THE ROLE OF FAMILY NURSE PRACTITIONERS: PROMOTING ORAL MEDICATION ADHERENCE TO MAINTENANCE TREATMENT AMONG ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

by

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Abstract

The role of family nurse practitioners (FNPs) in promoting medication adherence in adolescents with inflammatory bowel disease (IBD) has not been established. This project provides intervention strategies that FNPs can use to promote oral medication adherence to maintenance treatment in adolescents with IBD. This is a critical need because non-adherence to maintenance therapy is the most significant factor associated with relapses of IBD and a serious health issue in adolescents with IBD. There are no current best practice guidelines in promoting adherence to maintenance medications in IBD patients. Findings from the literature review suggest that non-adherence to maintenance therapy is complex and multi-factorial. No single intervention strategy has been shown to be effective for all patients and conditions. However, individually tailored interventions that attend to behavioural, educational and psychosocial factors appear promising. The bio-psychosocial model is used as a conceptual framework to examine the factors affecting medication adherence and to explore the intervention strategies for improving medication adherence. Findings of this project are limited by the paucity of research on medication adherence in adolescents with IBD. Implications and recommendations for family nurse practitioner practice, education and research are discussed.
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Introduction

Inflammatory bowel disease (IBD) is a chronic, autoimmune disease of the gastrointestinal tract characterized by clinical remissions and unpredictable relapses. The peak onset of IBD coincides with adolescence, as the median age of diagnosis is age 15, and approximately 25% of IBD occurs before the age of 20 years (Kappelman et al., 2007). According to Crohn's and Colitis Canada (CCC), Canada has one of the higher rates of IBD in the world, with the number of new cases of IBD in Canadian children almost doubling since 1995 (CCC, 2014).

The management of IBD aims to induce and maintain a clinical remission, prevent disease relapse and improve quality of life. Pharmacological interventions represent the cornerstone of management for IBD by targeting the underlying inflammatory response (Diefenach & Breuer, 2006). Life long maintenance therapy is required to prevent relapses of the disease and colorectal cancer (Zheng & Kennedy, 2009). Successful management of IBD necessitates adherence to maintenance medications. The demands of adhering to maintenance medications are perceived as a major burden by adolescents (Leleiko et al., 2013).

Non-adherence to maintenance medications is the most significant factor associated with relapses of IBD. No studies have reported the impacts of non-adherence to maintenance medications on relapse rates of the disease in an adolescent population. In adult patients with IBD, non-adherence resulted in more than a five times greater risk of relapses of the disease than adherent patients (Kane, Huo, Aikens, & Hanauer, 2003). Adherence to maintenance medications has significant implications for prevention of complications and morbidities, improvement of disease outcomes and quality of life, and reduction in healthcare costs (Hawthorne, Rubin, & Ghosh, 2008; Hommel, Denson, & Baldassano, 2011; Horne, Parham,
Driscol, & Robinson, 2009; Quittner, Modi, Lemanek, Levers-Landis, & Rapoff, 2008). Therefore, improving medication adherence is an important step in the effective management of IBD in adolescents.

Promoting medication adherence in adolescents with IBD is challenging for healthcare providers, in part because best practice in promoting medication adherence is not well defined. As primary care providers, family nurse practitioners (FNPs) have a role in promoting medication adherence and improving the quality of care for adolescents with IBD. A review of the literature in this area is timely to identify best practice for FNPs to promote medication adherence. A holistic approach is essential to develop strategies to identify adolescents at risk for non-adherence and provide effective interventions to improve adherence.

A conceptual framework can provide a useful lens to examine and analyze literature. The bio-psychosocial (BPS) model is chosen for this paper to explore the role of FNPs in promoting medication adherence in adolescents with IBD. The BPS model suggests that healthcare professionals take into account the interactions of psychological, social factors and biological processes to fully understand disease progression and changes (Engel, 1980). The bio-psychosocial perspective provides a comprehensive approach to frame effective promotion of medication adherence in adolescents with IBD.

The World Health Organization (WHO) defines an adolescent as any person between the ages of 10 and 19, and adolescence is marked by a transitional phase of growth and development between childhood and adulthood (WHO, 2014). During this transitional period of life, adolescents undergo profound changes in biologic, social and psychological realms and also experience role changes within family and peer groups. It is a time when adolescents strive to
become more independent, along with increased academic and social demands (Mamula, Markowitz, & Baldassano, 2003).

Compounded with the developmental characteristics of adolescence, medication adherence in adolescents becomes complex and challenging. Adolescents with IBD are susceptible to anxiety/depressive symptoms, and thus can experience greater difficulties with adherence to IBD treatment (Gray, Denson, Bladassano, & Hommel, 2012). Adolescents are more frequently non-adherent to maintenance treatment than adults with IBD (Kamperidis et al., 2012). Depending on the medication type and method of assessment, non-adherence rates for medications range from 50% to 88% among adolescents with IBD (Hommel, Davis, & Baldassano, 2009; Mackner & Crandall, 2005; Oliva-Hemker, Abadom, Cuffari, & Thompson, 2007).

Given the prevalence of IBD, along with the high rates of non-adherence in adolescents with IBD and the significant impacts of non-adherence on health outcomes and healthcare services, there is need to address this issue in FNP practice. The intent of this paper is to explore the role of FNPs in promoting medication adherence in adolescents with IBD by answering two questions: 1) in adolescents with IBD, what factors affect their adherence to oral medications for maintenance treatment? And 2) what are the intervention strategies that FNPs can use to promote oral medication adherence in adolescents with IBD?

To answer these questions, the context for understanding IBD and maintenance therapy in an adolescent population will be first provided, along with definition of adherence and methods for assessing medication adherence. The challenges for adolescents adhering to medication and the need for promoting medication adherence are also addressed. Second, application of the BPS model will be introduced. Third, literature will be reviewed to determine
and describe factors affecting medication adherence and current intervention strategies for improving medication adherence. Through analysis of the literature using the BPS model, implications and recommendations for FNP practice, education and future research will be presented.
Chapter One: Background

This section aims to provide a context to better understand the disease process, treatment regimens and medication adherence. First, an overview of IBD, maintenance therapy, definition of adherence and non-adherence, and methods of measuring medication adherence will be presented. Second, the significance of promoting adherence to maintenance medications among adolescents with IBD will be addressed. Last, the BPS model will be introduced as a conceptual framework to address non-adherence.

Overview of Inflammatory Bowel Disease

IBD is a term used for two major gastrointestinal inflammatory disorders: Crohn’s disease (CD) and ulcerative colitis (UC). IBD is characterized by unpredictable and fluctuating cycles of remissions and exacerbations (mild, moderate or severe) throughout a patient’s lifetime (Higuchi & Bousvaros, 2014). In an adolescent population, IBD presents with unique patterns of incidence and clinical manifestations.

Incidence

In Canada, the prevalence of IBD is 1 in 150 compared to 1 in 350 in other nations (CCC, 2014). The peak incidence of IBD occurs in patients between the ages of 15 and 25 years, with a possible second peak between 50 and 80 years. Approximately 25% to 30% of CD and 20% of UC present before the age of 20 years. The incidence of CD is higher than UC in children and the incidence of paediatric CD has been increasing, whereas the incidence of UC has remained stable (Dubinsky, 2008; Rufo & Bousvaros, 2006).

Pathophysiology

IBD is an immune-mediated inflammatory disease. The aetiology and pathogenesis of IBD remain poorly understood. Although the exact pathophysiology of IBD has not been fully
defined, there is both a genetic and environmental component. IBD likely results from a complex interaction of genetic, immune and environmental factors (Peppercorn & Cheifetz, 2014). IBD is more common in individuals with Jewish ancestry and Caucasians. Approximately 10-25% of affected patients have a first-degree relative with either UC or CD. Cigarette smoking increases the risk for CD but may be protective for the development of UC. It is not certain whether there is a direct connection between psychosocial factors and the risk of developing IBD. However, it is likely that psychological factors have a role in the exacerbation of symptoms in patients with established IBD (Peppercorn & Cheifetz, 2014).

Clinical Manifestations

CD and UC share similarities in pathogenesis, symptoms and treatment, but CD can involve any part of the gastrointestinal tract from mouth to anus, most commonly in the ileum and ileocecal regions. Inflammation can be focal and transmural from the mucosa to the serosa. In UC, the inflammation is superficial and limited to the mucosa of the colon and rectum in a diffuse and continuous fashion. Adults and children with IBD have similar gastrointestinal symptoms, such as weight loss, abdominal pain, diarrhea, rectal bleeding, or extra-intestinal manifestations such as iritis, erythema nodosum or arthritis (Higuchi & Bousvaros, 2014). Patients with IBD have an increased risk of small bowel adenocarcinoma and colon cancer. The risk increases with the extent and severity of the disease, the age of onset and duration of the disease (Diefenbach & Breuer, 2006).

When IBD develops earlier in life, there are other challenges that are not encountered with the onset of this disease in adults. Challenges found in adolescents with IBD include growth and/or sexual maturation impairment, such as subnormal gains in height or weight and delayed or failed sexual maturation (Higuchi & Bousvaros, 2014). Moreover, adolescents with IBD have
relatively high rates of psychosocial morbidity, such as depression and anxiety. Emotional and/or behavioural issues may take the form of child-parent conflict, non-adherence to medications and difficulties with school activities or socializing with peers (Mackner, Sission, & Crandall, 2004).

**Goal of Management**

Treatment of IBD is complex, involving medications, dietary modifications and sometimes surgery. Currently, there is no permanent cure for IBD. Management of IBD aims to induce and maintain a clinical remission, improve quality of life and decrease the need for surgical interventions (Diefenach & Breuer, 2006). The goal of medical management for IBD is to achieve clinical and histological remission by suppressing inflammation with a minimum of side effects from medications. Once a remission is induced, the patient can be transitioned to maintenance therapy, typically involving medications with a slower onset of action and fewer side effects (Bousvaros & Leichtner, 2014).

Surgical intervention usually involves resection of the diseased bowel segment and is reserved primarily for patients who do not respond to aggressive medical management, or who develop complications. A total colectomy for UC is curative, but most patients do not desire surgery. Colectomy and ileoanal reservoirs are an option, but may result in significant complications. Elective surgery is generally avoided in CD because of the high recurrence risk. Moreover, the intestinal inflammation and extra-intestinal symptoms may occur after surgical interventions in both CD and UC (Bousvaros, Leichtner & Burpee, 2014). Therefore, pharmacological intervention represents the cornerstone of management for IBD to sustain remission by targeting the underlying inflammatory response (Diefenach & Breuer, 2006).
Maintenance Therapy

The primary goal of maintenance therapy is to maximize therapeutic efficacy, minimize toxicity, maximize medication adherence and quality of life, maintain physical and psychosocial wellbeing and prevent disease complications (Dubinsky, 2008). The main oral medications for maintaining medically or surgically induced remissions in children with IBD include anti-inflammatory agents (i.e. aminosalicylates) and immune-modulators (Bousvaros & Leichtner, 2014). Over-the-counter medications may be needed for maintenance treatment. These agents will now be described.

Aminosalicylates

Preparations containing 5-aminosalicylic acid (5-ASA) are formulated to release the drug at specific sites in the gastrointestinal tract, since efficacy is dependent on luminal concentration. Common agents of 5-ASA used for maintenance treatment in adolescents with IBD include sulfasalazine and mesalamine. These medications inhibit synthesis of pro-inflammatory prostaglandins and leukotricenes. If 5-ASA medications are effective in eliminating symptoms and avoiding frequent relapses, they are generally preferable to immune-modulators because of the lower toxicity. Abrupt discontinuation of 5-ASA is not recommended and may result in relapse (Bousvaros & Leichtner, 2014).

The most common side effects of 5-ASA are headache, dizziness, increased sensitivity of skin to sunlight, itchiness, anorexia, upset stomach, nausea, vomiting, abdominal pain, cramps and diarrhea. Common adverse effects of 5-ASA may include haemolytic anemia and hepatotoxicity. Reversible oligospermia has been reported with sulfasalazine. Many of these side effects are dose related. They can be mild or severe, temporary or permanent (Chami & Feagan, 2011). It is suggested that monitoring of patients with 5-ASA should include complete blood
counts at least twice a year, and liver function tests and urinalysis at least annually (Bousvaros & Leichtner, 2014).

**Immuno-modulators**

Immuno-modulators for maintenance therapy in adolescents with IBD include thiopurines, i.e., azathioprine (AZA) and 6-mercaptopurine (6-MP). They have been shown to be effective in maintaining remission because of the long onset of action. AZA is metabolized into 6-MP and these two drugs are equally effective and differ only in their dosage. In the liver, these drugs are converted to 6-thioguanine nucleotides (6-TGN) and 6-methylmercaptopurine nucleotide (6-MMPN), which inhibit lymphocyte proliferation by impairing DNA synthesis. Metabolite monitoring of serum levels of 6-TGN and 6-MMPN can be helpful in assessing thiopurine metabolism, medication adherence and in optimizing drug dosing (Bousvaros & Leichtner, 2014). It is important to treat with appropriate dosing, as under-dosing is the most common cause of treatment failure in maintaining remission (Diefenbach & Bureuer, 2006).

Side effects of thiopurines include anorexia, nausea, GI discomfort, diarrhea and arthralgia. Adverse effects of thiopurines include increased risk of opportunistic infection, bone marrow suppression, blood dyscrasias and rarely pancreatitis, hepatotoxicity, hypersensitivity, or pneumonitis (Chami & Feagan, 2011). These have been associated with an inherited inability to metabolize thiopurines. Patients with an alteration in the gene of thiopurine methyltransferase (TPMT) have deficit TPMT activity and are at risk for marked elevations of the active 6-thioguanine nucleotides which result in severe leucopenia. A screening test is available to determine TPMT genotype as well as thiopurine metabolism (Diefenbach & Bureuer, 2006). Patients treated with 6-MP or AZA require frequent monitoring for complete blood count and
aminotransferase levels. If patients are stable, they should be monitored every 3 months and 2 to 3 weeks after a change in dose (Bousvaros & Leichtner, 2014).

**Over-the-Counter Medications**

Over-the-counter medications, such as vitamins, minerals and other supplements, may be recommended along with the above maintenance medications. They are required due to malabsorption following intestinal inflammation and due to the effects of maintenance medications. For example, since sulfasalazine competitively inhibits folate absorption, patients should be treated simultaneously with folate (Reed-Knight, Lewis, & Blount, 2011). Adherence to folate supplementation and 5-ASA maintenance therapy may reduce the risk of colon cancer (Bousvaros & Leichtner, 2014).

The choice of maintenance medications and the dose of medications depend on the patient’s disease severity and initial response to medications. Although medications for maintenance therapy expose patients to a number of medication-related side effects or adverse events, appropriate maintenance therapy throughout childhood and adolescence is required to prevent relapses of the disease and colorectal cancer (Zheng & Kennedy, 2009). Monitoring for both safety and adherence is a challenge in management of IBD. The following section will define medication adherence and discuss methods for measuring adherence.

**Defining and Measuring Medication Adherence**

To improve medication adherence, FNPs need to understand how medication adherence is defined and measured in order to identify adolescents who are non-adherent or at risk for non-adherence to maintenance medications.
Definition of Adherence and Non-adherence

Adherence to long-term therapy is defined as the extent to which an individual’s behaviour corresponds with a healthcare provider’s recommendations, including taking medications, following a diet, or modifying a lifestyle (WHO, 2003). This paper is focused specifically on adherence to oral medications. According to the International Society for Pharmacoeconomics and Outcomes Research, medication adherence is defined as the extent to which a patient takes medication in accordance with the prescribed interval and dose (Hawthorne et al., 2008).

In studies of medication adherence in adolescents with IBD, medication adherence was defined as 80% of the medications taken in the past seven days or one month in accordance with the prescribed interval and dose. Non-adherence was considered when medications were taken less than 80% in accordance with the prescribed interval and dose. To quantify adherence, the number of prescribed doses minus the number of missed doses is divided by the number of prescribed doses and multiplied by 100 (Zelikovsky & Schast, 2008).

In clinical settings and literature, the terms compliance and adherence are often used synonymously. The term compliance has fallen out of favour, because it implies that patients need to be obedient. Adherence has become more widely used, because it suggests that patients’ behaviour is concordant with healthcare providers’ recommendations. Moreover, patients are considered active partners with health professionals in their own care. Adherence reflects collaboration between the patient and the provider with regards to a treatment plan (Hommel, Greenley, Maddux, Gray, & Mackner, 2013).
Methods of Measuring Medication Adherence

In the context of family practice, common methods for measuring adherence rates include subjective and objective assessments. Subjective assessments include patient reports via standardized interviews and/or questionnaires. For adolescents with IBD, both adolescent and parent reports of adherence are often used because of the high level of parent involvement in medication administration (Wu, Pai, Gray, Denson, & Hommel, 2013). Objective assessments include pill count, checking prescription refills, the use of electronic medication monitors and drug assays.

Each method of adherence assessment has its inherent strengths and weaknesses. Subjective assessments are cost-effective and feasible clinic-based assessments. However, self-reports tend to overestimate medication adherence and may be somewhat time consuming to administer (Hommel et al., 2009). A study of 42 adolescents with IBD by Hommel et al. (2009) found that non-adherence rates were 10% for 6-MP/AZA and 2% for 5-ASA using adolescent interviews as a subjective assessment. In contrast, non-adherence rates for these same patients were 64% for 6-MP/AZA and 88% for 5-ASA using objective assessments (pill count and drug assays). This study highlights the significant discrepancy between subjective and objective assessment of non-adherence, suggesting both subjective and objective methods may be required to effectively monitor adherence in adolescents taking maintenance medications for IBD.

A second study that illustrates how subjective assessments overestimate adherence compared to objective assessments was a prospective observational study conducted by Gifford, Berg, Lahiff, Cheifetz, Horowitz and Moss (2012) in 93 patients with UC taking mesalamine for maintenance therapy. A random urine salicylate level above 15 mg/dL distinguished patients who had recently taken mesalamine from controls. The researchers found that approximately
one-third of patients who self-identified as “high adherers” by an adherence questionnaire had random levels of urine salicylates below the threshold of 15 mg/dL. This study again identifies that subjective assessments can overestimate medication adherence.

Compared to subjective assessments, objective methods can provide more reliability but also have drawbacks. Data from pill count, checking prescription refills and use of electronic medication monitors are based on the assumption that patients do not discard their medications, for example, adolescents do not discard medications that are to be taken during school hours. These data cannot confirm actual medication ingestion or whether the appropriate number of pills was taken. Electronic medication monitoring devices can malfunction, as they contain an integral electronic microcircuit that records the time and date of each opening and closing of the container. Another drawback is they are expensive and may not be available in all primary care settings (Leleiko et al., 2013).

Bioassays are also an objective measure of drug metabolites in blood or urine, but they can be affected by individual pharmacokinetics and are subject to bias due to white coat compliance, i.e., adolescents more conscientiously taking medications prior to medical appointments (Wu et al., 2013). Metabolite monitoring of serum levels of 6-TGN and 6-MMPN can be helpful in assessing medication adherence in patients treated with 6-MP/AZA. Measuring serum levels of 5-ASA as well as its metabolites in urine can be useful in assessing medication adherence, and is practical for routine use in clinic settings. Patients taking 5-ASA excrete a proportion of the ingested dose as 5-ASA or n-acetyl-5-ASA in the urine, which can be detected and quantified within 4 hours after an ingested dose and remains detectable for up to 5 days after discontinuation. Random urine screening for a salicylate level provides a better indication of medication adherence to 5-ASA (Gifford et al., 2012).
Both subjective and objective measures offer unique data for assessing medication adherence. The discrepancy between subjective and objective assessments of adherence and the drawbacks of each method underscore the importance of multiple methods for adherence assessment. Application of multiple methods to assess adherence is current practice, as it may provide more reliable and realistic adherence estimates (Hommel, Herzer, Ingerski, Hente & Denson, 2011).

The Significance of Promoting Medication Adherence

Adherence to medications throughout the maintenance phase is central to maintaining remission. Addressing medication adherence should be considered a major component in managing patients with IBD (Kane et al., 2012). The need for promoting medication adherence in adolescents with IBD is important for several reasons, including preventing relapses, complications and morbidities, improving physical and psychosocial wellbeing and reducing healthcare costs.

Preventing Relapses, Complications and Morbidities

Non-adherence to maintenance medications has significant consequences on relapses of IBD, disease activity, complications and morbidities (Hawthorne et al., 2008). No studies were found to report the impacts of non-adherence to maintenance medications on disease activity, complications and morbidities in adolescents with IBD. In adult patients with quiescent UC, non-adherence to 5-ASA resulted in relapse in 61% of patients over 2 years, whereas only 11% of adherent patients experienced relapses. Only about 40% of patients on 5-ASA were fully adherent to maintenance therapy. Relapse rates over 2 years are significantly higher in non-adherent patients with UC (Kane et al., 2003).
Non-adherence or disruption of maintenance therapy destabilizes disease activity, leading to exacerbations of symptoms, such as nausea, abdominal pain, fatigue, diarrhea, fistulae or abscesses (Robinson, Hankins, Wiseman, & Jones, 2013). In the long term, adherence to maintenance medications significantly reduces the risk of developing colorectal cancer by up to 75% in UC patients (Van et al., 2005).

**Improving Physical and Psychosocial Wellbeing**

Growth failure in adolescents with IBD can be reversed if the disease is controlled medically, use of maintenance therapy is maximized, and sufficient dietary energy and nutrients are provided (Bousvaros & Leichtner, 2014). Adolescents with non-adherence are more likely to experience poorer overall quality of life in physical, emotional, social and school areas, and have greater anxiety and depressive symptoms (Gray et al., 2012; Hommel, Davis, & Baldassano, 2008). Achieving disease remission results in significant improvement of bowel symptoms, but also overall physical and psychosocial wellbeing. Exacerbations of clinical symptoms can be a source of psychological issues in adolescents (Robinson et al., 2013).

**Reducing Healthcare Costs**

Non-adherence to maintenance medications contributes to the high costs associated with treatment of relapses of IBD. Adolescents who are not adherent are more likely to have greater disease severity, potentiating the need for more aggressive and costly medical treatment (Gray et al., 2012). Poor adherence poses the risk of increasing dosages to toxic levels or needlessly or prematurely stepping up therapy, when what is actually needed is better adherence to the original treatment regime (Leleiko et al., 2013). Although there is no data available pertinent to an adolescent population, there is evidence that for adults with IBD, disease relapses are associated with a two or three fold increase in costs for non-hospitalized cases and a 20-fold increase in
costs for hospitalized cases compared with quiescent cases of IBD (Bassi, Dodd, Williamson, & Bodger, 2004).

Given that non-adherence rates for maintenance medications in adolescents with IBD range from 50% to 88% (Hommel et al., 2009; Mackner & Crandall, 2005; Oliva-Hemker at al., 2007) and its considerable impacts on health outcomes and healthcare costs, it is important for healthcare providers to understand the factors affecting adherence in adolescents with IBD and to develop and implement intervention strategies to promote medication adherence.

In primary care settings, FNPs not only diagnose and manage medical issues; they also focus on the effects of illness on the life of individual patients and families, and emphasize health promotion, patient education/counselling and disease prevention (College of Registered Nurses of British Columbia, [CRNBC], 2012). According to the scope of practice of FNPs in BC, FNPs cannot initiate IBD treatment and maintenance medications or continue prescribing immune-modulators. But, they can continue prescribing 5-ASA agents, such as sulfasalazine. FNPs are involved in the continuity of care for patients of all ages with IBD and are responsible for monitoring maintenance therapy and assessing adherence as part of the team providing care. Therefore, FNPs need to understand maintenance therapy for IBD, factors affecting adherence and intervention strategies that can be used to improve adherence as needed.

The Bio-psychosocial Model

The bio-psychosocial (BPS) model was originally described by Engel (1980). Engel suggested that healthcare professionals move beyond the biomedical model to gain a comprehensive understanding of the aetiology and progression of disease; the interactions between physical and psychosocial variables must be examined in order to successfully provide
effective care of patient health and wellbeing. This bio-psychosocial perspective provides a comprehensive approach to examine the issue of non-adherence in adolescents with IBD.

Adolescents with IBD have a greater vulnerability with physical, social and psychological issues. In adolescence, there are a number of developmental milestones, such as a greater desire for autonomy, more need and interest in activities with peers rather than with family and an increased awareness of fitting in with peers. These normative transformations challenge adolescents to adhere to maintenance medications of IBD (Hommel, Greenley et al., 2013). Adolescents with IBD often express frustration and anger about the unpredictable disease activity, energy levels, body image and decreased physical and social activities. They are more vulnerable to psychosocial issues than healthy peers, due to disturbing symptoms, altered physical appearance, invasive medical procedures or surgical interventions. This may influence their overall adjustment and coping strategies (Mamula et al., 2003).

Examining the issue of non-adherence with a bio-psychosocial perspective facilitates the identification of the psychosocial issues associated with the disease and medication adherence. Many adolescents with IBD have fears about how the disease will affect their future school and employment, as well as the long-term side effects of medications. Feelings of helplessness, dependency and low self-esteem, anxiety and depressive symptoms can have direct implications on adherence to treatment plans (Mackner & Crandall, 2006). Because these issues are associated with poor adherence, it has been suggested that psychotherapy addressing these areas may contribute to improved medication adherence (Mackner & Crandall, 2005). Given the significance of psychosocial issues associated with the disease and medication adherence among adolescents with IBD, examination of non-adherence is likely best conceptualized with the BPS model.
Using the BPS model to explore the role of FNPs in promoting medication adherence also fits with the philosophy of primary health care (PHC). A PHC model embraces five types of care, namely promotive, preventative, curative, rehabilitative, supportive and palliative (Canadian Nurses Association [CNA], 2000). Health promotion and disease prevention are an element of the PHC approach and are integrated in FNP practice in primary care settings. In contrast, a primary care model, or a biomedical model, is largely medical-centered and illness-oriented (CNA, 2000). The BPS model integrates the biomedical and psychosocial perspectives and emphasizes the roles of psychosocial variables in disease progression, health promotion and illness prevention. Application of the BPS model enables healthcare providers to examine the biological, psychological and social variables in relation to non-adherence and to provide promotive, preventative and supportive care of adolescents and their families.

Biomedical solutions, when applied without attention to psychosocial issues, are not likely to maximize adherence that can be provided in a BPS approach (Leleiko et al., 2013). It is for these reasons that the BPS model was chosen as a conceptual framework to examine the literature and analyze the review in this paper. If FNPs have knowledge of the disease processes, treatment goals and regimens, tools for assessing medication adherence, and employ a BPS approach to medication adherence, they are well prepared to understand the complexities of factors affecting medication adherence and plan intervention strategies in a relevant and appropriate manner to improve medication adherence. To explore factors affecting adherence and intervention strategies for improving medication adherence, a literature search was conducted and will be presented in the next chapter.
Chapter Two: Literature Search Strategy

This paper aims to provide intervention strategies for improving medication adherence in adolescents with IBD. This literature review was guided by two research questions: 1) in adolescents with IBD, what factors affect their adherence to oral medications for maintenance treatment? 2) What are intervention strategies that FNPs can use to improve oral medication adherence in adolescents with IBD? This chapter will summarize the search methods and the articles retrieved for conducting an integrative literature review.

Literature Search Methods

The literature search was conducted using the electronic online databases through the University of Northern British Columbia and Interior Health Authority libraries. The search terms or key words were based on the research questions and were combined variously using “AND” or “OR” (see Box 1). A search realm was defined in medicine, nursing, pharmacology and psychology. Electronic databases include Medline, CINAHL, PsycINFO, Cochrane and Google Scholar. Additionally, reference lists of review papers were hand searched for applicable papers. The website of Crohn’s and Colitis Canada was also included.

<table>
<thead>
<tr>
<th>Box 1. Search terms for Medline, CINAHL, PsycINFO, Cochrane and Google Scholar</th>
</tr>
</thead>
<tbody>
<tr>
<td>inflammatory bowel disease OR ulcerative colitis OR Crohn’s disease OR Crohn* AND adhere* OR complian* OR concordanc* OR non-adheren* OR non-complian* AND medication OR treatment OR therapy OR intervent* OR strateg* AND adolescen* OR paediatric OR teenager</td>
</tr>
</tbody>
</table>

Limits: from the year 2000 onward.
The collection of relevant literature followed three steps. First, literature was initially selected by screening the titles of the articles. Second, literature was sampled by reviewing the abstracts of the articles. The inclusion criteria for keeping abstracts were based on their relevance to the topic of the project (see Box 2). Third, literature was collected by examining the full texts of primary research articles, review articles and clinical reports. The full texts of articles were retrieved based on the inclusion (see Box 3) and exclusion criteria (see Box 4). Preliminary literature review had suggested that medication adherence started to become a major topic of interest around 2000. Therefore, 2000 was chosen as the starting point for this literature search.

<table>
<thead>
<tr>
<th>Box 2. Inclusion criteria for keeping abstracts</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Published in English</td>
</tr>
<tr>
<td>• Adolescents with IBD (10-19 years old according to WHO).</td>
</tr>
<tr>
<td>• Adherence to oral medications (including supplements)</td>
</tr>
<tr>
<td>• Maintenance therapy</td>
</tr>
<tr>
<td>• Rates/impacts of non-adherence.</td>
</tr>
<tr>
<td>• Methods of measuring adherence.</td>
</tr>
<tr>
<td>• Factors affecting non-adherence to maintenance medication.</td>
</tr>
<tr>
<td>• Interventions/strategies for improving medication adherence.</td>
</tr>
<tr>
<td>• Published from the year 2000 onward</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Box 3. Inclusion criteria for keeping full texts of articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>The inclusion criteria for keeping abstracts and plus:</td>
</tr>
<tr>
<td>• Original research articles</td>
</tr>
<tr>
<td>• Qualitative, quantitative or mixed studies</td>
</tr>
<tr>
<td>• Clinical reports and review articles</td>
</tr>
<tr>
<td>• Peer-reviewed journal articles</td>
</tr>
</tbody>
</table>
 Articles Retrieved

A combination of different search terms yielded 64 articles in the selected electronic databases. Forty articles were kept after screening the titles of articles. After reviewing the abstracts of articles, 31 articles were kept based on the inclusion criteria. A total of 20 articles with full texts were kept after reviewing the full texts of articles, including 12 articles on factors affecting medication adherence and 8 articles on intervention strategies. The number of articles included and excluded at each step is presented in Box 5. The number and the themes of final articles reviewed are presented in Box 6.

Of note, the literature review was carried out in two sections: factors affecting non-adherence using the 12 articles (see Chapter three) and intervention strategies for improving medication adherence using the 8 articles (see Chapter four). A paucity of literature was found for intervention strategies in adolescents with IBD. Of the 8 articles, 4 studies were conducted in adolescents between the ages 11 and 18 years, 4 other studies that included both adolescents and adults were also included, because these 4 studies included older adolescents between the ages of 17 and 19 years and provided a value-added source of intervention strategies for improving medication adherence.
### Box 5. Numbers of the articles included and excluded at each step

| Articles yielded with combination of different search terms cross databases and reference search | 64 |
| Articles yielded after screening the titles | Included: 40 | Excluded: 24 |
| Articles yielded after reviewing the abstracts | Included: 31 | Excluded: 9 |
| Articles with full texts retrieved that met the inclusion criteria | Included: 20 | Excluded: 11 |

### Box 6. Numbers and themes of the articles retrieved with full texts

<table>
<thead>
<tr>
<th>Numbers of the articles (total 20)</th>
<th>Themes of the articles</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 original studies</td>
<td>factors affecting medication adherence</td>
</tr>
<tr>
<td>8 original studies</td>
<td>intervention strategies for improving medication adherence</td>
</tr>
</tbody>
</table>
Chapter Three: Factors Affecting Medication Adherence

Identifying the factors that affect medication adherence is a first step in targeting interventions to improve medication adherence (Kane & Robinson, 2010). For this purpose, twelve studies were retrieved and reviewed to answer the first research question: “In adolescents with IBD, what factors affect their adherence to oral medications for maintenance treatment?”

Before delving deeper into understanding the factors affecting medication adherence, tools used in the literature to identify factors will be briefly introduced in the following section.

**Assessment Tools to Identify Factors Affecting Adherence**

Common tools employed in literature to identify factors affecting adherence are presented in Box 7, and are described later, including tools for assessing knowledge, behavioural factors, psychosocial issues, family functioning and coping strategies.

<table>
<thead>
<tr>
<th>Assessing knowledge and behavioural factors</th>
<th>Assessing psychosocial issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Medication Adherence Measure (MAM)</td>
<td>The Child Behavioural Checklist (CBCL)</td>
</tr>
<tr>
<td>The Medication Adherence Interview (MAI)</td>
<td>The Youth Self-Report (YSR)</td>
</tr>
<tr>
<td>The Treatment Adherence Interview (TAI)</td>
<td>The Children’s Depression Inventory (CDI)</td>
</tr>
<tr>
<td></td>
<td>The Multidimensional Anxiety Scale for Children (MASC-2)</td>
</tr>
<tr>
<td></td>
<td>The Medication Adherence Interview (MAI)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Assessing family functioning</th>
<th>Assessing coping strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Family Assessment Device (FAD)</td>
<td>The Coping Strategies Inventory (CSI)</td>
</tr>
<tr>
<td>IBD Family Responsibility Questionnaire (IBD-FRQ)</td>
<td>The Piers Harris Self-Concept Scale (PHSCS)</td>
</tr>
<tr>
<td>The Issue Checklist</td>
<td></td>
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</tbody>
</table>
Tools for Assessing Knowledge and Behavioural Factors

The Medical Adherence Measure (MAM), the Medication Adherence Interview (MAI) and the Treatment Adherence Interview (TAI) were commonly used to assess knowledge of treatment and medication regimens and behavioural factors affecting adherence.

The MAM is a validated and reliable semi-structured interview administered during standard clinical care (validity 0.40 and reliability 0.89). The MAM contains 12 commonly identified barriers to medication adherence. Respondents answer yes, if they perceive each item to be a barrier to adherence. This tool also asks respondents to report the number of doses of medication they have missed in the past 7 days (Zelikovsky & Schast, 2008). With its two fold purposes, i.e. measuring medication adherence and assessing barriers to adherence, the MAM was used in seven studies (see Table 1). It was conducted jointly or separately with adolescents and their parents, based on the aims of the clinician, patient population, or purpose of research.

The MAI designed by Mackner and Crandall (2005) is a semi-structured interview for assessing barriers to adherence in children with IBD. These factors include educational (knowledge of treatment and medications, etc.), organizational (placement of medication in house, who refills pill organizer, etc.), behavioural (refusal to take medications) and emotional (anxiety and depressive symptoms) domains. The TAI was modeled after the MAI by Hommel and Baldassano (2010). It only contains eight questions and was used during a routine clinic visit in two studies (Hommel & Baldassano, 2010; Hommel, Odell, Sander, Baldassano, & Barg, 2011).

There has been no report about reliability or validity of the MAI and TAI. However, they were specifically used to assess barriers to adherence in children with IBD. The interview questions were well designed with input from a psychologist, gastroenterologist and
anthropologist representing expertise in paediatric behavioural medicine and medication adherence.

**Tools for Assessing Psychosocial Issues**

The Child Behavioural Check List (CBCL), the Youth Self-Report (YSR), the Children’s Depression Inventory (CDI), the Multidimensional Anxiety Scale for Children (MASC-2) and the MAI were commonly used in the studies for assessing psychosocial issues.

The CBCL is a validated and reliable measure used to assess a range of behavioural and psychosocial problems of children aged 6 to 18 years. It contains 113 items that yield 8 factors: aggressive behaviour, anxious/depressed, attention problems, rule-breaking behaviour, social problems, somatic complaints, thought problems and withdrawal (Achenbach & Rescorla, 2001). The YSR is a version of the CBCL, but for use only with children 11 years and older. Both tools have been found to be reliable (test-retest reliability from 0.70 to 0.74) and valid (internal consistency from 0.82 to 0.96). The child or adolescent completes the YSR, whereas parents complete the CBCL (Achenbach & Rescorla, 2001).

The CDI is a 27-item self-report measure widely used to assess the severity of depression and/or dysthymic disorder in children and adolescents aged 7 to 17 years. The CDI has been found to be reliable (internal consistency for the total score $\alpha=0.86$) (Finch, Saylor, Edwards, & McIntosh, 1987). The MASC-2 is a comprehensive assessment of anxiety dimensions in children and adolescents aged 8 to 19 years, including physical symptoms, harm avoidance, social anxiety and separation/panic. The MASC-2 has been found to be reliable (internal consistency $\alpha$ from 0.73 to 0.89 for child report and from 0.7 to 0.9 for parent report) (Baldwin & Dadds, 2007).
Tools for Assessing Family Functioning

The Family Assessment Device (FAD) and IBD Family Responsibility Questionnaire (IBD-FRQ) and the Issues Checklist were commonly used in the studies for assessing family functioning.

The FAD contains 60 questions used to evaluate family functioning in seven areas: problem solving, communication, roles, emotional responsiveness, emotional involvement, behavioural control and general functioning. These questions are completed by all family members over the age of 12. The FAD has been found to be reliable and valid. The internal consistency (α) for the subscale ranged from 0.93 to 0.90, predictive validity $r = 0.47$ (Miller, Epstein, Bishop, & Keitner, 1985).

The IBD-FRQ is a measure of adolescent and parental involvement in IBD management. It contains 26 items and includes adolescent, maternal and paternal report forms. IBD-FRQ has been found to be reliable. Internal consistency estimates for adolescent and parent report were good with $\alpha \geq 0.88$ and $\alpha \geq 0.92$, respectively (Greenley, Doughty, Stephens, & Kugathasan, 2010).

The Issues Checklist is a scale containing a list of 44 issues that can lead disagreements between parents and adolescents. It can be assessed with adolescent and parent reports regarding the frequency and common sources of conflicts between the adolescent and parents during the previous two weeks. Internal consistency estimates were good with $\alpha = 0.68$ for adolescent report of conflict frequency and $\alpha = 0.89$ for parent report of conflict frequency (Greenley, Doughty et al., 2010).
Tools for Assessing Coping Strategies

The Coping Strategies Inventory (CSI) and the Piers Harris Self-Concept Scale (PHSCS) were used in studies for assessing coping strategies. The CSI was to assess coping thoughts and behaviours that children and adolescents use to deal with stressful situations during the past month. It is a 72-item self-report questionnaire and contains 8 primary subscale items, including problem solving, cognitive restructuring, social support, express emotions, problem avoidance, wishful thinking and social withdrawal subscales. The internal consistency (α) for the subscales ranged from 0.71 to 0.94 (Tobin, 2001).

The PHSCS was designed by Piers to assess self-esteem in children between the ages of 7 and 18 years. The scale yields a general measure of the respondent’s overall self-concept, and includes six domain subscales including behavioural adjustment, intellectual and school status, physical appearance, attitudes, freedom from anxiety and happiness and satisfaction. This measure is widely used in both schools and clinical settings to determine specific areas of conflict, typical coping and defence mechanisms and appropriate intervention techniques. This scale was found to be reliable. The internal consistency (α) for the subscales ranged from 0.88 to 0.93 (Alexopoulos & Foudoulaki, 2002).

In summary, among these tools for assessing factors affecting adherence, the MAI, the TAI and the IBD-FRQ were designed specifically to assess specific barriers to adherence in children with IBD. The other assessment tools were not developed specifically for IBD patients, but are commonly used to assess knowledge and behavioural factors, psychosocial issues, family functioning and coping strategies in children and families. Understanding these tools will help FNPs to identify specific factors affecting adherence in adolescents with IBD.
Factors Affecting Medication Adherence

A literature matrix was created to analyze the twelve studies reviewed, including the above methods for measuring medication adherence and the tools for assessing factors affecting adherence (See Table 1). Literature revealed that factors affecting adherence included disease and medication-related factors, psychosocial and behavioural issues and knowledge and health beliefs about treatment and medications. These factors will be presented in the following section.

Disease and Medication-Related Factors

Four quantitative studies identified that non-adherence was related to disease activity and treatment regimens, such as patient being asymptomatic in remission (when they felt well so they might not take medications regularly), complex medication regimens (multiple daily doses and number of pills per dose), medication side effects (headache, nausea or diarrhea), or difficulty swallowing pills due to the size and taste of pills (Gray et al., 2012; Greenley, Stephens, Doughty, Raboin, & Kugathasan, 2010; Hommel & Baldassano, 2010; Hommel, Denson et al., 2011).

Greenley, Stephens et al. (2010) conducted a study to examine demographic, disease-related and treatment regimen-related factors for adherence in 64 adolescents (11-18 years old) with IBD. The goal of this study was to investigate relationships between the frequencies of barriers and levels of non-adherence. Barriers to adherence and medication adherence rates were assessed via patient and parent reports with the Medication Adherence Questionnaire. This study revealed that concerns about medication side effects and multiple daily doses of medications were common adherence barriers reported by adolescents and parents. Approximately 14% of adolescents and 19% of their parents reported concerns about medication side effects. Adolescents whose regimen involved more than one daily medication administration reported
having more barriers to adherence. Adolescents also reported discontinuing medication was due to feeling well.

The prevalence of adherence barriers in this study was not significantly associated with adolescent age, gender and time since diagnosis (in months). Findings of this study could be affected by limitations, such as use of cross-sectional data, homogeneous characteristics of participants and a small sample size (Greenley, Stephens et al., 2010).

Three other studies reported that along with complex treatment regimens and medication side effects, large pill sizes, difficulty swallowing pills and the unpleasant taste of pills were reported by adolescents to be barriers to adherence (Gray et al., 2012; Hommel & Baldassano, 2010; Hommel, Denson et al., 2011). These three studies will be discussed further in the sections on psychological/psychosocial and behavioural factors.

In addition to the above factors affecting medication adherence, the association between non-adherence and disease duration was also examined. Non-adherence was found to be associated with longer disease duration in two studies (Kitney et al., 2009; Reed-Knight et al., 2011). However, the prevalence of adherence barriers was not significantly associated with time since diagnosis (Greenley, Stephens et al., 2010).

Psychosocial Factors

The literature identified that psychosocial factors in the adolescents themselves as well as in their families affected medication adherence. Psychosocial factors such as anxiety and depressive symptoms, helplessness, dependency and low self-esteem were associated with non-adherence in adolescents with IBD (Gray et al., 2012; Hommel, Denson, et al., 2011; Leleiko et al., 2013; Mackner & Crandall, 2005). Family psychosocial distress was related to non-adherence in adolescents in the forms of parent-child conflicts, family dysfunction, poor coping
strategies and less parental involvement (Hommel, Odell et al., 2011; Mackner & Crandall, 2005; Reed-Knight et al., 2011).

**Psychosocial issues in adolescents.** In four studies, non-adherence in adolescents with IBD was found to be related to anxiety and depressive symptoms, helplessness, dependency and low self-esteem in adolescents (Gray et al., 2012; Hommel, Denson, et al., 2011; Leleiko et al., 2013; Mackner & Crandall, 2005).

Gray et al. (2012) examined the collective impact of barriers to adherence and anxiety/depressive symptoms on medication adherence in 79 adolescents with IBD. Barriers to adherence were assessed with the Medical Adherence Measure (MAM) and psychological functioning was assessed with the Child Behaviour Check List (CBCL). Results revealed that one in eight adolescents reported borderline or clinically elevated levels of anxiety/depressive symptoms. Anxiety/depressive symptoms had a negative additive impact on behavioural factors for adherence. Forgetfulness, being away from home and interference with activities were the mostly commonly reported behavioural barriers to adherence (Gray et al., 2012).

This study used multi-site data collection, which allows for the recruitment of a sample larger than typically included in paediatric IBD research. But findings might be affected by limitations, such as the cross-sectional nature of data, the relatively homogeneous sample and the use of self-report for adherence assessment (Gray et al., 2012).

Mackner and Crandall (2005) examined factors associated with poor adherence in 50 children with IBD 11-17 years of age and their parents. Patients and parents were interviewed separately with the Medication Adherence Interview. Personnel who did not provide direct medical care conducted the interviews. Self-esteem was assessed in intellectual and school status, physical appearance, popularity and behaviour. Coping strategies were assessed with a
range of thoughts and behaviours that adolescents used to deal with stressful situations.

Problems/emotional problems were assessed with the CBCL and the Children’s Depression Inventory (CDI).

This study revealed that disease-associated psychosocial distress and vulnerability, such as helplessness, dependency and low self-esteem, were identified as impediments for adherence in adolescents. There was a significant correlation between more behavioural and/or emotional problems and lower adherence (Mackner & Crandall, 2005). Although data were obtained from adolescent and parent reports, the authors used well-structured and validated assessment tools. Moreover, findings were improved with parent-child concordance, as personnel who did not provide direct medical care conducted interviews with parents and children separately.

Hommel, Denson et al. (2011) and Leleiko et al. (2013) investigated the association between behavioural and emotional problems and medication adherence. Both studies suggested that psychosocial functioning, anxiety and depressive symptoms, especially among older adolescents, substantially contributed to non-adherence. Medication adherence was assessed with different methods in these two studies. Subjective method with the MAM (adolescent and parent reports) was used in Hommel, Denson et al. (2011), while objective method with electronic medication monitoring device was used in Leleiko et al. (2013).

In Hommel, Denson et al. (2011), the relationship of barriers to adherence and adolescent behavioural functioning and psychosocial distress was examined in 62 adolescents with 5-ASA and/or 6-MP/AZA. Barriers to adherence were assessed with the MAM, using adolescent and parent reports. Psychosocial distress and psychological functioning were assessed with the CBCL and the CDI (adolescents and parents completed questionnaires). Results revealed that 15% of adolescents reported clinically elevated depressive symptoms and 24% reported
clinically elevated internalizing behavioural problems. Increased incidence of clinically significant emotional problems, particularly depression, was found to be associated with a greater number of reported barriers to adherence.

The findings from this study may be limited by a small sample size and homogeneous characteristics of participants. The majority of families in this study did not represent families of various socio-economic backgrounds, but of upper middle socio-economic class. The subjective assessment of adherence may have resulted in overestimates of adherence (Hommel, Denson et al., 2011).

In Leleiko et al. (2013), whether behavioural and emotional problems predicted non-adherence to maintenance medications was investigated in 79 adolescents. Psychosocial distress and psychological functioning were assessed with the CBCL and the CDI (adolescents and parents completed questionnaires). Results revealed that adolescents aged 15 or older had significantly lower adherence rates. Anxiety and depressive symptoms, especially among older adolescents, significantly contributed to non-adherence. A limitation to this study is that medication adherence rates derived from the electronic medication monitoring device may represent an overestimate of adherence, as this device can only document the times that it was opened, but not the actual ingestion (Leleiko et al., 2013).

**Psychosocial issues in families.** In three studies, non-adherence to maintenance medications was identified related to psychosocial distress in families, including parent-child conflicts, family dysfunction and less maternal involvement (Hommel, Odell et al., 2011; Mackner & Crandall, 2005; Reed-Knight et al., 2011).

As discussed previously, Mackner and Crandall (2005) highlighted correlation between emotional/behavioural problems and lower adherence. In particular, this study identified that
family functioning was a key dynamic affecting adherence. Parent-child concordance in reports of adherence was also examined in this study. Family functioning was assessed in the areas of problem solving, communication, roles and emotional and behavioural control. Coping strategies were assessed using the range of thoughts and behaviours that adolescents used to deal with stressful situations. Results revealed that poorer adherence was associated with family dysfunction, which included characteristics such as poor family structure, a lack of cohesion and child discipline. Better family functioning and child coping strategies were significantly correlated with medication adherence. Specifically, families with appropriate rules and consequences for behaviours had children who were more adherent. This suggests adherence should be monitored in families that lack appropriate child discipline (Mackner & Crandall, 2005).

Hommel, Odell et al. (2011) and Reed-Knight et al. (2011) both found parent-child conflicts were associated with non-adherence. However, these two studies had different foci. Hommel, Odell et al. (2011) used a qualitative individual interview approach to 16 adolescents and their parents. Parent-child dyads identified parent-child conflicts and oppositional behaviours as barriers to adherence. Despite the richness and diversity of the qualitative data obtained, the sample size was fairly modest (n=16). Parents and adolescents were interviewed together in order to encourage identification and discussion of different perspectives. While this is a substantial advantage, an important disadvantage of this approach is the potential to have adolescents defer answers and opinions to their parents and this approach may have inhibited some responses by both participants. In addition, this study was conducted during regular scheduled clinic visits, which makes prolonged interviews unfeasible.
Reed-Knight et al. (2011) used quantitative data to examine factors associated with adherence to both prescription and over-the-counter (OTC) medications. This study revealed that a lack of autonomous motivation, less maternal involvement and more perceived parent-child conflicts were associated with poor adherence to both prescription and OTC medications. Parents who perceived more conflicts in their relationship with their adolescents were less likely to promote adherence to avoid another conflict. Despite several limitations in this study, such as adolescent and parent reports of adherence, cross-sectional data and a homogeneous sample, the results are an important addition to the literature on adherence in adolescents with IBD.

Psychosocial factors affecting medication adherence summarized from the above studies included anxiety and depressive symptoms, disease-associated psychosocial distress and vulnerability such as helplessness, dependency and low self-esteem of adolescents, family dysfunction, parent-child conflicts and less maternal involvement. Psychosocial issues in both adolescents and families correlated with behavioural issues of adolescents contributing to non-adherence to IBD treatment (Mackner & Crandall, 2005).

**Behavioural Factors**

In five studies, forgetfulness was identified as the most common factor affecting adherence, followed by interference with activities, not being home and medications not being refilled (Gray et al., 2012; Hommel & Baldassano, 2010; Hommel, Denson et al., 2011; Hommel, Odell et al., 2011; Ingerski, Baldasano, Denson, & Hommel, 2010). In addition, non-adherence was found associated with behavioural function specific to levels of attention and conduct problems (Reed-Knight, Lewis, & Blount, 2013).

A study using both qualitative and quantitative data was conducted by Hommel and Baldassano (2010). The purpose of the study was to examine adolescents' and their parents'
perceived barriers to medication adherence and the relationship between non-adherence rates to perceived barriers to adherence. Sixteen adolescents with IBD and their parents participated in an open-ended interview regarding barriers to adherence using the MAM. Medication adherence was assessed with a combined method including self-reports and pill counts. The most commonly identified barriers to adherence were forgetfulness, interference with activities and not being home. Non-adherence frequency was 42% for 6-MP/AZA and 50% for 5-ASA. This study also revealed the significant correlation between non-adherence rates and perceived barriers to adherence by adolescents and their parents.

This is the only study using qualitative and quantitative data to examine barriers to adherence and the frequency of non-adherence to maintenance medications. Using mixed methods, i.e. forced choice and semi-structured, open-ended interview approach to identify factors affecting medication adherence, and a combined measurement of assessing adherence, make this study outstanding from other studies. However, responses to interview questions might have been inhibited, when adolescents and their parents were interviewed jointly. The findings are limited by the small sample size (n=16) and homogenous sample (primary Caucasian and fairly high annual incomes of the families). Therefore, generalization of these findings to ethnic minorities or individuals with lower annual incomes is limited.

Using the same participants in the study by Hommel and Baldassano (2010), Hommel, Odell et al. (2011) conducted an extensive qualitative study to examine factors affecting adherence perceived by 16 adolescents and their parents. The authors administered a qualitative individual interview during a clinic appointment, using open-ended, semi-structured questions of the TAI to elicit discussion by adolescents and parents. Adolescents and parents identified forgetfulness, interference with activities, parent-child conflicts, oppositional behaviours and
inadequate planning for medications as major factors affecting adherence. Other factors affecting adherence included poor understanding of the purpose of medications, regimen complexity, embarrassment about taking medications around peers and financial and work/school issues (Hommel, Odell et al., 2011).

This qualitative study also identified factors that could facilitate medication adherence, including family support, good parent-child relationships, calm discussion of non-adherence when it occurs, establishing a routine of taking medications, parental monitoring and reminders, keeping medications accessible and in the same location, using a pillbox, planning for medication-taking and perceived benefits of taking medications (Hommel, Odell et al., 2011).

The two studies of Hommel and Baldassano (2010) and Hommel, Odell et al. (2011) have several limitations, such as small sample size (n=16) and homogeneous characteristics of participants. Moreover, the interviews were conducted jointly in adolescents and their parents during regularly scheduled clinic appointments, which make prolonged interviews and detailed qualitative data collection unfeasible.

Behavioural function specific to attention and conduct problems was examined in relation to non-adherence in a study by Reed-Knight et al. (2013). The purpose of this study was to identify the associations between attention and conduct problems, perceived barriers to adherence and adherence to maintenance medications in 85 adolescents with IBD. This study used the validated Externalizing Clinical Scales to measure attention and conduct problems and the MAM to assess barriers to adherence. Adolescents with known attention deficit hyperactivity disorder or oppositional defiant disorder were excluded from the study sample. Results revealed that the majority of participants reported normative levels of attention and conduct problems. Attention problems and conduct symptoms (e.g., rule breaking, lying, oppositional behaviours
and low motivation) were associated with high levels of barriers and poorer medication adherence. High levels of attention and conduct problems were found to interfere with behaviours contributing to non-adherence, such as forgetfulness and poor organization and plan (Reed-Knight et al., 2013).

These findings were reported by parents but not by adolescents, suggesting that parents are more adept at recognizing behavioural problems and barriers that their children experienced, or that adolescents are less willing to acknowledge barriers. This is the only study examining the effects of attention and conduct problems on adherence in adolescents with IBD. Findings suggest that addressing attention or conduct problems in adolescents may be an effective intervention for promoting adherence. However, study limitations should be considered while interpreting and generalizing these findings, such as a subjective method of assessing adherence, homogeneous sample and the cross-sectional data.

Ingerski et al. (2010) conducted a study to identify family-reported adherence barriers to 5-ASA and 6-MP/AZA in 74 adolescents and their caregivers. Factors for medication adherence were assessed with the MAM, adherence rates were assessed with pill counts and serum assays of 6-MP/AZA. Adolescents and their caregivers jointly completed adherence barriers with the MAM. Results revealed that demographic variables were not related to adherence barriers. The most commonly reported barriers included forgetfulness, being away from home and interference with activities. Most families experienced at least one barrier to medication adherence. Significant correlations were found between total number of barriers and adherence. Fewer total numbers of barriers were related to better adherence. Strengths of this study include multi-site data collection, multiple methods of adherence assessment and inclusion of both adolescents and their caregivers. However, findings may be limited with cross-sectional and quantitative data.
Key behavioural factors for adherence summarized from the above four studies included forgetfulness, interference with activities, not being home, medications not being refilled and attention and conduct problems. Non-adherence is not only limited to behavioural problems, but also related to knowledge or concerns about maintenance treatment. Even when forgetfulness is the reason for non-adherence, knowledge and beliefs about maintenance treatment should be assessed.

Factors related to Knowledge and Beliefs

Five quantitative studies revealed that non-adherence was associated with a lack of knowledge about IBD treatment and medications, and beliefs that treatment was not necessary or medications were ineffective (Gray et al., 2012; Greenley, Stephens et al., 2013; Hommel, Denson et al., 2011; Ingerski et al., 2010; Kitney et al., 2009).

Greenley, Stephens et al. (2013) examined the adherence rates to multivitamins, iron and calcium supplements in 49 adolescents with IBD in the USA and the relationship between non-adherence and knowledge about supplements. Supplemental knowledge and adherence were assessed with the MAM. Results revealed that mean adherence rates ranged from 32% to 44% across these supplements. Approximately 25% of participants did not know the reason for supplements. Adolescents who lacked knowledge about all supplements displayed substantially poorer adherence than those with moderate or high levels of knowledge. This suggests knowledge of supplements is a predictor of adherence. Although the findings could have been affected by the subjective assessment method (self-reports on the MAM may have overestimated adherence), they still illuminate an important gap between a lack of knowledge and non-adherence. Use of multiple measures of adherence and qualitative data could have allowed for
more careful evaluation of the levels of knowledge and adherence (Greenley, Stephens et al., 2013).

The only Canadian study examining medication adherence among paediatric IBD patients was conducted by Kitney and colleagues (2009) in Edmonton, Alberta. The purpose of this study was to examine adherence rates to prescribed IBD medications, non-prescribed supplements and self-use of herbal medications and to determine factors affecting adherence in 119 IBD patients (a mean age of 13.2 ± 3.4 years). Adherence was assessed based on patient reports in a survey adapted from a published questionnaire. The questions used in the survey were designed to determine frequency and reasons for non-adherence as well as overall health awareness. Demographic data of the patients were obtained from chart reviews and an IBD patient database.

Results revealed that non-adherence was significantly associated with older adolescents (14.6 years versus 13.0 years). Approximately 10% of patients reported using herbal medicines. The use of herbal medicines was found to be related to non-adherence to maintenance medications. Moreover, results showed that non-adherence rates were found higher in those with a parent or guardian education level of high school or lower. Adherent patients reported seeing their healthcare providers more frequently than non-adherent patients. This is the only study about levels of parent education and the use of herbal medications regarding medication adherence in paediatric IBD patients. Limitations of the findings include the subjective assessment of adherence and cross-sectional quantitative data.

The other three studies identified that non-adherence was influenced by the beliefs that treatment was not necessary or medications were ineffective (Gray et al., 2012; Hommel, Denson et al., 2011; Ingerski et al., 2010). These three studies were presented in the sections of behavioural and psychosocial factors. They all examined barriers to adherence to 5-ASA and 6-
MP/AZA, based on adolescent and/or parent reports on the MAM, but each study had different foci and purposes.

Gray et al. (2012) focused on the negative additive impact of psychological issues on the relationship between barriers and adherence, and revealed that 10.1% of adolescents did not think the treatment necessary. Hommel, Denson et al. (2011) and Ingerski et al. (2010) both examined the relationship of medication adherence and perceived barriers to adherence, based on both adolescent and parent reports. Ingerski et al. (2010) also used objective methods (pill counts and serum assays of 6-MP/AZA) to assess medication adherence. Both studies found that the parents and adolescents did not believe the treatment medications were necessary.

The above studies indicated that non-adherence was associated with knowledge and beliefs about IBD treatment and medications and the education levels of parents or caregivers of adolescents with IBD. Use of herbal medications was associated with non-adherence. This may reflect a lack of confidence in or distrust of the effectiveness of prescribed maintenance medications (Kitney et al., 2009).

In summary, findings of this review implied that factors affecting adherence were complex and multi-factorial. Disease and medication-related factors were associated with the disease activity, treatment regimens and medications. Psychosocial factors were associated with anxiety and depressive symptoms, helplessness, dependency, low self-esteem of adolescents, parent-child conflicts, family dysfunction, poor coping strategies and less parental involvement. Common behavioural factors were identified as forgetfulness, interference with activities, not being home, medications not being refilled and levels of attention and conduct problems. Non-adherence was also significantly influenced by a lack of knowledge about IBD treatment and medications and beliefs of the need for treatment and medications.
In addition to these factors, two studies revealed that demographic factors, such as age, gender, ethnicity and levels of family annual income, were not significantly associated with non-adherence in adolescents with IBD (Greenley, Stephens et al. 2010; Ingerski et al., 2010). However, two other studies identified that older adolescents (15 years and older) were at greatest risk of poor adherence, compared with adolescents younger than 12 years (Kitney et al., 2009; Leleiko et al., 2013). The relationship between barriers to adherence and adherence was investigated in four studies (Greenley, Stephens et al., 2010; Hommel & Baldassano, 2010; Hommel, Denson et al., 2011; Ingerski et al., 2010).

Of the twelve studies, eleven were conducted in the United States of America and one in Canada. Methods included mixed methods, both qualitative and quantitative, in one study (Hommel & Baldassano, 2010), qualitative with individual interviews in one study (Hommel, Odell et al., 2011) and quantitative in ten other studies (Gray et al., 2012; Greenley, Stephens et al., 2010; Greenley, Stephens et al., 2013; Hommel, Danson et al., 2011; Ingerski et al., 2010; Kitney et al., 2009; Leleiko et al., 2013; Mackner & Crandall, 2005; Reed-Knight et al., 2011; Reed-Knight et al., 2013). Adherence to 5-ASA and 6-MP/AZA was also examined in five studies, with subjective and/or objective methods (Greenley, Stephens et al., 2013; Hommel & Baldassano, 2010; Hommel, Denson et al., 2011; Kitney et al., 2009; Leleiko et al., 2013). Findings of literature review about intervention strategies will be discussed in the next chapter.
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample/ Age</th>
<th>Tools to identify factors</th>
<th>Commonly Identified Factors</th>
<th>Strengths</th>
<th>Weaknesses</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gray et al. (2012)</td>
<td>Sample: n=79, Age: 13-17yr</td>
<td>Medical Adherence Measure (assessing factors and measuring adherence)</td>
<td>Forget, not being home, interference with activities, refusal/defiance, did not fill, hate</td>
<td>Multiple factors examined.</td>
<td>Homogeneous Sample.</td>
<td>Adherence was significantly lower with higher barriers</td>
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<td></td>
<td>Quantitative</td>
<td>Youth Self-Report (behavioural and emotional functioning over the past six months)</td>
<td>the taste, difficulty swallowing pill, not feeling well, belief that medications were</td>
<td>Multi-site data collected.</td>
<td>Adherence measured with Self report.</td>
<td>and higher anxiety and depressive symptoms.</td>
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<td></td>
<td>USA</td>
<td></td>
<td>unnecessary, dislike medication side effects. Anxiety/depression moderate the</td>
<td>Well-validated tools used.</td>
<td>Cross-sectional data.</td>
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<td></td>
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<td>relationship between barriers to adherence and adherence.</td>
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<td>Greenley, Stephens et al. (2010)</td>
<td>Sample: n=64, Age: 11-18yr</td>
<td>Medication Adherence Questionnaires (written format of the Medication Adherence Interview to assess adherence rate). Six questions used to assess barriers to adherence during the past one year.</td>
<td>Lack of time, medication side effects, multiple daily doses of medications, feeling well, belief that medication was ineffective. Adherence barriers were significantly higher in families reporting imperfect adherence compared to those reporting perfect adherence.</td>
<td>Adolescents and parents included.</td>
<td>Homogeneous Sample.</td>
<td>Barriers to adherence were not consistently associated with adolescent age, sex and time since diagnosis</td>
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<td></td>
<td>Quantitative</td>
<td>USA</td>
<td></td>
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<td>Cross-sectional data.</td>
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<td>Only six barriers examined.</td>
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<tr>
<td>Greenley et al. (2013)</td>
<td>Sample: n=49, Age: 11-18yr</td>
<td>Medical Adherence Measure (assessing knowledge about supplements as prescribed and measuring supplement adherence over the past one week).</td>
<td>Lack of knowledge about the reasons for supplements (multivitamin, iron and calcium regimens). Rates of non-adherence ranged from 68 to 56% cross supplements. Poorer adherence was significantly related to lower levels of knowledge across all supplements.</td>
<td>Adherence and knowledge were assessed with a validated tool.</td>
<td>Small sample size.</td>
<td>Lack of knowledge associated non-adherence to supplements as prescribed.</td>
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<tr>
<td></td>
<td>Quantitative</td>
<td>USA</td>
<td></td>
<td></td>
<td>Adolescent-reports.</td>
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<td>Focused solely on knowledge.</td>
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<td>Hommel &amp; Baldassano (2010)</td>
<td>Sample: n=16, Age: 13-17yr</td>
<td>Medical Adherence Measure (assessing factors and adherence over the past week).Treatment Adherence Interview (assessing knowledge of regimens, organizational and behavioural factors).</td>
<td>Forget, interference with activities, difficulty swallowing pill and not being home. Number of reported barriers was positively correlated with objective measure of non-adherence (pill count). Non-adherence frequency was 42% for 6-MP/AZA and 50% for 5-ASA.</td>
<td>Subjective and objective methods of adherence assessment. Quantitative and qualitative data for assessing factors. Inclusion of patients and parents.</td>
<td>Homogeneous Sample.</td>
<td>Use a combined approach to adherence assessment. Use quantitative and qualitative data to assess factors affecting adherence.</td>
</tr>
<tr>
<td>Study</td>
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<tr>
<td>Hommel, Denson et al. (2011) Quantitative USA</td>
<td>Sample n=62 Age: 13-17yr</td>
<td>Medical Adherence Measure. Child Behaviour Check List Youth Self-Report Children’s Depression Inventory.</td>
<td>Forget, not being home, interference with activities, refusal/defiance, did not fill, not feeling well, belief that medication was unnecessary, difficulty swallowing pill, hate the taste. Perceived barriers to adherence were related to non-adherence and increased behavioural and emotional problems (oppositional behaviours, depression and anxiety, etc.)</td>
<td>Inclusion of adolescents and parents. Heterogeneous sample.</td>
<td>Subjective measure of assessing adherence.</td>
<td>Oppositional behaviours, depression and anxiety are potential factors affecting adherence.</td>
</tr>
<tr>
<td>Hommel, Odell et al. (2011) Qualitative USA</td>
<td>Sample n=16 Age: 13-17yr</td>
<td>Treatment Adherence Interview (assessing knowledge of regimens, organizational and behavioural factors).</td>
<td>Forget, interference with activities, a lack of planning ahead for medication-taking, difficulty swallowing pills, child oppositional behaviours, embarrassment about taking medications with peers, regimen complexity, limited knowledge about IBD, treatment and medications, parent-child conflicts.</td>
<td>A semi-structured open-ended interview. Inclusion of patients and parents.</td>
<td>Homogeneous Sample. Small sample size.</td>
<td>Family support and good parent-child relationships, parental monitoring and reminders were highly valued.</td>
</tr>
<tr>
<td>Ingerski et al. (2010) Quantitative USA</td>
<td>Sample n=74 Age: 13-17yr</td>
<td>Medical Adherence Measure (assessing barriers to adherence and measuring adherence in the past one week).</td>
<td>Forget, not being home, interference with activities, refusal/defiance, did not fill, not feeling well, belief that medication was not necessary. Fewer total reported barriers was related to better adherence. Demographic was not related to the total number of reported barriers.</td>
<td>Subjective and objective (pill count, serum assay) methods of assessing adherence. Multi-site data collections. Adolescents and parents included.</td>
<td>Homogeneous Sample. Cross-sectional data.</td>
<td>Total number of barriers was significantly correlated to adherence.</td>
</tr>
<tr>
<td>Kitney et al. (2009) Quantitative Canada</td>
<td>Sample n=119 Mean age: 13.2±3.4</td>
<td>A survey (published questionnaire with 24 domains to determine frequency and reasons for non-adherence to IBD prescribed medications, vitamins and complementary medicines in the past three months)</td>
<td>Forget, feeling better, too many medications, lower level of parent education, multiple daily doses and infrequent clinic visits. Non-adherence was significantly associated with older age (14.6 yr versus 13.0 yr), longer disease duration, and use of herbal medications, but not demographics (gender, place of residence, ethnicity or first language).</td>
<td>Descent sample size. Heterogeneous sample.</td>
<td>One subjective measure of adherence. Cross-sectional data.</td>
<td>Pay attention to use of herbal medications in IBD patients, educate them the possible drug interactions.</td>
</tr>
</tbody>
</table>
Table 1. (Continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample/Age</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Leleiko et al. (2013)</td>
<td>Sample n=79 Age: 8-17.5yr</td>
<td>Child Behaviour checklist. Children's Depression Inventory. Multidimensional Anxiety Scale for Children.</td>
<td>Adolescents aged 15 yr or older had significant lower adherence rates to 5-ASA and 6-MP/AZA compared with younger adolescents. Behavioural and emotional issues were significantly related to non-adherence.</td>
<td>Use of medication electronic monitoring devices as a single measure of adherence.</td>
<td>Screen for emotional and behavioural problems, especially among older adolescents.</td>
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<tr>
<td>Mackner &amp; Crandall (2005)</td>
<td>Sample n=50 Age: 11-17yr</td>
<td>Parents completed medication adherence interview, the Child Behaviour Checklist, Family Assessment Device and demographics questionnaires. Separately, adolescents completed medication adherence interview, the Piers Harris Self-Concept Scale, Children's Depression Inventory and Coping Strategies Inventory questionnaires.</td>
<td>Family dysfunction, child poor coping strategies and behavioural/emotional problems were significantly associated with non-adherence. Demographic and treatment regimen factors were not associated with non-adherence. The rates of non-adherence were 52% adolescent reported and 62% parent reported.</td>
<td>Well-validated measures of behavioural and emotional issues. Study over a 6-month period.</td>
<td>Use of interview as a sole measure of adherence.</td>
<td>Monitor family dysfunction, adolescent behavioural and emotional problems, poor coping strategies and consider psychotherapy.</td>
</tr>
<tr>
<td>Reed-Knight et al. (2013)</td>
<td>Sample n=85 Age: 11-18yr</td>
<td>Medical Adherence Measure (assess adherence over the past one week), Parent/Adolescent Medication Barriers Scales (assessing parent- and adolescent-reported barriers) Behaviour Assessment System for Children (assessing attention and conduct problems by parents).</td>
<td>Attention problems and conduct symptoms (e.g., rule breaking, lying) interfered with adherence. Barriers to adherence included forgetfulness, poor organization/planning, being busy, relying on a parental reminder. Barriers mediated the effects of attention and conduct problems.</td>
<td>Inclusion of parent and adolescent. Validated questionnaire measuring attention and conduct problems.</td>
<td>Subjective measure of adherence. Homogeneous sample. Cross-sectional data.</td>
<td>Barriers to adherence contribute to the relationship between attention and behavioural problems and adherence.</td>
</tr>
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</table>
Chapter Four: Intervention Strategies to Improve Medication Adherence

Given the high rates of non-adherence in adolescents with IBD and its significant impacts on individual health outcomes and healthcare costs, development and implementation of intervention strategies to target specific factors affecting adherence is imperative. For this purpose, a total of eight studies were retrieved and reviewed to answer the second research question: “What are the intervention strategies that FNPs can use to promote oral medication adherence in adolescents with IBD?”

Literature is limited on intervention strategies for non-adherence in adolescents with IBD. Of the eight studies, four were focused on adolescents aged 11 to 18 years with smaller sample sizes. Four other studies were focused on adult patients and adolescents aged 17 years and older. These four studies involved older adolescent patients and had larger sample sizes. Therefore, they were included to provide a broader research-based evidence of intervention strategies.

Among the eight studies, one study was conducted in Canada (Waters, Jensen, & Fedorak, 2005), one in Denmark and Ireland (Elkjaer et al., 2010), one in the United Kingdom (Moshkovska, Stone, Smith, Bankart, Baker, & Mayberry, 2011) and five in the USA (Cook, Emiliozzi, El-Hajj, & McCabe, 2010; Greenley et al., 2011; Hommel, Herzer et al., 2011; Hommel et al., 2012; Hommel, Hente, Herzer, Ingerski, & Denson, 2013).

The intervention strategies provided in these studies included behavioural, psychosocial, educational and multi-component interventions. These interventions were justified with the factors identified in the previous literature review (See Chapter three), because they targeted disease and medication-related factors (such as complex dosing regimen, adverse effects of medications), psychosocial issues (such as depression, anxiety, psychosocial distress, low
motivation), behavioural problems (such as forgetfulness, oppositional behaviours) and a lack of knowledge about the disease, maintenance treatment and medications.

Multi-component intervention strategies were evaluated in four studies (Hommel et al., 2012; Hommel, Hente et al., 2013; Hommel, Herzer et al., 2011; Moshkovska et al., 2011). No study was found to evaluate behavioural interventions as a single intervention strategy. Instead, behavioural interventions were provided as part of multi-component interventions. Psychosocial interventions were provided as a single strategy in two studies (Cook et al., 2010; Greenley et al., 2011). Educational interventions were provided as a single strategy in two studies (Elkjaer et al., 2010; Waters et al., 2005).

Adherence interventions, methods of adherence assessment, intervention outcomes of each study, along with its strengths and weaknesses were examined and presented in Table 2. Multi-component interventions will be presented first, followed by behavioural interventions, psychosocial interventions and educational interventions.

**Multi-component Interventions**

Multi-component intervention strategies combined educational, behavioural, or psychosocial interventions (Greenley, Kunz, Walter, & Hommel, 2013). These interventions focused on behavioural and emotional problems, a lack of knowledge and psychosocial issues of adolescents and families, which were identified associated with non-adherence and reviewed in Chapter three. Given that factors affecting medication adherence are complex and multi-factorial in adolescents with IBD, using multi-component interventions was reasonable.

Four studies provided the evidence to support the efficacy of multi-component interventions on adherence in adolescents with IBD (Hommel et al., 2012; Hommel, Hente et al., 2013; Hommel, Herzer et al., 2011; Moshkovska et al., 2011). Approaches to multi-component
interventions were different in these four studies, depending on the purpose of each study. An individually tailored intervention was delivered in a clinical setting in Hommel, Herzer et al. (2011). An individually tailored intervention was delivered through online Skype in Hommel, Hente et al. (2013). A family-based group intervention was provided in a clinical setting in Hommel et al. (2012). In these three studies, multi-component interventions were delivered by doctoral level clinical psychologists or postdoctoral psychology fellows. A one-on-one education and motivation program was provided by the researchers (Moshkovska et al., 2011).

Hommel, Herzer et al. (2011) conducted a pilot randomized trial in a clinical setting to evaluate the feasibility, acceptability and efficacy of an individually tailored, multi-component approach that targeted educational, behavioural and psychosocial factors related to adherence. These multi-component interventions focused on educational and behavioural interventions, problem solving skills and adolescent/family psychosocial support. Fourteen adolescents with IBD aged 11 to 18 years were randomly assigned to an immediate care group or a wait list control group. Patients in the immediate care group attended four weekly intervention sessions, each session lasting 60-75 minutes. The interventions were provided by doctoral-level clinical psychologists or postdoctoral fellows. Medication adherence was measured with pill count at each visit.

Results revealed that improvements in adherence were substantially better for 5-ASA (mesalamine) than for 6-MP/AZA, with an increase of 4% of adherence to 6-MP/AZA and an increase of 25% of adherence to 5-ASA. The 100% retention rate of patients indicated the four-session interventions were a feasible approach for improving adherence. Additionally, the interventions were rated favourably in terms of acceptability by both patients and parents,
suggesting that a multi-component individually tailored approach is a viable intervention strategy.

Hommel et al. (2012) conducted a randomized-controlled trial of a family-based group intervention in 40 adolescents with IBD aged 11-18 years. They provided similar multi-component interventions used in Hommel, Herzer et al. (2011), including educational and behavioural interventions, problem solving skills and adolescent/family psychosocial support. These interventions targeted educational, behavioural and psychosocial factors related to adherence, and were delivered in a clinical setting. The purpose of this trial was to evaluate the feasibility, acceptability and efficacy of a family-based group approach to multi-component interventions to improve medication adherence.

Forty adolescents with their parents were randomly assigned to a family-based intervention group (n = 20) and a usual care group (n = 20). Participants in the intervention group attended four weekly family-based group intervention sessions led by doctoral level clinical psychologists or postdoctoral psychology fellows. Patients in the control group received standard care over a 6-week period. There were no significant differences between the two groups at baseline across demographic, disease activity and adherence parameters. Medication adherence to 5-ASA (mesalamine) and 6-MP/AZA was assessed with adolescent and parent reports, pill count and electronic medication monitoring.

Results revealed no significant differences between the intervention and usual care groups from baseline to post intervention assessments across pill counts, electronic monitor and parent-reported adherence. From adolescent-reports, there was no significant difference for adherence to 6-MP/AZA between the two groups, but there was a significant increase (25%) in 5-ASA adherence in the intervention group, whereas there was only a 1% increase in 5-ASA
adherence in the usual care group. Excellent feasibility was demonstrated by the 99% attendance in the intervention group. The intervention was also highly acceptable to both patients and parents, as evidenced by 70-100% reporting a high degree of acceptability.

This trial utilized a multi-method, multi-informant assessment approach to compensate for the limitations of each measure. However, the findings are limited by the small sample size and homogenous sample. There were some unseen challenges for using electronic monitor devices in participants, which could affect the adherence results. High baseline levels of adherence across self-report assessment might have prevented significant differences in adherence between the two groups (Hommel et al., 2012).

Hommel, Hente et al. (2013) conducted a single-arm pilot clinical trial in adolescents with IBD. They provided the same intervention strategies used in Hommel, Herzer et al. (2011), i.e. an individually tailored, multi-component intervention approach that targeted educational, behavioural and psychosocial factors related to adherence. The multi-component interventions included educational and behavioural interventions, problem solving skills and adolescent/family psychosocial support. But the interventions were delivered through tele-health (skype) with patients and families, not through clinic visits. The purpose of this trial was to evaluate the feasibility, acceptability and preliminary efficacy of this tele-health-based approach to improve medication adherence and reduce costs.

Nine adolescents with IBD aged 11-18 years and their parents completed four weekly intervention sessions, each session lasting 60-90 minutes though Skype and webcam. Patients and parents were seen independently, without other families present. Interventions were provided by doctoral-level clinical psychologists or postdoctoral clinical psychology fellows. Each patient was treated by the same clinician for the duration of their treatment. Medication adherence to 5-
ASA and 6-MP/AZA was measured with pill count over the telephone at baseline and post-intervention time points. Baseline and post-treatment measures were completed by participants and were mailed to study staff.

Results revealed that there was a marked increase in 5-ASA adherence from 62% at baseline to 91% post intervention. But, adherence to 6-MP/AZA decreased modestly from 61% to 53% post intervention. The feasibility was indicated by 100% attendance for all participants in the trial. Acceptability ratings by patients and parents were highly favourable and ratings of convenience were high, with 78% of patients and parents providing ratings in the ideal range. Utilizing this tele-health approach resulted in a per-patient cost savings of over $100 and more than 4 hours of travel time over the course of treatment. Findings suggest that a tele-health approach to individually tailored, multi-component interventions is feasible, acceptable and shows preliminary efficacy of improving medication adherence.

Both Hommel, Herzer et al. (2011) and Hommel, Hente et al. (2013) had similar limitations, such as small sample size, homogeneous sample and a single measure for adherence assessment (pill count). The two studies revealed a better improvement in adherence to 5-ASA than to 6-MP/AZA. The discrepant effects of the two medications may suggest there is an unknown barrier to 6-MP/AZA adherence. This may also be related to the difference in regimen complexity of these two medications (6-MP/AZA usually requires 2-3 times daily and 5-ASA requires once daily). However, the findings of these two studies imply that individually tailored, multi-component interventions, delivered either via tele-health or in a clinical setting, are feasible, acceptable and effective in promoting medication adherence.

Similar multi-component interventions were provided and delivered with different approaches in the above three studies (Hommel, Herzer et al., 2011; Hommel et al., 2012).
Hommel, Hente et al., 2013). These studies revealed the feasibility, acceptability and efficacy of multi-component interventions to improve medication adherence in adolescents with IBD, either an individually tailored approach in a clinical setting, via Skype, or a family-based group approach in a clinical setting.

Moshkovska et al. (2011) conducted a study among 71 patients aged 18 to 80 years on 5-ASA for maintenance treatment of UC. The purpose of this study was to evaluate the impact of multi-faceted interventions on adherence to 5-ASA in patients with UC, changes in health beliefs and satisfaction with information. The interventions included educational, motivational and behavioural components tailored to patient preferences. Patients in the intervention group attended a one-on-one education and motivation session conducted by the researchers. They were also offered up to three practical adherence enhancing interventions, including simplifying of dosing regimen (if clinically appropriate), medication reminder charts, visual medication reminders, daily/weekly electronic pillbox organizers, or mobile telephone alarm set-up. Patients in the control group received standard prescribed care from their clinical team.

Medication adherence was objectively assessed based on the levels of urinary 5-ASA and N-acetyl-5-ASA concentration at baseline, mid-study (24 weeks) and at the end of study (48 weeks). Disease flare-up data were collected from medical records during the study period. A flare-up was defined as an unscheduled hospital appointment or admission related to UC. Changes in health beliefs and satisfaction with information were measured using validated questionnaires. Results revealed that at follow-up adherence in the intervention group was 44% greater than in the control group. Changes in questionnaire scores suggested a positive effect of these combined interventions on patient knowledge, satisfaction with information and greater adherence in the intervention group.
Although it is difficult to accurately assess the contribution made by the various components of multi-faceted interventions, this study suggested combining interventions tailored to individual preference of practical reminders was an effective way of improving adherence to 5-ASA. There are several limitations to this study, such as a relatively small sample size and a single measure used for adherence assessment. This study was focused on patients aged 18 years and older. It is difficult to know whether these interventions would apply directly to adolescents who are 17 years and younger. Further studies exploring the impact of this approach to adolescents with IBD are therefore required.

**Behavioural Interventions**

Behavioural interventions aim to reinforce medication adherence by providing practical strategies, include using different type of reminder systems, daily/weekly pillbox organizers, development of behavioural contracting or reward systems. Dosage simplification was considered one component of behavioural interventions (Greenley, Kunz et al., 2013). Behavioural interventions were provided in conjunction with other interventions in three studies using multi-component interventions (Hommel, Herzer et al., 2011; Hommel et al., 2012; Moshkovska et al., 2011). These studied were reviewed in the above section on multi-component interventions.

In Moshkovska et al. (2011), three practical strategies: were used, including simplifying of dosing regimen (if clinically appropriate), medication reminder aids (charts, visual and audio reminders), or use of daily/weekly electronic pillbox organizers. These practical interventions targeted forgetfulness and complex medication regimens. As part of multi-component interventions, these practical interventions were tailored to an individual preference that may have played a role in the significant improvement to adherence to 5-ASA in this study.
In addition to these practical interventions, development of behavioural contracting or reward systems was also provided in multi-component interventions in Hommel, Herzer et al. (2011) and Hommel et al. (2012). Behavioural contracting or reward systems targeted on adolescents who had attention conduct problems, low motivation, or oppositional behaviours. These studies demonstrated that behavioural contracting and reward systems, when used appropriately in combination with other interventions, contributed to improvement of adherence. These were particularly helpful for adolescents with oppositional behaviours and/or low motivation to adhere to medications.

Behavioural factors were identified correlated to other factors contributing to non-adherence, such as psychosocial factors or a lack of knowledge about the disease, treatment regimens and medications. Psychological issues affected the relationship between behavioural factors and medication adherence (Gray et al., 2012; Mackner & Crandall, 2005). Therefore, behavioural interventions were provided in combination with psychosocial or educational interventions to improve medication adherence in adolescents with IBD.

**Psychosocial Interventions**

Psychosocial interventions included cognitive-behavioural interventions and problem-solving skills training to support adolescents and families. Cognitive-behavioural interventions enhanced adherence by altering thinking patterns that contributed to non-adherence while also establishing behavioural patterns that supported adherence using behavioural intervention strategies (Greenley, Kunz et al., 2013). Psychosocial interventions were provided as a single intervention strategy in two studies (Cook et al., 2010; Greenley et al., 2011). They were also provided in multi-component interventions in three other studies (Hommel, Herzer et al., 2011; Hommel et al., 2012; Hommel, Hente et al., 2013).
Cook et al. (2010) conducted a preliminary test of telephone nurse counselling to address cognitive and emotional barriers to medication adherence in 278 patients with UC aged 18 years and older. The purpose of this study was to evaluate the effects of motivational interviewing and cognitive-behavioural techniques (CBT) on adherence to 5-ASA (mesalamine). Interventions were delivered by a registered nurse (RN) who received training on CBT and motivational interviewing counselling techniques. During phone calls, the RN assessed adherence and offered interventions, using motivational interviewing questions to reduce ambivalence about treatment, and using CBT to address negative beliefs about treatment and help patients cope with adverse drug effects.

All participants received telephone follow-ups. On average, two more calls from the RN were made at different times on different days of the week. Written materials that addressed cognitive barriers (e.g., information about UC and 5-ASA) or emotional barriers to adherence were mailed to participants. The referring healthcare provider received a progress note after each call, noting the participant's adherence level and any concerns. Up to 6 months, adherence to mesalamine was measured by a structured interview and was compared to mesalamine adherence of an expected population rate using a binomial test. After 6 months patients at low-risk for non-adherence were called once and patients at high risk for non-adherence received additional calls from the same RN.

Disease and medication-related factors were tackled through the interventions. The RN addressed adverse effects of medications and symptoms associated with the disease activity, helped patients cope with these issues and effectively communicate with healthcare providers about their concerns. Results revealed that patients' 6-month adherence was significantly higher than the expected rate in a similar population. This study suggested telephone nurse counselling
to address cognitive and emotional barriers was feasible to improve mesalamine adherence in patients with UC. Because this was a pilot study and used self-report data for adherence assessment, results require further confirmation in a randomized control trial with more objective adherence data.

Greenley et al. (2011) conducted a randomised trial to evaluate the acceptability and feasibility of a phone-delivered problem-solving skills training (PSST) intervention to reduce adherence barriers and improve adherence to maintenance medications in adolescents with IBD. PSST consisted of teaching families a structured approach to defining problems and generating and evaluating solutions. Thirty-three participants (parent-child dyads or triads) were randomised to either to immediate treatment and a wait list comparison (control) group. In the immediate group, 15 adolescents aged 11-18 years and their parents completed a baseline assessment of adherence barriers, as well as assessments at the midway point and post intervention. Those in the immediate treatment group received four phone intervention sessions.

Medication adherence was assessed with electronic monitoring. Knowledge about IBD, management regimens and family problem solving skills were assessed with patient and family reports. Compared with the control group, medication adherence was significantly improved in the immediate group. More than 70% of parents and adolescents indicated increased knowledge about IBD and management regimens, improved family problem solving skills, and the intervention helped them to identify barriers to adherence. Moreover, 78% of parents and 80% of adolescents reported plans to use solutions generated in PSST in medication regimen management. Findings were limited by the homogeneous and small size sample. However, data were analyzed both subjectively (patient/family reports) and objectively (electronic monitoring).
This study supports a phone-delivered PSST as an acceptable and feasible method of intervention to reduce adherence barriers and improve adherence in adolescents with IBD.

**Educational Interventions**

A lack of knowledge about the disease, treatment regimens or medications was identified to be associated with non-adherence in adolescents with IBD. Educational interventions aim to improve patient knowledge of the disease, treatment regimens and mechanisms of medications, enhance patient motivation and increase their awareness of consequences of non-adherence (Greenley, Kunz et al., 2013). Educational interventions were provided either as a single strategy or as part of multi-component intervention strategies.

The effects of educational interventions as a single intervention strategy were evaluated in two studies, but with different formats of education (Elkjaer et al., 2010; Waters et al., 2005). Waters et al. (2005) provided a formal IBD education program designed and delivered by a gastroenterology nurse practitioner in a clinical setting. Elkjaer et al. (2010) provided web-based specific education and constant care using e-health resources.

A formal educational intervention was developed and evaluated by Waters et al. (2005). The purpose of this study was to assess the effects of increased knowledge on medication adherence in patients with IBD aged 17 and older. Sixty-nine patients were randomly assigned to a formal IBD education group (n = 38) or standard of care group (n = 31). Patients in the formal IBD education group, in addition to standard of care, attended a 12-hour, structured education program provided in 3-hour blocks over four consecutive weeks. Patients in the standard of care group were provided with educational pamphlets and regular physician education.

Medication adherence was assessed with self-reports. Knowledge was assessed in diet, gut anatomy and physiology, general IBD knowledge, complications and medications.
Healthcare use was assessed with records of physician visits and hospital admissions related to IBD and the associated complications. Patient satisfaction with medical care and the education program was assessed with questionnaires.

Results revealed that the formal IBD education group had a lower rate of non-adherence and healthcare use compared to the standard of care group, but the differences were not significant. The education group demonstrated significantly higher knowledge scores compared to the standard of care group. Patients' satisfaction ratings were high for both groups, but the education group had a significantly greater degree of patient satisfaction. Findings of this study may be limited by the subject reports as a sole measure of adherence and time constrains on part of patient and provider.

Elkjaer and colleagues (2010) evaluated the effects of web-based specific IBD education on medication adherence, disease outcomes and healthcare costs. This study was undertaken in Denmark and Ireland. A total of 333 patients aged 18 to 69 years on 5-ASA maintenance treatment for UC participated. Patients were randomized to either a web-based group (n =169) or a control group (n = 164). Patients in the web-group were provided access to a 3-hour, web-guided specific education session about IBD aetiology, pathology, disease course, adherence and complications of IBD. Patients in the control group continued the conventional treatment and follow-ups in the IBD outpatient clinic. Patients in the two groups could contact the web-doctor by e-mail, text messages or phone calls.

Medication adherence was assessed with refilling of medications from the e-prescription pharmacy database. At 12 months, adherence was improved significantly in web-patients. More than 88% of the web patients found this new approach feasible and wanted to continue using it. At the end of the trial, a significant improvement in IBD knowledge and medication adherence
was observed in the web group compared to the control group. No significant difference in relapse frequency was observed between the two groups during the study period, but median days of relapses in the web group were of a shorter duration than in the control group.

The number of visits to the outpatient clinic was significantly lower in the web than in the control group. Moreover, during 12 months web-patients contacted the web doctor more often than control-patients. The numbers of contacts were converted into a saving of 189 euro per patient per year for the out clinic (about 265 Canadian dollars per patient per year). The strengths of this study include large sample size, multi-component, multisite data collection and a longer period of study. Results of medication adherence may be limited by using an objective assessment as a single measure. Findings indicate the web-guided approach is feasible and cost effective in improving adherence to maintenance medications in UC. This web-based, specific IBD educational intervention was targeted to older adolescent and adult patients, but might not be appropriate for younger adolescents.

In summary, intervention strategies for improving medication adherence aimed to target multi-factorial barriers to adherence, such as complex treatment regimens, medication side effects or adverse drug events, emotional and behavioural problems, problem solving skills, knowledge about the disease, treatment and medications. Educational, psychosocial, behavioural or multi-component interventions were delivered individually or in a group setting, via telephone calls, websites, or during clinical visits. Compared with group-based interventions that focus on issues shared by multiple families, an individually tailored intervention provides more time for individualized problem solving of families' unique barriers. A multi-component individually tailored approach appears a promising intervention option.
Findings of the review are limited by the paucity of literature. However, they provide implications for the role of FNPs in promoting medication adherence. Discussion of implications and recommendations for FNP practice, education and research will be provided in next chapter.
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (n)</th>
<th>Adherence interventions</th>
<th>Methods of adherence assessment</th>
<th>Intervention outcomes</th>
<th>Strengths</th>
<th>Weaknesses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook et al. (2010) USA</td>
<td>n= 278 Age: 18 yr and older, UC</td>
<td>Telephone counselling conducted by a RN who used cognitive-behavioural techniques and motivational interviewing, reinforced with written follow-up materials that were sent to patients (M= 2.1 calls).</td>
<td>Patient report with structured interview. 5-ASA</td>
<td>Overall, participants’ 6-month adherence was significantly higher than the expected population rate. Self-efficacy predicted adherence, not demographic and clinical variables did not.</td>
<td>Large sample size. Multi-component strategies. Telephone counselling inexpensive and feasible, reduces patient travel.</td>
<td>Pre-post design, with no control group. Increase workload for RNs. RNs received special training.</td>
</tr>
<tr>
<td>Elkjaer et al. (2010) Denmark and Ireland</td>
<td>n= 333 Age: 18-69 yr, UC</td>
<td>Web-based intervention strategy. Patients in a web-group (web-guided approach via <a href="http://www">www</a>. constant-care.dk) received constant care with specific education and self-treatment for 12 months. Interaction with a physician through e-mail, text messages or phone was also provided. Patients in a control group continued the usual care.</td>
<td>E-pharmacy database for adherence to 5-ASA maintenance therapy.</td>
<td>Medication adherence, IBD knowledge was significantly improved in the web-group patients. Median relapse duration was 18 days in the web group versus 77 days in the control group. The number of visits to the outpatient clinic was lower in the web than in the control group, resulting in a saving of 189 euro/patient/year.</td>
<td>Large sample size. Multi-component, multisite RCT. Wide age range and large sample size. Education and feedback on IBD symptoms using an automated system reduced provider burden.</td>
<td>Significant cost associated with use of automated tracking system.</td>
</tr>
<tr>
<td>Greenley et al. (2011) USA</td>
<td>n= 31 Age: 11-18 yr, IBD</td>
<td>Phone-delivered cognitive behavioural problem-solving skill training (PSST) intervention (2 phone sessions). PSST consists of teaching patients and parents a structured approach to defining problems and generating and evaluating solutions.</td>
<td>Electronic monitoring, patient and parent reports.</td>
<td>Increased knowledge of IBD and treatment regimen, improved families’ problem solving skills, helped to identify adherence barriers and plan to use solutions generated in PSST.</td>
<td>Randomized trial. Multiple measures of adherence. Telephone delivered intervention reduces patient travel.</td>
<td>Small sample size, single method of adherence, interventionists had psychology background.</td>
</tr>
<tr>
<td>Hommel et al. (2011) USA</td>
<td>n= 14 Age: 11-18 yr IBD</td>
<td>Four weekly sessions of family-based individually tailored multi-component interventions, targeting educational, organizational, behavioural and family factors (problem solving skills and adaptive family functioning), each session 60-75 minutes.</td>
<td>Pill count. Patient and parent report, 5-ASA 6-MP/ASA</td>
<td>Adherence to 6-MP in intervention group significantly increased compared with controls, but no significant difference in adherence to 5-ASA. Intervention resulted in a 4% gain of adherence in 6-MP/ASA and a 25% gain in 5-ASA from baseline to post-intervention.</td>
<td>Randomized trial. Subjective and objective methods of adherence assessment.</td>
<td>Small sample size, lack of socioeconomic and ethnic diversity, interventionists had graduate-level training in psychology.</td>
</tr>
<tr>
<td>Study</td>
<td>Sample (n)</td>
<td>Age (yr)/ Diagnosis</td>
<td>Adherence interventions</td>
<td>Methods of Adherence assessment</td>
<td>Intervention outcomes</td>
<td>Strengths</td>
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<tr>
<td>Hommel et al. (2012)</td>
<td>n= 40</td>
<td>Age: 11-18 yr IBD</td>
<td>Four weekly sessions of group-based multi-component interventions, targeting educational, organizational, behavioural and family factors (problem solving skills, adaptive family functioning) over 6 weeks, each session 60-90 minutes.</td>
<td>Patient and caregiver report, pill count, electronic monitoring. 5-ASA 6-MP/AZA</td>
<td>Adherence rates increased from 66% to 89% for 6-MP/AZA and 51% to 93% for 5-ASA across assessment methods. Patient reported a significant improvement in adherence to 5-ASA, but not significant for 6-MP/AZA.</td>
<td>Randomized trial, with family-based intervention and usual care groups. Multiple methods of adherence assessment.</td>
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<tr>
<td>The USA</td>
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<tr>
<td>Hommel et al. (2013)</td>
<td>n= 9</td>
<td>Age: 11-18 yr IBD</td>
<td>Individually tailored intervention through tele-health delivery (online Skype and webcam), targeting educational, organizational, behavioural and family psychosocial factors. Four weekly sessions, each 60-90 minutes.</td>
<td>Patient and caregiver report, pill count, 5-ASA 6-MP/AZA</td>
<td>Adherence increased from 62% at baseline to 91% for 5-ASA, but decreased slightly from 61% to 53% for 6-MP/AZA.</td>
<td>Subjective and objective methods of adherence assessment.</td>
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<tr>
<td>USA</td>
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<tr>
<td>Moshkovska et al. (2011)</td>
<td>n= 71</td>
<td>Age: 18-80 yr UC</td>
<td>Tailored patient preference intervention over 48 weeks, including educational and motivational components, options of simplified dosing regimen and practical reminders.</td>
<td>Urinary 5-ASA levels. 5-ASA 6-MP/AZA</td>
<td>Adherence in the intervention group was 44% greater than in the control group, but no significant difference in the two groups. Intervention group status had a significant positive impact on maintaining adherence levels.</td>
<td>Randomized trial, intervention group (one-on-one) and control group (standard care), conducted by the researchers.</td>
</tr>
<tr>
<td>The United Kingdom (UK)</td>
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<tr>
<td>Waters et al. (2005)</td>
<td>n= 69</td>
<td>Age: 17yr and older IBD</td>
<td>Formal education intervention in 3-hour blocks over 4 consecutive weeks, including general information about IBD, treatment and group discussion of worries and concerns. Individual dietary counselling. Assessment of knowledge of IBD and quality of life at baseline, immediately and 8 weeks post-education.</td>
<td>Survey, validated questionnaires, patient self report.</td>
<td>The intervention group had significantly higher knowledge scores, significantly greater degree patient satisfaction and a lower rate of medication adherence, but no significant difference. Increased healthcare use significantly correlated with poorer medication adherence.</td>
<td>Randomized trial, intervention group (education with standard care) and control group (standard care). Education program designed and provided by nurse practitioner.</td>
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</table>
Chapter Five: Implications and Recommendations

This paper was an initial review of factors affecting medication adherence in adolescents with IBD and intervention strategies to improve medication adherence. To explore the role of FNPs in promoting medication adherence, implications and recommendations for FNP practice, education and research will be discussed.

Implications and Recommendations for FNP Practice

Findings from the reviews have implications for FNPs to engage in collaborative practice within a multidisciplinary team, and apply the BPS model to support the psychosocial wellbeing of adolescents and families. A stepwise approach to medication adherence is recommended, including measuring adherence, identifying factors affecting adherence and implementing individualized interventions targeting specific factors.

Engaging in Collaborative Practice

A team that may include paediatricians, gastroenterologists and nutritionists primarily cares for children and adolescents with IBD. Other healthcare professionals may also be involved, such as psychiatrists, gastrointestinal nurse specialists, social workers, or adjunctive paediatric subspecialists, such as rheumatologists, ophthalmologists, dermatologists and endocrinologists (Bousvaros & Leichtner, 2014). Although maintenance medications for IBD are initiated by specialists or physicians, according to the Scope of Practice for Nurse Practitioners (CRNBC, 2012), FNPs are able to continue prescribing 5-ASA and 6-MP/AZA, and provide continuity of support and care to adolescents and families based on the longitudinal relationship they have with patients and families in a primary care setting. FNPs have a role in promoting medication adherence in collaborative practice. They need to collaborate and consult with
physicians, specialists, psychiatrists and other healthcare professionals, and work with nurses, pharmacists together in a multidisciplinary team to manage medication adherence.

Given the role in primary care, FNPs can be important resources to facilitate and encourage optimal medication adherence. Through follow-up visits for adolescents who are stable and/or require medication monitoring, FNPs are able to assess adolescents who are non-adherent or at risk for non-adherence, identify factors affecting medication adherence, monitor medication side effects, adverse effects or drug toxicity, provide interventions to maximize medication adherence and assist patients to optimize health outcomes. Through engagement in collaborative practice in a multidisciplinary team, FNPs can serve as a liaison between patients/families and healthcare providers, consulting physicians, specialists and other healthcare professionals and referring patients to other professionals for early interventions as needed.

**Applying the BPS Model**

Given the significant of psychosocial issues associated with IBD and non-adherence in adolescents with IBD, applying the BPS model will facilitate FNPs to manage medication adherence. Psychological issues influence adolescents and parents’ coping strategies and problem-solving skills and affect quality of life and medication adherence (Mackner & Crandall, 2005). The interactions between disease and medication-related factors and psychosocial issues should be integrated into the assessment of medication adherence. FNPs need to understand the interplay between psychosocial issues and maladaptive behaviours and coping strategies, and explore how adolescents deal with stressful situations. FNPs need to have knowledge about the appropriate tools to assess the psychological functioning of adolescents and families.

Family is undisputed as the primary social context for children. Parent-child conflicts, family dysfunction, poor coping strategies and less parental involvement affect medication
adherence among adolescents with IBD (Mackner & Crandall, 2005). Parents may continue to assume full responsibility for their adolescent’s medical management, which may conflict with the adolescent’s desire to develop independence, resulting in parent-child conflicts. On the other hand, parents may turn full responsibility over to the adolescent. The adolescent may stop taking medications unknown to the parents, if he fails to see the consequences of not taking maintenance medications.

Therefore, FNPs need to assist parents and adolescents to share responsibility for taking medications, manage parent-child conflicts, anticipate and reduce barriers to adherence. Particular attention should be paid to the families that lack appropriate child discipline and family cohesion, and the parents who have psychosocial distress and poor coping strategies. Providing families with information or referral for assistance with regard to forming partnerships between parents and adolescents, sustaining parental involvement and minimizing conflicts between adolescents and their parents are valuable in encouraging adherence to treatment regimens.

A positive social network serves preventive as well as ameliorative functions in those experiencing various kinds of stress. When assessing psychosocial functioning in adolescents, FNPs should pay attention to any social withdrawal, interpersonal difficulty with peers, difficulty participating in school and social activities. FNPs can advocate for resources and social supports for children with IBD and encourage patients and parents to participate in support groups, such as the Crohn’s and Colitis Canada camp held at community levels or province and national levels. Attending an IBD camp or activities may improve social interactions and quality of life of IBD patients (CCC, 2014). In conclusion, attention to psychosocial issues with the BPS perspectives will facilitate FNPs to improve medication adherence in adolescents with IBD.
A Stepwise Approach to Medication Adherence

In conjunction with the BPS model, a stepwise approach to management of medication adherence is recommended for FNP practice. First, FNPs need to measure adherence with a combined subjective and objective method. Second, once the levels of non-adherence are identified, FNPs need to factors affecting adherence with validated assessment tools. Third, FNPs need to implement relevant interventions targeting specific factors.

**Measuring medication adherence.** The methods used to assess adherence have an impact on the estimates of adherence. It is important to understand the strengths and drawbacks of both subjective and objective methods of measuring medication adherence. The majority of the studies of adherence in IBD rely on subjective self-reports using standardized interviews and questionnaires. FNPs should keep in mind that self-ratings on subjective measures tend to overestimate medication adherence. At least two measures of adherence should be used to measure medication adherence in adolescents with IBD, including one objective measure. When using bioassays to assess medication adherence, FNPs should be aware that adolescents may intentionally take medications prior to lab work. Random urine screening for a salicylate level may be a better choice if clinically applicable, as it has a better indication of medication adherence to 5-ASA (Gifford et al., 2012).

Using standardized interviews and/or questionnaires to quantify adherence may be somewhat time-consuming during a clinic visit because of its length, such as the MAM. FNPs should use this scale, if a visit can be dedicated to assessing adherence. The Morisky Medication Adherence Scale (MMAS-8) is a valid instrument containing eight questions and can be completed in a routine clinic visit (See Table 3). The MMAS-8 allows healthcare providers to take an initial step to identify patients who are non-adherent or at risk for non-adherence to oral
medications in adult patients with IBD (Trindade, Ehrlich, Kornbluth, & Ullman, 2011). This scale was not used in the studies reviewed.

However, if adherence appears to be of pressing concern in a routine follow-up visit, FNPs might consider using the MMAS-8 as an initial screening tool to assess the levels of adherence, because it is shorter. Depending on the levels of adherence, patients can be further assessed with a combination of objective and subjective measures to quantify medication adherence. FNPs should exercise caution in administering this scale because it has not been studied in an adolescent population.

Assessing factors affecting adherence. Effective interventions start with an accurate identification of factors affecting adherence. It is important for FNPs to understand and use appropriate tools to identify factors affecting adherence. After baseline levels of non-adherence are obtained, or the FNP suspects there may be an issue with adherence, i.e., adherence rate is less than 80% according to the cut-off used in literature, or adherence rate is medium or low according to the MMAS-8, then specific factors affecting adherence should be identified with appropriate assessment tools. FNPs need to determine which tool to use for assessing specific factors in an individual patient or family.

Tools for assessing factors affecting adherence in the twelve studies were presented in Chapter three. Among these tools, only the TAI provides qualitative data; the other tools provided quantitative data. The TAI was designed specifically to assess barriers to adherence in children with IBD (Hommel & Baldassano, 2010; Hommel, Odell et al., 2011). It contains eight questions (see Box 8) and was used at a regular clinic visit. Therefore, FNPs may use this tool as an initial screening tool to collect preliminary data at each clinic visit, then book a longer visit or
multiple visits to further complete an in-depth assessment with the MAI or other specific tools to identify specific factors affecting medication adherence.

When using the TAI or other tools, FNPs need to involve adolescents and their parents or caregivers and to enable participants to discuss their concerns and identify barriers to adherence using an open-ended interview approach. Adolescents and parents may be interviewed separately or jointly. FNPs need to understand the advantages of each approach. When adolescents and parents are interviewed separately, different responses may have occurred with their own answers without embarrassment or inhibition. When they were interviewed together, they can be encouraged to identify and discuss different perspectives, during which the dynamics between adolescents and parents can be observed. Conducting interviews separately or jointly with adolescents and their parents or caregivers may be time-consuming, and may not fit into a regular clinic visit. However, since FNPs can be flexible in their schedules, they could book a longer clinic visit or multiple visits to obtain qualitative and quantitative data.

Of importance, medication adherence to maintenance medications is a dynamic process in adolescents with IBD. Assessing adherence and identifying factors affecting adherence should be ongoing in an individual patient and family for effective and efficient interventions.
Table 3. The Morisky medication adherence scale (MMAS-8) for IBD patients.

<table>
<thead>
<tr>
<th>Morisky Medication Adherence Scale Questions</th>
<th>Scoring</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
</tr>
<tr>
<td>1 Do you sometimes forget to take your IBD pills?</td>
<td>0</td>
</tr>
<tr>
<td>2 Over the past 2 weeks, were there any days when you did not take your pills for reasons other than forgetting?</td>
<td>0</td>
</tr>
<tr>
<td>3 Have you ever cut back or stopped taking your pills because you felt worse when you took it?</td>
<td>0</td>
</tr>
<tr>
<td>4 When you travel or leave home, do you sometimes forget to bring along your IBD pills?</td>
<td>0</td>
</tr>
<tr>
<td>5 Did you take your IBD pills yesterday?</td>
<td>1</td>
</tr>
<tr>
<td>6 When you feel like your IBD symptoms are under control, do you sometimes stop taking your pills?</td>
<td>0</td>
</tr>
<tr>
<td>7 Do you ever feel hassled about sticking to your IBD treatment plan?</td>
<td>0</td>
</tr>
<tr>
<td>8 How often do you have difficulty remembering to take all your IBD pills?</td>
<td>Rarely/never</td>
</tr>
</tbody>
</table>

Low adherence <6  
Medium adherence 6-7  
High adherence 8  

(Trindade, Ehrlich, Kornbluth, & Ullman, 2011).

Box 8. The treatment adherence interview for adolescents with IBD

1. Tell me what you know about IBD in terms of how someone gets, how it is treated and how long someone has it.
2. Tell me about your medication regimen and how each medication is supposed to work.
3. How is your medication organized and who is in charge of making sure medication is taken?
4. What gets in the way or prevents you from taking your medication? What makes it easier to take medication?
5. Why do you think it is easy or difficult for you to take medication?
6. When you miss a dose, whom do you tell? What happens when you tell you them?
7. What type of relationship does you and your parents have, related to your IBD and in general? How do you reconcile differences?
8. What do you think would make things less or more difficult on you and your family with respect to taking medications?

Choosing relevant practical interventions. Adherence to maintenance medications is a multi-dimensional issue affected by complex and multiple factors in adolescents with IBD. Each patient may have one or more factors affecting medication adherence and each patient and family may benefit from different intervention approaches. Relevant practical interventions targeting specific factors are summarized for FNP practice (see Table 4). Additional explanations of intervention strategies will be provided in the following section.

Interventions for disease/medication-related factors. Adolescents need to understand the goal of maintenance treatment and the importance of adherence to medications, even if they are asymptomatic in remission. FNPs need to appropriately manage medication side effects or adverse effects, monitor lab work as recommended for drug toxicity and consult with specialists or physicians for dose simplification if clinically appropriate. FNPs should work with adolescents together to develop practical strategies to minimize difficulty swallowing and symptoms associated with medication side effects, such as splitting pills, taking them with food, or avoiding food that can cause nausea or diarrhea.

Interventions for psychosocial factors. Psychosocial interventions are justified with the BPS model in promoting medication adherence. Problematic psychosocial functioning was found to be associated with maladaptive behaviours and negative thinking and poor coping strategies and problem-solving skills. Promoting psychosocial wellbeing of adolescents and families improved quality of life and medication adherence (Mackner & Crandall, 2005). Supporting psychosocial wellbeing of adolescents and families is an integral part of psychosocial interventions, which was covered in the section of applying the BPS model. Other psychosocial interventions will be discussed in the following section.
Cognitive-behavioural interventions (CBI) were found to have the most empirical evidence for therapeutic effects on physical symptoms, depression/anxiety, behavioural and psychosocial issues in adolescents with IBD. These effects were maintained during a 12-month period (Cook et al., 2010). The intent of CBI is to empower patients through education, coping strategies, problem-solving skills training to effectively deal with the impact of psychosocial issues on medication adherence and disease management. Problem-solving skills training (PSST) was a promising modality used to improve medication adherence by teaching patients and parents a structured approach to defining problems and generating and evaluating solutions (Greenley et al., 2010).

CBI and PSST are best provided by a mental health professional with training in understanding paediatric chronic illnesses, such as psychiatrist, therapist, social worker and counsellor. FNPs should make a timely referral to these health professionals for early psychosocial interventions in adolescents and families with psychosocial issues. Doing so will be beneficial for improving medication adherence. In addition to CBI and PSST, FNPs need to explore other effective and practical intervention strategies to facilitate psychosocial wellbeing.

Complementary therapies have proven effective in stress coping, including exercise, relaxation techniques, meditation, yoga, dance, music therapy and journaling (Schneider & Fletcher, 2008). To help patients and families engage in practicing these techniques to reduce physiological and psychosocial distress, FNPs need to be aware of community resources for these programs and provide adolescents and parents with the information about these stress management techniques. FNPs may recommend the website of the Crohn’s and colitis Canada to patients and families. This website also offers information for handling psychosocial stress and social network services.
No interventions have focused solely on social functioning and social support in improving medication adherence in adolescents with IBD. FNPs need to identify family coping strategies and availability of social support networks. FNPs work in collaboration with mental health professionals, social workers and community nurses to ensure that families have access to support resources. FNPs may refer patients and families to social workers or mental health professionals for early interventions, if the social distress significantly affects their psychosocial wellbeing and interferes with medication adherence.

*Interventions for behavioural factors.* FNPs need to work with adolescents and families to develop practical strategies such as memory aids to improve medication taking. FNPs may encourage adolescents and parents to discuss perceived barriers and responsibility for medication taking and refilling, and make a plan for medications ahead of activities. To avoid medications not being refilled, FNPs may first discover any financial barriers in families and make an effort in assisting families to receive an appropriate coverage of medications. FNPs may collaborate with pharmacists for automatic medication renewals/delivery or 90 days of medication supplies to facilitate continuity of medication supplies.

Memory aids should be simple, useful and individualized, such as medication dispensers, pharmacy bubble packs and reminders. Visual reminders include posted notes, phone text messages or medication charts. Patients could be reminded about taking their medications via simple pill-taking cues, such as placing pills close to something they use daily, e.g., toothpaste, breakfast table, glasses, contact lenses case, night-time beverage, etc. Auditory reminders can be alarm set-up, phone or video calls or voice messages. Most adolescents have a smart phone. FNPs can encourage them to program their phones for specific reminders tailored to patient preferences. Reminder systems with specific information about which medication is to be taken
at a given time, along with dosing instructions, are likely to be most beneficial for adolescents who forget to take medications (Greenley, Stephens et al., 2013).

Reward systems or behavioural contracting was particularly helpful for adolescents with oppositional behaviours and/or low motivation to adhere to medications (Hommel, Herzer et al., 2011; Hommel et al., 2012). They suggested that behavioural contracting should be developed with the input of adolescents to enhance their motivating values. Rewards for taking medications should provide concrete reinforcement for engaging in a task. Rewards can take the forms of objects or privileges, and should be tied to attainable and positive goals rather than unattainable goals or loss of privileges.

**Interventions for modifying knowledge and beliefs.** Assessment of the levels of education and health literacy of adolescents and parents should be an initial step required for effective educational interventions. Health literacy is defined the degree to which people are able to access, understand, evaluate and communicate information to promote and maintain good health across the life-course (Kwan, Frankish, & Rootman, 2006). FNPs need to adapt an individually tailored approach to educational interventions based on the levels of education and health literacy of patients and parents. FNPs may also consider a group-based educational intervention if it is in the best interest of patients and families, as it is generally cost-effective and allows for social networking among patients and families.

Infrequent clinic visits of adolescents were recognized associated with non-adherence (Kitney et al., 2009), FNPs should make an effort in increasing the frequency of clinical visits for adolescents who have difficulty with medication adherence, and building a professional rapport with adolescents and their parents. FNPs or clinic assistants or other members such as RNs
should phone or text adolescents/parents in advance to remind them of the time of appointments and encourage them to attend educational programs for improving medication adherence.

Written information should be provided when reinforced verbally in educational interventions. Patients who received written information with verbal reinforcement were more likely to adhere to therapy than those receiving written information alone (Hawthorne et al., 2008). Detailed information about the names of medications, dosing schedules and mechanisms of action, medication side effects, potential adverse effects and the goal of maintenance treatment should be provided in written or verbally. Part of educational interventions could also be accomplished through the development of a patient handbook that addresses their concerns with respect to medications and treatment.

FNPs may use different approaches to educational interventions. FNPs should consider routine visits as an excellent teaching and learning environment, and book longer visits as needed. The formal educational program designed and delivered by a gastroenterologist nurse practitioner (Waters et al., 2005) and the IBD-focused motivational interviewing counselling delivered by a RN (Cook et al., 2010) demonstrated the feasibility and acceptability in improving medication adherence. These IBD-focused educational interventions can be applied to FNP practice.

Today, internet is one popular medium that adolescents use often. FNPs may consider utilizing a tele-health approach to adolescents and families whose schedules do not fit regular clinical visits or for whom long travel may be a burden. A web-guided approach is feasible and cost effective in improving adherence to maintenance medications and healthcare resources utilization. The numbers that patients contacted their web doctor saved 189 euro per patient per
year for clinic services (Elkjaer et al., 2010), which is about 265 Canadian dollars per patient per year.

In summary, given that there is no single factor affecting adherence in adolescents with IBD, it makes a sense that no one generic intervention can be identified. Rather, evidence indicates that proper multi-informant assessment of key factors affecting adherence based on the BPS framework increases the likelihood of selecting appropriate effective, evidence-informed interventions that are inclusive of consideration to patient and family preferences.

No single intervention strategy or package of strategies can be effective across all patients and families, conditions or settings. To accomplish this, FNPs need to choose relevant interventions targeting specific factors and tailored to each individual patient and family's situations. Given the complex and multiple factors affecting medication adherence, multi-component interventions are likely to be superior to any single intervention in promoting medication adherence in adolescents. Adherence to maintenance medications is a dynamic process in adolescents with IBD. Therefore, reassessing adherence and outcomes of interventions should be ongoing in routine practice in conjunction with this stepwise approach to medication adherence.
# Table 4. Factors affecting adherence and relevant practical interventions

<table>
<thead>
<tr>
<th>Factors for non-adherence</th>
<th>Practical interventions</th>
</tr>
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<tbody>
<tr>
<td><strong>Disease/medication-related factors:</strong></td>
<td></td>
</tr>
<tr>
<td>• Patient being asymptomatic in remission</td>
<td>• IBD formal education program</td>
</tr>
<tr>
<td>• Medication complex regimens</td>
<td>• Dose simplification: once or twice daily if clinically appropriate</td>
</tr>
<tr>
<td>• Side effects or adverse events of medications</td>
<td>• Manage side effects: headache, anorexia, nausea, vomiting, abdominal pain</td>
</tr>
<tr>
<td>• Difficulty swallowing pills due to the size and taste of pills</td>
<td>• Monitor lab work regularly for drug toxicity</td>
</tr>
<tr>
<td>• Medication complex regimens clinically appropriate</td>
<td>• Split pills and take them with food</td>
</tr>
<tr>
<td>• Side effects or adverse events of medications</td>
<td></td>
</tr>
<tr>
<td>• Difficulty swallowing pills due to the size and taste of pills</td>
<td></td>
</tr>
<tr>
<td><strong>Psychosocial factors:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Adolescent related</strong></td>
<td></td>
</tr>
<tr>
<td>• Anxiety</td>
<td>• Cognitive-behavioural interventions</td>
</tr>
<tr>
<td>• Depressive symptoms</td>
<td>• Problem solving skills training</td>
</tr>
<tr>
<td>• Helplessness</td>
<td>• Adolescent social support group</td>
</tr>
<tr>
<td>• Dependency</td>
<td>• IBD camps or activity groups</td>
</tr>
<tr>
<td>• Low self-esteem</td>
<td>• Increase the frequency of clinical visits</td>
</tr>
<tr>
<td><strong>Family related:</strong></td>
<td>• Manage anxiety and depression</td>
</tr>
<tr>
<td>• Family dysfunction</td>
<td>• Refer to a mental health team/social worker</td>
</tr>
<tr>
<td>• Parent-child conflicts</td>
<td>• Promote adaptive coping strategies</td>
</tr>
<tr>
<td>• Less maternal involvement</td>
<td>• Shared family responsibility for medications</td>
</tr>
<tr>
<td><strong>Behavioural factors:</strong></td>
<td>• Sustain maternal involvement</td>
</tr>
<tr>
<td>• Forgetfulness</td>
<td>• Family social support/network</td>
</tr>
<tr>
<td>• Interference with activities</td>
<td></td>
</tr>
<tr>
<td>• Not being home</td>
<td></td>
</tr>
<tr>
<td>• Medications not being refilled</td>
<td></td>
</tr>
<tr>
<td>• Attention and conduct problems</td>
<td></td>
</tr>
<tr>
<td>• Oppositional behaviours</td>
<td></td>
</tr>
<tr>
<td><strong>Factors related to knowledge and beliefs:</strong></td>
<td></td>
</tr>
<tr>
<td>• A lack of knowledge about IBD treatment and medications</td>
<td>• Assess levels of education and health literacy of patients and parents</td>
</tr>
<tr>
<td>• Beliefs that treatment was not necessary or medications were ineffective</td>
<td>• IBD formal education program</td>
</tr>
<tr>
<td>• Concerns of medication side effects or adverse events</td>
<td>• Enhance patient-provider relationship</td>
</tr>
<tr>
<td></td>
<td>• Increase the frequency of clinical visits</td>
</tr>
<tr>
<td></td>
<td>• Discuss beliefs and concerns about treatment and medications</td>
</tr>
<tr>
<td></td>
<td>• Convey a non-judgmental understanding of the patient’s perspectives</td>
</tr>
<tr>
<td></td>
<td>• No blame but support</td>
</tr>
</tbody>
</table>
Implications and Recommendations for FNP Education

Given the multi-factorial and complex factors affecting medication adherence in adolescents with IBD, promoting medication adherence presents challenges in FNP knowledge and skills. Of the eight studies of intervention strategies for improving medication adherence, interventions were delivered by the healthcare professionals who had specific training or higher levels of clinical psychology, such as gastroenterology nurse practitioner, a RN who received CBT and motivational interviewing counselling training, or master-or doctoral-level psychology clinicians. This implies that FNPs need to continue receiving specific education and training to be competent in fulfilling the role in promoting medication adherence.

To provide effective patient education and counselling, FNPs need to explain the concept of maintenance treatment and justify the need for maintaining remission and maximizing medication adherence. FNPs need to ensure that adolescents and parents understand the detailed information, such as the names of medications, dosing regimens and mechanisms of action, medication side effects potential adverse events, goals of maintenance treatment and consequences of non-adherence. With the philosophy of primary health care, FNPs are expected to take a leadership role in promoting medication adherence and preventing relapses of the disease. To accomplish the role, FNPs need to receive sufficient education on medication adherence and have access to specific training in adherence management.

FNPs will seek out opportunities to expand knowledge and improve skills, such as attending conferences, in-services and continuing education programs, to be competent in management of medication adherence, conducting multi-formant adherence assessment, identifying factors affecting adherence and delivering relevant interventions tailored to individual patient and family’s preferences. The healthcare organizations in which they work
should design and support delivery systems that empower healthcare professionals an adherence toolkit.

With appropriate knowledge and skills, not only can FNPs be able to provide education for adolescents and parents, but also they will be an important resource for other healthcare professionals in promoting medication adherence. Within a multidisciplinary team, FNPs should raise the significance of addressing non-adherence in adolescents with IBD and share knowledge, information and intervention strategies for improving medication adherence. The knowledge and skills of improving medication adherence will also benefit FNPs in promoting medication adherence in adolescents with other chronic diseases.

**Implications and Recommendations for Research**

The literature review is restricted by the paucity of studies on medication adherence in adolescents with IBD, but findings of the review present some challenges and variations, which warrants future studies. Implications and recommendations for research will be provided in this section.

Defining and assessing adherence to maintenance medication is one of the challenges. For maintenance medications, the level of adherence necessary to achieve a clinical remission is not fully known. There is no operational definition to distinguish arbitrary cut-off of adherence from non-adherence, although the majority of the studies of adherence considered 80% as cut-off. There is no clinical significance to this arbitrary cut-off (Leleiko et al., 2013). Whether 80% adherence is enough or 100% adherence is necessary has not been identified. Research needs to define the level of adherence to sustain clinical remission or whether the cut-off adherence depends on how individual patients metabolize medications.
Another challenge presents in measurement of medication adherence, which varied among the studies and might result in inconsistent findings. Self-reports were commonly used as a primary assessment of adherence. Research needs to reveal data from combined measures of subjective and objective assessments of medication adherence. The MMAS-8 is a valid scale of assessing levels of medication adherence among adults with IBD, but its validity and reliability need to be investigated in adolescents with IBD.

As previously discussed, the majority of studies on factors affecting adherence provided quantitative data with the tools that utilized a forced-choice format of commonly endorsed barriers related to adherence. Factors were assessed with qualitative or mixed data in only two studies (Hommel & Baldassano, 2010; Hommel, Odell et al., 2011). Use of an open-ended interview format for qualitative data analyses may have provided greater breath of data in regard to specific factors affecting adherence in an individual patient and family. Research needs to obtain both quantitative and qualitative data to identify factors affecting adherence, combining a quantitative forced-choice questionnaire and a qualitative open-ended interview assessment.

The majority of studies had a small sample size with homogeneous geographic characteristics, such as Caucasians. This is likely influenced by the fact that Caucasians are disproportionately diagnosed with IBD. Homogeneous samples of Caucasian families with higher levels of annual income may not easily generalize findings to minority and low income families. Socio-economic situations should be explored in research of medication adherence in an adolescent population. In addition, cross-sectional data were exclusively utilized in the studies on factors affecting adherence. This precludes the ability to make conclusions concerning the directionality of the findings. Findings revealed that older adolescents had higher non-adherence
rates and more psychosocial issues. Longitudinal research is needed to identify casual
relationships between factors and medication adherence, especially in older adolescents.

Current studies were focused on primary care practice and examined from the view of
physicians. Examination on non-adherence from the view of nursing, the philosophy of primary
health care with a BPS approach is needed in research. In addition, little research has been
carried out on the effects of healthcare provider-related and healthcare system-related factors on
adherence. Whether non-adherence is linked to these factors in adolescents with IBD needs to be
investigated in research.

Although the benefits from appropriate maintenance therapy throughout childhood and
adolescence are considerable, the views on the duration for maintenance treatment in IBD
patients remain varying among physicians, particularly in patients with quiescent UC (Zheng &
Kennedy, 2009). This may have an impact on adherence management and disease outcomes.
Only one study reported non-adherence to 5-ASA resulted in relapse in 61% of patients over 2
years in adults with quiescent UC (Kane et al., 2003). No studies have reported the impacts of
non-adherence to maintenance medications on disease activity in children and adolescent
populations. Relapse rates with regard to duration of medication adherence in adolescents with
IBD should be investigated.
Conclusion

This paper provided an initial review on the issue of non-adherence to oral maintenance medications in adolescents with IBD. Twelve studies were reviewed for identifying factors affecting medication adherence and eight studies were reviewed for exploring intervention strategies for improving medication adherence in this population. Findings of this paper are limited by the paucity of literature on this issue. However, they provide implications for FNP practice, education and research in promoting medication adherence.

The BPS model assists FNPs to examine non-adherence in adolescents with a comprehensive approach. With the BPS perspectives, FNPs gain a better understanding of factors affecting medication adherence, the significance of psychosocial issues related to medication adherence and the interactions of the disease/medication related, behavioural and psychosocial factors. To optimize medication adherence, the impact of psychosocial issues of adolescents and families on medication adherence should be addressed. FNPs play an important role in providing psychosocial interventions and supporting the psychosocial wellbeing of adolescents and families. In collaborative practice, FNPs cooperate with patients/families and healthcare providers, consult physicians, specialists and other healthcare professionals and refer patients to multidisciplinary professionals for early psychosocial assessments and interventions.

A stepwise approach to medication adherence is recommended for FNP practice. An initial step is to measure medication adherence using both subjective and objective methods. At a routine visit, medication adherence may be initially screened with the MMAS-8, and then can be estimated with a combined method of subjective and objective measurements, such as the MAM and urinary levels of ASA. If non-adherence is identified or suspected, specific factors affecting adherence should be identified with appropriate assessment tools.
There are several validated and reliable tools used for identifying disease/medication-related, behavioural and psychosocial factors, assessing family psychosocial functioning, knowledge and beliefs of treatment and medications. FNPs need to understand these tools and use them appropriately for accurate assessments of factors affecting adherence. Among those assessment tools used in literature, the TAI, the MAI and the IBD-FRQ were designed specifically for adolescents with IBD. The TAI provides qualitative data and can be used at a routine clinic visit as an initial screening tool to collect preliminary information. An in-depth assessment with appropriate tools to identifying specific factors will be completed with in a longer visit or multiple visits.

Precise assessment of factors affecting adherence is required for effective and efficient interventions. Behavioural, educational, psychosocial and multi-component interventions were provided in literature. No single intervention strategy has been shown to be effective for all patients. A combination of multiple intervention strategies tailored to individual patient and family’s preferences appears a promising intervention strategy. In adolescents with IBD, medication adherence is a dynamic process. An ongoing reassessment of adherence and outcomes of interventions with a stepwise approach is recommended.

Promoting medication adherence challenges FNP knowledge, skills and practice. To accomplish the role in promoting medication adherence, FNPs need to continue receiving specific education and training to improve their capacity and competence. FNPs are expected to be an educator, an advocate and a coordinator in management of medication adherence. FNPs take a leadership role and are expected to participate in research to develop effective interventions that are feasible and manageable in FNP practice. Investigating whether factors of healthcare providers and/or healthcare system are associated with non-adherence will be a value-
added component of research that FNPs contribute to improve medication adherence in adolescents with IBD.
References


Canadian Nurses Association ([CNA], 2000). *The primary health care approach*. Ottawa, ON: Author.


