

Observational Study

Current practice and clinicians' perception of medication non-adherence in patients with inflammatory bowel disease: A survey of 98 clinicians

Anisah Soobraty, Sarah Boughdady, Christian P Selinger

Anisah Soobraty, Sarah Boughdady, Christian P Selinger, IBD Unit, Leeds Gastroenterology Institute, Leeds Teaching Hospitals NHS Trust, Leeds LS9 7TF, United Kingdom

Christian P Selinger, Leeds Institute of Biomedical and Clinical Sciences, University of Leeds, Leeds LS9 7TF, United Kingdom

Author contributions: Soobraty A and Boughdady S collected the data, performed the analysis and wrote the draft manuscript; Selinger CP designed the study, supervised data collection and analysis and critically reviewed the manuscript.

Institutional review board statement: The study was exempt from the requirement of research ethics committee approval as no patient data were elicited.

Informed consent statement: All study participants provided informed consent by return of the online questionnaire.

Conflict-of-interest statement: Christian P Selinger has received unrestricted research grants from Warner Chilcott, and Abbvie, has provided consultancy to Warner Chilcott, Dr Falk, Abbvie, Takeda and Janssen, and had speaker arrangements with Warner Chilcott, Dr Falk, Abbvie, MSD and Takeda; the other authors report no relevant conflict of interest.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Dr. Christian P Selinger, IBD Unit, Leeds Gastroenterology Institute, Leeds Teaching Hospitals NHS Trust,

St James University Hospital, Beckett St., Leeds LS9 7TF, United Kingdom. christian.selinger@web.de
Telephone: +44-113-2068768

Received: October 17, 2016
Peer-review started: October 19, 2016
First decision: November 22, 2016
Revised: November 24, 2016
Accepted: January 2, 2017
Article in press: January 3, 2017
Published online: February 6, 2017

Abstract

AIM

The survey ascertains perceptions and describes current practice of clinicians regarding medication non-adherence in patients with Inflammatory Bowel Disease.

METHODS

Gastroenterologists, trainees and inflammatory bowel disease (IBD) specialist nurses from the United Kingdom were invited to a web based survey collecting data on clinician demographics, patient volume and level of interest in IBD. Respondents were asked to estimate non-adherence levels and report use of screening tools and interventions to improve adherence.

RESULTS

Non-adherence was seen as an infrequent problem by 57% of 98 respondents. Levels of non-adherence were estimated lower than evidence suggests by 29% for mesalazine (5ASA), 26% for immunomodulators (IMM) and 21% for biologics (BIOL). Respondents reporting non-adherence as a frequent problem were more likely to report adherence levels in line with evidence (5ASA $P < 0.001$; IMM $P = 0.012$; BIOL $P = 0.015$). While 80% regarded screening as important only 25% screen

regularly (40% of these with validated assessment tools). Respondents stated forgetfulness, beliefs about necessity of medication and not immediately apparent benefits as the main reasons for non-adherence. Patient counselling on benefits and risks of medication was a commonly used intervention.

CONCLUSION

Clinicians treating IBD patients frequently underestimate non-adherence and use of validated screening tools is infrequent. Most respondents identified the main factors associated with non-adherence in line with evidence and often counselled patients accordingly. Professional education should focus more on non-adherence practice to avoid adverse treatment outcomes associated with non-adherence.

Key words: Non-adherence; Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Clinical practice

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Non-adherence to maintenance medication is a very common phenomenon occurring in up to 50% of patients with inflammatory bowel disease. This survey demonstrates that many clinicians underestimate the extent of non-adherence and screening for non-adherence is infrequent and not systematic. The lack of evidence for any intervention to improve adherence is reflected by the participants divergent practice to improve adherence. There is an urgent need for further clinician education on non-adherence and robustly tested interventions that are capable of improving adherence.

Soobraty A, Boughdady S, Selinger CP. Current practice and clinicians' perception of medication non-adherence in patients with inflammatory bowel disease: A survey of 98 clinicians. *World J Gastrointest Pharmacol Ther* 2017; 8(1): 67-73 Available from: URL: <http://www.wjgnet.com/2150-5349/full/v8/i1/67.htm> DOI: <http://dx.doi.org/10.4292/wjgpt.v8.i1.67>

INTRODUCTION

Inflammatory bowel disease (IBD) refers to a group of conditions that mainly affect the gastrointestinal tract. The two primary conditions Crohn's disease and ulcerative colitis are chronic and debilitating diseases that can have very serious consequences including hospitalisation, surgery and an increased risk of developing colorectal cancer (CRC)^[1]. However, evidence has shown that if IBD is treated appropriately and patients are adherent to IBD maintenance medications, disease morbidity is improved by reducing the frequency and severity of relapses^[1,2]. Adherence can lessen the risk of developing CRC and can improve other treatment outcomes for patients, for example, by providing a

better quality of life^[3,4].

However, despite this, there is evidence that approximately 30%-40% of patients do not adhere to their prescribed medication^[4-11]. The literature also suggests that the level of non-adherence varies according to the type of medication. IBD can be treated using a wide range of medications, including mesalazine (5ASA), immunomodulators (IMMs) and biological agents (BIOL) such as infliximab, and adalimumab. Non-adherence occurs in 30%-45% with mesalazine^[8-10], 15%-20% with IMMs^[10,12], 5%-10% with biologics^[13].

Low adherence to medication leads to poor disease control, which not only has an impact on the patient, but also the economy incurred through the cost of absenteeism, medical care and hospitalisation. Non-adherence is therefore a cause of financial burden to health services^[14-16].

While forgetfulness is the main reason for non-intentional non-adherence, several reasons for intentional non-adherence have been identified^[4]. Apart from psychological comorbidities and quiescent disease activity the most constant findings relate to the patient perception of their medication. Non-adherent patients were more likely to express doubts over the necessity for maintenance medication and had greater concerns over potential adverse effects^[5,10].

Though there are numerous methods to determine adherence, studies have found that clinicians find this difficult to gauge amongst their patients^[17,18]. Methods used to screen for adherence as identified by the literature include measuring drug metabolic levels, using scales such as the Morisky Scale^[18] or Medication Adherence Report Scale (MARS)^[5] and the use of simple questioning. Currently, little is known about screening behaviour of health professionals in the United Kingdom or how they manage non-adherence. In addition, there is not much information on how clinicians perceive the problem of non-adherence amongst those they are treating for IBD^[17,18].

The aim of this study was to assess clinicians' awareness of the extent of non-adherence in IBD. We also aimed to explore clinicians' perception of factors associated with non-adherence and identify potential differences in perception by profession, experience or level of interest in IBD. Finally, we aimed to investigate the use of screening tools and the management of non-adherence in patients with IBD amongst health professionals.

MATERIALS AND METHODS

We developed an online survey assessing clinicians' perceptions and practice based on a literature search. The survey was piloted with 8 IBD specialists and some clarifying minor amendments were based on their feedback. The survey containing both open and closed questions is available as a supplement (S1).

The survey questionnaire collected data on the parti-

Table 1 Respondents' demographics, self-reported expertise and scope of inflammatory bowel disease practice

		Frequency	Percentage
Sex	Male	46	47%
	Female	52	53%
Age, yr	20-29	7	7%
	30-44	45	46%
	45-60	40	41%
	> 60	6	6%
	< 5	11	11%
Years in practice, yr	5-9	21	22%
	10-14	17	17%
	15-19	10	10%
	≥ 20	39	40%
Profession	Gastroenterology trainee	17	17%
	Gastroenterology consultant	51	52%
	IBD nurse specialist	28	29%
	Other	2	2%
Geographic region	England	92	95%
	Scotland	2	2%
	Wales	2	2%
	Northern Ireland	1	1%
Self-rated level of IBD interest in medically qualified staff	General gastroenterologist	32	46%
	Interest in IBD	18	27%
	Expert IBD physician	18	27%
IBD patients per week	Range 0-150		
	Mean 25		

IBD: Inflammatory bowel disease.

Participants' demographics, level of interest in IBD and the number of patients with IBD typically seen in a week. Participants were asked about their overall impression of non-adherence amongst their local patient population. Furthermore we asked respondents to estimate the levels of non-adherence amongst those being managed with mesalazine (5ASA), IMMs and biologics (BIOL) therapy. Perceived reasons for non-adherence were explored by asking respondents to rank the significance of 8 pre-specified reasons (derived by the authors from the literature) with 1 being the most important and 8 being the least. Analysis of ranking preferences was performed by counting the number of times respondents had stated a particular reason to be in the top 3. Moreover, the survey gathered data on participants' practice regarding the use of screening tools and any interventions used in their practice to improve adherence.

The survey was distributed by email to consultant gastroenterologists, trainees *via* the British Society Gastroenterology IBD section (775 members) and IBD specialist nurses from the United Kingdom *via* the UK IBD nurse network (approximately 200 members). We aimed to include different staff groups (consultants, trainees and nurses) in order to collect the views and opinions of those involved in all aspects of patient care. The survey and data compilation were performed through Bristol Online Surveys, an academic online survey system, over a 3 mo period.

Quantitative data were analysed with SPSS Statistics (IBM, version 22) using χ^2 tests to compare responses between the different participant groups. The qualitative data responses were collated and key themes were identified and described.

In the United Kingdom Ethical approval is not required for survey studies examining the views and opinions of clinicians only.

RESULTS

Respondents

Of the 98 study participants (response rate 10%) 52 (53%) were female, 46 (47%) male, and 47% of participants were older than 44 years. Respondents included 51 consultants, 17 trainees, 28 IBD specialist nurses, 1 IBD dietitian and 1 biologics nurse specialist (Table 1). Approximately half of respondents had 15 years' experience or more. Of the 68 medically qualified respondents 32 classed themselves as general gastroenterologists, 18 had an IBD interest and 18 stated that they were IBD experts. The number of patients seen in an average week varied greatly amongst the study's participants between less 10 to over 100 patients with a mean of 25 patients per week.

Respondents' perception of non-adherence

Non-adherence in their local patient cohort was perceived as a frequent problem by 43%, as an infrequent problem by 49%, while 7% reported few cases only and 1% reported no adherence issues. Overall 57% of respondents reported non-adherence at best to be an infrequent problem. Older respondents were more likely to report non-adherence as an at best infrequent problem ($P = 0.043$). No other correlations between overall perception of non-adherence and other factors displayed in Table 1 were found.

Respondents estimated level of non-adherence considerably lower than suggested by the evidence base in 31% for 5ASA, in 28% for IMM and in 23% for BIOL (Table 2). Respondents who perceived non-adherence as a frequent problem were more likely to report adherence levels in line with the evidence base (5ASA $P < 0.0001$, IMM $P = 0.002$, BIOL $P = 0.006$; Table 3). Self-declared level of interest in IBD did not affect whether or not participants estimated non-adherence for 5ASA and IMM in line with evidence. However, a higher level of interest in IBD was found to significantly correlate with estimating level of non-adherence for biologics therapy in line with evidence ($P = 0.012$; Table 4). No other correlations between perception of non-adherence for 5ASA, IMM or BIOL and other factors displayed in Table 1 were found.

Perceived reasons for non-adherence

The most commonly identified reasons for non-adherence were patient's forgetfulness (rank 1), lack of belief in the necessity for medication (rank 2), benefits of

Table 2 Estimation of non-adherence levels by respondents and percentage in line with evidence

Medication	Column A: literature-based non-adherence levels	Column B: perceived mean non-adherence levels	Proportion who estimated non-adherence levels below the levels in column A
Mesalazine	30%-45%	20%	31%
Immunomodulator therapy	15%-20%	10%	28%
Biological agents	5%-10%	1%	23%

Table 3 Association between perception of non-adherence as a frequent problem and reporting non-adherence levels in line with the evidence base

Medication	χ^2 value	Degrees of freedom	P value
Mesalazine	33.226	1	0.000
Immunomodulator therapy	12.592	2	0.002
Biological agents	7.459	1	0.006

medication not immediately apparent (rank 3) and concerns over potential side effects (rank 4; Table 5).

Screening practice

Nearly all (99%) respondents thought that improving adherence to medication would improve health-related outcomes in IBD and 80% regarded screening as important. However, only 58% reported ever using screening tools and only 25% stated that they screen their patients on a regular basis. In addition, it was found that only 40% use validated assessment tools to screen for adherence on a regular basis. Among the respondents who used screening tools, 60% used simple questioning asking their patients whether they were taking all their medications and 37% used Drug metabolic levels to assess non-adherence. No participants reported using the Morisky scale or the MARS and only 3% used the Visual Analogue Scale.

Thematic coding of qualitative data found that while some screen for non-adherence routinely, others only screen if a patient is not responding to medication or if they are treating someone who has regular flares or relapses. Reasons stated for not using screening tools included not having enough time during consultations and a lack of knowledge on the different screening tools available.

Managing non-adherence

Ninety-six percent of respondents believed that non-adherence can be addressed and that determining low adherence is important because interventions can increase adherence. Participants were asked to rank the effectiveness of certain interventions as a part of our survey. Fifty-two percent thought that involving patients in their treatment was the most effective intervention (rank 1). Other highly ranked interventions included "general education on the disease" (rank 2) and "less frequent dosing" (rank 3) and patient counselling was ranked 4th and most commonly included information on

Table 4 Association between level of interest in inflammatory bowel disease and estimation of non-adherence to biological therapy

Pearson χ^2 test	What percentage of your patients on biological therapy are non-adherent?	
Level of interest in IBD for medical staff	χ^2 value	8.863
	Degrees of freedom	2.000
	P value	0.012

IBD: Inflammatory bowel disease.

benefits and risks of medication.

DISCUSSION

Non-adherence is a common issue amongst cohorts of patients with chronic diseases and especially in those with IBD. In contrast to the well-established evidence on the extent of adherence^[4,19,20] and factors associated with it^[10], little is known on how clinicians perceive non-adherence and how they combat it^[17]. Yet identification of non-adherence is the vital first step in attempting to avoid the increased health burden for the patient and financial burden for the healthcare system associated with non-adherence. This study is only the 2nd survey of clinicians views overall and the first in the United Kingdom.

Our study shows that clinicians have a tendency to underestimate the extent of non-adherence as only 43% of respondents thought that non-adherence was a frequent issue. It is interesting to note that older health professionals are more likely to underestimate the problem of non-adherence more often than other clinicians. No other respondents' characteristics (nurse vs doctor, scope of IBD practice, self-reported level of IBD expertise) were associated with the overall impression of non-adherence. Perception of non-adherence may therefore be a generational issue that could be influenced by different methods of training over time and associated changes in practitioner-patient relationships. Further work is required to elicit why non-adherence rates are wrongly perceived as low in general. Clinicians may feel uncomfortable with the thought of patients not following agreed treatment plans and may also feel helpless when tasked with improving non-adherence given the lack of evidence based interventions.

Table 5 Perception of reasons for non-adherence

Rank	Actual side effects of medication	Patient forgets to take medication	Benefits of medication not immediately apparent	Anxiety or depression	Poor patient knowledge of disease	Frequency of dosing	Beliefs about necessity of medication	Concerns over potential side effects
Ranked 1 st	14.60%	32.30%	13.70%	5.30%	7.30%	9.60%	12.40%	11.30%
Ranked 2 nd	9.40%	25%	20%	7.40%	11.50%	18.10%	23.70%	14.40%
Ranked 3 rd	7.30%	11.50%	18.90%	8.40%	8.30%	21.30%	20.60%	23.70%
Ranked 4 th	14.60%	7.30%	11.60%	7.40%	18.80%	11.70%	15.50%	12.40%
Ranked 5 th	10.40%	12.50%	16.80%	13.70%	14.60%	9.60%	10.30%	16.50%
Ranked 6 th	24%	3.10%	9.50%	16.80%	18.80%	13.80%	8.20%	9.30%
Ranked 7 th	10.40%	4.20%	5.30%	16.80%	14.60%	8.50%	3.10%	9.30%
Ranked 8 th	9.40%	4.20%	4.20%	24.20%	6.30%	7.40%	6.20%	3.10%
Ranked in top 3	30	66	50	20	26	46	55	48
by <i>n</i> =								
Overall rank	6	1	3	8	7	5	2	4

Levels of non-adherence were underestimated for all medications enquired about in our survey (5ASA, IMM and BIOL). The authors elicited observed non-adherence rates found in the majority of published cohort studies^[8-10,12,13] and compared the survey respondents' perceptions with these levels. Between 23%-31% estimated the levels of non-adherence to the different medication in their local patient population much lower than the evidence suggests. This may go some way in explaining why non-adherence to maintenance medication often goes undetected. We have demonstrated that those practitioners who perceive non-adherence as a frequent issue, however, estimate non-adherence levels closer to the levels derived from the evidence base.

Respondents ranked unintentional non-adherence (patient's forgetfulness) and three reasons associated with intentional nonadherence (lack of belief of necessity for medication, benefits not immediately apparent, concerns over potential side effects) as the most common reasons for non-adherence. This closely mirrors the evidence base as these factors are most consistently associated with non-adherence^[4,10,20]. Respondents ranked factors that are only inconsistently or not associated with non-adherence (frequency of dosing, anxiety or depression, patient knowledge) as less important thereby demonstrating a good understanding of the factors associated with non-adherence.

Though the majority of respondents (80%) stated that they thought screening was an important issue and that adherence to medication would improve disease outcomes, this was not reflected in the participants' clinical practice. 76% said that they screened at least occasionally for non-adherence, but of those 52% said that they only use it "rarely" or "sometimes". A similar study to this one, carried out by Trindade *et al.*^[18] in the United States found that 77% of participants self-reportedly screened for adherence, however, the frequency of screening is unknown^[18]. The commonest screening method used was simple questioning of the patient (as in Trindade's study), which is known to be unreliable in assessing adherence as it vastly

underestimates non-adherence^[18,21,22]. Evidence based adherence report tools were only used by a minority and these were largely restricted to blood tests. A strong effort should be made to encourage health professionals to use validated screening tools such as the 8-item Morisky Medication Adherence Scale (MMAS-8) and MARS, which are effective at detecting non-adherence non-invasively^[18].

The conundrum presented by our findings is that while 96% of respondents believed that non-adherence can be addressed and that interventions can improve adherence, only 25% of respondents reported that they screen their patients regularly. It is perceivable that respondents believe that non-adherence can be improved yet have limited experience, resources or faith in interventions' success to actually implement regular screening for non-adherence. In view of the low screening rates, interventions targeting clinicians' knowledge, skills and practices need to be found. This should include education about non-adherence, efforts at raising general awareness, especially associated consequences in terms of morbidity, and financial cost. Clinicians should also be trained in the use of validated screening tools available such as the MMAS-8 and MARS.

The field of interventions aimed at improving non-adherence is difficult as the evidence consists of under-powered studies^[23], studies with non-reproducible complex interventions^[24], ongoing studies^[25] and review articles having to base advice on associated factors alone due to the lack of rigorously tested interventions. This dilemma is revealed by the high ranking of interventions without any positive evidence base ("general disease education", "less frequent dosing") and the high ranking of important but insufficiently defined interventions such as "patient involvement in treatment" and "counselling". Those engaged in patient counselling reassuringly report using themes around medication information concerning the evidence based necessity and concerns framework^[5,10,26]. A number of technological advances allow for frequent reminders for patients, but most of these systems fail to address intentional non-adherence.

Whether patient counselling can be effectively delivered in a remote, technology based way has not been rigorously tested so far. Arguably, personal contact with clinicians and especially IBD nurses may facilitate counselling more effectively.

There are a number of limitations to our study. First of all the response rate of 10% is low, but this is in line with other surveys of health care professionals^[27,28]. A degree of selection bias is inherent in survey studies but the spread of self-reported expertise among respondents in our study suggest a reasonably balanced sample. We believe that the sample is likely representative of IBD clinicians in the United Kingdom, but there are no reliable data to verify this assumption. Whether non-responders hold the same views as responders is unclear. Furthermore, subjective bias may have occurred as respondents may have given answers that they thought were expected of them or answers that they think the researchers were looking for, which in turn may explain the discrepancy between the generally positive perceptions of screening and the lack of regular screening in practice. We asked respondents to rank pre-specified reasons for non-adherence and pre-specified interventions based on our valuation of the existing literature to allow for a meaningful analysis. Naturally this list will have not been comprehensive and items such as "clinician-patient relationship" were not included.

In conclusion, we found that clinicians often underestimate the problem of non-adherence in patients with IBD. We also found that the use of validated screening tools was infrequent. This is a phenomenon, which occurs across all grades and professions. In addition, we found that the factors associated with non-adherence were correctly identified by participants. Based on our findings, it seems sensible to focus educational efforts for clinicians on the issue of non-adherence and its negative impact on patients with IBD. Further research is needed to establish simple and effective interventions to manage non-adherence.

COMMENTS

Background

Non-adherence to inflammatory bowel disease (IBD) maintenance medication occurs in up to 50% of patients. It is associated with adverse clinical outcomes and increased healthcare costs. While there are a number of methods that can detect non-adherence clinicians often struggle in routine clinical practice to detect it. There is a lack of robustly tested interventions capable of improving non-adherence to IBD medication.

Research frontiers

In the absence of clear guidelines and evidence for interventions little is known how clinicians perceive and how they address the issue of non-adherence. This survey ascertained perceptions and describes current practice to inform education, research and guidelines for clinical practice.

Innovations and breakthrough

A multitude of studies have aimed to identify factors associated with non-adherence. The most frequently found modifiable factors for intentional non-

adherence are a lack of belief in the necessity for medication and concerns over potential side effects. Patient friendly and easily implementable self-report tools to detect non-adherence have been assessed and validated ready for use in routine clinical practice.

Application

Further education about non-adherence is required as clinicians treating IBD patients frequently underestimate non-adherence. The use of validated screening tools should be encouraged. The respondents clearly identified the main factors associated with non-adherence and aimed to address them by counselling. A formally tested evidence based intervention to improve non-adherence is urgently required.

Terminology

IBD comprises ulcerative colitis and Crohns's disease, which are chronic inflammatory disorders of the gastrointestinal tract. Non-adherence is defined as a patient driven deviation from an agreed treatment plan.

Peer-review

This manuscript is well written and gives a clear overview of the perception of clinicians about medication non-adherence in IBD. As non-adherence is still a major problem in chronic diseases.

REFERENCES

- 1 **Mowat C**, Cole A, Windsor A, Ahmad T, Arnott I, Driscoll R, Mitton S, Orchard T, Rutter M, Younge L, Lees C, Ho GT, Satsangi J, Bloom S. Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011; **60**: 571-607 [PMID: 21464096 DOI: 10.1136/gut.2010.224154]
- 2 **Kane S**, Huo D, Aikens J, Hanauer S. Medication nonadherence and the outcomes of patients with quiescent ulcerative colitis. *Am J Med* 2003; **114**: 39-43 [DOI: 10.1016/S0002-9343(02)01383-9]
- 3 **Moody GA**, Jayanthi V, Probert CS, Mac Kay H, Mayberry JF. Long-term therapy with sulphasalazine protects against colorectal cancer in ulcerative colitis: a retrospective study of colorectal cancer risk and compliance with treatment in Leicestershire. *Eur J Gastroenterol Hepatol* 1996; **8**: 1179-1183 [PMID: 8980937 DOI: 10.1097/00042737-199612000-00009]
- 4 **Selinger CP**, Robinson A, Leong RW. Clinical impact and drivers of non-adherence to maintenance medication for inflammatory bowel disease. *Expert Opin Drug Saf* 2011; **10**: 863-870 [PMID: 21548837 DOI: 10.1517/14740338.2011.583915]
- 5 **Horne R**, Parham R, Driscoll R, Robinson A. Patients' attitudes to medicines and adherence to maintenance treatment in inflammatory bowel disease. *Inflamm Bowel Dis* 2009; **15**: 837-844 [PMID: 19107771 DOI: 10.1002/ibd.20846]
- 6 **Cervený P**, Bortlík M, Kubena A, Vlcek J, Lakatos PL, Lukás M. Nonadherence in inflammatory bowel disease: results of factor analysis. *Inflamm Bowel Dis* 2007; **13**: 1244-1249 [PMID: 17538983 DOI: 10.1002/ibd.20189]
- 7 **Cervený P**, Bortlík M, Vlcek J, Kubena A, Lukás M. Non-adherence to treatment in inflammatory bowel disease in Czech Republic. *J Crohns Colitis* 2007; **1**: 77-81 [PMID: 21172188 DOI: 10.1016/j.crohns.2007.08.002]
- 8 **Shale MJ**, Riley SA. Studies of compliance with delayed-release mesalazine therapy in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2003; **18**: 191-198 [PMID: 12869079 DOI: 10.1046/j.1365-2036.2003.01648.x]
- 9 **Kane SV**, Cohen RD, Aikens JE, Hanauer SB. Prevalence of nonadherence with maintenance mesalamine in quiescent ulcerative colitis. *Am J Gastroenterol* 2001; **96**: 2929-2933 [PMID: 11693328 DOI: 10.1111/j.1572-0241.2001.04683.x]
- 10 **Selinger CP**, Eaden J, Jones DB, Katelaris P, Chapman G, McDonald C, Smith P, Lal S, Leong RW, McLaughlin J, Robinson A. Modifiable factors associated with nonadherence to maintenance medication for inflammatory bowel disease. *Inflamm Bowel Dis* 2013; **19**: 2199-2206 [PMID: 23899547 DOI: 10.1097/

- MIB.0b013e31829ed8a6]
- 11 **Bernal I**, Domènech E, Garcia-Planella E, Marín L, Mañosa M, Navarro M, Cabré E, Gassull MA. Medication-taking behavior in a cohort of patients with inflammatory bowel disease. *Dig Dis Sci* 2006; **51**: 2165-2169 [PMID: 17086434 DOI: 10.1007/s10620-006-9444-2]
 - 12 **Goodhand JR**, Kamperidis N, Sirwan B, Macken L, Tshuma N, Koodun Y, Chowdhury FA, Croft NM, Direkze N, Langmead L, Irving PM, Rampton DS, Lindsay JO. Factors associated with thiopurine non-adherence in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2013; **38**: 1097-1108 [PMID: 24099471 DOI: 10.1111/apt.12476]
 - 13 **Ma C**, Evaschese CJ, Gracias G, Huang VW, Fedorak DK, Kroeker KI, Dieleman LA, Halloran BP, Fedorak RN. Inflammatory bowel disease patients are frequently nonadherent to scheduled induction and maintenance infliximab therapy: A Canadian cohort study. *Canadian J Gastroenterol Hepatol* 2015; **29**: 309-314 [DOI: 10.1155/2015/378628]
 - 14 **Kane S**, Shaya F. Medication non-adherence is associated with increased medical health care costs. *Dig Dis Sci* 2008; **53**: 1020-1024 [PMID: 17934828 DOI: 10.1007/s10620-007-9968-0]
 - 15 **Lakatos PL**. Prevalence, predictors, and clinical consequences of medical adherence in IBD: how to improve it? *World J Gastroenterol* 2009; **15**: 4234-4239 [PMID: 19750566 DOI: 10.3748/wjg.15.4234]
 - 16 **Munger MA**, Van Tassell BW, LaFleur J. Medication nonadherence: an unrecognized cardiovascular risk factor. *MedGenMed* 2007; **9**: 58 [PMID: 18092064]
 - 17 **Trindade AJ**, Morisky DE, Ehrlich AC, Tinsley A, Ullman TA. Current practice and perception of screening for medication adherence in inflammatory bowel disease. *J Clin Gastroenterol* 2011; **45**: 878-882 [PMID: 21555953 DOI: 10.1097/MCG.0b013e3182192207]
 - 18 **Trindade AJ**, Ehrlich A, Kornbluth A, Ullman TA. 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. *Inflamm Bowel Dis* 2011; **17**: 599-604 [PMID: 20848512 DOI: 10.1002/ibd.21310]
 - 19 **Hawthorne AB**, Rubin G, Ghosh S. Review article: medication non-adherence in ulcerative colitis--strategies to improve adherence with mesalazine and other maintenance therapies. *Aliment Pharmacol Ther* 2008; **27**: 1157-1166 [PMID: 18384664 DOI: 10.1111/j.1365-2036.2008.03698.x]
 - 20 **Jackson CA**, Clatworthy J, Robinson A, Horne R. Factors associated with non-adherence to oral medication for inflammatory bowel disease: a systematic review. *Am J Gastroenterol* 2010; **105**: 525-539 [PMID: 19997092 DOI: 10.1038/ajg.2009.685]
 - 21 **Hommel KA**, Davis CM, Baldassano RN. Objective versus subjective assessment of oral medication adherence in pediatric inflammatory bowel disease. *Inflamm Bowel Dis* 2009; **15**: 589-593 [PMID: 18985746 DOI: 10.1002/ibd.20798]
 - 22 **Wu YP**, Pai AL, Gray WN, Denson LA, Hommel KA. Development and reliability of a correction factor for family-reported medication adherence: pediatric inflammatory bowel disease as an exemplar. *J Pediatr Psychol* 2013; **38**: 893-901 [PMID: 23804406 DOI: 10.1093/jpepsy/jst043]
 - 23 **Waters BM**, Jensen L, Fedorak RN. Effects of formal education for patients with inflammatory bowel disease: a randomized controlled trial. *Can J Gastroenterol* 2005; **19**: 235-244 [DOI: 10.1155/2005/250504]
 - 24 **Moshkovska T**, Stone MA, Smith RM, Bankart J, Baker R, Mayberry JF. Impact of a tailored patient preference intervention in adherence to 5-aminosalicylic acid medication in ulcerative colitis: results from an exploratory randomized controlled trial. *Inflamm Bowel Dis* 2011; **17**: 1874-1881 [PMID: 21830265 DOI: 10.1002/ibd.21570]
 - 25 **Chan JT**, Selinger C, Kariyawasam VC, Collins GD, Leong RW. An inflammatory bowel disease clinical pharmacist significantly improves medication rates through personalised counselling. *J Gastroenterol Hepatol* 2012; **27**: 99
 - 26 **Hall NJ**, Rubin GP, Hungin AP, Dougall A. Medication beliefs among patients with inflammatory bowel disease who report low quality of life: a qualitative study. *BMC Gastroenterol* 2007; **7**: 20 [PMID: 17559670 DOI: 10.1186/1471-230X-7-20]
 - 27 **Tan M**, Holloway RH, Lange K, Andrews JM. General practitioners' knowledge of and attitudes to inflammatory bowel disease. *Intern Med J* 2012; **42**: 801-807 [PMID: 21883783 DOI: 10.1111/j.1445-5994.2011.02586]
 - 28 **Kashkooli S**, Andrews J, Robert M, Selinger C, Leong R. Inflammatory bowel disease-specific pregnancy knowledge of gastroenterologists against general practitioners and obstetricians. *UEG J* 2015; **3**: 462-470 [DOI: 10.1177/2050640615580893]

P- Reviewer: Cibor D, Coenen S, Duran NE, Katsanos KH

S- Editor: Qi Y **L- Editor:** A **E- Editor:** Wu HL





Published by **Baishideng Publishing Group Inc**

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

Help Desk: <http://www.wjgnet.com/esps/helpdesk.aspx>

<http://www.wjgnet.com>

