., "Ran out/didn't fill," "Not feeling well"), reveal that adolescents with

IBD report an average of 2.6–2.9 distinct barriers to adherence (Hommel, Denson, & Baldassano, 2011; Ingerski, Baldassano, Denson, & Hommel, 2010). Commonly reported barriers include forgetting (85%–94%; Gray, Denson, Baldassano, & Hommel, 2012; Hommel & Baldassano, 2010), not being home (43%–75%; Gray et al., 2012; Hommel & Baldassano, 2010), medication interfering with an activity (34%–69%; Gray et al., 2012; Hommel & Baldassano, 2010), regimen complexity (63%; Hommel & Baldassano, 2010), difficulty swallowing pills (56%; Hommel & Baldassano, 2010), and running out due to not refilling a prescription in time (15%; Gray et al., 2012). The time of day can also act as a barrier, and adolescents are least likely to miss a dose during lunchtime at school (10%) and dinner time (12%; Ingerski et al., 2010). Barriers to adherence have also been found to interact with other predictors. As noted above in Gray et al. (2012), anxiety/depressive symptoms moderate the barriers–adherence relationship, with high anxiety/depression adolescents reporting poorer adherence in relation to barriers, compared with low anxiety/depression adolescents. Barriers to adherence have also been shown to mediate the relationship between both attention problems and conduct problems with parent-reported adherence, underscoring the potential significance of behavioral functioning in identifying youth at-risk of nonadherence (Reed-Knight et al., 2013). Peer victimization is associated with lower adherence, and prosocial support moderates its impact (Janicke et al., 2009). As such, several publications have recommended the development of problem-solving skills among adolescents with IBD as a means of maneuvering barriers and optimizing adherence (Greenley, Gumidyala, et al., 2015; Hommel, Denson, et al., 2011; Hommel et al., 2012).

There are several factors that can influence the adherence of adolescents. Kim et al. (2016) compared the attitudes of adolescents aged 10–20 years and adults aged 30–50 years in a sample of 287 individuals with IBD. Although the overall risk of nonadherence due to age was unremarkable in this sample, the differences in attitudes between groups revealed attitudes that risk nonadherence. Compared with adults, adolescents were significantly more likely to endorse indifferent or skeptical attitudes toward medication and less likely to hold accepting or ambivalent attitudes. With regard to risk of nonadherence, indifferent or skeptical attitudes towards medication predicted nonadherence.

Knowledge about medication also affects adherence. Greenley, Stephens, et al. (2013) assessed the level of knowledge regarding nutritional supplements in IBD among 68 adolescent IBD patients. Comparing those who did not know and those who knew specifically how a multivitamin helped them, a large effect size was found on adherence with those having specific knowledge of the medication. Another consideration is whether the adherence is reported by the adolescent or parent, as Greenley et al. (2010) found that the relationship between adolescent and maternal reported adherence was not strong. Regarding intentional and unintentional nonadherence in adolescents, less research has been undertaken compared with adults (Schurman, Cushing, Carpenter, & Christenson, 2011). In a sample of 100 adolescent IBD patients, Schurman et al. (2011) found that the rate of unintentional nonadherence (73%) was higher than intentional (35%), and that the two kinds of nonadherence were not significantly correlated. Intentional nonadherence predicted 8%–10% additional variance in disease severity beyond age and gender alone.

The approach to risk factors for poor adherence differs between adults and adolescents. In adults, the emphasis is placed upon developing a positive and trusting physician–patient relationship, rather than demographic factors. Trust, regular contact, understanding the purpose of the medications, and integrating with an established routine are very important. Most frequently, when nonadherence occurs, it is unintentional and less-well integrated with the patient's routine. For adolescents, the terminology for unintentional nonadherence is barriers (e.g., Hommel & Baldassano, 2010). Assessing and adjusting barriers help to manifest support and better medication habits. As the literature thus far indicates, the best results are seen when adolescents understand and feel accepting toward their medications, and when their environment is conducive toward establishing and maintaining successful and lasting medication adherence habits.

Recent Diagnosis

Adult IBD Cohorts

For adults, there are mixed results to whether time since diagnosis impacts adherence rates. In a sample of 491 patients with IBD, D'inca et al. (2008) found that patients with a longer diagnosis (≥5 years; 15%) were more likely to be adherent than patients with a shorter diagnosis (<5 years; 24%). However, it should be noted that Červený, Bortlík, Kuběna, et al. (2007) did not find a significant difference when comparing at 10 years or greater time, irrespective of Crohn disease, ulcerative colitis, or medication type.

Adolescent IBD Cohorts

In predicting prescription medication adherence, Reed-Knight, Lewis, and Blount (2011) found a weak negative influence of time since diagnosis in a block that explained 20% of the variance. Similarly, Kitney et al.

(2009) found more adherent adolescents with IBD tended to have a shorter disease duration compared with nonadherent adolescents. In regard to specific medications, LeLeiko, Lobato, Hagin, McQuaid, et al. (2013) found that in IBD individuals prescribed 5-ASA medication, newly diagnosed individuals were more likely to be adherent than longer term diagnosed individuals (77% vs. 62%). However, this difference was not found in 6-MP medication users. Although these findings suggest a common theme toward greater adherence in newly diagnosed individuals, this finding may be masked by patient characteristics.

Greenley, Karazsia, et al. (2015) closely monitored the trajectory of adherence among 96 adolescents with IBD using an objective method of an electronic bottle cap that records the time and date of medication doses. Using group-based trajectory modelling, a two-group solution was established. Individuals who were high adherers maintained a trajectory of high adherence over time. In contrast, individuals who are mild nonadherers initially progressed to poorer adherence over time. As such, adherence tends to worsen over time only if a good and sustainable regimen is not established early.

The opposite trend is found in the literature between adults and adolescents in time since diagnosis. Adults can be slower to develop good medication adherence. In contrast, adolescents tend to become less adherent over time if they are not supported to establish good adherence habits early.

Impact of Nonadherence

Adult IBD Cohorts

Nonadherence to medication is associated with impaired health outcomes for individuals with IBD (Selinger et al., 2011). Comparing low adherers with medium/high adherers (N = 110), Trindade, Ehrlich, Kornbluth, and Ullman (2011) found that low adherers were significantly more likely to report higher disease activity on the Harvey Bradshaw Index (HBI). Low adherence to medication is also associated with up to a 3.5-fold increased risk of symptom relapse (Bhatt, Patil, Joshi, Abraham, & Desai, 2009; Feagins et al., 2014; Robinson, Hankins, Wiseman, & Jones, 2013; Tae et al., 2016). However, it should also be noted that among individuals who are adherent to the mesalazine medication, a change in regimen is associated with a 3.5-fold greater risk of symptom relapse than persisting with the same regimen (Robinson et al., 2013).

Adolescent IBD Cohorts

There is comparatively less research for adolescents with IBD. In a study of 100 parent/adolescent dyads, Schurman et al. (2011) found that volitional (i.e., intentional) nonadherence predicted an additional 10% (for parents and 8% for adolescents) of the variance in IBD disease severity beyond age and gender. The consequences of nonadherence to medication in both adults and adolescents is a worsening of IBD symptoms and risk of relapse. Consequently, consistent adherence to medication plays an important role in symptom control. A summary of the differences in adolescent and adult non-adherence-related evidence can be seen in Supplemental Digital Content 1 (available at http://links.lww.com/GNJ/A58).

Implications for Practice

There are multiple promising strategies that may enhance medication among IBD patients, and nurses are likely to play a central role in implementing these. As suggested by Greenley, Kunz, Walter, and Hommel (2013), educational approaches in particular are a promising strategy for enhancing adherence in adults and adolescents. Nurses are an invaluable conduit for improving patient knowledge about their condition and medication. The involvement of nurses in adherence promotion strategies may range from simple and informal recommendations during clinic visits (e.g., medication reminder strategies, pill boxes) to more complex, resource-intensive multicomponent interventions (e.g., Cook, Emiliozzi, El-Hajj, & McCabe, 2010; Cross et al., 2012).

There are clear benefits to patient adherence, with an additional 26% of individuals with chronic health conditions achieving a good health outcome when adherent (Dimatteo, Giordani, Lepper, & Croghan, 2002). For individuals with IBD specifically, nonadherence is associated with increased disease activity (Trindade et al., 2011), and an approximately threefold increased risk of relapse (Bhatt et al., 2009; Feagins et al., 2014; Tae et al., 2016). Atreja, Bellam, and Levy (2005) developed a simple model of medication adherence that uses the mnemonic "SIMPLE" to guide healthcare providers toward effective interventions that promote adherence. Based on this mnemonic, recommendations to enhance adherence are provided and split across adolescents and adult patient groups (see Table 1).

This review provides an IBD-specific evidence-based review of the literature on treatment adherence, with a further specific focus on practical adherence-promoting solutions across the life span for health providers working in this area. Supporting individuals with IBD to optimize their adherence has the potential to avoid costly flares/relapses that cause discomfort, time in in- or outpatient services, and hospital or insurance resources (Wan, Kozma, Slaton, Olson, & Feagan, 2014), which carries benefits for all. A key limitation of research on this subject is the

TABLE 1. Summary of the SIMPLE Mnemonic of Adherence Integrated With IBD Adherence Research

SIMPLE Mnemonic (Atreja et al., 2005)		IBD Adolescent Research	IBD Adult Research
S	Simplify regimen characteristics with easy administration that can be tied with a patient's activities of daily living.	When adolescents with IBD are supported to establish good medication habits, they tend to endure, whereas early mild nonadherence decays over time progressively into poorer adherence (Greenley, Karazsia, et al., 2015). The longer the time since their IBD diagnosis, the less likely adolescents are to have remained adherent to their medication (Kitney et al., 2009; LeLeiko, Lobato, Hagin, McQuaid, et al., 2013; Reed-Knight et al., 2011). Simplifying the medication regimen has been shown to improve adherence in adult IBD cohorts and, as such, is a promising strategy for reducing instances of accidental nonadherence among pediatric IBD patients (Greenley, Kunz, et al., 2013).	Needing to take medications three times daily (Shale & Riley, 2003), having four or more types of medication (Kane et al., 2001), or being in the process of changing regimen (Robinson et al., 2013), increase the likelihood of poor adherence. Conversely, simpler once-per-day dosing schedules are associated with greater adherence among adult UC patients (Dignass & Veerman, 2008; Kane, Huo, & Magnanti, 2003). The use of pill boxes and visual or auditory reminder systems may also improve adult adherence rates (Greenley, Kunz, et al., 2013).
I	Impart appropriate knowledge to help patients understand the purpose of their prescription.	Higher levels of knowledge regarding nutritional supplementation in IBD have been shown to predict greater supplemental adherence (Greenley, Stephens, et al., 2013). Oral medication adherence may be enhanced through family-based problem-solving training, which enhance adolescents' abilities to identify and address barriers to adherence (Greenley, Kunz, et al., 2013; Greenley et al., 2011). Hommel, Herzer, Ingerski, Hente, and Denson (2011) targeted patient education as part of a multicomponent intervention, finding improved adherence. Problem-solving skills training has been shown to benefit oral medication adherence in youth IBD patients (Greenley et al., 2011).	Help adults to understand their medication and why they take it, as a low understanding of their condition, symptoms and medication predict nonadherence (Tae et al., 2016; Waters, Jensen, & Fedorak, 2005). Formal IBD education was found to be associated with greater medication adherence, and lower healthcare use (Waters et al., 2005). A multicomponent intervention by Elkjaer et al. (2010) utilizing educational strategies report enhanced adherence. Problem-solving training has shown some benefit for pediatric IBD cohorts, indicating the potential value of this strategy for enhancing adherence among adults (Greenley, Kunz, et al., 2013).
M	Modifying beliefs and behavior to perceive risks and benefits of adopting healthy behavior.	Skeptical attitudes toward the medication regime (Kim et al., 2016) also hurt adherence. On average, adolescents will be confronted with an average of 2.6–2.9 barriers (Hommel, Denson, et al., 2011; Ingerski et al., 2010) (nonintentional nonadherence), which are commonly forgetting, not being home, and interfering with an activity (Spekhorst, Hummel, Benninga, Van Rheenen, & Kindermann, 2016). Nonadherent adolescents also report not filling a prescription in time (Gray et al., 2012) and having less success taking them at particular times of the day (Ingerski et al., 2010). Target and improve problem-solving skills to reduce the barriers to adherence to help improve adherence (Greenley, Gumidyala, et al., 2015; Hommel, Denson, et al., 2011; Hommel et al., 2012).	Patients are only 40%–67% accepting of their medication regimen (Campos et al, 2016; Horne et al., 2009; Kim et al., 2016; Moshkovska et al., 2009). Integrate the regimen with individual daily routine and values to improve acceptance of adherent behaviors. Motivational interviewing strategies delivered as part of multicomponent interventions (Cook et al., 2010; Moshkovska et al., 2011) have been associated with enhanced adherence.

(*continues*)

TABLE 1. Summary of the SIMPLE Mnemonic of Adherence Integrated With IBD Adherence Research (*Continued*)

SIMPLE Mnemonic (Atreja et al., 2005)		IBD Adolescent Research	IBD Adult Research
P	Patient–provider communication with an open and trusting collaborative dialogue.	Anxiety/depression can interact with barriers to produce poorer adherence (Gray et al., 2012). Open and trusting patient–doctor communication may encourage patients to disclose and seek treatment for such psychological distress. A discordant patient–physician relationship is associated with greater nonadherence (Sewitch et al., 2003). Nguyen et al. (as cited in Greenley, Kunz, et al., 2013) found increased frequency of contact between the patient and the GI provider to be associated with improved oral thiopurine adherence among youths with IBD in the 3 days prior to, the day of, and 3 days after their GI appointment.	It is recommended to form a positive provider–patient relationship as distrust (Nguyen et al., 2009), negativity, and/or missed or infrequent contact (Mountifield et al., 2014; Tae et al., 2016) with healthcare providers predict nonadherence. Pay attention to general mental health factors as they can contribute to poor adherence (Long et al., 2014; Nahon et al., 2012; Nahon et al., 2011; Nigro, Angelini, Grosso, Caula, & Sategna-Guidetti, 2001; Shale & Riley, 2003). Women either pregnant or attempting to conceive can also stop taking medications without consultation out of concern for safety (Gallinger, Rumman, & Nguyen, 2016).
L	Leave the bias of demographic and personal characteristics such as gender, marital, education, ethnicity, or income, out of focus.	Demographics are not modifiable or reliable, instead focus on what is modifiable, such as thinking on an individual basis, building a good patient–provider relationship, addressing concerns about medication, and paying attention to general psychological factors (Lenti & Selinger, 2017; Selinger et al., 2011).	
E	Evaluate adherence using standardized and reliable methods.	Evaluation with a multimethod including both self-report such as Medication Adherence Report Scale (Ediger et al., 2007) or Morisky Medication Adherence Score (Morisky et al., 1986) and an objective measure such as pill count or biological assay to help ensure that unintentional nonadherence does not occur (Gifford et al., 2013; Hommel et al., 2009).	

Note. GI = gastrointestinal; IBD = inflammatory bowel disease.

heterogeneity of available data. For example, the measurement of adherence and the interpretation of adherence scores often vary between studies. Such inconsistencies make it difficult to compare findings across studies and reach comprehensive conclusions. Furthermore, there is considerably less evidence available for adolescents than for adults.

Future research should focus on areas such as barriers for adults and looking at intentional versus unintentional nonadherence in adolescents. This study identified that psychological disorders (e.g., anxiety/depression) can moderate the effect of barriers for adolescents (Gray et al., 2012), and that interventions that include a cognitive–behavioral therapy component helps adults (Cook et al., 2010; Elkjaer et al., 2010; Moshkovska et al., 2011). As such, future research could explore the interaction of thinking styles, psychological disorders, and coping strategies on medication adherence.

Conclusion

Nonadherence to medication for individuals with IBD is estimated to occur in 65%–90% of adolescents (Greenley et al., 2010, 2012; LeLeiko, Lobato, Hagin, Hayes, et al., 2013; LeLeiko, Lobato, Hagin, McQuaid, et al., 2013; Reed-Knight et al., 2013) and 55%–70% of adults (Jackson et al., 2010). Overall there has been less research with respect to adherence in adolescents compared with adults; however, there appears to be greater focus on unintentional nonadherence (barriers) in adolescents than in adults and more promising interventions. Although less is spent on medication when one is nonadherent, the cost of complications associated with nonadherence on the healthcare system is significantly higher (Wan et al., 2014).

Adherence is important for individuals with IBD as nonadherence is associated with increased disease activity (Trindade et al., 2011), and an approximately threefold increased risk of relapse (Bhatt et al., 2009; Feagins et al., 2014; Tae et al., 2016). Modifiable factors are considered the best target to help increase adherence (Selinger et al., 2011). IBD treatment has changed significantly with the widespread use of biological therapies, which may reduce patient burden due to their infrequent administration through intravenous infusions or self-injections. Nonetheless, research has reported suboptimal adherence rates (Lopez et al., 2013; Wentworth et al., 2018), especially for self-administered biologics (adalimumab, certolizumab). Furthermore, the practice of combined biological/immunomodulator therapy means that many patients undergoing biological therapies are subject to the same challenges and barriers surrounding daily medication adherence as those on non-biological daily oral medication regimens. Adolescents (Greenley, Gumidyala, et al., 2015; Lenti & Selinger, 2017) and women considering pregnancy (de Lima, Zelinkova, Mulders, & van der Woude, 2016) are particularly responsive to intervention. Health providers supporting patients with IBD can use the "SIMPLE" mnemonic (Atreja et al., 2005), which promotes establishing good communication, information, simple regimen, overcoming barriers, focusing on the modifiable, and multimethod evaluation. ✪

Acknowledgments

The authors thank Mr Stephan Moller, Miss Sarina Cook, and Dr Sally Woodhouse for their editorial assistance in bringing this paper to fruition.

REFERENCES

Arnett, J. J. (2000). Emerging adulthood: A theory of development from the late teens through the twenties. *American Psychologist*, *55*(5), 469–480.

Atreja, A., Bellam, N., & Levy, S. R. (2005). Strategies to enhance patient adherence: Making it simple. *MedGenMed: Medscape General Medicine*, *7*(1), 4.

Baert, F., Noman, M., Vermeire, S., Van Assche, G., D'haens, G., Carbonez, A., … Rutgeerts, P. (2003). Influence of immunogenicity on the long-term efficacy of infliximab in Crohn's disease. *New England Journal of Medicine*, *348*(7), 601–608.

Bermejo, F., Lopez-San Roman, A., Algaba, A., Guerra, I., Valer, P., Garcia-Garzon, S., & Rodriguez-Agullo, J. L. (2010). Factors that modify therapy adherence in patients with inflammatory bowel disease. *Journal of Crohn's and Colitis*, *4*(4), 422–426. doi:10.1016/j.crohns.2010.01.005

Bernal, I., Domènech, E., Garcia-Planella, E., Mañín, L., Mañosa, M., Navarro, M., … Gassull, M. A. (2006). Medication-taking behavior in a cohort of patients with inflammatory bowel disease. *Digestive Diseases and Sciences*, *51*(12), 2165–2169. doi:10.1007/s10620-006-9444-2

Bhatt, J., Patil, S., Joshi, A., Abraham, P., & Desai, D. (2009). Self-reported treatment adherence in inflammatory bowel disease in Indian patients. *Indian Journal of Gastroenterology*, *28*(4), 143–146. doi:10.1007/s12664-009-0050-z

Bokemeyer, B., Teml, A., Roggel, C., Hartmann, P., Fischer, C., Schaeffeler, E., & Schwab, M. (2007). Adherence to thiopurine treatment in out-patients with Crohn's disease. *Alimentary Pharmacology and Therapeutics*, *26*(2), 217–225. doi:10.1111/j.1365-2036.2007.03365.x

Bucci, C., Zingone, F., Tammaro, S., Iovino, P., Santonicola, A., & Ciacci, C. (2017). Factors predicting the adherence to the therapy of Italian IBD patients. *Gastroenterology Research and Practice, 2017*, 1–6.

Campos, S., Portela, F., Sousa, P., & Sofia, C. (2016). Inflammatory bowel disease: Adherence to immunomodulators in a biological therapy era. *European Journal of Gastroenterology and Hepatology*, *28*(11), 1313–1319. doi:10.1097/MEG.0000000000000704

Červený, P., Bortlík, M., Kuběna, A., Vlček, J., Lakatos, P. L., & Lukáš, M. (2007). Nonadherence in inflammatory bowel disease: Results of factor analysis. *Inflammatory Bowel Diseases*, *13*(10), 1244–1249. doi:10.1002/ibd.20189

Červený, P., Bortlik, M., Vlcek, J., Kubena, A., & Lukás, M. (2007). Non-adherence to treatment in inflammatory bowel disease in Czech Republic. *Journal of Crohn's and Colitis*, *1*(2), 77–81. doi:10.1016/j.crohns.2007.08.002

Cook, P. F., Emiliozzi, S., El-Hajj, D., & McCabe, M. M. (2010). Telephone nurse counseling for medication adherence in ulcerative colitis: A preliminary study. *Patient education and Counseling*, *81*(2), 182–186. doi:10.1016/j.pec.2009.12.010

Cross, R. K., Cheevers, N., Rustgi, A., Langenberg, P., & Finkelstein, J. (2012). Randomized, controlled trial of home telemanagement in patients with ulcerative colitis (UC HAT). *Inflammatory Bowel Diseases*, *18*(6), 1018–1025. doi:10.1002/ibd.21795

D'inca, R., Bertomoro, P., Mazzocco, K., Vettorato, M., Rumiati, R., & Sturniolo, G. (2008). Risk factors for non adherence to medication in inflammatory bowel disease patients. *Alimentary Pharmacology & Therapeutics*, *27*(2), 166–172.

de Lima, A., Zelinkova, Z., Mulders, A. G., & van der Woude, C. J. (2016). Preconception care reduces relapse of inflammatory bowel disease during pregnancy. *Clinical Gastroenterology and Hepatology*, *14*(9), 1285–1292. doi:10.1016/j.cgh.2016.03.018

Depont, F., Berenbaum, F., Filippi, J., Le Maitre, M., Nataf, H., Paul, C., … Thibout, E. (2015). Interventions to improve adherence in patients with immune-mediated inflammatory disorders: A systematic review. *PLoS One*, *10*(12), e0145076. doi:10.1371/journal.pone.0145076

Devlen, J., Beusterien, K., Yen, L., Ahmed, A., Cheifetz, A. S., & Moss, A. C. (2014). Barriers to mesalamine adherence in patients with inflammatory bowel disease: A qualitative analysis. *Journal of Managed Care & Specialty Pharmacy*, *20*(3), 309–314. doi:10.18553/jmcp.2014.20.3.309

Dignass, A., & Veerman, H. (2008). Once versus twice daily mesalazine (Pentasa) granules for the maintenance of remission in ulcerative colitis: Results from a multi-national randomized controlled trial. *Gut, 57*(suppl 1), A1.

Dimatteo, M. R., Giordani, P. J., Lepper, H. S., & Croghan, T. W. (2002). Patient adherence and medical treatment outcomes: A meta-analysis. *Medical Care*, *40*(9), 794–811. doi:10.1097/00005650-200209000-00009

Ediger, J. P., Walker, J. R., Graff, L., Lix, L., Clara, I., Rawsthorne, P., … Bernstein, C. N. (2007). Predictors of medication adherence in inflammatory bowel disease. *American Journal of Gastroenterology*, *102*(7), 1417–1426. doi:10.1111/j.1572-0241.2007.01212.x

Elkjaer, M., Shuhaibar, M., Burisch, J., Bailey, Y., Scherfig, H., Laugesen, B., … Munkholm, P. (2010). E-health empowers patients with ulcerative colitis: A randomised controlled trial of the web-guided "Constant-care" approach. *Gut*, *59*(12), 1652–1661. doi:10.1136/gut.2010.220160

Feagins, L. A., Iqbal, R., & Spechler, S. J. (2014). Case–control study of factors that trigger inflammatory bowel disease flares. *The World Journal of Gastroenterology*, *20*(15), 4329–4334. doi:10.3748/wjg.v20.i15.4329

Fidder, H., Schnitzler, F., Ferrante, M., Noman, M., Katsanos, K., Segaert, S., … Rutgeerts, P. (2009). Long-term safety of infliximab for the treatment of inflammatory bowel disease: A single-centre cohort study. *Gut*, *58*(4), 501–508.

Gallinger, Z. R., Rumman, A., & Nguyen, G. C. (2016). Perceptions and attitudes towards medication adherence during pregnancy in inflammatory bowel disease. *Journal of Crohn's & Colitis*, *10*(8), 892–897. doi:10.1093/ecco-jcc/jjw052

Gifford, A. E., Berg, A. H., Lahiff, C., Cheifetz, A. S., Horowitz, G., & Moss, A. C. (2013). A random urine test can identify patients at risk of mesalamine non-adherence: A prospective study. *American Journal of Gastroenterology*, *108*(2), 249–255. doi:10.1038/ajg.2012.419

Goodhand, J. R., Kamperidis, N., Sirwan, B., Macken, L., Tshuma, N., Koodun, Y., … Lindsay, J. O. (2013). Factors associated with thiopurine non-adherence in patients with inflammatory bowel disease. *Alimentary Pharmacology and Therapeutics*, *38*(9), 1097–1108. doi:10.1111/apt.12476

Govani, S. M., Noureldin, M., Higgins, P. D., Heisler, M., Saini, S. D., Stidham, R. W., … Waljee, A. K. (2018). Defining an optimal adherence threshold for patients taking subcutaneous anti-TNFs for inflammatory bowel diseases. *American Journal of Gastroenterology*, *113*(2), 276.

Gray, W. N., Denson, L. A., Baldassano, R. N., & Hommel, K. A. (2012). Treatment adherence in adolescents with inflammatory bowel disease: The collective impact of barriers to adherence and anxiety/depressive symptoms. *Journal of Pediatric Psychology*, *37*(3), 282–291. doi:10.1093/jpepsy/jsr092

Greenley, R. N., Gumidyala, A. P., Nguyen, E., Plevinsky, J. M., Poulopoulos, N., Thomason, M. M., … Kahn, S. A. (2015). Can you teach a teen new tricks? Problem solving skills training improves oral medication adherence in pediatric patients with inflammatory bowel disease participating in a randomized trial. *Inflammatory Bowel Diseases*, *21*(11), 2649–2657. doi:10.1097/mib.0000000000000530

Greenley, R. N., Karazsia, B., Schurman, J. V., Gumidyala, A. P., Nguyen, E. U., Thomason, M. M., … Kahn, S. A. (2015). Trajectories of oral medication adherence in youth with inflammatory bowel disease. *Health Psychology*, *34*(5), 514–521. doi:10.1037/hea0000149.

Greenley, R. N., Kunz, J. H., Biank, V., Martinez, A., Miranda, A., Noe, J., … Stephens, M. C. (2012). Identifying youth nonadherence in clinical settings: Data-based recommendations for children and adolescents with inflammatory bowel disease. *Inflammatory Bowel Diseases*, *18*(7), 1254–1259. doi:10.1002/ibd.21859

Greenley, R. N., Kunz, J. H., Walter, J., & Hommel, K. A. (2013). Practical strategies for enhancing adherence to treatment regimen in inflammatory bowel disease. *Inflammatory Bowel Diseases*, *19*(7), 1534–1545.

Greenley, R. N., Nguyen, E., Kunz, J. H., Biank, V., Blank, E., Miranda, A., … Stephens, M. (2011). Phone intervention to improve pediatric oral medication adherence: Preliminary acceptability and feasibility: P-148. *Inflammatory Bowel Diseases*, *17*(Suppl. 2), S57–S57.

Greenley, R. N., Stephens, K. A., Nguyen, E. U., Kunz, J. H., Janas, L., Goday, P., & Schurman, J. V. (2013). Vitamin and mineral supplement adherence in pediatric inflammatory bowel disease. *Journal of Pediatric Psychology*, *38*(8), 883–892. doi:10.1093/jpepsy/jst037

Greenley, R. N., Stephens, M., Doughty, A., Raboin, T., & Kugathasan, S. (2010). Barriers to adherence among adolescents with inflammatory bowel disease. *Inflammatory Bowel Diseases*, *16*(1), 36–41. doi:10.1002/ibd.20988

Higgins, P. D. R., Rubin, D. T., Kaulback, K., Schoenfield, P. S., & Kane, S. (2009). Systematic review: Impact of non-adherence to 5-aminosalicylic acid products on the frequency and cost of ulcerative colitis flares. *Alimentary Pharmacology and Therapeutics*, *29*(3), 247–257. doi:10.1111/j.1365-2036.2008.03865.x

Hommel, K. A., & Baldassano, R. N. (2010). Brief report: Barriers to treatment adherence in pediatric inflammatory bowel disease. *Journal of Pediatric Psychology*, *35*(9), 1005–1010. doi:10.1093/jpepsy/jsp126

Hommel, K. A., Davis, C. M., & Baldassano, R. N. (2009). Objective versus subjective assessment of oral medication adherence

in pediatric inflammatory bowel disease. *Inflammatory Bowel Diseases*, *15*(4), 589–593. doi:10.1002/ibd.20798

Hommel, K. A., Denson, L. A., & Baldassano, R. N. (2011). Oral medication adherence and disease severity in pediatric inflammatory bowel disease. *European Journal of Gastroenterology and Hepatology*, *23*(3), 250–254. doi:10.1097/MEG.0b013e328344019c

Hommel, K. A., Hente, E., Herzer, M., Ingerski, L. M., & Denson, L. A. (2013). Telehealth behavioral treatment for medication nonadherence: A pilot and feasibility study. *European Journal of Gastroenterology and Hepatology*, *25*(4), 469–473. doi:10.1097/MEG.0b013e32835c2a1b

Hommel, K. A., Hente, E. A., Odell, S., Herzer, M., Ingerski, L. M., Guilfoyle, S. M., & Denson, L. A. (2012). Evaluation of a group-based behavioral intervention to promote adherence in adolescents with inflammatory bowel disease. *European Journal of Gastroenterology and Hepatology*, *24*(1), 64–69. doi:10.1097/MEG.0b013e32834d09f1

Hommel, K. A., Herzer, M., Ingerski, L. M., Hente, E., & Denson, L. A. (2011). Individually tailored treatment of medication nonadherence. *Journal of Pediatric Gastroenterology and Nutrition*, *53*(4), 435.

Horne, R., Parham, R., Driscoll, R., & Robinson, A. (2009). Patients' attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. *Inflammatory Bowel Diseases*, *15*(6), 837–844. doi:10.1002/ibd.20846

Ingerski, L. M., Baldassano, R. N., Denson, L. A., & Hommel, K. A. (2010). Barriers to oral medication adherence for adolescents with inflammatory bowel disease. *Journal of Pediatric Psychology*, *35*(6), 683–691. doi:10.1093/jpepsy/jsp085

Jackson, C. A., Clatworthy, J., Robinson, A., & Horne, R. (2010). Factors associated with non-adherence to oral medication for inflammatory bowel disease: A systematic review. *American Journal of Gastroenterology*, *105*(3), 525–539. doi:10.1038/ajg.2009.685

Janicke, D. M., Gray, W. N., Kahhan, N. A., Follansbee Junger, K. W., Marciel, K. K., Storch, E. A., & Jolley, C. D. (2009). Brief report: The association between peer victimization, prosocial support, and treatment adherence in children and adolescents with inflammatory bowel disease. *Journal of Pediatric Psychology*, *34*(7), 769–773. doi:10.1093/jpepsy/jsn116

Kamperidis, N., Goodhand, J. R., Chowdhury, F. A., Koodun, Y., Direzke, N. C., Naik, S., … Lindsay, J. O. (2012). Factors associated with nonadherence to thiopurines in adolescent and adult patients with inflammatory bowel disease. *Journal of Pediatric Gastroenterology and Nutrition*, *54*(5), 685–689. doi:10.1097/MPG.0b013e3182475e71

Kane, S., Cohen, R. D., Aikens, J. E., & Hanauer, S. B. (2001). Prevalence of nonadherence with maintenance mesalamine in quiescent ulcerative colitis. *American Journal of Gastroenterology*, *96*(10), 2929–2933. doi:10.1111/j.1572-0241.2001.04683.x

Kane, S., Huo, D., Aikens, J., & Hanauer, S. (2003). Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. *American Journal of Medicine*, *114*(1), 39–43. doi:10.1016/S0002-9343(02)01383-9

Kane, S., Huo, D., & Magnanti, K. (2003). A pilot feasibility study of once daily versus conventional dosing mesalamine for maintenance of ulcerative colitis. *Clinical Gastroenterology and Hepatology*, *1*(3), 170–173.

Kawakami, A., Tanaka, M., Nishigaki, M., Yoshimura, N., Suzuki, R., Maeda, S., … Yamamoto-Mitani, N. (2014). A screening instrument to identify ulcerative colitis patients with the high possibility of current non-adherence to aminosalicylate medication based on the Health Belief Model: A cross-sectional study. *BMC Gastroenterology*, *14*, 220. doi:10.1186/s12876-014-0220-z

Khanna, R., Bressler, B., Levesque, B. G., Zou, G., Stitt, L. W., Greenberg, G. R., … Vermeire, S. (2015). Early combined immunosuppression for the management of Crohn's disease (REACT): A cluster randomised controlled trial. *The Lancet*, *386*(10006), 1825–1834.

Kim, S. B., Kim, K. O., Jang, B. I., Kim, E. S., Cho, K. B., Park, K. S., … Jeon, S. W. (2016). Patients' beliefs and attitudes about their treatment for inflammatory bowel disease in Korea. *European Journal of Gastroenterology and Hepatology*, *31*(3), 575–580. doi:10.1111/jgh.13155

Kitney, L., Turner, J. M., Spady, D., Malik, B., El-Matary, W., Persad, R., & Huynh, H. Q. (2009). Predictors of medication adherence in pediatric inflammatory bowel disease patients at the Stollery Children's Hospital. *Canadian Journal of Gastroenterology*, *23*(12), 811–815.

Lakatos, P. L. (2009). Prevalence, predictors, and clinical consequences of medical adherence in IBD: How to improve it? *World Journal of Gastroenterology*, *15*(34), 4234–4239. doi:10.3748/wjg.15.4234

Lakatos, P. L., Czegledi, Z., David, G., Kispal, Z., Kiss, L. S., Palatka, K., … Lakatos, L. (2010). Association of adherence to therapy and complementary and alternative medicine use with demographic factors and disease phenotype in patients with inflammatory bowel disease. *Journal of Crohn's & Colitis*, *4*(3), 283–290. doi:10.1016/j.crohns.2009.11.011

LeLeiko, N. S., Lobato, D., Hagin, S., Hayes, C., McQuaid, E. L., Seifer, R., … Bancroft, B. (2013). 6-Thioguanine levels in pediatric IBD patients: Adherence is more important than dose. *Inflammatory Bowel Diseases*, *19*(12), 2652–2658. doi:10.1097/01.MIB.0000436960.00405.56

LeLeiko, N. S., Lobato, D., Hagin, S., McQuaid, E., Seifer, R., Kopel, S. J., … Bancroft, B. (2013). Rates and predictors of oral medication adherence in pediatric patients with IBD. *Inflammatory Bowel Diseases*, *19*(4), 832–839. doi:10.1097/MIB.0b013e3182802b57

Lenti, M. V., & Selinger, C. P. (2017). Medication non-adherence in adult patients affected by inflammatory bowel disease: A critical review and update of the determining factors, consequences and possible interventions. *Expert Review of Gastroenterology and Hepatology*, *11*(3), 215–226. doi:10.1080/17474124.2017.1284587

Long, M. D., Kappelman, M. D., Martin, C. F., Chen, W., Anton, K., & Sandler, R. S. (2014). Risk factors for depression in the elderly inflammatory bowel disease population. *Journal of Crohn's & Colitis*, *8*(2), 113–119. doi:10.1016/j.crohns.2013.07.002

Lopez, A., Billioud, V., Peyrin-Biroulet, C., & Peyrin-Biroulet, L. (2013). Adherence to anti-TNF therapy in inflammatory bowel diseases: A systematic review. *Inflammatory Bowel Diseases*, *19*(7), 1528–1533.

López San Román, A., Bermejo, F., Carrera, E., Pérez-Abad, M., & Boixeda, D. (2005). Adherence to treatment in inflammatory bowel disease. *Revista Espanola de Enfermedades Digestivas*, *97*(4), 249–257.

Maddux, M., Ricks, S., Delurgio, S., & Hommel, K. (2017). A pilot study evaluating the impact of an adherence-promoting intervention among nonadherent youth with inflammatory bowel disease. *Journal of Pediatric Nursing*, *35*, 72–77. doi:10.1016/j.pedn.2017.03.006

Mantzaris, G. J., Roussos, A., Kalantzis, C., Koilakou, S., Raptis, N., & Kalantzis, N. (2006). How adherent to treatment with azathioprine are patients with Crohn's disease in long-term remission? *Inflammatory Bowel Diseases*, *13*(4), 446–450.

Miloh, T., Shub, M., Montes, R., Ingebo, K., Silber, G., & Pasternak, B. (2017). Text messaging effect on adherence in children with inflammatory bowel disease. *Journal of Pediatric Gastroenterology and Nutrition*, *64*(6), 939–942.

Morisky, D. E., Green, L. W., & Levine, D. M. (1986). Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care*, *24*(1), 67–74.

Moshkovska, T., Stone, M. A., Clatworthy, J., Smith, R. M., Bankart, J., Baker, R., … Mayberry, J. F. (2009). An investigation of medication adherence to 5-aminosalicylic acid therapy in patients with ulcerative colitis, using self-report and urinary drug excretion measurements. *Alimentary Pharmacology and Therapeutics*, *30*(11/12), 1118–1127. doi:10.1111/j.1365-2036.2009.04152.x

Moshkovska, T., Stone, M. A., Smith, R. M., Bankart, J., Baker, R., & Mayberry, J. F. (2011). Impact of a tailored patient preference intervention in adherence to 5-aminosalicylic acid medication in ulcerative colitis: Results from an exploratory randomized controlled trial. *Inflammatory Bowel Disease*, *17*(9), 1874–1881. doi:10.1002/ibd.21570

Mountifield, R., Andrews, J. M., Mikocka-Walus, A., & Bampton, P. (2014). Covert dose reduction is a distinct type of medication non-adherence observed across all care settings in inflammatory bowel disease. *Journal of Crohn's and Colitis*, *8*(12), 1723–1729.

Nahon, S., Lahmek, P., Durance, C., Olympie, A., Lesgourgues, B., Colombel, J. F., & Gendre, J. P. (2012). Risk factors of anxiety and depression in inflammatory bowel disease. *Inflammatory Bowel Diseases*, *18*(11), 2086–2091. doi:10.1002/ibd.22888

Nahon, S., Lahmek, P., Saas, C., Durance, C., Olympie, A., Lesgourgues, B., & Gendre, J. P. (2011). Socioeconomic and psychological factors associated with nonadherence to treatment in inflammatory bowel disease patients: Results of the ISSEO survey. *Inflammatory Bowel Diseases*, *17*(6), 1270–1276. doi:10.1002/ibd.21482

Nguyen, G. C., LaVeist, T. A., Harris, M. L., Datta, L. W., Bayless, T. M., & Brant, S. R. (2009). Patient trust-in-physician and race are predictors of adherence to medical management in inflammatory bowel disease. *Inflammatory Bowel Diseases*, *15*(8), 1233–1239. doi:10.1002/ibd.20883

Nigro, G., Angelini, G., Grosso, S. B., Caula, G., & Sategna-Guidetti, C. (2001). Psychiatric predictors of noncompliance in inflammatory bowel disease: Psychiatry and compliance. *Journal of Clinical Gastroenterology*, *32*(1), 66–68.

Oliva-Hemker, M. M., Abadom, V., Cuffari, C., & Thompson, R. E. (2007). Nonadherence with thiopurine immunomodulator and mesalamine medications in children with Crohn disease. *Journal of Pediatric Gastroenterology and Nutrition*, *44*(2), 180–184.

Pittet, V., Rogler, G., Mottet, C., Froehlich, F., Michetti, P., de Saussure, P., … Vader, J. P. (2014). Patients' information-seeking activity is associated with treatment compliance in inflammatory bowel disease patients. *Scandinavian Journal of Gastroenterology*, *49*(6), 662–673. doi:10.3109/00365521.2014.896408

Reed-Knight, B., Lewis, J. D., & Blount, R. L. (2011). Association of disease, adolescent, and family factors with medication adherence in pediatric inflammatory bowel disease. *Journal of Pediatric Psychology*, *36*(3), 308–317. doi:10.1093/jpepsy/jsq076

Reed-Knight, B., Lewis, J. D., & Blount, R. L. (2013). Behavioral functioning in youth with inflammatory bowel disease: Perceived barriers as mediator of medication adherence. *Journal of Pediatric Psychology*, *38*(3), 309–320. doi:10.1093/jpepsy/jss122

Robinson, A., Hankins, M., Wiseman, G., & Jones, M. (2013). Maintaining stable symptom control in inflammatory bowel disease: A retrospective analysis of adherence, medication switches and the risk of relapse. *Alimentary Pharmacology and Therapeutics*, *38*(5), 531–538. doi:10.1111/apt.12396

Schurman, J. V., Cushing, C. C., Carpenter, E., & Christenson, K. (2011). Volitional and accidental nonadherence to pediatric inflammatory bowel disease treatment plans: Initial investigation of associations with quality of life and disease activity. *Journal of Pediatric Psychology*, *36*(1), 116–125. doi:10.1093/jpepsy/jsq046

Selinger, C. P., Eaden, J., Jones, D. B., Katelaris, P., Chapman, G., McDonald, C., … McLaughlin, J. (2013). Modifiable factors associated with nonadherence to maintenance medication for inflammatory bowel disease. *Inflammatory Bowel Diseases*, *19*(10), 2199–2206.

Selinger, C. P., Robinson, A., & Leong, R. W. (2011). Clinical impact and drivers of non-adherence to maintenance medication for inflammatory bowel disease. *Expert Opinion on Drug Safety*, *10*(6), 863–870. doi:10.1517/14740338.2011.583915

Sewitch, M. J., Abrahamowicz, M., Barkun, A., Bitton, A., Wild, G. E., Cohen, A., & Dobkin, P. L. (2003). Patient nonadherence to medication in inflammatory bowel disease. *American Journal of Gastroenterology*, *98*(7), 1535.

Shale, M. J., & Riley, S. A. (2003). Studies of compliance with delayed-release mesalazine therapy in patients with inflammatory bowel disease. *Alimentary Pharmacology and Therapeutics*, *18*(2), 191–198. doi:10.1046/j.1365-2036.2003.01648.x

Spekhorst, L. M., Hummel, T. Z., Benninga, M. A., Van Rheenen, P. F., & Kindermann, A. (2016). Adherence to oral maintenance treatment in adolescents with inflammatory bowel disease. *Journal of Pediatric Gastroenterology and Nutrition*, *62*(2), 264–270. doi:10.1097/MPG.0000000000000924

Tabibian, A., Tabibian, J. H., Beckman, L. J., Raffals, L. L., Papadakis, K. A., & Kane, S. (2015). Predictors of health-related quality of life and adherence in Crohn's disease and ulcerative colitis: Implications for clinical management. *Digestive Diseases and Sciences*, *60*(5), 1366–1374. doi:10.1007/s10620-014-3471-1

Tae, C. H., Jung, S. A., Moon, H. S., Seo, J. A., Song, H. K., Moon, C. M., … Jung, H. K. (2016). Importance of patients' knowledge of their prescribed medication in improving treatment adherence in inflammatory bowel disease. *Journal of Clinical Gastroenterology*, *50*(2), 157–162. doi:10.1097/mcg.0000000000000431

Taft, T. H., Keefer, L., Leonhard, C., & Nealon-Woods, M. (2009). Impact of perceived stigma on inflammatory bowel disease patient outcomes. *Inflammatory Bowel Diseases*, *15*(8), 1224–1232.

Trindade, A. J., Ehrlich, A., Kornbluth, A., & Ullman, T. A. (2011). Are your patients taking their medicine? Validation of a new adherence scale in patients with inflammatory bowel disease and comparison with physician perception of adherence. *Inflammatory Bowel Diseases*, *17*(2), 599–604. doi:10.1002/ibd.21310

Vitale, D. S., Greenley, R. N., Lerner, D. G., Mavis, A. M., & Werlin, S. L. (2015). Adherence to infliximab treatment in a pediatric inflammatory bowel disease cohort. *Journal of Pediatric Gastroenterology and Nutrition*, *61*(4), 408–410.

Wan, G. J., Kozma, C. M., Slaton, T. L., Olson, W. H., & Feagan, B. G. (2014). Inflammatory bowel disease: Healthcare costs for patients who are adherent or non-adherent with infliximab therapy. *Journal of Medical Economics*, *17*(6), 384–393. doi:10.3111/13696998.2014.909436

Waters, B. M., Jensen, L., & Fedorak, R. N. (2005). Effects of formal education for patients with inflammatory bowel disease: A

randomized controlled trial. *Canadian Journal of Gastroenterology and Hepatology*, *19*(4), 235–244.

Wentworth, B. J., Buerlein, R. C., Tuskey, A. G., Overby, M. A., Smolkin, M. E., & Behm, B. W. (2018). Nonadherence to biologic therapies in inflammatory bowel disease. *Inflammatory Bowel Diseases*, *24*(9), 2053–2061.

Yu, H., MacIsaac, D., Wong, J., Sellers, Z., Wren, A., Bensen, R., … Park, K. (2018). Market share and costs of biologic therapies for inflammatory bowel disease in the USA. *Alimentary Pharmacology & Therapeutics*, *47*(3), 364–370.

Zelikovsky, N., & Schast, A. P. (2008). Eliciting accurate reports of adherence in a clinical interview: Development of the medical adherence measure. *Pediatric Nursing*, *34*(2), 141–146.

For 5 additional continuing education articles related to the topic of medication compliance, go to www.NursingCenter.com.

Instructions for Taking the CE Test Online:

- Read the article. The test for this CE activity can be taken online at www.nursingcenter.com. Tests can no longer be mailed or faxed.
- You will need to create a free login to your personal CE Planner account before taking online tests. Your planner will keep track of all your Lippincott Professional Development online CE activities for you.
- There is only one correct answer for each question. A passing score for this test is 12 correct answers. If you pass, you can print your certificate of earned contact hours and the answer key. If you fail, you have the option of taking the test again at no additional cost.
- For questions, contact Lippincott Professional Development: 1-800-787-8985.

Registration Deadline: December 3, 2021

Disclosure Statement:
The authors and planners have disclosed that they have no financial relationships related to this article.

Provider Accreditation:
Lippincott Professional Development will award 1.5 contact hours for this continuing nursing education activity.

Lippincott Professional Development is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation. This activity is also provider approved by the California Board of Registered Nursing, Provider Number CEP 11749 for 1.5 contact hours. Lippincott Professional Development is also an approved provider of continuing nursing education by the District of Columbia, Georgia, and Florida, CE Broker #50-1223. Your certificate is valid in all states.

Payment:

- The registration fee for this test is $10.50 for members; $15.00 for nonmembers.

DOI: 10.1097/SGA.0000000000000507

