REPRODUCTIVE KNOWLEDGE SPECIFIC TO INFLAMMATORY BOWEL DISEASE AMONG WOMEN WITH IBD AND PHYSICIANS WHO TREAT WOMEN WITH IBD

by

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ABSTRACT

Background: Inflammatory Bowel Disease (IBD) affects women in their reproductive years. Women with IBD often choose not to have children, and this voluntary childlessness may be due to their concerns regarding the adverse effects of their IBD and its treatment on fertility, pregnancy, and the newborn. Patients often obtain information from their physicians, yet physician IBD-specific reproductive knowledge has not been well studied.

Objectives: The objectives of this study were to characterize the relationship between IBD-specific reproductive knowledge and childlessness among women with IBD, and to characterize the relationship between IBD-specific reproductive knowledge and practice patterns (relative to reproductive issues) among physicians who treat women with IBD.

Methods: This was a cross-sectional survey of women with IBD (18 to 45 years old) and of physicians who treat women with IBD. IBD-specific reproductive knowledge was measured on a 0-17 point scale by the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey with scores grouped as: poor (0 to 7), adequate (8 to 10), good (11 to 13), very good (14 to 17). Multivariable logistic regression was used to obtain adjusted odds ratios and 95% confidence intervals for estimating the effects of exposure variables on the outcomes of interest.

Results and Conclusions: There was an inverse relationship between IBD-specific reproductive knowledge; increases in the CCPKnow score corresponded to decreases in the odds of childlessness. Women with IBD had significant IBD-specific reproductive

knowledge deficits, concerns, and beliefs/opinions. Women with IBD often changed their family plans once they were diagnosed with IBD. Discussion of family planning with a physician, specifically with a gastroenterologist, corresponded to lower odds of having poor CCPKnow scores relative to not discussing family planning with a physician. Although almost two-thirds of physicians had very good CCPKnow scores, physician knowledge of IBD-medication use during pregnancy and breastfeeding was highly variable, revealing knowledge deficits in many physicians who treat women with IBD. The Internet was an important source of information for both women with IBD and physicians. Thus, internet-based educational activities aimed at both patients and physicians may be effective targets for improving IBD-specific reproductive knowledge among women with IBD. Improving IBD-specific reproductive knowledge among women and physicians will help ensure that women with IBD can make informed choices about having children.

PREFACE

This thesis is an original work by Vivian Wai-Mei Huang. The research project, of which this thesis is a part, received research ethics approval from the University of Alberta Research Ethics Board, Project Name "Patient Knowledge and Family Planning in Inflammatory Bowel Disease", no. Pro00033798, October 10, 2012.

Chapter 4 of this thesis is the basis for a pending manuscript titled "Poor IBD-specific Reproductive Knowledge is Associated with Childlessness among Women with IBD" co-authored by HJ Chang, KI Kroeker, KJ Goodman, K Hegadoren, LA Dieleman, and RN Fedorak. VWH contributed to study design, data collection, data analysis, and manuscript drafting and editing. HJC contributed to data analysis and manuscript editing. KIK contributed to study design, data collection, manuscript editing. KJG contributed to study design, data analysis, and manuscript editing. KH and LAD contributed to study design and manuscript editing. RNF contributed to study design, data collection, data analysis, manuscript editing.

The introduction and factual statements in the discussion in Chapter 8 of this thesis is in part modeled after a published manuscript titled "From conception to delivery: Managing the pregnant inflammatory bowel disease patient" co-authored by VW Huang and FM Habal. VWH reviewed the literature and drafted the manuscript. FMH reviewed the literature and revised the manuscript. VWH and FMH contributed to the conception and design of the review, and approved the final version for publication.

DEDICATION

“Life is a journey, not a destination”

Ralph Waldo Emerson

I would like to dedicate this thesis to all people who journey through life burdened with inflammatory bowel disease. I hope that the knowledge obtained from the results of this thesis will help them, or help their physicians help them, in their journey through life. Especially, I hope this thesis will contribute towards helping women with IBD make informed decisions regarding family plans as they journey through life.

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LIST OF SYMBOLS, NOMENCLATURE, ABBREVIATIONS

ADA - Adalimumab (Humira®)
AZA – Azathioprine (Imuran®)

CD – Crohn's disease
Cipro – Ciprofloxacin

FP – family planning

GI - gastroenterologist
GP – general practitioner
GIT – gastroenterology trainee

IBD – inflammatory bowel disease
ID – indeterminate colitis
IFX – infliximab (Remicade ®)

METRO - metronidazole
MTX – methotrexate

UC – ulcerative colitis

χ**2** = Chi square

6-MP – 6-mercaptopurine (Purinethol®)

1 INTRODUCTION: Inflammatory Bowel Disease is a Chronic Disease That Affects Women in Their Reproductive Years

1.1 Chronic Disease and Family Planning

Chronic diseases, such as inflammatory bowel disease (IBD), have a significant influence on major decisions throughout one's life. Having a chronic disease means a lifetime of periods of relapse and periods of remission. Most chronic diseases require lifelong medications and in severe cases may require surgical intervention or other invasive procedures. Chronic diseases and treatments can affect quality of life, social functioning, psychological state, and many other aspects of life. They therefore impact important life decisions such as those related to having children, marriage and divorce, job and career choice, social life, holidays, travelling and education[1].

In addition, women with chronic diseases can be at higher risk of pregnancy-related complications and higher risk of disease-related complications during pregnancy; there is always increased concern regarding reproduction and pregnancy in women with chronic diseases. The disease itself, as well as the medications and surgeries used to manage the disease, can affect fertility, pregnancy outcomes, and neonatal outcomes. In addition, measures taken to control reproduction and the pregnancy itself can affect the disease course and decisions regarding treatment strategies.

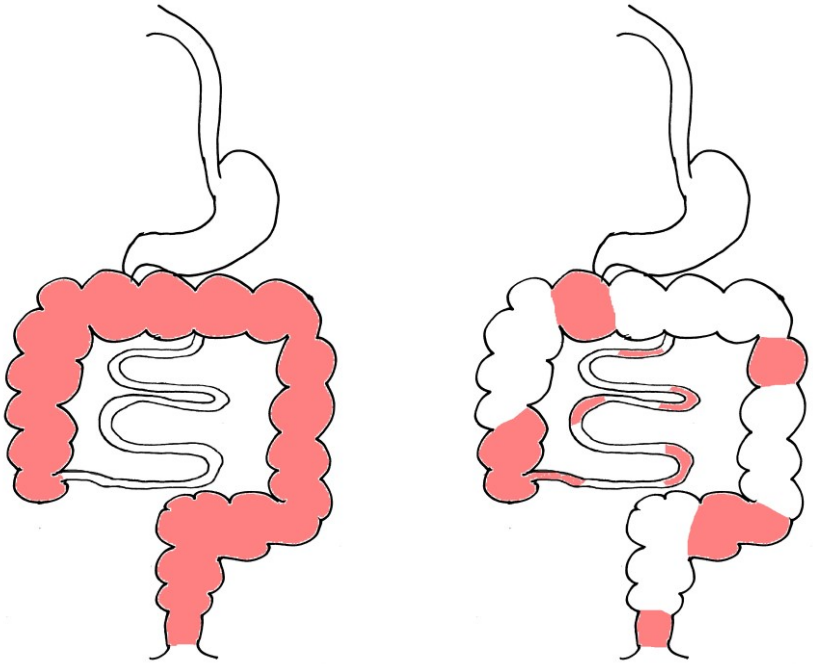
Among women with chronic diseases such as hemophilia, HIV, epilepsy, and multiple sclerosis, concerns about passing on their disease, and disease related issues are major concerns[2-4]. In one study on women with hemophilia, for 54% of the women, hemophilia was found to be a major factor in their decision "not to have children/any more children"; the main reasons cited were fear of passing hemophilia onto their child, previous experience with hemophilia, and stress of going through prenatal tests[2]. Similarly, women with HIV often choose to not become pregnant after learning of their HIV diagnosis; fears of transmitting HIV to their child and personal health concerns are weighed against their pre-existing desire to have children[3]. For women with epilepsy, concerns about the ability to care for a child and passing on epilepsy to the child are major concerns associated with the decision to have fewer children[4]. In a study of multiple sclerosis (MS) patients, about a third of patients reported MS-related reasons for not becoming pregnant following diagnosis of MS; the main reasons cited were symptoms interfering with parenting, concerns about burdening the partner, and concern about children inheriting MS[5]. A study involving focus groups of women with diabetes, hypertension, and obesity reported deficits in knowledge about pregnancy-related risks, and "lack of intent to engage in preconception health promotion and family planning"[6].

Recently, a systematic review on the childbearing concerns and related information needs and preferences of women with chronic diseases found that studies reported a high prevalence of women with a chronic health condition expressing concern about

childbearing and having questions about the reproductive implications of their condition[7]. The major common factors that appear to affect family planning decisions in women with chronic diseases include (1) fear of passing on the disease to their child, (2) concerns about the impact of reproduction on their own health, and (3) lack of knowledge regarding pregnancy-related risks.

1.2 Inflammatory Bowel Disease is a Chronic Disease

Inflammatory bowel disease (IBD) is a group of chronic intestinal diseases that typically present during childhood, adolescence, and young adulthood. IBD includes Crohn's disease (CD), ulcerative colitis (UC), and IBD-unspecified (IBD-U). Crohn's disease can affect any part of the gastrointestinal tract, from mouth to anus, as shown in Figure 1-1, and can present with fistulae, abscesses, or obstruction. Ulcerative colitis affects only the large bowel, as shown in Figure 1-1, and rarely presents with fistulae, abscesses, or obstruction. IBD-U refers to IBD that does not completely fit a CD or UC diagnosis. Symptoms of IBD include abdominal pain, cramping, (bloody) diarrhea, rectal urgency, weight loss, and fatigue. IBD can also have extra-intestinal manifestations with effects on other body systems. Treatment of IBD includes the use of various medications such as 5-aminosalicylates, immunosuppressants, steroids, and biologics, each of which has various side effects including effects on reproduction[8]. Typically, these medications are used in the "pyramid" of treatment shown in Figure 1-2, and in some cases, surgery is required.



Ulcerative Colitis (UC) Crohn's Disease (CD)

Figure 1-1: The Different Types of Inflammatory Bowel Disease Affect Different Parts of the Gastrointestinal System

Ulcerative colitis (UC) affects the large bowel only. Crohn's disease (CD) affects any part of the gastrointestinal system, from mouth, to anus.

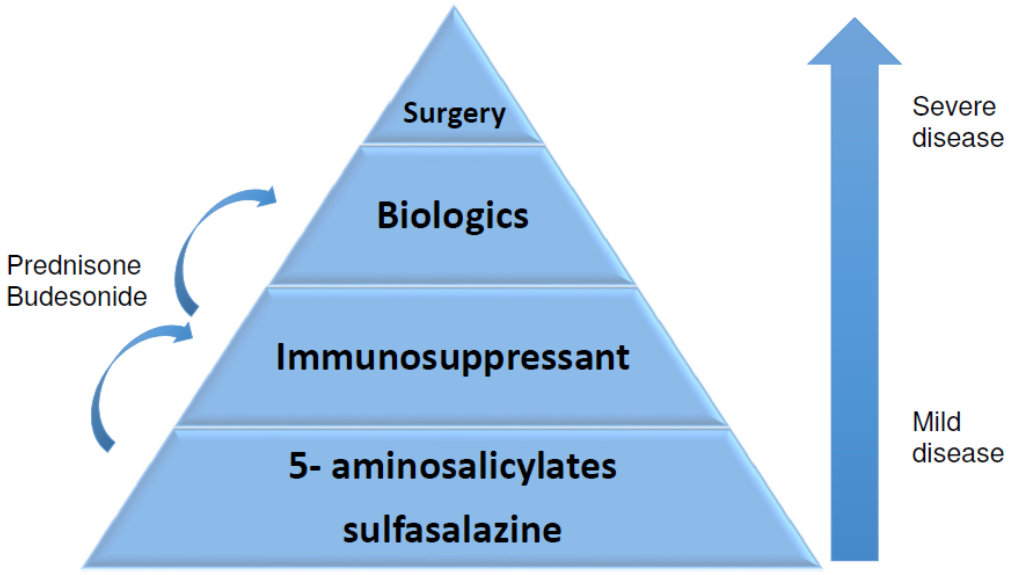


Figure 1-2: The Pyramid of Treatment for Inflammatory Bowel Disease

Some types of surgical interventions, such as colectomy with creation of an internal pouch, have been shown to adversely affect fertility in women with IBD[8].

Since IBD is often diagnosed during the reproductive years, management is challenging for both women with IBD and physicians who treat women with IBD. Physicians and patients alike need to consider issues regarding the effects of IBD, and of its treatment, on fertility, pregnancy, breastfeeding, and maternal and neonatal outcomes. In addition, they need to consider the effects of pregnancy, delivery method, and the breastfeeding and postpartum periods on the IBD disease course.

1.3 Inflammatory Bowel Disease and Reproduction

Women with IBD have been reported to have decreased fertility, which previously was thought to be due to their IBD disease[9, 10]. However, many studies have reported similar fertility rates among women with IBD compared to the general population[11-13]. Low fertility rates observed in some studies have been theorized to be due to "voluntary childlessness" where women with IBD choose not to have children due to fears and concerns regarding reproduction given their IBD status[10, 11, 13-15].

The voluntary childlessness rate among women with IBD was reported to be as high as 36%[16] in early studies, however, more recent studies estimated that up to 18% of women with IBD choose not to have children because of their IBD[9, 10, 14]. A recently

published systematic review and meta-analysis reported that studies of women with CD estimated that the proportion with children was 17 – 44 per hundred lower in women with CD than in women without CD[15]. Studies estimated that 14% to 36% of women with CD and 14% to 21% of women with UC were voluntarily childless[15]. The reviewed publications and the published systematic review with meta-analysis showed that the involuntary infertility rate in women with IBD was similar to the general population[15].

Recent publications have reported deficits in patient knowledge about reproduction and IBD, and unwarranted fears and anxiety regarding this topic in women with IBD[17, 18]. This lack of patient knowledge and unwarranted fears regarding reproduction in IBD has been hypothesized to contribute to voluntary childlessness in IBD patients[17, 18].

Previous studies have estimated that up to 50% of IBD patients were given medical advice against conception and pregnancy[9, 14], and that only about 50% of women with IBD indicate that they discussed reproductive issues with their IBD physician[10]. A recent chart review study estimated that only 19% of female IBD patients have reproductive counseling documented in the medical chart[19].

There have been two published studies that address physician knowledge about IBD in general or about reproductive issues in women with IBD; both studies looked at general practitioner knowledge[18, 20]. In the Toomey et al. study, only 8% of GPs reported feeling that they could address on their own family planning with IBD patients themselves, and

only 18% of FPs reported that they routinely raised the issue of family planning with IBD patients[20]. In the Tan et al. study, 37% of GPs categorized themselves as "uncomfortable" with IBD management, specifically the use of immunosuppressants and biologics[18]. Systematic search of relevant databases yields no published reports of investigations of gastroenterologist knowledge of reproductive issues in IBD patients. Inadequate physician knowledge regarding reproduction in IBD patients and lack of comfort with managing pregnant IBD patients may be leading physicians to avoid discussing family planning with IBD patients or offering misguided medical advice to women with IBD in their reproductive years. This inadequacy in physician knowledge may also be contributing to the voluntary childlessness seen in IBD patients.

1.4 Purpose of the Study

The purposes of this study were to characterize the relationship between IBD-specific reproductive knowledge and childlessness among women with IBD, and to characterize the relationship between IBD-specific reproductive knowledge and practice patterns of practice pertaining to reproductive issues among physicians who treat women with IBD.

1.5 Objectives of the Study

1.5.1 Patient Study Objectives

The primary objective of the patient study was to estimate among women with IBD the effect of IBD-specific reproductive knowledge level on childlessness.

The secondary objectives of the patient portion of this study were:

- To estimate associations of selected variables, particularly discussion of family planning with a physician, with patient IBD-specific reproductive knowledge.
- To characterize differences between childless women and women who have children in IBD-specific reproductive concerns and beliefs.
- To characterize the medication knowledge of women with IBD, and to characterize differences between childless women and women who have children in medication knowledge.
- To characterize the change in family plans after IBD diagnosis of women with IBD.

1.5.2 Physician Study Objectives

The primary objective of the physician study was to characterize IBD-specific reproductive knowledge among physicians.

The secondary objectives of the physician portion of this study were:

- To estimate associations of selected factors with IBD-specific reproductive knowledge among physicians.
- To estimate the effect of IBD-specific reproductive knowledge level on physician discussion of family planning with patients.

- To characterize physician knowledge about medication use in pregnancy and breastfeeding.

1.6 Significance of the Study

Family planning is an important part in the course of life. Many factors are involved when deciding whether or not to have children. If women with IBD lack IBD-specific reproductive knowledge and this is contributing to women with IBD choosing to remain childless due to the perpetuation of unwarranted fears and concerns, then educational activities can be developed to address these deficits. If women with IBD are making decisions regarding the management of their disease (e.g. non-adherence to medications) based on reproductive concerns due to lack of understanding of the impact of their disease and treatment on reproduction, then this needs to be addressed for optimal management of IBD in women during their reproductive years.

If physicians who treat women with IBD in their reproductive years lack IBD-specific reproductive knowledge, and impart unwarranted fears and concerns, or incorrect information to their patients, then this needs to be addressed with educational activities targeted to specific physician groups.

Identifying relevant knowledge deficits among factors affecting reproduction decisions among women with IBD and among physicians who treat women with IBD during their

reproductive years will permit development of targeted educational activities to ensure that women with IBD are equipped to make informed family planning decisions and that physicians treating women with IBD during their reproductive years are equipped to make appropriate practice decisions.

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2 METHODS: A Cross-sectional Survey of Women with IBD and Physicians who Treat Women with IBD

2.1 Overall Study Design

This is a cross-sectional study of IBD-specific reproductive knowledge and related factors of interest among women with IBD and physicians who treat women with IBD, with data collected by questionnaire. This study design is suitable for an exploratory study and was chosen in order to reach the most patients and physicians as possible in a feasible time period.

2.2 Setting and Participants

The study was conducted from the Gastroenterology Inflammatory Bowel Disease Consultation and Research Clinic, Zeidler Ledcor Centre (ZLC), University of Alberta Hospital (Edmonton, Alberta, Canada). All questionnaire packages were mailed from ZLC with return address to ZLC. Physicians were recruited from various conferences across Canada, but all questionnaires were returned to ZLC and stored in the secured triple-locked office of the research investigators. Alternative electronic surveys were hosted via the Internet engine SurveyMonkey and responses were retrieved and stored in the secured database of the Gastroenterology Division research group.

2.3 Patient Study

2.3.1 Patient Study Population

The population of interest was women with IBD who met the following inclusion criteria:

1) female, 18 to 45 years of age;
2) seen in the IBD clinic from 2010 through 2013;
3) willing to participate and able to give informed consent.

Women with IBD were excluded if they met the following exclusion criteria:

1) unable to read or write in English;
2) unwilling to complete questionnaires.

2.3.2 Patient Recruitment

An electronic health records database was used to identify female patients with IBD who had been seen or were coming to clinic between January 2010 and June 2013.

The patient study package consisted of:

1) a checklist with room for return address (Appendix A-1);
2) an information sheet and consent form (Appendix A-2);
3) a self-administered patient questionnaire (Appendix A-3);
4) a stamped, self-addressed return envelope.

The patient study package was either mailed to the targeted patients, or directly handed to patients during a clinic visit.

Those who had not responded within 3 months were sent reminders via mail or, if an email address was available, via email (Appendix A-4) with a link to a web-based version of the questionnaire (Appendix A-5). In order to improve the response rate, a second reminder via telephone occurred approximately 3 months after the first reminder.

Packages were returned by mail or in–person by patients who consented to participate in the study. Return of the questionnaires with a signed consent form, and submission of the electronic consent form with the electronic survey, were taken as informed consent.

As the questionnaires took an average of 15-20 minutes (based on testing among 4 secretaries working for the IBD clinic), patients were reimbursed in the form of a $10 coffee shop gift card upon return of the completed survey.

The number of eligible women identified from the electronic database and the subsequent response rate determined the sample size for the patient study.

Figure 2-1 illustrates the groups of study factors collected by the questionnaires and the resulting classification of women with respect to key variables.

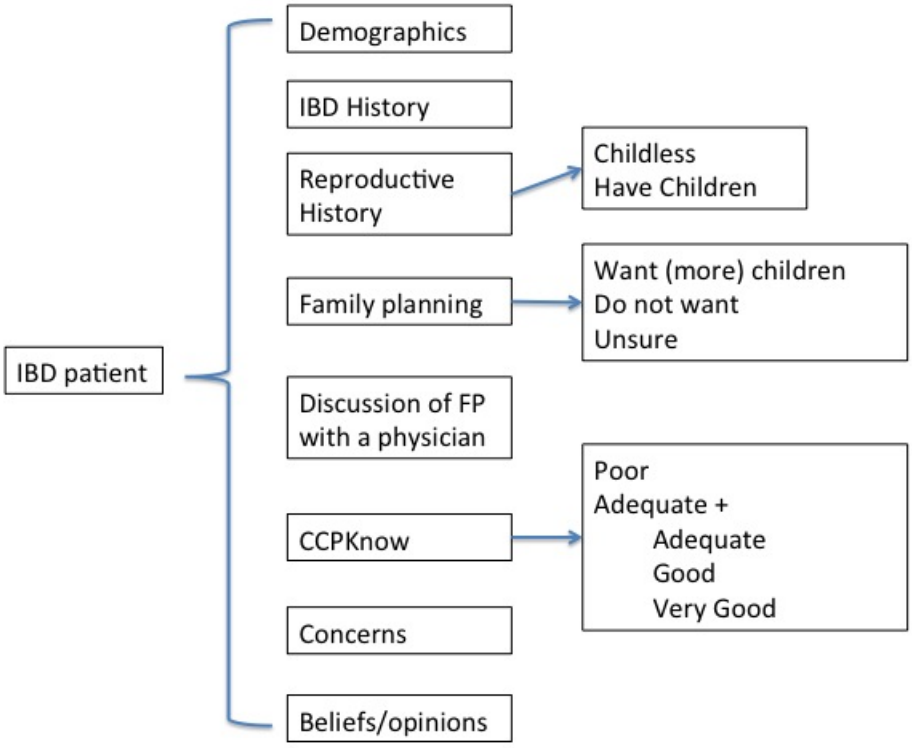

Figure 2-1: Patient Study Factor Scheme

IBD – inflammatory bowel disease
CCPKnow – Crohn's and Colitis Pregnancy Knowledge score
FP – family planning

2.3.3 Patient Data Sources and Variable Definitions

Questions for the patient questionnaire (Appendix A-3), with the exception of the IBD-specific reproductive knowledge survey (Crohn's and Colitis Pregnancy Knowledge or CCPKnow survey), were developed after an extensive review of the literature on: patient knowledge of and concerns about reproductive issues in IBD[1-3]; and focus groups about reproduction in women with other chronic medical conditions[4-7].

The investigator developed the candidate questions and revised them after discussion with 3 IBD clinicians, 1 epidemiologist, and 1 PhD nurse. The patient questionnaires were tested for readability among the 4 female secretaries working for the IBD clinic, and 1 female student with post-secondary education.

The questionnaire set was initially piloted among patients by sending them out to the first 60 patients from the database-generated list. Based on the 24 returned surveys, changes were made to clarify wording and numbering of response options, and additional questions were incorporated for medical history, to produce the final questionnaire (Appendix A-3).

The sections of the patient questionnaire are as follows:

- **Demographic section (#1-10):** These included variables that may affect knowledge and/or childlessness: education, employment status, number of siblings, family

history of IBD, ethnicity, current marital status, diagnosis of IBD in partner, IBD in partner's family.

- **Medical history section (#1):** These included disorders that may affect knowledge and/or childlessness: diagnosed mood disorder, irritable bowel syndrome, diabetes, gynecologic and other chronic conditions.
- **IBD history (#1-9):** These asked about the patient's IBD history: self-reported diagnosis as CD, UC, or Indeterminate (patients who selected more than one diagnosis were coded as Indeterminate, in order to capture that they were unsure about their diagnosis); which IBD medications they had ever been treated with; whether they were put on steroids for a flare during the past year; whether they had a history of perianal disease, colectomy with creation of an internal pouch, or ostomy (external bag).
- **Discussion of family planning (#8, #9):** Patients were asked who they discussed family planning with and where they obtain information regarding family planning and IBD.
- **Reproductive history (#1-5):** Reproductive history was ascertained because it could affect knowledge and childlessness. Patients were asked if they had ever seen a fertility specialist, or had fertility treatment; if they were currently pregnant, or had ever been pregnant. If patients had ever been pregnant, they were asked to fill out a table for their pregnancy outcomes to indicate the number of pregnancies that: occurred before IBD diagnosis and after IBD diagnosis; were planned or not planned; resulted in therapeutic abortions, spontaneous abortions/miscarriages, stillbirths,

preterm and low birth weight, full term and low birth weight, full term and healthy. They were also asked if they had any adopted children.

- **Contraception use (#7, #8, #9):** There were 3 questions on the use of contraception. These were asked in order to understand the contribution of contraception use toward childlessness.
- **Family Planning Status (#6, #10, #11, #12, #13):** In order to capture patient's views on reproduction given their IBD, they were asked for their current status with respect to having children (#6), as well as their status before IBD diagnosis (#10), and since IBD diagnosis (#11). They were also asked if they had been pregnant after being diagnosed with IBD, and if the course of the pregnancy influenced their decision to become pregnant again (#12, #13). Question #12 and #13 were modified from #23 and #24 from the previously published Marri et al study[1].
- **Concerns (#14, #15, #16):** Depending on their current desire to become pregnant or not, they were guided to complete questions #14, 15, or 16. Question #14 was based on question #21 from the Marri et al study[1]. Question #15 was modified from questions used in a multiple sclerosis study[7]. Question #16 was for patients who planned to have more pregnancies, but was identical to Question #14, and thus these two questions were analyzed together.
- **Medication adherence (#17, #18, #19, #20):** Patients were asked about medication adherence during reproduction and IBD. Question #17 was modified from Question #22 of the Marri et al. study[1].

- **Information requests (#21):** Question #21 was added after the pilot because a large number of the 24 pilot patients wrote in various topics they wished to obtain more information on.
- **Beliefs and Opinions (A – L):** This series of Likert questions was developed to better characterize the viewpoints of women with IBD regarding sources of worry that include genetics, medications, effect of pregnancy on IBD, effect of IBD and medications on pregnancy. These topics were based on previous studies reporting women's concerns in IBD[1,2]. The scale ranged from 1) strongly disagree to 5) strongly agree.
- **Crohn's and Colitis Pregnancy Knowledge (CCPKnow) Score:** The CCPKnow score was developed by Selinger et al. in a similar manner to the CCKnow (Crohn's and Colitis Knowledge) IBD disease-specific questionnaire using feedback from a focus group of patients, IBD specialist nurses, and gastroenterologists[8]. Selinger et al reported that the CCPKnow instrument had a Flesch-Kincaid Grade level of 3.6, indicating that the reading difficulty corresponds to what is typical for grade 3 in the USA; this score is calculated by the formula 0.39 (total words/total sentences) + 11.8 (total syllables/total worlds) – 15.59. It was validated using as a gold standard four groups of healthy volunteers with different levels of IBD education (16 clerical staff, 11 general staff nurses, 15 junior doctors, and 17 IBD specialists nurses); differences in scores between these groups were analyzed using the Kruskal-Wallis test for non-parametric data[8]. The CCPKnow survey was initially developed with 18 questions, but question 4 discriminated poorly, and thus the score is based on responses to 17

questions. CCPKnow scores are calculated by summing up the number of correct responses. The median CCPKnow scores in the gold standard groups were as follows: 5.5 among clerical staff, 9 among general nurses, 10 among junior doctors, and 16 among specialist nurses ($p<0.001$ for the null hypotheses of equal medians) (see reference article for a graph showing the distribution of scores)[8]. The ROC (Receiver Operating Characteristic) curve, using IBD nurse-specialist knowledge as the gold standard, revealed an area under the curve (AUC) of 0.973 for differentiating individuals with IBD-nurse level knowledge from those with lower levels of knowledge; AUC scores closer to 1.0 indicate better accuracy for discriminating between groups. Using the validation group, a CCPKnow score cut-off of 14 had a sensitivity of 94% and a specificity of 95% for very good knowledge (IBD nurse specialist level knowledge) and a cut-off of 8 had a sensitivity of 78% and a specificity of 70% for at least adequate knowledge (general nurse level knowledge). CCPKnow scores were then grouped into levels: poor (0 to 7, clerical staff level), adequate (8 to 10, general nurse level), good (11 to 13, junior doctor level), very good (14 to 17, IBD nurse specialist level). Selinger et al. reported that the CCPKnow score had a Cronbach alpha value of 0.94, based on the validation group results, indicating high internal consistency; the Cronbach alpha score is calculated by $\alpha = [Kc/[\upsilon +(K-1)c)]$ where K = number of components, υ = average variance of each component, c = average of all covariances; the score increases as inter-correlation of test items increases. Selinger et al. reported the score had a Spearman correlation coefficient (ρ) = 0.641 ($p<0.001$) for the comparison with the CCKnow instrument

that, which measures general IBD knowledge, within the validation group. For the purpose of this study, the complete CCPknow questionnaire was administered, but question 4 was not included in the total CCPKnow score, based on the validation study. After validation, Selinger et al. administered it to a group of 145 female IBD patients aged 18 to 45 years, who were also given the CCKnow (Crohn's and Colitis Knowledge) survey for comparison.

2.3.4 Patient Study Methods Used to Reduce Bias

Attempts were made to reduce selection bias by inviting all eligible patients identified from the database, and by attempting to reach each non-responder multiple times. Attempts were made to reduce measurement bias by using the investigator-developed detailed questions, in various formats, to accurately classify reproductive history and family planning status. A standard measurement tool (the CCPKnow survey) was used to measure the IBD-specific reproductive knowledge.

2.4 Physician Study

2.4.1 Physician Study Population

The population of interest was physicians who were involved in the treatment of women with IBD. There were no inclusion or exclusion criteria for physicians, except that inclusion required them to identify themselves as managing women with IBD in their clinical practice.

2.4.2 Physician Recruitment

Physician recruitment occurred in stages:

1) physicians attending the national Mentoring in IBD conference in November 2012;
2) physicians attending the Gastroenterologists (GI) for General Practitioners (GP) conference in December 2012;
3) physicians referring patients to the IBD clinic;
4) members of the Canadian Association of Gastroenterology (CAG).

Physicians in groups 1 and 2 were given a package consisting of:

1) a letter of invitation (Appendix B-1);
2) an information and consent sheet (Appendix B-2);
3) a self-administered questionnaire (Appendix B-3).

The investigator distributed the packages at the conferences, and asked participating physicians to return the surveys after completion.

Physicians in group 3 were mailed a package consisting of:

1) a letter of invitation (Appendix B-4);
2) an information and consent sheet (Appendix B-5);
3) a self-administered questionnaire (Appendix B-3);
4) a stamped, self-addressed envelope.

Physicians in group 4 were invited to participate via:

1) an e-posting (Appendix B-6) placed on the Canadian Association of Gastroenterology (CAG) website, with a link to the electronic version of the survey (Appendix B-7);
2) a posting CAG included in their monthly e-newsletters.

A final attempt to increase response rate was made in June 2013, when personalized invitation letters (Appendix B-8) were faxed to referring physicians. These invitation letters included the link to the electronic version of the survey.

Physician participants were not required to return a signed consent form; returned paper questionnaires, and submitted electronic questionnaires were taken as implied informed consent. Physicians were not given an incentive for participation.

Figure 2-2 illustrates the groups of study factors collected for the physician study and the resulting classification of physicians with respect to key variables.

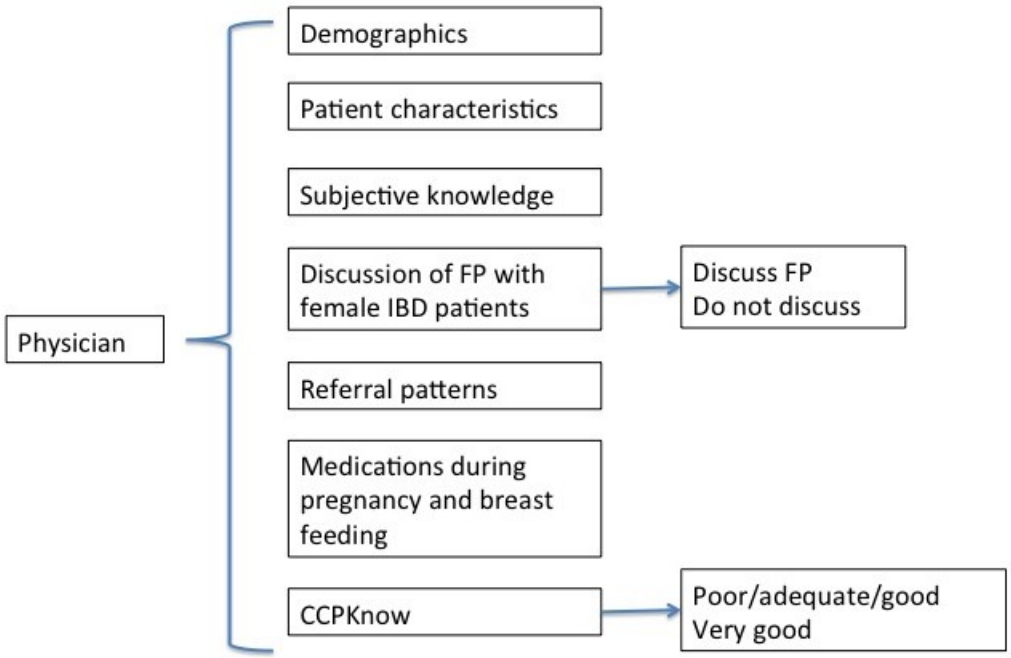

Figure 2-2: Physician Study Factor Scheme

IBD – inflammatory bowel disease
CCPKnow – Crohn's and Colitis Pregnancy Knowledge score
FP – family planning

2.4.3 Physician Data Sources and Variable Definitions

The physician questionnaire (Appendix B-3) was piloted at the Mentoring in IBD conference. There were no problems noted in the initial sample from the Mentoring in IBD conference, thus no changes were made to the questionnaire.

The physician questionnaire included the following sections:

- **Demographics and characteristics of practice (#1 – 9):** These included variables that may affect knowledge and practice patterns: gender; training status; years in practice; type of practice setting; type of practice; population of city they practice in; estimated percentage of their patients with IBD; how many IBD patients they see each year; how many pregnant IBD patients they managed in the past year.
- **Comfort managing pregnant IBD patients (#10, #11):** Physicians were asked how they feel about their IBD knowledge in general and whether they feel comfortable managing pregnant IBD patients, as these variables were felt to potentially affect knowledge and practice patterns.
- **Practice patterns pertaining to reproduction in IBD (#12 -17):** Physicians were asked if they routinely bring up the topic of family planning (discussion of family planning) with female IBD patients of reproductive age; what percentage they think inform them when they are trying to become pregnant; whether they refer female IBD patients who have been trying to conceive for more than one year to a fertility specialist or gynecologist; what percentage they think inform them when they are pregnant; whether they routinely refer pregnant IBD patients to an obstetrician.

- **Medication use in pregnancy and breastfeeding (#17, #18):** Physicians were asked to indicate whether they would stop or continue (or were unsure) a list of medications commonly used in IBD if a patient informed them she was trying to conceive or that she was pregnant. They were then asked the same question with respect to a patient informing them she was breastfeeding.
- **Information sources (#19):** Physicians were asked where they obtain information regarding reproductive issues in IBD.
- **Crohn's and Colitis Pregnancy Knowledge (CCPKnow) Score:** To assess physicians' level of IBD-specific reproductive knowledge, the CCPKnow score was used because there has not been any questionnaire developed to assess physicians' IBD-specific reproductive knowledge.

2.4.4 Physician Study Methods Used to Reduce Bias

Attempts were made to reduce selection bias by inviting all participating physicians attending all conferences listed, and also by inviting all members of the Canadian Association of Gastroenterology. In addition, physician surveys were collected anonymously to reduce selection bias from physician non-participation due to concern about being labeled as having poor knowledge.

2.5 Data Entry and Data Analysis

Patient and physician survey responses were entered into separate files using coded study numbers and no personal identifiers. Data was entered directly into SPSS (Statistical Program version 20.0 and 21.0) and data analysis performed within SPSS. Graphs and charts were created using Excel 2011 version 14.3.9. In cases where a question was unanswered, the answer was considered missing for that question, and the denominator was reduced, so that the proportion reported is out of all respondents who replied to that question.

Variables were recoded as explained below.

Patient questions:

1) **Education:** Categorized as "grade 1 to grade 12", "college/university", "graduate degree", "professional school degree", "other"; the "other" category included respondents with trade school and other training that did not fit into academic degree categories.
2) **Medication history:** Responses of "Mesalamine" or "Sulfasalazine" were recoded as "5-ASA/sulfasalazine", as they are similar in terms of efficacy and side effects in the treatment of IBD. Responses of "Steroids (prednisone, solumedrol)" or "Budesonide" were recoded as "Steroids" as prednisone, solumedrol, and

budesonide are all corticosteroids and are used in an overlapping manner in the treatment of IBD.

3) **Child status:** Dichotomized as “childless” or “have children” – responses of “preterm and low birth weight”, “full term and low birth weight”, “full term and healthy” were coded as “has children”, while the lack of any successful outcomes of pregnancy were coded as “childless”. Patients were also asked if they had any adopted children. Women who were “childless” but had adopted children were classified as “childless”, because many of the concerns and knowledge issues relate to concepts revolving around biologic/genetic and physiological interactions between pregnancy and IBD. This study focuses on differences between women who choose not to have their own biological children (voluntary childlessness) and women who want to have children or already have children. Further sub-analysis will be done subsequent to this study regarding the effects of a history of pregnancy and IBD-specific reproductive knowledge, concerns, and beliefs or opinions.
4) **Concerns** (Reproductive history questions #14 and #16): These two questions listed the same concerns, thus they were analyzed together, and subsequent sub-group analysis was conducted to compare responses in childless women and women who have children.

Physician Questions:

1) **Training Status:** Categorized as “Gastroenterologist”, “Gastroenterology trainee”, “General Practitioner”, “Other”. The number of respondents who were “general

internist", "surgical trainee", "surgeon" or "other health care professional" were small, so these categories were included under the new category "other".

2) **Type of practice setting:** Dichotomized as "community" or "academic". The categories of "clinical, community hospital" and "private outpatient clinic" were categorized as "community", while "clinical, academic hospital" and "research, academic hospital" were classified as "academic".
3) **Type of practice:** Categorized as "Gastroenterology focus", "Gastroenterology/ Hepatology", "General practice", "Other". The categories of "hepatobiliary focus", "general medicine", "general surgery", and "other" were classified as "Other".
4) **Population of city:** Categorized as "0 to 99,999", "100,000 to 499,999", or ">500,000". Any population <100,000 was recoded as "0 to 99,999".
5) **Number of pregnant IBD patients managed in past year:** Categorized as "none", "1 to 10", "11 or more". Categories of "11 to 20" and ">20" were recoded as "11 or more".

2.6 Statistical Analysis

Distributions of all variables were inspected to determine if responses were normally distributed. The continuous variables current age, age at diagnosis, and duration of IBD did not have normal distributions and thus their distributions are described as medians and interquartile ranges (IQR).

The statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests. For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions

The CCPKnow score can be reported as either a numerical score from 0 to 17, or as a qualitative level of knowledge, with levels of knowledge covering ranges of scores. The analyses presented in this study include comparisons of the median CCPKnow scores across subgroups, as well as comparisons of the proportion of respondents with specific qualitative knowledge levels across subgroups.

The cross-sectional design limits the measures of outcome event frequency to the prevalence proportion (cases divided by population at risk) or prevalence odds (case/noncase ratio). The ratio of prevalence odds (i.e., prevalence odds ratio) is the preferred measure of association in a cross-sectional study when the outcomes have not occurred within a defined risk period[9]. To estimate the effect of independent variables on dependent variables, unadjusted odds ratios (OR) were estimated using binary logistic regression; reported ORs were rounded to two significant figures and presented with 95% confidence intervals (CI). To estimate ORs adjusted for selected covariates, multivariable logistic regression was used to obtain adjusted ORs and 95% CIs.

Covariates were identified based on whether they could affect both the independent variable of interest and the outcome of interest, without being affected by the independent variable. Causal relation diagrams, or directed acyclic graphs (DAGs) for the associations between independent variables and dependent variables were created to identify variables to be included as covariates in each multivariable logistic regression analyses. DAGs were created using DAGitty Version 2.0 (www.dagitty.net)[10].

2.7 Ethics

This study was approved by the Health Research Ethics Board (HREB) of the University of Alberta. Patients and physicians were aware that participation in this study was voluntary. Patients were aware that participation status in this study did not affect their regular clinical care. All study packages included a study information sheet and consent form. For patients, the paper study materials included signed consent forms, while the electronic version only allowed the participant to complete and submit the questionnaire if they completed the electronic consent form. Patients received a $10 coffee shop gift card upon return of the completed study materials. Physicians did not receive any incentive for participation.

2.8 References

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3 RESULTS: A Description of the Patient and Physician Study Populations

3.1 Patient Results

The initial electronic database search using the inclusion criteria listed in Chapter 2 retrieved a list of 434 IBD female patients. Some patients had moved and their surveys were returned unopened, and they could not be reached to update their mailing addresses. Initially, these patients were categorized separately from non-responders; however, as we could not confirm that questionnaires that were not returned in the mail had indeed reached the targeted patient, all patients who did not return a questionnaire were considered non-responders. A total of 252 patients returned study packages. Of these, 4 questionnaires were incomplete, with blank CCPKnow or missing demographic responses; this resulted in a final response rate of 57.1% (248/434).

3.1.1 Patient Characteristics and Prevalence of Childlessness

Table 3-1 shows the distribution of the 248 respondents by demographic variables and the prevalence of childlessness within each demographic category. There were 128 (51.6%) childless women and 120 (48.4%) women who have children. The median patient age was 32.0 (26.0 – 38.0) years. Childless women were younger, with a median age of 26.0 (IQR 22.0 – 33.0) years, than women with children, whose median age was 36.0 (IQR 32.0 – 41.0) years ($p<0.001$ for the difference in these medians). As shown in Table 3-1, the prevalence of childlessness decreased with increasing age. There were 67 (27.0%) single women and 173 (69.8%) partnered women. Compared to single women,

Table 3-1: Characteristics and Prevalence of Childlessness by Selected Study Variables among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	Total patients (N=248)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Current age (years)					
18 to 24	49	19.8	47/49	95.9	<0.001
25 to 29	50	20.2	34/50	68.0	
30 to 34	56	22.6	24/56	42.9	
35 to 39	47	19.0	12/47	25.5	
40 to 45	47	19.0	12/47	25.5	
Marital status					
Single	67	27.0	60/67	89.6	<0.001
Partnered	173	69.8	66/173	38.2	
Divorced	8	3.2	2/8	25.0	
Education					
Grade 1 to Grade 12	56	22.6	29/56	51.8	0.26
College/university	157	63.3	76/157	48.4	
Graduate degree	11	4.4	7/11	63.6	
Professional school degree	5	2.0	2/5	40.0	
Other	19	7.7	14/19	73.7	
Employment (n=229)*					
Unemployed	28	12.2	13/28	46.4	0.019
Part time	46	20.1	24/46	52.2	
Full time	117	51.1	73/117	62.4	
Other	38	16.6	13/38	34.2	
Family history of IBD					
Yes	107	43.1	52/107	48.6	0.41
No	141	56.9	76/141	53.9	
Other Medical History					
Mood (n=227)*					
Yes	61	26.9	30/61	49.2	0.40
No	166	73.1	92/166	55.4	
Irritable bowel (n=229)*					
Yes	65	28.4	36/65	55.4	0.75
No	164	71.6	87/164	53.0	
Gynecological (n=230)*					
Yes	28	12.2	15/28	53.6	0.97
No	202	87.8	109/202	54.0	

Category	Total patients (N=248)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Diabetes (n=230)*					
Yes	5	2.2	3/5	60.0	0.78
No	225	97.8	121/225	53.8	
Other (n=229)*					
Yes	47	20.5	23/47	48.9	0.42
No	182	79.5	101/182	55.5	
Have discussed family planning with a physician					
Yes	154	62.1	72/154	46.8	0.050
No	94	37.9	56/94	59.6	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

the prevalence of childlessness was 51.4 per 100 lower among married women, and 64.6 per 100 lower among divorced women. The prevalence of childlessness was similar across education levels. More than half the respondents had full time employment (117/229 (51.1%)); compared to the unemployed group, the prevalence of childlessness was 16.0 per 100 higher in the full time employment group. Almost half (107/248 (43.1%)) of the patients reported having a relative with IBD. The prevalence of childlessness was similar among women with or without family history of IBD. The distribution of co-morbid disorders is also shown in Table 3-1; less than a third of respondents indicated they had any of these co-morbid disorders. The prevalence of childlessness was similar among those with or without these co-morbid disorders.

A large percentage of women (154/248 (62.1%)) indicated they had discussed family planning with a physician. The prevalence of childlessness was 12.8 per 100 higher among women who had not discussed family planning with a physician compared to women who had discussed family planning with a physician.

3.1.2 Patient IBD History and Prevalence of Childlessness

There were more respondents with CD (150/248 (60.5%)) than UC (88/248 (35.5%)) or indeterminate (10/248 (4.0%)) (Table 3-2). The prevalence of childlessness was similar across disease types. The median age at IBD diagnosis was 21.0 (IQR 17.0 – 27.0) years, with the majority (183/248 (73.8%)) of respondents reporting diagnosis after the age of 18 years. The median age at IBD diagnosis was lower in childless women than women

who have children (19.0 (IQR 15.0 – 22.5) years v. 25.0 (IQR 20.0 – 30.0) years, respectively; p<0.001). The prevalence of childlessness was 32.2 per 100 women higher in the group diagnosed before age 18 years compared to those diagnosed between the ages of 18 to 45 years (p<0.001). The median duration of disease was 9.0 (IQR 5.0 – 15.0) years, with the majority (191/248 (77.0%)) of patients having 5 or more years with the disease.

The prevalence of childlessness was similar across women with different disease durations. Just under a quarter of patients (54/225 (24.0%)) had a history of perianal disease. The prevalence of childlessness was similar among women with and without perianal disease. A few patients (17/248 (6.9%)) had history of colectomy with internal pouch. A small percentage of patients (24/248 (9.7%)) had surgery involving an ostomy (external bag). The prevalence of childlessness was 26.7 per 100 women higher in the group with a history of colectomy compared to those without a history of colectomy (p=0.034 for this comparison), and 25.9 per 100 women higher in the group with a history of ostomy compared to those without an ostomy (p=0.016 for this comparison).

Table 3-2 also shows the distribution of medication use (collapsed as described in Chapter 2). Sulfasalazine and 5-aminosalicylates were categorized together; budesonide, prednisone and solumedrol were categorized together. The majority of respondents had been on 5-ASA/sulfasalazine (218/248 (87.9%)), steroids (216/248 (87.1%)), azathioprine/6-MP (180/248 (72.6%)), or antibiotics (152/248, (61.3%)).

Table 3-2: IBD History and Prevalence of Childlessness by Selected Study Variables among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	Total patients (N=248)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Type of IBD					
Crohn's disease	150	60.5	76/150	50.7	0.49
Ulcerative colitis	88	35.5	45/88	51.1	
Indeterminate	10	4.0	7/10	70.0	
Age diagnosed with IBD					
Younger than 18 years	65	26.2	49/65	75.4	<0.001
18 to 45 years	183	73.8	79/183	43.2	
Duration of IBD					
0 to 4 years	57	23.0	33/57	57.9	0.28
5 or more years	191	77.0	95/191	49.7	
Perianal disease (n=225)*					
Yes	54	24.0	29/54	53.7	0.99
No	171	76.0	92/171	53.8	
Colectomy with pouch					
Yes	17	6.9	13/17	76.5	0.034
No	231	93.1	115/231	49.8	
Ostomy					
Yes	24	9.7	18/24	75.0	0.016
No	224	90.3	110/224	49.1	
Medication History					
Do not remember					
Yes	8	3.2	3/8	37.5	0.42
No	240	96.8	125/240	52.1	
5-ASA/sulfasalazine					
Yes	218	87.9	113/218	51.8	0.85
No	30	12.1	15/30	50.0	
Steroids					
Yes	216	87.1	114/216	52.8	0.34
No	32	12.9	14/32	43.8	
Methotrexate					
Yes	42	16.9	19/42	45.2	0.36
No	206	83.1	109/206	52.9	
Azathioprine/6-MP					
Yes	180	72.6	97/180	53.9	0.24
No	68	27.4	31/68	45.6	

	Total patients (N=248)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Anti-TNF					
Yes	117	47.2	62/117	53.0	0.68
No	131	52.8	66/131	50.4	
Antibiotics					
Yes	152	61.3	77/152	50.7	0.71
No	96	38.7	51/96	53.1	
Other (clinical trials)					
Yes	32	12.9	16/32	50.0	0.85
No	216	87.1	112/216	51.9	
Steroids for a flare					
Yes	64	25.8	33/64	51.6	0.99
No	184	74.2	95/184	51.6	
CCPKnow level					
Poor (0 to 7)	131	52.8	78/131	59.5	0.070
Adequate (8 to 10)	49	19.8	21/49	42.9	
Good (11 to 13)	48	19.4	21/48	43.8	
Very good (14 to 17)	20	8.1	8/20	40.0	
Dichotomized CCPKnow level					
Poor (0 to 7)	131	52.8	78/131	59.5	0.008
Adequate + (8 to 17)	117	47.2	50/117	42.7	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

About half (117/248 (47.2%)) of the respondents had been on anti-TNF therapy, and 12.9% (32/248) had been on other medications (clinical trials). The prevalence of childlessness was similar across groups of women exposed to different medications. Just over a quarter (64/248 (25.8%)) of respondents had been given steroids in the past year to treat a flare of their IBD. The prevalence of childlessness was similar in women who had been treated with steroids for a flare in the past year and in those who had not. Finally Table 3-2 shows the distribution of CCPKnow levels; the prevalence of childlessness was 16.8 per 100 women higher among women in the "poor" CCPKnow category compared to women with "adequate +" levels (p=0.008 for this comparison).

3.1.3 Patient Reproductive History and Prevalence of Childlessness

As shown in Table 3-3, a small percentage of women reported seeing a fertility specialist, or having fertility treatment (28/248 (11.3%)). Just over half (136/248 (54.8%)) of all respondents had ever been pregnant (Table 3-3). Of the 223 who responded to the question about being currently pregnant, 11 (4.9%) were currently pregnant. Seventeen of the 128 (13.3%) childless women had been pregnant at one time. Table 3-3 also shows the proportion of women who reported each of the listed pregnancy outcomes. The prevalence of childlessness was 35.5 per 100 women higher in the group that reported having had a therapeutic abortion compared to women who had never had a therapeutic abortion (p<0.001) and 14.0 per 100 women higher in the group that reported having had a miscarriage compared to women who had never had miscarriage (p=0.016).

Table 3-3: Reproductive History and Prevalence of Childlessness by Selected Study Variables among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	Total patients (n=248)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Had fertility treatment					
Yes	28	11.3	14/28	50.0	0.86
No	220	88.7	114/220	51.8	
Ever been pregnant					
Yes	136	54.8	17/136	12.5	<0.001
No	112	45.2	111/112	99.7	
If have been pregnant, timing in relation to IBD diagnosis (n=135*)					
Before only	36	26.7	4/36	11.1	0.50
After only	78	57.8	11/78	14.1	
Before and After	21	15.6	1/21	4.8	
Pregnancy outcomes (n=136*)					
Therapeutic abortion					
Yes	16	11.8	7/16	43.8	<0.001
No	120	88.2	10/120	8.3	
Miscarriage					
Yes	52	30.1	11/52	21.1	0.016
No	84	61.8	6/84	7.1	
Stillbirth					
Yes	2	1.5	1/2	50.0	0.11
No	118	88.1	16/118	11.9	
Preterm/LBW					
Yes	13	9.6	0/13	0	0.15
No	123	90.4	17/123	13.8	
Full term/LBW					
Yes	8	5.9	0/8	0	0.27
No	128	94.1	17/128	13.3	
Full term/healthy					
Yes	99	72.8	0/99	0	<0.001
No	37	27.2	17/37	45.9	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

3.2 Physician Results

3.2.1 Physician Characteristics and Proportion who Discuss Family Planning

There were 225 returned surveys, of which 215 had complete responses for analysis. Almost two-thirds (136/215 (63.3%)) of physicians reported that they "routinely bring up the topic of family planning".

As shown in Table 3-4, the majority (147/215 (68.4%)) were male physicians. The proportion of physicians who discuss family planning was similar across genders. The majority of respondents were GI physicians (100/215 (46.5%)) and GP physicians (79/215 (36.7%)). Compared to the proportion that discuss family planning among GI physicians (85/100 (85.0%)), this proportion was lower by 39.2 per 100 physicians among GI trainees, 43.2 per 100 physicians among GP physicians, and 26.7 per 100 physicians among Other physicians (85/100 (85.0%) GI physicians, 11/214 (45.8%) GI trainees, 33/79 (41.8%) GP physicians, 7/12 (58.3%) Other physicians; $p<0.001$ for the comparison across all categories).

Most of the physician respondents had more than 10 years of practice; the proportion of physicians who discuss family planning was similar by duration of practice.

Table 3-4: Characteristics and the Proportion of Physicians who Discuss Family Planning by Selected Study Variables among 215 Canadian Physicians

	Total physicians (n=215)*		Proportion who Discuss FP		Chi-square p-value
	N	% of total*	N	% of category	
Gender					
Male	147	68.4	93/147	63.3	1.0
Female	68	31.6	43/68	63.2	
Training status					
Gastroenterologist (GI)	100	46.5	85/100	85.0	<0.001
GI trainee (GIT)	24	11.2	11/24	45.8	
General practitioner (GP)	79	36.7	33/79	41.8	
Other	12	5.6	7/12	58.3	
Years in practice (n=186)*					
0 to 4 years	28	15.1	20/28	71.4	0.22
5 to 10 years	26	14.0	21/26	80.8	
11 to 20 years	48	25.8	28/48	58.3	
> 20 years	84	45.2	53/84	63.1	
Population of city (n=152) *					
0 to 99,999	50	32.9	27/50	54.0	0.78
100,000 to 499,999	33	21.7	20/33	60.6	
>500,000	69	45.4	37/69	53.6	
Type of practice (n=183) *					
Community	129	70.5	73/129	56.6	<0.001
Academic	54	29.5	46/54	85.2	
Percentage of patients with IBD (n=212) *					
0 – 9%	96	45.3	42/96	43.8	<0.001
10 – 24%	68	32.1	56/68	82.4	
25 – 50%	32	15.1	22/32	68.8	
51 – 100%	16	7.7	13/16	81.3	
Number of IBD patients each year (n=212) *					
0 to 9	36	16.7	16/36	44.4	0.005
10 to 50	77	35.8	43/77	55.8	
51 to 100	29	13.5	20/29	69.0	
101 to 150	21	9.8	16/21	76.2	
more than 150	52	24.2	41/52	78.9	
Number of pregnant IBD patients managed in past year					
None	87	40.5	38/87	43.7	<0.001
1 to 10	80	37.2	69/80	86.3	
11 or more	48	22.3	29/48	60.4	

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator. FP = family planning

Most of the physician respondents worked in a city with a population >500,000. The proportion of physicians who discuss family planning was similar across physicians grouped by population of the city.

Most of the physician respondents were in community practice (129/183 (70.5%)) with 65 (35.5%) in “clinical, community hospital” practice, and 64 (35.0%) in “private outpatient clinic” practice. The other 54 (29.5%) were in academic practice, with 43 (23.5%) in “clinical, academic hospital” practice, and 11 (6.0%) in “research, academic hospital” practice. The proportion of physicians who discuss family planning was 28.6 per 100 physicians higher among those who were in academic practice compared to those in community practice (46/54 (85.2%) v. 73/129 (56.5%), respectively; $p<0.001$)

As shown in Table 3-4, the majority of physicians had practices with IBD patients comprising 0 – 9% of patients; compared to the proportion that reported that they discuss family planning in this group of physicians (42/96 (43.8%)), the proportion was higher by 38.6 per 100 physicians among physicians with practices in which 10 – 24% of patients have IBD (56/68 (82.4%)); higher by 25 per 100 physicians among physicians with practices in which 25 – 50% of patients have IBD (22/32 (68.8%)); and higher by 37.5 per 100 physicians among physicians with practices in which more than 50% of patients have IBD (13/16 (81.3%)) ($p<0.001$ for the comparison across all categories).

Most physicians reported seeing between 10 to 50 IBD patients per year. The proportion of physicians who discuss family planning increased monotonically with increasing number of IBD patients seen per year, from 44.4% among those who reported seeing 0 to 9 IBD patients per year to 78.9% among those who reported seeing more than 150 IBD patients per year (p=0.005 for this comparison).

Most physicians fell into the none or 1 to 10 pregnant IBD patients managed in the past year categories. Compared to physicians who managed pregnant IBD patients, a lower proportion of those who did not manage any such patients discuss family planning (38/87 (43.7%) if managed no pregnant IBD patients, 69/80 (86.3%) if managed 1 to 10 pregnant IBD patients, 29/48 (60.4%) if managed 11 or more pregnant IBD patients; p<0.001).

3.3 Discussion of the Accuracy of Data Obtained from Patient and Physician Respondents for this Analysis

More than half of the patient respondents were childless, which is similar to previously reported estimates of the prevalence of childlessness among respondents of questionnaire-based studies on childlessness in IBD patients. In the Selinger et al.[1] study, 50.3% of the respondents were childless; in the Marri et al.[2] study, 51% (28% temporary, 18% voluntary, 5% non-voluntary) of CD patients were childless and 29.3% (13.6% temporary, 14% voluntary, 1.7% non-voluntary) of UC patients were childless; in the Mountifield et al.[3] study, 42% of respondents were childless, although this included male and female respondents.

It may be that childless patients, or patients with a particular interest in this topic due to other study factors, were more likely to respond to the invitation to participate in this study. This would have increased the frequency of childlessness and related factors among women in the study population relative to the target population. If women with higher levels of IBD-specific knowledge were either more or less likely to participate if they were childless, or had related attributes, this would have distorted associations between the study factors of interest. However, given that the prevalence of childlessness in this study population is similar to previously reported studies, there is no evidence that this study population does not represent the target population of female IBD patients in term of the prevalence of childlessness. Similarly, there is no evidence that the distribution of IBD-specific reproductive knowledge levels in this study population differs from that of the target population.

The patient response rate of this study (57.1%) is higher than previously reported response rates when considering only female respondents. The response rates in previous studies varied as follows: 20% (637/3147)[2], 28% (101/361 postal return rate)[1], 43% (31/73)[4], and 59% (217/365)[3]. However, Marri et al.[2] included males, thus for analysis, they had 169 female IBD patients; Mountifield et al.[3] also included males, leaving 168 female IBD patients.

The University of Alberta IBD clinic services a large referral basis, covering most of the western provinces and the northern territories of Canada. The patient population is

diverse in terms of demographics and IBD history. As such, the respondents in this study were drawn from a broad population of women with IBD. However, there could be determinants of participation that altered the distribution of disease severity, baseline history of medication use, and perhaps baseline IBD-specific knowledge. If the distribution of key variables was altered to different degrees across comparison groups, this may have led to biased estimates of the associations of interest.

This is one of the first studies to characterize and compare different physician groups, including gastroenterologists, gastroenterology trainees, general practitioners, and other physician groups, in terms of IBD-specific reproductive knowledge and practice patterns. Previous published studies included general practitioners only[4,5]. Tan et al. studied general IBD knowledge and attitudes among 409 GPs in Australia, but not IBD-specific reproductive knowledge[5]. Toomey et al. reported on 49 out of 112 (44% response rate) general practitioners, but did not use a specific IBD-specific reproductive knowledge survey[4].

The physicians in this study were recruited from local, provincial, and national settings. As such, this study population captures a variety of physicians involved in the management of female IBD patients. The respondents mainly consisted of gastroenterologists, and general practitioners. The physicians varied on years in practice, percentage of patients with IBD and number of IBD patients seen each year.

The majority of physicians had managed 10 or fewer pregnant IBD patients in the past year, with 40% not managing any IBD patients.

Among the physician respondents, the majority (63.3%) indicated they "routinely bring up the topic of family planning". The proportion that discuss family planning was higher among gastroenterologists, those with less than 10 years of practice, those in academic practice, those with practices in which 10% or more of the patients have IBD, those who see more IBD patients per year, and those who managed 10 or more pregnant IBD patients in the past year.

Factors that influenced the participation of physicians may include the varied recruitment methods, along with the physicians' knowledge level and workload. Physicians with higher IBD-specific reproductive knowledge may have been more likely to complete and submit the questionnaire than physicians with lower knowledge levels. Physicians with busier practices may not have had time to complete and submit the questionnaires. Nevertheless, the recruitment methods targeted a variety of physician groups and efforts were made to encourage participation to the extent possible.

3.4 Conclusion

The patient sample provides a broad sample of the female IBD patient population. The physician sample provides a broad sample of physicians involved in the management of female IBD patients.

3.5 References

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5. Tan M, Holloway RH, Lange K, et al. General practitioners' knowledge of and attitudes to inflammatory bowel disease. Intern Med J. 2012;42:801–807.

4 Among Women with IBD, Does Discussion of Family Planning with a Physician Influence IBD-specific Reproductive Knowledge & Does IBD-specific Reproductive Knowledge Influence Childlessness?

4.1 Introduction

Inflammatory bowel disease (IBD) is a chronic intestinal disease that often affects patients in their reproductive years. Management of IBD can therefore be challenging when considering the interactions and effects of IBD and IBD-treatments on fertility, pregnancy, breastfeeding, and maternal and neonatal outcomes. Women with IBD have been reported to have fewer children than women without IBD, with reported ranges of 14% to 36% of women with IBD choosing not to have children, a concept termed "voluntary childlessness" in the literature[1-3], compared to reported ranges of 2.5% to 28% of the general population[3]. Previous reports have documented that the reasons women with IBD choose voluntary childlessness include concerns related to medication-associated teratogenicity[2,4], the impact of pregnancy on their IBD[1], the risk of passing IBD to their child[1,2], and not being able to care for their child[1]. Many of these concerns are based on beliefs that conflict with scientific evidence, as studies have shown that women with IBD, in general, have similar fertility as the general population, and are able to carry successful pregnancies and care for their infants, especially if their IBD is in remission[5-11]. In addition, most medications used to treat IBD have not been shown to cause significant adverse pregnancy or neonatal outcomes.

Recent publications have reported significant patient knowledge deficits regarding pregnancy and IBD, and unwarranted fears and concerns among women with IBD[2,4,12,13]. Thus, a lack of knowledge and consequent negative views regarding reproduction given IBD may be contributing to the voluntary childlessness seen among women with IBD. However, an objective measure of IBD-specific reproductive knowledge, the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey, has only recently been developed[14].

Given that studies have reported deficits in IBD-specific reproductive knowledge and investigators have postulated that voluntary childlessness was due to lack of knowledge leading to unwarranted fears and concerns, it is important to investigate the association between IBD-specific reproductive knowledge and childless in women with IBD. In addition, there has been little research on the associations of physician-patient discussion of family planning with patient IBD-specific reproductive knowledge, concerns, and childlessness.

The objectives of this analysis were to estimate (1) the effect of IBD-specific reproductive knowledge on childlessness among women with IBD and (2) the effect of family planning discussion with a physician on (a) IBD-specific reproductive knowledge and (b) childlessness.

4.2 Methods

4.2.1 Recruitment and Questionnaire

Female IBD patients aged 18 to 45 years were identified from the University of Alberta Inflammatory Bowel Disease clinic, and invited to complete the patient questionnaire that included the CCPKnow survey as well as questions on their demographic characteristics, IBD history, and reproductive history. Full details have been presented in Chapter 2 Methods.

4.2.2 Data Sources and Variable Definitions

IBD-specific reproductive knowledge (CCPKnow)

Raw scores were calculated by summing the number of correct responses. Women were categorized into having a poor CCPKnow knowledge level (CCPKnow scores of 0 to 7) or an adequate+ CCPKnow knowledge level (CCPKnow scores of 8 to 17).

Childlessness

Women were categorized as childless if they had no biological children; and as having children if they had at least one biological child from any pregnancy.

Discussion of Family Planning with a Physician

The classification of women as having discussed family planning with a physician was based on the response to the questionnaire item: “who have you discussed family

planning with?" with responses classified as "yes" or "no" as shown in Table 4-1:

Table 4-1: Categorization of Responses to Discussion of Family Planning with a Physician

Responses	Have Discussed FP with a Physician?
Have not discussed with anyone	No
Gastroenterologist	Yes
General Medicine specialist	Yes
Specialist (gynecologist, obstetrician)	Yes
Family physician	Yes
IBD nurse	No
Pharmacist	No
Family and Friends	No
Other	No

4.2.3 Statistical Analysis

This analysis aimed to estimate the effects of IBD-specific reproductive knowledge on childlessness by:

1) comparing the median CCPKnow scores of childless women to the median CCPKnow scores of women with children
2) estimating ORs for the dose-response association between the incremental CCPKnow score and the prevalence odds of childlessness.

The analysis aimed additionally to estimate the effects of having discussed family planning with a physician on IBD-specific reproductive knowledge and childlessness by:

1) comparing the median CCPKnow scores of women who had discussed family planning with a physician to the median CCPKnow scores of those who had not discussed family planning with a physician

2) estimating the OR for the effect of having discussed family planning with a physician on the prevalence odds of childlessness.

For continuous variables, medians and interquartile ranges (IQR) were tabulated, and medians were compared across subgroups; the statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests. For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions.

To estimate the effect of independent variables on childlessness, multivariable logistic regression was used to estimate odds ratios and 95% CI adjusted for selected covariates. Covariates were selected based on whether they could affect both the independent variable of interest and the outcome of interest while not being affected by the independent variable of interest. DAGs used to identify adjustment variables were created using DAGitty Version 2.0 (www.dagitty.net). The resulting multivariable models were repeated with stratification by age and marital status, as the prevalence of childlessness was lower among older women and among married women (see Chapters 3 and 4).

4.3 Results

4.3.1 Characteristics of the Study Population

Complete data was available from 248 women who returned questionnaires that had complete responses for all variables included in the final multivariable analysis. Of the 248 women, 128 (51.6%) were childless and 120 (48.4%) have children. Tables 3-1, 3-2, 3-3 show the distributions of demographic variables for this patient group. (Appendix C-2 Tables C2-0-1, C2-0-2, and C2-0-3 show these distributions separately for women with poor CCPKnow levels compared to women with adequate+ CCPKnow levels).

4.3.2 IBD-specific Reproductive Knowledge (as measured by CCPKnow)

The distribution of CCPKnow scores is shown in Figure 4-1. The median CCPKnow score was 7.0 (IQR 3.0 – 11.0), with 52.8% (131/248) of women having poor CCPKnow scores. The median CCPKnow score and the proportion of women with poor CCPKnow scores are shown within subgroups in Table 4-2. Childless women had median CCPKnow scores that were two full units lower than median scores of women who have children (6.0 (IQR 3.0 – 9.0) v. 8.0 (IQR 5.0 – 11.0), respectively; p=0.017). The prevalence of childlessness was 16.8 per 100 women higher among women with poor CCPKnow scores than among women with adequate + CCPKnow scores (78/131 (59.5%) v. 50/117 (42.7%), respectively; p=0.008). Women who were single had median CCPKnow scores that were 3.0 points lower than the median scores of women who were married/ partnered (p<0.001). The proportion of women with poor CCPKnow scores was 34.2 per

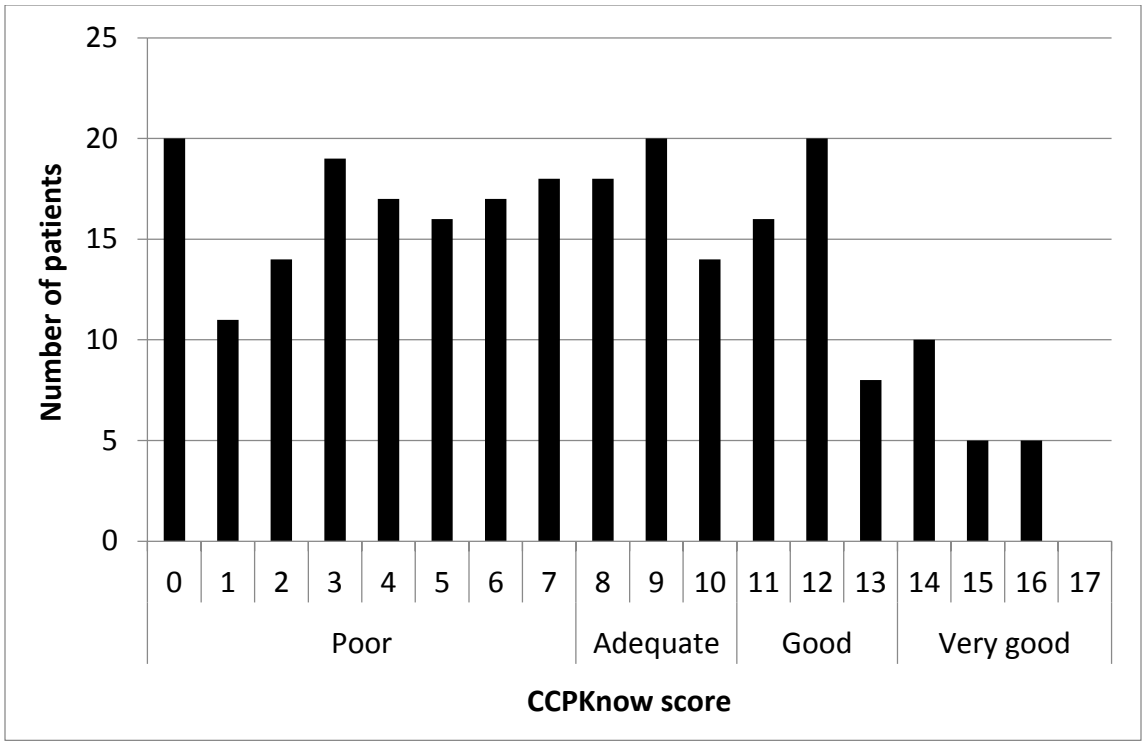

Figure 4-1: Distribution of CCPKnow Scores Measuring IBD-specific Reproductive Knowledge among 248 women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Total number of patients n = 248.
"Poor" n = 131/248, 52.8%;
"Adequate" n = 49/248, 19.8%;
"Good" n=48/248, 19.4%;
"Very good" n = 20/248, 8.1%.

100 women higher among single women compared to partnered women (52/67 (77.6%) v. 75/173 (43.4%), respectively; p<0.001 for this comparison). The proportion of women with poor CCPKnow scores differed across subgroups based on level of education completed (p=0.007).

The median CCPKnow score was lower among women diagnosed before 18 years of age compared to women diagnosed at older ages (6.0 (IQR 3.0 – 9.0) v. 7.0 (4.0 – 11.0), respectively; p=0.03). The proportion of women with poor CCPKnow scores differed across subgroups based on age at diagnosis (p=0.043). The median CCPKnow scores and the proportion of women with poor CCPKnow scores were similar across subgroups based on duration of IBD, and history of perianal disease, colectomy, or ostomy.

Women who had ever been pregnant had a median CCPKnow score that was 2.0 units higher than the median score among those who had never been pregnant (8.0 (IQR 5.0 – 11.0) v. 6.0 (3.0 – 9.0), respectively; p<0.001), and the proportion of women with poor CCPKnow scores was 17.6 per 100 women lower among women who had been pregnant compared to those who had not been pregnant (p<0.001).

Table 4-2: Description of IBD-specific Reproductive Knowledge in 248 Women with IBD: Median CCPKnow Score and the Proportion with a Poor CCPKnow Score by Selected Study Variables among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	CCPKnow score	Mann-Whitney	Proportion with Poor CCPKnow		Chi-square
	Median (IQR)	p-value	N	%	p-value
Total cohort (n=248)	7.0 (3.0-11.0)	-	131/248	52.8	
Age (years)					
18 to 24	4.0 (2.0 – 8.0)	0.001	34/49	69.4	0.043
25 to 29	8.0 (4.0 – 12.0)		23/50	46.0	
30 to 34	9.0 (6.0 – 12.0)		23/56	41.1	
35 to 39	6.0 (3.0 – 9.0)		27/47	57.4	
40 to 45	7.0 (4.0 – 11.0)		24/46	52.2	
Marital status					
Single	5.0 (2.0 – 7.0)	<0.001	52/67	77.6	<0.001
Partnered	8.0 (4.0-11.0)		75/173	43.4	
Divorced	8.0 (5.0 – 10.0)		4/8	50.06	
Education status					
Grade 1 to Grade 12	4.0 (2.0 – 8.0)	0.004	39/56	69.6	0.007
College/university	8.0 (4.0 – 11.0)		79/157	50.3	
Graduate degree	9.0 (8.0 – 11.0)		2/11	18.2	
Professional school degree	9.0 (8.0 – 14.0)		1/5	20.0	
Other	7.0 (5.0 – 10.0)		10/19	52.6	
Employment status					
Unemployed	6.0 (3.0 – 9.0)	0.38	18/28	64.3	0.47
Part time	8.0 (3.0 – 12.0)		21/46	45.7	
Full time	7.0 (4.0 – 11.0)		61/118	52.1	
Other	7.0 (4.0 – 10.0)		21/39	55.3	
Family history of IBD					
Yes	7.0 (4.0 – 11.0)	0.39	54/107	50.5	0.52
No	7.0 (3.0 – 11.0)		77/141	54.6	
Type of IBD					
Crohn's disease	7.0 (4.0 – 11.0)	0.37	77/150	51.3	0.51
Ulcerative colitis	7.0 (4.0 – 11.0)		47/88	53.4	
Indeterminate	3.0 (1.0 – 10.0)		7/10	70.0	
Age diagnosed with IBD					
Younger than 18 years	6.0 (3.0 – 9.0)	0.027	40/65	61.5	0.10
18 to 45 years	7.0 (4.0 – 11.0)		91/183	49.7	

	CCPKnow score	Mann-Whitney	Proportion with Poor CCPKnow		Chi-square
	Median (IQR)	p-value	N	%	p-value
Duration of IBD					
0 to 4 years	6.0 (3.0 – 10.0)	0.22	34/57	59.6	0.24
5 or more years	7.0 (4.0 – 11.0)		97/191	50.8	
Perianal disease					
Yes	6.0 (3.0 – 11.0)	0.67	32/54	59.3	0.28
No	7.0 (3.0 – 11.0)		87/171	50.9	
Colectomy with pouch					
Yes	6.0 (3.0 – 9.0)	0.24	12/17	70.6	0.13
No	7.0 (3.0 – 11.0)		119/231	51.5	
Ostomy					
Yes	6.0 (4.0 – 10.0)	0.56	15/24	62.5	0.32
No	7.0 (3.0 – 11.0)		116/226	51.8	
Ever pregnant					
Yes	8.0 (5.0 – 11.0)	<0.001	61/136	44.9	0.006
No	6.0 (3.0 – 9.0)		70/112	62.5	
Have children					
Yes	6.0 (3.0 – 9.0)	0.001	78/131	59.5	0.008
No	8.0 (5.0 – 11.0)		50/117	42.7	
Have discussed Family Planning with a physician					
Yes	8.0 (5.0 – 11.0)	<0.001	66/154	42.9	<0.001
No	4.0 (2.0 – 8.0)		65/94	69.1	
Have discussed FP with a physician					
Did not discuss	4.0 (2.0 – 8.0)	<0.001	65/94	69.1	<0.001
GI physician	9.0 (7.0 – 12.0)		34/105	32.4	
Non-GI physician	6.0 (3.0 – 9.0)		32/49	65.3	
Obtain Information					
Yes	8.0 (5.0 – 12.0)	<0.001	68/161	42.2	<0.001
No	3.0 (1.0 – 8.0)		63/87	72.4	
Obtain Info from a physician					
Yes	9.0 (6.0 – 12.0)	<0.001	51/125	40.8	<0.001
No	5.0 (2.0 – 9.0)		80/123	65.0	

4.3.3 Identifying Covariates for the Multivariable Logistic Regression Model for Estimating the Effect of CCPKnow on Childlessness

The unadjusted odds ratios estimating the effects of various study variables on childlessness and on having poor CCPKnow scores are shown in Appendix C-2 Table C2-0-4. Using these values, as well as background knowledge of the relationships of candidate covariates with childlessness and IBD-specific reproductive knowledge, candidate variables were entered into a directed acyclic graph (DAG) (Figure 4-2), with arrowed lines indicating the hypothesized causal pathway from IBD-specific reproductive knowledge to childlessness. As shown in the diagram, education was assumed to affect the CCPKnow score but not to be independently associated with childlessness. Therefore, education was not included as a covariate in the multivariable logistic regression analysis.

The covariates identified for the multivariable logistic regression model for the effect of IBD-specific reproductive knowledge, captured by the CCPKnow score, on childlessness were 1) current age and 2) marital status. Both of these covariates were associated with CCPKnow score and with childlessness. As there were only 8 patients classified under the marital status “divorced”, these patients were combined with “partnered” patients, making the assumption that they must have once been married to be “divorced”. Assuming the causal relation diagram captures all causal pathways, adjusting for these covariates would control for effects of the remaining candidate covariates: 1) age at diagnosis, 2) duration of disease, 3) discussion of family planning.

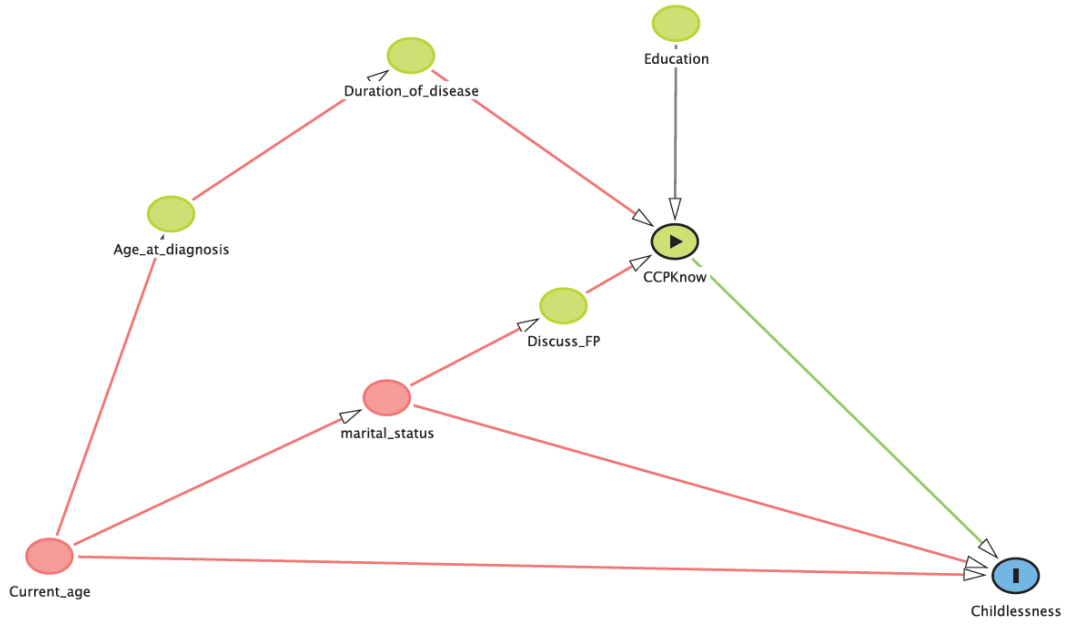

Figure 4-2: Directed Acyclic Graph for Patient CCPKnow and Childlessness

CCPKnow = Crohn's and Colitis Pregnancy Knowledge score. Outcome = childlessness. Exposure = CCPKnow. FP = family planning. Created with DAG 2.0 (www.dagitty.net).

4.3.4 Estimating the Effect of IBD-specific Reproductive Knowledge (as measured by the CCPKnow Score) on Childlessness

In order to estimate the effect of IBD-specific reproductive knowledge (as measured by the CCPKnow score) on childlessness, multivariable logistic regression was used to estimate odds ratios and 95% CI adjusted for current age and marital status. As shown in Table 4-3, multivariable logistic regression estimated an OR adjusted for current age and marital status of 0.92 (95% CI: 0.86 – 0.99) for the dose-response relationship between CCPKnow unit increments and the odds of childlessness. Thus each one-point increase in the CCPKnow score corresponded to an 8% decrease in the odds of childlessness.

The effect of CCPKnow score remained among women 34 years of age and younger, and women age 34 years and younger who were partnered, but the magnitude of the effect diminished among women above 34 years of age, and among those above 34 years who were partnered (Table 4-4).

Table 4-3: Multivariable Logistic Regression Model for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Childlessness among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Variable	OR	95% CI
CCPKnow score (per unit increase)	0.92	0.86 - 0.99
Marital status		
Single (n=67)	1.0	-
Partnered (n=181)	0.21	0.08 – 0.53
Current age (per year increase)	0.86	0.82 – 0.91

Table 4-4: Multivariable Logistic Regression Models for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Childlessness Stratified by Age and Marital Status among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Variable	OR	95% CI
34 years and younger		
CCPKnow score (per unit increase)	0.88	0.79 – 0.97
Marital status		
Single (n=62)	1.0	-
Partnered (n=93)	0.17	0.051 – 0.56
Current age (per year increase)	0.80	0.71 – 0.90
Older than 34 years		
CCPKnow score (per unit increase)	0.99	0.88 – 1.1
Marital status		
Single (n=5)	1.0	-
Partnered (n=88)	0.52	0.078 – 3.5
Current age (per year increase)	0.06	0.84 – 1.1
34 years and younger AND partnered		
CCPKnow score (per unit increase)	0.87	0.70 – 0.91
Current age (per year increase)	0.80	0.70 – 0.91
Older than 34 years AND partnered		
CCPKnow score (per unit increase)	0.98	0.86 – 1.1
Current age (per year increase)	0.96	0.83 – 1.1
34 years and younger AND single		
CCPKnow score (per unit increase)	0.92	0.70 – 1.2
Current age (per year increase)	0.78	0.60 – 1.0

NB: unable to complete for women 34 years and older who are Single, as n=5.

4.3.5 Estimating the Effect of Family Planning Discussion With a Physician on CCPKnow and Childlessness

Among the respondents, 154 of 248 (62.1%) reported having discussed family planning with a physician. The proportion of women with poor CCPKnow scores was lower among women who had discussed family planning with a physician. Women who had discussed family planning with a physician had median CCPKnow scores that were 4.0 units higher than those who had not discussed family planning with a physician (8.0 (IQR 5.0 – 11.0) v. 4.0 (IQR 2.0 – 8.0), respectively; $p<0.001$). Women who had discussed family planning with a GI physician had a median CCPKnow score that was 3.0 units higher than those who had discussions with a non-GI physician and 5.0 units higher than the median score of those who had not had discussions with a physician (9.0 (IQR 7.0 – 12.0) v. 6.0 (IQR 3.0 – 9.0) v. 4.0 (IQR 2.0 – 8.0), respectively; $p<0.001$).

As shown in Table 4-5, the multivariable logistic regression model estimated an OR adjusted for current age and marital status of 0.44 (95% CI: 0.25 -0.77) for the effect of having discussed family planning with a physician (compared to not having done so) on the odds of having a poor CCPKnow score; thus discussion of family planning with a physician corresponded to a 56% decrease in the odds of having a poor CCPKnow score. Table 4-5 shows that the multivariable logistic regression model estimated an OR adjusted for current age and marital status of 0.28 (95% CI: 0.15 – 0.53) for the effect of having discussed family planning with a GI physician on the odds of having a poor CCPKnow score; thus discussion of family planning with a GI physician corresponded to a

Table 4-5: Multivariable Logistic Regression Model for Estimating the Effect of Having Discussed Family Planning with a Physician on Having Poor IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR	95% CI
Have discussed family planning with a physician		
No (n=94)	1.0	-
Yes (n=154)	0.44	0.25 – 0.77
Marital status		
Single (n=67)	1.0	-
Partnered (n=181)	0.22	0.10 – 0.48
Current age (per year increase)	1.0	0.98 – 1.1

Table 4-6: Multivariable Logistic Regression Model for Estimating the Effect of Having Discussed Family Planning with a GI Physician on Having Poor IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR	95% CI
Have discussed family planning with a physician		
No (n= 94)	1.0	-
GI physician (n=105)	0.28	0.15 – 0.53
Non-GI physician (n=49)	1.0	0.48 – 2.2
Marital status		
Single (n=67)	1.0	-
Partnered (n=181)	0.24	0.11 – 0.52
Current age (per year increase)	1.0	0.98 – 1.1

72% decrease in the odds of having a poor CCPKnow score. The estimated OR adjusted for current age and marital status, however, for the effect of having discussed family planning with a non-GI physician on the odds of having a poor CCPKnow score was 1.0 (95% CI: 0.48 – 2.2); thus discussion of family planning with a non-GI physician did not correspond to a decrease in the odds of having a poor CCPKnow score. Relatively fewer childless women compared to women who have children (72/128 (56.3%) v. 82/120 (68.3%), respectively; p=0.050) reported having discussed family planning with a physician. The prevalence of childlessness was 12.8 per 100 women fewer among women who had discussed family planning with a physician compared to those who had not (72/154 (46.8%) v. 56/94 (59.6%), respectively; p=0.050).

As shown in Table 4-7, the multivariable logistic regression model estimated an OR adjusted for current age and marital status of 1.0 (95% CI: 0.51 – 2.0) for the effect of having discussed family planning with a physician on childlessness. As shown in Table 4-8, having discussed family planning with a GI physician corresponded to a 21% decrease in the odds of childlessness (p=0.52) compared to the 90% increase in the odds of childlessness associated with having discussed family planning with a non-GI physician or with no physician (p=0.17). However, as shown in Table 4-9, for women above 34 years of age, and the subset of those above 34 years of age who were partnered, the models estimated ORs in the positive direction for the effect of having discussed family planning with a physician on childlessness. However, there was a loss of precision in estimates for subgroups, as shown by the wider confidence intervals.

Table 4-7: Multivariable Logistic Regression Model for Estimating the Effect of Having Discussed Family Planning with a Physician on Childlessness among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR	95% CI
Have discussed family planning with a physician		
No (n=94)	1.0	-
Yes (n=154)	1.0	0.51 – 2.0
Marital status		
Single (n=67)	1.0	-
Partnered (n=181)	0.17	0.07 – 0.43
Current age (per year increase)	0.87	0.83 – 0.91

Table 4-8: Multivariable Logistic Regression Model for Estimating the Effect of Having Discussed Family Planning with a GI Physician on Childlessness among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR	95% CI
Have discussed family planning with a physician		
No (n= 94)	1.0	-
GI physician (n=105)	0.79	0.38 – 1.6
Non-GI physician (n=49)	1.9	0.76 – 4.6
Marital status		
Single (n=67)	1.0	-
Partnered (n=181)	0.17	0.066 – 0.44
Current age (per year increase)	0.87	0.82 – 0.91

Table 4-9: Age and Marital Status Stratified Multivariable Logistic Regression Model for Estimating the Effect of Having Discussed Family Planning with a Physician on Childlessness among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR	95% CI
34 years and younger		
Have discussed family planning with a physician		
No (n=59)	1.0	-
Yes (n=96)	0.51	0.19 – 1.4
Marital status		
Single (n=62)	1.0	-
Partnered (n=93)	0.14	0.043 – 0.44
Current age (per year increase)	0.81	0.73 – 0.91
34 years and younger, type of physician		
Have discussed family planning with a physician		
No (n=59)	1.0	-
GI physician (n=68)	0.42	0.15 – 1.2
Non-GI physician (n=28)	0.94	0.25 – 3.6
Marital status		
Single (n=62)	1.0	-
Partnered/divorced (n=93)	0.14	0.044 – 0.45
Current age (per year increase)	0.82	0.73 – 0.91
Older than 34 years		
Have discussed family planning with a physician		
No (n=35)	1.0	-
Yes (n=58)	4.0	1.0 – 15
Marital status		
Single (n=5)	1.0	-
Partnered (n=88)	0.17	0.019 – 1.5
Current age (per year increase)	0.99	0.86 – 1.1
Older than 34 years, type of physician		
Have discussed family planning with a physician		
No (n=35)	1.0	-
GI physician (n=37)	3.3	0.79 – 13
Non-GI physician (n=21)	5.4	1.2 - 24
Marital status		
Single (n=5)	1.0	-
Partnered (n=88)	0.17	0.020 – 1.5

	OR	95% CI
Current age (per year increase)	0.99	0.85 – 1.1
34 years and younger AND partnered		
Have discussed family planning with a physician		
No (n=23)	1.0	-
Yes (n=70)	0.54	0.18 – 1.6
Current age (per year increase)	0.82	0.72 – 0.93
34 years and younger AND partnered, type of physician		
Have discussed family planning with a physician		
No (n=23)	1.0	-
GI physician (n=54)	0.44	0.14 – 1.4
Non-GI physician (n=16)	1.2	0.27 – 5.1
Current age (per year increase)	0.82	0.72 – 0.93
Older than 34 years AND partnered		
Have discussed family planning with a physician		
No (n=30)	1.0	-
Yes (n=58)	4.0	1.1 - 15
Current age (per year increase)	0.99	0.86 – 1.1
Older than 34 years AND partnered, type of physician		
Have discussed family planning with a physician		
No (n=30)	1.0	-
GI physician (n=37)	3.3	0.79 – 13
Non-GI physician (n=21)	5.5	1.2 – 24
Current age (per year increase)	0.99	0.85 – 1.1
34 years and younger AND single		
Have discussed family planning with a physician		
No (n=36)	1.0	-
Yes (n=26)	0.37	0.032 – 4.3
Current age (per year increase)	0.79	0.61 – 1.0
34 years and younger AND single, type of physician		
Have discussed family planning with a physician		
No (n=36)	1.0	-
GI physician (n=14)	0.39	0.028 – 5.6
Non-GI physician (n=12)	0.34	0.017 – 6.5
Current age (per year increase)	0.78	0.60 – 1.0

NB: unable to complete for women 34 years and older who are single, as n=5.

4.4 Discussion

The health state of having a chronic disease influences major life-changing decisions, such as having relationships, having children, job and career choices, and lifestyle decisions[15]. Having a chronic medical condition may influence women's views about pregnancy, but the influence of disease specific knowledge and attitudes about pregnancy varies by disease type[16]. Having IBD is no exception; the influence of IBD-specific reproductive knowledge and attitudes about pregnancy may influence the views of women with IBD regarding pregnancy.

Based on review of the literature to date, this is the largest reported study of women with IBD focused on IBD-specific reproductive knowledge that examines the relationship between IBD-specific reproductive knowledge, discussion of family planning with a physician, and childlessness. In the current study, we had a relatively high response rate (57.1%) and a high prevalence of childlessness (51.6%) in our study population. There was also a higher prevalence of women with poor IBD-specific reproductive knowledge (52.8%) than reported from the Selinger et al. CCPKnow study (44.8%)[14].

This current study estimated an inverse relationship between IBD-specific reproductive knowledge, as measured by the CCPKnow survey, and childlessness; that is the odds of being childless decreased with increasing CCPKnow score. This study also estimated higher IBD-specific reproductive knowledge scores among women with IBD who had

discussed family planning with a physician compared to women who had not discussed family planning with a physician.

The Effect of IBD-specific Reproductive Knowledge on Childlessness

Previously, Selinger et al.[14] developed and validated the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey, providing a standard measure of IBD-specific reproductive knowledge; they reported that childless women had lower CCPKnow scores than women who have children. However, they had a mixed population of 44 women from clinics and 101 women from postal return with a reported low postal return rate (28% (101/361)); women with higher knowledge levels may have been more likely to participate, thus Selinger et al.'s study population may have included an over-representation of women with higher knowledge levels. Toomey et al.[13] attempted to characterize patient knowledge of reproductive issues in IBD, and although they showed there was a knowledge deficit among patients, they also had a small number of respondents (31/73 (42% response rate)). The current study had a larger number of respondents, and a higher response rate from both clinic and mail recruitment strategies.

Knowledge regarding reproductive issues in IBD was not the only factor associated with childlessness in our study population. Other factors associated with childlessness included current age, marital status, age at diagnosis, and duration of disease. Even after adjusting for the confounding effects of current age and marital status, the results

still showed the inverse gradient of increasing levels of CCPKnow scores associated with decreasing odds of childlessness.

The multivariable logistic regression models stratified by age and marital status showed that the estimated effect IBD-specific knowledge as measured by the CCPKnow score was most apparent among women of ages 34 years and younger who had partners, compared to women older than 34 years, or women of all ages who were single. Thus, women of ages 34 years and younger who have partners may be the patient group that benefits the most in terms of decreasing childlessness from improving IBD-specific reproductive knowledge.

The Effect of Having Discussed Family Planning with a Physician on IBD-specific Reproductive Knowledge

In this study, the odds of having a poor CCPKnow score was 56% lower among women who had discussed family planning with a physician compared to women who had not discussed family planning with a physician. Previously, Toomey et al.[13] reported that 32% of female IBD patients had discussed family panning with a physician, while Marri et al.[1] reported that 68% of their respondents at some point had discussed issues concerning pregnancy with their physician. In this study, we found that a large proportion of women (154/248 (62.1%)) had discussed family planning with a physician. In particular, the CCPKnow scores were highest among women who had discussed family planning with a gastroenterologist, suggesting that there may be a difference in the type of information exchanged between gastroenterologists and female IBD

patients, compared to the information exchanged between general practitioners and female IBD patients. Thus a potential way to improve women's IBD-specific reproductive knowledge would be through increasing the proportion of physicians, especially gastroenterologists, discussing family planning with their IBD patients. In addition, gastroenterologists may have information on how to counsel female IBD patients that can be shared with general practitioners.

The Effect of Having Discussed Family Planning with a Physician on Childlessness

The prevalence of childlessness was slightly lower among women who had discussed family planning with a physician, compared to women who had not discussed family planning with a physician, but having discussed family planning with a physician did not correspond to a decrease in the odds of childlessness after adjustment for identified confounders. Thus, there is an apparent discrepancy in the observation that increasing CCPKnow score was associated with decreasing odds of childlessness, and having discussed family planning with a physician was associated with increased odds of having adequate+ CCPKnow scores, yet having discussed family planning with a physician was not associated with decreased odds of childlessness.

The multivariable logistic regression models stratified by age and marital status showed that there was a difference in the direction of the estimated effects of having discussed family planning with a physician within subgroups that differed on age and marital status. For women of ages 34 years and younger, the estimated effect of having

discussed family planning with a physician showed a decrease in the odds of childlessness, but for women older than 34 years, the estimated effect of having discussed family planning with a physician showed an increase in the odds of childlessness.

This discrepancy suggests there may be causal pathways between having discussed family planning with a physician and childlessness other than that shown in the DAG, which hypothesized that the causal pathway was through improving IBD-specific reproductive knowledge as measured by the CCPKnow score. The depicted pathway or alternate pathways that are not depicted may be dependent on age. Another possible explanation is that the pathway is not a simple unidirectional relationship. Perhaps the relationship between discussion of family planning with a physician and childlessness is reversed in childless women who are older than 34 years; these women may discuss family planning with a physician in attempts to become pregnant and therefore have better CCPKnow scores. It is possible that erroneous assumptions used to construct the DAG led to errors in selecting variables for the multivariable model. The sensitivity of the results to errors in selecting the set of adjustment variables will be examined in future work. In addition, this discrepancy may be due to the wording of the question, as "family planning" could be interpreted to also mean contraceptive planning and this interpretation may be dependent on age. If this were the case, it would distort the estimated effects by lumping together women who discussed family planning when they

wanted to prevent pregnancy with those who discussed family planning when they were deciding whether or not to have children.

Although there was a relatively high response rate, there are several limitations to this analysis. The patient population was taken from a single tertiary centre, and these women may be more knowledgeable than the general female IBD population. However, as described in Chapter 3, this centre services a large referral base encompassing western Canada, and the patient population is quite diverse in terms of demographic factors and IBD disease history. Another limitation of this cross sectional survey is its inability to establish a time sequence of events. This study cannot measure each woman's IBD-specific reproductive knowledge level at the time she made the decision to remain childless or to have children, or when she discussed family planning with a physician. It is possible that women who decided to remain childless have lower IBD-specific reproductive knowledge because they were not yet thinking of this issue and had not sought knowledge related to pregnancy at this time in their lives. The results of this study which show that women in the youngest age group (18 to 24 years) and those who were currently single had the lowest median CCPKnow scores supports this possibility.

This study showed that female IBD patients' current IBD-specific reproductive knowledge level was associated with prior discussion of family planning with a physician. However, the study questionnaire did not inquire whether the patient or the

physician initiated the discussion, or what the discussion encompassed (particularly, contraception v. pregnancy planning). These would be important pieces of information to capture in future studies, to examine whether standards of practice should recommend physician-initiated discussion of reproductive issues in IBD and what specific topics for discussion should be addressed.

4.5 Conclusion

Overall, this analysis shows a strong inverse association of increasing IBD-specific reproductive knowledge with decreasing odds of childlessness among women with IBD. Discussion of family planning with a physician, and specifically with a gastroenterologist, was associated with increased IBD-specific reproductive knowledge. Thus, future research should focus on addressing determinants of patients' IBD-specific reproductive knowledge, and on the impact of encouraging physicians to discuss family planning with their female IBD patients of reproductive age. Even among single women in the younger 18 to 24 year age group, opening the conversation to address patient questions and concerns may help young women with IBD understand their options with respect to reproduction.

4.6 References

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5 Among Women with IBD, Does IBD-specific Reproductive Knowledge and Discussion of Family Planning Influence IBD-specific Reproductive Concerns?

5.1 Introduction

Knowledge about disease-specific reproductive issues plays an important role in decisions regarding family planning. Disease-specific concerns such as the risk of genetically passing on the disease to the child, the effect of the disease on fertility and pregnancy outcome, the effect of the pregnancy on the disease, and issues pertaining to delivery and breast-feeding, also play an important role in decisions regarding family planning. Women with IBD may have unfounded fears and concerns about reproductive issues in IBD which may be contributing to "voluntary childlessness" among women with IBD[1-8]. These reproductive concerns include concerns about infertility due to IBD, inheritability of IBD, risk of congenital abnormalities as a result of IBD or medications used to treat IBD, and about the effects of IBD on pregnancy and pregnancy on IBD[4,7,9].

As shown in Chapter 4, childless women with IBD had lower IBD-specific reproductive knowledge than women with IBD who have children. The prevalence of childlessness was higher among women with lower IBD-specific reproductive knowledge, as measured by the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey; 59.5% of women with poor CCPKnow scores were childless compared to 42.7% of women with adequate + CCPKnow scores (Chapter 4). Selinger et al. previously reported some

associations between CCPKnow scores and concerns about medication use during pregnancy, but not with all reproductive concerns[7]. The Selinger et al. study was the first published study to report any association between knowledge (measured by the CCPKnow survey) and attitudes[7]. Thus, the association of IBD-specific reproductive knowledge with specific patient concerns and beliefs/opinions regarding reproductive issues in IBD is still not well characterized.

Chapter 4 presented estimates of a positive association between discussion of family planning with a physician and patient IBD-specific reproductive knowledge. Whether discussion of family planning with a physician is associated with specific topics in IBD-reproductive knowledge, or with specific patient concerns, and sources of worry pertaining to IBD-specific reproductive issues is not well characterized.

The objectives of this analysis were 1) to describe IBD-specific reproductive knowledge deficits and to compare these deficits in childless women and women who have children; 2) to estimate the effect of discussion of family planning with a physician on having certain knowledge deficits, IBD-specific reproductive concerns, and IBD-specific reproductive sources of worry; and 3) to estimate the effect of IBD-specific reproductive knowledge on (a) reporting certain IBD-specific reproductive concerns and (b) reporting certain IBD-specific reproductive sources of worry.

5.2 Methods

5.2.1 Recruitment and Questionnaire

Female IBD patients who were between 18 and 45 years of age were identified from the University of Alberta Inflammatory Bowel Disease Clinic, and invited to complete the CCPKnow survey along with questionnaires aimed at obtaining information about socio-demographic characteristics, IBD history, reproductive history, discussion of family planning, IBD-specific reproductive concerns, and sources of worry. Full details have been presented in Chapter 2 Methods.

5.2.2 Data Sources and Variable Definitions

IBD-specific Reproductive Knowledge (CCPKnow)

For each CCPKnow survey question, the proportion that selected each response category was calculated separately for childless women and women who have children. These proportions were depicted in bar graphs. The responses were categorized into binary outcomes (incorrect v. correct) for subsequent logistic regression analyses.

IBD-specific Reproductive Concerns

To estimate the differences in IBD-specific reproductive concerns in childless women and women who have children, questions #14 and #16 were combined for analysis; the proportion that reported having each concern was calculated and presented in figures.

IBD-specific Reproductive Statements of Sources of Worry

This section was developed to better characterize the viewpoints of women with IBD regarding genetics, medications, effect of pregnancy on IBD, effect of IBD and medications on pregnancy. Comparing childless women and women who have children, the proportion that selected each Likert response is presented in figures. As the objective of this analysis was to estimate the effect of the exposure variable on the odds of reporting concerns or the odds of agreeing with specific statements of sources of worry, women were categorized into two groups as shown in Table 5-1 for logistic regression analysis:

Table 5-1: Categorization of Responses to Statements of Sources of Worry

Original Likert response	Category
Strongly agree	Agree
Agree	Agree
Unsure	Do not agree
Disagree	Do not agree
Strongly disagree	Do not agree

Discussion of Family Planning with a Physician

The classification of women as having discussed family planning with a physician was based on the response to the questionnaire item: "who have you discussed family planning with?" with responses regrouped as "yes" or "no" as shown in Table 5-2:

Table 5-2: Categorization of Discussion of Family Planning with a Physician

Responses	Have Discussed Family Planning with a Physician?
Have not discussed with anyone	No
Gastroenterologist	Yes
General Medicine specialist	Yes
Specialist (gynecologist, obstetrician)	Yes
Family physician	Yes
IBD nurse	No
Pharmacist	No
Family and Friends	No
Other	No

5.2.3 Statistical Analysis

This analysis aimed:

1) To characterize IBD-specific reproductive knowledge deficits among women with IBD:
    a. by comparing childless women and women who have children on the proportion that selected the correct response for each individual CCPKnow questions.
2) To estimate the effect of having discussed family planning with a physician on patient knowledge, concerns, and sources of worry:
    a. by estimating the ORs for the effect of having discussed family planning with a physician
        i. on selecting the correct response for specific CCPKnow questions
        ii. on reporting specific concerns
        iii. on agreeing with statements on specific sources of worry.

3) To estimate the effect of IBD-specific reproductive knowledge on reporting specific concerns, and specific sources of worry
    a. by estimating the ORs for the effect of having poor CCPKnow knowledge level
        i. on reporting specific concerns
        ii. on agreeing with statements on specific sources of worry.

For continuous variables, medians and interquartile ranges (IQR) were tabulated, and medians were compared across subgroups; the statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests. For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions.

To estimate the effect of independent variables on the outcome of interest, multivariable logistic regression was used to obtain odds ratios and 95% CI adjusted for selected covariates. Covariates were selected based on whether they could affect both the independent variable of interest and the outcome of interest, while not being an intervening variable between the two. For the section on individual CCPKnow questions, individual experience and history could affect the odds of selecting the

correct response. Unadjusted odds ratios and 95% CI are presented for exposure variables relevant to the individual CCPKnow question. These same variables were then included as covariates in the multivariable logistic regression analyses. It was not felt that other study variables would affect the odds of selecting the correct response for each individual CCPKnow question, and thus the covariates used in Chapter 4 were not included in the multivariable logistic regression models.

5.3 Results

5.3.1 Characteristics of Study Population

Complete data pertaining to the CCPKnow survey was available from 248 women who returned questionnaires that had complete responses for all variables included in the final multivariable analysis of IBD-specific reproductive knowledge. The distributions of demographic variables in this patient population have been presented in Chapter 3. Only 211 women completed the patient concerns sections; their demographic characteristics are shown in Appendix C-3 Table C3-0-1.

5.3.2 IBD-specific Reproductive Knowledge Deficits (CCPKnow questions)

More than half of the respondents selected the correct responses for CCPKnow questions #1 (inheritance), #5 and #6 (disease activity), #8 (drugs), #13 (mode of delivery), and #17 (pregnancy outcomes), as shown in Appendix C-3 Table C3-0-2, while less than half of the respondents selected correct responses for the remaining

questions. Appendix C-3 Table C-3-0-2 shows the proportions of childless women and women who have children who correctly responded to each CCPKnow question.

a) Inheritance (#1, #2)

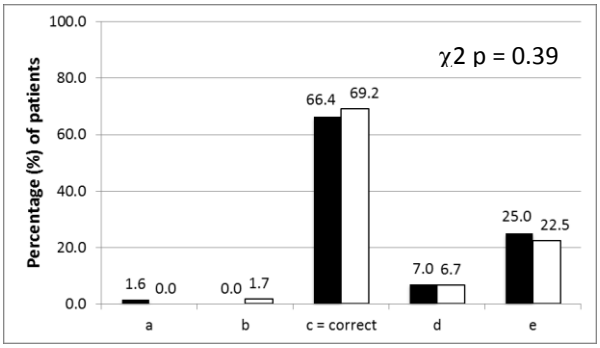
As shown in Figure 5-1, the majority of childless women and women who have children (85/128 (66.4%) v. 83/120 (69.2%), respectively; p=0.64) selected the correct response that IBD is more likely to affect a child if the mother or father suffers from it. Women with a family history of IBD had 1.1 (95% CI: 0.65 – 1.9) times the odds of correctly answering this question compared to women who had no family history of IBD. A minority of childless women and women who have children (32/128 (25.0%) v. 37/120 (30.8%), respectively; p=0.31) selected the correct response that the risk of passing on IBD to a child is less than 10% (Figure 5-1). Women with a family history of IBD had 0.57 (95% CI: 0.32 – 1.0) times the odds of correctly answering this question compared to women who had no family history of IBD.

b) Fertility (#3, #4)

Similar proportions of childless women and women who have children (26/128 (20.3%) v. 37/130 (30.8%), respectively; p=0.057) selected the correct response that men with inflammatory bowel disease usually do not have problems with infertility (Figure 5-2). Women who had UC had 3.6 (95% CI: 1.9 – 7.0) times the odds of correctly answering this question compared to women who had CD.

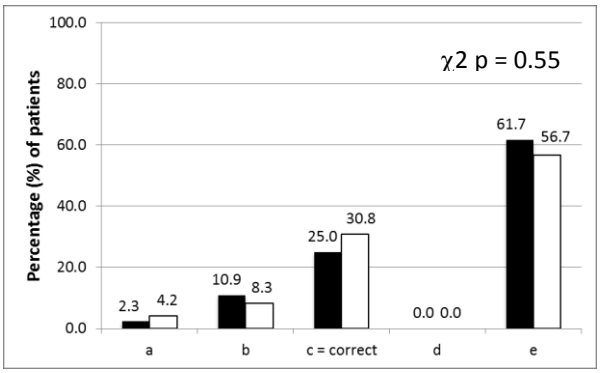
1) Inflammatory bowel disease …

a) will always pass from a parent to a child
b) will never pass from a parent to a child
c) is more likely to affect a child if mother or father are suffering from it
d) does not run in families
e) don't know



2) The risk of passing on inflammatory bowel disease to a child …

a) is zero
b) can be exactly determined by genetic testing
c) is less than 10%
d) can be reduced by medication
e) don't know

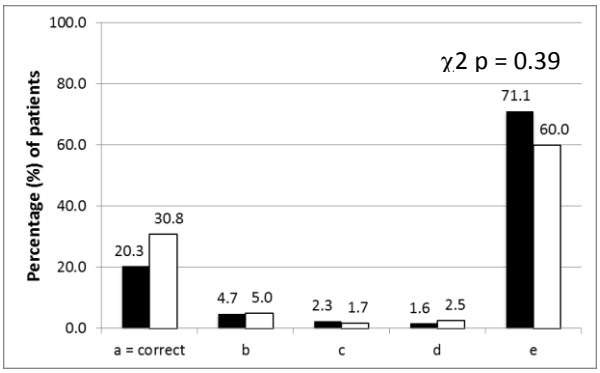


■ Childless n=128 □ Have children n = 120

Figure 5-1: Knowledge Regarding Genetics and IBD among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

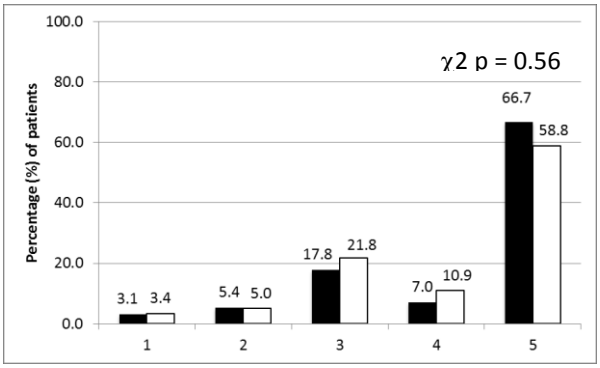
3) Men with inflammatory bowel disease...

a) usually do not have problems with infertility
b) should avoid all medications when trying for a baby
c) should not have children with women suffering from IBD
d) should not father children after the age of 40
e) don't know



4) The chances of a woman becoming pregnant…

a) are not reduced if her ulcerative colitis is active
b) are not reduced if she has an ileo-anal pouch
c) are generally good if she suffers from ulcerative colitis
d) are not influenced by the activity of Crohn's disease
e) don't know



■ Childless n=128 □ Have children n = 120

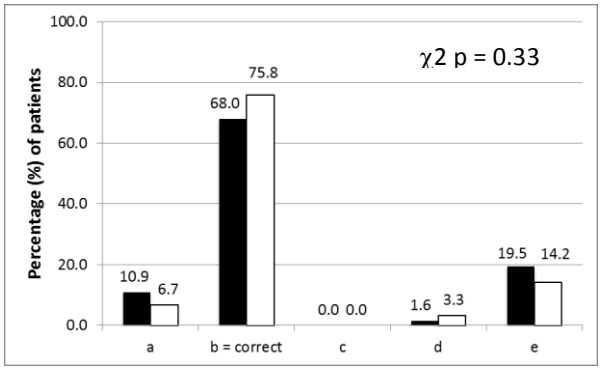
Figure 5-2: Knowledge Regarding Fertility and IBD among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

c) Disease activity (#5, #6, #7)

The majority of childless women and women who have children (87/128 (68.0%) v. 91/120 (75.8%), respectively; p=0.17) selected the correct response that IBD should be well controlled before becoming pregnant (Figure 5-3). Similar large proportions of childless women and women who have children (82/128 (64.1%) v. 82/120 (68.3%), respectively; p=0.48) also selected the correct response that women with IBD should delay trying for a baby until their disease has been controlled by medication (Figure 5-3). However, the proportion that knew that active IBD during pregnancy should be treated with some types of drugs to protect the pregnancy was 19 per 100 women fewer among childless women compared to women who have children (45/128 (35.2%) v. 65/120 (54.2%), respectively; p=0.003) (Figure 5-3).

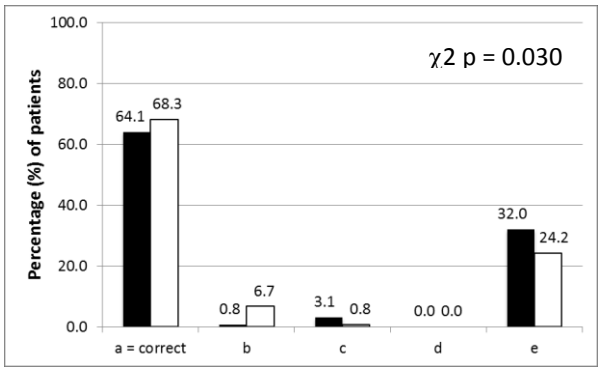
5) What is most important when trying for a baby?

a) women should come off all drugs before becoming pregnant
b) inflammatory bowel disease should be well controlled before becoming pregnant
c) there is no need for women to discuss it with her doctor before becoming pregnant
d) women with Crohn's disease should not stop smoking
e) don't know



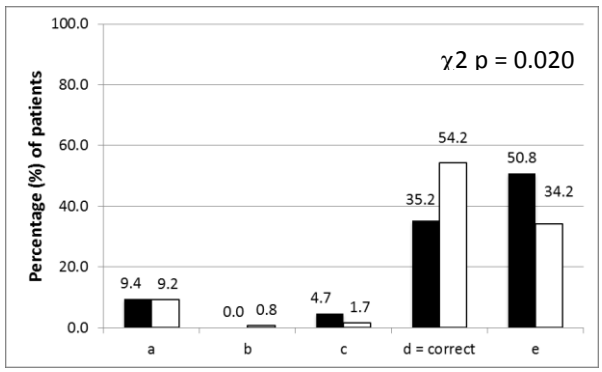
6) Women with inflammatory bowel disease…

a) should delay trying for a baby until their disease has been controlled by medication
b) never experience flares of their disease during pregnancy
c) will always experience a flare during their pregnancy
d) often need surgery during pregnancy
e) don't know



7) Active inflammatory bowel disease during pregnancy …

a) does not affect the chance of having a healthy baby
b) does not cause early birth
c) should be put up with to protect the unborn from drug effects
d) should be treated with some types of drugs to protect the pregnancy
e) don't know



■ Childless n=128 □ Have children n = 120

Figure 5-3: Knowledge Regarding the Effects of IBD Disease Activity on Pregnancy Outcomes among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

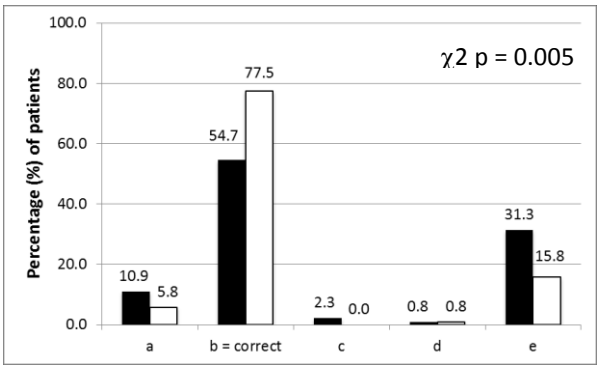
d) Drugs (#8 to 12)

As shown in Figure 5-4, the proportion that selected the correct response that pregnant women with IBD should continue some medications was 22.8 per 100 women fewer among childless women compared to women who have children (70/128 (54.7%) v. 93/120 (77.5%), respectively; p<0.001). However, similarly low proportions of childless women and women who have children (22/128 (17.2%) v. 26/130 (21.7%), respectively; p=0.37) selected the correct response that Infliximab or Adalimumab are generally seen as 'probably safe' in pregnancy (Figure 5-4). Women with a history of anti-TNF therapy had 8.0 (95% CI: 3.6 - 18) times the odds of correctly answering this question compared to women who had never been on anti-TNF therapy.

Similar proportions of childless women and women who have children (36/128 (28.1%) v. 30/120 (25.0%), respectively; p=0.58) selected the correct response that Methotrexate should be stopped 3 -6 months before trying for a baby (Figure 5-4). Women with a history of methotrexate therapy had 6.7 (95% CI: 3.3 – 14) times the odds of correctly answering this question compared to women who had no history of methotrexate therapy.

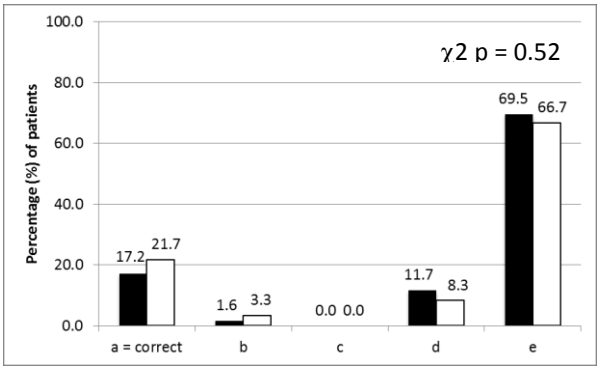
8) Pregnant women with inflammatory bowel disease …

a) should avoid all drugs
b) should continue some medications
c) should use herbal medications only
d) do not need to discuss drugs with their doctor
e) don't know



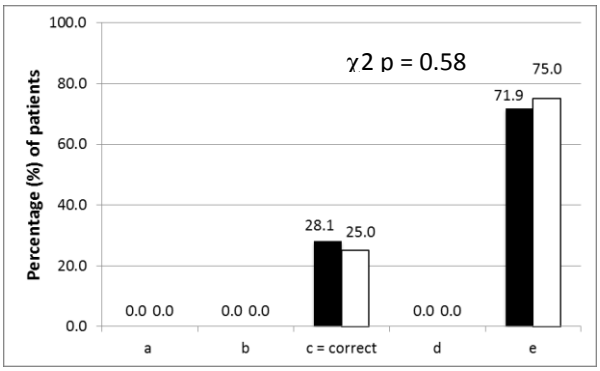
9) Infliximab or Adalimumab …

a) are generally seen as "probably safe" in pregnancy
b) cause serious harm to babies
c) do not work in pregnant women
d) should always be stopped prior to conception
e) don't know



10) The drug Methotrexate …

a) does not cause birth defects
b) is safe in pregnancy when taken as a tablet
c) should always be stopped 3-6 months before trying for a baby
d) does not need to be stopped in males who are taking it when they are trying for a baby
e) don't know



■ Childless n=128 □ Have children n = 120

Figure 5-4: Knowledge Regarding IBD Medications in Pregnancy (part A) among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Regarding Mesalazine, the proportion that selected the correct response that during pregnancy Mesalazine is safe and should be continued was 14.4 per 100 women fewer among childless women than women who have children (37/128 (28.9%) v. 52/120 (43.3%), respectively; p=0.018) (Figure 5-5). Women with a history of Mesalazine treatment had 11 (95% CI: 2.7 - 49) times greater odds of correctly answering this question compared to women who had no history of Mesalazine treatment.

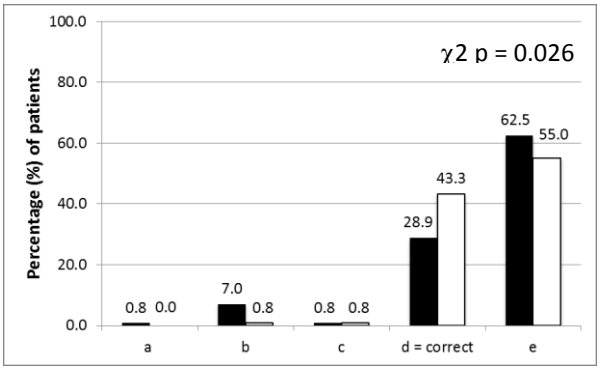
Small proportions of childless women and women who have children selected the correct response that during pregnancy azathioprine or 6-MP can be continued, though this proportion was nearly twice as large among women who have children (15/128 (11.7%) v. 25/120 (20.8%), respectively; p=0.051) (Figure 5-5). All women who correctly responded to this question had been on azathioprine or 6-MP therapy (40/40 (100%)); however, only 22.2% (40/180) of the women who had been on azathioprine or 6-MP therapy correctly answered this question.

e) Mode of delivery (#13, #14)

As shown in Figure 5-6, the proportion that selected the correct response that they can have a vaginal delivery was 27.3 per 100 women more in women who have children compared to childless women (91/120 (75.8%) v. 63/130 (48.5%), respectively; p<0.001). The majority of women did not know that peri-anal disease that occurs after a normal vaginal delivery is more likely if a woman suffered from it previously (Figure 5-6).

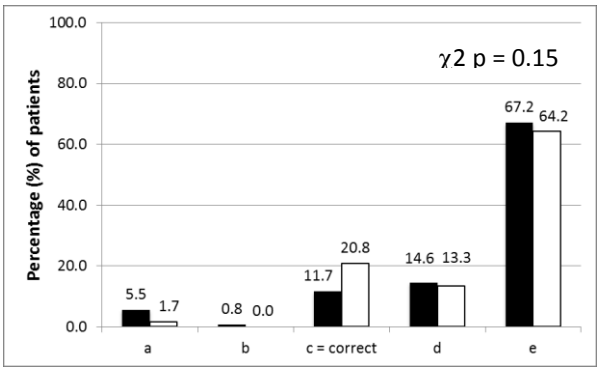
11) During pregnancy Mesalazine …

a) should not be taken as a suppository or enema
b) should be avoided at all cost
c) does not work
d) is safe and should be continued
e) don't know



12) During pregnancy Azathioprine or 6-Mercaptopurine …

a) cause serious harm to babies
b) do not work
c) can be continued
d) are considered unsafe
e) don't know

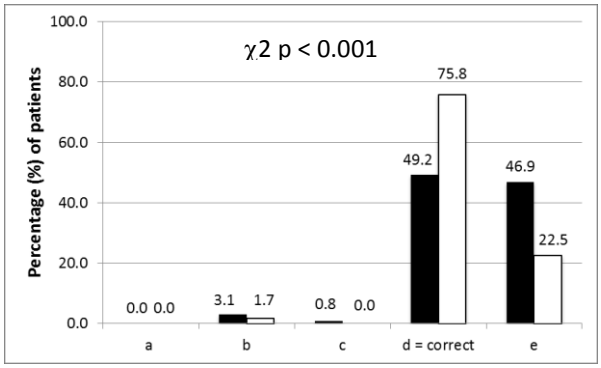


■ Childless n=128 □ Have children n = 120

Figure 5-5: Knowledge Regarding IBD Medications in Pregnancy (Part B) 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

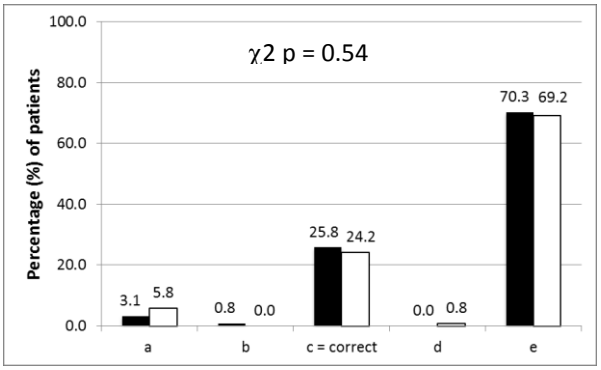
13) Women with inflammatory bowel disease …

a) should never have a caesarean section
b) must have a caesarean section
c) and peri-anal disease are advised against having a caesarean section
d) can have a vaginal delivery in most cases
e) don't know



14) Peri-anal disease that occurs after a normal vaginal delivery …

a) is common in ulcerative colitis
b) responds well to creams
c) is more likely if a woman suffered from it previously
d) is never seen in women with Crohn's disease
e) don't know



■ Childless n=128 □ Have children n = 120

Figure 5-6: Knowledge Regarding IBD and Delivery Methods among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

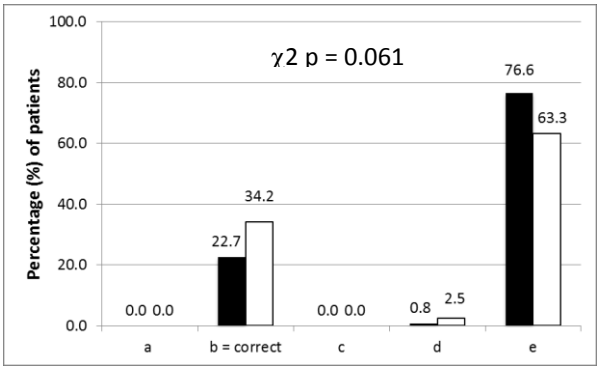
Women with a history of perianal disease had 2.2 (95% CI: 1.2 – 4.3) times the odds of correctly responding to this question compared to women without this history.

f) Pregnancy outcomes (#15, 16, 17)

Regarding pregnancy outcomes, the proportion that selected the correct response that women suffering from IBD often give birth a bit early was 11.5 per 100 women fewer among childless women compared to women who have children (29/128 (22.7%) v. 41/120 (34.2%), respectively; p=0.006) (Figure 5-7). Few women selected the correct response that birth defects occur slightly more often in babies of mothers with IBD than in babies of mothers without IBD (Figure 5-7).

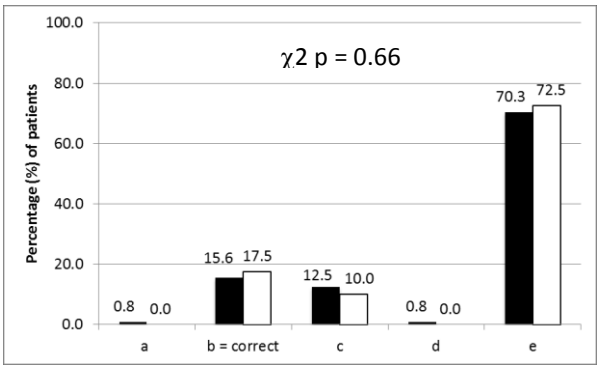
15) Women suffering from inflammatory bowel disease …

a) usually have bigger and heavier babies than other women
b) often give birth a bit early
c) often give birth late
d) always have their baby on time even when Crohn's disease flares
e) don't know



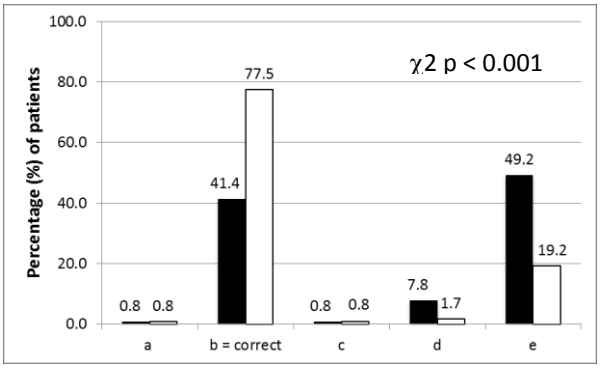
16) Birth defects in babies of mothers with inflammatory bowel disease …

a) are a common problem
b) occur slightly more often than in babies of mothers without IBD
c) are usually due to drug side effects
d) can be prevented by vaccinations
e) don't know



17) The chances of having a healthy baby for mothers suffering from inflammatory bowel disease …

a) are less than 50%
b) are very good
c) depend on the method of delivery
d) can be improved by avoiding medication
e) don't know



■ Childless n=128 □ Have children n = 120

Figure 5-7: Knowledge Regarding IBD and Pregnancy Outcomes among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Regarding having a healthy baby, the proportion that selected the correct response that the chances of having a healthy baby for mothers suffering from IBD are very good was 36.1 per 100 women fewer among childless women than among women who have children (53/128 (41.4%) v. 93/120 (77.5%), respectively; $p<0.001$) (Figure 5-7).

c) Breastfeeding

Similar proportions of women who have children and childless women were aware that mothers suffering from IBD may have tiny amounts of medications in their breast milk (Figure 5-8).

18) Mothers suffering from inflammatory bowel disease …

a) should not breast feed to avoid passing the disease on to the child
b) never experience a flare of disease when breastfeeding
c) may have tiny amounts of medication in their breast milk
d) do not need to discuss breast feeding with their midwife or doctor
e) don't know

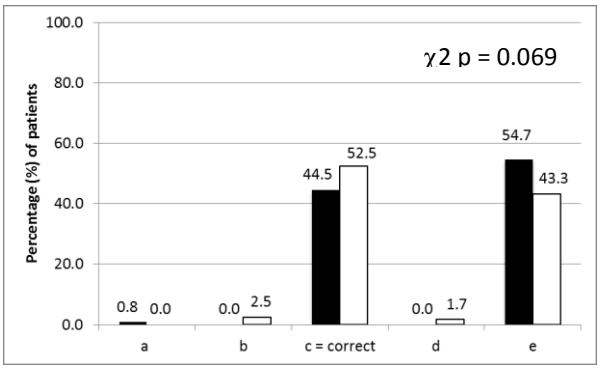


Figure 5-8: Knowledge Regarding Breast feeding and IBD among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

5.3.3 The Effect of Having Discussed Family Planning with a Physician on Correctly Answering CCPKnow Questions

Multivariable logistic regression was performed to estimate the effect of having discussed family planning with a physician on the odds of correctly answering each CCPKnow question, adjusted for selected variables specific to each question (unadjusted odds ratios and 95% CI for having discussed family planning with a physician are presented in Appendix C-3 Table C3-0-3).

As shown in Table 5-3, women who had discussed family planning with a physician had increased odds of correctly answering the CCPKnow questions compared to women who had not discussed family planning with a physician, for all questions except for question #2 (the risk of passing on IBD to a child is less than 10%). However, when analyzed further by type of physician, most of the effects were larger in magnitude if the patient had discussed family planning with a GI physician compared to a non-GI physician or no physician.

Table 5-3: Multivariate Logistic Regression Estimating the Effect of Having Discussed Family Planning with a Physician on the Odds of Correctly Answering Individual CCPKnow Questions among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR*	95% CI
INHERITANCE		
1. Inflammatory bowel disease … *is more likely to affect a child if mother or fathers are suffering from it.*		
Have discussed family planning with a physician [1]	1.8	1.0 – 3.1
Family history of IBD (yes v. no)	1.1	0.61 – 1.8
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	2.4	1.3 – 4.5
Non-GI physician (v.no physician)	1.1	0.52 – 2.2
Family history of IBD (yes v. no)	1.1	0.61 – 1.9
2. The risk of passing on inflammatory bowel disease to a child … *is less than 10%.*		
Have discussed family planning with a physician [1]	1.5	0.85 – 2.8
Family history of IBD (yes v. no)	0.54	0.3 – 0.97
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	2.1	1.1 – 3.9
Non-GI physician (v. no physician)	0.69	0.28 – 1.7
Family history of IBD (yes v. no)	0.54	0.30 – 0.97
FERTILITY		
3. Men with inflammatory bowel disease … *usually do not have problems with infertility.*		
Have discussed family planning with a physician[1]	3.3	1.7 – 6.8
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.9	1.9 – 8.0
Non-GI physician (v. no physician)	2.5	1.0 – 5.9
4. The chances of a woman becoming pregnant … *are generally good if she has ulcerative colitis.*		
Have discussed family planning with a physician[1]	2.9	1.3 – 6.2
Type of IBD (UC v. CD)	3.8	1.9 – 7.4
Type of IBD (ID v. CD)	1.1	0.13 – 10

	OR*	95% CI
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.4	1.5 – 7.6
Non-GI physician (v. no physician)	1.9	0.69 – 5.2
Type of IBD (UC v. CD)	3.8	1.9 – 7.5
Type of IBD (ID v. CD)	1.1	0.12 – 9.3
DISEASE ACTIVITY		
5. When trying for a baby... *inflammatory bowel disease should be well controlled before becoming pregnant.*		
Have discussed family planning with a physician[1]	3.1	1.7 – 5.4
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	4.8	2.4 – 9.7
Non-GI physician (v. no physician)	1.5	0.74 – 3.2
6. Women with inflammatory bowel disease … *should delay trying for a baby until their disease has been controlled.*		
Have discussed family planning with a physician[1]	2.9	1.7 – 5.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	4.6	2.4 – 8.9
Non-GI physician (v. no physician)	1.4	0.69 – 2.8
7. Active inflammatory bowel disease during pregnancy *… should be treated with some types of drugs to protect the pregnancy.*		
Have discussed family planning with a physician[1]	3.7	2.1 – 6.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	5.6	3.0 – 10
Non-GI physician (v. no physician)	1.5	0.73 – 3.3
DRUGS		
8. Pregnant women with inflammatory bowel disease … *should continue some medications.*		
Have discussed family planning with a physician[1]	3.3	1.9 – 5.7
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	6.3	3.2 - 12
Non-GI physician (v. no physician)	1.3	0.64 – 2.6

	OR*	95% CI
9. Infliximab or Adalimumab … *are generally seen as 'probably safe' in pregnancy.*		
Have discussed family planning with a physician[1]	2.0	0.96 – 4.3
Have been on anti-TNF therapy (yes v. no)	7.9	3.5 – 18
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.3	1.5 – 7.4
Non-GI physician (v. no physician)	0.38	0.098 – 1.5
Have been on anti-TNF therapy (yes v. no)	9.0	3.9 – 21
10. The drug Methotrexate … *should always be stopped 3-6 months before trying for a baby.*		
Have discussed family planning with a physician	2.6	1.3 – 5.1
Have been on methotrexate therapy (yes v. no)	7.2	3.4 – 15
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.3	1.6 – 6.9
Non-GI physician (v. no physician)	1.4	0.56 – 3.6
Have been on methotrexate therapy (yes v. no)	8.0	3.7 – 17
11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc) … *is safe and should be continued.*		
Have discussed family planning with a physician[1]	2.0	1.1 – 3.6
Have been on Mesalamine therapy (yes v. no)	8.8	2.0 – 38
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	2.8	1.5 – 5.3
Non-GI physician (v. no physician)	0.89	0.39 – 2.0
Have been on Mesalamine therapy (yes v. no)	11	2.5 – 48
12. During pregnancy Azathioprine or 6-Mercaptopurine … *can be continued.*		
Have discussed family planning with a physician[1]	5.4	2.0 – 15
Have been on AZA/6MP therapy (yes v. no)	#	-
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	7.5	2.7 – 21
Non-GI physician (v. no physician)	2.0	0.55 – 7.6
Have been on AZA/6MP therapy (yes v. no)	n/a#	

	OR*	95% CI
MODE OF DELIVERY		
13. Women with inflammatory bowel disease … *can have a vaginal delivery in most cases.*		
Have discussed family planning with a physician[1]	2.8	1.7 – 4.9
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	4.5	2.4 – 8.5
Non-GI physician (v. no physician)	1.3	0.64 – 2.6
14. Peri-anal disease that occurs after a normal vaginal delivery … *is more likely if a woman suffered from it previously.*		
Have discussed family planning with a physician[1]	2.8	1.4 – 5.6
Have history of perianal disease (yes v. no)	2.3	1.2 – 4.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.3	1.6 – 7.0
Non-GI physician (v. no physician)	1.8	0.72 – 4.4
Have history of perianal disease (yes v. no)	2.2	1.1 – 4.4
PREGNANCY OUTCOMES		
15. Women suffering from inflammatory bowel disease … *often give birth a bit early.*		
Have discussed family planning with a physician[1]	2.6	1.4 – 5.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.3	1.7 – 6.3
Non-GI physician (v. no physician)	1.6	0.68 – 3.7
16. Birth defects in babies of mothers with inflammatory bowel disease … *occur slightly more often than in babies of mothers without inflammatory bowel disease.*		
Have discussed family planning with a physician[1]	2.5	1.1 – 5.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	3.0	1.3 – 6.7
Non-GI physician (v. no physician)	1.6	0.55 – 4.5

	OR*	95% CI
17. The chances of having a healthy baby for mothers suffering from inflammatory bowel disease … *are very good.*		
Have discussed family planning with a physician[1]	3.5	2.0 – 5.9
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	5.3	2.8 – 9.8
Non-GI physician (v. no physician)	1.7	0.83 – 3.3
BREASTFEEDING		
18. Mothers suffering from inflammatory bowel disease … *may have tiny amounts of medication in their breast milk.*		
Have discussed family planning with a physician[1]	2.1	1.2 – 3.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	2.6	1.5 – 4.7
Non-GI physician (v. no physician)	1.3	0.63 – 2.6

*Adjusted for variables listed under each question

[1] Reference category: Have not discussed family planning with a physician

unable to adjust because all women who correctly responded had been on AZA/6MP

5.3.4 Concerns about Reproductive Issues in IBD

There were 211 patient responses to this section of the questionnaire; 107 childless women, and 104 women who have children. The median number of concerns per woman was 4.0 (ICR 1.0 – 6.0). Table 5-4 shows detailed percentages of childless women and women who have children who reported each concern. Significant differences in the proportions of childless women and women who have children existed for various concerns.

Compared to the proportion with specific concerns among women who have children, this proportion among childless women was: 25.1 per 100 more for genetically passing their disease ($p<0.001$); 39.8 per 100 more for decreased fertility ($p<0.001$); 21.1 per 100 more for stillbirth or miscarriage ($p<0.001$); 24.8 per 100 more for chronic illness leading to birth defects ($p<0.001$); 26.1 per 100 more for IBD-medications causing birth defects ($p<0.001$); 15.7 per 100 more for worsening of their disease ($p=0.022$); 14.2 per 100 more for added stress of raising a child ($p=0.030$); and 13.0 per 100 more for IBD-related fatigue ($p=0.053$).

Table 5-4: Proportion of Women Reporting IBD-specific Reproductive Concerns among 107 Childless Women with IBD and 104 Women with IBD who have children from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Concern	Total (n=211)		Proportion of Childless Women (n=107)		Proportion of Women Who have children (n=104)		Chi-square
	N	%	N	%	N	%	p-value
• Medical advice against conception	46	21.8	33	30.8	13	12.5	0.001
• Genetically passing IBD to child	110	52.1	69	64.5	41	39.4	<0.001
• Not able to care for child	55	26.1	32	29.9	23	22.1	0.20
• Added stress of raising a child	72	34.1	44	41.1	28	26.9	0.030
• Chronic illness leading to birth defects	61	28.9	44	41.1	17	16.3	<0.001
• Stillbirth or miscarriage	49	23.2	36	33.6	13	12.5	<0.001
• IBD-medication causing birth defects	99	46.9	64	59.8	35	33.7	<0.001
• Worsening of disease	98	46.4	58	54.2	40	38.5	0.022
• Decreased fertility	69	32.7	56	52.3	13	12.5	<0.001
• Negative body image	28	13.3	20	18.7	8	7.7	0.019
• IBD-related fatigue	85	40.3	50	46.7	35	33.7	0.053

The proportion that reported having been given medical advice against conception was thirteen per 100 more among childless women compared to women who have children (p=0.001). Childless women had on average 3 more concerns than women who have children (5.0 (IQR 3.0 – 7.0) v. 2.0 (IQR 0.0 – 6.0) concerns, respectively; p<0.001). The top concern of all women was "concern for the possibility of genetically passing my disease to my child", but the next top 4 concerns differed in order of importance among childless women and women who have children, as shown in Table 5-5.

Open-ended responses to "other concerns" are shown in Appendix C-3 Table C3-0-4. Grouping of the open-ended responses identified additional concerns which include the following: 1) clotting risk, 2) concern that they would have to stop medications in order to become pregnant, which could lead to flare or surgery, 3) medication-related fatigue, 4) poor control of IBD post-partum, 5) potential for low birth weight and premature delivery, 6) prior surgeries and scar tissue affecting fertility.

Table 5-5: Top IBD-specific Reproductive Concerns of 107 Childless Women with IBD and 104 Women with IBD who have children from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	Total patients	Childless	Have children
Concern about …	**Ranking by highest proportion of women**		
• Genetically passing my disease to my child	1	1	1
• IBD medications causing birth defects	2	2	3
• Worsening of my disease as a result of pregnancy	3	3	2
• IBD related fatigue	4	5	4
• Added stress of raising a child	5	6 (tied)	5
• Decreased fertility	6	4	9 (tied)
• Chronic illness leading to birth defects	7	6 (tied)	8
• Stillbirth or miscarriage	8	7	9 (tied)
• Medical advice against conception	9	8	9 (tied)
• Other concerns	10	10	7
• Negative body image restricts sexual activity	11	9	7.7
• No concerns	12	12	6
• Unsure	13	11	10

5.3.5 The Effect of Having Discussed Family Planning with a Physician on Concerns

Multivariable logistic regression was used to estimate the effect of having discussed family planning with a physician on the odds of reporting specific concerns, adjusted for appropriate covariates depending on the concern, as shown in Table 5-6. As shown in Table 5-6, having discussed family planning with a physician did not correspond to a decrease in the odds of reporting specific concerns; to the contrary, it was associated with increased odds of reporting concerns about having a stillbirth or miscarriage, and about IBD-related fatigue. Having discussed family planning with a physician corresponded to a 4.8 (95% CI: 2.0 – 11) -fold increase in the odds of reporting the concern about stillbirth or miscarriage, and a 2.0 (95% CI: 1.1 – 3.5) -fold increase in the odds of reporting the concern about IBD-related fatigue.

The type of physician with whom respondents had discussions with did not clearly modify the OR for reporting specific concerns, except that having discussed family planning with a non-GI physician corresponded to a 2.3 (95% CI: 1.1 – 4.9) -fold increase in the odds of reporting a concern about IBD-related fatigue.

Having a family history of IBD corresponded to a 2.3 (95% CI: 1.3 – 4.0) fold increase in the odds of reporting the concern about genetically passing IBD to the child. Having a history of AZA treatment corresponded to a 2.4 (95% CI: 1.3 – 4.4) -fold increase in the odds of reporting the concern about IBD-medication induced birth defects.

Table 5-6: Multivariable Logistic Regression Models for Estimating the Effect of Family Planning Discussion with a Physician (and Type of Physician) on Patient Concerns among 211 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Concern	OR*	95% CI
Medical advice against conception		
Have discussed family planning with a physician[1]	1.9	0.94 – 4.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	2.1	0.97 – 4.5
Non-GI physician (v. no physician)	1.6	0.65 – 4.2
Genetically passing my disease to my child		
Have discussed family planning with a physician[1]	1.3	0.75 – 2.4
Family history of IBD (yes v. no)	2.3	1.3 – 4.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.4	0.73 – 2.5
Non-GI physician (v. no physician)	1.3	0.60 – 2.7
Family history of IBD (yes v. no)	2.3	1.3 – 4.0
Not being able to care for a child		
Have discussed family planning with a physician[1]	1.3	0.9 – 2.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.3	0.67 – 2.7
Non-GI physician (v. no physician)	1.3	0.55 – 3.0
Added stress of raising a child		
Have discussed family planning with a physician[1]	0.76	0.43 – 1.4
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.76	0.40 – 1.4
Non-GI physician (v. no physician)	0.76	0.35 – 1.7
Chronic illness leading to birth defects		
Have discussed family planning with a physician[1]	1.5	0.78 – 2.8
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.5	0.74 – 2.9
Non-GI physician (v. no physician)	1.5	0.65 – 3.3

Concern	OR*	95% CI
Stillbirth or a miscarriage		
Have discussed family planning with a physician[1]	4.8	2.0 – 11
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	4.8	2.0 – 12
Non-GI physician (v. no physician)	4.8	1.8 - 13
IBD medications causing birth defects		
Have discussed family planning with a physician[1]	1.1	0.6 – 1.9
AZA treatment (yes v. no)	2.4	1.3 - 4.4
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.1	0.59 – 2.1
Non-GI physician (v. no physician)	0.98	0.46 – 2.1
AZA treatment (yes v. no)	2.4	1.3 – 4.4
Worsening of my disease as a result of pregnancy		
Have discussed family planning with a physician[1]	1.1	0.66 – 2.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.1	0.62 – 2.1
Non-GI physician (v. no physician)	1.1	0.55 – 2.4
Decreased fertility		
Have discussed family planning with a physician[1]	1.6	0.86 – 2.9
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.7	0.86 – 3.2
Non-GI physician (v. no physician)	1.4	0.64 – 3.2
Negative body image, restrict my sexual activity		
Have discussed family planning with a physician[1]	1.6	0.66 – 4.1
Marital status		
Partnered (v. single)	0.84	0.32 – 2.2
Divorced (v. single)	2.3	0.36 - 15
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	2.0	0.76 – 5.4
Non-GI physician (v. no physician)	1.1	0.31 – 3.6

Concern	OR*	95% CI
Marital status		
Partnered (v. single)	0.78	0.29 – 2.1
Divorced (v. single)	2.8	0.43 – 18
IBD related fatigue		
Have discussed family planning with a physician[1]	2.0	1.1 – 3.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.8	0.96 – 3.5
Non-GI physician (v. no physician)	2.3	1.1 – 4.9

*Adjusted for variables listed under each question

[1] Reference category: Have not discussed family planning with a physician

5.3.6 The Effect of Having Poor CCPKnow on Concerns

Multivariable logistic regression was used to estimate the effect of having a poor CCPKnow score on reporting specific concerns, as shown in Table 5-7. (Unadjusted ORs are shown in Appendix C3 Table C3-0-5). As shown in Table 5-7, having a poor CCPKnow score did not correspond to a substantial increase in the odds of reporting specific concerns, with the exception that patients who had poor CCPKnow scores had 2.0 (95% CI: 1.0 – 4.0) times the odds of reporting that they had been given medical advice against conception compared to patients with higher CCPKnow levels.

Other factors were associated with reporting specific concerns. Having a family history of IBD corresponded to a 2.3 (95% CI: 1.3 – 4.0) -fold increase in the odds of reporting the concern about genetically passing IBD to the child. Having a history of AZA treatment was associated with a 2.4 (95% CI: 1.3 – 4.5) -fold increase in the odds of reporting the concern about IBD-medication induced birth defects.

Table 5-7: Multivariable Logistic Regression Models for Estimating the Effect of Having Poor IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on the Odds of Reporting Specific Concerns among 211 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Concern	OR*	95% CI
Medical advice against conception		
Poor CCPKnow (v. higher CCPKnow levels)	2.0	1.0 – 4.0
Genetically passing my disease to my child		
Poor CCPKnow (v. higher CCPKnow levels)	0.83	0.48 – 1.4
Family history of IBD (yes v. no)	2.3	1.3 – 4.0
Not being able to care for a child		
Poor CCPKnow (v. higher CCPKnow levels)	0.87	0.47 – 1.6
Added stress of raising a child		
Poor CCPKnow (v. higher CCPKnow levels)	0.76	0.43 – 1.4
Chronic illness leading to birth defects		
Poor CCPKnow (v. higher CCPKnow levels)	0.87	0.48 – 1.6
Stillbirth or a miscarriage		
Poor CCPKnow (v. higher CCPKnow levels)	1.2	0.63 - 2.3
IBD medications causing birth defects		
Poor CCPKnow (v. higher CCPKnow levels)	0.77	0.44 – 1.3
AZA use (yes v. no)	2.4	1.3 – 4.5
Worsening of my disease as a result of pregnancy		
Poor CCPKnow (v. higher CCPKnow levels)	0.95	0.56 – 1.6
Decreased fertility		
Poor CCPKnow (v. higher CCPKnow levels)	1.3	0.75 – 2.4
Negative body image, restrict my sexual activity		
Poor CCPKnow (v. higher CCPKnow levels)	1.6	0.67 – 3.6
Marital status		
Partnered (v. single)	1.1	0.43 – 2.9
Divorced (v. single)	2.9	0.46 – 18
IBD related fatigue		
Poor CCPKnow (v. higher CCPKnow levels)	0.80	0.46 – 1.4

*Adjusted for variables listed under each question

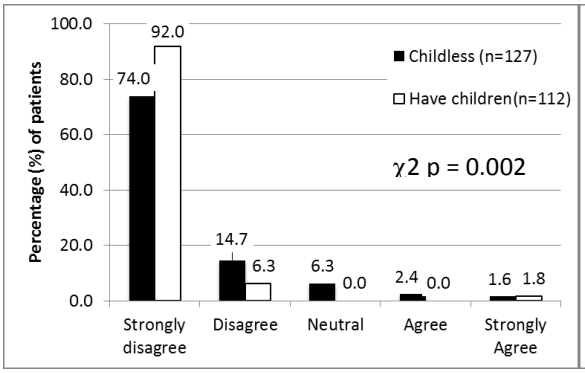
5.3.7 IBD-specific Reproductive Statements of Sources of Worry

Various numbers of childless women and women who have children responded to each of the statements of sources of worry. Therefore, the percentages are calculated using the total number of responses to a particular question as the denominator for that question.

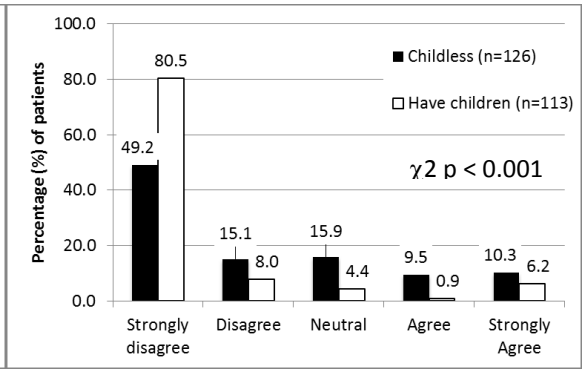
For the statement "I do not like children", comparing childless women to women who have children, the proportion was: 18 per 100 less for strongly disagree; 9.4 per 100 more for disagree, 6.3 per 100 more for neutral, 2.4 per 100 more for agree, and 0.2 per 100 less for strongly agree ($p=0.002$), as shown in Figure 5-9 A.

For the statement "Being a mother is not a major goal in my life", comparing childless women to women who have children, the proportion among was: 31.3 per 100 less for strongly disagree, 7.1 per 100 more for disagree, 11.5 per 100 more for neutral, 8.6 per 100 more for agree, and 4.1 per 100 more for strongly agree ($p<0.001$), as shown in Figure 5-9 B.

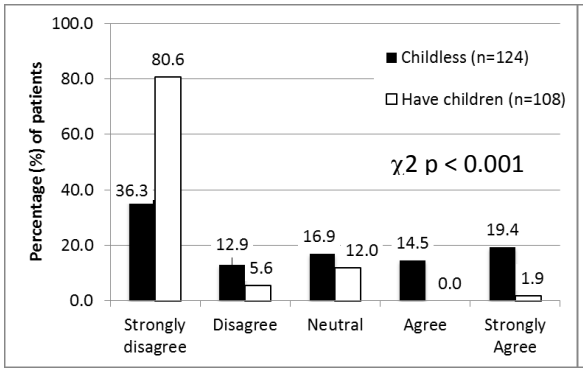
For the statement "I am not in a relationship and I am not ready to have children", comparing childless women to women who have children, the proportion was: 44.3 per 100 less for strongly disagree, 7.3 per 100 more for disagree, 4.9 per 100 more for neutral, 14.5 per 100 more for agree, and 17.5 per 100 more for strongly agree ($p<0.001$), as shown in Figure 5-9 C.



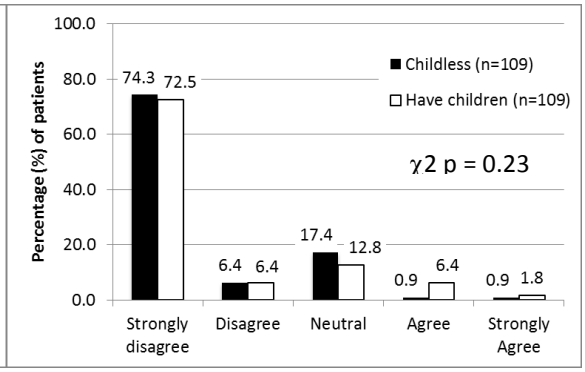
A) I do not like children.



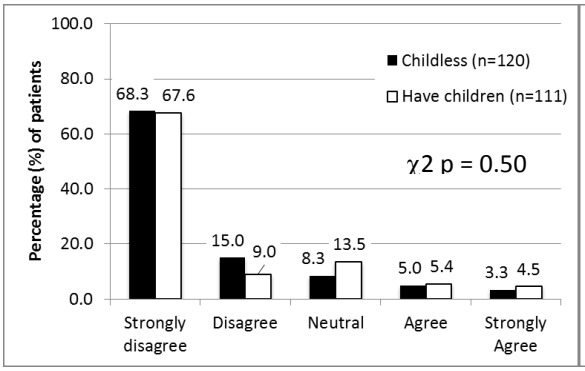
B) Being a mother is not a major goal in my life.



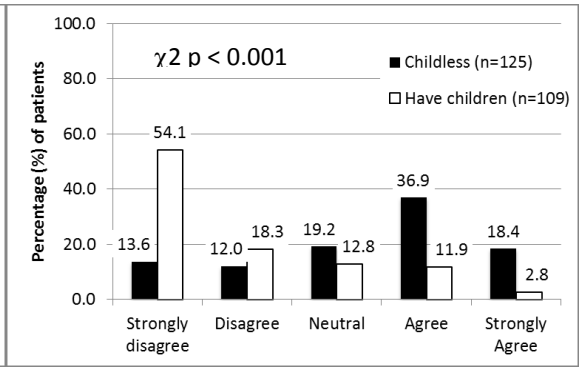
C) I am not in a relationship and I am not ready to have children.



D) I do not plan to have children because of the poor outcome of my previous pregnancies.



E) My physician told me not to become pregnant.



F) I am worried that having IBD decreases my chances of successful conception.

Figure 5-9: Pre-conception Reproductive Sources of Worry among Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

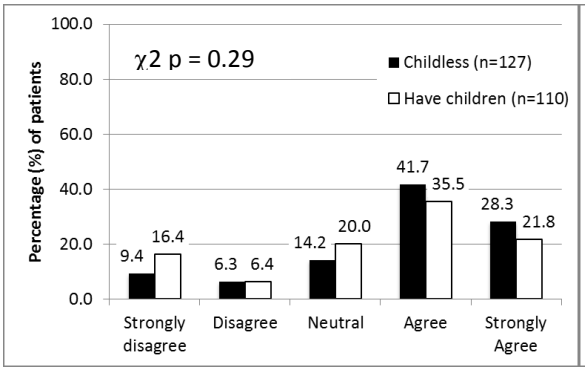
For the statement “I do not plan to have children because of the poor outcome of my previous pregnancies”, comparing childless women to women who have children, the proportion was: 1.8 per 100 more for strongly disagree, the same for disagree, 4.6 per 100 more for neutral, 5.5 per 100 less for agree, 0.9 per 100 less for strongly agree ($p=0.230$), as shown in Figure 5-9 D.

For the statement “My physician told me not to become pregnant”, comparing childless women to women with children the proportion was: 0.7 per 100 more for strongly disagree, 6 per 100 more for disagree, 5.2 per 100 more for neutral, 0.4 per 100 less for agree, and 1.2 per 100 less for strongly agree ($p=0.50$), as shown in Figure 5-9 E. Response to this statement correlated well to a woman’s response to reporting that she had been given “medical advice that conception is not possible/inadvisable with IBD” (in Section on IBD-specific reproductive concerns) ($p=0.004$).

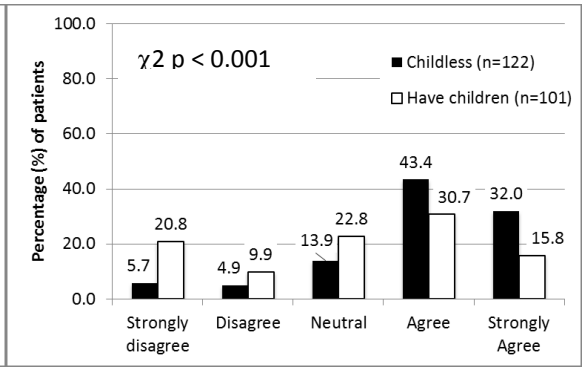
For the statement “I am worried that having IBD decreases my chances of successful conception”, comparing childless women to women who have children, the proportion was: 40.6 per 100 less for strongly disagree, 6.3 per 100 less for disagree, 6.4 per 100 more for neutral, 24.9 per 100 more for agree, and 15.6 per 100 more for strongly agree ($p<0.001$), as shown in Figure 5-9 F. Responses to this statement correlated to responses to the “concern of the possibility of being unable to have a baby due to possible decreased fertility” (in Section on IBD-specific reproductive concerns) ($p<0.001$).

Most women agreed or strongly agreed with the statement “I am worried that I will pass my IBD genetically to my child”. Comparing childless women to women who have children, the proportion was: 7 per 100 less for strongly disagree, 0.1 per 100 less for disagree, 5.8 per 100 less for neutral, 6.2 per 100 for agree, and 6.5 per 100 more for strongly agree ($p=0.29$), as shown in Figure 5-10 G. Responses to this statement correlated with the “concern for the possibility of genetically passing my disease to my child” (in Section on IBD-specific reproductive concerns) ($p<0.001$).

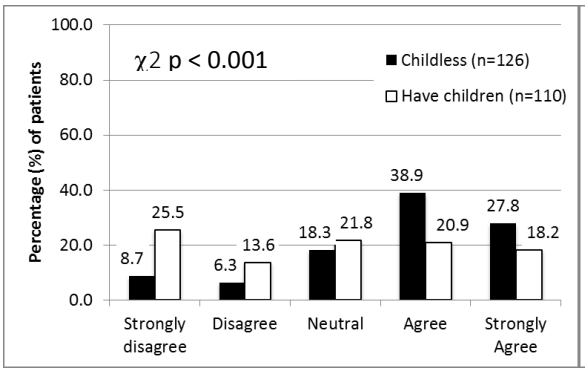
Regarding the statement “I am worried about the effects of IBD on pregnancy”, comparing childless women to women who have children, the proportion was: 15.2 per 100 less for strongly disagree, 5.0 per 100 less for disagree, 8.9 per 100 less for neutral, 12.7 per 100 more for agree, and 16.2 per 100 more for strongly agree ($p<0.001$), as shown in Figure 5-10 H.



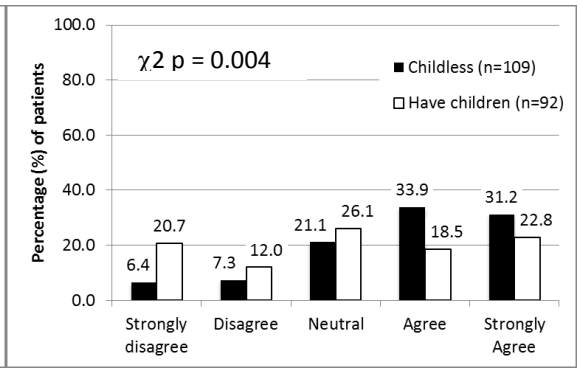
G) I am worried that I will pass my IBD genetically to my child.



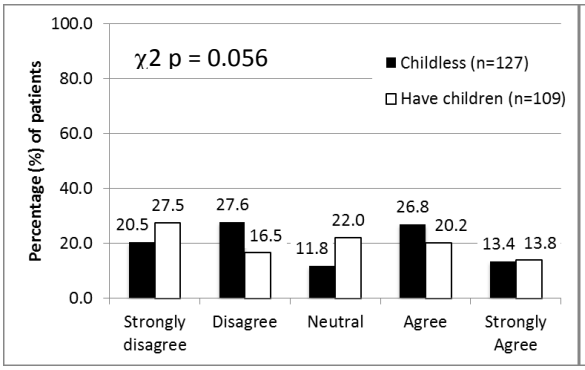
H) I am worried about the effects of IBD on pregnancy.



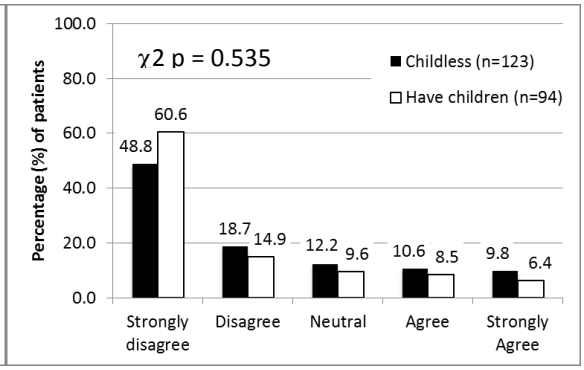
I) I am worried that my pregnancy may worsen my disease (cause a flare).



J) I am worried that the medications I am on to control my IBD may cause birth defects.



K) I am worried that I may not be able to care for my child as a result of my child.



L) I am considering not having children because of my IBD.

Figure 5-10: Pre-conception Reproductive Sources of Worry among Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Regarding the statement “I am worried that pregnancy may worsen my disease”, comparing childless women to women who have children, the proportion was 16.8 per 100 less for strongly disagree, 7.3 per 100 less for disagree, 3.5 per 100 less for neutral, 18 per 100 more for agree, and 9.6 per 100 more for strongly agree ($p<0.001$), as shown in Figure 5-10 I. Responses to this statement correlated with the “concern of the possibility of having a worsening of my disease as a result of pregnancy” (Section on IBD-specific reproductive concerns) ($p<0.001$).

Regarding the statement “I am worried that the medications I am on to control my IBD may cause birth defects”, comparing childless women to women who have children, the proportion was 14.3 per 100 less for strongly disagree, 4.7 per 100 less for disagree, 5 per 100 less for neutral, 15.4 per 100 more for agree, and 8.4 per 100 more for strongly agree ($p=0.004$), as shown in Figure 5-10 J. Responses to this statement correlated with the “concern of the possibility of IBD medications causing birth defects” (Section on IBD-specific reproductive concerns) ($p<0.001$).

Regarding the statement “I am worried that I may not be able to care for my child as a result of my disease”, comparing childless women to women who have children, the proportion was 7 per 100 less for strongly disagree, 11.1 per 100 more for disagree, 10.2 per 100 less for neural, 6.6 per 100 more for agree, and 0.4 per 100 less for strongly agree ($p=0.056$), as shown in Figure 5-10 K. Responses correlated with the “concern for

not being able to care for a child" (Section on IBD-specific reproductive concerns) ($p<0.001$).

For the statement "I am considering not having children because of my IBD", comparing childless women to women who have children, the proportion was 11.8 per 100 less for strongly disagree, 3.9 per 100 more for disagree, 2.6 per 100 more for neutral, 2.1 per 100 more for agree, and 3.4 per 100 more for strongly agree ($p=0.54$), as shown in Figure 5-10 L.

5.3.8 The Effect of Having Discussed Family Planning with a Physician on Sources of Worry about IBD and Reproduction

Multivariable logistic regression was used to estimate the effect of having discussed family planning with a physician on the odds of agreeing with statements on specific worries pertaining to IBD and reproduction, adjusted for appropriate covariates depending on the source of worry. As shown in Table 5-8, having discussed family planning with a physician was not strongly associated with the odds of agreeing with statements on specific sources of worry. However, when the type of physician with whom the respondent reported having discussed family planning was analyzed, having discussed family planning with a non-GI physician corresponded to an increase in the odds of agreeing with the statement "I am worried that having IBD decreases my chances of successful conception", as well as in the odds of agreeing with the statement

Table 5-8: Multivariable Logistic Regression Models for Estimating the Effect of Having Discussed Family Planning on Agreeing with Statements of Sources of Worry about IBD and Reproduction among Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Sources of Worry	OR*	95% CI
F) I am worried that having IBD decreases my chances of successful conception.		
Have discussed family planning with a physician[1]	1.7	0.97 – 3.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.4	0.77 – 2.7
Non-GI physician (v. no physician)	2.5	1.2 – 5.2
G) I am worried that I will pass my IBD genetically to my child.		
Have discussed family planning with a physician[1]	0.72	0.40 – 1.3
Family history of IBD (yes v. no)	4.0	2.2 – 7.2
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.78	0.41 – 1.5
Non-GI physician (v. no physician)	0.62	0.29 – 1.3
Family history of IBD (yes v. no)	4.0	2.2 – 7.3
H) I am worried about the effects of my IBD on pregnancy.		
Have discussed family planning with a physician[1]	1.5	0.84 – 2.6
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	1.3	0.71 – 2.4
Non-GI physician (v. no physician)	1.9	0.90 – 4.2
I) I am worried that my pregnancy may worsen my disease.		
Have discussed family planning with a physician[1]	0.77	0.45 – 1.3
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.56	0.31 – 0.99
Non-GI physician (v. no physician)	1.5	0.74 – 3.3
J) I am worried that the medication I am on to control my IBD may cause birth defects.		
Have discussed family planning with a physician[1]	1.01	0.56 – 1.8
AZA treatment (yes v. no)	3.6	1.8 – 6.8

Sources of Worry	OR*	95% CI
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.80	0.42 – 1.5
Non-GI physician (v. no physician)	1.6	0.72 – 3.6
AZA treatment (yes v. no)	3.7	1.9 – 7.1
Have discussed family planning with a physician[1]	1.0	0.57 – 1.8
IFX/ADA treatment	1.9	1.1 – 3.3
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.83	0.44 – 1.6
Non-GI physician (v. no physician)	1.5	0.71 – 3.4
IFX/ADA treatment (yes v. no)	1.9	1.1 – 3.3
K) I am worried that I may not be able to care for my child as a result of my disease.		
Have discussed family planning with a physician[1]	0.87	0.51 – 1.5
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.87	0.48 – 1.57
Non-GI physician (v. no physician)	0.87	0.42 – 1.8
L) I am considering not having children because of my IBD.		
Have discussed family planning with a physician[1]	0.97	0.47 – 2.0
Have discussed family planning with a physician[1]		
GI physician (v. no physician)	0.88	0.40 – 1.9
Non-GI physician (v. no physician)	1.1	0.56 – 2.9

*Adjusted for variables listed under each question

[1] Reference category: Have not discussed family planning with a physician

"I am worried that the medications I am on to control my IBD may cause birth defects", and to a somewhat lesser extent in the odds of agreeing with the statement "I am worried that pregnancy may worsen my disease".

Other factors were associated with some of these sources of worry. Having a family history of IBD corresponded to a 4.0 (95% CI: 2.2 – 7.3) -fold increase in the odds of agreeing with the statement "I am worried that I will pass my IBD genetically to my child". Having a history of AZA treatment corresponded to a 3.6 (95% CI: 1.1 – 7.9) -fold increase in the odds of agreeing with the statement "I am worried that the medications I am on to control my IBD may cause birth defects"; having a history of IFX/ADA treatment corresponded to a 1.9 (95% CI: 1.1 – 3.9) -fold increase in the odds of agreeing with the statement "I am worried that the medications I am on to control my IBD may cause birth defects".

5.3.9 The Effect of Having Poor CCPKnow on the Odds of Agreeing with Statements of Sources of Worry about IBD and Reproduction

Multivariable logistic regression was used to estimate the effect of having a poor CCPKnow score on agreeing with statements of specific sources of worry, adjusted for appropriate covariates depending on the source of worry. As shown in Table 5-9, having a poor CCPKnow score showed weak associations with the odds of agreeing with statements of specific sources of worry.

Table 5-9: Multivariable Logistic Regression Models for Estimating the Effect of Having Poor IBD-specific Reproductive Knowledge (as measured by the CCPKnow score) on the Odds of Agreeing with Statements of Specific Sources of Worry about IBD and Reproduction among Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Source of Worry	OR*	95% CI
F) I am worried that having IBD decreases my chances of successful conception.		
Poor CCPKnow (v. higher CCPKnow levels)	1.4	0.81 – 2.4
G) I am worried that I will pass my IBD genetically to my child.		
Poor CCPKnow (v. higher CCPKnow levels)	0.95	0.55 – 1.7
Family history of IBD (yes v. no)	3.8	2.1 – 6.9
H) I am worried about the effects of my IBD on pregnancy.		
Poor CCPKnow (v. higher CCPKnow levels)	0.88	0.51 – 1.5
I) I am worried that my pregnancy may worsen my disease (cause a flare).		
Poor CCPKnow (v. higher CCPKnow levels)	1.1	0.64 – 1.8
J) I am worried that the medication I am on to control my IBD may cause birth defects.		
Poor CCPKnow (v. higher CCPKnow levels)	1.2	0.67 – 2.1
AZA treatment (yes v. no)	3.5	1.8 – 6.8
Poor CCPKnow (v. higher CCPKnow levels)	1.2	0.69 – 2.1
IFX/ADA treatment (yes v. no)	1.9	1.1 – 3.3
K) I am worried that I may not be able to care for my child as a result of my disease.		
Poor CCPKnow (v. higher CCPKnow levels)	0.72	0.43 – 1.2
L) I am considering not having children because of my IBD.		
Poor CCPKnow (v. higher CCPKnow levels)	0.89	0.44 – 1.8

*Adjusted for variables listed under each question

5.4 Discussion

Women with IBD have been characterized as having unfounded fears and concerns regarding reproduction and IBD, which has been hypothesized to contribute to "voluntary childlessness" among women with IBD[3,4,7]. In this analysis, we have identified key knowledge deficits among women with IBD, and key concerns and sources of worry regarding reproduction and IBD. This analysis also showed that higher CCPKnow scores did not correspond to decreases in the odds of agreeing with statements of specific sources of worry. In addition, this analysis estimated that having discussed family planning with a physician corresponded to an increase in the odds of reporting concern about stillbirth or miscarriage, and about IBD-related fatigue, but not with other concerns or sources of worry.

Pre-conception concerns, sources of worry

Chronic illness may affect a woman's sexual desire and functioning, or her goals in life regarding family planning and children. In this study, the proportion that reported having the concern of a negative body image restricting sexual activity was 11 per 100 women more among childless women than among women who have children. IBD and chronic diseases have been associated with negative self-esteem and decreased sexual function among patients[10]. In a large case-control study, Marin et al. observed that in half of the female patients, sexual desire and satisfaction worsened after IBD diagnosis, and that women with IBD had lower mean sexual function index scores, and a higher prevalence of sexual dysfunction compared to women who did not have IBD[10].

In the statements of sources of worry section of this study, similar proportions of childless women and women who have children reported that they did "not like children". However, more women who have children than childless women indicated they strongly disagree with the statement that "being a mother is not a major goal in my life". More childless women selected agree or strongly agree that "I am not in a relationship and I am not ready to have children", indicating that part of childlessness may be due to relationship status and goals to have children, rather than directly related to fears or concerns about IBD and medications.

Genetics and inheritance

Passing on a chronic illness to one's child may be a major concern among mothers and women who are considering becoming mothers. In the study by Mountifield et al.[4], only 7/48 (15%) women reported having a concern about "the genetic risk of my child having IBD". Selinger et al.[7] reported that among the childless women (n=96) in their survey study, 74.7% were concerned about the inheritability of IBD to offspring.

Most women in this study (67.7%) knew about the increased risk of a child having IBD if the mother or father suffer from it, but few women (27.8%) knew that the risk is less than 10%. Having discussed family planning with a physician was associated with a 1.8-fold increase in the odds of selecting the correct response to this question on genetics, while having a family history of IBD was associated with decreased odds of selecting the correct response. When analyzing the type of physician they discussed family planning

with, women who had discussed family planning with a GI physician had increased odds of selecting the correct responses to the genetics questions. However, this question (CCPKnow question #2) may not accurately reflect knowledge about genetics and inheritance, as the correct answer "less than 10%" may not be true for some subgroups of IBD cases. For example, for patients who have a strong family history of IBD, or certain genes, the risk may be higher than 10%.

Nevertheless, this topic was addressed in the other concerns and statements of sources of worry sections of the questionnaire, where more than half (52.1%) of the women reported having a "concern for the possibility of genetically passing my disease to my child". The majority of women also indicated that they agreed or strongly agreed with the statement "I am worried that I will pass my IBD genetically to my child", confirming the high proportion of women who have this concern. The proportion of childless women reporting this concern (64.5%) was almost twice the proportion of women who have children reporting this concern (39.4%).

Knowledge (CCPKnow score) and discussion of family planning with a physician was not associated with decreased odds of having this concern about genetics and inheritance, but having a family history of IBD corresponded to an increase in the odds of reporting this concern. This suggests that the concern about passing on one's disease to one's child may be affected by personal family history and that because they developed IBD, women may believe that it may have been passed on to them by their mother or other

family member; perhaps this concern can only be alleviated by a personal history of having a child unaffected by IBD.

Fertility

IBD, medications to treat IBD, and surgery to treat IBD can affect fertility; however, in general, a woman who is in remission and who has not had pelvic surgery (e.g. ileoanal pouch) has similar fertility as the general female population. In this study, women were more likely to correctly answer the fertility-related CCPKnow questions if they had discussed family planning with a physician. A third of women reported having a concern for the possibility of decreased fertility. More childless women than women who have children reported having this concern, as well as agreeing with the statement "I am worried that having IBD decreases my chances of successful conception".

In addition, a third of childless women and proportionally fewer women who have children reported that they had been given "medical advice that conception is not possible/inadvisable with IBD". Interestingly, women with "poor" CCPKnow scores had increased odds of reporting that they had been given medical advice against conception. Women who previously had discussed family planning with a physician were slightly more likely to report having been given medical advice against conception and having the concern of decreased fertility.

When the type of physician with whom they had discussed family planning with was analyzed, women who reported having discussed family planning with a non-GI physician had higher odds of agreeing with the statement "I am worried that having IBD decreases my chances of successful conception". This raises the question of whether physicians, and specifically non-GI physicians, are informing their patients that they have an increased risk of decreased fertility and that conception is not advised during IBD. While this may be the case for selected patients, it does not apply to all patients. This warrants further study into IBD-specific reproductive knowledge among physicians and the quality of their discussions about family planning with patients.

Disease Activity and Medications

Women who are in remission when they become pregnant are more likely to stay in remission during pregnancy, while women with active disease at conception are more likely to have continued disease activity, or worsened disease during pregnancy. To stay in remission, women should continue required medications throughout pregnancy. However, medication use during conception and pregnancy is of major concern to women because of the potential effects on the pregnancy and fetus. Fear of adverse effects of medications on pregnancy has been reported to be one of the top concerns of women with IBD, with up to 84% of women with IBD in previous studies reporting this concern[4].

The majority of women in this study knew that “IBD should be well controlled before becoming pregnant”, and that “women with IBD should delay trying for a baby until their disease has been controlled by medication”. Having discussed family planning with a physician corresponded to an increase in the odds of selecting the correct response to each of the disease activity CCPKnow questions. However, this effect was mainly seen only if the physician with whom the respondent discussed family planning was a GI physician compared to a non-GI physician.

Almost half of the women reported concerns about the possibility of IBD medications causing birth defects. However, a higher proportion of childless women compared to women who have children had this concern; it was the second highest concern among childless women, in contrast to the third highest concern among women who have children. Similarly almost a third of childless women strongly agreed and a third agreed with the statement “I am worried that the medications I am on to control my IBD may cause birth defects”. Again, this finding suggests that a woman’s personal experience with pregnancy and having a healthy child may affect their knowledge, concerns, and beliefs/opinions regarding the possibility of IBD medications causing birth defects.

The majority of women were unaware of IBD-medication specifics such as Infliximab or Adalimumab being “probably safe” in pregnancy, that Methotrexate should be stopped 3-6 months before trying for a baby, or that Azathioprine and 6-MP can be continued during pregnancy. Having discussed family planning with a physician corresponded to

an increase in the odds of selecting the correct responses to drug-related CCPKnow questions except for the anti-TNF question (#9). Assuming that patients obtain information from their physicians, this may suggest that physician knowledge of anti-TNF use is limited. Discussion with a GI physician corresponded to an increase relative to discussion with a non-GI physician in the odds of selecting the correct answers to drug-related CCPKnow questions. Prior treatment with specific medications increased the odds of correctly answering the associated CCPKnow questions, thus patient knowledge pertaining to specific drugs may be enhanced by personal experience with the specific drug.

Mode of delivery

The mode of delivery is relevant to certain women with IBD; those who have had a colectomy and ileoanal pouch formation are often advised against vaginal delivery, due to risk of damage to the anal sphincter resulting in fecal incontinence; CD patients with active perianal disease are advised to have caesarean section. In this study, childless women were less likely than women who have children to select the correct response to the CCPKnow question on vaginal delivery, and both childless women and women who have children were unlikely to select the correct response to the question regarding peri-anal disease. Discussion of family planning with a physician corresponded to an increase in the odds of selecting the correct response to these CCPKnow questions, and a history of peri-anal disease corresponded to an increase in the odds of selecting the

correct response to the peri-anal disease question (#14), again supporting the inference that women's IBD-specific reproductive knowledge is enhanced by personal experience.

Pregnancy outcomes and Breastfeeding

Previous publications have reported that up to 67.9% of women with IBD believe that they can have a healthy baby[7]. However, among women who choose not to have children, up to 18% report having a fear of IBD-related congenital abnormalities[4]. In this study, only 58.9% of respondents believed that the chances of having a healthy baby were very good; 41.4% of childless women and 77.5% of women who have children reported this belief. Discussion of family planning with a physician corresponded to an increase in the odds of selecting the correct response for each of the CCPKnow questions about pregnancy outcomes and breastfeeding, indicating the importance of a transfer of knowledge from physician to patient.

Other concerns of women

The CCPKnow survey covers the majority of reproductive issues in IBD, but there are many concerns that women with IBD have which are not within the CCPKnow survey. A large proportion of women were concerned about worsening of their disease as a result of pregnancy, with fewer women who have children compared to childless women (38.5% v. 54.2%) reporting this concern. Similarly, more childless women than women who have children agreed with the statement "I am worried that pregnancy may worsen

my disease". Again, this suggests that personal experience with pregnancy may affect a woman's concerns and sources of worry.

Other significant concerns reported by respondents of this study were IBD-related fatigue, not being able to care for a child, and the added stress of raising a child. Again, personal history of having children was associated with these concerns, as a higher proportion of childless women compared to women who have children were concerned about the added stress of raising a child.

Personal Experience and Knowledge, Concerns, Beliefs/Opinions

The analysis estimated positive effects of personal experiences including family history of IBD, specific disease phenotypes (perianal disease), or being on specific medications on the odds of selecting the correct responses to the corresponding individual CCPKnow questions, and also on the odds of reporting specific concerns and beliefs/opinions. This supports the observation that knowledge framed in terms of factual information differs from sources of worry, and that personal experience may have more of an effect than factual knowledge does on concerns, and beliefs or opinions; this may explain why knowledge as measured by CCPKnow did not show clear effects on the odds of reporting specific concerns, and sources of worry.

Limitations

A limitation of this analysis is the cross-sectional design, which does not allow for inferring any temporal relationship between IBD-specific reproductive knowledge, concerns, sources of worry, and voluntary childlessness. In addition, as the responses for the statements on beliefs or opinions were scaled using the Likert scale of degrees of agreement, women who responded "unsure" were categorized as "not in agreement" for the purpose of the logistic regression analysis. This was felt to be appropriate as the analysis aimed to estimate the effect of exposure variables on the odds of having specific concerns and sources of worry, indicated by the responses "strongly agree" or "agree". However, it is possible that this method of categorization may have underestimated the effects of the exposure variables on the outcomes if women who indicated "unsure" were more in agreement than disagreement. Additionally, the degrees of agreement with statements about having particular worries may not correspond to beliefs about the probability of specific undesired consequences.

5.5 Conclusion

Women with IBD, especially childless women with IBD, have knowledge deficits and concerns regarding IBD-specific reproductive issues that range from pre-conception to breastfeeding. Increased IBD-specific reproductive knowledge did not correspond to a decrease in the odds of having IBD-specific reproductive concerns. Having discussed family planning with a physician corresponded to an increase in the odds of selecting the correct responses to the CCPKnow questions, but also corresponded to an increase

in the odds of having been given medical advice that conception is not possible/ inadvisable with IBD, of having the concern of decreased fertility, and of having the concern of having a stillbirth or miscarriage. However, the analysis showed that the type of physician the patient discussed family planning with modified the odds of having certain concerns and sources of worry. Thus, a further study on physician knowledge is warranted in order to address any knowledge deficits among physicians.

5.6 References

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6 Family Planning Decisions Change Over Time and With IBD Diagnosis among Women with IBD

6.1 Background

Individuals with chronic inflammatory diseases are burdened with lifelong symptoms, medications and other treatments, and with the effects of the disease and subsequent treatment on their quality of life, life decisions, and interactions with family and friends. In particular, having an inflammatory disease has been shown to affect decisions regarding family planning. Inflammatory bowel disease is a chronic disease that tends to affect patients during the reproductive adolescent and young adult years when individuals are considering family planning.

As presented in Chapters 4 and 5, women with IBD in this study population had a high prevalence of poor IBD-specific reproductive knowledge and a large number of IBD-specific reproductive concerns; in particular, compared to women with children, childless women had lower IBD-specific reproductive knowledge and more IBD-specific reproductive concerns. Prior publications have reported the concept of "voluntary childlessness" based on the hypothesis that women with IBD have fears and concerns about reproduction in IBD and thus may choose not to have children[1-6]. The recent systematic review published by Tavernier et al.[6] summarizes the publications that reported involuntary and voluntary childlessness among Crohn's disease (CD) and ulcerative colitis (UC) patients; Tavernier et al. estimated prevalence of "voluntary

childlessness" ranging from 14% to 46% among women with IBD, compared to 2.5% to 28% among women without IBD.

Marri et al. estimated that there was a higher prevalence of "voluntary childlessness" among women with IBD (CD 18%, UC 15%) compared to women in the general population (6.2%)[3]. Mountifield et al. reported that up to 14% of childless women with IBD made the decision to remain childless as a direct result of having a diagnosis of IBD[4]. In the Selinger et al.[7] study, 29.7% of nulliparous women with IBD reported considering "voluntary childlessness" because of their IBD. Up to 42% of patients in the Toomey et al.[8] study reported that they would allow IBD to influence their family planning decisions.

However, the definition of "voluntary childlessness" differed across studies; Marri et al.[3] used the National Center for Health Statistics definition of "women who are fecund and do not wish to have any children or who are surgically sterile for contraceptive reasons". Mountifield et al.[4] suggested that an indication of "voluntary childlessness" among IBD patients was the observation that IBD patients did not seek medical fertility advice any more than the general female population despite the fact that IBD patients have a higher prevalence of concern regarding infertility than the general female population (>40% v. 9%). In the Selinger et al[7] study, women who responded "agree" or "totally agree" to the question "I am considering not having children because of inflammatory bowel disease" were considered to be voluntarily childless. Tommey et al.[8] considered

women who indicated that they would allow IBD to influence their family planning decisions to be voluntarily childless. Thus, the definition of "voluntary childlessness" has not been consistent among studies, and may not capture the complexity involved when a woman with IBD chooses to remain childlessness.

The objectives of this analysis were to characterize voluntary childlessness among women with IBD by asking them about their family planning status and contraception use at various times in their disease history in order to investigate how IBD diagnosis affects family planning and childlessness among women with IBD. The analysis also aimed to estimate the association of IBD-specific reproductive knowledge with voluntary childlessness.

6.2 Methods

6.2.1 Setting and Participants

Female IBD patients who were between 18 to 45 years old were identified from the University of Alberta Inflammatory Bowel Disease Clinic, and invited to complete the CCPKnow survey along with questionnaires about demographics, IBD history, reproductive history, and whether they had discussions of family planning. The questionnaires also asked about their family planning status before IBD diagnosis, after IBD diagnosis, and currently. Full details for patient recruitment and questionnaire development have been presented in Chapter 2 Methods.

6.2.2 Data Sources and Variable Definitions

Before IBD diagnosis family planning status

Question 10 of the REPRODUCTIVE HISTORY section of the questionnaire asked

> "10. Just BEFORE your IBD diagnosis, which of the following was true for you:"

with responses categorized as shown in Table 6-1.

Table 6-1: Categorization of responses to Question 10

Questionnaire responses	New categorization
I had not given birth but planned to some day	Planned to have (more) children
I had not given birth and planned to have adopted children only	Did not plan to have (more) children
I had not given birth and did not plan to give birth or raise adopted children	Did not plan to have (more) children
I had given birth and planned to get pregnant again	Planned to have (more) children
I had given birth and did not plan to get pregnant again	Did not plan to have (more) children
Other - free-text responses indicated they had not thought about it, or were unsure, or were too young at age of diagnosis to have considered family planning	Unsure

After IBD diagnosis family planning status

Question 11 of the REPRODUCTIVE HISTORY section of the questionnaire asked

> "11. SINCE being diagnosed with IBD, have you changed your feelings/perspectives about having your own children?"

with responses categorized as shown in Table 6-2.

Table 6-2: Categorization of responses to Question 11

Questionnaire responses	New categorization
No	Remains as for question 10
Yes	Depends on sub-response
Now I plan to not have children because of my illness	Did not plan to have (more) children
Now I plan to have children despite my illness	Planned to have (more) children

Not I plan to adopt children because of my illness	Did not plan to have (more) children
Other - free-text responses indicated they had not thought about it, or were unsure, or were too young at age of diagnosis to have considered family planning	Unsure

Current family planning status

Question 6 of the REPRODUCTIVE HISTORY section of the questionnaire asked

"6. What is your current status in life regarding children?"

with responses categorized as shown in Table 6-3.

Table 6-3: Categorization of responses to Question 6

Questionnaire responses	New categorization
Do not want to have children	Do not want (more) children
Would like adopted children only	Do not want (more) children
Trying to become pregnant	Want (more) children
Have children, would like more	Want (more) children
Have children, completed family	Do not want (more) children
Don't have children, would like to later on	Want (more) children
Unsure	Unsure

This analysis categorized women who wished to have adopted children only as childless, and as not wanting or planning to have children. The reason for this is that the analysis aimed to characterize the desire or plans to have biological children, as the majority of concerns regarding reproduction and IBD revolve around issues of genetics, adverse maternal and fetal outcomes, medication-induced teratogenicity, and pregnancy effects on IBD.

Change in family planning status

Changes in family planning status were compared across the following time periods: BEFORE IBD diagnosis, SINCE IBD diagnosis, and CURRENT.

Contraception use

Questions 7, 8, 9 of the REPRODUCTIVE HISTORY section of the questionnaire asked about contraception use. For question 7, only women who responded to question 6 with "trying to become pregnant" were included. Change in contraception use was then determined by classifying patients as "no change", "yes to no", and "no to yes".

Voluntary childlessness

Women were categorized as "voluntarily childless" if they met the criteria:

1) currently childless

AND 2) currently do not plan to have children (as indicated by response to question 6 on current family planning status).

6.2.3 Statistical analysis

This analysis aimed to characterize changes in family planning status over time by:

1) estimating the proportions of women in each family planning status subgroup BEFORE IBD diagnosis, SINCE IBD diagnosis, and at the CURRENT time
2) describing the patterns of change in family planning status over the three time points

3) comparing childless women and women who have children on the distribution of each of the patterns of change in family planning status.

This analysis aimed to characterize trends in contraception use by:

1) estimating the proportions of women who used contraception and of women who did not use contraception BEFORE IBD diagnosis and at the time of the survey (CURRENT time)
2) describing the patterns of change in contraception use over time
3) comparing the proportion of childless women and women who have children for each of the patterns of change in contraception use.

This analysis also aimed to estimate the effect of IBD-specific reproductive knowledge on the odds of voluntary childlessness by:

1) estimating ORs and 95% CI for the effect of the CCPKnow score on the odds of voluntary childlessness
2) among childless women, estimating ORs and 95% CI for the effect of the CCPKnow score on the odds of having the family planning status “trying to become pregnant”.

For continuous variables, medians and interquartile ranges (IQR) were tabulated, and medians were compared across subgroups; the statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests.

For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions.

To estimate the effect of independent variables on the outcome of interest, multivariable logistic regression was used to obtain odds ratios and 95% CI adjusted for selected covariates. Covariates were selected based on whether they could affect both the independent variable of interest and the outcome of interest, while not being an intervening variable between the two. For marital status, as there were only 2 patients classified under the marital status "divorced", these patients were combined with "partnered" patients, making the assumption that they must have once been married to be "divorced".

6.3 Results

6.3.1 Characteristics of Study Population

Complete data was available from 223 women who returned questionnaires that had complete responses for all variables included in the final multivariable analysis. Demographic data for all patients are shown in Table 6-4. The median age was 32.0 (IQR 26.0 – 37.0) yrs. There were 116 (52.0%) childless women and 107 (48.0%) women

Table 6-4: Prevalence of Childlessness by Selected Study Variables among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	Total patients (N=223)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Age (years)					
18 to 24	44	19.7	42/44	95.5	<0.001
25 to 29	47	21.1	31/47	66.0	
30 to 34	51	22.9	22/51	43.1	
35 to 39	41	18.4	10/41	24.4	
40 to 45	40	17.9	11/40	27.5	
Marital status (current)					
Single	66	29.6	59/66	89.4	<0.001
Partnered	155	69.5	57/155	36.8	
Divorced	2	0.9	0/2	0	
Marital status (before IBD diagnosis)					
Single	155	69.5	103/155	66.5	<0.001
Partnered	68	30.5	13/68	19.1	
Education					
Grade 1 to Grade 12	50	22.4	26/50	52.0	0.24
College/university	141	63.2	68/141	48.2	
Graduate degree	11	4.9	7/11	63.6	
Professional school degree	4	1.8	2/4	50.0	
Other	17	7.6	13/17	76.5	
Employment					
Unemployed	28	13.6	13/28	46.4	0.037
Part time	40	19.4	21/40	52.5	
Full time	104	50.5	65/104	62.5	
Other	34	16.5	12/34	35.3	
Family history of IBD					
Yes	97	43.5	46/97	47.4	0.23
No	126	56.5	70/126	55.6	
Type of IBD					
Crohn's disease	134	60.1	68/134	50.7	0.65
Ulcerative colitis	80	35.9	42/80	52.5	
Indeterminate	9	4.0	6/9	66.7	
Age at IBD diagnosis					
Before 18 years	59	26.5	44/59	74.6	<0.001
18 to 45 years	164	73.5	72/164	43.9	

Category	Total patients (N=223)*		Prevalence of childlessness		Chi-square p-value
	N	% of total*	N	% of category	
Duration of IBD					
0 to 4 years	52	23.3	31/52	59.6	0.21
5 or more years	171	76.7	85/171	49.7	
Perianal disease (n=202)*					
Yes	49	24.3	26/49	53.1	0.89
No	153	75.7	83/153	54.2	
Colectomy with pouch					
Yes	15	6.7	11/15	73.3	0.087
No	208	93.3	105/208	50.5	
Ostomy					
Yes	20	9.0	15/20	75.0	0.031
No	203	90.9	106/203	45.9	
Have discussed family planning with a physician					
Yes	140	62.8	67/140	47.9	0.11
No	83	37.2	49/83	59.0	
Ever been pregnant					
Yes	123	55.2	16/123	13.0	<0.001
No	100	44.8	100/100	100.0	
Pregnancy timing (n=121)*					
Before IBD diagnosis only	31	25.6	4/31	12.9	0.58
After IBD diagnosis only	71	58.7	10/71	14.1	
Before and after IBD diagnosis	19	15.7	1/19	5.3	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

who have children. The median age of childless women was 9 years lower than the median of age of women who have children (26.0 (IQR 22.0 – 33.0) years v. 35.0 (IQR 31.0 – 41.0) years, respectively; p<0.001). The median age at diagnosis of all patients was 21.0 (IQR 17.0 -27.0) years. The median age at diagnosis among childless women was 6.0 years younger than that of women who have children (19.0 (IQR 15.0 – 22.0) years v. 25.0 (IQR 20.0 – 29.0) years, respectively; p<0.001). The median duration of disease of all patients was 9.0 (IQR 5.0 – 15.0) years. The median duration of disease among childless women was 1.0 year less than that of women who have children (9.0 (IQR 5.0 – 13.0) years v. 10.0 (IQR 6.0 – 16.0) years, respectively; p=0.040).

6.3.2 Family Planning Status Before IBD Diagnosis

Table 6-5 shows the distribution of family planning status BEFORE IBD diagnosis of childless women and women who have children. As shown in Table 6-5, although there were differences in the proportion of women in each family planning status subgroup, when this variable was re-categorized into three groups, the proportion of childless women who planned to have children was similar to the proportion of women who have children who planned to have (more) children (91/116 (78.4%) v. 74/107 (69.2%), respectively; p=0.053).

Table 6-5: Family Plans BEFORE IBD Diagnosis of 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	Total patients (n=223)		Childless (n=116)		Have children (n=107)		Chi-square p-value
	N	%	N	%	N	%	
Original responses							
I had not given birth but planned to some day	151	67.7	91	78.4	60	39.7	<0.001
I had not given birth and planned to have adopted children only	1	0.4	0	0	1	0.9	
I had not given birth and did not plan to give birth or raise adopted children	19	8.5	14	12.1	5	4.7	
I had given birth and planned to get pregnant again	14	6.3	0	0	14	13.1	
I had given birth and did not plan to get pregnant again	20	9.0	0	0	20	18.7	
Other	18	8.1	11	61.1	7	38.9	
Categorized responses							
Planned to have (more) children	165	74.0	91	78,4	74	69.2	0.053
Did not plan to have (more) children	40	17.9	14	12.1	26	24.3	
Unsure	18	8.1	11	9.5	7	6.5	

6.3.3 Family Planning Status Since IBD Diagnosis

Table 6-6 shows the distribution of family planning status SINCE IBD diagnosis among childless women and women who have children. As shown in Table 6-6, comparing childless women to women who have children, the proportion was 26.8 per 100 more for those who had changed family planning status SINCE IBD diagnosis (56/116 (48.3%) v. 23/107 (21.5%), respectively; p<0.001). There were a large number of patients who specified "other" responses, listed in Appendix C4 Table C4-0-1.

Table 6-6: Changes in Plans to Have Children SINCE IBD Diagnosis among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	Total patients (n=223)		Childless (n=116)		Have children (n=107)		Chi-square
	N	%	N	%	N	%	p-value
Changed family planning status since diagnosis							
No	144	64.6	60	51.7	84	78.5	<0.001
Yes	79	35.4	56	48.3	23	21.5	
If yes, how?	**(n=77)**		**(n=54)**		**(n=23)**		
Now I plan to not have children because of my illness	14	18.2	6	11.1	8	34.8	0.074
Now I plan to have children despite my illness	20	26.0	15	27.8	5	21.7	
Now I plan to adopt children because of my illness	3	3.9	3	5.6	0	0	
Other	40	51.9	30	55.6	10	43.5	
Categorized							
Plan to have (more) children	149	66.8	75	64.7	74	69.2	0.17
Do not plan to have (more) children	48	21.5	23	19.8	25	23.4	
Unsure	26	11.7	18	15.5	8	7.5	

These could not easily be classified into the three listed responses for the sub question to Question 11, as some response overlapped, or were unrelated. Therefore, women were categorized as shown in Table 6-3, based on the categorization from Question 10 (do not plan/plan/unsure), the response from Question 11 (No/Yes), and the response to the sub question of "if Yes, how did they change", and the analysis of the specified "other" responses.

6.3.4 Current Family Planning Status

Table 6-7 shows the distribution of responses for current family planning status regarding plans for having children, as well as the re-categorized status. Regarding current plans to have children, comparing childless women to women who have children, the proportion was 9.3 per 100 more for currently trying to become pregnant, (14/116 (12.1%) v. 3/107 (2.8%), respectively; $p<0.001$), and 21.0 per 100 women more for being unsure about current plans to have children (19/116 (16.4%) v. 5/107 (4.7%), respectively; $p<0.001$).

When analyzing the family planning status variable with 3 categories, comparing childless women to women who have children, the proportion was 38.0 per 100 more for planning to have children (82/116 (70.7%) v. 35/107 (32.7%), respectively; $p<0.001$) and 11.7 per 100 more for being unsure (19/116 (16.4%) v. 5/107 (4.7%), respectively; $p<0.001$). However, 15 of 116 (12.9%) childless women indicated they did not plan to have children.

Table 6-7: CURRENT Family Plans of 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	Total patients (n=223)		Childless (n=116)		Have children (n=107)		Chi-square p-value
	N	%	N	%	N	%	
Status							
Do not want to have children	13	5.8	10	8.6	3	2.8	<0.001
Would like adopted children only	3	1.3	3	2.6	0	0	
Trying to become pregnant	17	7.6	14	12.1	3	2.8	
Have children, would like more	33	14.8	1	0.9	32	29.9	
Have children, completed family	66	29.6	2	1.7	64	59.8	
Do not have children, would like to later on	67	30.0	67	57.8	0	0	
Unsure	24	10.8	19	16.4	5	4.7	
Status recoded							
Plan to have (more) children	117	52.5	82	70.7	35	32.7	<0.001
Do not plan to have (more) children	82	36.8	15	12.9	67	62.6	
Unsure	24	10.8	19	16.4	5	4.7	

6.3.5 Changes in Family Planning Status Over Time

Table 6-8 shows the change in family planning status from before IBD diagnosis to since IBD diagnosis. Comparing childless women to women who have children, the proportion was 10.1 per 100 less for not planning to have children before and since IBD diagnosis (10/116 (8.6%) v. 20/107 (18.7%) respectively; p<0.001). Comparing childless women to women who have children, the proportion was 5.6 per 100 more for planning to have children before but no longer planning to have children since IBD diagnosis (12/116 (10.3%) v. 5/107 (4.7%), respectively, p<0.001).

Table 6-9 shows the distribution of women as they changed family planning status across the 3 time points. Only 23 of the 223 (10.3%) women did not plan to have children at all three time points, while 96 of the 223 (43.0%) women planned to have children at all three time points. Comparing childless women to women who have children, the proportion was 12.5 per 100 less for not planning to have children at all three time points (5/116 (4.3%) v. 18/107 (16.8%), respectively; p<0.001); 27.0 per 100 more for planning to have children at all three time points (65/116 (56.0%) v. 31/107 (29.0%), respectively; p<0.001); and 30.1 per 100 less for changing from planning to have children before IBD diagnosis and since IBD diagnosis, but currently not planning to have children (2/116 (1.7%) v. 34/107 (31.8%), respectively; p<0.001).

Table 6-8: Change in Family Plans comparing BEFORE IBD Diagnosis to SINCE IBD Diagnosis among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Before diagnosis			Since diagnosis							
				Total		Childless (n=116)		Have Children (n=107)		Chi-square p-value
	N	%		N	%	N	%	N	%	
DNP	40	17.9	**DNP**	30	13.5	10	8.6	20	18.7	<0.001
			P	9	4.0	4	3.4	5	4.7	
			U	1	0.4	0	0	1	0.9	
P	165	74.0	**DNP**	17	7.6	12	10.3	5	4.7	
			P	140	62.8	71	61.2	69	64.5	
			U	8	3.6	8	6.9	0	0	
U	18	8.1	**DNP**	1	0.4	1	0.9	0	0	
			P	0	0	0	0	0	0	
			U	17	7.6	10	8.6	7	6.5	

DNP: do not plan; P: plan; U: unsure

Table 6-9: Change in Family Plans over Time among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Before diagnosis			Since diagnosis			Currently					
						Total			Childless (n=116)		Have Children (n=107)	
	N	%		N	%		N	%	N	%	N	%
DNP	40	17.9	DNP	30	13.5	**DNP**	**23**	**10.3**	**5**	**4.3**	**18**	**16.8**
						P	3	1.3	1	0.9	2	1.9
						U	4	1.8	4	3.4	0	0
			P	9	4.0	DNP	5	2.2	0	0	5	4.7
						P	4	1.8	4	3.4	0	0
						U	0	0	0	0	0	0
			U	1	0.4	DNP	1	0.4	0	0	1	0.9
						P	0	0	0	0	0	0
						U	0	0	0	0	0	0
P	165	74.0	DNP	17	7.6	DNP	9	4.0	6	5.2	3	2.8
						P	4	1.8	3	2.6	1	0.9
						U	4	1.8	3	2.6	1	0.9
			P	140	62.8	**DNP**	**36**	**16.1**	**2**	**1.7**	**34**	**31.8**
						P	**96**	**43.0**	**65**	**56.0**	**31**	**29.0**
						U	8	3.6	4	3.4	4	3.7
			U	8	3.6	DNP	0	0	0	0	0	0
						P	5	2.2	5	4.3	0	0
						U	3	1.3	3	2.6	0	0
U	18	8.1	DNP	1	0.4	DNP	1	0.4	1	0.9	0	0
						P	0	0	0	0	0	0
						U	0	0	0	0	0	0
			P	0	0	DNP	0	0	0	0	0	0
						P	0	0	0	0	0	0
						U	0	0	0	0	0	0
			U	17	7.6	DNP	7	3	1	0.9	6	5.6
						P	5	2.2	4	3.4	1	0.9
						U	5	2.2	5	4.3	0	0

DNP = do not plan; P = plan; U = unsure

6.3.6 Contraception use

As shown in Table 6-10, comparing childless women to women who have children, the proportion was 20.4 per 100 less for using contraception before IBD diagnosis (70/115 (60.9%) v. 87/106 (82.1%), respectively; p<0.001), and 20.2 per 100 more for using contraception at the time of the survey (63/115 (54.8%) v. 37/107 (34.6%), respectively; p<0.001).

As shown in Table 6-10, comparing childless women to women who have children, the proportion was 10.3 per 100 more for changing from not using contraception before IBD diagnosis to using contraception at the time of the survey (14/115 (12.2%) v. 2/106 (1.9%) respectively; p<0.001), and 21.3 per 100 more for changing from using contraception before IBD diagnosis to not using contraception at the time of the survey (88/106 (82.2%) v. 70/115 (60.9%), respectively; p<0.001).

Table 6-10: Contraception Use BEFORE IBD Diagnosis and CURRENT Contraception Use among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	Total patients (n=222)		Childless (n=115)		Have children (n=107)		Chi-square p-value
	N	%	N	%	N	%	
Before (n=221)							
No	64	29.0	45	39.1	19	17.9	0.001
Yes	157	71.0	70	60.9	87	81.3	
Currently (n=222)							
No	122	55.0	52	45.2	70	65.4	0.003
Yes	100	45.0	63	54.8	37	34.6	
	Total patients (n=221)		**Childless (n=115)**		**Have children (n=106)**		**Chi-square p-value**
	N	**%**	**N**	**%**	**N**	**%**	
Before/Current (n=221)							
No/No	48	21.6	31	27.0	17	15.9	<0.001
No/Yes	16	7.2	14	12.2	2	1.9	
Yes/No	158	71.2	70	60.9	88	82.2	
Yes/Yes	0	0	0	0	0	0	

6.3.7 Voluntary Childlessness

Women who were 1) currently childless, and 2) currently do not plan to have children were categorized as having "voluntary childlessness". There were 15 women who met these criteria (15/116 (12.9%) of childless women; 15/223 (6.7%) of total patients).

Voluntary Childless Women Compared to All Patients

Compared to all patients, the voluntarily childless women were similar in the median current age (36.0 (IQR 30.0 – 45.0) years v. 32.0 (IQR 26.0 – 37.0) years, respectively; p=0.082), median age at diagnosis (22.0 (IQR 20.0 – 26.0) years v. 21.0 (17.0 – 27.0) years, respectively; p=0.38) and median duration of disease (13.0 (IQR 6.0 – 20.0) years v. 9.0 (IQR 5.0 – 15.0) years, respectively; p=0.12). They had a median CCPKnow score similar to the median CCPKnow score of the rest of the patients (4.0 (IQR 2.0 – 10.0) v. 7.0 (IQR 4.0 – 11.0), respectively; p=0.15). Similar proportions of women who were voluntarily childless and other women in the study population reported having discussed family planning with a physician (8/15 (53.3%) v. 132/208 (63.5%), respectively; p=0.43). As shown in Table 6-11 multivariable logistic regression estimated an OR adjusted for current age (years) and marital status of 0.90 (95% CI: 0.78 – 1.0) for the association of the CCPknow score with the odds of voluntary childlessness. Thus each one-point increase in the CCPKnow score corresponded to a 10% decrease in the odds of voluntary childlessness.

Table 6-11: Multivariable Logistic Regression Model Estimating the Effect of IBD-specific Reproductive Knowledge (as measured by the CCPKnow score) on Voluntary Childlessness among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Variable	OR	95%CI
CCPKnow score	0.91	0.79 – 1.0
Current age (years)	1.1	1.0 – 1.2
Marital status		
Single	1.0	-
Partnered	0.87	0.21 – 3.6

Voluntarily childless women compared to non-voluntarily childless women

These voluntarily childless women were of older median age than the rest of the childless women (36.0 (IQR 30.0 – 45.0) years v. 26.0 (22.0 – 32.0) years, respectively; p=0.001). They were diagnosed at an older median age (22.0 (IQR 20.0 – 26.0) years v. 18.0 (IQR15.0 – 22.0) years, respectively; p=0.007), and had a longer median duration of disease (13.0 (IQR 6.0 – 20.0) years v. 8.0 (IQR 5.0 – 12.0) years, respectively; p=0.032). The median CCPKnow scores were similarly low for voluntarily childless women and for the other childless women (4.0 (IQR 2.0 – 10.0) v. 6.0 (3.0 – 9.0), respectively; p=0.52). The prevalence of voluntary childlessness was similar among childless women with poor CCPKnow scores (19/70 (14.3%)) and childless women with adequate+ CCPKnow scores (5/46 (10.9%)) (p=0.59).

The prevalence of voluntary childlessness was similar among childless women who had discussed family planning with a physician and those who had not discussed family planning with a physician (8/67 (11.9%) v. 7/49 (14.3%), respectively; p=0.71). The prevalence of voluntary childlessness was similar among childless women who reported at least one IBD-specific reproductive concern and childless women who reported no concerns (11/85 (12.9%) v. 2/10 (20.0%), respectively; p=0.54).

As shown in Table 6-12, multivariable logistic regression estimated an OR adjusted for current age in years and marital status of 0.91 (95% CI: 0.79 – 1.0) for the association between the CCPknow score and voluntary childlessness among childless women. Thus

each one-point increase in the CCPKnow score corresponded to a 9% decrease in the odds of voluntary childlessness among childless women. The confidence interval for this estimate excluded values greater than 1.0, indicating uncertainty about the magnitude of this effect but not about its direction.

Table 6-12: Multivariable Logistic Regression Model for Estimating the Effect of IBD-specific Reproductive Knowledge (as measured by the CCPKnow score) on Voluntary Childlessness among 116 Childless Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Variable	OR	95%CI
CCPKnow score	0.91	0.79 – 1.0
Current age (yrs)	1.2	1.1 – 1.3
Marital status		
Single	1.0	-
Partnered	1.2	0.27 – 5.2

6.3.8 Childless Women: Trying to Become Pregnant

Childless women were also categorized as "trying to become pregnant" or "not trying" based on their responses to Question 6. There were 14 women who were "trying to become pregnant" (14/116 (12.1%) of childless women; 14/223 (6.3%) of total cohort). These women had an older median age than the rest of the childless women (34.0 (IQR 31.0 – 37.0) years v. 26.0 (21.0 – 32.0) years, respectively; p<0.001). Their median age at diagnosis was the same as the median age at diagnosis of the rest of the childless women (19.0 (IQR 17.0 – 28.0) years v. 19.0 (IQR 15.0 – 22.0) years, respectively; p=0.19) and their median duration of disease was 6.0 years longer than the median duration of disease of the rest of the childless women (14.0 (IQR 8.0 – 17.0) years v. 8.0 (IQR 5.0 – 12.0) years, respectively; p=0.065). They also had a higher median CCPKnow score than the rest of the childless women (10.0 (IQR 9.0 – 12.0) v. 5.0 (2.0 – 9.0), respectively; p=0.001).

As shown in Table 6-13, multivariable logistic regression estimated an OR adjusted for current age in years, marital status, and having at least one IBD-specific reproductive concern, of 1.2 (95% CI: 1.0 – 1.4) for the association of the CCPknow score with the odds of trying to become pregnant among childless women. Thus, each one-point increase in the CCPKnow score corresponded to a 20% increase in the odds of trying to become pregnant.

Table 6-13: Multivariable Logistic Regression Model for Estimating the Effect of IBD-specific Reproductive Knowledge (as measured by the CCPKnow survey) on the Odds of "trying to become pregnant" among 116 Childless Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Variable	OR	95% CI
CCPKnow score	1.1	0.99 – 1.3
Current age (years)	1.0	0.94 – 1.1
Marital status		
Single	1.0	-
Partnered	4.9	0.57 - 43

6.4 Discussion

Women with IBD have been reported to have an increased infertility rate, partly due to medical or health reasons, but more recently postulated as being due to a choice made by women with IBD to remain childless[3,4,9,10]. This study characterized women's family planning status at time points that spanned before IBD diagnosis, since IBD diagnosis, and at the current time, in an attempt to identify true "voluntary childlessness" among women with IBD. About 4.3% of the childless women did not want children at any time point, while 56% of the childless women wanted children at all three time points. Specifically, when women who were 1) currently childless and 2) currently did not want to have children were classified as "voluntarily childless", the "voluntary childlessness" prevalence among the childless study participants (12.9%) was slightly lower than reported elsewhere[3,4,9,10].

Changes in family plans over time with diagnosis of IBD

This is the one of the first studies to describe changes in family plans over time. The change from planning to have children before IBD diagnosis to not planning to have children since IBD diagnosis was more common in childless women than in women who have children. This change in plans to have children was consistent with the finding that the change from not using contraception to using contraception was also more common in childless women (12.2%) compared to women who have children (1.9%). These results support the hypothesis that some of the childlessness in women with IBD can be attributed to a conscious decision to remain childless ("voluntary childlessness").

Voluntary Childlessness

The concept of "voluntary childlessness" as reported in the literature was attributed to concerns and beliefs based on incorrect knowledge regarding reproduction in IBD. Estimates of voluntary childlessness from previous studies, summarized in the recent systematic review by Tavernier et al., range from 14% to 36% of women with IBD and from 2.5% to 28% of women without IBD[6]. However, the definition of voluntary childlessness differed across studies. Measures of voluntary childlessness used in previous studies included the prevalence of contraception use, as well as intentions inferred from responses to various questions.

In a previous study by Marri et al. women with IBD were grouped into "temporarily childless", "voluntarily childless", and "non-voluntarily childless" categories, according to National Institute of Health (NIH) definitions[3]. By the NIH definitions, temporarily childless women have no children currently but expect to have children in the future, and voluntarily childless women are fecund and do not wish to have children or are surgically sterile for contraceptive reasons[3]. In the current analysis, women with IBD were asked about their plans to have children before IBD diagnosis, since IBD diagnosis, and at the current time, in an attempt to describe changes in intentions regarding family planning status. Further analysis of these changes over time in relation to IBD diagnosis may be helpful in understanding the concept of temporary childlessness and temporary voluntary childlessness among women with IBD.

When evaluating childless women who were categorized as having voluntary childlessness, increases in the CCPKnow score corresponded to decreases in the odds of voluntary childlessness. Childless women who were actively trying to become pregnant at the time of the survey had a higher median CCPKnow score than childless women who were not trying to become pregnant. There was a positive association between the CCPKnow score and the odds of trying to become pregnant among childless women. This suggests that IBD-specific reproductive knowledge may play an important role in the decision to have children. However, as this is a cross-sectional survey, it is difficult to determine if childless women who were trying to become pregnant had higher levels of IBD-specific reproductive knowledge because they sought knowledge they felt they needed after they made the decision to try to have children, or if they had obtained higher IBD-specific reproductive knowledge and were thus more comfortable with the decision to try to have children.

Limitations of the analysis

A potential limitation of the analysis was that women who wished to have adopted children only were categorized as childless, and as not wanting or planning to have children. This analysis aimed to characterize the desire or plan to have biological children, as the majority of concerns regarding reproduction and IBD revolve around issues of genetics, disease-associated adverse maternal and fetal outcomes, medication-induced teratogenicity, and pregnancy effects on IBD. Women who indicated they only wished to adopt children may have made this decision based on some of these

concerns, and therefore they were not included in the category of women who have children or women who wanted to have children. However, women were not questioned about the reason they chose to have adopted children only, and potentially some of the concerns and beliefs may apply even to the desire to have adopted children or no children at all.

In addition, analysis aimed to estimate the effects of exposure variables on the outcome of voluntary childlessness, which was defined as currently being childless and currently not wanting to have children. Therefore, women who responded that they were "unsure" about their family planning status were considered to not yet have decided that they wanted to have children, and thus were categorized as not wanting to have children at the time of the survey. It is possible this method of categorization may have overestimated the prevalence of voluntary childlessness, as some women who indicated they were "unsure" may have been "unsure" due to non-IBD related reasons.

Another potential limitation of the analysis was that women were not questioned about sexual activity with respect to contraception use; some reported changes in contraception use may have been due to changes in sexual activity rather than to the IBD diagnosis.

6.5 Conclusion

Decisions regarding having children among women with IBD are fluid decisions that change over time with respect to IBD diagnosis. Childless women in this study were more likely than women who have children to change from planning to have children before IBD diagnosis to not planning to have children since IBD diagnosis. Increases in IBD-specific reproductive knowledge as measured by the CCPKnow score corresponded decreases in the odds of voluntary childlessness and to increases in the odds of trying to become pregnant. IBD-specific reproductive knowledge is only one of many factors affecting the fluid decisions and plans to have children among women with IBD.

6.6 References

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7 Among Physicians Who Treat Women with IBD, Does IBD-specific Reproductive Knowledge and Degree of Comfort Managing Pregnant IBD Patients Influence Discussion of Family Planning?

7.1 Introduction

Women with IBD obtain information regarding reproduction in IBD from various sources. Chapters 4 and 5 showed that women with IBD who had discussed family planning with a physician had higher IBD-specific reproductive knowledge on average than women who had not discussed family planning with a physician. Only 62.1% of women with IBD reported having discussed family planning with a physician. However, it is unclear whether these discussions were initiated by the women with IBD or by their physicians.

Knowledge levels and degree of comfort with providing advice on this topic may affect whether physicians discuss family planning with their IBD patients. In 2011, Tan et al. reported results from a large survey in South Australia assessing general practitioner (GP) comfort with managing IBD; 37% of GPs reported being generally 'uncomfortable' with IBD management; specifically, GPs were uncomfortable with the use of immunosuppressants and biologics[1]. In a survey conducted by Toomey et al., only 18% of surveyed GPs routinely raised the topic of family planning[2]. A recent chart review study estimated that only 19% of female patients with IBD had reproductive counseling documented in their charts[3]. As Andrews et al. indicated, "sexuality, fertility, family

planning, and pregnancy" has been considered one of the "un-promoted issues in IBD" because the topic is not often brought up during patient-physician encounters[4]. To date, the effect of physicians' knowledge regarding reproductive issues in IBD and their degree of comfort with managing reproduction in IBD on their practice patterns pertaining to reproduction in IBD is not clearly understood.

The objectives of this analysis were to estimate among physicians the effects of IBD-specific reproductive knowledge and degree of comfort with managing pregnant IBD patients on the odds of discussing family planning with their female IBD patients.

7.2 Methods

7.2.1 Settings and Participants

Physicians were recruited from the physicians referring to the IBD clinic, physicians attending various gastroenterology and IBD conferences in Canada, and physician members of the Canadian Association of Gastroenterology. Full details of physician recruitment were described in Chapter 2.

7.2.2 Data Sources and Variable Definitions

Physicians were asked to complete the study questionnaire, which included the CCPKnow survey along with questions on socio-demographic factors, characteristics of their practice and patient population, whether they discuss family planning with

patients, degree of comfort with managing pregnant IBD patients. Full details were presented in Chapter 2.

IBD-specific Reproductive Knowledge

IBD-specific reproductive knowledge among physicians was assessed using the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey (described in Chapter 2). The CCPknow scores, calculated by summing the correct responses to each question, range from 0 to 17; respondents were categorized as having poor (0 to 7), adequate (8 to 10), good (11 to 13), or very good (14-17) CCPKnow levels, which were then dichotomized as "poor/adequate/good" or "very good".

Degree of comfort managing pregnant IBD patients

The questionnaire asked physicians the following question:

11) Do you feel comfortable managing pregnant IBD patients?

Responses were categorized as shown in Table 7-1.

Table 7-1: Categorization of Degree of Comfort Managing Pregnant IBD Patients

Questionnaire responses	New categorization
Not comfortable at all	Not comfortable
Not comfortable	Not comfortable
Somewhat	Somewhat
Fairly comfortable	Comfortable
Very comfortable	Comfortable

Discussion of family planning with patients

The questionnaire asked physicians the following question:

12) With a female IBD patient of reproductive age, do you routinely bring up the topic of family planning?

with responses being No or Yes. Those who replied Yes were classified as physicians who discuss family planning.

7.2.3 Statistical Analysis

This analysis aimed to estimate among physicians the effect of IBD-specific reproductive knowledge on the odds of discussing family planning by

(1) comparing the proportion that discuss family planning across categories of study variables

(2) estimating ORs and 95% CI for the effect of IBD-specific reproductive knowledge as measured by the CCPKnow score on the odds of discussing family planning.

The analysis also aimed to estimate the effect of the degree of comfort with managing pregnant IBD patients on the odds of discussing family planning by

(1) comparing the proportion that discusses family planning across categories of degrees of comfort

(2) estimating ORs and 95% CI for the effect of the degree of comfort on the odds of discussing family planning.

For continuous variables, medians and interquartile ranges (IQR) were tabulated, and medians were compared across subgroups; the statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests.

For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions.

To estimate the effect of independent variables on the outcome of interest, multivariable logistic regression was used to obtain odds ratios and 95% CI adjusted for selected covariates. Covariates were identified based on whether they could affect both the independent variable of interest and the outcome of interest, while not being an intervening variable between the two. DAGs (directed acyclic graphs) that depict the associations between independent variables and dependent variables were created using DAGitty Version 2.0 (www.dagitty.net).

7.3 Results

7.3.1 Characteristics of the Study Population

Complete data was available from 215 physicians who returned questionnaires that had complete responses for all variables included in the final multivariable analysis. Table 3-4 shows characteristics of the 215 physician respondents. As the final multivariable logistic regression models include demographic factors related to practice characteristics, only questionnaires submitted by practicing physicians (n=183) were included in this analysis.

7.3.2 Discussion of Family Planning

Almost two thirds (119/183, 65.0%) of the physicians discuss family planning. As shown in Table 7-2, the proportion of physicians who discuss family planning was 44.5 per 100 physicians higher among GI physicians compared to GP physicians ($p<0.001$), 29.0 per 100 physicians higher among academic physicians compared to community physicians ($p<0.001$), and 46.2 per 100 physicians higher among physicians with practices in which 11 - 24% of patients have IBD compared to physicians with practices in which 0 to 10% of patients have IBD ($p=0.005$ for this comparison). In addition, the proportion of physicians who discuss family planning increased with IBD knowledge level, and with the degree of comfort with managing pregnant IBD patients. More physicians with very good CCPKnow scores discuss family planning compared to those with poor/adequate/good CCPKnow scores (89/110 (80.9%) v. 30/73 (41.1%), respectively; $p<0.001$).

Appendix C-5 Table C5-0-1 shows the distribution of variables within each physician group. The percent female was 21.6% among GI physicians, 44.0% among GP physicians, and 18.2% among Other physicians ($p<0.001$ for all comparisons). Other variables that differed between physician groups included years of practice, with more GP physicians and Other physicians falling into the 11-20 years and >20 years categories, whereas GI physicians were more evenly distributed. Higher proportions of GP physicians and Other physicians relative to GI physicians practiced in the community

Table 7-2: Characteristics and the Proportion of Physicians who Discuss Family Planning by Selected Variables among 183 Practicing Canadian Physicians

	Total physicians (n=183)*		Proportion who discuss family planning		Chi-square p-value
	N	% of total*	N	% of category	
Gender					
Male	127	69.4	83/127	65.4	0.89
Female	56	30.6	36/56	64.3	
Training status					
Gastroenterologist (GI)	97	53.0	82/97	84.5	<0.001
General practitioner (GP)	75	41.0	30/75	40.0	
Other	11	6.0	7/11	63.6	
Years in practice					
0 to 4 years	27	14.8	19/27	70.4	0.21
5 to 10 years	26	14.2	21/26	80.8	
11 to 20 years	47	25.7	27/47	57.4	
>20 years	83	45.4	52/83	62.7	
Population of city (n=131)*					
0 to 99,999	46	35.1	24/46	52.2	0.74
100,000 to 499,999	28	21.4	17/28	60.7	
>500,000	57	43.5	33/57	57.9	
Type of practice (n=180)*					
Community	127	70.6	71/127	55.9	<0.001
Academic	53	29.4	45/53	84.9	
Percentage of patients with IBD					
0 – 10%	91	49.7	40/91	44.0	<0.001
11 – 24%	51	27.9	46/51	90.2	
25 – 50%	27	14.8	20/27	74.1	
51 – 100%	14	7.7	13/14	92.9	
Number of IBD patients each year					
0 to 9	33	18.0	14/33	42.4	<0.001
10 to 50	66	36.1	36/66	54.5	
51 to 100	18	9.8	15/18	83.3	
101 to 150	18	9.8	14/18	77.8	
more than 150	48	26.2	40/48	83.3	
Number of pregnant IBD patients managed in past year					
None	76	41.5	33/76	43.4	<0.001
1 to 10	70	38.3	61/70	87.1	
11 or more	37	20.2	25/37	67.6	

	Total physicians (n=183)*		Proportion who discuss family planning		Chi-square p-value
	N	% of total*	N	% of category	
Self-assessed IBD knowledge					
Inadequate	16	8.7	5/16	31.3	<0.001
Enough to get by	83	45.4	48/83	57.8	
Very good	84	45.9	66/84	78.6	
Degree of comfort managing pregnant IBD patients					
Not comfortable	59	32.2	22/59	37.3	<0.001
Somewhat comfortable	37	20.2	25/37	67.6	
Comfortable	87	47.5	72/87	82.8	
CCPKnow level					
Poor (0 to 7)	17	9.3	6/17	35.3	<0.001
Adequate (8 to 10)	18	9.8	6/18	33.3	
Good (11 to 13)	38	20.8	18/38	47.4	
Very good (14 to 17)	110	60.1	89/110	80.9	
Dichotomized CCPKnow level					
Poor/Adequate/Good (0 to 13)	73	39.9	30/73	41.1	<0.001
Very good (14 to 17)	110	60.1	89/110	80.9	

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator.

(98.6% v. 63.6% v. 50.0%, respectively; p<0.001). Other differences are shown in Appendix C-5 Table C5-0-1.

7.3.3 Physician IBD-specific Reproductive Knowledge (as measured by the CCPKnow score)

Figure 7-1 shows the distribution of CCPKnow scores among physicians. The median CCPKnow score was 15.0 (IQR 11.0 – 17.0) with almost two-thirds of physicians (110/183 (60.1%)) having very good CCPknow scores. The median CCPKnow score was 17.0 (IQR 16.0 – 17.0) for GI physicians, and 11.0 (IQR 8.0 – 13.0) for GP physicians. Table 7-3 shows the proportion with very good CCPknow scores across categories of study variables. Compared to the proportion of GI physicians with very good CCPKnow scores, the proportion was 72.8 per 100 physicians lower among GP physicians and 47.3 per 100 physicians lower among Other physicians (90/97 (92.8%) GI physicians, 15/75 (20.0% GP physicians, 5/11 (45.5%) Other physicians; p<0.001). Proportionally more physicians who began to practice medicine more recently had very good CCPKnow scores. The proportion of physicians with very good CCPKnow scores was 40.7 per 100 more among physicians in academic practice compared to physicians in community practice (61/127 (48.0%) v. 47/53 (88.7%), respectively; p<0.001). The proportion with very good CCPKnow scores was higher among physicians who had managed more IBD patients in their practice, and who had managed at least one or more pregnant IBD patients.

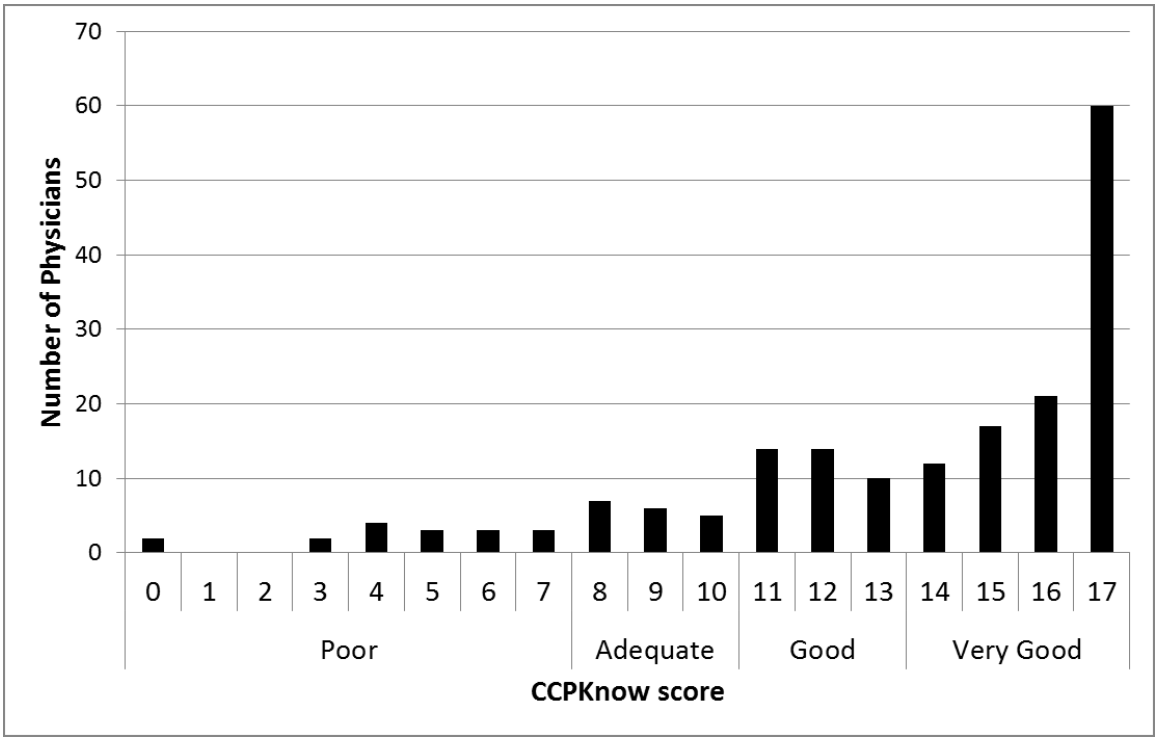

Figure 7-1: Distribution of CCPKnow Scores, Measuring IBD-specific Reproductive Knowledge, among 183 Practicing Canadian Physicians

Poor n=17/183, 9.3%;
Adequate n=18/283, 9.8%;
Good n=38/183, 20.8%
Very good n=110/183, 60.1%.

Table 7-3: Characteristics and the Proportion with Very Good IBD-specific Reproductive Knowledge (as Measured by the CCPKnow score) by Selected Study Variables among 183 Practicing Canadian Physicians

	Total (n=183)*		Proportion with very good CCPKnow scores		Chi-square p-value
	N	% of total*	N	% of category	
Gender					
Male	127	69.4	84/127	66.1	0.012
Female	56	30.6	26/56	46.4	
Training status					
Gastroenterologist (GI)	97	53.0	90/97	92.8	<0.001
General practitioner (GP)	75	41.0	15/75	20.0	
Other	11	6.0	5/11	45.5	
Years in practice					
0 to 4 years	27	14.8	23/27	85.2	<0.001
5 to 10 years	26	14.2	23/26	88.5	
11 to 20 years	47	25.7	23/47	48.9	
>20 years	83	45.4	41/83	49.4	
Population of city (n=131)*					
0 to 99,999	46	35.1	16/46	34.8	0.064
100,000 to 499,999	28	21.4	14/28	50.0	
>500,000	57	43.5	33/57	57.9	
Type of practice (n=180)*					
Community	127	70.6	61/127	48.0	<0.001
Academic	53	29.4	47/53	88.7	
Percentage of patients with IBD					
0 – 10%	91	49.7	26/91	28.6	<0.001
11 – 24%	51	27.9	45/51	88.2	
25 – 50%	27	14.8	25/27	92.6	
51 – 100%	14	7.7	14/14	100.0	
Number of IBD patients each year					
0 to 9	33	18.0	6/33	18.2	<0.001
10 to 50	66	36.1	27/66	40.9	
51 to 100	18	9.8	17/18	94.4	
101 to 150	18	9.8	15/18	83.3	
more than 150	48	26.2	45/48	93.8	
Number of pregnant IBD patients managed in past year					
None	76	41.5	22/76	28.9	<0.001
1 to 10	70	38.3	64/70	91.4	
11 or more	37	20.2	24/37	64.9	

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator.

7.3.4 Identifying Covariates for the Multivariable Logistic Regression Model for Estimating the Effect of the CCPKnow Score on the Odds of Discussing Family Planning with Patients among Physicians

Study variables that may affect both the CCPKnow score and whether physicians discuss family planning were entered into a DAG (Figure 7-2), with arrowed lines indicating the direction of the association between the CCPKnow score and discussion of family planning. The directions of the associations between study variables were based on assumptions that training status (GI physician, GP physician, Other physician) may influence whether a physician practiced in the community or in academia, and years in practice (as different physicians with diverse training status differ on the years of training, which dictates when physicians can enter practice). In addition, the assumption was made that the number of pregnant IBD patients a physician had managed in the past year would influence their degree of comfort, rather than degree of comfort affecting whether they had managed pregnant IBD patients in the past year (presumably, physicians do not explicitly choose their patient characteristics in terms of gender and pregnancy status).

In addition, the assumption was made that IBD-specific reproductive knowledge (measured by the CCPKnow score) influenced the degree of comfort managing pregnant IBD patients. The total effect of the CCPKnow score on the odds of discussing family planning includes the estimated direct effect of the CCPKnow score and the estimated indirect effect of the CCPKnow score acting through an intermediate variable, the

degree of comfort with managing pregnant IBD patients,) on the odds of discussing family planning. Both the total and direct effects of the CCPKnow score on the odds of discussing family planning were estimated separately to examine whether the CCPKnow score had a direct effect on the odds of discussing family planning, or if the total effect of the CCPKnow score on the odds of discussing family planning was fully mediated by the degree of comfort. The valid estimation of the direct effect depends on the assumption that there is no interaction between the main exposure and the intermediate variable.

The identified covariates for the multivariable logistic regression model for the total effect of IBD-specific knowledge as measured by the CCPKnow score on the odds of discussing family planning among physicians were 1) years in practice and 2) # of pregnant IBD patients managed in the past year.

The covariates for the multivariable logistic regression model for the direct effect of the CCPKnow score on the odds of discussing family planning among physicians were 1) years in practice, 2) # pregnant IBD patients managed in the past year, 3) degree of comfort with managing pregnant IBD patients.

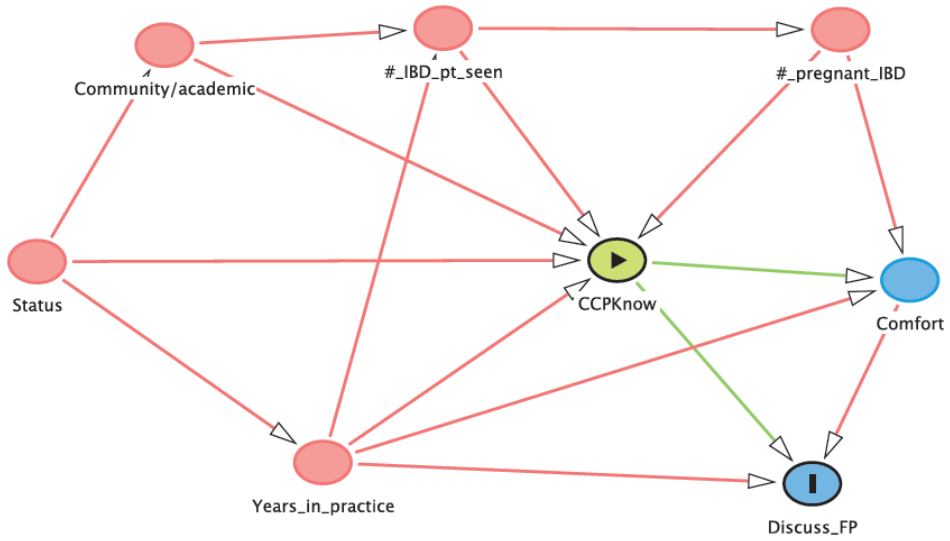

Figure 7-2: Directed Acyclic Graph for the CCPKnow Score and Discussion of Family Planning among Physicians

CCPKnow = Crohn's and Colitis Pregnancy Knowledge score. Outcome = discussion of family planning. Exposure = CCPKnow. FP = family planning. IBD= inflammatory bowel disease. Yellow circle with arrow = exposure, blue circle with I = primary outcome, blue circle empty = outcome of exposure but exposure to primary outcome.

7.3.5 The Association of IBD-specific Reproductive Knowledge with Discussion of Family Planning among Physicians

The proportion that discusses family planning was 39.8 per 100 physicians higher among physicians with very good CCPKnow scores than among physicians with poor/adequate/good CCPKnow scores (89/110 (80.9%) v. 30/73 (41.1%), respectively; p<0.001). Appendix C-5 Table C5-0-2 shows the proportion that responded correctly to the CCPKnow question of interest, among those who discuss family planning and those who do not. For most CCPKnow questions, proportionally more physicians who discuss family planning than those who do not discuss family planning answered the question correctly.

As shown in Table 7-4, multivariable logistic regression estimated an OR adjusted for years in practice and # of pregnant IBD patients managed in the past year of 1.2 (95% CI: 1.0 – 1.3) for the total effect of IBD-specific reproductive knowledge (the CCPKnow score) on the odds of discussing family planning (the effect of the CCPKnow score directly, or indirectly through the degree of comfort, on the odds of discussing family planning); thus each one-point increase in the CCPKnow score corresponded to a 20% increase in the odds of discussing family planning among physicians. The estimated OR for the direct effect of the CCPKnow score (the effect not mediated by degree of comfort) was 1.1 (95% CI: 1.0-1.3), corresponding to a 10% increase in the odds of discussing family planning among physicians. Thus, assuming no interaction between the CCPKnow score and the degree of comfort, these estimates suggest that half of the

total effect of the CCPKnow score is mediated by the degree of comfort; however, it must be noted that the 95% CIs for the two estimates are the same, thus this analysis does not have adequate statistical power for precise estimation of these two effects.

Table 7-4: Multivariable Logistic Regression Model for the Total and Direct Effects of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on the Odds of Discussion of Family Planning among 183 Practicing Canadian Physicians

	OR	95% CI
TOTAL effect		
CCPKnow score	1.2	1.0 – 1.3
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.2	0.31 – 5.0
11 to 20 years	0.83	0.27 – 26
> 20 years	1.2	0.40 – 3.3
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	4.4	1.7 – 12
11 or more	1.1	0.38 – 3.3
DIRECT effect		
CCPKnow score	1.1	1.0 – 1.3
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.3	0.32 – 5.4
11 to 20 years	0.83	0.26 – 2.6
>20 years	1.2	0.39 – 3.4
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.1	1.0 – 9.4
11 or more	1.5	0.55 – 4.1
Degree of comfort with managing pregnant IBD patients		
Not comfortable	1.0	-
Somewhat comfortable	1.8	0.66 – 4.9
Comfortable	2.2	0.72 – 6.8

7.3.6 Degree of Comfort Managing Pregnant IBD Patients

Almost half the physicians (87/183 (47.5%)) reported that they feel comfortable managing pregnant IBD patients. As shown in Table 7-5, study variables associated with degree of comfort included gender, training status, population of city, type of practice, percentage and number of IBD patients in practice, and knowledge level.

The proportion of physicians who reported that they feel comfortable managing pregnant IBD patients was 54.0 per 100 physicians higher among physicians with very good CCPKnow scores than among physicians with poor/adequate/good CCPKnow scores (76/110 (69.1%) v. 11/73 (15.1%), respectively; $p<0.001$).

Table 7-5: Characteristics and the Proportion that Reports Feeling Comfortable Managing Pregnant IBD Patients by Selected Study Variables among 183 Practicing Canadian Physicians

	Total Physicians (n=183)*		Proportion that reports feeling comfortable managing pregnant IBD patients		Chi-square p-value
	N	% of total*	N	% of category	
Gender					
Male	127	69.4	70/127	55.1	0.008
Female	56	30.6	17/56	30.4	
Training status					
Gastroenterologist (GI)	97	53.0	74/97	76.3	<0.001
General practitioner (GP)	75	41.0	11/75	14.7	
Other	11	6.0	2/11	18.2	
Years in practice					
0 to 4 years	27	14.8	15/27	55.6	0.29
5 to 10 years	26	14.2	17/26	65.4	
11 to 20 years	47	25.7	19/47	40.4	
> 20 years	83	45.4	36/83	43.4	
Population of city (n=131)*					
0 to 99,999	46	35.1	10/46	21.7	0.015
100,000 to 499,999	28	21.4	11/28	39.3	
>500,000	57	43.5	30/57	52.6	
Type of practice (n=180)*					
Community	127	70.6	46/127	36.2	<0.001
Academic	53	29.4	39/53	73.6	
Percentage of patients with IBD					
0 – 9%	91	49.7	18/91	19.8	<0.001
10 – 24%	51	27.9	35/51	68.6	
25 – 50%	27	14.8	21/27	77.8	
51 – 100%	14	7.7	13/14	92.9	
Number of IBD patients each year					
0 to 9	33	18.0	4/33	12.1	<0.001
10 to 50	66	36.1	15/66	22.7	
51 to 100	18	9.8	12/18	66.7	
101 to 150	18	9.8	15/18	83.3	
more than 150	48	26.2	41/48	85.4	
Number of pregnant IBD patients managed in past year					
None	76	41.5	8/76	10.5	<0.001
1 to 10	70	38.3	47/70	81.4	
11 or more	37	20.2	22/37	59.5	

	Total Physicians (n=183)*		Proportion that reports feeling comfortable managing pregnant IBD patients		Chi-square p-value
	N	% of total*	N	% of category	
CCPKnow level					
Poor (0 to 7)	17	9.3	1/17	5.9	<0.001
Adequate (8 to 10)	18	9.8	2/18	11.3	
Good (11 to 13)	38	20.8	8/38	21.1	
Very good (14 to 17)	110	60.1	76/110	69.1	
Dichotomized CCPKnow level					
Poor/Adequate/Good (0 to 13)	34	18.6	11/34	15.1	<0.001
Very good (14 to 17)	149	81.4	76/149	69.1	

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator.

7.3.7 Identifying Covariates for the Multivariable Logistic Regression Model for Estimating the Effect of Degree of Comfort on the Odds of Discussing Family Planning among Physicians

Variables that may affect both physician subjective comfort level managing pregnant IBD patients and whether physicians discuss family planning were entered into a DAG (Figure 7-3), with arrowed lines indicating the direction of the association between the degree of comfort and discussion of family planning. For this model, it was assumed that IBD-specific reproductive knowledge (the CCPKnow score) and practice characteristics influenced degree of comfort and that the associations were not in the other direction.

Based on this model, the degree of comfort had no indirect effect on the odds of discussing family planning, so the total and direct effects are the same. The selected covariates for the multivariable logistic regression model for the effect of the degree of comfort on discussion of family planning among physicians were: 1) # of pregnant IBD patients managed in the past year, 2) years in practice, 3) the CCPKnow score.

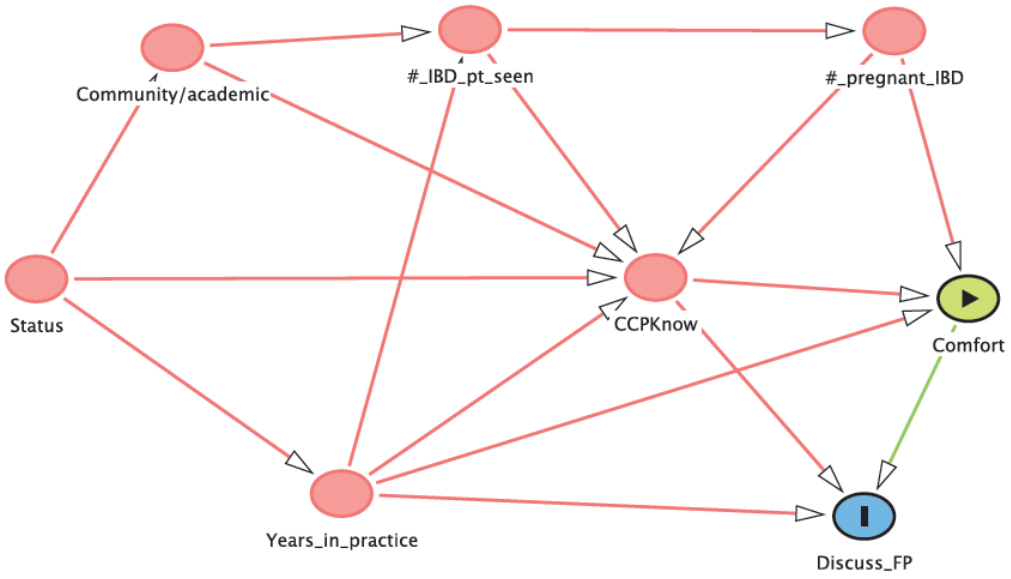

Figure 7-3: Directed Acyclic Graph for the Degree of Comfort with Managing Pregnancy IBD Patients and the Odds of Discussion of Family Planning among Physicians

CCPKnow = Crohn's and Colitis Pregnancy Knowledge score. Outcome = discussion of family planning. Exposure = CCPKnow. FP = family planning. IBD= inflammatory bowel disease. Yellow circle with arrow = exposure, blue circle with I = primary outcome, blue circle empty = outcome to exposure but exposure to primary outcome.

7.3.8 The Association between the Degree of Comfort with Managing Pregnant IBD Patients and Discussion of Family Planning among Physicians

Among physicians who reported that they feel comfortable managing pregnant IBD patients, the proportion that discusses family planning was 15.2 per 100 physicians higher than this proportion among those who reported that they feel somewhat comfortable (72/87(82.8%) comfortable v. 25/37 (67.6%) somewhat comfortable), and 45.5 per 100 physicians higher than among those who reported that they did not feel comfortable managing pregnant IBD patients (22/59 (37.3%) not comfortable; $p<0.001$).

As shown in Table 7-6, multivariable logistic regression estimated an OR adjusted for years in practice, # of pregnant IBD patients managed in the past year, and the CCPKnow score, of 2.2 (95% CI: 0.72 – 6.8) for the effect of the degree of comfort with managing pregnant IBD patients on the odds of discussion of family planning.

Table 7-6: Multivariable Logistic Regression Model for Estimating the Effect of the Degree of Comfort with Managing Pregnant IBD Patients on the Odds of Discussion of Family Planning among 183 Practicing Canadian Physicians

	OR	95% CI
Reported degree of comfort with managing pregnant IBD patients		
Not comfortable	1.0	-
Somewhat comfortable	1.8	0.66 – 4.9
Comfortable	2.2	0.72 – 6.8
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.3	0.32 – 5.4
11 to 20 years	0.83	0.26 – 2.6
> 20 years	1.2	0.39 – 3.4
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.1	1.0 – 9.4
11 or more	1.5	0.55 – 4.1
CCPKnow Score (per unit increase)	1.1	1.0 – 1.3

7.4 Discussion

Discussion of family planning with a physician was associated with higher levels of IBD-specific reproductive knowledge among patients in analyses presented in chapters 4 and 5. Almost two-thirds (62.1%) of patients reported having discussed family planning with a physician. The proportion of patients who reported having discussed family planning with a physician was similar to the proportion of physicians who reported that they discuss family planning with their female IBD patients of reproductive age.

In a recent multi-national survey assessing family planning and pregnancy issues for women with systemic inflammatory diseases, including IBD, the proportion that reported having talked about family planning and pregnancy with their female patients of reproductive age varied from 32% to 56% of the physicians surveyed in each nation[5]. In a random sample of charts reviewed for a study conducted in an academic gastroenterology practice, only 24% of female IBD patients' charts had documentation of a contraceptive method (limited to medications), and only 19% of female IBD patients' charts had documentation of reproductive counseling[3]. Gawron et al. reported that counseling was primarily driven by the patient, and in particular, by women who were already pregnant or considering pregnancy. The higher rates of discussion of family planning reported by physician respondents in the current analysis and other reported findings may be due to self-reporting bias towards the affirmative; however, the lower frequency observed in the Gawron et al. chart review study may

underestimate the frequency of physician-led discussion of family planning if physicians had not consistently recorded their discussions[3]. In the current analysis, similar proportions of patients and physicians reported having discussed family planning, suggesting that about 2/3 of patients consult physicians who discuss family planning.

Higher proportions of physicians who had more training and experience, as well as more IBD-specific reproductive knowledge, reported that they discuss family planning with their female IBD patients of reproductive age. The majority of gastroenterologists (84.5%) indicated they discuss family planning, while only 40% of general practitioners indicated that they discussed family planning. However, this study estimated a higher proportion of general practitioners who routinely discuss family planning with their female IBD patients than the 18% estimated by Toomey et al.[2].

In this study, there was a positive relationship between IBD-specific reproductive knowledge (as measured by the CCPKnow score) and physicians reporting that they discussed family planning with their female IBD patients of reproductive age. Even after adjusting for the potential confounding study variables of years in practice, type of practice, and number of pregnant IBD patients managed within the past year, the analysis estimated that increases in the CCPKnow score corresponded to increases in the odds of discussing family planning among physicians.

Increasing degrees of comfort managing pregnant IBD patients was associated with increasing proportions of physicians who discuss family planning. Feeling comfortable managing pregnant IBD patients corresponded to a 2.2-fold increase in the odds of discussing family planning, although there was imprecision in the effect estimate (95% CI: 0.72 - 6.8).

The pattern of findings suggest that training and experience contribute to knowledge and the degree of comfort with managing pregnant IBD patients, which, in turn, may affect whether a physician discusses family planning with their female IBD patients of reproductive age. However, improving IBD-specific reproductive knowledge (as measured by the CCPKnow score) among physicians may be sufficient to improve the frequency of discussion of family planning among physicians.

Therefore, targeted educational activities to improve physician IBD-specific reproductive knowledge may increase the frequency with which physicians discuss family planning with IBD patients.

Perhaps targeting general practitioners for interventions aimed at improving IBD-specific reproductive knowledge will help ensure that all physicians involved in the care of female IBD patients of reproductive age have sufficient knowledge to discuss family planning with IBD patients effectively. This is important because, previously in chapters 4 and 5, we showed that the type of physician (GI vs. non-GI) was important in the

effect of having discussed family planning with a physician on patient IBD-specific reproductive knowledge, concerns, and beliefs/opinions.

There are a few limitations to this cross-sectional study. This study aimed to ascertain information that can only be obtained by asking physicians to report their behavior, and such reporting may be inaccurate. Physicians may have over-reported their inclination to discuss family planning with their patients. However, as a similar proportion of women in the parallel patient study reported having discussed family planning with a physician, this source of agreement suggests that over-reporting my physicians may be minimal.

7.5 Conclusion

IBD-specific reproductive knowledge is associated with discussion of family planning among physicians. Therefore, educational activities aimed at improving physician IBD-specific reproductive knowledge should be further studied in order to determine whether this improves the proportion of physicians who discuss family planning with female IBD patients.

7.6 References

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8 Physician Knowledge Regarding Medication Use During Pregnancy and Breastfeeding in IBD

8.1 Introduction

Inflammatory bowel disease (IBD) requires lifelong medications. IBD is often managed using the "pyramid of treatment" approach. At the bottom level of the treatment pyramid (Figure 1-2) are the sulfasalazine and the mesalamines or 5-aminosalicylate (5-ASA) medications. Some IBD patients require stronger medications such as immunosuppressants (azathioprine, 6-mercaptopurine, and methotrexate), corticosteroids (prednisone, budesonide), and biologics (infliximab, adalimumab). Patients who continue to have active disease despite 5-ASA or immunosuppressants, or who have specific disease phenotypes (for example, fistulizing Crohn's disease) require biologics.

Each of these IBD medications is assigned an FDA (Food and Drug Administration) classification (Table 8-1) of safety for use during pregnancy and breastfeeding based on the available level of evidence from animal and human studies[1]. However, despite recent publications reporting more data supporting the continuation of certain IBD-medications during pregnancy and breastfeeding with relatively low risk of congenital malformations or adverse pregnancy and neonatal outcomes, patients and physicians continue to be concerned and unsure about the use of IBD-medications during pregnancy among women with IBD[2-4].

Table 8-1: Federal Drug Administration (FDA) Classifications of Commonly Used IBD Medications

FDA	Definition	IBD Medications
A	Controlled studies in animals and women have shown no risk in the first trimester, possible fetal harm is remote	N/A
B	Either animal studies have not demonstrated a fetal risk but no controlled studies exist in pregnant women, or animal studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester.	Adalimumab, Infliximab Mesalamine Metronidazole Sulfasalazine
C	No controlled studies in humans have been performed, and animal studies have shown adverse events, or studies in humans and animals not available; give if potential benefit outweighs the risk	Budesonide, Prednisone Ciprofloxacin Mesalamine (Asacol with DBP coating)
D	Positive evidence of human fetal risk is available, but the benefits may outweigh the risk if life-threatening or serious disease	Azathioprine/6-MP
X	Studies in animals or humans show fetal abnormalities; drug contraindicated	Methotrexate

6-MP = 6-mercaptopurine, DBP – dibutyl phthalate

IBD patients' reproductive wishes are influential to their treatment plans; Zelinkova et al. reported that a third of IBD patients who have reproduction plans require medication changes[5]. In addition, female IBD patients receive significantly less immuno-suppressants compared to male IBD patients, although they may have higher disease activity, suggesting that there is a gender-specific difference in the therapeutic management of IBD patients[6]. This gender-specific difference in management may be related to inadequate knowledge or experience regarding the use of IBD-medications during the reproductive period. For example, even among expert gastroenterologists who have published on the use of thiopurines (azathioprine) in IBD, 89% would continue azathioprine (which can be continued during pregnancy) until delivery, while 9% would never administer azathioprine during pregnancy[7].

The objectives of this analysis were to (1) characterize physicians' use of IBD medications during (a) pregnancy and (b) breastfeeding, and (2) estimate the effect of IBD-specific reproductive knowledge on the appropriate use of IBD-medications during (a) pregnancy and (b) breastfeeding.

8.2 Methods

8.2.1 Settings and Participants

Physicians were recruited from physicians referring to the IBD clinic, physicians attending various Gastroenterology and IBD conferences in Canada, and physician

members of the Canadian Association of Gastroenterology. Full details of physician recruitment were described in Chapter 2.

8.2.2 Data Sources and Variable Definitions

Physicians were asked to complete the study questionnaire, which included the CCPKnow survey and questions on socio-demographic variables, characteristics of their practice and patient population, and how they prescribe IBD medications to their female IBD patients during pregnancy and breastfeeding. Full details were presented in Chapter 2.

IBD-specific Reproductive Knowledge

IBD-specific reproductive knowledge was assessed using the CCPKnow survey (see chapter 2 for details). Raw scores were calculated by summing the number of correct responses. Physicians were categorized into having either a "poor/adequate/good" knowledge level (CCPKnow scores of 0 to 13) or a "very good" knowledge level (CCPKnow scores of 14 to 17).

Physician Use of IBD Medications during Pregnancy and Breastfeeding

To characterize physician use of IBD-medications, physicians were asked to complete questions #17 and #18 of the study questionnaire.

17) Please indicate if you would stop the medication, continue the medication, continue adjusted, or are unsure, if your patient informed you she was trying to conceive, or that she was pregnant.

18) Please indicate if you would stop the medication, continue the medication, continue adjusted, or are unsure, if your patient informed you she was breastfeeding.

For both questions 17 and 18, responses were dichotomized as shown in Table 8-2 according to whether best practice is to continue or stop the medication of interest.

Table 8-2: Dichotomization of responses to questions regarding medication continuation during pregnancy and breastfeeding

Response	Categorized	If best practice is to continue	If best practice is to stop or not use
Stop	Stop	Not continue	Stop
Continue	Continue	Continue	Not stop
Continue adjusted	Continue	Continue	Not stop
Unsure	Unsure	Not continue	Not stop

Both questions 17 and 18 asked about the following medications: sulfasalazine, mesalmine (oral and topical), prednisone (oral and topical), budesonide/entocort (oral and topical), azathioprine/6-MP, ciprofloxacin, metronidazole, methotrexate, and biologics (infliximab and adalimumab).

8.2.3 Statistical Analysis

This analysis aimed to estimate for each IBD medication, the proportion of physicians that indicated the appropriate use during pregnancy and breastfeeding across variables of interest.

The analysis also aimed to estimate the effect of IBD-specific reproductive knowledge on the odds of appropriate use of each IBD medication during pregnancy and breastfeeding by:

(1) estimating ORs for the effect of IBD-specific reproductive knowledge as measured by the CCPknow score on the odds of appropriate use of each IBD medication of interest during (a) pregnancy and (b) breastfeeding.

For continuous variables, medians and interquartile ranges (IQR) were tabulated, and medians were compared across subgroups; the statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests. For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions.

To estimate the effect of independent variables on the appropriate use of IBD-medications, multivariable logistic regression was used to obtain odds ratios and 95% CI adjusted for selected covariates. Covariates were selected based on whether they could affect both the independent variable of interest and the outcome of interest, without being affected by the independent variable. DAGs were created using DAGitty Version 2.0 (www.dagitty.net).

8.3 Results

8.3.1 Characteristics of Study Population

Characteristics of the full group of physicians have been presented in Table 3-4. As the final multivariable logistic regression models include factors related to practice characteristics, only questionnaires submitted by practicing physicians (n=183) were included for analysis in this chapter. Table 8-3 shows the characteristics of the physicians included in this analysis.

Table 8-3: Characteristics of 183 Practicing Canadian Physicians

	Total physicians (n=183)*	
	N	(%)
Gender		
Male	127	69.4
Female	56	30.6
Training status		
Gastroenterologist (GI)	97	53.0
General practitioner (GP)	75	41.0
Other	11	6.0
Years in practice		
0 to 4 years	27	14.8
5 to 10 years	26	14.2
11 to 20 years	47	25.7
>20 years	83	45.4
Population of city (n=131)*		
0 to 99,999	46	35.1
100,000 to 499,999	28	21.4
>500,000	57	43.5
Type of practice (n=180)*		
Community	127	70.6
Academic	53	29.4
Percentage of patients with IBD		
0 – 9%	91	49.7
10 – 24%	51	27.9
25 – 50%	27	14.8
51 – 100%	14	7.7
Number of IBD patients each year		
0 to 9	33	18.0
10 to 50	66	36.1
51 to 100	18	9.8
101 to 150	18	9.8
more than 150	48	26.2
Number of pregnant IBD patients managed in past year		
None	76	41.5
1 to 10	70	38.3
11 or more	37	20.2

	Total physicians (n=183)*	
	N	(%)
Self-assessed IBD knowledge		
Inadequate	16	8.7
Enough to get by	83	45.4
Very good	84	45.9
Degree of comfort managing pregnant IBD patients		
Not comfortable	59	32.2
Somewhat comfortable	37	20.2
Comfortable	87	47.5
CCPKnow level		
Poor (0 to 7)	17	9.3
Adequate (8 to 10)	18	9.8
Good (11 to 13)	38	20.8
Very good (14 to 17)	110	60.1
Dichtomized CCPKnow level		
Poor/Adequate/Good (0 to 13)	73	39.9
Very good (14 to 17)	110	60.1

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator.

8.3.2 Physicians' Knowledge of IBD Medication Use during Pregnancy and Breastfeeding

As shown in Table 8-4, the majority of physicians correctly responded to the CCPKnow questions pertaining to IBD-medication use during pregnancy and breastfeeding; 92.3% correctly responded that pregnant women with IBD should continue some medications, and 89.1% responded that tiny amounts of medication can be found in the breast milk. However fewer physicians correctly responded to the question about Infliximab/Adalimumab safety (61.7%), and to the questions regarding the use of Mesalazine (Mesalamine) (69.9%) and Azathioprine/6-MP (56.8%).

Table 8-4: Responses to Medication Related CCPKnow Questions of 183 Practicing Canadian Physicians

	Correct responses	
DRUGS	**N***	**%**
8. Pregnant women with inflammatory bowel disease … *should continue some medications*	169	92.3
9. Infliximab or Adalimumab … *are generally seen as 'probably safe' in pregnancy*	113	61.7
10. The drug Methotrexate … should always be stopped 3-6 months before trying for a baby	157	85.8
11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc) … *is safe and should be continued*	128	69.9
12. During pregnancy Azathioprine or 6-Mercaptopurine … *can be continued*	104	56.8
BREASTFEEDING		
18. Mothers suffering from inflammatory bowel disease … *may have tiny amounts of medication in their breast milk*	163	89.1

* Total N = 183

8.3.3 Identifying Covariates for the Multivariable Logistic Regression Model for Estimating the Effect of Physician CCPKnow on the Odds of Appropriate Use of Medications

Study variables that may affect both physician CCPKnow and physician use of medications during pregnancy and breastfeeding were entered into a DAG (Figure 8-1), with arrowed lines indicating the direction of the association between CCPKnow and use of the medication. Several assumptions were made and previously described in Chapter 7.

The total effect includes the estimated direct effect of knowledge on the odds of appropriately using the medication during pregnancy or breastfeeding and the estimated indirect effect of knowledge acting through an intermediate variable on the odds of appropriately using the medication during pregnancy or breastfeeding. Based on the model, the CCPKnow score did not have any indirect effects on the odds of appropriately using the medication during pregnancy or breastfeeding. Therefore the total and direct effects of the CCPKnow score on the odds of appropriately using the medication of interest during pregnancy or breastfeeding are equal in this model. The covariates identified for the multivariable logistic regression model for the effect of CCPKnow on physician use of medications were 1) # of pregnant IBD patients managed in the past year, 2) years in practice, 3) community/academic practice.

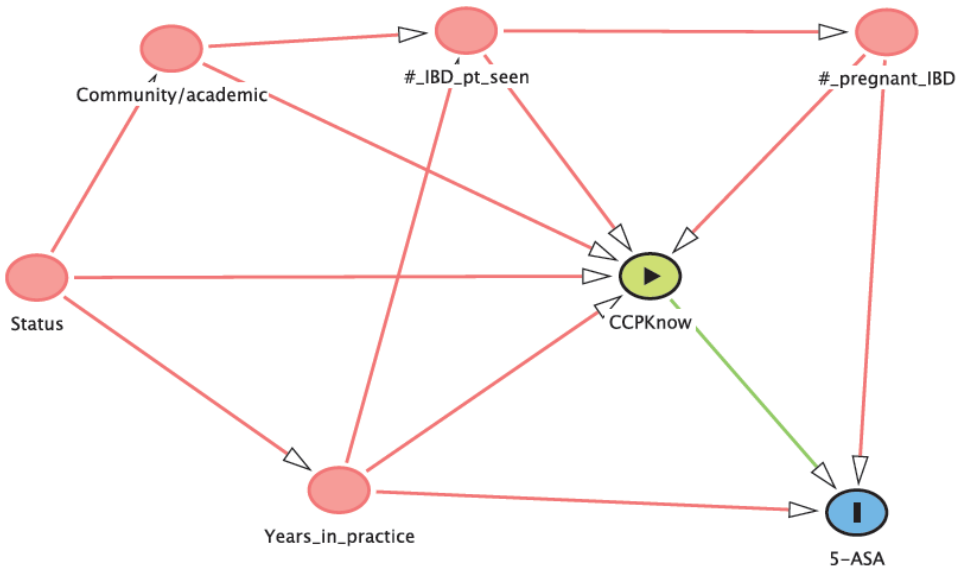

Figure 8-1: Directed Acyclic Graph for Physician CCPKnow score and Physician Use of Medication during Pregnancy and Breastfeeding

CCPKnow = Crohn's and Colitis Pregnancy Knowledge score. Outcome = Use of medication. Exposure = CCPKnow. IBD= inflammatory bowel disease. Yellow circle with arrow = exposure, blue circle with I = outcome.

8.3.4 Use of Sulfasalazine/Mesalamine Medications

As shown in Figure 8-2, although the majority of physicians indicated that they would continue sulfasalazine (SSZ) or mesalamine (MESAL) during pregnancy and breastfeeding, many physicians would stop or were unsure about the use of these medications during pregnancy or breastfeeding.

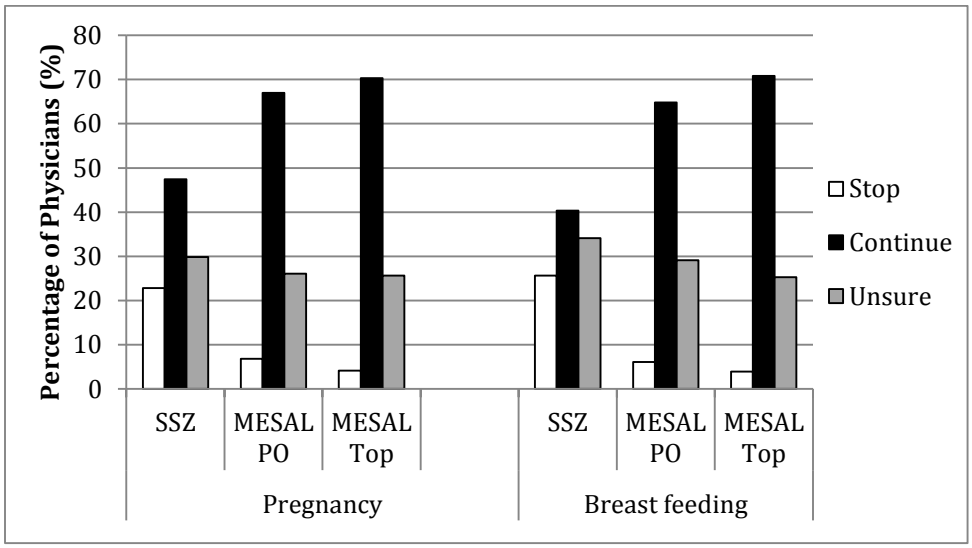

Figure 8-2: Use of Sulfasalazine/Mesalamine during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

SSZ = Sulfasalazine, MESAL = Mesalamine, PO = oral, TOP = topical. Best practice is to continue these medications if needed (Black bars)

In Figures 8-3 and 8-4, the use of sulfasalazine and mesalamine during pregnancy and breastfeeding is shown. Regarding sulfasalazine, compared to the proportion of GI physicians who would continue sulfasalazine during pregnancy, this proportion was 40.5 per 100 physicians lower among GP physicians, and 32.6 per 100 lower among physicians (60/91 (65.9%) GI physicians, 18/71 (25.4%) GP physicians, 3/9 (33.3%) Other physicians; $p<0.001$). Regarding oral mesalamine, compared to GI physicians who

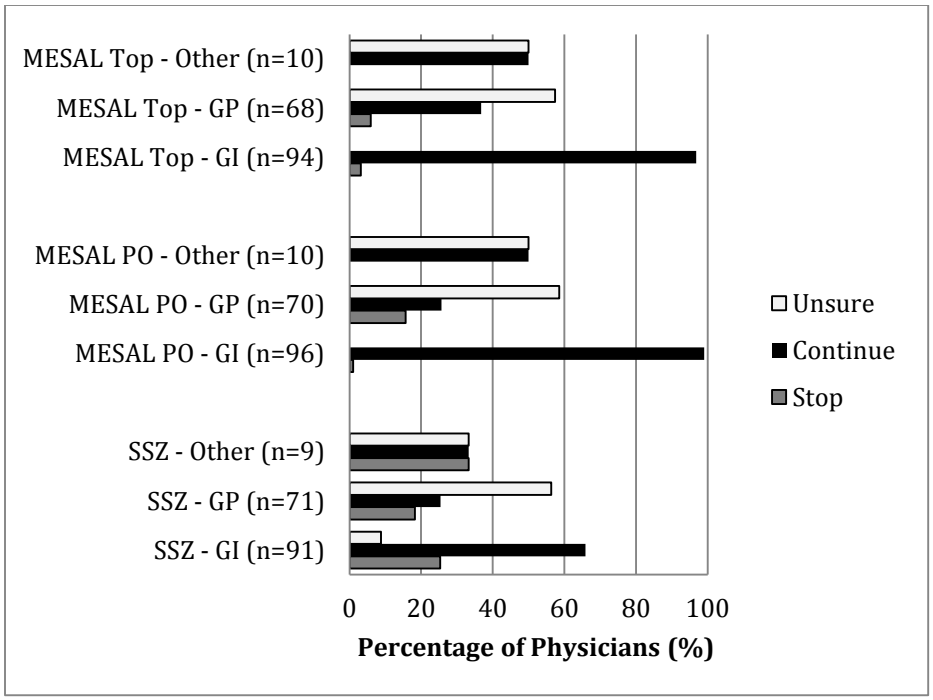

Figure 8-3: Use of Sulfasalazine/Mesalamine during Pregnancy by Training among 183 Practicing Canadian Physicians

GI = gastroenterologist, GP = general practitioner, SSZ = Sulfasalazine, MESAL = Mesalamine, PO = oral, TOP = topical. Best practice is to continue these medications if needed (Black bars)

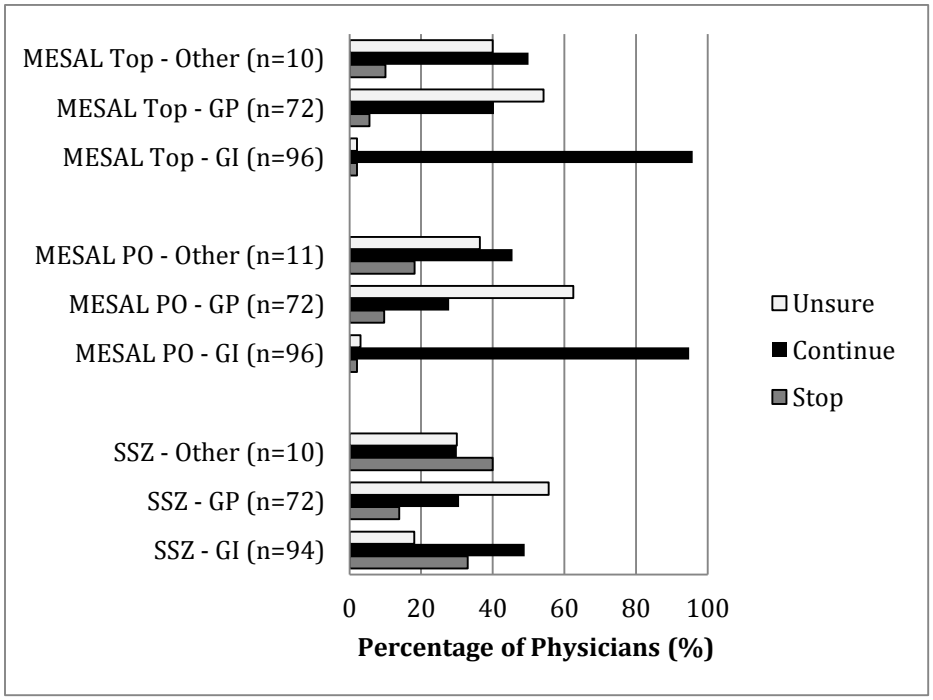

Figure 8-4: Use of Sulfasalazine/Mesalamine during Breastfeeding, by Training among 183 Practicing Canadian Physicians

GI = gastroenterologist, GP = general practitioner, SSZ = Sulfasalazine, MESAL = Mesalamine, PO = oral, TOP = topical. Best practice is to continue these medications if needed (Black bars)

would continue Mesalazine during pregnancy, this proportion was 73.3 per 100 physicians lower among GP physicians, and 49.0 per 100 physicians lower among Other physicians (95/96 (99.0%) GI physicians, 18/70 (25.7%) GP physicians, 5/10 (50.0%) Other physicians; p<0.001). Regarding topical Mesalamine, compared to GI physicians who would continue topical Mesalamine during pregnancy, this proportion was 60.0 per 100 physicians lower among GP physicians, and 46.8 per 100 physicians lower Other physicians (91/94 (96.8%) GI physicians, 25/68 (36.8%) GP physicians, 5/10 (50.0%) Other physicians; p<0.001). The proportions of GI and Other physicians that continue sulfasalazine and mesalamine during breastfeeding were similar to those who continue these medications during pregnancy. However, for GI physicians, the proportion that continues sulfasalazine during breastfeeding was 17 per 100 physicians lower than this proportion among those who continue sulfasalazine during pregnancy (46/94 (48.9%) v. 60/91 (65.9%), respectively; p=0.019).

Table 8-5 shows the effect of the CCPKnow score on appropriate use of sulfasalazine and mesalamine during pregnancy and breastfeeding. Full results of multivariable logistic regression models including the ORs for covariates are shown in Appendix C6 Table C6-0-1. Table 8-5 shows that for sulfasalazine and mesalamine, each unit increase in the CCPKnow score corresponded to an increase in the odds of correctly continuing the medication, with increases ranging from a 20% increase in odds for sulfasalazine in breastfeeding, to almost double the odds for mesalamine PO in pregnancy.

Table 8-5: Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Sulfasalazine/Mesalamine during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Sulfasalazine, pregnancy (continue vs. stop)	1.3	1.1 – 1.5
Mesalamine PO, pregnancy (continue vs. stop)	1.9	1.5 – 2.5
Mesalamine Top, pregnancy (continue vs. stop)	1.3	1.2 – 1.5
Sulfasalazine, breast feeding (continue vs. stop)	1.2	1.1 – 1.4
Mesalamine PO, breast feeding (continue vs. stop)	1.5	1.2 – 1.7
Mesalamine Top, breast feeding (continue vs. stop)	1.3	1.2 – 1.5

Reference response is Stop (not best practice): OR = 1.0

8.3.5 Use of Corticosteroids (Prednisone, Budesonide)

As shown in Figure 8-5, most physicians continue corticosteroids during pregnancy and breastfeeding. The proportion of physicians who continue topical prednisone during pregnancy was 10.8 per 100 physicians higher than the proportion who continue oral prednisone during pregnancy (141/179 (78.8%) v. 119/175 (68.0%), respectively; p=0.022). The proportion of physicians who continue topical budesonide was 13.4 per 100 physicians higher than the proportion who continue oral budesonide during pregnancy (129/172 (75.0%) v. 106/172 (61.6%), respectively; p=0.008). Similarly, the proportion of physicians who continue topical prednisone during breastfeeding was 10.9 per 100 physicians higher than the proportion who continue oral prednisone during breastfeeding (149/177 (84.2%) v. 132/180 (73.3%), respectively; p=0.012). The proportion of physicians who continue topical budesonide was 10 per 100 physicians more than the proportion who continue oral budesonide (138/173 (79.8%) v. 121/173 (69.9%), respectively; p=0.035).

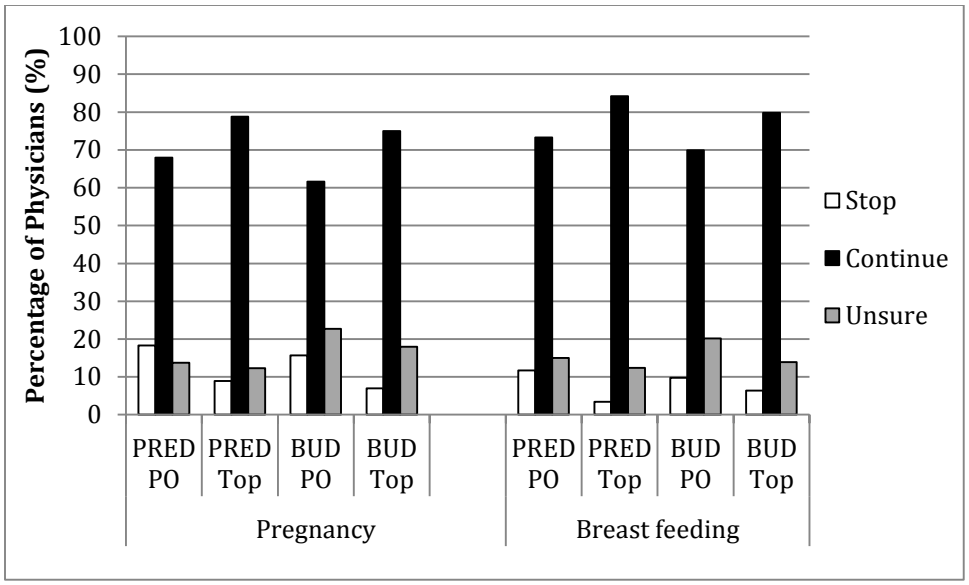

Figure 8-5: Use of Corticosteroids during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

PRED = Prednisone, BUD = budesonide, PO: oral, TOP: topical. Best practice is to continue these medications if needed (Black bars)

Figure 8-6 shows the distribution of responses for the use of corticosteroids during pregnancy by physician training. Regarding oral prednisone, compared to the proportion of GI physicians who continue oral prednisone during pregnancy, this proportion was 41.8 per 100 physicians lower among GP physicians, and 12.6 per 100 physicians lower among Other physicians (81/95 (85.3%) GI physicians, 30/69 (43.5%) GP physicians, 8/11 (72.7%) Other physicians; $p<0.001$). Regarding topical prednisone, compared to the proportion of GI physicians who continue topical prednisone during pregnancy, this proportion was 21.8 per 100 physicians lower among GP physicians, and 15.8 per 100 physicians lower among Other physicians (85/96 (88.5%) GI physicians, 48/72 (66.7%) GP physicians, 8/11 (72.7%) Other physicians; $p<0.001$). The distribution of responses was similar for the use of oral and topical budesonide during pregnancy.

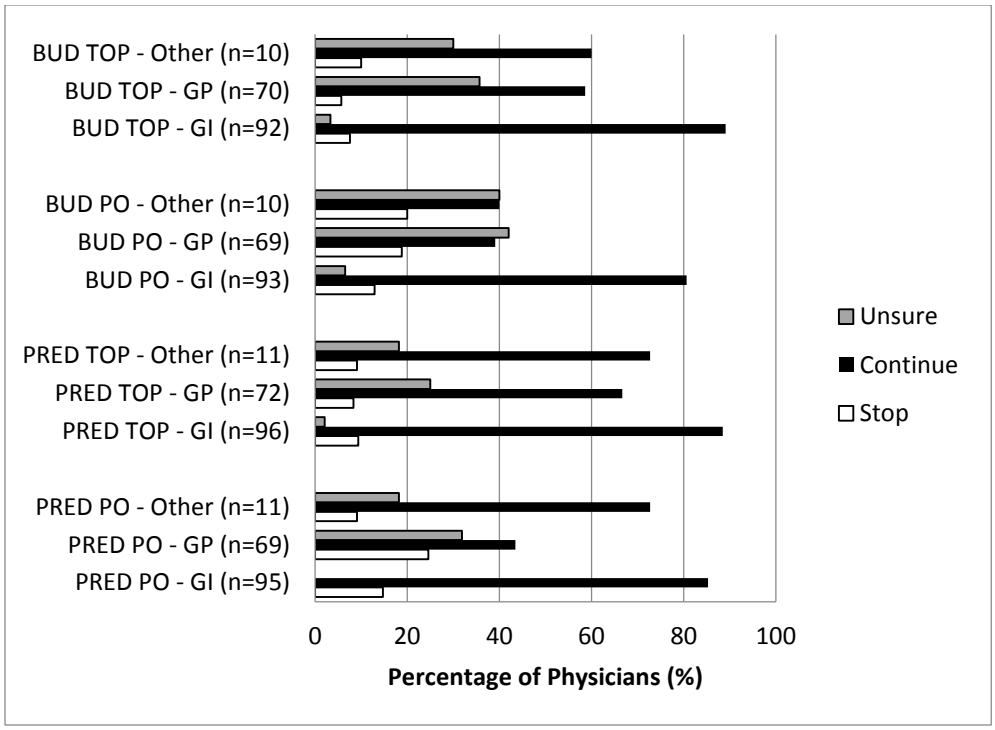

Figure 8-6: Use of Corticosteroids during Pregnancy by Training Status among 183 Practicing Canadian Physicians

GP = general practitioner, GI = gastroenterologist, PRED = Prednisone, BUD = budesonide, PO = oral, TOP = topical. Best practice is to continue these medications if needed (Black bars).

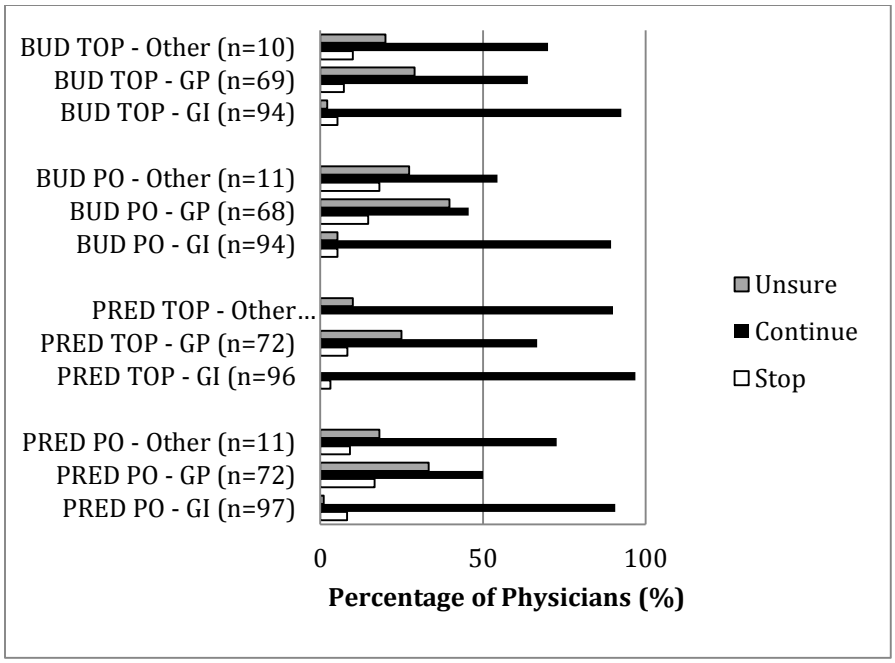

Figure 8-7: Use of Corticosteroids during Breastfeeding by Training Status among 183 Practicing Canadian Physicians

GP = general practitioner, GI = gastroenterologist, PRED = Prednisone, BUD = budesonide, PO = oral, TOP = topical. Best practice is to continue these medications if needed (Black bars).

Figure 8-7 shows the distribution of responses for the use of corticosteroids during breastfeeding by physician training. Across training categories, similar proportions continue prednisone and budesonide PO and Top during breastfeeding, and during pregnancy.

Table 8-6 shows the effect of CCPKnow on the odds of physicians indicating the appropriate use of corticosteroids during pregnancy and breastfeeding. Full results from multivariable logistic regression models including ORs for covariates are shown in Appendix C6 Table C6-0-2. Table 8-6 shows that each unit increase in the CCPKnow score corresponded to a 10% to 30% increase in the odds of physicians indicating the appropriate continuation of corticosteroids during pregnancy and breastfeeding.

Table 8-6: Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Corticosteroids during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Prednisone PO, pregnancy (continue vs. stop)	1.1	0.97 – 1.2
Prednisone Top, pregnancy (continue vs. stop)	1.2	1.1 – 1.3
Budesonide PO, pregnancy (continue vs. stop)	1.3	1.1 – 1.5
Budesonide Top, pregnancy (continue vs. stop)	1.2	1.1 – 1.4
Prednisone PO, breastfeeding (continue vs. stop)	1.1	0.98 – 1.2
Prednisone Top, breastfeeding (continue vs. stop)	1.3	1.1 – 1.4
Budesonide PO, breastfeeding (continue vs. stop)	1.3	1.1 – 1.5
Budesonide Top, breastfeeding (continue vs. stop)	1.3	1.1 – 1.5

Reference response is Stop (not best practice): OR = 1.0

8.3.6 Use of Antibiotics (Ciprofloxacin, Metronidazole)

As shown in Figure 8-8, the majority of physicians stop Ciprofloxacin (CIPRO) during pregnancy (127/176 (72.2%)), but only half stop Ciprofloxacin during breastfeeding (88/178 (49.4%)). Just over half of physicians stop Metronidazole (METRO) during pregnancy (96/175 (54.9%)); 41.5% (73/176) stop Metronidazole during breastfeeding.

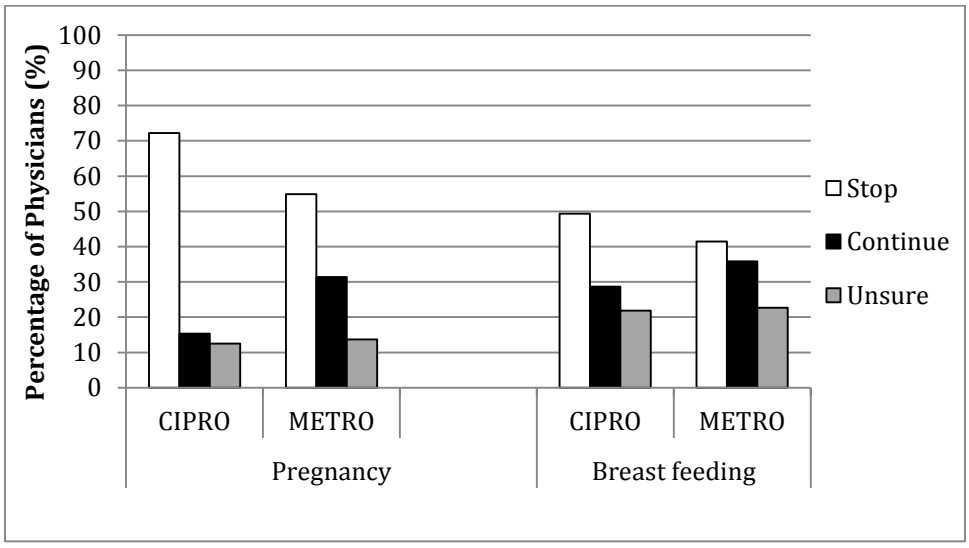

Figure 8-8: Use of Antibiotics during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

CIPRO = ciprofloxacin, METRO = metronidazole. Best practice is to stop ciprofloxacin (white), and metronidazole (white) although they may be used if absolutely needed (black).

Figure 8-9 shows the distribution of responses for the use of ciprofloxacin and metronidazole during pregnancy by training status. Regarding antibiotic use, compared to the proportion of GI physicians who continue ciprofloxacin during pregnancy, this proportion was 15.1 per 100 physicians lower among GP physicians, and 12.1 per 100 lower among Other physicians (5/71 (7.0%) GI physicians, 21/95 (22.1%) GP physicians, 1/10 (10.0%) Other physicians; p=0.016). Regarding metronidazole, compared to the proportion of GI physicians who continue metronidazole during pregnancy, this proportion was 17.2 per 100 physicians higher among GP physicians and 24.6 per 100 more GP physicians than Other physicians indicated they were unsure about the use of metronidazole during pregnancy (7/95 (7.4%) GI physicians, 17/69 (24.6%) GP physicians, 0/11 (0.0%) Other physicians; p=0.003).

Figure 8-10 shows the distribution of responses to the use of ciprofloxacin and metronidazole during breastfeeding by training status. The distribution of responses for the use of ciprofloxacin during breastfeeding was similar among GI physicians, GP physicians, and Other physicians (p=0.13). However, compared to the proportion of GI who stop metronidazole during breastfeeding, this proportion was 20.4 per 100 physicians lower among GP physicians and 24.8 per 100 physicians higher among Other physicians (46/96 (47.9%) GI physicians, 19/69 (27.5%) GP physicians, 8/11 (72.7%) Other physicians; p=0.014).

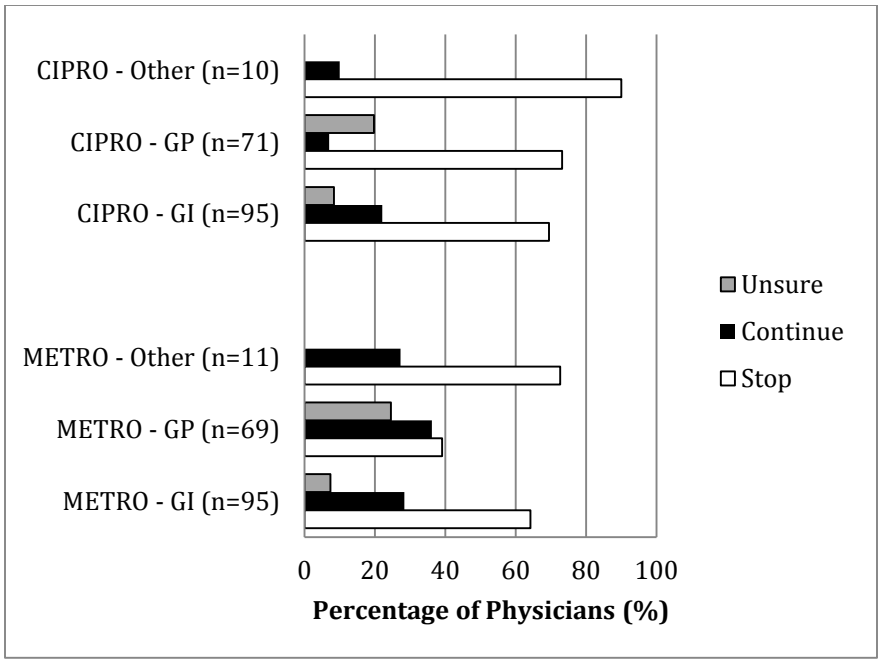

Figure 8-9: Use of Antibiotics during Pregnancy by Training Status among 183 Practicing Canadian Physicians

GI = gastroenterologist, GP = general practitioner, CIPRO = ciprofloxacin, METRO = metronidazole. Best practice is to stop (white), although they may be used if needed (black).

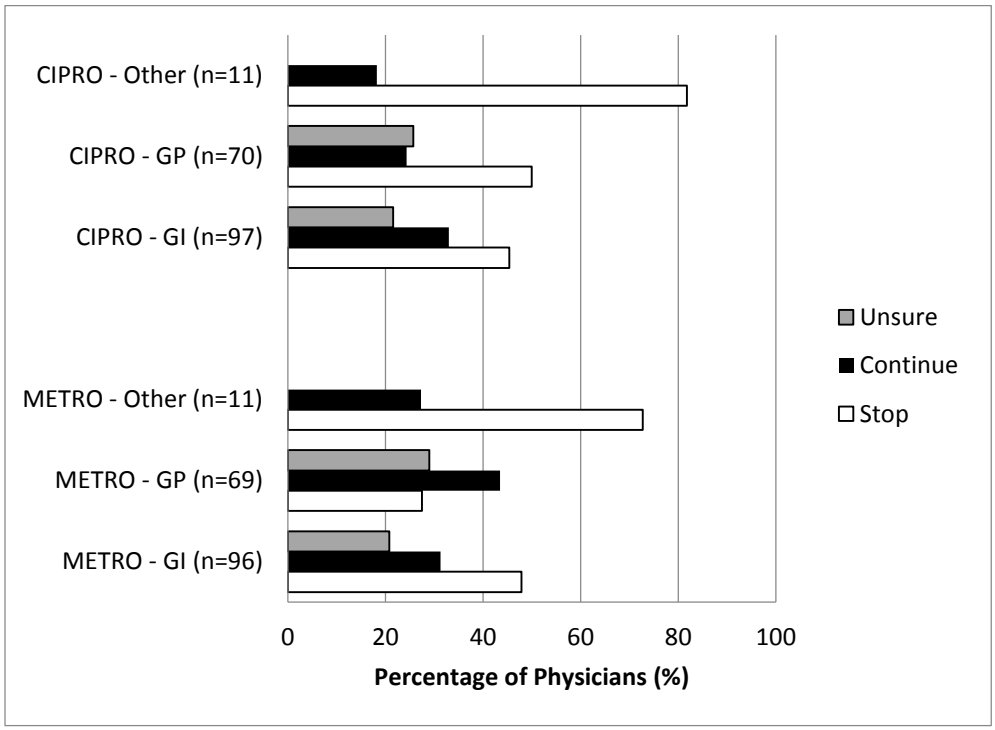

Figure 8-10: Use of Antibiotics during Breastfeeding by Training Status among 183 Practicing Canadian Physicians

GI = gastroenterologist, GP = general practitioner, CIPRO = ciprofloxacin, METRO = metronidazole. Best practice is to stop (white) although they may be used if needed (white).

Table 8-7 shows the effect of CCPKnow on appropriate use of these antibiotics during pregnancy and breastfeeding. Full multivariable logistic regression models with OR for covariates are shown in Appendix C6 Table C6-0-3. Table 8-7 shows that an increase in the CCPKnow score did not correspond to notable increases in the odds of physicians indicating appropriate use of these antibiotics during pregnancy and breastfeeding, except that each one point increase in the CCPKnow score corresponded to a 20% increase in the odds of stopping ciprofloxacin during pregnancy and breastfeeding.

Table 8-7: Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Antibiotics during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Ciprofloxacin, pregnancy (stop v. continue)	1.2	1.1 – 1.3
Metronidazole, pregnancy (continue v. stop)	1.1	0.94 – 1.2
Ciprofloxacin, breast feeding (stop v. continue)	0.96	0.85 – 1.1
Metronidazole, breast feeding (continue v. stop)	1.1	0.95 – 1.2

Reference response for ciprofloxacin is not stop (not best practice): OR = 1.0
Reference response for metronidazole is stop (not best practice): OR = 1.0

8.3.7 Use of Immunosuppressants (Azathioprine/6-mercaptopurine/ Methotrexate)

As shown in Figure 8-11, just over a quarter of physicians would stop Azathioprine (AZA)/6-mercaptopurine (6-MP) during pregnancy (46/175 (26.3%)) and breastfeeding (47/176 (26.7%)). Almost all (159/177 (89.8%)) of physicians would stop Methotrexate (MTX) during pregnancy and approximately 70% (122/176 (69.3%)) of physicians would stop MTX during breastfeeding.

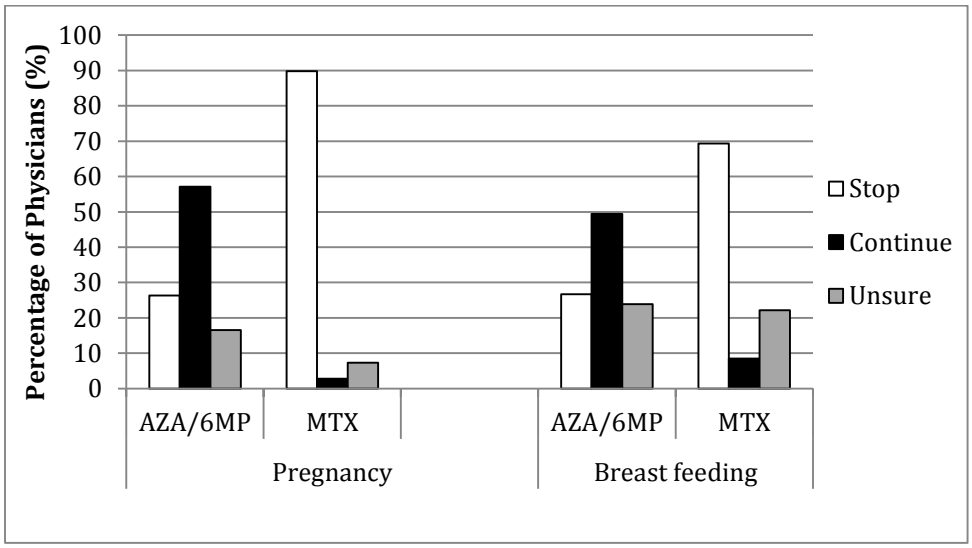

Figure 8-11: Use of Immunosuppressants during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

AZA = Azathioprine; 6-MP = 6-mercaptopurine; MTX = Methotrexate. Best practice is to continue AZA/6MP (black bars) and to stop MTX (white bars).

Figure 8-12 shows the distribution of response to use of immunosuppressants during pregnancy by training status. Regarding AZA/6MP, compared to the proportion of GI physicians who continue AZA/6MP during pregnancy, this proportion was 73.7 per 100 lower among GP physicians, and 43.9 per 100 lower among Other physicians (84/94 (89.4%) GI physicians, 11/70 (15.7%) GP physicians, 5/11 (45.5%) Other physicians; $p<0.001$). Regarding MTX, compared to the proportion of GI physicians who stop MTX during pregnancy, this proportion was 9.5 per 100 physicians lower among GP physicians, and 2.9 per 100 physicians lower among Other physicians (90/96 (93.8%) GI physicians, 59/70 (84.3%) GP physicians, 10/11 (90.9%) Other physicians; $p=0.039$).

Figure 8-13 shows the distribution of responses to the use of AZA/6MP and MTX during breastfeeding by training status. Regarding AZA/6MP, compared to the proportion of GI physicians who continue AZA/6MP during breastfeeding, this proportion was 71.4 per 100 physicians lower among GP physicians, and 34.5 per 100 physicians lower among Other physicians (76/95 (80.0%) GI physicians, 6/70 (8.6%) GP physicians, 5/11 (45.5%) Other physicians; $p<0.001$). Regarding MTX, compared to the proportion of GI physicians who stop MTX during breastfeeding, this proportion was 8.7 per 100 physicians lower among GP physicians, and 19.3 per 100 physicians lower Other physicians (68/95 (71.6%) GI physicians, 44/70 (62.9%) GP physician, 10/11 (90.9%) Other physicians; $p=0.004$).

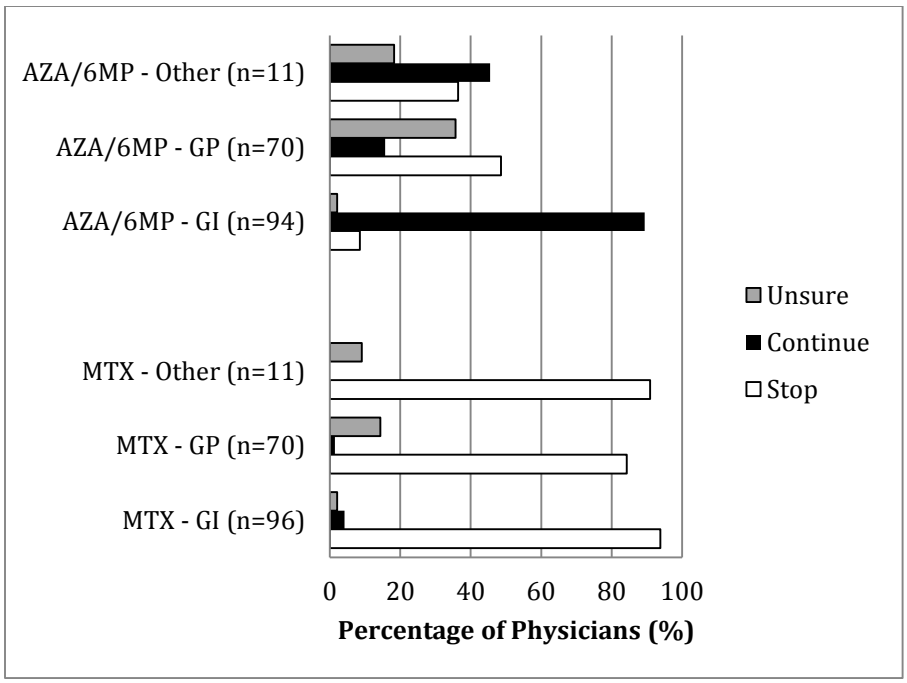

Figure 8-12: Use of Immunosuppressants during Pregnancy by Training Status among 183 Practicing Canadian Physicians

GP = general practitioner, GI = gastroenterologist, AZA = Azathioprine; 6-MP = 6-mercaptopurine; MTX = Methotrexate. Best practice is to continue AZA/6MP (black) and stop MTX (white).

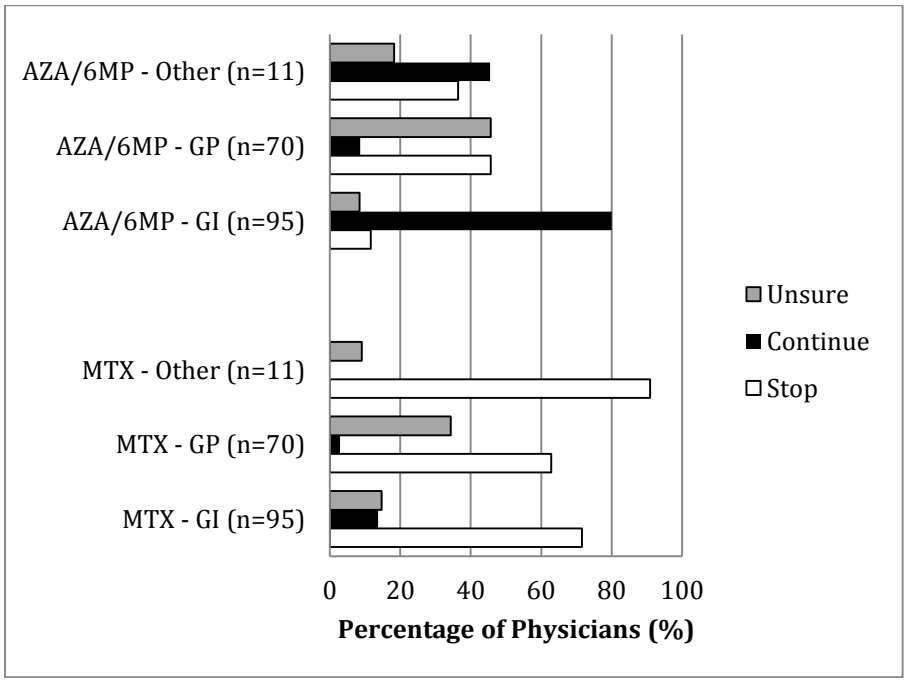

Figure 8-13: Use of Immunosuppressants during Breastfeeding by Training Status among 183 Practicing Canadian Physicians

GP = general practitioner, GI = gastroenterologist, AZA = Azathioprine; 6-MP = 6-mercaptopurine; MTX = Methotrexate. Best practice is to continue AZA/6MP (black) and to stop MTX (white).

Table 8-8 shows the effect of CCPKnow on appropriate use of immunosuppressant medications during pregnancy and breastfeeding. Full multivariable logistic regression models with OR for covariates are shown in Appendix C6 Table C6-0-4. Table 8-8 shows that each unit increase in the CCPKnow score corresponded to a substantial increase in the odds of physicians appropriately continuing AZA/6MP during pregnancy and breast feeding, and to a smaller increase in the odds of appropriately stopping MTX during pregnancy and breast feeding.

Table 8-8: Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Immunosuppressants during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
AZA/6MP, pregnancy (continue v. stop)	1.6	1.3 – 2.0
MTX, pregnancy (stop v. continue)	1.2	1.1 – 1.4
AZA/6MP, breastfeeding (continue v. stop)	1.4	1.2 – 1.7
MTX, breastfeeding (stop v. continue)	1.1	1.0 – 1.3

AZA = azathioprine, 6-MP = 6-mercaptopurine, MTX = methotrexate
Reference response for AZA/6MP is stop (not best practice): OR = 1.0
Reference response for MTX is not stop (not best practice): OR = 1.0

8.3.8 Use of Biologics (Infliximab, Adalimumab)

As shown in Figure 8-14, just over half of physicians continue infliximab (IFX) (99/178 (55.6%)) and adalimumab (ADA) (96/177 (54.2%)) during pregnancy, with similar proportions of physicians continuing infliximab (92/176 (52.3%)) and adalimumab (89/176 (50.6%)) during breastfeeding.

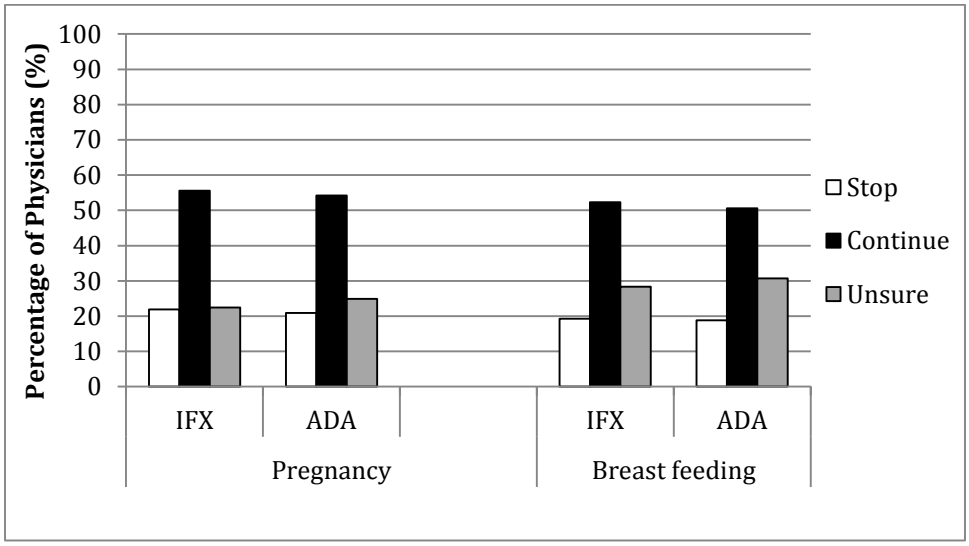

Figure 8-14: Use of Biologics during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians.
IFX = Infliximab, ADA = Adalimumab. Best practice is to continue IFX and ADA during pregnancy and breastfeeding if needed (black bars).

Figure 8-15 shows the distribution of use of infliximab and adalimumab during pregnancy by training status. Regarding infliximab, compared to the proportion of gastroenterologists who continue infliximab during pregnancy, this proportion was 79.3 per 100 physicians lower among GP physicians, and 54.2 per 100 physicians lower among Other physicians (87/96 (90.6%) GI physicians, 8/71 (11.3%) GP physicians, 4/11 (36.4%) Other physicians; p<0.001). Regarding adalimumab, compared to the proportion of GI physicians who continue adalimumab during pregnancy, this proportion was 77.1 per 100 physicians lower among GP physicians, and 52.0 per 100 lower among Other physicians (84/95 (88.4%) GI physicians, 8/71 (11.3%) GP physicians, 4/11 (36.4%) Other physicians; p<0.001).

Figure 8-16 shows the distribution of use of infliximab and adalimumab during breastfeeding by training status. Regarding infliximab, compared to the proportion of GI physicians who continue infliximab during breastfeeding, this proportion was 80.3 per 100 physicians lower among GP physicians, and 51.0 per 100 physicians lower among Other physicians (83/95 (87.4%) GI physicians, 5/70 (7.1%) GP physicians, 4/11 (36.4%) Other physicians; p<0.001). Regarding adalimumab, compared to the proportion of GI physicians who continue adalimumab during breastfeeding this proportion was 71.1 per 100 physicians lower among GP physicians, and 47.8 per 100 physicins lower among Other physicians (80/95 (84.2%) GI physicians, 5/70 (7.1%) GP physicians, 4/11 (36.4%) Other physicians; p<0.001).

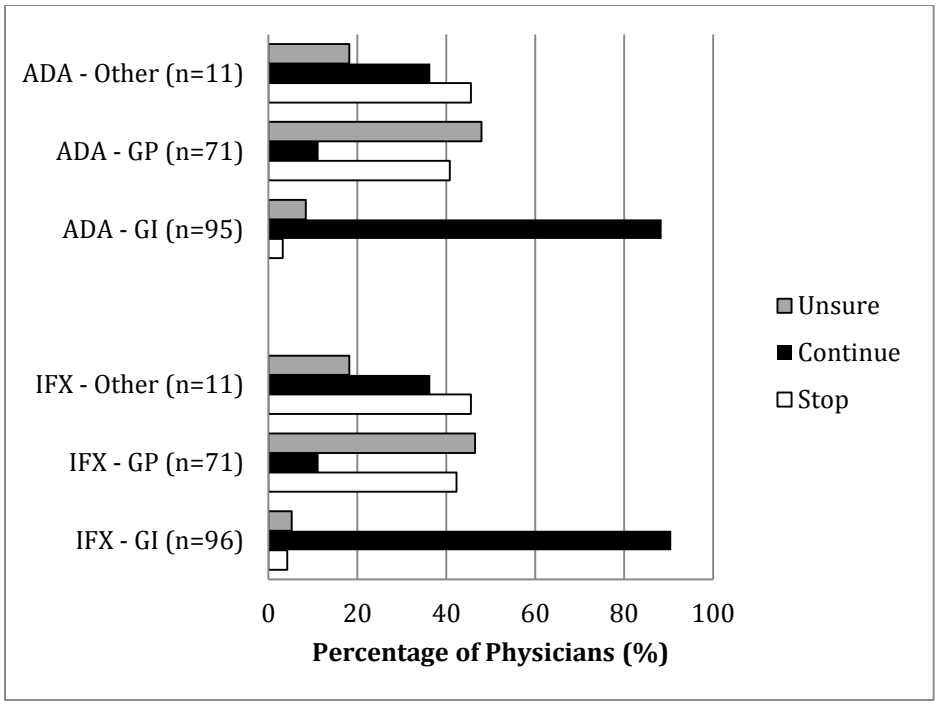

Figure 8-15: Use of Biologics during Pregnancy by Training Status among 183 Practicing Canadian Physicians

GP = general practitioner, GI = gastroenterologist, IFX = Infliximab, ADA = Adalimumab. Best practice is to continue IFX and ADA during pregnancy and breastfeeding if needed (black bars).

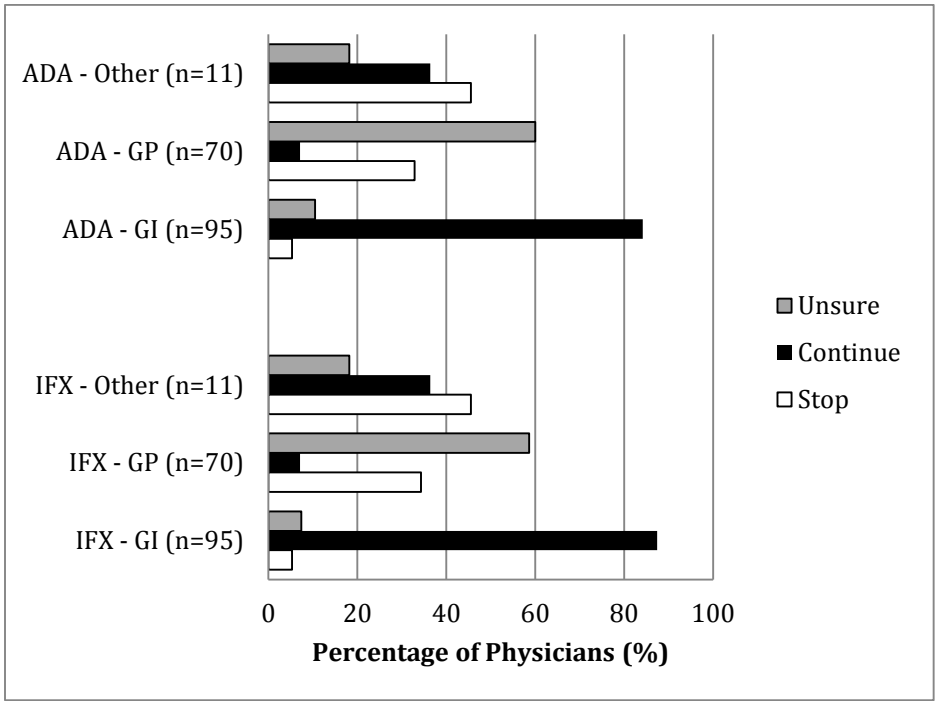

Figure 8-16: Use of Biologics during Breastfeeding by Training Status among 183 Practicing Canadian Physicians

GP = general practitioner, GI = gastroenterologist, IFX = Infliximab, ADA = Adalimumab. Best practice is to continue IFX and ADA during pregnancy and breastfeeding if needed (black bars).

Table 8-9 shows the effect of CCPKnow score on appropriate use of immunosuppressant medications during pregnancy and breastfeeding. Full multivariable logistic regression models with OR for covariates are shown in Appendix C6 Table C6-0-5. Table 8-9 shows that each unit increase in CCPKnow score corresponded to substantial increases in the odds of physicians continuing IFX and ADA during pregnancy and breastfeeding.

Table 8-9: Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Biologics during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
IFX, pregnancy (continue v. stop)	1.7	1.3 – 2.1
ADA, pregnancy (continue v. stop)	1.6	1.3 – 2.0
IFX, breastfeeding (continue v. stop)	1.8	1.4 – 2.3
ADA, breastfeeding (continue v. stop)	1.7	1.4 – 2.2

IFX = infliximab, ADA = adalimumab
Reference response for both is stop (not best practice): OR = 1.0

8.4 Discussion

Management of chronic disorders such as Inflammatory Bowel Disease (IBD) in pregnancy and breastfeeding can be challenging because of concerns of the effects of the medications on pregnancy and neonatal outcomes. There are guidelines and there are "safety classifications", however, as many of the medications used to treat IBD are relatively new in terms of the evidence regarding the interaction with the pregnancy and neonatal outcomes, physicians are often still unclear and uncomfortable using these medications.

Recently, over the last several years, more studies have been published supporting the relative safety of IBD medications during pregnancy and breastfeeding. However, results of this cross-sectional survey show that there is still significant variation in physician practice patterns regarding the use of IBD-medications in women who are considering pregnancy or are pregnant, or who are breastfeeding.

Most of the survey respondents (92.3%) correctly understood that pregnant women with IBD should continue some medications. This is the most important concept that physicians must understand, in order to accept that they can continue to use IBD-medications in their pregnant IBD patients. Most publications report that active IBD at the time of conception and during pregnancy increases the risk of adverse pregnancy outcomes, such as spontaneous abortion[8-10], and preterm delivery[11]. In addition, active

disease at the time of conception is associated with increased risk of having active disease during pregnancy[12]. Therefore, medication adherence in order to maintain remission is important during the pre-conception and reproductive period.

Aminosalicylates (Mesalazine/Mesalamine)/Sulfasalazine

Only two-thirds (69.9%) of physicians correctly responded to the CCPKnow question that during pregnancy Mesalamine medications (e.g. Asacol, Mesavant, Pentasa, Salofalk etc.) are safe and should be continued. Gastroenterologists were more likely to continue Sulfasalazine and Mesalamine medications during pregnancy and breastfeeding, while general practitioners were more likely to be unsure of the usage of these medications. Overall, studies estimate no increased risk of poor pregnancy outcomes, or adverse neonatal outcomes[13-19] among women with IBD treated with 5-ASA medications. Both sulfasalazine and mesalamine medications can be continued during pregnancy and breastfeeding. Patients who are maintained on these medications typically have milder disease and may tend to follow up regularly with their general practitioner. Therefore, it is important for general practitioners to understand and be comfortable with the continued usage of these medications during pregnancy and breastfeeding.

Corticosteroids

In this study, more physicians continue topical corticosteroids than oral corticosteroids, likely because of assumed lower systemic absorption and thus lower exposure of the

neonate. More gastroenterologists than general practitioners or other physicians continue corticosteroids during pregnancy and breastfeeding. Corticosteroids are used to treat severe flares of IBD, and can be used during pregnancy and breastfeeding if required. Avoidance in the first trimester of pregnancy is recommended to decrease the potential risk of cleft palate, and as the highest levels appear in the breast milk in the first 4 hours after consumption, it is recommended to "pump and dump" the first 4 hours of breast milk after taking steroid medication[1, 20, 21]. Although decisions should be made on a case-by case basis, corticosteroids can be used to treat IBD flares during pregnancy and breastfeeding, and physicians, especially general practitioners, should be educated regarding this option, in case their female patients with IBD are flaring during pregnancy and require corticosteroids.

Antibiotics: Metronidazole and ciprofloxacin

The majority of physician respondents stop ciprofloxacin (72.2%) and metronidazole (54.9%) during pregnancy in IBD, but fewer stop ciprofloxacin (49.4%) and metronidazole (41.5%) during breastfeeding. More gastroenterologists than general practitioners or other physicians continue ciprofloxacin during pregnancy even though it is recommended to avoid ciprofloxacin during pregnancy. For metronidazole, most gastroenterologists and other physicians stop during breastfeeding, but general practitioners were divided with some continuing, some stopping, and some unsure.

Metronidazole (FDA Class B) and Ciprofloxacin (FDA Class C) are commonly used to treat abscesses and fistulae in IBD. Animal studies showed carcinogenic effects from Metronidazole, and early studies suggested a risk of cleft lip[21], but this has not been reported in humans[22]. If required, metronidazole can be used during pregnancy[21, 22]. Since metronidazole is excreted in breast milk, and prolonged exposure to metronidazole is associated with potential toxicity, it is not recommended during breastfeeding; although if required it can be used and it has been suggested to wait 12 to 24 hours after receiving a dose of metronidazole before breastfeeding[21]. Previously, there was concern that quinolones increase the risk of arthropathies in the offspring; although studies have reported no significant increase in major congenital anomalies, including musculoskeletal problems from the use of ciprofloxacin[23, 24], because of the known possible effect of ciprofloxacin on bone and cartilage, it has been recommended to avoid this medication during pregnancy[21]. Ciprofloxacin is also detectable in the breast milk in small amounts[25], but short term treatment can be used if indicated[21]. Therefore, these antibiotics can be used during pregnancy and breastfeeding if absolutely required, although best practice is to avoid ciprofloxacin, which may explain the variation in physician responses. Better knowledge regarding the recommended use of these medications during pregnancy and breastfeeding is required.

Immunosuppressants: Azathioprine, 6-mercaptopurine, Methotrexate

Only 57.7% of physicians surveyed correctly responded that “during pregnancy Azathioprine or 6-Mercaptopurine can be continued”, and 26.3% of physicians would

stop AZA/6MP during pregnancy. There was a clear difference in the use of these drugs among physician groups; 89.4% of gastroenterologists continue Azathioprine/6-MP during pregnancy compared to only 15.7% of general practitioners. Almost half of the general practitioners indicated they would stop AZA/6-MP during pregnancy and breastfeeding. Although thiopurines are classified as FDA class D drugs because of teratogenicity in earlier animal studies, most studies report that the use of AZA/6-MP during pregnancy in women with IBD is not associated with significant increased risk of preterm birth, low birth weight, neonatal adverse outcomes, or congenital abnormalities[17, 26-31]. Expert opinion is to continue thiopurine use during pregnancy and breast feeding to maintain remission of disease[1, 20, 21, 32].

Peyrin-Biroulet et al. recently conducted an international survey and reported that 89% of the surveyed gastroenterologists continue azathioprine until delivery and 9% never use azathioprine during pregnancy[7]. Thus, it is important to educate physicians, in particular, general practitioners, about the relative safety of continuing AZA/6-MP during pregnancy and breastfeeding in IBD.

The majority of physicians surveyed correctly indicated that they stop Methotrexate if their patient was considering pregnancy or was pregnant. However, there was still a concerning proportion (10.1%) of physicians who continue or were unsure about the use of Methotrexate during pregnancy. There was an even larger (30.7%) proportion that continue or were unsure about the use of Methotrexate during breastfeeding. Even

some gastroenterologists continue or were unsure about using Methotrexate during pregnancy (6.2%) and breastfeeding (28.4%).

Methotrexate is a commonly used immunosuppressant for the treatment of IBD, mainly for Crohn's disease. However, it is a known teratogen, causing congenital malformations, and is an abortifacient; therefore it is contraindicated during conception and pregnancy. Patients should discontinue methotrexate for at least 3 to 6 months prior to attempting to conceive[1, 20, 21]. Methotrexate crosses into the breast milk[33] and because of its teratogenicity, it is contraindicated during breast feeding[34, 35]. Despite multiple guidelines and reviews advising against the use of Methotrexate during pregnancy and breastfeeding, there is an important knowledge deficit regarding the use of this teratogenic medication in pregnancy and breastfeeding in IBD. However, this may also be a result of the study design (i.e. physicians in a hurry may have accidently selected the wrong response).

Biologics: Infliximab and Adalimumab

There was a clear lack of knowledge regarding the use of infliximab and adalimumab among physicians. Only half of physicians continue infliximab and adalimumab during pregnancy and breastfeeding, the majority being gastroenterologists. General practitioners indicated they would stop or were unsure about the use of these biologics during pregnancy and breast feeding, with approximately a third stopping them during pregnancy and breast feeding.

Anti-tumour necrosis factor inhibitors are commonly used to treat moderate to severe IBD, and fistulizing Crohn's disease. Initially infliximab and adalimumab use was reported in a few cases of pregnant women with IBD which did not show any adverse effects[36-43]. Larger observational studies, registry studies, and systematic reviews have shown its safety for use during pregnancy[44-48]. It is recommended to stop infliximab and adalimumab at the onset of the third trimester to decrease the amount of placental transport[49, 50]. However, in high risk patients, or patients with active disease, these biologics should be continued throughout the pregnancy. Studies have shown nil to minimal levels of infliximab and adalimumab in the breast milk and no significant adverse events have been reported in the infant[25, 40, 51-55]. It is thought that any detectable levels in the neonate after delivery may be due to placental transfer during pregnancy[54]. Therefore, if a patient requires these medications, the risk of having a severe flare increases with discontinuation, and this could cause harm to the pregnancy and neonate. Thus, there is a need to improve physician knowledge regarding the use of biologics in the treatment of IBD during pregnancy and breastfeeding.

Effect of IBD-specific reproductive knowledge on physician use of IBD-medications

Higher IBD-specific reproductive knowledge as measured by the CCPKnow survey was associated with appropriate physician use of IBD-medications. Even for the use of 5-ASA and sulfasalazine medications, for each increase in CCPKnow score, the odds of continuing these drugs during pregnancy and breastfeeding increased. Similarly a

higher CCPKnow score was associated with increased odds of physicians continuing corticosteroids during pregnancy and breastfeeding.

However, increasing CCPPKnow score was not associated with increased odds of physician appropriate use of antibiotics, likely because ciprofloxacin and metronidazole, although recommended to avoid use during pregnancy, can still be used if required. Therefore, although the analysis for this study used best practice as stopping ciprofloxacin during pregnancy and breastfeeding, and continuing metronidazole during pregnancy and breastfeeding, theoretically continuing both medications if needed is not contraindicated.

Higher IBD-specific reproductive knowledge was associated with increased odds of physicians continuing AZA/6MP during pregnancy and breastfeeding, and of physicians stopping MTX during pregnancy and breastfeeding. The effect of increasing IBD-specific reproductive knowledge was greatest on the odds of physician use of infliximab and adalimumab during pregnancy and breastfeeding; for each incremental point increase in CCPKnow score, physicians were 60 to 80% more likely to continue infliximab and adalimumab during pregnancy and breastfeeding.

Knowledge of IBD-specific reproductive issues includes knowing that women with IBD who require medications for maintenance of remission should continue certain IBD-

medications. This study shows a clear association between increased IBD-specific reproductive knowledge and appropriate physician use of IBD-medications.

Conclusion

Physicians have variable knowledge regarding the use of IBD-medications during pregnancy and breastfeeding among women with IBD. Physicians with subspecialty training (gastroenterologists), and those with higher IBD-specific reproductive knowledge are more likely to appropriately use IBD-medications. This knowledge deficit regarding medications used to treat IBD should be addressed with targeted educational activities, specifically for non-sub specialty physicians (general practitioners). Further studies addressing other health care professional knowledge, including obstetricians, maternal fetal medicine specialists, pharmacists, and nurses should be conducted as well to identify knowledge deficits, and targets for educational activities.

8.5 References

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9 Where do Patients and Physicians Obtain Their IBD-specific Reproductive Information? Where Should We Target Educational Activities to Improve IBD-specific Reproductive Knowledge among Patients and Physicians?

9.1 Introduction

Inflammatory bowel disease (IBD) can be challenging to manage because of patient and physician concerns regarding interactions between the disease, treatments, and surgeries, and fertility, pregnancy, and breastfeeding. There was a significant knowledge deficit among both patients and physicians regarding IBD-specific reproductive issues (Chapters 4 and 7). Having identified these specific knowledge deficits, the challenge remains on how to translate the knowledge to patients and physicians. There have been multiple studies and review articles published on the relative safety of various IBD medications during pregnancy and breastfeeding, and on the management of IBD. However, patients and physicians continue to lack knowledge regarding these issues (Chapters 4, 5, 7, 8).

The best method for providing information effectively to patients and physicians is still unclear. A recent Canadian publication reported that patients with longstanding IBD rate as acceptable, the following sources of information: medical specialists (81%), brochures (79%), family doctors (64%), and website recommended by health care provider (64%)[1]. Just over half of the respondents in that survey (51%) selected the medical specialist as their first choice[1]. Among recently diagnosed Canadian IBD

patients, gastroenterologists (36%) and the Internet (38%) were the most frequent sources of information[2]. However, 24% of patients were dissatisfied with the information they were given at initial diagnosis[2]. Similarly, in a European study conducted by Politi et al., 66% of IBD patients selected the specialist as their primary source of information, with 77% being satisfied with their current information[3]. Other preferred sources of information reported in the literature include paper (bulletin, brochures, etc.), and international organizations[3-5].

The objectives of this analysis, conducted separately in patients and physicians, were to:

- characterize information-obtaining behavior and preferences for information sources regarding family planning or reproductive issues and IBD
- estimate the effect of obtaining information from multiple sources on IBD-specific reproductive knowledge
- estimate the effects of specific information sources on IBD-specific reproductive knowledge.

9.2 Methods

9.2.1 Setting and Participants

Patients and physicians were recruited as described in Chapter 2. Full details were presented in Chapter 2.

9.2.2 Data Sources and Variable Definitions

IBD-specific reproductive knowledge

IBD-specific reproductive knowledge of patients and physicians was assessed using the CCPKnow survey (see chapter 2 for details). Raw scores were calculated by summing the number of correct responses. Patients were dichotomized into having a poor CCPKnow knowledge level (CCPKnow scores of 0 to 7) or an adequate or better (adequate+) CCPKnow knowledge level (CCPKnow scores of 8 to 17). In contrast, due to higher knowledge levels on average, physicians were dichotomized into having a poor/adequate/good CCPKnow knowledge level (CCPKnow scores of 0 to 13) or a very good CCPKnow knowledge level (CCPKnow scores of 14 to 17).

Patients: Information-Obtaining Behavior and Information Sources

Table 9-1 shows the categorization of patients' responses to question 9 of the Inflammatory Bowel Disease History section of the patient questionnaire.

> 9. Where do you obtain your information regarding family planning and inflammatory bowel disease?

Table 9-1: Patients: Categorization of Variables Pertaining to Information-Obtaining Behavior and Information Sources

Questionnaire responses	Information obtaining	Information Sources
I have not sought information	Do not obtain	None
Gastroenterologist	Obtain information	Gastroenterologist
Family Physician	Obtain information	Family Physician
IBD nurse	Obtain information	IBD nurse
Pharmacist	Obtain information	Pharmacist
Internet	Obtain information	Internet
Pamphlets/brochures	Obtain information	Pamphlets/brochures
Books	Obtain information	Books

Support Groups	Obtain information	Support Groups
Family and Friends	Obtain information	Family and Friends
Other	Obtain information	Other

Physicians: Information Obtaining Behavior and Information Sources

Table 9-2 shows the categorization of physicians' responses to question 19 of the physician questionnaire.

> 19. Where do you obtain information regarding reproductive issues in inflammatory bowel disease?

Table 9-2: Physicians: Categorization of Variables Pertaining to Information-obtaining Behavior and Information Sources

Questionnaire responses	Information obtaining	Information sources
I have not sought information	Do not obtain	None
IBD-related conferences	Obtain information	IBD-related conferences
Gastroenterology conferences	Obtain information	Gastroenterology conferences
Medical journal subscriptions	Obtain information	Medical journal subscriptions
Internet websites	Obtain information	Internet websites
Literature reviews and searches	Obtain information	Literature reviews and searches
Textbooks	Obtain information	Textbooks
Specialist colleague	Obtain information	Specialist colleague
Other	Obtain information	Other

9.2.3 Statistical Analysis

This analysis aimed to characterize information-obtaining behavior of patients and physicians by estimating the proportion that obtain and do not obtain information by subgroups of interest.

The analysis also aimed to estimate the effect of obtaining information on IBD-specific reproductive knowledge by:

(1) comparing the proportion with adequate+ CCPKnow scores in patients who do and do not obtain information
(2) comparing the proportion with very good CCPKnow scores in physicians who do and do not obtain information
(3) estimating the OR for the effect of obtaining information on having poor CCPknow scores among patients
(4) estimating the OR for the effect of obtaining information on having very good CCPKnow scores among physicians
(5) estimating the OR for the effect of information source on having poor CCPKnow scores among patients
(6) estimating the OR for the effect of information source on having very good CCPKnow scores among physicians.

For continuous variables, medians and interquartile ranges (IQR) were tabulated, and medians were compared across subgroups; the statistical hypothesis that the medians did not differ was tested using non-parametric Mann-Whitney and Kruskall Wallis tests. For categorical variables, frequency distributions of categories were tabulated, and differences in distributions were compared across subgroups; the statistical hypothesis that the distributions did not differ was tested using the Chi-square ($\chi 2$) test. P-values for the null hypothesis of no difference are reported for the comparison of medians and frequency distributions.

To estimate the effect of independent variables on outcome variables, multivariable logistic regression was used to obtain odds ratios and 95% CI adjusted for selected covariates. Covariates were selected based on whether they could affect both the independent variable of interest and the outcome of interest, without being affected by the independent variable. DAGs were created using DAGitty Version 2.0 (www.dagitty.net).

For the effects of obtaining information and of each information source on having poor CCPKnow scores among patients, the selected covariates were (1) current age, (2) marital status, and (3) education level. For the effects of obtaining information and of each information source on having very good CCPKnow scores among physicians, the selected covariates were (1) years in practice and (2) percentage IBD patients in practice.

9.3 Results

9.3.1 Patients: Characteristics of Study Population

Complete data was available from 248 women who returned questionnaires that had complete responses for all variables included in the final multivariable analysis. Table 9-3 shows the patient characteristics and the proportion of patients in each category who obtain information about family planning and IBD. Almost two-thirds (161/248 (64.9%)) of respondents indicated they obtain information about family planning and IBD.

9.3.2 Patients: Information-obtaining Behavior

The information-obtaining behavior varied by age group with the peak frequency (49/56 (87.5%)) falling in the 30 to 34 year-old age group. As shown in Table 9-3, the proportion that obtains information among single women was 21.2 per 100 women lower than this proportion among women with partners, and 24.3 per 100 women higher than this proportion among divorced women (33/67 (49.3%) single women, 122/173 (70.5%) women with partners, 2/8 (25.0%) divorced women; p=0.007).

Of the women who had been pregnant, compared to the proportion that obtains information among women who had only been pregnant before their IBD diagnosis, this proportion was 36.5 per 100 women higher among women who had only been pregnant after their IBD diagnosis, and 20.2 per 100 women higher among women who had been pregnant both before and after their IBD diagnosis (15/36 (41.7%) v. 61/78 (78.2%) v. 13/21 (61.9%), respectively; p=0.001). Similar proportions of childless women (81/128 (63.3%)) and women who have children (80/120 (66.7%)) obtain information regarding family planning and IBD (p=0.58).

Compared to the proportion that obtain information among women who have poor CCPKnow scores, this proportion was 27.6 per 100 women higher among women who

Table 9-3: Characteristics and Proportion Who Obtain Information about Family Planning by Selected Study Variables among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	Total patients (N= 248)*		Proportion who obtain information		Chi-square p-value
	N	% of total*	N	% of category	
Current age (years)					
18 to 24	49	19.8	24/49	49.0	0.001
25 to 29	50	20.2	32/50	64.0	
30 to 34	56	22.6	49/56	87.5	
35 to 39	47	19.0	29/47	61.7	
40 to 45	46	19.0	27/46	58.7	
Marital status					
Single	67	27.0	33/67	49.3	0.007
Partnered	173	69.8	122/173	70.5	
Divorced	8	3.2	2/8	25.0	
Education					
Grade 1 to Grade 12	56	22.6	26/56	46.4	0.009
College/university	157	63.3	110/157	70.1	
Graduate degree	11	4.4	9/11	81.8	
Professional school degree	5	2.0	2/5	40.0	
Other	19	7.7	14/19	73.7	
Employment (n=229)*					
Unemployed	28	12.2	15/28	53.6	0.48
Part time	46	20.1	32/46	69.6	
Full time	117	51.1	78/117	66.7	
Other	38	16.6	23/38	60.5	
Family history of IBD					
Yes	107	43.1	76/107	71.0	0.079
No	141	56.9	85/141	60.3	
Type of IBD					
Crohn's disease	150	60.5	100/150	66.7	0.54
Ulcerative colitis	88	35.5	56/88	63.6	
Indeterminate	10	4.0	5/10	50.0	
Age IBD diagnosed					
Younger than 18 years	65	26.2	34/65	52.3	0.013
18 to 45 years	183	73.8	127/183	69.4	
Duration of IBD					
0 to 4 years	57	23.0	34/57	59.6	0.34
5 or more years	191	77.0	127/191	66.5	

Category	Total patients (N= 248)*		Proportion who obtain information		Chi-square p-value
	N	% of total*	N	% of category	
Ever been pregnant					
Yes	136	54.8	89/136	65.4	0.850
No	112	45.2	72/112	64.3	
If have been pregnant, timing in relation to IBD diagnosis (n=135)*					
Before only	36	26.9	15/36	41.7	0.001
After only	78	57.8	61/78	78.2	
Before and after	21	15.7	13/21	61.9	
Have children					
No, childless	128	51.6	81/128	63.3	0.577
Yes, have children	120	48.4	80/120	66.7	
CCPKnow level					
Poor (0 to 7)	131	52.8	68/131	51.9	<0.001
Adequate (8 to 10)	49	19.8	36/49	73.5	
Good (11 to 13)	48	19.4	39/48	81.3	
Very good (14 to 17)	20	8.1	18/20	90.0	
CCPKnow level					
Poor (0 to 7)	131	52.8	68/131	51.9	<0.001
Adequate plus (8 to 17)	117	47.2	93/117	79.5	
Have discussed family planning with a physician					
No	94	37.9	26/94	27.7	<0.001
Yes	154	62.1	135/154	87.7	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

have adequate + CCPKnow scores (68/131 (51.9%) v. 93/117 (79.5%), respectively; p<0.001). As shown in Table 9-3, as the CCPKnow level increased, the proportion that obtains information also increased (p<0.001). Compared to the proportion that obtains information among women who had discussed family planning with a physician, this proportion was 60 per 100 women lower among women who had not discussed family planning with a physician (135/154 (87.7%) v. 26/94 (27.7%), respectively; p<0.001).

9.3.3 Patients: Sources of Information Regarding Family Planning and IBD

As shown in Figure 9-1, the most frequently indicated sources of information were: GI physician (106/248 (42.7%)), GP physician (81/248 (32.7%)) and Internet (86/248 (34.7%)). The next most frequent sources of information were pamphlets (47/248 (19.0%)), family and friends (43/248 (17.3%)), IBD nurse (37/248 (14.9%)). Books (30/248 (12.1%)), pharmacist (15/248 (6.0%)), support group (11/248 (4.4%)), and other (18/248 (7.3%) sources of information were less frequently selected. Appendix C7 Table C7-0-1 shows the free text responses patients wrote under other sources of information. As shown in Figure 9-2, the proportion that obtains information from their GI physician among women who have children was 15.6 per 100 women higher than this proportion among childless women (61/120 (50.8%) v. 45/128 (35.2%), respectively; p=0.013). The proportion that obtains information from their GP physician among women who have children was 12.6 per 100 women higher than this proportion among childless women (47/120 (39.2%) v. 34/128 (26.6%), respectively; p=0.034). However,

the proportion that obtains information from the internet among women who have children was 10.6 per 100 women lower than this proportion among childless women (35/120 (29.2%) v. 51/128 (39.8%), respectively; p=0.077).

In chapter 4, the analysis estimated different effects of discussion of family planning on childlessness in older (35+ years) and younger women (<=34 years). As shown in Figure 9-3, the proportion that obtains information from their IBD nurse among women 35 years and older was 10.1 per 100 women lower than this proportion among women 34 years and younger (8/93 (8.6%) v. 29/155 (18.7%), respectively; p=0.031). The proportion that obtains information from the Internet among women 35 years and older was 12.5 per 100 women lower than this proportion among women 34 year and younger (25/93 (26.9%) v. 61/155 (39.4%), respectively; p=0.046) as their information source.

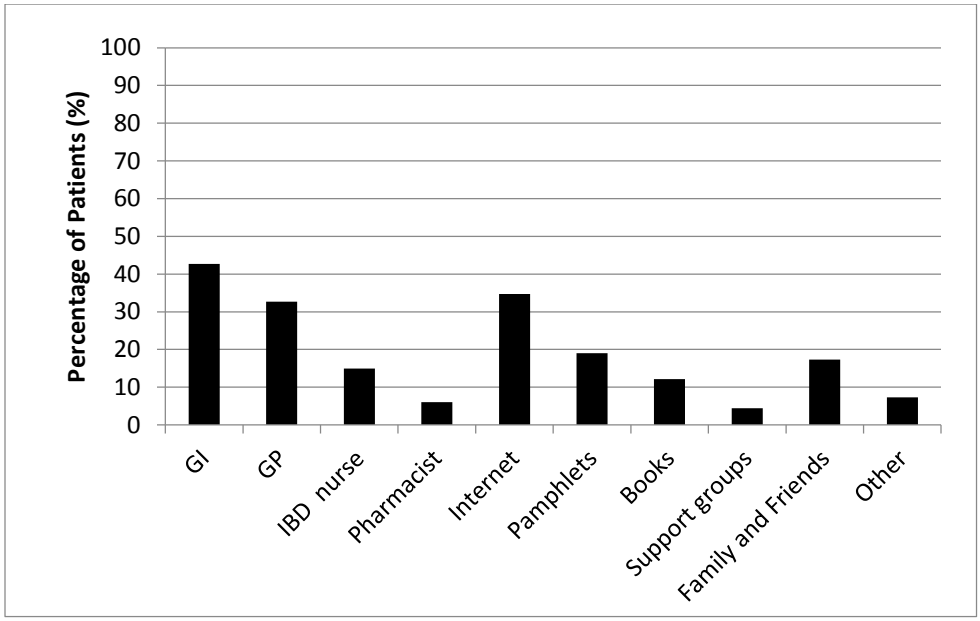

Figure 9-1: Information Sources Regarding Family Planning and IBD of 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

GI = gastroenterologist, GP = general practitioner

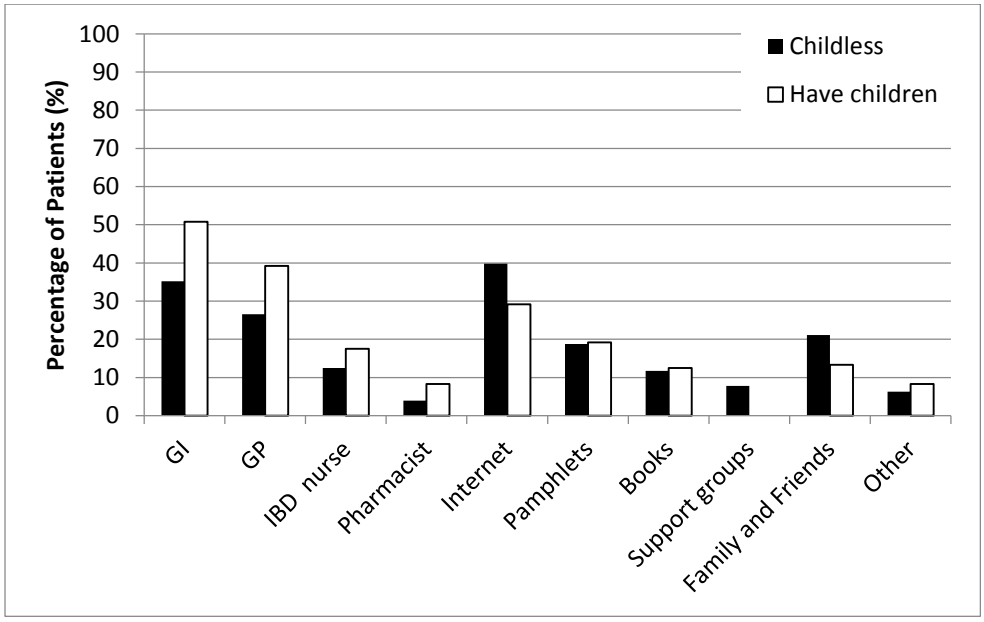

Figure 9-2: Information Sources Regarding Family Planning and IBD Differ Between Childless Women with IBD and Women with IBD who have children

GI = gastroenterologist, GP = general practitioner

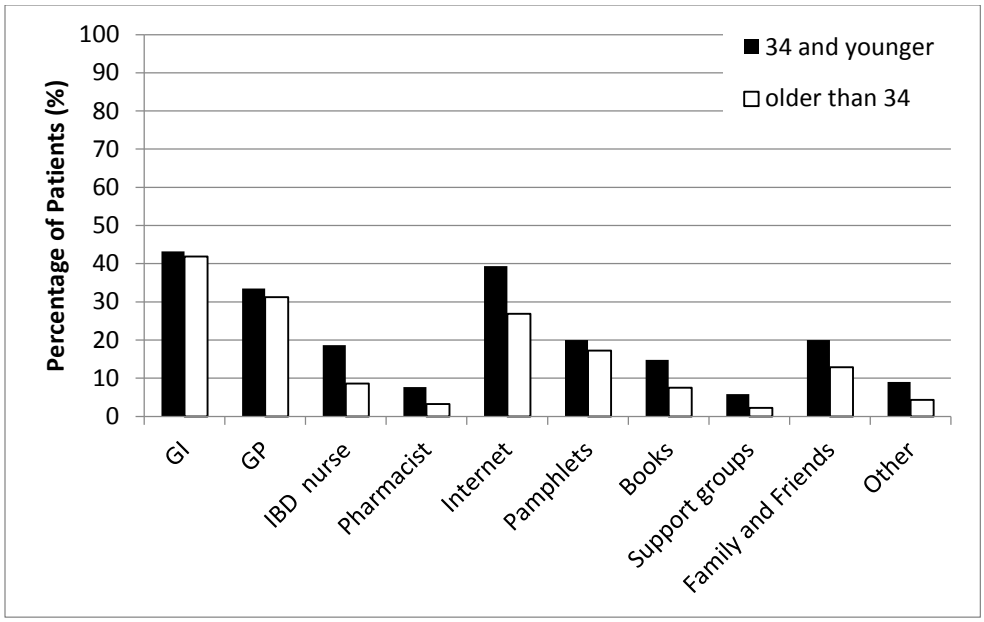

Figure 9-3: Information Sources Regarding Family Planning and IBD Differ Between Women 34 years or younger Compared to Women Older than 34 years.

GI = gastroenterologist, GP = general practitioner

9.3.4 Patients: The Association of Information-obtaining Behavior Regarding Family Planning and IBD, and of Each Information Source with Having Poor CCPKnow Scores

The Effect of Obtaining Information on Having Poor CCPKnow Scores

The median CCPKnow score of patients who obtain information was 5.0 units higher than the median CCPKnow score of patients who do not obtain information (8.0 (IQR 5.0 – 12.0) v. 3.0 (1.0 – 8.0), respectively; $p<0.001$). As shown in Table 9-4, multivariable logistic regression estimated an OR adjusted for current age, marital status, and education level of 0.35 (95% CI: 0.19 – 0.64) for the effect of obtaining information on having poor CCPKnow scores; the odds of having poor CCPKnow levels was 65% lower among women who obtain information regarding family planning and IBD relative to women who do not obtain such information.

The Effect of Information Source on Having Poor CCPknow Scores

As shown in Table 9-4, the following sources of information decreased the odds of having poor CCPKnow levels: gastroenterologist, family physician, IBD nurse, pharmacist, internet, pamphlets and brochures, books, and family and friends. Support groups, and other sources of information did not clearly affect the odds of having poor CCPKnow levels. Appendix C7 Table C7-0-2 shows the full multivariable logistic regression models with ORs for the selected covariates.

Table 9-4: Multivariable Logistic Regression Models for Estimating the Effects of Information-obtaining Behavior and Information Sources on Having Poor IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	OR	95% CI
Model for effect of patient information-obtaining behavior on having Poor CCPKnow		
Obtain information		
No	1.00	-
Yes	0.34	0.18 – 0.63
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.20	0.09 – 0.44
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.62	0.31 – 1.3
Graduate degree	0.084	0.013 – 0.52
Professional school degree	0.13	0.013 – 1.3
Other	0.67	0.21 – 2.2
Model for effect of information sources on having Poor CCPKnow*#		
Source of information		
Gastroenterologist	0.52	0.30 – 0.91
Family Physician	0.34	0.19 – 0.62
IBD nurse	0.40	0.18 – 0.89
Pharmacist	0.22	0.059 – 0.79
Internet	0.47	0.26 – 0.84
Pamphlets and brochures	0.34	0.17 – 0.70
Books	0.36	0.14 – 0.88
Support Groups	2.2	0.46 – 11
Family and Friends	0.45	0.21 – 0.94
Other	0.31	0.21 – 1.6

* reference category for each OR is the negative response to that source of information
# see Appendix for full multivariable logistic regression models with OR for covariates

9.3.5 Physicians: Characteristics of Study Population

Complete data was available from 215 physicians who returned questionnaires that had complete responses for all variables included in the final multivariable analysis. Table 3-4 previously showed full physician demographics. As the final multivariable logistic regression models include demographic factors related to practice characteristics, only questionnaires submitted by practicing physicians (n=183) were included for analysis in this chapter. Table 9-5 shows the characteristics of the 183 physicians included in this analysis and the proportion of physicians in each category who obtain information regarding reproductive issues in IBD. More than three quarters (155/183 (84.7%)) of physicians obtain information regarding reproductive issues in IBD.

9.3.6 Physicians: Information-obtaining Behaviour

As shown in Table 9-5, compared to the proportion that obtains information among GI physicians, this proportion was 32.0 per 100 physicians lower among GP physicians and 36.4 per 100 physicians lower among Other physicians (97/97 (100.0%) GI physicians, 51/75 (68.0%) GP physicians, 7/11 (63.6%) Other physicians; $p<0.001$). With increasing years of practice by 5-year increments, the proportion that obtains information decreased ($p=0.041$). The proportion that obtains information among physicians in academic practice was 16.7 per 100 physicians more than this proportion among physicians in community practice (51/53 (96.2%) academic and 101/127 (79.5%)

Table 9-5: Characteristics and the Proportion who Obtain Information Regarding Reproductive Issues in IBD by Selected Study Variables among 183 Practicing Canadian Physicians

	Total (n=183)*		Proportion who obtain information		Chi-square p-value
	N	% of total*	N	% of category	
Gender					
Male	127	69.4	108/127	85.0	0.85
Female	56	30.6	47/56	83.9	
Training status					
Gastroenterologist (GI)	97	53.0	97/97	100.0	<0.001
General practitioner (GP)	75	41.0	51/75	68.0	
Other	11	6.0	7/11	63.6	
Years in practice					
0 to 4 years	27	14.8	25/27	92.6	0.041
5 to 10 years	26	14.2	26/26	100.0	
11 to 20 years	47	25.7	38/47	80.9	
>20 years	83	45.4	66/83	79.5	
Population of city (n=131)*					
0 to 99,999	46	35.1	37/46	80.4	0.92
100,000 to 499,999	28	21.4	22/28	78.6	
>500,000	57	43.5	44/57	77.2	
Type of practice (n=180)*					
Community	127	70.6	101/127	79.5	0.005
Academic	53	29.4	51/53	96.2	
Percentage of patients with IBD					
0 – 9%	91	49.7	63/91	69.2	<0.001
10 – 24%	51	27.9	51/51	100.0	
25 – 50%	27	14.8	27/27	100.0	
51 – 100%	14	7.7	14/14	100.0	
Number of IBD patients each year					
0 to 9	33	18.0	20/33	60.6	<0.001
10 to 50	66	36.1	51/66	77.3	
51 to 100	18	9.8	18/18	100.0	
101 to 150	18	9.8	18/18	100.0	
more than 150	48	26.2	48/48	100.0	
Number of pregnant IBD patients managed in past year					
None	76	41.5	52/76	68.4	<0.001
1 to 10	70	38.3	69/70	98.6	
11 or more	37	20.2	34/37	91.9	

	Total (n=183)*		Proportion who obtain information		Chi-square p-value
	N	% of total*	N	% of category	
Subjective IBD knowledge					
Inadequate	16	8.7	9/16	56.3	<0.001
Enough to get by	83	45.4	63/83	75.9	
Very good	84	45.9	83/84	98.8	
Feel about managing pregnant IBD patients					
Not comfortable	59	32.2	35/59	59.3	<0.001
Somewhat comfortable	37	20.2	33/37	89.2	
Comfortable	87	47.5	87/87	100.0	
CCPKnow level					
Poor (0 to 7)	17	9.3	10/17	58.8	<0.001
Adequate (8 to 10)	18	9.8	10/18	55.6	
Good (11 to 13)	38	20.8	27/38	71.1	
Very good (14 to 17)	110	60.1	108/110	98.2	
Dichotomized CCPKnow level					
Poor/Adequate/Good (0 to 13)	73	39.9	47/73	64.4	<0.001
Very good (14 to 17)	110	60.1	108/110	98.2	
Discuss family planning					
No	64	35.0	45/64	70.3	<0.001
Yes	119	65.0	110/119	92.4	

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator.

community; p=0.005). Compared to the proportion that obtains information in the group of physicians with practices in which 0 - 10% of patients have IBD, this proportion was 30.8 per 100 physicians higher in the groups of physicians with higher percentages of IBD patients (10 - 24%, 25 - 50%, and >50%, with respective proportions of 63/91 (69.2%), 51/51 (100%), 27/27 (100.0%), 14/14 (100.0%); p<0.001). Compared to the proportion that obtains information among physicians who had not managed any pregnant IBD patients in the last year, this proportion was 30.2 per 100 physicians more among physicians who had managed 0 to 10 pregnant IBD patients in the past year, and 23.5 per 100 physicians more among physicians who had managed 11 or more pregnant IBD patients in the past year (52/76 (68.4%) v. 69/70 (98.6%) v. 34/37 (91.9%), respectively; p<0.001).

Compared to the proportion that obtains information among physicians who ranked their IBD knowledge as “inadequate”, this proportion was 19.6 per 100 physicians more among physicians who ranked their IBD knowledge as “was enough to get by” and 41.8 per 100 physicians more among physicians who ranked their IBD knowledge as “very good” (9/11 (56.3%) v. 63/83 (75.9%) v. 83/84 (98.8%), respectively; p<0.001). Similarly, compared to the proportion that obtains information among physicians who reported feeling “not comfortable” managing pregnant IBD patients, this proportion was 29.9 per 100 physicians more among physicians who reported feeling “somewhat comfortable” managing pregnant IBD patients, and 40.7 per 100 physicians more among physicians

who reported feeling “comfortable” managing pregnant IBD patients (35/59 (59.3%) v. 33/37 (89.2%) v. 87/87 (100.0%), respectively; p<0.001).

The proportion that obtains information was 22.1 per 100 physicians higher among physicians who discuss family planning compared to this proportion among physicians who do not discuss family planning (45/64 (92.4%) v. 110/119 (70.3%), respectively; p<0.001).

9.3.7 Physicians: Sources of Information Regarding Reproductive Issues and IBD

As shown in Figure 9-4, GI conferences, IBD conferences, specialist colleagues, internet, and literature review were the most frequently reported information sources among physicians. Medical journals, textbooks, and other sources of information were less frequently selected.

As shown in Figure 9-5, the proportion that obtains information from GI conferences was 38.9 per 100 physicians higher among physicians who discuss family planning than this proportion among physicians who do not discuss family planning (76/119 (63.9%) v. 16/64 (25.0%), respectively; p<0.001). Similarly, the proportion that obtains information from IBD conferences was 29.7 per 100 physicians higher among physicians who discuss family planning than this proportion among physicians who do not discuss family planning (67/119 (56.3%) v. 17/64 (26.6%), respectively; p<0.001).

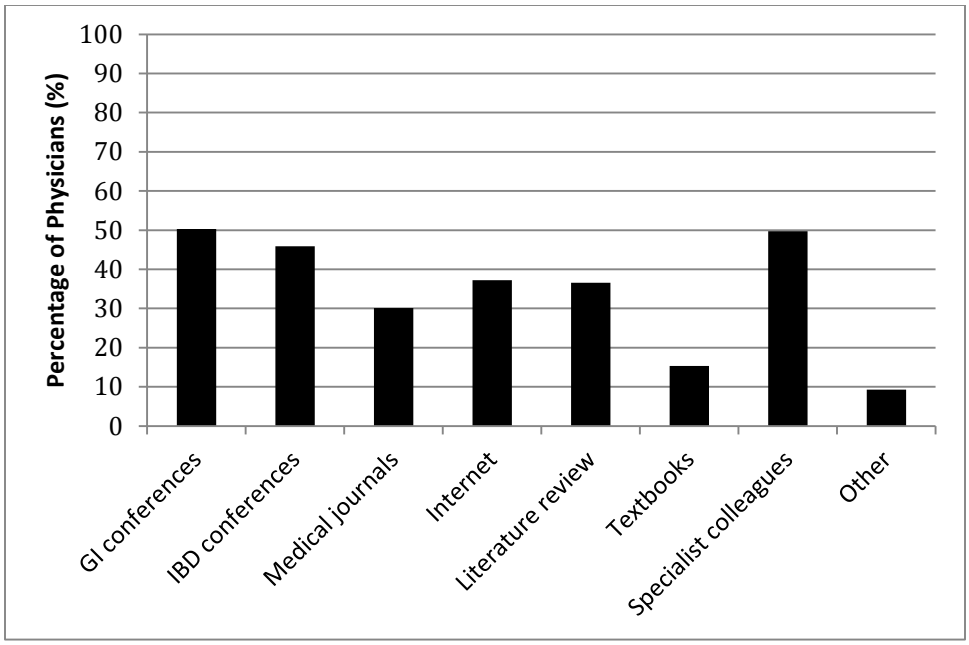

Figure 9-4: Sources of Information Regarding Reproductive Issues and IBD of 183 Practicing Canadian Physicians

GI = gastroenterology, IBD = inflammatory bowel disease

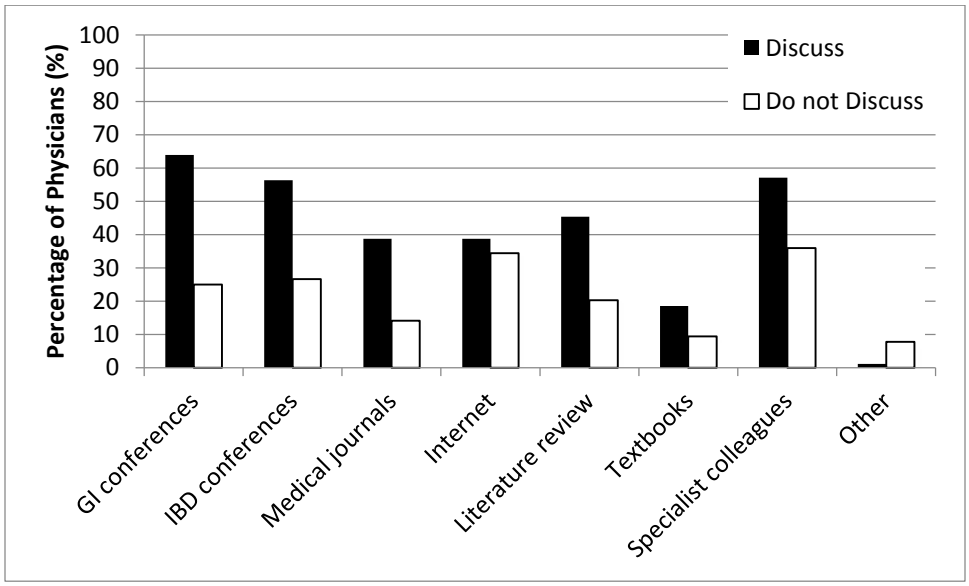

Figure 9-5: Sources of Information Regarding Reproductive Issues and IBD by Discussion of Family Planning of 183 Practicing Canadian Physicians

GI = gastroenterology, IBD = inflammatory bowel disease

9.3.8 Identifying Covariates for the Multivariable Logistic Regression Model for Estimating the Effect of Information-obtaining Behaviour on the Odds of Having Very Good IBD-specific Reproductive Knowledge as Measured by the CCPKnow Score among Physicians

Study variables that may affect both information-obtaining behavior and the CCPKnow score among physicians were entered into a DAG (Figure 9-6), with arrowed lines indicating the direction of the association. The total and direct effects are equal in this model because there is no indirect pathway from information-obtaining behavior to the CCPKnow score. The covariates identified for the multivariable logistic regression model for the effect among physicians of information-obtaining behaviour on CCPKnow scores were 1) # of pregnant IBD patients managed in the past year, 2) years in practice, 3) community/academic position, and 4) training status.

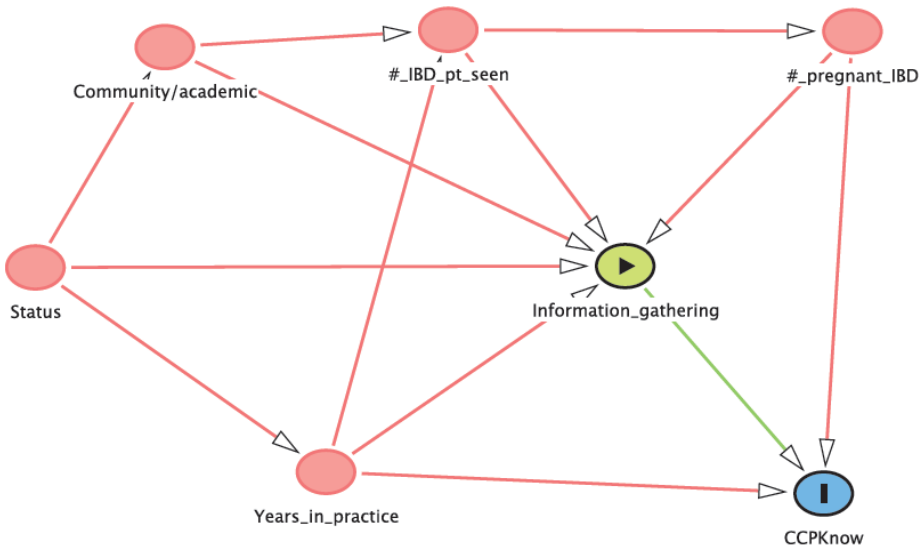

Figure 9-6: Directed Acyclic Diagram for Information-obtaining Behaviour and Having Very Good CCPKnow Scores among Physicians

9.3.9 The Association among Physicians of Information-obtaining Behavior with Having Very Good CCPKnow Scores

Effect of Obtaining Information on the Odds of Having a Very Good CCPKnow Level

The median CCPKnow score of physicians who obtain information was 7.0 units higher than the median CCPKnow score of physicians who do not obtain information (16.0 (IQR 13.0 – 17.0) v. 9.0 (IQR 8.0 – 12.0), respectively; p<0.001). As shown in Table 9-6, multivariable logistic regression estimated an OR, adjusted for years in practice and percentage of IBD patients in practice, of 5.4 (95% CI: 9.5 - 30) for the effect of obtaining information on the odds of having a very good CCPKnow level. Thus, physicians who obtain information regarding reproduction and IBD have 5.4 times the odds of having very good CCPKnow scores compared to physicians who do not obtain such information.

Effect of Source of Information on the Odds of Having a Very Good CCPknow Level

As shown in Table 9-6, reporting GI conferences as a source of information corresponded to a 3.6 (95% CI: 1.1 – 12)-fold increase in the odds of having a very good CCPKnow score. Table 9-6 also shows the multivariable logistic regression model OR and 95% CI estimates of the effect of each information source on the odds of having a very good CCPKnow score. Appendix C7 Table C7-0-3 shows the full multivariable logistic regression models with ORs for the selected covariates.

Table 9-6: Physicians: Multivariable Logistic Regression Models for Estimating the Effects of Information-Obtaining Behavior and Information Sources on the Odds of Having Very Good IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) among 183 Practicing Canadian Physicians

	OR	95% CI
Model for the effect of information-obtaining behavior on the odds of having a Very Good CCPKnow Level		
Obtain information		
No	1.00	-
Yes	5.4	9.5 – 30
Years in practice (years)		
0 to 4 years	1.0	-
5-10 years	0.47	0.055 – 4.0
11-20 years	0.18	0.032 – 0.97
>20 years	0.17	0.44 – 7.3
Type of practice		
Community	1.0	-
Academic	1.8	0.44 – 7.3
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.4	0.74 – 15
11 or more	4.2	1.3 – 14
Training Status		
GI	1.0	-
GP	0.063	0.013 – 0.30
Other	0.23	0.038 – 1.4
Model for the effect of information sources on the odds of having a Very Good CCPKnow Level**#		
Source of information		
IBD-related conferences	2.1	0.69 – 6.2
Gastroenterology conferences	3.6	1.1 – 12
Medical journal subscriptions	1.9	0.54 – 6.5
Internet websites	1.0	0.37 – 2.9
Literature reviews and searches	1.3	0.43 – 3.9
Textbooks	1.9	0.50 – 7.5
Specialist colleague consultations	1.5	0.57 – 3.9
Other	1.2	0.22 – 6.1

* reference category for each OR is the negative to that source of information
# see Appendix for multivariable logistic regression models with OR for covariates

9.4 Discussion

Decisions regarding family planning in the context of having a chronic disease such as inflammatory bowel disease can be complex. Poor IBD-specific reproductive knowledge is associated with childlessness, and family planning discussion with a physician was associated with decreased odds of having poor knowledge (see chapter 4). However, less than two-thirds of women report having discussed family planning with a physician (see chapter 4). Discussions about family planning can be initiated by the patient or the physician. Physicians with very good IBD-specific reproductive knowledge and those who feel comfortable managing pregnant IBD patients are more likely to discuss family planning with their female IBD patients of reproductive age (see chapter 7).

In this analysis, obtaining information on IBD-specific reproductive knowledge was associated among patients and physicians with having higher knowledge scores. In addition, certain sources of information had stronger estimated effects on IBD-specific reproductive knowledge than other sources.

Patient information-obtaining behavior and information sources

Patients who actively obtain information regarding family planning and IBD had higher CCPKnow scores, and 65% lower odds of having poor IBD-specific reproductive knowledge than women who do not obtain information. Patients obtain information most frequently from their gastroenterologist (42.7%), general practitioner (32.7%), and

the Internet (34.7%). These patient preferences are similar to those reported in the literature, with medical specialists, family doctors, and Internet/websites being the most frequently reported preferred sources of information for patients with IBD[1-3].

All three of these sources of information (gastroenterologist/general practitioner/ Internet) were associated with higher levels of IBD-specific reproductive knowledge among patients; conversely, women who obtained information from these sources of information had decreased odds of having poor CCPKnow scores. Other sources of information that were associated with decreased odds of having poor CCPKnow scores included IBD nurse, pharmacist, pamphlets and brochures, and books. However, women also obtained information from family and friends and support groups, but these sources of information were less clearly associated with poor CCPKnow scores.

This finding suggests that there may be something different about either the content and quality of the information women obtain from the first group of sources of information (gastroenterologist, general practitioner, internet, IBD nurse, pharmacist, pamphlets and books) compared to the second group (family and friends, support groups); or about the exchange of information, translation into knowledge, and retention of knowledge by the patient depending on the source of information. Specifically, the content of the information women obtain through the first group of information sources may specifically address issues assessed by the CCPKnow survey. Therefore, targets to improve patient IBD-specific reproductive knowledge should

include any of the sources listed in the first group, but definitely should include the gastroenterologist, the general practitioner, and the Internet.

The Internet can be a double-edged sword, as patients will encounter information that may be unreliable and of poor quality. Multiple reviews of IBD information resources on the Internet have found that most websites are of poor quality[6,7], and may be too difficult for patients to comprehend[7]. However, there are certain websites that have been assessed and are recommended for patient use to obtain information about IBD[6-8]. The Internet as a source of information should not be dismissed and patients' preferences or requests for obtaining information from recommended Internet sites should be acknowledged; patients should be directed to accurate recommended sources[8]. It has been suggested based on patient survey responses that IBD referral centres develop their own IBD-dedicated websites[5]. Since Internet websites are one of the most frequently reported sources of information among women with IBD, and among patients with IBD in general, ensuring that there are websites that have appropriate, correct, and easy to comprehend information regarding reproductive issues and IBD is very important.

In the previous analyses, women who had discussed family planning with a physician had higher IBD-specific reproductive knowledge (as measured by CCPKnow score). This analysis also found that women who obtain information regarding family panning from physicians (gastroenterologists, general practitioner) have higher CCPKnow scores.

However, as shown in chapter 7, physicians' IBD-specific reproductive knowledge is variable, and there were notable deficits in overall IBD-specific reproductive knowledge, as well as in the appropriate use of medications during pregnancy and breastfeeding (Chapter 8). In addition, physicians with lower levels of IBD-specific reproductive knowledge and those who were less comfortable managing pregnant IBD patients discussed family planning with their patients less frequently (Chapter 7). Therefore, these knowledge deficits among physicians need to be addressed in order to ensure that physicians are equipped with the correct information, so they feel comfortable managing pregnant IBD patients, and discussing family planning with their patients.

Physician information obtaining behavior and information sources

This analysis also assessed the effect of physicians' information-obtaining behavior and sources of information on physician IBD-specific reproductive knowledge. Physicians who actively obtain information regarding reproductive issues and IBD had higher CCPKnow scores, and had 6.6 times the odds of having very good CCPKnow scores compared to physicians who do not actively obtain information. Physicians obtained information in order of frequency from gastroenterology (50.3%) and IBD-related (45.9%) conferences, specialist colleagues (49.7%), the Internet (37.2%), literature reviews (36.6%), medical journals (30.1%), and textbooks (15.3%).

Only gastroenterology and IBD-related conferences as information sources were associated with a 2-fold increase in the odds of having very good CCPKnow scores. This

finding suggests that conferences may be an effective venue for improving physician knowledge. Therefore, efforts to improve IBD-specific reproductive knowledge among physicians should include targeted activities in gastroenterology and IBD-related conferences.

9.5 Conclusion

In summary, information-obtaining behavior among both patients and physicians is associated with increased IBD-specific reproductive knowledge, and certain information sources have stronger associations with increased IBD-specific reproductive knowledge than other sources. Educational targets to improve patients' IBD-specific reproductive knowledge should include gastroenterologists, general practitioners, and the Internet. Educational targets to improve physicians' IBD-specific reproductive knowledge should include gastroenterology and IBD-conferences and the Internet.

9.6 References

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10 Gastroenterology Trainees: Learners are Important Targets for Improving IBD-specific Reproductive Knowledge

10.1 Introduction

IBD-specific reproductive knowledge among physicians varies with specialty training and experience; as shown in Chapter 7, gastroenterologists have higher IBD-specific reproductive knowledge as measured by the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey, compared to general practitioners. Gastroenterology trainees (GI trainees) were excluded from previous analyses because practice characteristics were important covariates for multivariable logistic regression models. However, characterization of IBD-specific reproductive knowledge and relevant sources of information among GI trainees is useful for identifying differences in knowledge and information-obtaining behavior of GI trainees compared to practicing gastroenterologists and general practitioners.

The objectives of this analysis were to characterize the IBD-specific reproductive knowledge of GI trainees, as well as their practice patterns and use of medications for pregnant and breastfeeding patients. In addition, this analysis will characterize GI trainees' information-obtaining behavior and information sources regarding reproduction and IBD.

10.2 Methods

All GI trainee respondents were selected from the total group of 215 respondents, resulting in 24 questionnaires for analysis. Analyses similar to that done in Chapters 7, 8 and 9 were performed for GI trainee questionnaires. However, due to small numbers, hypothesis testing comparing outcomes across sub groups of GI trainees was not feasible. For specific outcome variables, comparisons were made to previously measured outcomes for practicing physicians (gastroenterologists and general practitioners – Chapters 7, 8, 9).

10.3 Results

10.3.1 Characteristics of Study Population

Table 10-1 shows the characteristics of the GI trainees. There were more males than females, and most trainees had seen 51 to 100 IBD patients each year, but almost a third (29.2%) had not managed any pregnant IBD patients in the past year.

10.3.2 Trainee IBD-specific Reproductive Knowledge (measured by the CCPKnow Score)

The median CCPKnow score for GI trainees was 15.0 (IQR 14.0 – 16.0), which is slightly lower than the median CCPKnow score of gastroenterologists (17.0 (IQR 16.0 – 17.0)) and substantially higher than the median CCPKnow score of general practitioners (11.0

Table 10-1: Characteristics and the Proportion with Very Good IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) among 24 Canadian Gastroenterology Trainees

Category	Total trainees (n=24)		Proportion with Very Good CCPKnow Scores	
	N	% of total	N	% of category
Gender				
Male	17	70.8	14/17	82.4
Female	7	29.2	5/7	71.4
Number of IBD patients each year				
0 to 9	0	0	0/0	0
10 to 50	7	29.2	4/4	57.1
51 to 100	11	45.8	10/11	90.9
101 to 150	2	8.3	1/2	50.0
more than 150	4	16.7	4/4	100.0
Number of pregnant IBD patients managed in past year				
None	7	29.2	5/7	71.4
1 to 10	7	29.2	6/7	85.7
11 to 20	9	37.5	7/9	77.8
>20	1	4.2	1/1	100.0

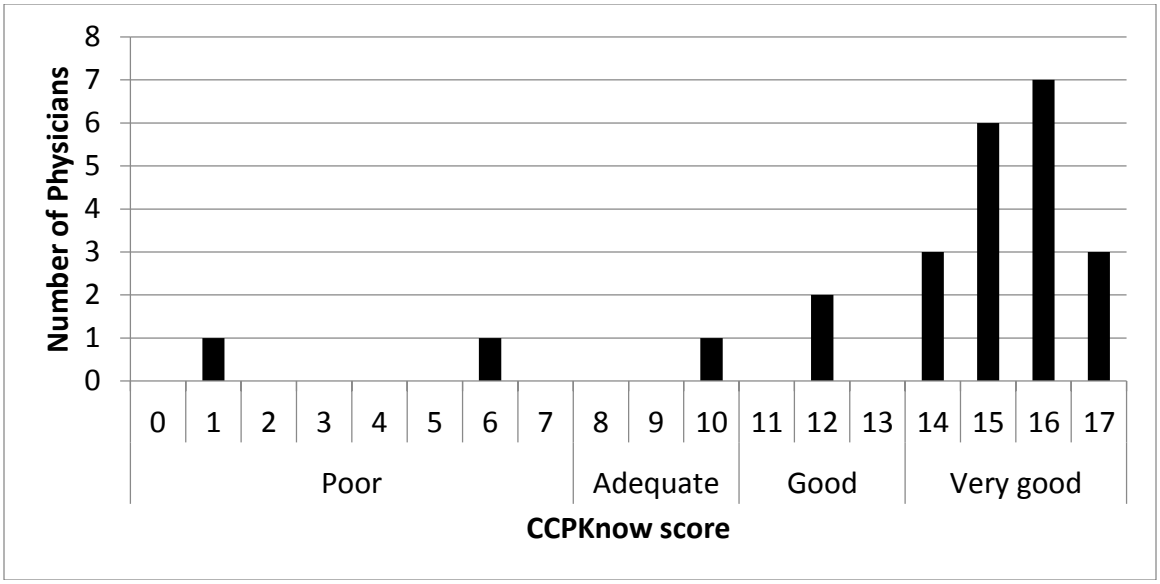

Figure 10-1: Distribution of CCPKnow Score Measuring IBD-specific Reproductive Knowledge among 24 Gastroenterology Trainees

Poor n=2/24, 8.3%; Adequate n=1/24, 4.2%; Good n=2/24, 8.3%; Very good n=19/24, 79.2%

(IQR 8.0 – 13.0)). The proportion of GI trainees with very good CCPKnow scores was 79.2% (19/24) (Figure 10-1). This proportion is between the proportions of gastroenterologists (92.8%) and general practitioners (45.5%) who had very good CCPKnow scores.

Table 10-1 also shows that the proportions of GI trainees with very good CCPKnow scores were similar across gender and varied by number of IBD patients and experience with pregnant IBD patients, though the statistical precision is low due to small numbers in comparison groups.

10.3.3 Trainee Discussion of Family Planning

Less than half (11/24 (45.8%)) of GI trainees discuss family planning with female patients of reproductive age. Table 10-2 shows the proportion that discusses family planning in each category of selected study variables. The proportions that discuss family planning were similar across gender and varied by number of IBD patients and experience with pregnant IBD patients, though the statistical precision is low due to small numbers in comparison groups.

Table 10-2: Characteristics and the Proportion that Discusses Family Planning by Selected Study Variables among 24 Canadian Gastroenterology Trainees

	Total trainees (n=24)		Proportion who Discuss FP	
	N	% of total	N	% of category
Gender				
Male	17	70.8	7/17	41.2
Female	7	29.2	4/7	57.1
Number of IBD patients each year				
0 to 9	0	0	0/9	0
10 to 50	7	29.2	4/7	57.1
51 to 100	11	45.8	5/11	45.5
101 to 150	2	8.3	1/2	50.0
more than 150	4	16.7	1/4	25.0
Number of pregnant IBD patients managed in past year				
None	7	29.2	2/7	28.6
1 to 10	7	29.2	5/7	71.4
11 to 20	9	37.5	4/9	44.4
>20	1	4.2	0/1	0

FP family planning

10.3.4 Trainee Medication Use During Pregnancy and Breastfeeding

Gastroenterology Trainee Use of Sulfasalazine and Mesalamine Medications

As shown in Figure 10-2, the majority of GI trainees continue sulfasalazine (15/24 (62.5%)) or oral mesalamine (19/24 (79.2%)) during pregnancy and breastfeeding (sulfasalazine 12/23 (52.2%); oral mesalamine 17/23 (73.9%)).

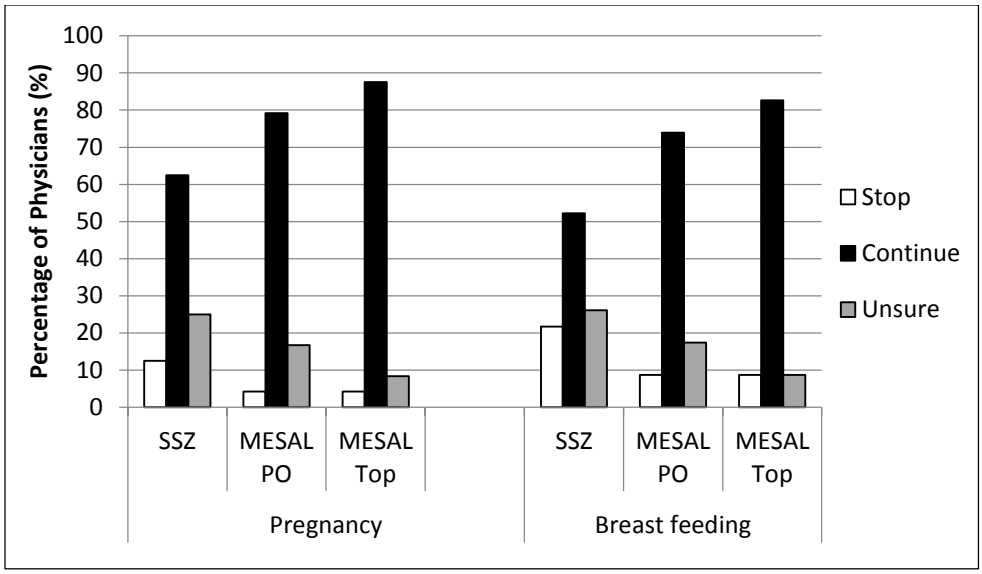

Figure 10-2: Gastroenterology Trainee Use of Sulfasalazine/Mesalamine during Pregnancy and Breastfeeding

SSZ = Sulfasalazine, MESAL = Mesalamine, PO = oral, TOP = topical. Best practice is to continue these medications if needed (Black bars)

Gastroenterology Trainee Use of Corticosteroid Medications

As shown in Figure 10-3, the majority of GI trainees continue oral prednisone (19/24 (79.2%)), topical prednisone (22/23 (95.7%)), oral budesonide (22/24 (91.7%)) and topical budesonide (22/24 (91.7%) during pregnancy.

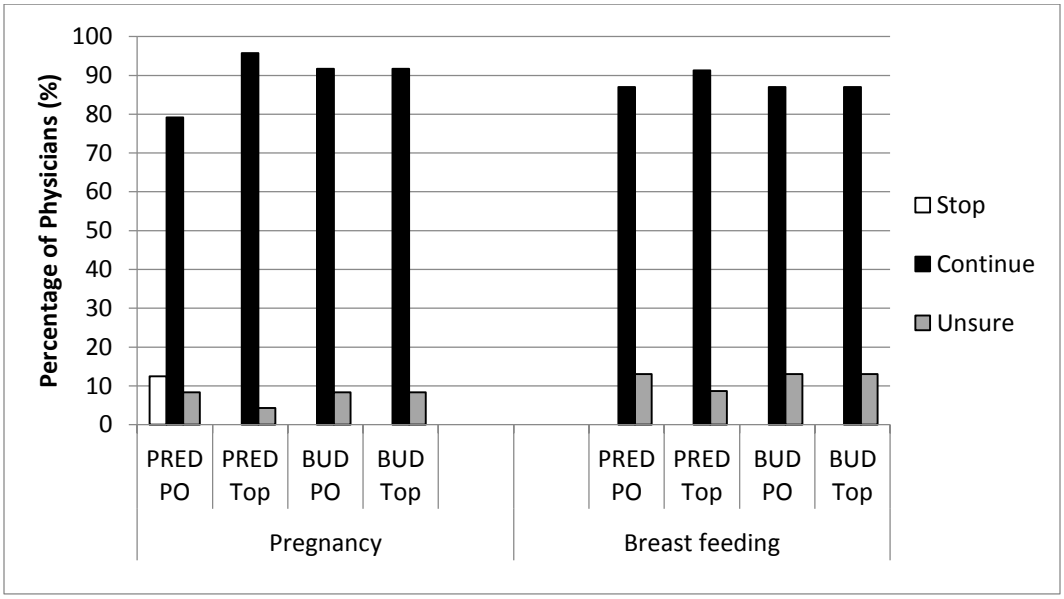

Figure 10-3: Gastroenterology Trainee Use of Corticosteroids during Pregnancy and Breastfeeding

PRED = Prednisone, BUD = budesonide, PO: oral, TOP: topical. Best practice is to continue these medications if needed (Black bars)

Gastroenterology Trainee Use of Antibiotics (Ciprofloxacin/Metronidazole)

As shown in Figure 10-4, the majority of GI trainees stop ciprofloxacin during pregnancy (16/24 (66.7%)) and slightly fewer stop ciprofloxacin during breastfeeding (10/23 (43.5%)). Almost half the trainees stop metronidazole during pregnancy (10/24 (41.7%)) and almost a half continue metronidazole during pregnancy (11/24 (45.8%)). Almost half the trainees stop metronidazole during breastfeeding (11/23 (47.8%)) and less than half continue metronidazole during breastfeeding (9/23 (39.1%)).

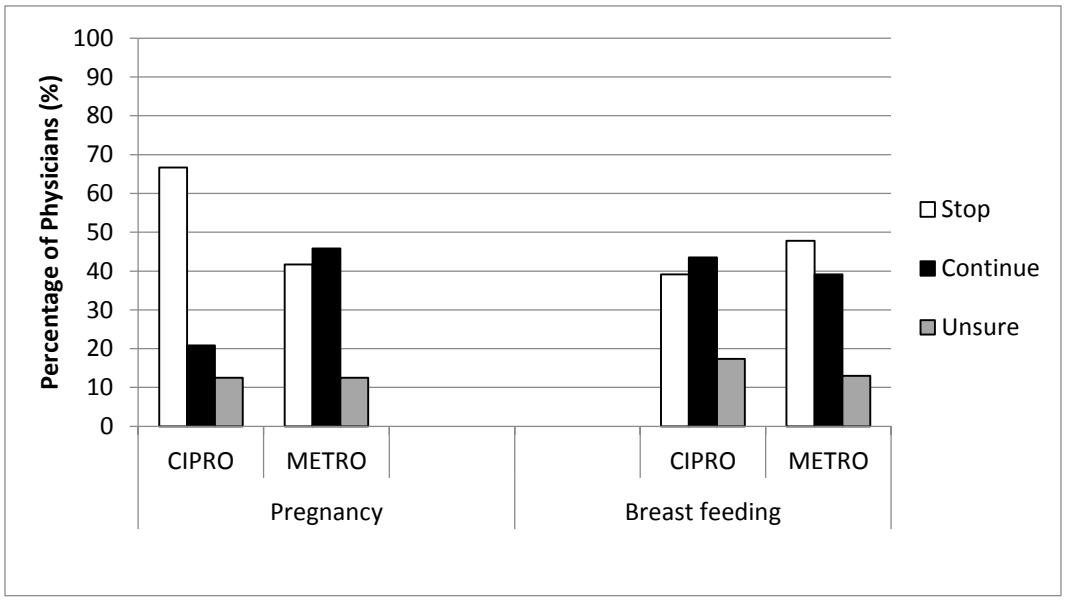

Figure 10-4: Gastroenterology Trainee Use of Antibiotics during Pregnancy and Breastfeeding

CIPRO = ciprofloxacin, METRO = metronidazole. Best practice is to stop ciprofloxacin (white), and metronidazole (white) although they may be used if absolutely needed (black).

Gastroenterology Trainee Use of Immunosuppressants (Azathioprine/6MP and Methotrexate)

As shown in Figure 10-5, the majority of GI trainees continue Azathioprine during pregnancy (15/24 (62.5%)) and the majority of GI trainees stop Methotrexate during pregnancy (22/24 (91.7%)). The majority of GI trainees continue Azathioprine during pregnancy (20/23 (87.0%)). About half of GI trainees stop Methotrexate (12/23 (52.2%)) but just over a quarter continue Methotrexate (6/23 (26.1%)) during breastfeeding.

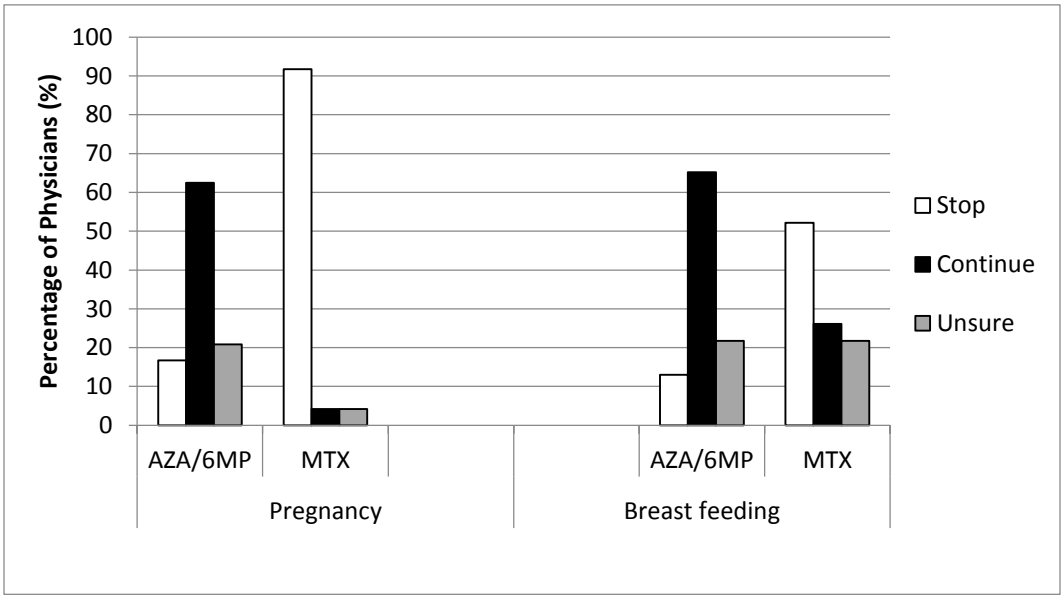

Figure 10-5: Gastroenterology Trainee Use of Immunosuppressants during Pregnancy and Breastfeeding

AZA = Azathioprine; 6-MP = 6-mercaptopurine; MTX = Methotrexate. Best practice is to continue AZA/6MP (black bars) and to stop MTX (white bars).

Gastroenterology Trainee Use of Biologics (Infliximab/Adalimumab)

As shown in Figure 10-6, the majority of GI trainees continue biologics during pregnancy and breastfeeding. However, there was still a proportion of GI trainees who were unsure about infliximab (3/24 (12.5%)) and adalimumab (6/24 (25.0%)) use during pregnancy. Some GI trainees stop infliximab (2/23 (8.7%)) and adalimumab (2/23 (8.7%)) during breastfeeding.

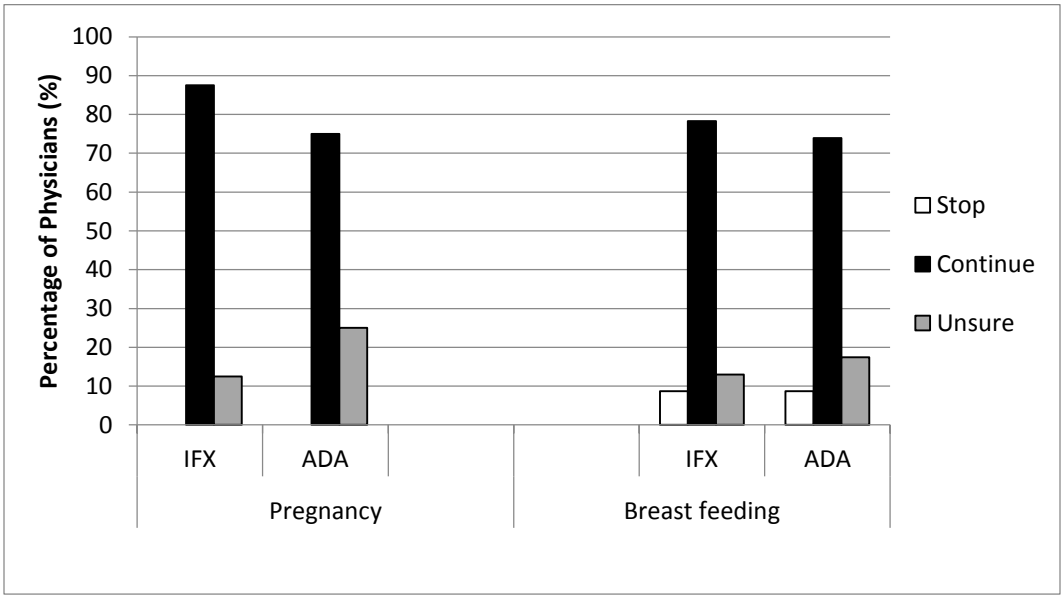

Figure 10-6: Gastroenterology Trainee Use of Biologics during Pregnancy and Breastfeeding

IFX = Infliximab, ADA = Adalimumab. Best practice is to continue IFX and ADA during pregnancy and breastfeeding if needed (black bars).

10.3.5 Trainee Information Obtaining Behaviour and Information Sources

The majority of GI trainees obtain information regarding reproduction and IBD (21/24 (87.5%)). As shown in Figure 10-7, specialist colleagues, internet, literature review, and IBD conferences were the most frequently reported physician information sources. GI conferences, textbooks, medical journal and other sources were less frequently selected.

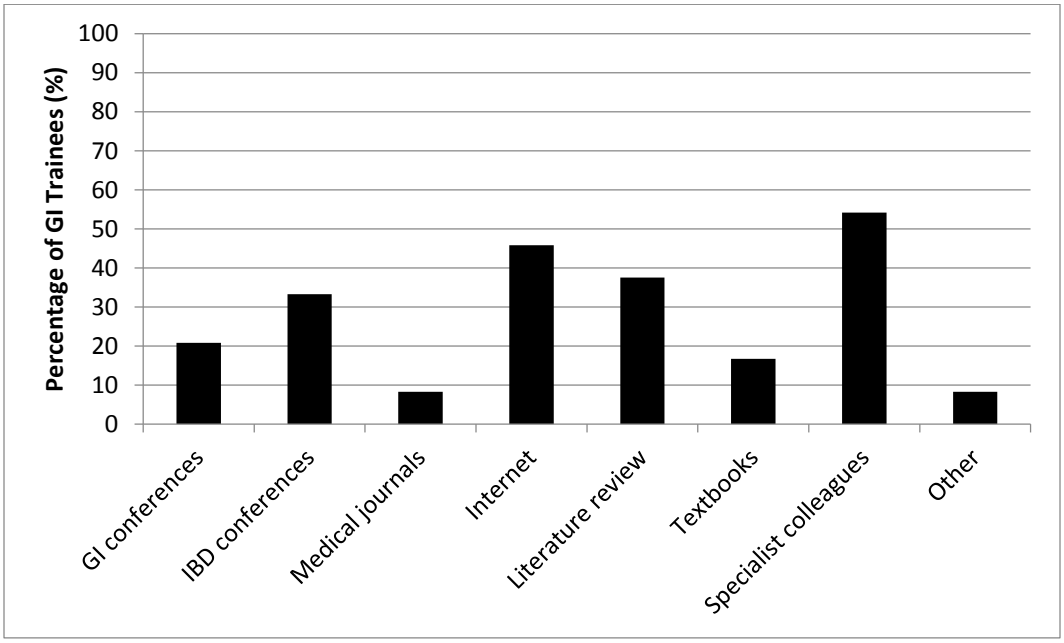

Figure 10-7: Gastroenterology Trainee Sources of Information Regarding Family Planning and IBD

GI = gastroenterology, IBD = inflammatory bowel disease

10.4 Discussion

Physicians of different specialty training have different levels of knowledge regarding reproductive issues and IBD; those with less gastroenterology-specific training such as general practitioners have less IBD-specific reproductive knowledge compared to gastroenterologists who have subspecialty training (Chapter 7). In this analysis, IBD-specific reproductive knowledge, as measured by median scores on the Crohn's and Colitis Pregnancy Knowledge (CCPKnow) survey, of GI trainees approached that of gastroenterologists but less than half of the trainees (45.8%) discuss family planning with their female IBD patients of reproductive age compared to 65.0% of the gastroenterologists.

The similarity of GI trainees' and gastroenterologists' median CCPKnow scores supports the concept that having specialty training in gastroenterology and some exposure to IBD contributes to IBD-specific reproductive knowledge. Compared to general practitioners, GI trainees would receive more basic instruction about IBD in general, and should be more familiar with the IBD medications and IBD-specific concepts asked in the CCPKnow survey.

The low percentage of GI trainees that discuss family planning may represent the lack of clinical interaction or exposure to female IBD patients of reproductive age, given that GI residency training programs are often focused on acute in-patient care. In addition, although GI trainees have very good IBD-specific reproductive knowledge, they may not

yet have acquired the communication skills that would enable them to discuss family planning with patients.

GI trainee continuation of medications prescribed to pregnant or breastfeeding women with IBD was similar to that of Gastroenterologists. Again, this may be a reflection of their exposure to instruction on IBD and medications, and experience managing IBD patients during their GI training.

Only 87.5% of GI trainees obtain information regarding reproduction and IBD, which is less than the 100% of gastroenterologists (Chapter 9), but more than the 68% of general practitioners (Chapter 9) who obtain such information. GI trainees obtain information from colleagues, internet, literature review, and IBD conferences, in that order of frequency, which differs from the order reported by practicing physicians (GI conferences, IBD conferences, specialist colleagues, internet, and literature review) (Chapter 9).

This difference in preference of information source should be kept in mind when considering optimal methods for targeting specific groups of physicians to improve knowledge regarding reproductive issues and IBD. For example, a recent US survey of GI program directors, their colleagues, and their fellows, on the learning preferences of GI fellows and attending physicians, showed that although fellows (equivalent to Canadian GI residents) and attending physicians (GI staff) regularly attended national conferences,

relatively more attending physicians than GI fellows found that their knowledge improved by their participation in the Gastroenterology Core Curriculum (a specialized intensive program with a series of educational activities at the Digestive Diseases Week conference)[1]. The Koczka et al. study also found that GI fellows felt they learned more from pharamaceutical-sponsored dinner lectures than from other educational activities[1].

In the USA, training in women's health issues in gastroenterology was mandated in the Gastroenterology Core Curriculum in 2003; inflammatory bowel diseases falls under general topics (female fertility compromise secondary to GI disorders) and pregnancy topics (chronic GI disorders management during pregnancy)[2]. At Brown University, Rhode Island, Saha et al. started a women's health program in 1996; their curriculum included a 2-month rotation in GI women's health inpatient and outpatient activities, as well as a three-year women's health pathway fellowship program, and an educational program through the Department of Obstetrics and Gynecology that includes pathobiology, research, statistical methods, scientific publishing, and grant writing[3]. From the experiences of the 13 fellows who participated in the program, >80% felt prepared to evaluate and treat GI disorders in pregnancy, and nearly 65% felt prepared to address general GI women's health issues[3]. Saha et al. also surveyed the USA GI program directors and fellows about women's health training, and found that more fellows than program directors perceive training in women's GI health issues to be low[4]. They identified multiple barriers to this training including low number of pregnant

patients treated, low number of referrals from obstetrics and gynecology, and lack of faculty interest in women's health[4].

A recent AGA (American Gastroenterological Association) institute report emphasizes the importance of a multidisciplinary effort in establishing a curriculum in women's GI health; they present as well a sample curriculum that includes inpatients and procedures, outpatients, and didactic educational actvities (as shown in Figure 10-8)[5].

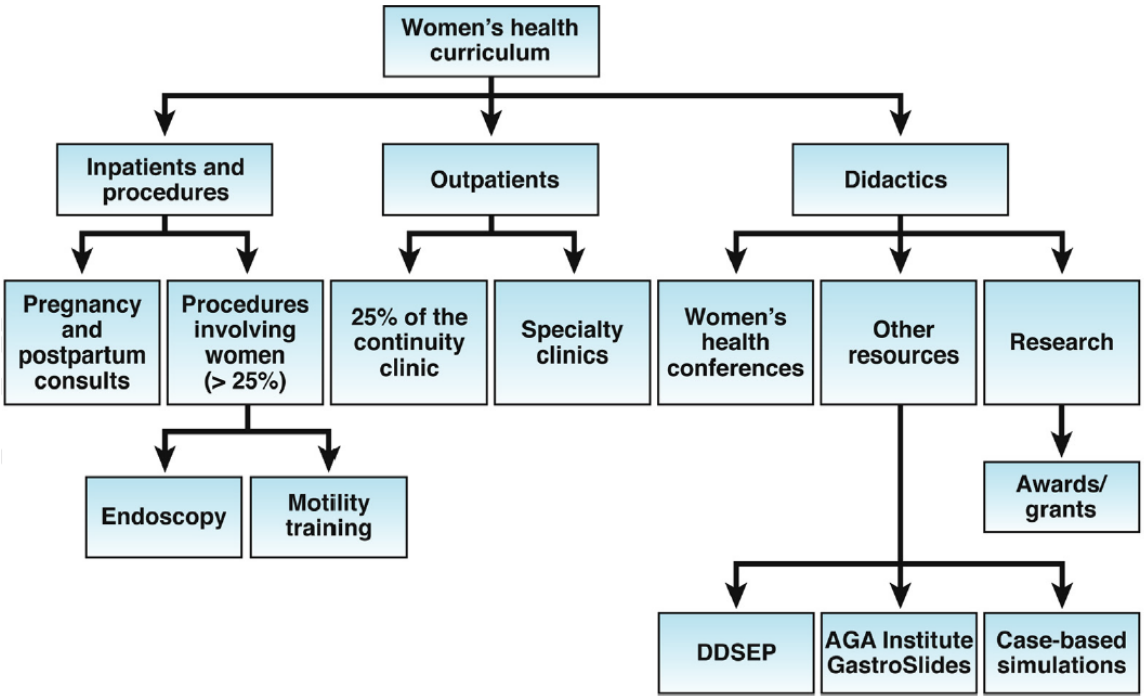

Figure 10-8: Sample Curriculum Components for Women's Health Curriculum

Figure 1 from Devuni D and Chokshi RV[5].

Previous studies have attempted to determine the best method to teach medical trainees evidence-based medicine - lecture v. online, direct v. self-directed,

multidisciplinary v. discipline-specific groups, lecture v. active small group methods of teaching[6]. However, to date, no specific method has been found to be superior in terms of learner outcomes[6].

The results of this analysis suggest that trainees may benefit more from educational activities that are internet based. In general surgery, Internet-based interactive modules were found to have potential in introducing general surgery residents to bariatric surgery[7]. A study investigating virtual clinical encounter as a method to train medical students and ease communication and socioemotional interactions with patients was found to be engaging and useful[8]. Perhaps a similar virtual tool could be used to train GI trainees and other trainees regarding how to bring up reproduction and family planning with IBD patients.

A limitation of this analysis is that there were only 24 GI trainee respondents, which is only a fraction of all the GI trainees in Canada. In addition, the trainees were not questioned about their year of training, or whether they had exposure to managing IBD patients. As mentioned, experience and exposure to IBD patients, and specifically pregnant IBD patients, may be an important factor affecting knowledge of IBD-specific reproductive issues among GI trainees.

10.5 Conclusion

Gastroenterology trainees have similar levels of IBD-specific reproductive knowledge and continuation of medications prescribed to pregnant or breastfeeding women with IBD as do practicing gastroenterologists, however fewer GI trainees discuss family planning with female IBD patients of reproductive age. There is a need for improving education about reproduction and IBD in the Canadian Gastroenterology Residency training programs. Further studies that investigate the women's health in gastroenterology component of Canadian Gastroenterology Residency programs, and aim to identify the most effective methods for improving trainee knowledge and practice patterns regarding reproduction and IBD are required.

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11 Summary of Objectives and Findings: Need for Improving IBD-specific Reproductive Knowledge

11.1 There is a Lack of Patient IBD-specific Reproductive Knowledge

11.1.1 Patient Study Primary Objective and Conclusion

The primary objective of the patient study was to estimate among women with IBD the effect of IBD-specific reproductive knowledge on childlessness (Chapter 4):

- There is a strong inverse relationship between IBD-specific reproductive knowledge and childlessness among women with IBD, with an estimated OR of 0.92 (95% CI: 0.86 – 0.99) for the association of the CCPKnow score with childlessness, adjusted for current age and marital status.

11.1.2 Patient Study Secondary Objectives and Findings

The secondary objectives of the patient portion of this study were:

- To estimate associations of selected variables, and in particular, discussion of family planning with a physician, with IBD-specific reproductive knowledge (Chapters 4 and 5):
  - The odds of having poor CCPKnow scores (adjusted for current age and marital status) were lower (OR 0.44, 95% CI: 0.25 -0.77) among women who had discussed family planning with a physician compared to women who had not discussed family planning with a physician. The odds were even lower (OR 0.28,

95% CI: 0.15 – 0.53) among women who had discussed family planning with a gastroenterologist compared to non-gastroenterologists.

- To characterize differences between childless women and women who have children on IBD-specific reproductive concerns and beliefs (Chapter 5):
  - Women with IBD, especially childless women with IBD, have notable knowledge deficits, concerns, and sources of worry regarding IBD-specific reproductive issues that range from pre-conception to breastfeeding.
- To characterize the medication knowledge of women with IBD, and to study differences between childless women and women who have children in medication knowledge (Chapter 5):
  - Almost half of the women were concerned about the possibility of IBD medications causing birth defects.
  - Relatively fewer childless women than women who have children know that pregnant women with IBD should continue some medications.
  - Prior treatment with specific medications was associated with increased odds of correctly answering the associated CCPKnow questions, and thus knowledge pertaining to specific drugs appears to be associated with personal experience with the specific drug.
- To characterize the change in family plans over time among women with IBD (Chapter 6):

- There was a decrease in the proportion of women who planned to have children, comparing this proportion before IBD diagnosis (74.0%) to this proportion since IBD diagnosis (66.8%), and to this proportion currently (52.5%).
- Relatively more childless women (10.3%) than women who have children (4.7%) changed from planning to have children before IBD diagnosis to no longer planning to have children since IBD diagnosis.

11.2 IBD-specific Reproductive Knowledge among Physicians

11.2.1 Physician Study Primary Objective and Findings

The primary objective of the physician study was to characterize IBD-specific reproductive knowledge among physicians using the CCPKnow survey.

- The median physician CCPKnow score was 15.0 (IQR 11.0 – 17.0), indicating very good IBD-specific reproductive knowledge. The median CCPKnow score was 17.0 (IQR 16.0 – 17.0) for gastroenterologists, 15.0 (IQR 14.0 – 16.0) for GI trainees, and 11.0 (IQR 8.0 – 13.0) for general practitioners.
- Almost two-thirds of physicians (60.1%) had very good CCPKnow scores. Relatively more gastroenterologists than general practitioners had very good CCPKnow scores.

11.2.2 Physician Study Secondary Objective and Findings

The secondary objectives of the physician portion of this study were:

- To estimate associations of selected study factors with IBD-specific reproductive knowledge among physicians:
  - Factors associated with very good CCPKnow scores included training status; years of practice; type of practice; % of IBD patients in practice; and # of pregnant IBD patients managed in the past year.
- To estimate the effect of IBD-specific reproductive knowledge level on the odds of discussing family planning with patients:
  - There was a positive association between IBD-specific reproductive knowledge and discussion of family planning, with an estimated OR of 1.2 (95% CI: 1.0 – 1.3) for the association of the CCPKnow score with the odds of discussing family planning, adjusted for years in practice, type of practice, and # of pregnant IBD patients managed in the past year.
  - The degree of comfort managing pregnant IBD patients was not clearly associated with increased odds of discussing family planning with patients.
- To characterize physician knowledge about medication use in pregnancy and breastfeeding:
  - Most physicians (92.3%) knew that pregnant women with IBD should continue some medications. Physician knowledge and use of IBD-medications during pregnancy and breastfeeding was highly variable.

12 From Bench to Bedside: Improving Knowledge Regarding Reproduction and Pregnancy in IBD

12.1 Addressing IBD-specific Reproductive Knowledge and Concerns among Patients and Physicians: University of Alberta Pregnancy in IBD Consultation and Research Clinic

The initial results of this survey study on IBD-specific reproductive knowledge reveal that a lack of knowledge among patients and physicians regarding reproduction and pregnancy issues as they relate to the management of IBD. This lack of knowledge among patients may be contributing to patient concerns and unwarranted fears. Female IBD patients who are childless may be choosing to remain childless (voluntary childlessness) due to concerns about genetically passing the disease to their offspring, IBD-medication induced teratogenicity, pregnancy-induced flare of their IBD, or adverse pregnancy and neonatal outcomes because of their IBD. Physicians, especially general practitioners, vary in their continuation of medications prescribed to pregnant and breastfeeding women with IBD, often stopping medications that can be continued during pregnancy and breastfeeding. Adherence to maintenance medication is important as, in general, clinical remission at the time of conception and during pregnancy is associated with improved pregnancy and neonatal outcomes. However, adherence to treatment may be affected by physician advice, in which case it is important to ensure that physicians have appropriate knowledge regarding IBD-medication use during pregnancy and breastfeeding.

The University of Alberta IBD clinic, in an attempt to address this lack of IBD-specific reproductive knowledge among patients and physicians and to improve outcomes for pregnant IBD patients and their offspring, initiated a Pregnancy in IBD Research Program as shown in Figure 12-1. This Pregnancy in IBD Research Program includes the Pregnancy in IBD Consultation and Research Clinic as well as the Pregnancy in IBD Knowledge Translation Program.

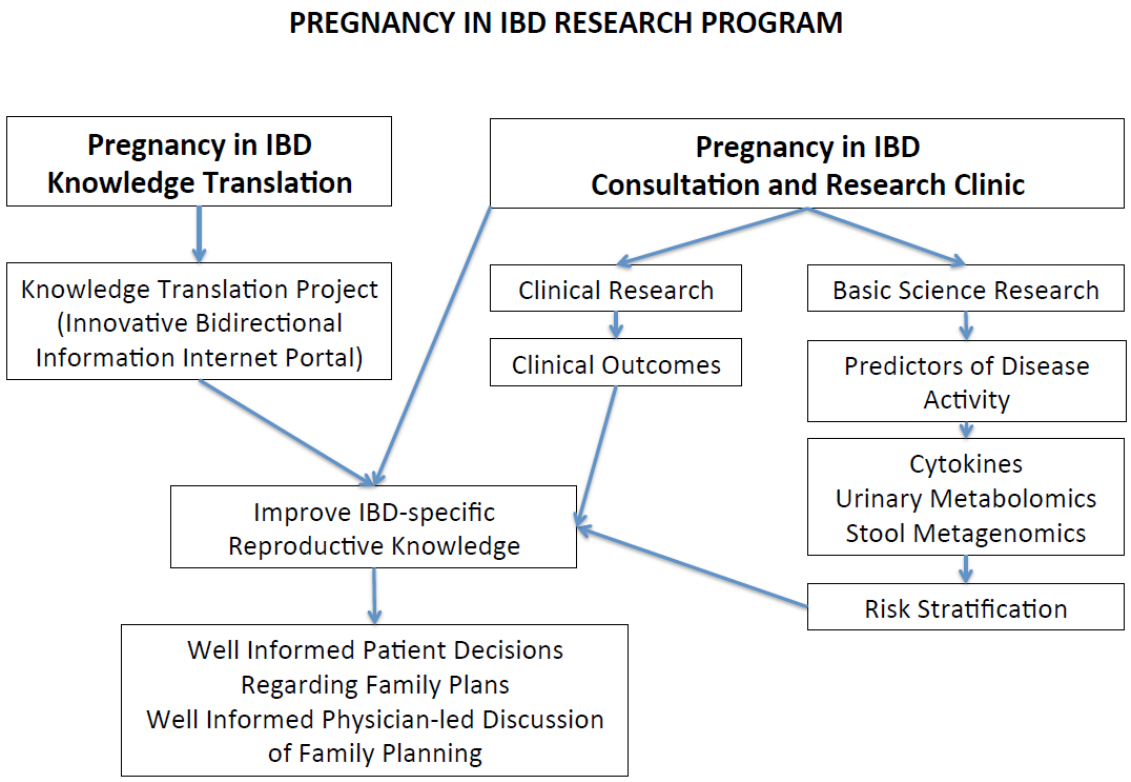

Figure 12-1: Pregnancy in IBD Research Program, University of Alberta Hospital, 2013-2014

12.2 Pregnancy in IBD Consultation and Research Clinic

The main objective of this clinic is to provide a specialized preconception and pregnancy clinic that provides education and counseling, close monitoring, and prompt urgent assessments with adjustments of medications, in order to optimize maternal and neonatal outcomes. The clinic is also designed to provide long-term prospective follow-up with detailed clinical and biological evaluation for research purposes.

All patients seen at the U of A Pregnancy in IBD Consultation and Research Clinic receive an in-depth personalized consultation regarding their IBD and gastroenterological health, and how this relates to pregnancy. They are enrolled into the clinic schedule, which includes a visit pre-conception, a visit in each trimester, and visits within 3 months, 6 months, 9 months, and 12 months post-partum. Patients who are flaring are seen with extra visits as needed. Patients are counseled regarding the use of the medications they are currently taking during the pre-conception, pregnancy, and post-partum and breastfeeding periods, as appropriate. If needed, adjustments to their medications are recommended with communication back to the referring physicians.

Patients who are not already being followed by an obstetrician are referred to the Maternal Fetal Medicine (MFM) Clinic at the Royal Alexandra Hospital. The MFM clinic is a multidisciplinary clinic with a perinatologist, maternal medicine specialist, genetic counselor, and nurses. The MFM clinic follows the growth of the fetus and makes

recommendations regarding necessary optimization of maternal and fetal health. They will make referrals to obstetricians who are comfortable managing women with IBD. All communications to referring physicians include educational tips regarding medications and IBD effect on pregnancy.

12.2.1 Clinical Research Program

Women who consent to participate in the clinical research program are enrolled into CEGIIR (Centre of Excellence for Gastroenterological Inflammation and Immunity Research). A special Pregnancy in IBD module for CEGIIR includes questionnaires on patient background, IBD history, reproductive history, and current medications and supplements. The module also includes questionnaires regarding clinical disease activity using the Harvey Bradshaw Index (HBI) for Crohn's disease, and Mayo score for ulcerative colitis, as well as the Short IBD Quality of Life (SIBDQ) survey. Additional questions include pregnancy specific symptoms and signs of complications. The patients' clinical laboratory indices of disease activity (C-reactive protein (CRP), ferritin, CBC (hgbn)) are also being recorded at each visit.

Eventually, the proposed clinical research study will be to assess whether this model of intensive counselling and monitoring is associated with improved maternal and fetal outcomes. The study will also assess the changes in clinical disease activity, and in quality of life, during pregnancy in IBD patients. Finally, the study will assess whether pre-conception and 1st trimester (i.e. baseline) measurements of clinical disease activity

(either by questionnaires or by laboratory measurements) can predict IBD disease course during pregnancy.

12.2.2 Basic Science Research Program

Patients who consent to the basic science research component of the clinic are enrolled into CEGIIR and provide blood, urine, and stool samples at each visit. The samples will be analyzed for serum cytokine profile, urinary metabolomics and stool metagenomics (which is indicative of the microbiome or gut bacterial flora) changes, c-reactive protein (CRP), and fecal calprotectin (FCP) (a marker specific for gut inflammation) changes during the reproductive and pregnancy period.

Studies on pregnancy, and pregnancy in inflammatory conditions, have shown that pregnancy is an immunological time period, with changes in the cytokine milieu[1-3]. It recently was hypothesized that the gut microbiome may play a role in pregnancy and IBD[4]. Therefore, the analysis on changes in serum cytokines and stool microbiome will contribute to the overall understanding of the pathophysiological interaction between reproduction and pregnancy and IBD. CRP and FCP will be studied as biomarkers for current disease activity, and as biomarkers to predict future disease activity. For example, the question is - can the CRP or FCP of a woman with IBD who is pre-conception or in early pregnancy objectively identify disease activity even if she is clinically well? Or can the pre-conception CRP or FCP act as biomarkers to predict

disease activity during pregnancy and thus be used to stratify women with IBD based on risk as they approach the pregnancy period?

Biomarkers that can identify current disease activity in pre-conception or pregnant women with IBD would be important to identify for use, as they would allow clinicians to identify women who are asymptomatic but actually have disease activity. Especially if the woman is already pregnant, these biomarkers may be able to distinguish IBD disease activity from non-inflammatory etiology of her gastrointestinal symptoms, and hopefully avoid the need for endoscopic evaluation during pregnancy. These biomarkers could also hopefully predict future disease activity and thus stratify women with IBD based on risk of disease activity during her subsequent pregnancy; this would be important as it would provide knowledge regarding her disease behavior, and strengthen the need for her to adhere to medications or perhaps to escalate therapy.

12.3 Knowledge Translation Research Program

This study has shown that patients and physicians obtain information regarding reproduction and IBD from different sources. Patients obtain information from their gastroenterologist, general practitioner, and the Internet. A higher percentage of childless women compared to women who have children obtain information from the Internet. Physicians obtain information from GI and IBD-specific conferences, specialist colleagues, and the Internet. Therefore, educational activities targeting patients and physicians should flow, in part, through improving gastroenterologist and general

practitioner knowledge, since many patients obtain information from these sources, and also through the Internet since both patients and physicians obtain information from the Internet.

The U of A Pregnancy in IBD group has designed and will implement a Knowledge-to-Action project entitled “Improving Knowledge Regarding Pregnancy and IBD”. For this project, the Pregnancy in IBD clinic is developing an innovative online bidirectional educational portal to improve IBD-specific reproductive knowledge. The portal will consist of a series of educational video clips and informational text that will cover topics such as genetics, fertility, pregnancy, delivery, postpartum and breastfeeding, and medications during pregnancy and IBD. There will also be a FAQ section and an open forum by which patients can ask questions and the health care team will interact and provide answers. In order to evaluate the effectiveness of this KT tool, participants will be asked to complete pre- and post- surveys that will evaluate their IBD-specific reproductive knowledge (using the CCPKnow survey), their IBD-specific reproductive concerns and attitudes, as well as their usage of the website. Upon completion of the study, the portal will be opened to all IBD patients, and eventually modified to include physician-directed components.

This internet based educational module is only one aspect of the knowledge translation program. Two main objectives of this pilot project are to 1) to investigate the effectiveness of internet-based methods for improving knowledge, and 2) to conduct a

pilot to investigate the effectiveness of such a tool for reaching out to patients who live in more remote areas of Alberta. The results from this thesis reveal that the relationship between knowledge, concerns, and sources of worry about IBD-specific reproductive issues and decisions about having children is very complex and multifactorial. Therefore, future educational tools regarding reproductive issues in IBD will be developed based on feedback from women with IBD; this can be obtained from focus groups, having women with IBD test draft educational materials prior to launching or interactive seminars that include women with IBD. In addition, these educational activities can be opened up to include men with IBD, with further study on their IBD-specific reproductive knowledge and concerns. Finally, focus groups, seminars, and case studies can be designed to include physicians who treat women with IBD, in order identify effective ways to educate physicians.

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13 CONCLUSION: Increased IBD-specific Reproductive Knowledge is Associated with Decreased Odds of Childlessness among Women with IBD

Identifying IBD-specific reproductive knowledge deficits and the factors affecting knowledge and decisions among women with IBD and among physicians who manage women with IBD will allow development of targeted educational activities to ensure that women with IBD are equipped to make informed decisions regarding family planning and that physicians managing women with IBD are equipped to make informed practice decisions.

This thesis study has shown that there is a strong inverse relationship between IBD-specific reproductive knowledge and childlessness among women with IBD. It has also identified important IBD-specific reproductive knowledge deficits among women with IBD. The study has shown that discussion of family planning with a physician, and especially with a gastroenterologist, is associated with decreased odds of having poor knowledge among women with IBD. However, the study also showed that IBD-specific reproductive knowledge among physicians is variable, and that general practitioners have lower median levels of IBD-specific reproductive knowledge than gastroenterologists. In addition, it showed that physician continuation of medications prescribed to pregnant and breastfeeding women with IBD is highly variable, indicating knowledge deficits among physicians.

The study suggests that potential targets for educational activities to improve IBD-specific reproductive knowledge among women with IBD would be via their gastroenterologist, their general practitioner, and the Internet. Therefore, the "Improving Knowledge Regarding Pregnancy and IBD" Knowledge to Action project will be targeting patients via the Internet. The next step will be to educate and improve knowledge among gastroenterologists and general practitioners. The Pregnancy in IBD Research Program partly addresses these targets as better understanding of the pathophysiological interaction between pregnancy and IBD, and of biomarkers to predict disease activity and for risk stratification, will contribute to the medical community knowledge in general. In addition, the Pregnancy in IBD clinic also functions as a knowledge translation tool as communications are sent back to the referring physicians with educational tips.

Improving IBD-specific reproductive knowledge among patients with IBD and physicians who manage patients with IBD is one step towards addressing IBD-specific reproductive knowledge deficits, concerns, and sources of worry that may be contributing to voluntary childlessness among women with IBD.

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Appendix A-1: Patient Checklist

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

Zeidler Family Gastrointestinal Health & Research Institute
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Phone: 780-248-1031
Fax: 780-248-1041

PATIENT CHECKLIST

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning

Please READ THIS FIRST, and follow the instructions below:

- ☐ 1) Read the BLUE invitation letter. If you agree to participate, proceed to steps 2 and 3.
- ☐ 2) Read the PINK information sheet, initial each page, sign one Patient Consent Form, and keep the other copy for yourself.
- ☐ 3) Complete the WHITE Questionnaire

Once you have completed steps 1 to 3, please place the following documents in the provided envelope and return the envelope at any Canada post outlet or mailbox, or to the clinic.

- ☐ PINK information sheet and consent form, initialled and signed
- ☐ WHITE Questionnaire, completed
- ☐ YELLOW checklist, completed

Surveys should be returned June 11, 2013.

Please provide your full mailing address below so that we can mail you a $10 Tim Horton's gift card to reimburse you for your time:

Name: _____

Address: _____

_____

_____

Thank you for participating in this research study.

Appendix A-2: Patient Information Sheet and Consent Form

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

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Zeidler Ledcor Centre L-10B
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PATIENT INFORMATION SHEET

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning

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Principal Investigator: Dr. Richard N. Fedorak

Sub-Investigator(s): Dr. V. Huang, Dr. K. Kroeker, Dr. L. Dieleman, Dr. K. Goodman, Dr. K. Hegadoren

Dr. D. Kao	Dr. J. Liu	Dr. E. Semlacher	Dr. S. van Zanten
Dr. A. Lazarescu	Dr. J. McKaigney	Dr. C. Teshima	Dr. S. Zepeda

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BACKGROUND

Women with chronic illnesses, such as Inflammatory Bowel Diseases (IBD), often have difficulties making decisions regarding family planning compared to women who are healthy. Previous research has shown that concern regarding chronic illness and medication use can lead to decisions of voluntary childlessness. We aim to assess if certain views and knowledge, or lack of, surrounding these issues affects decision-making regarding family planning.

PURPOSE

You are being asked to participate in this research study in order to determine the impact of knowledge regarding fertility, pregnancy, and medication use in inflammatory bowel disease on decision-making regarding family planning.

You are being asked to participate for the following reasons:

a) You have Crohn's disease or ulcerative colitis
b) You are above the age of 18

DESCRIPTION OF STUDY

Participating in this study will involve completion and return of:

a) A questionnaire about your health, knowledge regarding reproductive issues in IBD, and your beliefs and decisions. This will take approximately 15-20 minutes.
b) Signed consent to allow us to access your medical records (including Alberta Netcare) if needed to obtain further details of your medical history (regarding diagnosis, treatment, extent of disease, etc.)

POSSIBLE RISKS

No risks are anticipated from participation in this study. If you have questions or concerns, you may contact the study investigator at the number provided below.

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease

POSSIBLE BENEFITS
You may not benefit directly from this study, but you will help researchers better understand whether knowledge regarding reproductive issues in IBD patients affects decision-making regarding family planning. If there is a relationship between knowledge and decision-making, future educational activities may be developed as a result of this study, in order to help patients such as yourself in their decision-making.

CONFIDENTIALITY
Personal health records relating to this study will be kept confidential. Any research data collected about you during this study will not identify you by name, only by your initials and a coded number. Your name will not be disclosed outside the research clinic. Any report published as a result of this study will not identify you by name.

For this study, the study doctor may need to access your personal health records (including electronic health records from Alberta Netcare) for health information such as past medical history and test results. The health information collected as part of this study will be kept confidential unless release is required by law, and will be used only for the purpose of the research study.

By signing the consent form you give permission to the study staff to access any personally identifiable health information, which is under the custody of other health care professionals as deemed necessary for the conduct of the research. Study documents and study data will be stored for a minimum of 5 years in secured locked storage of the principal investigator, and on the secured intranet at Division of Gastroenterology at the University of Alberta.

VOLUNTARY PARTICIPATION
You are free to withdraw from the research study at any time, and your continuing medical care will not be affected in any way. You are free to leave questions blank if you so choose. If the study is not undertaken or if it is discontinued at any time, the quality of your medical care will not be affected. If any knowledge gained from this or any other study becomes available which could influence your decision to continue in the study you will be promptly informed.

REIMBURSEMENT OF EXPENSES
Upon return of the questionnaire package, we will mail you a $10 Tim Horton's gift card.

CONTACTS:
If you have any questions about the study, you may contact:
Dr. Vivian Huang, IBD Fellow, at 780-248-1031 or vwhuang@ualberta.ca.

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615.

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
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PATIENT CONSENT FORM
Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning

Principal Investigator: Dr. Richard N. Fedorak

Sub-Investigator(s): Dr. V. Huang, Dr. K. Kroeker, Dr. L. Dieleman, Dr. K. Goodman, Dr. K. Hegadoren

Dr. D. Kao	Dr. J. Liu	Dr. E. Semlacher	Dr. S. van Zanten
Dr. A. Lazarescu	Dr. J. McKaigney	Dr. C. Teshima	Dr. S. Zepeda

	Yes	No
1) Do you understand that you have been asked to participate in this research study?	☐	☐
2) Have you read and received a copy of the attached Information Sheet?	☐	☐
3) Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
4) Have you had an opportunity to ask questions and discuss this study?	☐	☐
5) Do you understand that you are free to withdraw from the study at any time, without having to give a reason and without affecting your future medical care?	☐	☐
6) Do you understand the issue of confidentiality, and do you understand that the research team will have access to your medical record?	☐	☐

Who explained this study to you?_____

I agree to take part in this study: YES ☐ NO ☐

Signature of Research Subject *Date* *Printed Name* _____

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator or Delegate *Date* *Printed Name* _____

****

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A SIGNED AND DATED COPY GIVEN TO THE RESEARCH SUBJECT

Appendix A-3: Patient Questionnaire

UNIVERSITY OF ALBERTA

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Division of Gastroenterology
Department of Medicine

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PATIENT QUESTIONNAIRE
Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning

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Principal Investigator: Dr. Richard N. Fedorak

Sub-Investigator(s): Dr. V. Huang, Dr. K. Kroeker, Dr. L. Dieleman, Dr. K. Goodman, Dr. K. Hegadoren

Dr. D. Kao	Dr. J. Liu	Dr. E. Semlacher	Dr. S. van Zanten
Dr. A. Lazarescu	Dr. J. McKaigney	Dr. C. Teshima	Dr. S. Zepeda

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DEMOGRAPHICS:

1. In what year were you born? _____ (YYYY)

2. What is your highest level of education?
   - ☐ 0 Up to Grade 12 (Grades completed _____)
   - ☐ 1 College
   - ☐ 2 University Bachelor
   - ☐ 3 Graduate degree
   - ☐ 4 Professional school degree
   - ☐ 5 Other _____

3. What is your current employment status?
   - ☐ 0 unemployed
   - ☐ 1 part time employment
   - ☐ 2 full time employment
   - ☐ 3 Other _____

4. How many siblings do you have? _____

5. Please indicate how many of the following biological relatives have a diagnosis of IBD?
   - ☐ 0 None
   - ☐ 1 Mother
   - ☐ 2 Father
   - ☐ 3 Siblings (How many?_____)
   - ☐ 4 Paternal grandparent(s)
   - ☐ 5 Maternal grandparent(s)
   - ☐ 6 Other: _____

6. What is your ethnicity

☐0 Caucasian
☐1 Non-caucasian
Please describe: _____

7. What is your current marital status?

☐0 Single
☐1 Married/in a long-term relationship
☐2 Divorced
☐3 Widowed

If you are single, please skip #8-10 and go to MEDICAL HISTORY section

8. If applicable, in what year (after you turned 18) did you start living with your spouse/common-law partner? _____ (YYYY)

9. Does your partner have a diagnosis of IBD?

☐0 No
☐1 Yes

10. Does IBD run in your spouse' family?

☐0 No
☐1 Yes

MEDICAL HISTORY

1. Have you ever been diagnosed with any of the following? Please indicate the year diagnosed:
   a. Mood disorder, including depression
      ☐0 No
      ☐1 Yes _____(YYYY)
      please describe: _____
   b. Irritable bowel syndrome
      ☐0 No
      ☐1 Yes _____(YYYY)
   c. Gynecological condition causing infertility
      ☐0 No
      ☐1 Yes _____(YYYY)
      please describe: _____
   d. Diabetes
      ☐0 No
      ☐1 Yes _____(YYYY)
   e. Other chronic conditions
      ☐0 No
      ☐1 Yes _____(YYYY)
      please describe: _____

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease

INFLAMMATORY BOWEL DISEASE HISTORY

1. What is your diagnosis?
   - ☐ 0 Crohn's disease
   - ☐ 1 Ulcerative colitis
   - ☐ 2 Indeterminate colitis

2. When were you diagnosed? _____ (YYYY)

3. Which IBD medications have you ever been on? Please check off all that apply.
   - ☐ 0 Do not remember
   - ☐ 1 Sulfasalazine (Salazopyrine)
   - ☐ 2 Mesalamine/5-aminosalicylates (Asacol, Mesavant, Pentasa, Salofalk)
   - ☐ 3 Budesonide (Entocort)
   - ☐ 4 Steroids (Predisone, Solumedrol)
   - ☐ 5 Methotrexate (MTX)
   - ☐ 6 Azathioprine (Imuran)/6-mercaptopurine 6-MP, Purinethol)
   - ☐ 7 Anti-TNF/Biologics (Infliximab/Remicade, Adalimumab/Humira, Certolizumab/Cimzia)
   - ☐ 8 Antibiotics (Ciprofloxacin, Flagyl, other)
   - ☐ 9 Other, please list:

     _____

4. In the past year, has your physician ever put you on Corticosteroids (Prednisone) for a flare of your disease?
   - ☐ 0 No
   - ☐ 1 Yes

5. Have you ever had perianal disease (perianal fistula, abscess)?
   - ☐ 0 No
   - ☐ 1 Yes _____(YYYY)

6. Have you ever had surgery for colectomy (removal of colon) with creation of in internal pouch?
   - ☐ 0 No
   - ☐ 1 Yes (please specify the year: _____(YYYY)

7. Have you ever had surgery involving an ostomy (external bag)?
   - ☐ 0 No
   - ☐ 1 Yes (please specify the year: _____(YYYY)

8. Who have you discussed family planning with? Please select all that apply:
   - ☐ 0 I have not discussed with anyone
   - ☐ 1 Gastroenterologist
   - ☐ 2 General medicine specialist
   - ☐ 3 Specialist (gynaecologist, obstetrician)
   - ☐ 4 Family Physician
   - ☐ 5 IBD nurse
   - ☐ 6 Pharmacist
   - ☐ 7 Family and friends
   - ☐ 8 Other, please list: _____

9. Where do you obtain your information regarding family planning and inflammatory bowel disease? Please select all that apply:
   - ☐ 0 I have not sought information
   - ☐ 1 Gastroenterologist
   - ☐ 2 Family Physician
   - ☐ 3 IBD nurse
   - ☐ 4 Pharmacist
   - ☐ 5 Internet
   - ☐ 6 Pamphlets and brochures
   - ☐ 7 Books
   - ☐ 8 Support groups
   - ☐ 9 Family and Friends
   - ☐ 10 Other, please list: _____

REPRODUCTIVE HISTORY

1. Have you ever seen a fertility specialist, or had fertility treatment (hormones, in vitro fertilization)?
   - ☐ 0 No
   - ☐ 1 Yes

2. Are you currently pregnant?
   - ☐ 0 No
   - ☐ 1 Yes

3. Have you ever been pregnant (including miscarriages, abortions)?
   - ☐ 0 No
   - ☐ 1 Yes

If you have NOT been pregnant, please skip #4 and go to question 5.

4. Please fill out the following table for your pregnancy outcomes (indicate # for each):

   Age at IBD Diagnosis: _____

	BEFORE IBD Diagnosis		AFTER IBD Diagnosis	
Pregnancy Planned?	**PLANNED**	**NOT PLANNED**	**PLANNED**	**NOT PLANNED**
# therapeutic abortions				
# spontaneous abortions/miscarriage				
# stillbirths				
# preterm and low birth weight				
# full term and low birth weight				
# full term and healthy				

5. Do you have any adopted children?
   ☐$_0$ No
   ☐$_1$ Yes, how many? _____

6. What is your current status in life regarding children?
   ☐$_0$ do not want to have children
   ☐$_1$ would like adopted children only
   ☐$_2$ trying to become pregnant
   ☐$_3$ have children, would like more
   ☐$_4$ have children, completed family
   ☐$_5$ don't have children, would like to later on
   ☐$_6$ unsure

7. If you are trying to get pregnant, have you tried for more than 1 year (unprotected intercourse, no oral contraception or other forms of contraception)?
   ☐$_0$ No
   ☐$_1$ Yes

8. Did you use contraception before you were diagnosed with IBD?
   ☐$_0$ No
   ☐$_1$ Yes

9. Are you currently using contraception?
   ☐$_0$ No
   ☐$_1$ Yes

10. Just BEFORE your IBD diagnosis, which of the following was true for you:
    - ☐ 0 I had not given birth but planned to some day.
    - ☐ 1 I had not given birth and planned to have adopted children only.
    - ☐ 2 I had not given birth and did not plan to give birth or raise adopted children.
    - ☐ 3 I had given birth and planned to get pregnant again.
    - ☐ 4 I had given birth and did not plan to get pregnant again.
    - ☐ 5 Other _____

11. SINCE being diagnosed with IBD, have you changed your feelings/perspectives about having your own children?
    - ☐ 0 No
    - ☐ 1 Yes, in what way?
        - ☐ a Now I plan to not have children because of my illness
        - ☐ b Now I plan to have children despite my illness
        - ☐ c Now I plan to adopt children because of my illness
        - ☐ d other _____

12. If you have been pregnant after you were diagnosed with IBD, did the course of the pregnancy influence your decision to become pregnant again?
    - ☐ 0 Not applicable
    - ☐ 1 No
    - ☐ 2 Yes

13. If yes, how did it affect you?
    - ☐ 0 I chose not to become pregnant again
    - ☐ 1 I chose to become pregnant again
    - ☐ 2 I chose to adopt children in the future

If you do not want to become pregnant OR you have children but do not want to become pregnant again, please answer #14 and #15:

If you plan to have more pregnancies, please skip #14 and #15, and go to question #16:

14. Which of the following, if any, **because of your IBD**, had a part in your decision not to become pregnant? Please check all that apply:
    - ☐ 1 medical advice that conception is not possible/inadvisable with IBD
    - ☐ 2 concern for the possibility of genetically passing my disease to my child
    - ☐ 3 concern for not being able to care for a child
    - ☐ 4 concern about the added stress of raising a child
    - ☐ 5 concern of the possibility of chronic illness leading to birth defects
    - ☐ 6 concern of the possibility of having a stillbirth or a miscarriage
    - ☐ 7 concern of the possibility of IBD medications causing birth defects
    - ☐ 8 concern of the possibility of having a worsening of my disease as a result of pregnancy
    - ☐ 8 concern of being unable to have a baby due to possible decreased fertility
    - ☐ 10 having a negative body image of myself causes me to restrict my sexual activity
    - ☐ 11 IBD related fatigue
    - ☐ 12 Other reason _____
    - ☐ 13 unsure
    - ☐ 14 none of the above

15. Which of the following, if any, **not because of your IBD**, had a part in your decision not to become pregnant? Please check all that apply:

- ☐ 0 do not want to have biological children
- ☐ 1 chose to adopt
- ☐ 2 not ready to have children yet
- ☐ 3 I had already completed my family
- ☐ 4 Lifestyle choice (never wanted children)
- ☐ 5 not with a partner
- ☐ 6 age
- ☐ 7 still hoping to have children in the future
- ☐ 8 financial reasons
- ☐ 9 family support issues
- ☐ 10 because one of my previous pregnancies resulted in a miscarriage
- ☐ 11 have pre-existing fertility/gynaecological condition
- ☐ 12 partner has infertility issues
- ☐ 13 Other reason _____
- ☐ 14 unsure
- ☐ 15 none of the above

If you plan to have more pregnancies, please answer #16, otherwise skip to #17:

16. Which of the following, if any, **because of your IBD,** concerns you? Please check all that apply:

- ☐ 1 medical advice that conception is not possible/inadvisable with IBD
- ☐ 2 concern for the possibility of genetically passing my disease to my child
- ☐ 3 concern for not being able to care for a child
- ☐ 4 concern about the added stress of raising a child
- ☐ 5 concern of the possibility of chronic illness leading to birth defects
- ☐ 6 concern of the possibility of having a stillbirth or a miscarriage
- ☐ 7 concern of the possibility of IBD medications causing birth defects
- ☐ 8 concern of the possibility of having a worsening of my disease as a result of pregnancy
- ☐ 9 concern of being unable to have a baby due to possible decreased fertility
- ☐ 10 having a negative body image of myself causes me to restrict my sexual activity
- ☐ 11 IBD related fatigue
- ☐ 12 Other concern_____
- ☐ 13 unsure
- ☐ 14 none of the above

17. Have you ever been worried about taking certain medications and how they might interact with the possibility of becoming pregnant?

- ☐ 0 No
- ☐ 1 Yes

18. Has your gastroenterologist ever discussed the issue of whether or not to change the medications you are on for your IBD during pre-conception (trying to become pregnant) or during pregnancy with you?

- ☐ 0 No
- ☐ 1 Yes

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease

19. Have you changed or stopped your medications while trying to become pregnant without informing your physician?

☐ 0 No
☐ 1 Yes

20. If you were pregnant after you were diagnosed with IBD, did you change or stop your medication(s) during pregnancy without informing your physician?

☐ 0 No
☐ 1 Yes

21. Which of the following issues regarding reproduction in inflammatory bowel disease would you like more information on (please select all that apply):

☐ 1 IBD effect on fertility
☐ 2 IBD effect on pregnancy outcome
☐ 3 IBD effect on breastfeeding
☐ 4 IBD medications effect on fertility
☐ 5 IBD medications effect on pregnancy outcomes
☐ 6 IBD medications effect on breastfeeding
☐ 7 IBD related surgery effect on fertility
☐ 8 IBD related surgery effect on pregnancy outcome
☐ 8 other _____

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease

BELIEFS and OPINIONS

Considering your decision about having your own children, how strongly do you agree with the following statements?

1	2	3	4	5
Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree

A. I do not like children.	☐1	☐2	☐3	☐4	☐5
B. Being a mother is not a major goal in my life.	☐1	☐2	☐3	☐4	☐5
C. I am not in a relationship and I am not ready to have children.	☐1	☐2	☐3	☐4	☐5
D. I do not plan to have children because of the poor outcome of my previous pregnancies.	☐1	☐2	☐3	☐4	☐5
E. My physician told me not to become pregnant.	☐1	☐2	☐3	☐4	☐5
F. I am worried that having IBD decreases my chances of successful conception.	☐1	☐2	☐3	☐4	☐5
G. I am worried that I will pass my IBD genetically to my child.	☐1	☐2	☐3	☐4	☐5
H. I am worried about the effects of my IBD on pregnancy.	☐1	☐2	☐3	☐4	☐5
I. I am worried that pregnancy may worsen my disease (cause a flare).	☐1	☐2	☐3	☐4	☐5
J. I am worried that the medications I am on to control my IBD may cause birth defects.	☐1	☐2	☐3	☐4	☐5
K. I am worried that I may not be able to care for my child as a result of my disease.	☐1	☐2	☐3	☐4	☐5
L. I am considering not having children because of my IBD.	☐1	☐2	☐3	☐4	☐5

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease

Crohn's and Colitis Pregnancy Knowledge (CCPKnow) score

Please answer the following questions without using any help. Select only ONE answer for each question.

Inheritance

1. Inflammatory bowel disease
   - ☐ a will always pass from a parent to a child
   - ☐ b will never pass from a parent to a child
   - ☐ c is more likely to affect a child if mother or father are suffering from it
   - ☐ d does not run in families
   - ☐ e don't know

2. The risk of passing on inflammatory bowel disease to a child
   - ☐ a is zero
   - ☐ b can be exactly determined by genetic testing
   - ☐ c is less than 10%
   - ☐ d can be reduced by medication
   - ☐ e don't know

Fertility

3. Men with inflammatory bowel disease
   - ☐ a usually do not have problems with infertility
   - ☐ b should avoid all medication when trying for a baby
   - ☐ c should not have children with women suffering from inflammatory bowel disease
   - ☐ d should not father children after the age of 40
   - ☐ e don't know

4. The chances of a woman becoming pregnant
   - ☐ a are not reduced if her ulcerative colitis is active
   - ☐ b are not reduced if she has an ileo-anal pouch
   - ☐ c are generally good if she suffers from ulcerative colitis
   - ☐ d are not influenced by the activity of Crohn's disease
   - ☐ e don't know

Disease activity

5. What is most important when trying for a baby?
   - ☐ a women should come off all drugs before becoming pregnant
   - ☐ b inflammatory bowel disease should be well controlled before becoming pregnant
   - ☐ c there is no need for women to discuss it with her doctor before becoming pregnant
   - ☐ d women with Crohn's disease should not stop smoking
   - ☐ e don't know

6. Women with inflammatory bowel disease
   - ☐ a should delay trying for a baby until their disease has been controlled by medication
   - ☐ b never experience flares of their disease during pregnancy
   - ☐ c will always experience a flare during their pregnancy
   - ☐ d often need surgery during pregnancy
   - ☐ e don't know

7. Active inflammatory bowel disease during pregnancy
   - ☐ a does not affect the chance of having a healthy baby
   - ☐ b does not cause early birth
   - ☐ c should be put up with to protect the unborn from drug effects
   - ☐ d should be treated with some types of drugs to protect the pregnancy
   - ☐ e don't know

Drugs

8. Pregnant women with inflammatory bowel disease
   - ☐ a should avoid all drugs
   - ☐ b should continue some medications
   - ☐ c should use herbal medications only
   - ☐ d do not need to discuss drugs with their doctor
   - ☐ e don't know

9. Infliximab or Adalimumab
   - ☐ a are general seen as 'probably safe' in pregnancy
   - ☐ b cause serious harm to babies
   - ☐ c do not work in pregnant women
   - ☐ d should always be stopped prior to conception
   - ☐ e don't know

10. The drug Methotrexate
    - ☐ a does not cause birth defects
    - ☐ b is safe in pregnancy when taken as a tablet
    - ☐ c should always be stopped 3-6 months before trying for a baby
    - ☐ d does not need to be stopped in males who are taking it when they are trying for a baby
    - ☐ e don't know

11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc)
    - ☐ a should not be taken as a suppository or enema
    - ☐ b should be avoided at all cost
    - ☐ c does not work
    - ☐ d is safe and should be continued
    - ☐ e don't know

12. During pregnancy Azathioprine or 6-Mercaptopurine
    - ☐ a cause serious harm to babies
    - ☐ b do not work
    - ☐ c can be continued
    - ☐ d are considered unsafe
    - ☐ e don't know

Mode of delivery

13. Women with inflammatory bowel disease
    - ☐ a should never have a caesarean section
    - ☐ b must have a caesarean section
    - ☐ c and peri-anal disease (abscesses or fistulae around and outside the back passage) are advised against having a caesarean section
    - ☐ d can have a vaginal delivery in most cases
    - ☐ e don't know

14. Peri-anal disease (abscesses or fistulae around and outside the back passage) that occurs after a normal vaginal delivery
    - ☐ a is common in ulcerative colitis
    - ☐ b responds well to creams
    - ☐ c is more likely if a woman suffered from it previously
    - ☐ d is never seen in women with Crohn's disease
    - ☐ e don't know

Pregnancy outcomes

15. Women suffering from inflammatory bowel disease
    - ☐ a usually have bigger and heavier babies than other women
    - ☐ b often give birth a bit early
    - ☐ c often give birth late
    - ☐ d always have their baby on time even when Crohn's disease flares
    - ☐ e don't know

16. Birth defects in babies of mothers with inflammatory bowel diseases
    - ☐ a are a common problem
    - ☐ b occur slightly more often than in babies of mothers without inflammatory bowel disease
    - ☐ c are usually due to drug side effects
    - ☐ d can be prevented by vaccinations
    - ☐ e don't know

17. The chances of having a healthy baby for mothers suffering from inflammatory bowel disease
    - ☐ a are less than 50%
    - ☐ b are very good
    - ☐ c depend on the method of delivery
    - ☐ d can be improved by avoiding medication
    - ☐ e don't know

Breastfeeding

18. Mothers suffering from inflammatory bowel disease
    - ☐ a should not breast feed to avoid passing the disease on to the child
    - ☐ b never experience a flare of disease when breastfeeding
    - ☐ c may have tiny amounts of medication in their breast milk
    - ☐ d do not need to discuss breast feeding with their midwife or doctor
    - ☐ e don't know

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THANK YOU FOR PARTICIPATING IN THIS RESEARCH STUDY.

Please return this questionnaire with one signed PINK consent form and the YELLOW checklist in the envelope provided.

Appendix A-4: Patient Reminder

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

Zeidler Family Gastrointestinal Health & Research Institute
Zeidler Ledcor Centre L-10B
University of Alberta, 130 University Campus
Edmonton, Alberta, Canada T6G 2X8

vwhuang@ualberta.ca
www.departmentofmedicine.ualberta.ca/cegiir
Phone: 780-248-1031
Fax: 780-248-1041

PATIENT INVITATION LETTER
Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning

April 2013

Dear ,

Recently, you were given or mailed a survey package for a study being conducted by the Division of Gastroenterology. **If you have already responded, we thank you for your participation.**

As we are developing an IBD clinic for pregnancy, your views on reproductive issues in inflammatory bowel disease and decisions regarding family planning are very important to us. Your views will also increase our understanding of how to improve the quality of life for people with inflammatory bowel disease.

If you prefer to complete the questionnaire electronically, please go to the following Survey Monkey Link.

Survey Link: https://www.surveymonkey.com/s/GPRHGMC

To help compensate you for your time, we will reimburse you with a $10 Tim Horton's gift card for completion of the questionnaires.

Please submit your survey responses by June 7, 2013 as we will be hosting an online seminar on Pregnancy and IBD on Tuesday June 11, 2013 at 4pm. For further details, go to http://www.ibdclinic.ca/ibd-tv/

If you have any questions pertaining to this research study, please contact Dr. Vivian Huang, IBD fellow at vwhuang@ualberta.ca or 780-248-1031.

Sincerely,

VIVIAN HUANG, MD, FRCPC
Gastroenterology IBD Fellow

RICHARD N FEDORAK, MD, FRCPC, FRCP (London) FRS
Professor of Medicine

Dear ,

Recently, you were given or mailed a survey package for a study being conducted by the Division of Gastroenterology, **Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning.**

This is a reminder, that if you are interested in participating, the study is still ongoing. (If you have completed and returned the survey, but have not yet received your Tim Horton's gift card for reimbursement, please send me your name and address in reply to this email. There were a few surveys that were returned without this information. I cannot track and reimburse for completed surveys if I do not have the yellow sheet with the name and address.)

If you prefer to complete the questionnaire electronically, please click on the following Survey Monkey Link. Please note there is an electronic version of the consent form that must be completed prior to completion of the questionnaire.

Survey Link: https://www.surveymonkey.com/s/GPRHGMC

To help compensate you for your time, we will reimburse you with a $10 gift card for completion of the questionnaires. If you mail in the surveys, please include the yellow checklist form with your address. If you complete the electronic survey, please fill in the final address form before submission.

If you have any questions pertaining to this research study, please contact Dr. Vivian Huang, IBD fellow at vwhuang@ualberta.caor 780-248-1031.

Sincerely,
Vivian Huang

Patient Views Regarding Reproductive Issues in Inflammatory Bowel Disease and Decisions Regarding Family Planning

Appendix A-5: Electronic Web-based Version of Patient Questionnaire

INFORMATION SHEET, page 1

PATIENT VIEWS REGARDING REPRODUCTIVE ISSUES IN INFLAMMATORY BOWEL DISEASE and DECISIONS REGARDING FAMILY PLANNING

Principal Investigator: Dr. Richard N. Fedorak
Sub-Investigator(s): Dr. V. Huang, Dr. K. Kroeker, Dr. L. Dieleman, Dr. K. Goodman, Dr. K. Hegadoren

BACKGROUND
Women with chronic illnesses, such as Inflammatory Bowel Diseases (IBD), often have difficulties making decisions regarding family planning compared to women who are healthy. Previous research has shown that concern regarding chronic illness and medication use can lead to decisions of voluntary childlessness. We aim to assess if certain views and knowledge, or lack of, surrounding these issues affects decision-making regarding family planning.

PURPOSE
You are being asked to participate in this research study in order to determine the impact of knowledge regarding fertility, pregnancy, and medication use in inflammatory bowel disease on decision-making regarding family planning.

You are being asked to participate for the following reasons:
a) You have Crohn's disease or ulcerative colitis
b) You are above the age of 18

DESCRIPTION OF STUDY
Participating in this study will involve completion and return of:
a) A questionnaire about your health, knowledge regarding reproductive issues in IBD, and your beliefs and decisions. This will take approximately 15-20 minutes.
b) Consent to allow us to access your medical records (including Alberta Netcare) if needed to obtain further details of your medical history (regarding diagnosis, treatment, extent of disease, etc.)

POSSIBLE RISKS
No risks are anticipated from participation in this study. If you have questions or concerns, you may contact the study investigator at the number provided below.

POSSIBLE BENEFITS
You may not benefit directly from this study, but you will help researchers better understand whether knowledge regarding reproductive issues in IBD patients affects decision-making regarding family planning. If there is a relationship between knowledge and decision-making, future educational activities may be developed as a result of this study, in order to help patients such as yourself in their decision-making.

Appendix B-1: Physician letter of invitation – groups 1, 2

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

Zeidler Family Gastrointestinal Health & Research Institute
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www.departmentofmedicine.ualberta.ca/cegiir
Phone: 780-248-1031
Fax: 780-248-1041

Physician Knowledge Regarding Reproductive Issues in Inflammatory Bowel Disease

Dear Physician,

I hope you are enjoying the Inflammatory Bowel Disease conference. I am an IBD fellow from the University of Alberta, Edmonton, AB, and I would like to invite you to participate in my questionnaire study to assess physician knowledge regarding reproductive issues in IBD.

If you would like to participate, please find further details below. A copy of the information and consent form and questionnaire is attached. Completion and return of the questionnaire will be taken as implied consent. All responses are anonymous and confidential. Once completed please leave the questionnaire turned face down on your table.

Thank you for your time.

Sincerely,

VIVIAN HUANG, MD, FRCPC
Inflammatory Bowel Disease Fellow
The University of Alberta

Appendix B-2: Physician Information and Consent - groups 1, 2

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

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Fax: 780-248-1041

PHYSICIAN INFORMATION AND CONSENT FORM
Physician Knowledge Regarding Reproductive Issues in Inflammatory Bowel Disease

Principle Investigator: Dr. Richard Fedorak

Sub-Investigator(s): Dr. Vivian Huang, Dr. Karen Kroeker, Dr. Leo Dieleman, Dr. K. Goodman

BACKGROUND:
Women with chronic illnesses, such as inflammatory bowel diseases, often have difficulties making decisions regarding family planning compared to women who are healthy. Previous research has shown that concern regarding chronic illness and medication use can lead to decisions of voluntary childlessness. We want to assess physician knowledge regarding reproductive issues in inflammatory bowel disease, and to assess physician practice patterns with respect to discussing reproductive issues with IBD patients.

DESCRIPTION:
Participating in this study will involve completion of a questionnaire, which will take about 5 minutes.

CONFIDENTIALITY:
Your responses will be completely anonymous. No identifying information is requested.

IMPLIED CONSENT:
By completing and returning the questionnaire, you are providing your informed consent.

CONTACTS:

If you have any questions about the study, you may contact:

Dr. Vivian Huang, IBD Fellow, at 780-248-1031 or vwhuang@ualberta.ca

If you have concerns about your rights as a study participant, you may contact the Research Ethics Office at (780) 492-2615). This office has no affiliation with the study investigators.

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615.

Appendix B-3: Physician Questionnaire

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

Zeidler Family Gastrointestinal Health & Research Institute
Zeidler Ledcor Centre L-10B
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vwhuang@ualberta.ca
www.departmentofmedicine.ualberta.ca/cegiir
Phone: 780-248-1031
Fax: 780-248-1041

PHYSICIAN QUESTIONNAIRE:
Physician Knowledge Regarding Reproductive Issues in Inflammatory Bowel Disease

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Principal Investigator: Dr. Richard N. Fedorak

Sub-Investigator(s): Dr. V. Huang, Dr. K. Kroeker, Dr. L. Dieleman, Dr. K. Goodman

Dr. D. Kao	Dr. J. Liu	Dr. E. Semlacher	Dr. S. van Zanten
Dr. A. Lazarescu	Dr. J. McKaigney	Dr. C. Teshima	Dr. S. Zepeda

---

1) What is your gender?

- ☐ 0 Male
- ☐ 1 Female

2) Please indicate which of the following best describes you:

- ☐ 0 Gastroenterology trainee
- ☐ 1 Surgical trainee
- ☐ 2 General Internist
- ☐ 3 Gastroenterologist
- ☐ 4 Surgeon
- ☐ 5 General Practitioner
- ☐ 6 Other healthcare professional
  Specify_____

If you are a trainee, please skip # 3 – 5 and go to # 6.

3) How many years have you been in practice?

- ☐ 0 < 5 years
- ☐ 1 5 to 10 years
- ☐ 2 11 to 20 years
- ☐ 3 >20 years

4) What type of practice settting do you work in (>50%)?

- ☐ 0 clinical, community hospital
- ☐ 1 private outpatient clinic
- ☐ 2 clinical, academic hospital
- ☐ 3 research, academic hospital

5) What type of practice do you have?

- ☐ 0 Gastroenterology focus
- ☐ 1 Gastroenterology/Hepatology
- ☐ 2 Hepatobilary focus
- ☐ 3 General Medicine
- ☐ 4 General Surgery
- ☐ 5 Family practice
- ☐ 6 Other: specify _____

PHYSICIAN KNOWLEDGE OF REPRODUCTIVE ISSUES IN INFLAMMATORY BOWEL DISEASE

6) Approximately what is the population of the town/city that you practice in?

- ☐ 0 <1,000
- ☐ 1 1,000 to 2,499
- ☐ 2 2,500 to 4,999
- ☐ 3 5,000 to 9,999
- ☐ 4 10,000 to 49,999
- ☐ 5 50,000 to 99,999
- ☐ 6 100,000 to 499,999
- ☐ 7 >500,000

7) What percentage of your patients have IBD?

- ☐ 0 <10%
- ☐ 1 10-24%
- ☐ 2 25 – 50%
- ☐ 3 >50%

8) How many IBD patients do you see each year?

- ☐ 0 0 - 9
- ☐ 1 10 - 50
- ☐ 2 51 - 100
- ☐ 3 100 - 150
- ☐ 4 > 150

9) How many pregnant IBD patients have you managed in the past year?

- ☐ 0 None
- ☐ 1 up to 10
- ☐ 2 10 – 20
- ☐ 3 >20

10) How do you feel about your IBD knowledge in general?

- ☐ 0 Inadequate
- ☐ 1 Enough to get by
- ☐ 2 Very good

11) Do you feel comfortable managing pregnant IBD patients?

- ☐ 1 Not comfortable at all
- ☐ 2 Not comfortable
- ☐ 3 Somewhat
- ☐ 4 Fairly comfortable
- ☐ 5 Very comfortable

12) With a female IBD patient of reproductive age, do you routinely bring up the topic of family planning?

- ☐ 0 No
- ☐ 1 Yes

PHYSICIAN KNOWLEDGE OF REPRODUCTIVE ISSUES IN INFLAMMATORY BOWEL DISEASE

13) What percentage of your female IBD patients of reproductive age inform you when they are trying to become pregnant?

- ☐ 0 <10%
- ☐ 1 10-24%
- ☐ 2 25 – 50%
- ☐ 3 >50%

14) With a female IBD patient of reproductive age who has been trying to conceive for more than 1 year, would you refer to a fertility specialist or gynaecologist?

- ☐ 0 No
- ☐ 1 Yes

15) What percentage of your female IBD patients in your practice inform you when they are pregnant?

- ☐ 0 <10%
- ☐ 1 10-24%
- ☐ 2 25 – 50%
- ☐ 3 >50%

16) Do you routinely refer your pregnant IBD patients to an obstetrician?

- ☐ 0 No
- ☐ 1 Yes

17) Please indicate if you would stop the medication, continue the medication, or are unsure, if your patient informed you she was **trying to conceive, or that she was pregnant.**

Medication	STOP	CONTINUE unchanged	CONTINUE at an adjusted dose or frequency	UNSURE
Sulfasalazine				
Mesalamine (oral)				
Mesalamine (topical)				
Prednisone (oral)				
Prednisone (topical)				
Budesonide/Entocort (oral)				
Budesonide/Entocort (topical)				
Azathioprine/6-MP				
Ciprofloxacin				
Metronidazole				
Methotrexate				
Biologics (Infliximab)				
Biologics (Adalimumab)				

18) Please indicate if you would stop the medication, continue the medication, or are unsure, if your patient informed you she was **breastfeeding.**

Medication	STOP	CONTINUE unchanged	CONTINUE at an adjusted dose or frequency	UNSURE
Sulfasalazine				
Mesalamine (oral)				
Mesalamine (topical)				
Prednisone (oral)				
Prednisone (topical)				
Budesonide/Entocort (oral)				
Budesonide/Entocort (topical)				
Azathioprine/6-MP				
Ciprofloxacin				
Metronidazole				
Methotrexate				
Biologics (Infliximab)				
Biologics (Adalimumab)				

19) Where do you obtain information regarding reproductive issues in inflammatory bowel disease?

☐$_0$ I have not sought information
☐$_1$ IBD-related conferences
☐$_2$ Gastroenterology conferences
☐$_3$ Medical journal subscriptions
☐$_4$ Internet websites
☐$_5$ Literature reviews and searches
☐$_6$ Textbooks
☐$_7$ Specialist colleague consultations
☐$_8$ Other _____

Crohn's and Colitis Pregnancy Knowledge (CCPKnow) score

Select only one answer for each question.

Inheritance

1. Inflammatory bowel disease
   - ☐ a will always pass from a parent to a child
   - ☐ b will never pass from a parent to a child
   - ☐ c is more likely to affect a child if mother or father are suffering from it
   - ☐ d does not run in families
   - ☐ e don't know

2. The risk of passing on inflammatory bowel disease to a child
   - ☐ a is zero
   - ☐ b can be exactly determined by genetic testing
   - ☐ c is less than 10%
   - ☐ d can be reduced by medication
   - ☐ e don't know

Fertility

3. Men with inflammatory bowel disease
   - ☐ a usually do not have problems with infertility
   - ☐ b should avoid all medication when trying for a baby
   - ☐ c should not have children with women suffering from inflammatory bowel disease
   - ☐ d should not father children after the age of 40
   - ☐ e don't know

4. The chances of a woman becoming pregnant
   - ☐ a are not reduced if her ulcerative colitis is active
   - ☐ b are not reduced if she has an ileo-anal pouch
   - ☐ c are generally good if she suffers from ulcerative colitis
   - ☐ d are not influenced by the activity of Crohn's disease
   - ☐ e don't know

Disease activity

5. What is most important when trying for a baby?
   - ☐ a women should come off all drugs before becoming pregnant
   - ☐ b inflammatory bowel disease should be well controlled before becoming pregnant
   - ☐ c there is no need for women to discuss it with her doctor before becoming pregnant
   - ☐ d women with Crohn's disease should not stop smoking
   - ☐ e don't know

6. Women with inflammatory bowel disease
   - ☐ a should delay trying for a baby until their disease has been controlled by medication
   - ☐ b never experience flares of their disease during pregnancy
   - ☐ c will always experience a flare during their pregnancy
   - ☐ d often need surgery during pregnancy
   - ☐ e don't know

7. Active inflammatory bowel disease during pregnancy
   - ☐ a does not affect the chance of having a healthy baby
   - ☐ b does not cause early birth
   - ☐ c should be put up with to protect the unborn from drug effects
   - ☐ d should be treated with some types of drugs to protect the pregnancy
   - ☐ e don't know

Drugs

8. Pregnant women with inflammatory bowel disease
   - ☐ a should avoid all drugs
   - ☐ b should continue some medications
   - ☐ c should use herbal medications only
   - ☐ d do not need to discuss drugs with their doctor
   - ☐ e don't know

9. Infliximab or Adalimumab
   - ☐ a are general seen as 'probably safe' in pregnancy
   - ☐ b cause serious harm to babies
   - ☐ c do not work in pregnant women
   - ☐ d should always be stopped prior to conception
   - ☐ e don't know

10. The drug Methotrexate
    - ☐ a does not cause birth defects
    - ☐ b is safe in pregnancy when taken as a tablet
    - ☐ c should always be stopped 3-6 months before trying for a baby
    - ☐ d does not need to be stopped in males who are taking it when they are trying for a baby
    - ☐ e don't know

11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc)
    - ☐ a should not be taken as a suppository or enema
    - ☐ b should be avoided at all cost
    - ☐ c does not work
    - ☐ d is safe and should be continued
    - ☐ e don't know

12. During pregnancy Azathioprine or 6-Mercaptopurine
    - ☐ a cause serious harm to babies
    - ☐ b do not work
    - ☐ c can be continued
    - ☐ d are considered unsafe
    - ☐ e don't know

Mode of delivery

13. Women with inflammatory bowel disease
    - ☐ a should never have a caesarean section
    - ☐ b must have a caesarean section
    - ☐ c and peri-anal disease (abscesses or fistulae around and outside the back passage) are advised against having a caesarean section
    - ☐ d can have a vaginal delivery in most cases
    - ☐ e don't know

14. Peri-anal disease (abscesses or fistulae around and outside the back passage) that occurs after a normal vaginal delivery
    - ☐ a is common in ulcerative colitis
    - ☐ b responds well to creams
    - ☐ c is more likely if a woman suffered from it previously
    - ☐ d is never seen in women with Crohn's disease
    - ☐ e don't know

Pregnancy outcomes

15. Women suffering from inflammatory bowel disease
    - ☐ a usually have bigger and heavier babies than other women
    - ☐ b often give birth a bit early
    - ☐ c often give birth late
    - ☐ d always have their baby on time even when Crohn's disease flares
    - ☐ e don't know

16. Birth defects in babies of mothers with inflammatory bowel diseases
    - ☐ a are a common problem
    - ☐ b occur slightly more often than in babies of mothers without inflammatory bowel disease
    - ☐ c are usually due to drug side effects
    - ☐ d can be prevented by vaccinations
    - ☐ e don't know

17. The chances of having a healthy baby for mothers suffering from inflammatory bowel disease
    - ☐ a are less than 50%
    - ☐ b are very good
    - ☐ c depend on the method of delivery
    - ☐ d can be improved by avoiding medication
    - ☐ e don't know

Breastfeeding

18. Mothers suffering from inflammatory bowel disease
    - ☐ a should not breast feed to avoid passing the disease on to the child
    - ☐ b never experience a flare of disease when breastfeeding
    - ☐ c may have tiny amounts of medication in their breast milk
    - ☐ d do not need to discuss breast feeding with their midwife or doctor
    - ☐ e don't know

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THANK YOU!

Appendix B-4: Physician Letter of Invitation – group 3

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

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University of Alberta, 130 University Campus
Edmonton, Alberta, Canada T6G 2X8

vwhuang@ualberta.ca
www.departmentofmedicine.ualberta.ca/cegiir
Phone: 780-248-1031
Fax: 780-248-1041

Physician Knowledge Regarding Reproductive Issues in Inflammatory Bowel Disease

February 2013

Dear Dr.

I am an IBD fellow from the University of Alberta, Edmonton, AB, and I would like to invite you to participate in my questionnaire study to assess physician knowledge regarding reproductive issues in IBD.

If you would like to participate, please find further details below. A copy of the information and consent form and questionnaire is attached. Completion and return of the questionnaire will be taken as implied consent. All responses are anonymous and confidential. Once completed please return the questionnaire in the provided envelope.

Thank you for your time.

Sincerely,

VIVIAN HUANG, MD, FRCPC
Inflammatory Bowel Disease Fellow
The University of Alberta

Appendix B-5: Physician Information and Consent – group 3

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

Zeidler Family Gastrointestinal Health & Research Institute
Zeidler Ledcor Centre L-10B
University of Alberta, 130 University Campus
Edmonton, Alberta, Canada T6G 2X8

vwhuang@ualberta.ca
www.departmentofmedicine.ualberta.ca/cegiir
Phone: 780-248-1031
Fax: 780-248-1041

PHYSICIAN INFORMATION AND CONSENT FORM
Physician Knowledge Regarding Reproductive Issues in Inflammatory Bowel Disease

Principal Investigator: Dr. Richard Fedorak

Sub-Investigator(s): Dr. Vivian Huang, Dr. Karen Kroeker, Dr. Leo Dieleman, Dr. K. Goodman

BACKGROUND:
Women with chronic illnesses, such as inflammatory bowel diseases, often have difficulties making decisions regarding family planning compared to women who are healthy. Previous research has shown that concern regarding chronic illness and medication use can lead to decisions of voluntary childlessness. We want to assess physician knowledge regarding reproductive issues in inflammatory bowel disease, and to assess physician practice patterns with respect to discussing reproductive issues with IBD patients.

DESCRIPTION:
Participating in this study will involve completion of a questionnaire, which will take about 5 minutes.

POSSIBLE RISKS:
No risks are anticipated from participation in this study.

POSSIBLE BENEFITS:
You may not benefit directly from this study, but you will help researchers better understand physician practice patterns in discussing reproductive issues with IBD patients.

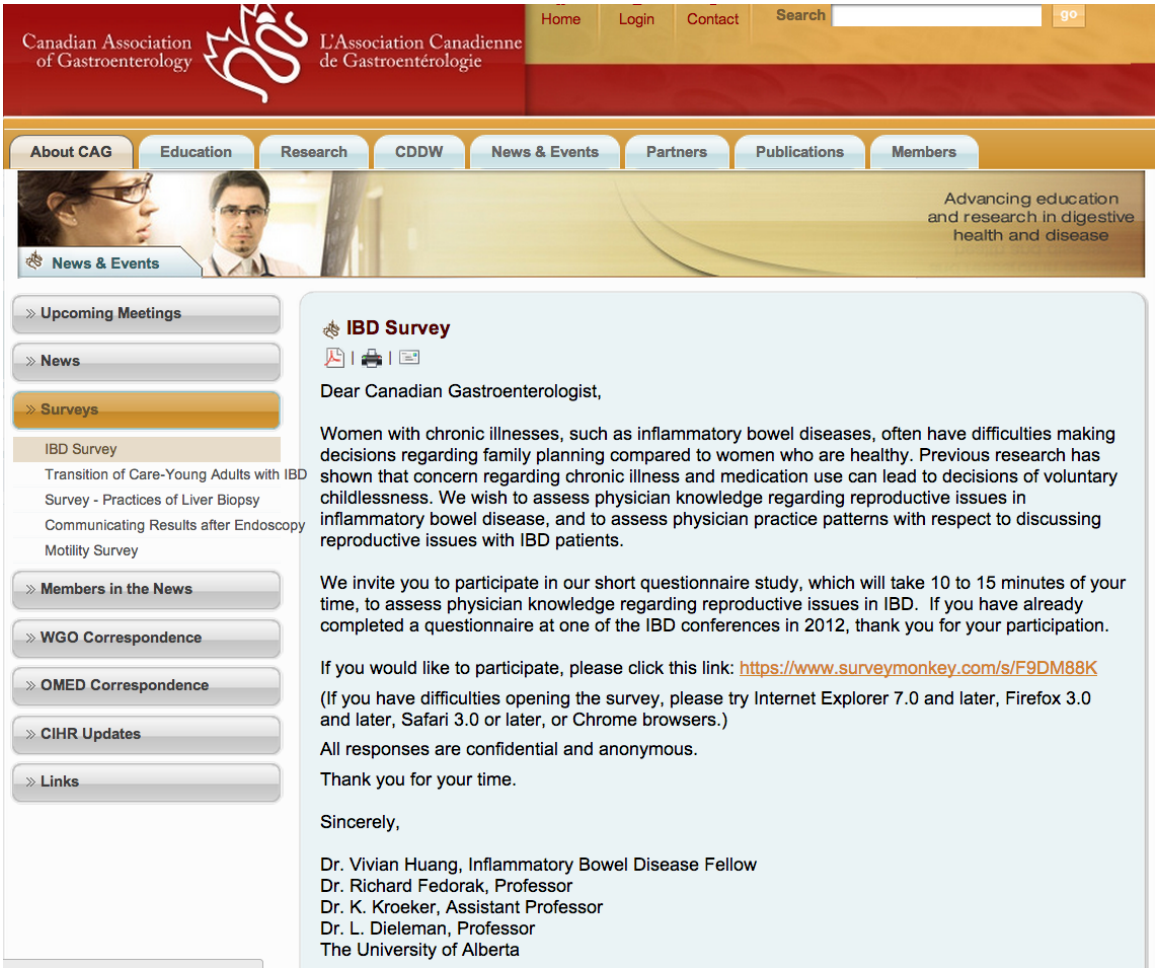
CONFIDENTIALITY:
Your responses will be completely anonymous. No identifying information is requested. Study documents and study data will be stored for a minimum of 5 years in secured locked storage of the principal investigator, and on the secured intranet at Division of Gastroenterology at the University of Alberta.

IMPLIED CONSENT:
By completing and returning the questionnaire, you are providing your informed consent.

CONTACTS:
If you have any questions about the study, you may contact:
Dr. Vivian Huang, IBD Fellow, at 780-248-1031 or vwhuang@ualberta.ca

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615.

Appendix B-6: Canadian Association of Gastroenterology e-posting – group 4



Appendix B-7: Electronic Web-based Version of Physician Questionnaire – group 4

1. Consent

PHYSICIAN KNOWLEDGE OF REPRODUCTIVE ISSUES IN INFLAMMATORY BOWEL DISEASE

Principal Investigator: Dr. Richard Fedorak

Sub-Investigator(s): Dr. Vivian Huang, Dr. Karen Kroeker, Dr. Leo Dieleman, Dr. K. Goodman

BACKGROUND:
Women with chronic illnesses, such as inflammatory bowel diseases, often have difficulties making decisions regarding family planning compared to women who are healthy. Previous research has shown that concern regarding chronic illness and medication use can lead to decisions of voluntary childlessness. We want to assess physician knowledge regarding reproductive issues in inflammatory bowel disease, and to assess physician practice patterns with respect to discussing reproductive issues with IBD patients.

DESCRIPTION:
Participating in this study will involve completion of a questionnaire, which will take about 10-15 minutes.

POSSIBLE RISKS:
No risks are anticipated from participation in this study.

POSSIBLE BENEFITS:
You may not benefit directly from this study, but you will help researchers better understand physician practice patterns in discussing reproductive issues with IBD patients.

CONFIDENTIALITY:
Your responses will be completely anonymous. No identifying information is requested. Survey Monkey houses its data on a US server and is therefore subject to the US Patriot Act. Study documents and study data will be stored for a minimum of 5 years in secured locked storage of the principal investigator, and on the secured intranet at Division of Gastroenterology at the University of Alberta.

IMPLIED CONSENT:
By completing the questionnaire, you are providing your informed consent.

CONTACTS:
If you have any questions about the study, you may contact:
Dr. Vivian Huang, IBD Fellow, at 780-248-1031 or vwhuang@ualberta.ca

The plan for this study has been reviewed for its adherence to ethical guidelines by a Research Ethics Board at the University of Alberta. For questions regarding participant rights and ethical conduct of research, contact the Research Ethics Office at (780) 492-2615.

Appendix B-8: Physician Reminder Letters

UNIVERSITY OF ALBERTA

Centre of Excellence for Gastrointestinal Inflammation and Immunity Research (CEGIIR)
Division of Gastroenterology
Department of Medicine

Zeidler Family Gastrointestinal Health & Research Institute
Zeidler Ledcor Centre L-10B
University of Alberta, 130 University Campus
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PHYSICIAN INVITATION LETTER
Physician Knowledge Regarding Reproductive Issues in Inflammatory Bowel Disease

April 2013

Dear ,

Recently, you were mailed a survey package for a study being conducted by the Division of Gastroenterology. **If you have already submitted your responses, we thank you for your participation.**

As we are developing an IBD clinic for pregnancy, your views on reproductive issues in inflammatory bowel disease are very important to us.

If you prefer to complete the questionnaire electronically, please go to the following Survey Monkey Link.

Survey Link: https://www.surveymonkey.com/s/XHMCZ9K

We would also appreciate your responses to the following questions (please return this sheet in the provided envelope or fax to (780) 248-1041):

1) Would you attend an educational CME event on reproductive issues/pregnancy in IBD?
- ☐ NO
- ☐ YES

2) Would you refer a pregnant IBD patient to a specialized pregnancy in IBD clinic?
- ☐ NO
- ☐ YES

Please submit your survey responses by June 7, 2013 as we will be hosting an online seminar on Pregnancy and IBD on Tuesday June 11, 2013 at 4pm. For further details, go to http://www.ibdclinic.ca/ibd-tv/

If you have any questions pertaining to this research study, please contact Dr. Vivian Huang, IBD fellow at vwhuang@ualberta.caor 780-248-1031.

Sincerely,

VIVIAN HUANG, MD, FRCPC
Gastroenterology IBD Fellow

RICHARD N FEDORAK, MD, FRCPC, FRCP (London) FRS
Professor of Medicine

Appendix C-1: Appendix for Chapter 3

Appendix Table C1-0-1: Characteristics of Childless Women and Women who have children among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	Total patients (N=248)		Childless (N=128)		Have children (N=120)		Chi-square p-value
	N	% of total*	N	% of total*	N	% of total*	
Current Age (years)							
18 to 24	49	19.8	47	36.7	2	1.7	<0.001
25 to 29	50	20.2	34	26.6	16	13.3	
30 to 34	56	22.6	24	18.8	32	26.7	
35 to 39	47	19.0	12	9.4	35	29.2	
40 to 45	46	18.5	11	8.6	35	29.2	
Marital status							
Partnered	173	69.8	66	51.6	107	89.2	<0.001
Divorced	8	3.2	2	1.6	6	5.0	
Single	67	27.0	60	46.9	7	5.8	
Education							
Grade 1 to Grade 12	56	22.6	29	22.7	27	22.5	0.26
College/university	157	63.3	76	59.4	81	67.5	
Graduate degree	11	4.4	6	5.5	4	3.3	
Professional school degree	5	2.0	2	1.6	3	2.5	
Other	19	7.7	14	10.9	5	4.2	
Employment (n=229)*							
Unemployed	28	12.2	13	10.6	15	14.2	0.02
Part time	46	20.1	24	19.5	22	20.8	
Full time	117	51.1	73	59.3	44	41.5	
Other	38	16.6	13	10.6	25	23.6	
Family history of IBD							
Yes	107	43.1	52	40.6	55	45.8	0.41
No	141	56.9	76	59.4	65	54.2	
Type of IBD							
Crohn's disease	150	60.5	76	59.4	74	61.7	0.49
Ulcerative colitis	88	35.5	45	35.2	43	35.8	
Indeterminate	10	4.0	7	5.5	3	2.5	
Age at IBD diagnosis							
Younger than 18 years	65	26.2	49	38.3	16	13.3	<0.001
18 to 45 years	183	73.8	79	61.7	104	86.7	
Duration of IBD							
0 to 4 years	57	23.0	33	25.8	24	20.0	0.28
5 years or more	191	77.0	95	74.2	96	80.0	
Worried about Meds (n=241)*							
Yes	154	63.9	86	68.8	68	58.6	0.100
No	87	36.1	39	31.2	48	41.1	

Category	Total patients (N=248)		Childless (N=128)		Have children (N=120)		Chi-square p-value
	N	% of total*	N	% of total*	N	% of total*	
GI discussed Meds (n=223)*							
Yes	80	35.9	31	26.1	49	47.1	‘0.001
No	143	64.1	88	73.9	55	52.9	
Have discussed family planning with a physician							
Yes	154	62.1	72	56.3	82	68.3	0.05
No	94	37.9	56	43.8	38	31.7	
CCPKnow level							
Poor (0 to 7)	131	52.8	78	60.9	53	44.2	0.008
Adequate+ (8-17)	117	47.2	50	39.1	67	55.8	
Dichotomized CCPKnow level							
Poor (0 to 7)	131	52.8	78	60.9	53	44.2	0.070
Adequate (8 to 10)	49	19.8	21	16.4	28	23.3	
Good (11 to 13)	48	19.4	21	16.4	27	22.5	
Very good (14 to 17)	20	8.1	8	6.3	12	10.0	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

Appendix Table C1-0-2: Unadjusted Odds of Patient Childlessness by Selected Study Variables among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	OR	95% CI
Current age (years)	0.91	0.83 - 0.98
Current age (years)		
18 to 24 (n=49)	1.0	-
25 to 29 (n=50)	0.090	0.019 - 0.42
30 to 34 (n=56)	0.032	0.0070 - 0.15
35 to 39 (n=47)	0.015	0.0030 - 0.069
40 to 45 (n=46)	0.013	0.0030 - 0.064
Marital status		
Single (n=67)	1.00	-
Partnered (n=173)	0.072	0.031 - 0.17
Divorced (n=8)	0.039	0.0070 - 0.23
Education		
Grade 1 to Grade 12 (n=56)	1.00	-
College/university (n=157)	0.87	0.47 – 1.6
Graduate degree (n=11)	1.6	0.43 – 6.2
Professional school degree (n=5)	0.62	0.096 – 4.0
Other (n=19)	2.6	0.83 – 8.2
Employment (n=229)*		
Unemployed (n=28)	1.0	-
Part time (n=46)	1.3	0.49 - 3.2
Full time (n=117)	1.9	0.83 - 4.4
Other (n=38)	0.60	0.22 - 1.6
Family history of IBD		
Yes (n=107)	1.2	0.75 - 20
No (n=141)	1.0	-
Type of IBD		
Crohn's disease (n=150)	1.0	-
Ulcerative colitis (n=88)	1.0	0.60 - 1.7
Indeterminate (n=10)	2.3	0.57 - 9.1
Age at diagnosis (years)	0.88	0.85 - 0.92
Age diagnosed with IBD		
Younger than 18 years (n=65)	1.0	-
18 to 45 years (n=183)	0.25	0.13 - 0.47
Duration of IBD		
0 to 4 years (n=57)	1.0	-
5 or more years (n=191)	0.72	0.40 - 1.3

Category	OR	95% CI
Perianal disease (n=225)*		
Yes (n=54)	1.0	0.54 - 1.8
No (n=171)	1.0	-
Colectomy with pouch		
Yes (n=17)	3.3	1.0 – 10
No (n-231)	1.0	-
Ostomy		
Yes (n=24)	3.1	1.2 - 8.1
No (n=224)	1.0	-
Have discussed family planning with a physician		
Yes (n=154)	0.60	0.35 - 1.0
No (n=94)	1.0	-

Appendix C-2: Appendix for Chapter 4

Appendix Table C2-0-1: Characteristics of Women with Poor v. Adequate plus CCPKnow Scores among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	Total patients (N=248)		Poor CCPKnow (N=131)		Adequate plus (N=117)		Chi-square p-value
	N	% of total*	N	% of total*	N	% of total*	
Median Age	32.0 (26.0 – 7.8)		32.0 (23.0 – 37.0)		32.0 (27.0 – 38.0)		0.92
Current Age (years)							
18 to 24	49	19.8	34	26.0	15	12.8	0.043
25 to 29	50	20.2	23	17.6	27	23.1	
30 to 34	56	22.6	23	17.6	33	28.2	
35 to 39	47	19.0	27	20.6	20	17.1	
40 to 45	46	18.5	24	18.3	22	18.8	
Marital status							
Partnered	173	69.8	75	57.3	98	83.8	<0.001
Divorced	8	3.2	4	3.1	4	3.4	
Single	67	27.0	52	39.7	15	12.8	
Education							
Grade 1 to Grade 12	56	22.6	39	29.8	17	14.5	0.007
College/university	157	63.3	79	60.3	78	66.7	
Graduate degree	11	4.4	2	1.5	9	7.7	
Professional school degree	5	2.0	1	0.8	4	3.4	
Other	19	7.7	10	7.6	9	7.7	
Employment (n=229)*							
Unemployed	28	12.2	18	14.9	10	9.3	0.468
Part time	46	20.1	21	17.4	25	23.1	
Full time	117	51.1	61	50.4	56	51.9	
Other	38	16.6	21	17.4	17	15.7	
Family history of IBD							
Yes	107	43.1	54	41.2	53	45.3	0.517
No	141	56.9	77	58.8	64	54.7	
Other Medical History							
Mood (n=227)*							
Yes	61	26.9	33	27.5	28	26.2	0.82
No	166	73.1	87	72.5	79	73.8	

Category	Total patients (N=248)		Poor CCPKnow (N=131)		Adequate plus (N=117)		Chi-square p-value
	N	% of total*	N	% of total*	N	% of total*	
Irritable bowel (n=229)*							
Yes	65	28.4	42	34.7	79	65.3	0.025
No	164	71.6	79	65.3	85	78.7	
Gynecological (n=230)*							
Yes	28	12.2	12	9.8	16	14.8	0.25
No	202	87.8	110	90.2	92	85.2	
Diabetes (n=230)*							
Yes	5	2.2	3	2.5	2	1.9	0.75
No	225	97.8	119	97.5	106	98.1	
Other (n=229)*							
Yes	47	20.5	26	21.3	21	19.5	0.75
No	182	79.5	96	78.7	86	80.4	
Have discussed family planning with a physician							
Yes	154	62.1	66	50.4	88	75.2	<0.001
No	94	37.9	65	49.6	29	24.8	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

Appendix Table C-2-0-2: IBD History among Women with Poor v. Adequate plus CCPKnow Scores among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	Total patients (N=248)		Poor CCPKnow (N=131)		Adequate plus (N=117)		Chi-square p-value
	N	% of total*	N	% of total*	N	% of total*	
Type of IBD							
Crohn's disease	150	60.5	77	58.8	73	62.4	0.51
Ulcerative colitis	88	35.5	47	35.9	41	35.0	
Indeterminate	10	4.0	7	5.3	3	2.6	
Median Age at IBD diag.	21.0		21.0		22.0		0.63
(IQR) years	(17.0 – 27.0)		(16.0 – 28.0)		(18.0 – 27.0)		
Age at IBD diagnosis							
Younger than 18 years	65	26.2	40	30.5	25	21.4	0.10
18 to 45 years	183	73.8	91	69.5	92	78.6	
Median Duration of IBD	10.0		9.0		10.0		0.44
(IQR) years	(6.0 – 17.0)		(5.0 – 14.0)		(6.0 – 16.0)		
Duration of IBD							
0 to 4 years	57	23.0	34	26.0	23	19.7	0.24
5 years or more	191	77.0	97	74.0	94	49.2	
Perianal disease (n=225)*							
Yes	54	24.0	32	26.9	22	20.8	0.28
No	171	76.0	87	73.1	84	79.2	
Colectomy with pouch							
Yes	17	6.9	12	9.2	5	4.3	0.13
No	231	93.1	119	90.8	112	95.7	
Ostomy							
Yes	24	9.7	15	11.5	9	7.7	0.32
No	224	90.3	116	88.5	108	92.3	
Medication History							
Do not remember							
Yes	8	3.2	127	96.9	113	96.6	0.87
No	240	96.8	4	3.1	4	3.4	
5-ASA/sulfasalazine							
Yes	218	87.9	21	16.0	9	7.7	0.044
No	30	12.1	110	84.0	108	92.3	
Steroids							
Yes	216	87.1	111	84.7	105	89.7	0.24
No	32	12.9	20	15.3	12	10.3	

	Total patients (N=248)		Poor CCPKnow (N=131)		Adequate plus (N=117)		Chi-square p-value
	N	% of total*	N	% of total*	N	% of total*	
Methotrexate							
Yes	42	16.9	22	16.8	20	17.1	0.95
No	206	83.1	109	83.2	97	82.9	
Azathioprine/6-MP							
Yes	180	72.6	96	73.3	84	71.8	0.79
No	68	27.4	35	26.7	33	28.2	
Anti-TNF							
Yes	117	47.2	61	46.6	56	47.9	0.84
No	131	52.8	70	53.4	61	52.1	
Antibiotics							
Yes	152	61.3	75	57.3	77	65.8	0.17
No	96	38.7	56	42.7	40	34.2	
Other (clinical trials)							
Yes	32	12.9	19	14.5	13	11.1	0.43
No	216	87.1	112	85.5	104	88.9	
Steroids for a flare							
Yes	64	25.8	39	29.8	25	21.4	0.13
No	184	74.2	92	70.2	92	78.6	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

Appendix Table C-2-0-3: Reproductive History among Women with Poor v. Adequate plus CCPKnow Scores among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	Total patients (N=248)		Poor CCPKnow (N=131)		Adequate plus (N=117)		Chi-square
	N	% of total*	N	% of total*	N	% of total*	
Had fertility treatment							
Yes	28	11.3	13	9.9	15	12.8	0.47
No	220	88.7	118	90.1	102	87.2	
Ever been pregnant							
Yes	136	54.8	61	46.6	75	64.1	0.006
No	112	45.2	70	53.4	42	35.9	
If have been pregnant, timing in relation to IBD diagnosis (n=135*)							
Before only	36	26.7	23	37.7	13	17.6	0.011
After only	78	57.8	27	44.3	51	68.9	
Before and After	21	15.6	11	18.0	10	13.5	
Pregnancy outcomes	**(n=136)**						
Therapeutic abortion							
Yes	16	11.8	10	16.4	6	8.0	0.13
No	120	88.2	51	83.6	69	92.0	
Miscarriage							
Yes	52	30.1	26	42.6	26	34.7	0.34
No	84	61.8	35	57.4	49	65.3	
Stillbirth							
Yes	2	1.5	1	1.6	1	1.3	0.88
No	118	88.1	60	98.4	74	98.7	
Preterm/LBW							
Yes	13	9.6	6	9.8	7	9.3	0.92
No	123	90.4	55	90.2	68	90.7	
Full term/LBW							
Yes	8	5.9	3	4.9	5	6.7	0.66
No	128	94.1	58	95.1	70	93.3	
Full term/healthy							
Yes	99	72.8	43	70.5	56	74.7	0.59
No	37	27.2	18	29.5	19	25.3	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

Appendix Table C-2-0-4: Unadjusted Odds Ratios Estimating the Effects of Selected Study Variables on Having Poor CCPKnow Scores among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Category	OR	95% CI
Current age (years)	0.98	0.94 - 1.0
Current age (years)		
18 to 24 (n=49)	1.0	-
25 to 29 (n=50)	0.38	0.17 - 0.86
30 to 34 (n=46)	0.31	0.14 - 0.69
35 to 39 (n=47)	0.60	0.26 - 1.4
40 to 45 (n=46)	0.48	0.21 - 1.1
Marital status		
Single (n=67)	1.0	-
Partnered (n=173)	0.22	0.12 - 0.42
Divorced (n=8)	0.29	0.064 - 1.3
Education		
Grade 1 to Grade 12 (n=56)	1.0	-
College/university (n=157)	0.44	0.23 – 0.85
Graduate degree (n=11)	0.097	0.019 – 0.50
Professional school degree (n=5)	0.11	0.011 – 1.0
Other (n=19)	0.48	0.17 – 1.4
Employment (n=229*)		
Unemployed (n=28)	1.0	-
Part time (n=46)	0.47	0.18 - 1.2
Full time (n=117)	0.61	0.26 - 1.4
Other (n=38)	0.69	0.25 - 1.9
Family history of IBD		
Yes (n=107)	0.85	0.50 - 1.4
No (n=141)	1.0	-
Type of IBD		
Crohn's disease (n=150)	1.0	-
Ulcerative colitis (n=88)	1.1	0.64 - 1.8
Indeterminate (n=10)	2.2	0.55 - 8.9
Age diagnosed with IBD (years)	1.0	0.97 - 1.0
Age diagnosed with IBD		
Younger than 18 years (n=65)	1.0	-
18 to 45 years (n=183)	0.62	0.35 - 1.1
Duration of IBD		
0 to 4 years (n=57)	1.0	
5 or more years (n=191)	0.70	0.38 - 1.3

Category	OR	95% CI
Perianal disease (n=225)*		
Yes (n=54)	1.4	0.76 - 2.6
No (n=171)	1.0	
Colectomy with pouch		
Yes (n=17)	2.3	0.77 - 6.6
No (n-231)	1.0	
Ostomy		
Yes (n=24)	1.6	0.65 - 3.7
No (n=224)	1.0	
Discussed family planning with a physician		
Yes (n=154)	0.34	0.20 - 0.58
No (n=94)	1.0	

* n=number of responses

Appendix C-3: Appendix for Chapter 5

Appendix Table C3-0-1: Characteristics and Prevalence of Childlessness by Selected Study Variables among 211 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Category	Total patients (N=211)		Prevalence of childlessness		Chi-square
	N	% of total*	N	% of category	p-value
Age (years)					
18 to 24	41	19.4	39/41	95.1	<0.001
25 to 29	39	18.5	26/39	66.7	
30 to 34	48	22.7	21/48	43.8	
35 to 39	41	19.4	11/41	26.8	
40 to 45	42	19.9	10/42	23.8	
Marital status					
Partnered	54	25.6	47/54	87.0	<0.001
Divorced	150	71.1	58/150	38.7	
Single	7	3.3	2/7	28.6	
Education					
Grade 1 to Grade 12	48	22.7	25/48	52.1	0.10
College/university	131	62.1	60/131	45.8	
Graduate degree	9	4.3	6/9	66.7	
Professional school degree	5	2.4	2/5	40.0	
Other	18	8.5	14/18	77.8	
Employment (n=210)*					
Unemployed	24	11.4	9/24	37.5	0.016
Part time	44	21.0	23/44	52.3	
Full time	105	50.0	63/105	60.0	
Other	37	17.6	12/37	32.4	
Family history of IBD					
Yes	91	43.1	45/91	49.5	0.75
No	120	56.9	62/120	51.7	
Type of IBD					
Crohn's disease	130	61.6	65/130	50.0	0.79
Ulcerative colitis	73	34.6	37/73	50.7	
Indeterminate	8	3.8	5/8	62.5	
Age IBD diagnosed					
Younger than 18 years	53	25.1	41/53	77.4	<0.001
18 to 45 years	158	74.9	66/158	41.8	

Category	Total patients (N=211)		Prevalence of childlessness		Chi-square
	N	% of total*	N	% of category	p-value
Duration of IBD					
0 to 4 years	42	19.9	23/42	54.8	0.56
5 or more years	169	80.1	84/169	49.7	
Meds: Sulfa/Mesalamine					
Yes	185	87.7	96/185	51.9	0.36
No	26	12.3	11/26	42.3	
Meds: Steroids					
Yes	182	86.3	95/182	52.2	0.28
No	29	13.7	12/29	41.4	
Meds: MTX					
Yes	35	16.6	16/35	45.7	0.52
No	176	83.4	91/176	51.7	
Meds: AZA/6MP					
Yes	149	70.6	79/149	53.0	0.30
No	62	29.4	28/62	45.2	
Meds: Anti TNF					
Yes	98	46.4	52/98	53.1	0.53
No	113	53.6	55/113	48.7	
Meds: Antibiotics					
Yes	130	61.6	65/130	50.0	0.79
No	81	38.4	42/81	51.9	
Flare in last 12 months					
Yes	52	24.6	26/52	50.0	0.91
No	159	75.4	81/159	50.9	
Perianal disease (n=206)*					
Yes	47	22.8	24/47	51.1	0.99
No	159	77.2	81/159	50.9	
Colectomy with pouch					
Yes	15	7.1	11/15	73.3	0.069
No	196	92.9	96/196	49.0	
Ostomy					
Yes	21	10.0	16/21	76.2	0.014
No	190	90.0	91/190	47.9	

Category	Total patients (N=211)		Prevalence of childlessness		Chi-square
	N	% of total*	N	% of category	p-value
Have discussed family planning with a physician					
Yes	132	62.6	62/132	47.0	0.16
No	79	37.4	45/79	57.0	
Ever been pregnant					
Yes	119	56.4	16/119	13.4	<0.001
No	92	43.6	91/92	98.9	

* n=number of responses; the percentages are calculated using the total number of patients with responses as the denominator.

Appendix Table C3-0-2: Percentage of Patients Reporting Correct CCPKnow Answers and Childlessness among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	Total patients (n=248)		Childless (n=128)		Have Children (n=130)		Chi-square*
	N	%	N	%	N	%	p-value
INHERITANCE							
1. Inflammatory bowel disease … *is more likely to affect a child if mother or father are suffering from it.*	168	67.7	85	66.4	83	69.2	0.64
2. The risk of passing on inflammatory bowel disease to a child … *is less than 10%.*	69	27.8	32	25.0	37	30.8	0.31
FERTILITY							
3. Men with inflammatory bowel disease … *usually do not have problems with infertility.*	63	25.4	26	20.3	37	30.8	0.057
4. The chances of a woman becoming pregnant … *are generally good if she suffers from ulcerative colitis.*	48	19.4	22	17.2	26	21.7	0.37
DISEASE ACTIVITY							
5. What is most important when trying for a baby? *Inflammatory bowel disease should be well controlled before becoming pregnant.*	178	71.8	87	68.0	91	75.8	0.17
6. Women with inflammatory bowel disease … *should delay trying for a baby until their disease has been controlled.*	164	66.1	82	64.1	82	68.3	0.48
7. Active inflammatory bowel disease during pregnancy … *should be treated with some types of drugs to protect the pregnancy*	110	44.4	45	35.2	65	54.2	0.003
DRUGS							
8. Pregnant women with inflammatory bowel disease … *should continue some medications*	163	65.7	70	54.7	93	77.5	<0.001
9. Infliximab or Adalimumab … *are generally seen as 'probably safe' in pregnancy*	48	19.4	22	17.2	26	21.7	0.37

	Total patients (n=248)		Childless (n=128)		Have Children (n=130)		Chi-square*
	N	%	N	%	N	%	p-value
10. The drug Methotrexate … should always be stopped 3-6 months before trying for a baby	66	26.6	36	28.1	30	25.0	0.58
11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc) … *is safe and should be continued*	89	35.9	37	28.9	52	43.3	0.018
12. During pregnancy Azathioprine or 6-Mercaptopurine … *can be continued*	40	16.1	15	11.7	25	20.8	0.051
MODE OF DELIVERY							
13. Women with inflammatory bowel disease … *can have a vaginal delivery in most cases*	154	62.1	63	49.2	91	75.8	<0.001
14. Peri-anal disease that occurs after a normal vaginal delivery … *is more likely if a woman suffered from it previously*	62	25.0	33	25.8	29	24.2	0.77
PREGNANCY OUTCOMES							
15. Women suffering from inflammatory bowel disease … *often give birth a bit early*	70	28.2	29	22.7	41	34.2	0.044
16. Birth defects in babies of mothers with inflammatory bowel disease … *occur slightly more often than in babies of mothers without inflammatory bowel disease*	41	16.5	20	15.6	21	17.5	0.69
17. The chances of having a healthy baby for mothers suffering from inflammatory bowel disease … *are very good*	146	58.9	54	41.4	93	77.5	<0.001
BREASTFEEDING							
18. Mothers suffering from inflammatory bowel disease … *may have tiny amounts of medication in their breast milk*	120	48.4	57	44.5	63	52.5	0.21

* Chi-square test comparing percentage of childless women v. women who have children

Appendix Table C3-0-3: Multivariable Logistic Regression Models for Estimating the Effect of Having Discussed Family Planning with a Physician on Correctly Answering CCPKnow Questions among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

	OR	95% CI	p-value
INHERITANCE			
1. Inflammatory bowel disease … *is more likely to affect a child if mother or father are suffering from it.*	1.8	1.1 - 3.1	0.032
2. The risk of passing on inflammatory bowel disease to a child … *is less than 10%.*	1.4	0.80 - 2.6	0.226
FERTILITY			
3. Men with inflammatory bowel disease … *usually do not have problems with infertility.*	3.4	1.7 - 6.8	0.001
4. The chances of a woman becoming pregnant … *are generally good if she suffers from ulcerative colitis.*	2.8	1.3 - 5.8	0.008
DISEASE ACTIVITY			
5. What is most important when trying for a baby? *Inflammatory bowel disease should be well controlled before becoming pregnant.*	3.1	1.7 - 5.4	<0.001
6. Women with inflammatory bowel disease … *should delay trying for a baby until their disease has been controlled.*	2.9	1.7 - 5.0	<0.001
7. Active inflammatory bowel disease during pregnancy … *should be treated with some types of drugs to protect the pregnancy*	3.3	1.9 - 5.7	<0.001
DRUGS			
8. Pregnant women with inflammatory bowel disease … *should continue some medications*	3.3	1.9 - 5.6	<0.001
9. Infliximab or Adalimumab … *are generally seen as 'probably safe' in pregnancy*	2.1	1.0 - 4.2	0.043
10. The drug Methotrexate … should always be stopped 3-6 months before trying for a baby	2.3	1.2 - 4.4	0.009
11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc) … *is safe and should be continued*	2.1	1.2 - 3.7	0.008
12. During pregnancy Azathioprine or 6-Mercaptopurine … *can be continued*	5.2	2.0 - 14	0.001
MODE OF DELIVERY			
13. Women with inflammatory bowel disease … *can have a vaginal delivery in most cases*	2.8	1.7 - 4.9	<0.001

	OR	95% CI	p-value
14. Peri-anal disease that occurs after a normal vaginal delivery … *is more likely if a woman suffered from it previously*	2.9	1.5 - 5.7	0.002
PREGNANCY OUTCOMES			
15. Women suffering from inflammatory bowel disease … *often give birth a bit early*	2.6	1.4 - 5.0	0.003
16. Birth defects in babies of mothers with inflammatory bowel disease … *occur slightly more often than in babies of mothers without inflammatory bowel disease*	2.5	1.1 - 5.5	0.024
17. the chances of having a healthy baby for mothers suffering from inflammatory bowel disease … *are very good*	3.5	2.0 - 5.9	<0.001
BREASTFEEDING			
18. Mothers suffering from inflammatory bowel disease … *may have tiny amounts of medication in their breast milk*	2.1	1.2 - 3.5	0.006

Appendix Table C3-0-4: Text Responses to IBD-specific Reproductive Concerns among 107 Childless Women with IBD and 104 Women with IBD who have children from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	Response
Childless	• Baby will not get proper nutrients due to my illness during pregnancy
	• Clotting risk
	• Concern that in order to become pregnant I would have to stop or change my meds which could lead to a flare of my disease. Also being sick and trying to get well took up a large part of child-bearing years. Now that I am finally well, I am too old to start a family.
	• Crohn's and procedures took away ability to carry a baby and produce eggs
	• Have always planned to adopt, despite Crohn's, more concerned with raising children than fertility.
	• If I wait too long will my disease be much worse and make it more difficult to conceive or be pregnant
	• Medication related fatigue, have to go off MTX and pain would get worse
	• Not ready to have children yet
	• Scar tissue from previous surgeries possibly decreasing fertility/ability to get pregnant
	• Trial drug
	• Worried about further complications from fertility treatments and scarring from multiple surgeries (6)
Have children	• 11 surgeries for Crohn's related issues after giving birth
	• all 3 babies pooping in vitro due to Imuran, caused them to be taken away at birth
	• Biologic becoming refractory after coming off it
	• Disease poorly controlled in post-partum period
	• Felt worse with pregnancies
	• Had to have hysterectomy after 2nd birth
	• I was able to complete a pregnancy when first diagnosed and was in remission for 2nd baby
	• Other medical problems as well, depression, financial problems due to illness
	• Potential for low birth weight and premature delivery
	• Radiation therapy for cancer
	• Stress on my partner should we lose another baby
	• Told IBD would be good while was pregnant and was true
	• Too many abdominal surg and scar tissue, obsgyn advised no more pregnancies
	• Too old, don't want any more children
	• Very ill with Crohn's less than 1 week after birth of daughter
	• Would have to stop medication so potential of another surgery, getting old, had fertility issues with first child

Appendix Table C3-0-5: Odds of Reporting Concern if Have Poor CCPKnow Scores among 211 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Concern	OR	95% CI
• Medical advice that conception is not possible/inadvisable with IBD	2.0	1.0 – 4.0
• Concern for the possibility of genetically passing my disease to my child	0.81	0.47 – 1.4
• Concern for not being able to care for a child	0.87	0.47 – 1.6
• Concern about the added stress of raising a child	0.76	0.43 – 1.4
• Concern of the possibility of chronic illness leading to birth defects	0.87	0.48 – 1.6
• Concern of the possibility of having a stillbirth or a miscarriage	1.2	0.63 – 2.3
• Concern of the possibility of IBD medications causing birth defects	0.79	0.46 – 1.4
• Concern about the possibility of having a worsening of my disease as a result of pregnancy	0.95	0.56 – 1.6
• Concern of being unable to have a baby due to possible decreased fertility	1.3	0.75 – 2.4
• Having a negative body image of myself causes me to restrict my sexual activity	1.5	0.68 – 3.4
• IBD related fatigue	0.80	0.46 – 1.4
• Other concern	0.80	0.39 – 1.7
• Unsure	1.4	0.39 – 5.2
• None of the above	1.6	0.73 – 3.5

Appendix Table 3-0-6: Odds of Reporting Concern if Have Discussed Family Planning with a Physician among 211 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Concern	OR	95% CI
• Medical advice that conception is not possible/inadvisable with IBD	1.9	0.94 – 4.0
• Concern for the possibility of genetically passing my disease to my child	1.4	0.80 – 2.5
• Concern for not being able to care for a child	1.3	0.69 – 2.5
• Concern about the added stress of raising a child	0.76	0.43 – 1.4
• Concern of the possibility of chronic illness leading to birth defects	1.5	0.78 – 2.8
• Concern of the possibility of having a stillbirth or a miscarriage	4.8	2.0 – 11
• Concern of the possibility of IBD medications causing birth defects	1.1	0.62 – 1.9
• Concern about the possibility of having a worsening of my disease as a result of pregnancy	1.1	0.66 – 2.0
• Concern of being unable to have a baby due to possible decreased fertility	1.6	0.86 – 2.9
• Having a negative body image of myself causes me to restrict my sexual activity	1.6	0.66 – 3.8
• IBD related fatigue	2.0	1.1 – 3.5
• Other concern	1.3	0.60 – 2.8
• Unsure	0.24	0.060 – 0.95
• None of the above	0.51	0.23 – 1.1

Appendix C-4: Appendix for Chapter 6

Appendix Table C4-0-1: Text Responses to Changes in Family Plans Since Being Diagnosed with IBD among 223 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010 – 2013

Childless	# of children wanted may change because of my illness
	Chose b (plan to have children despite illness) and c (plan to adopt because of illness)
	Complicates feelings, worried about implications, may not have children
	Considering not having children, may adopt
	Depression – worry become ill
	Even though pt checked not changed, selected b
	Fearful they will get UC but still plan to have my own
	Feel more apprehensive about "what iffs"
	Hesitant to have children because of illness, unsure at this time
	I am scared I won't be able to or my child will have IBD
	I am still not in a place in my life where children are planned in my immediate future, but since being diag and since starting remicade and Imuran, I now know that I will need to have some in-depth discussions about family planning with my gastro specialist
	I have adopted children but have chosen not to do IVF because of my illness
	I worry about the progression of the illness and think I should maybe have children sooner than later
	It has made me infertile
	It made me not consider changing my decision (I did not allow myself to consider having kids)
	Less desire to try for a family
	Might want to adopt eventually, concerned my illness will limit my options/abilities
	More aware about it, the changes of passing CD to child are very small
	Not sure if I am able to have kids due to surgery, still will try when the time comes
	Not sure if I'm able to carry to term with CD
	Not sure of genetic risks to my children
	Now I feel like an option I never concerned myself
	Now I plan to not have children BUT not necessarily because of my illness (adopting would be preferable because of the illness)
	Plan to have less children
	Cannot
	Still want to have children but planned pregnancy when feeling well
	Tried to get pregnant for over 6 years, then gave up, was told had unexplained infertility
	Unsure (2x responses)
	Unsure about giving my genetics to my children
	Unsure and scared about what could happen to child or myself

	Want children but worry that I cannot
	Wasn't sure I wanted to due to drugs/possibility of hereditary issues
	We are discussing possible IVF and/or surrogacy and also adoption
	Will plan if IVF works, otherwise adopt
	Worried about risks to the baby due to medications I am currently on
Have children	Cannot get healthy enough and don't want to take drugs while pregnant
	Had not planned on having children, but met husband
	Had one unhealthy, not sure I will have another
	Have them sooner while on mild medication or remission
	I plan to look into having more children
	I was very concerned about having issues conceiving and about passing on my illness to my children, but decided to still have my own
	I will have one less child because of my illness
	I would have had no children in fear of passing on my disease, which the disease was passed to my children
	It may have affected my choice
	One child is enough
	Plan to watch for signs keep them stress free
	Wanted more and decided no
	Wasn't sure if I could conceive or carry babies, would meds cause issues?

Appendix C-5: Appendix for Chapter 7

Appendix Table C5-0-1: Physician Characteristics by Training of 183 Practicing Canadian Physicians

	GI (n=97)		GP (n=84)		Other (n=11)		Chi square p-value
	N	% of total	N	% of total	N	% of total	
Gender							
Male	76	78.4	42	56.0	9	81.8	0.005
Female	21	21.6	42	44.0	2	18.2	
Years in practice							
0 to 4 years	20	20.6	6	8.0	1	9.1	0.001
5 to 10 years	22	22.7	3	4.0	1	9.1	
11 to 20 years	19	19.6	25	33.3	3	27.3	
>20 years	36	37.1	41	54.7	6	54.5	
Population of city (n=131)*							
0 to 99,999	7	14.9	35	46.7	4	44.4	0.007
100,000 to 499,999	12	25.5	15	20.0	1	11.1	
>500,000	28	59.6	25	33.3	4	44.4	
Type of practice (n=180)*							
Community	48	50.0	72	98.6	7	63.6	<0.001
Academic	48	50.0	1	1.4	5	36.4	
Percentage of patients with IBD							
0 – 9%	12	12.4	73	97.3	6	54.5	<0.001
10 – 24%	46	47.4	2	2.7	3	27.3	
25 – 50%	26	28.8	0	0	1	9.1	
51 – 100%	13	13.4	0	0	1	9.1	
Number of IBD patients each year							
0 to 9	1	1.0	29	38.7	3	27.3	<0.001
10 to 50	18	18.6	43	57.4	5	45.5	
51 to 100	15	15.5	2	2.7	1	9.1	
101 to 150	18	18.6	0	0	0	0	
more than 150	45	46.4	1	1.3	2	18.2	
Number of pregnant IBD patients managed in past year							
None	15	15.5	54	72.0	7	63.6	<0.001
0 to 10	67	69.1	2	2.7	1	9.1	
11 or more	15	15.5	19	25.3	3	27.3	

	GI (n=97)		GP (n=84)		Other (n=11)		Chi square p-value
	N	% of total	N	% of total	N	% of total	
Self-reported IBD knowledge							
Inadequate	0	0	14	18.7	2	18.2	<0.001
Enough to get by	25	25.8	53	70.7	5	45.5	
Very good	72	74.2	8	10.7	4	36.4	
Feel about managing pregnant IBD patients							
Not comfortable	6	6.2	46	61.3	7	63.6	<0.001
Somewhat comfortable	17	17.5	18	24.0	2	18.2	
Comfortable	74	76.3	11	14.7	2	18.2	
CCPKnow level							
Poor (0 to 7)	0	0	15	20	2	18.2	<0.001
Adequate (8 to 10)	2	2.1	15	20	1	9.1	
Good (11 to 13)	5	5.2	30	40	3	27.3	
Very good (14 to 17)	90	92.8	15	20	5	45.5	
Dichotomized CCPKnow level							
Poor/Adequate/Good (0 to 13)	7	7.2	60	80.0	6	54.5	<0.001
Very good (14 to 17)	90	92.8	15	20.0	5	45.5	

* n=number of responses; the percentages are calculated using the total number of physicians with responses as the denominator.

Appendix Table C5-0-2: Physician Responses to Individual CCPKnow Questions and Discussion of Family Planning among 215 Canadian Physicians

	Total cohort (n=215)		Do not discuss FP (n=79)		Discuss FP (n=130)		Chi-square
	N	%	N	% of total	N	% of total	p-value
INHERITANCE							
1. Inflammatory bowel disease … *is more likely to affect a child if mother or father are suffering from it.*	205	95.3	73	92.4	132	97.1	0.12
2. The risk of passing on inflammatory bowel disease to a child … *is less than 10%.*	159	74.0	46	58.2	113	83.1	<0.001
FERTILITY							
3. Men with inflammatory bowel disease … *usually do not have problems with infertility.*	155	72.1	52	65.8	103	75.7	0.12
4. The chances of a woman becoming pregnant … *are generally good if she suffers from ulcerative colitis.*	127	59.1	29	36.7	98	72.1	<0.001
DISEASE ACTIVITY							
5. What is most important when trying for a baby? *Inflammatory bowel disease should be well controlled before becoming pregnant.*	197	91.6	67	84.8	130	95.6	0.006
6. Women with inflammatory bowel disease … *should delay trying for a baby until their disease has been controlled.*	196	91.2	69	87.3	127	93.4	0.13
7. Active inflammatory bowel disease during pregnancy … *should be treated with some types of drugs to protect the pregnancy*	179	83.3	60	75.9	119	87.5	0.029
DRUGS							
8. Pregnant women with inflammatory bowel disease … *should continue some medications*	196	91.2	67	84.8	129	94.9	0.012
9. Infliximab or Adalimumab … *are generally seen as 'probably safe' in pregnancy*	137	63.7	30	38.0	107	78.6	<0.001

	Total cohort (n=215)		Do not discuss FP (n=79)		Discuss FP (n=130)		Chi-square
	N	%	N	% of total	N	% of total	p-value
10. The drug Methotrexate … should always be stopped 3-6 months before trying for a baby	183	85.1	56	70.9	127	93.4	<0.001
11. During pregnancy Mesalazine (this includes tablets like Asacol, Mesavant, Pentasa, Salofalk etc) … *is safe and should be continued*	150	69.8	37	46.8	113	83.1	<0.001
12. During pregnancy Azathioprine or 6-Mercaptopurine … *can be continued*	124	57.7	24	30.4	100	73.5	<0.001
MODE OF DELIVERY							
13. Women with inflammatory bowel disease … *can have a vaginal delivery in most cases*	184	85.6	62	78.5	122	89.7	0.024
14. Peri-anal disease that occurs after a normal vaginal delivery … *is more likely if a woman suffered from it previously*	172	80.0	54	68.4	118	86.8	0.001
PREGNANCY OUTCOMES							
15. Women suffering from inflammatory bowel disease … *often give birth a bit early*	160	74.4	50	63.3	110	80.9	0.004
16. Birth defects in babies of mothers with inflammatory bowel disease … *occur slightly more often than in babies of mothers without inflammatory bowel disease*	130	60.5	35	44.3	95	69.9	<0.001
17. The chances of having a healthy baby for mothers suffering from inflammatory bowel disease … *are very good*	190	88.4	64	81.0	126	92.6	0.010
BREASTFEEDING							
18. Mothers suffering from inflammatory bowel disease … *may have tiny amounts of medication in their breast milk*	193	89.8	68	86.1	125	91.9	0.17

Appendix C-6: Appendix for Chapter 8

Appendix Table C6-0-1: Multivariable Logistic Regression Models for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Sulfasalazine and Mesalamine Medications during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Model for the effect of CCPKnow score on continuing Sulfasalazine during pregnancy		
CCPKnow score (per unit increase)	1.3	1.1 – 1.5
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.57	0.17 – 1.9
11 to 20 years	0.68	0.22 – 2.1
>20 years	0.86	0.31 – 2.4
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.3	0.93 – 5.6
11 or more	2.1	0.79 – 4.8
Type of Practice		
Community	1.0	-
Academic	1.4	0.64 – 3.0
Model for the effect of CCPKnow score on continuing Mesalamine PO during pregnancy		
CCPKnow score (per unit increase)	1.9	1.1 – 3.2
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.0	-
11 to 20 years	0.036	0.002 – 0.67
>20 yrs	0.10	0.008 – 1.4
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.0	-
11 or more	2.1	0.33 – 14
Type of Practice		
Community	1.0	-
Academic	0.0	-
Model for the effect of CCPKnow score on continuing Mesalamine Top during pregnancy		
CCPKnow score (per unit increase)	1.3	1.2 – 1.5
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.43	0.072 – 2.5
11 to 20 years	0.34	0.083 – 1.5
>20 years	0.24	0.06 – 0.98
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	4.2	1.4 – 12
11 or more	1.1	0.4 – 3.2

	OR	95% CI
Type of Practice		
Community	1.0	-
Academic	1.4	0.50 – 3.8
Model for the effect of CCPKnow score on continuing Sulfasalazine during breastfeeding		
CCPKnow score (per unit increase)	1.2	1.1 – 1.4
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.2	0.37 – 3.7
11 to 20 years	1.1	0.38 – 3.0
>20 years	0.81	0.30 – 2.2
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.83	0.35 – 2.0
11 or more	2.0	0.81 – 5.2
Type of Practice		
Community	1.0	-
Academic	0.78	0.36 – 1.7
Model for the effect of CCPKnow score on continuing Mesalamine PO during breastfeeding		
CCPKnow score (per unit increase)	1.5	1.2 – 1.7
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.0	0.23 – 4.7
11 to 20 years	0.41	0.12 – 1.4
>20 years	0.57	0.18 – 1.8
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.6	1.0 – 6.7
11 or more	1.9	0.69 – 5.2
Type of Practice		
Community	1.0	-
Academic	0.63	0.25 – 1.6
Model for the effect of CCPKnow score on continuing Mesalamine Top during breastfeeding		
CCPKnow score (per unit increase)	1.3	1.2 – 1.5
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.3	0.25 – 6.8
11 to 20 years	0.39	0.11 – 1.4
>20 years	0.42	0.12 – 1.4
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	1.7	0.63 – 4.4
11 or more	1.5	0.55 – 4.1
Type of Practice		
Community	1.0	-
Academic	1.3	1.2 – 1.5

Appendix Table C6-0-2: Multivariable Logistic Regression Models for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Corticosteroids during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Model for the effect of CCPKnow score on continuing Prednisone PO during pregnancy		
CCPKnow score (per unit increase)	1.1	0.97 – 1.2
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.9	0.60 – 5.8
11 to 20 years	0.71	0.26 – 2.0
>20 years		
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	1.8	0.76 – 4.1
11 or more	1.7	0.70 – 4.3
Type of Practice		
Community	1.0	-
Academic	1.4	0.68 – 3.0
Model for the effect of CCPKnow score on continuing Prednisone Top during pregnancy		
CCPKnow score (per unit increase)	1.2	1.1 – 1.3
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.9	0.51 – 7.0
11 to 20 years	1.3	0.43 – 3.7
>20 years	1.0	0.38 – 2.7
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.98	0.41 – 2.4
11 or more	1.2	0.45 – 3.1
Type of Practice		
Community	1.0	-
Academic	0.93	0.41 – 2.1
Model for the effect of CCPKnow score on continuing Budesonide PO during pregnancy		
CCPKnow score (per unit increase)	1.3	1.1 – 1.5
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.93	0.28 – 3.1
11 to 20 years	0.55	0.18 – 1.7
>20 years		
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.55	0.18 – 1.7
11 or more	1.5	0.53 – 4.2
Type of Practice		
Community	1.0	-
Academic	1.8	0.80 – 3.9

	OR	95% CI
Model for the effect of CCPKnow score on continuing Budesonide Top during pregnancy		
CCPKnow score (per unit increase)	1.2	1.1 – 1.4
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.56	0.13 – 2.3
11 to 20 years	0.44	0.13 – 1.5
>20 years	0.34	0.11 – 1.1
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	1.1	0.45 – 2.8
11 or more	1.6	0.61 – 4.4
Type of Practice		
Community	1.0	-
Academic	1.2	1.1 – 1.4
Model for the effect of CCPKnow score on continuing Prednisone PO during breastfeeding		
CCPKnow score (per unit increase)	1.1	0.98 – 1.2
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.7	0.48 – 6.2
11 to 20 years	0.73	0.25 – 2.1
>20 years	1.0	0.37 – 2.7
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.4	1.0 – 5.6
11 or more	3.4	1.3 – 8.7
Type of Practice		
Community	1.0	-
Academic	13.0	1.3 – 6.9
Model for the effect of CCPKnow score on continuing Prednisone Top during breastfeeding		
CCPKnow score (per unit increase)	1.3	1.1 – 1.4
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	5.5x10^8	0.0 -
11 to 20 years	1.3	0.40 – 4.5
>20 years	2.0	0.65 – 6.0
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.71	0.25 – 2.0
11 or more	1.3	0.44 – 4.0
Type of Practice		
Community	1.0	-
Academic	2.0	0.65 – 6.0

	OR	95% CI
Model for the effect of CCPKnow score on continuing Budesonide PO during breastfeeding		
CCPKnow score (per unit increase)	1.3	1.1 – 1.5
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.8	0.47 – 7.1
11 to 20 years	0.67	0.22 – 2.0
>20 years	1.5	0.50 – 4.3
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	1.6	0.65 – 3.9
11 or more	3.0	1.1 – 8.4
Type of Practice		
Community	1.0	-
Academic	1.3	1.1 – 1.5
Model for the effect of CCPKnow score on continuing Budesonide Top during breastfeeding		
CCPKnow score (per unit increase)	1.3	1.1 – 1.5
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.4	0.32 – 6.2
11 to 20 years	0.87	0.26 – 3.0
>20 years	0.83	0.27 – 2.6
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.98	0.38 – 2.5
11 or more	2.3	0.77 – 7.2
Type of Practice		
Community	1.0	-
Academic	1.3	1.1 – 1.5

Appendix Table C6-0-3: Multivariable Logistic Regression Models for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Ciprofloxacin/Metronidazole during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Model for the effect of CCPKnow score on continuing ciprofloxacin during pregnancy		
CCPKnow score (per unit increase)	1.2	1.1 – 1.3
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.85	0.25 – 3.0
11 to 20 years	2.7	0.73 – 9.7
>20 years	0.70	0.25 – 2.0
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.48	0.18 – 1.2
11 or more	0.71	0.25 – 2.1
Type of Practice		
Community	1.0	-
Academic	0.31	0.13 – 0.70
Model for the effect of CCPKnow score on continuing Metronidazole during pregnancy		
CCPKnow score (per unit increase)	1.1	0.94 – 1.2
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.58	0.16 – 2.1
11 to 20 years	1.0	0.35 – 3.0
>20 years		
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.96	0.35 – 2.6
11 or more	3.5	1.3 – 9.5
Type of Practice		
Community	1.0	-
Academic	0.65	0.27 – 1.6
Model for the effect of CCPKnow score on continuing Ciprofloxacin during breastfeeding		
CCPKnow score (per unit increase)	9.96	0.85 – 1.1
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.1	0.29 – 3.9
11 to 20 years	1.0	0.31 – 3.3
>20 years	1.1	0.38 – 3.3
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.5	0.90 – 7.3
11 or more	7.0	2.5 – 20
Type of Practice		
Community	1.0	-
Academic	2.2	0.96 – 5.0

	OR	95% CI
Model for the effect of CCPKnow score on continuing Metronidazole during breastfeeding		
CCPKnow score (per unit increase)	1.1	0.95 – 1.2
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.4	0.41 – 4.9
11 to 20 years	0.94	0.31 – 2.9
>20 years	1.1	0.39 – 3.1
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.72	0.28 – 1.8
11 or more	3.9	1.5 – 9.9
Type of Practice		
Community	1.0	-
Academic	1.1	0.95 – 1.2

Appendix Table C6-0-4: Multivariable Logistic Regression Models for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of AZA/6MP and MTX during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Model for the effect of CCPKnow score on continuing AZA/6MP during pregnancy		
CCPKnow score (per unit increase)	1.6	1.3 – 2.0
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.96	0.22 – 4.2
11 to 20 years	1.7	0.44 – 6.4
>20 years	0.98	0.29 – 3.3
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	5.0	1.8 – 14
11 or more	1.7	0.59 – 5.0
Type of Practice		
Community	1.0	-
Academic	1.5	0.57 – 4.0
Model for the effect of CCPKnow score on stopping MTX during pregnancy		
CCPKnow score (per unit increase)	1.2	1.1 – 1.4
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	2.7	0.25 – 30
11 to 20 years	1.2	0.25 – 6.2
>20 years	1.5	0.34 – 6.8
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	1.2	0.30 – 5.1
11 or more	1.4	0.33 – 6.2
Type of Practice		
Community	1.0	-
Academic	0.44	0.12 – 1.6
Model for the effect of CCPKnow score on continuing AZA/6MP during breast feeding		
CCPKnow score (per unit increase)	1.4	1.2 – 1.7
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.82	0.23 – 2.9
11 to 20 years	0.67	0.21 – 2.2
>20 years	0.55	0.19 – 1.6
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	0.82	0.23 – 2.9
11 or more	0.67	0.21 – 2.2
Type of Practice		
Community	1.0	-
Academic	0.82	0.35 – 1.9

	OR	95% CI
Model for the effect of CCPKnow score on stopping MTX during breastfeeding		
CCPKnow score (per unit increase)	1.1	1.0 – 1.3
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.52	0.16 – 1.7
11 to 20 years	1.4	0.47 – 4.2
>20 years	1.4	0.33 – 1.7
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	1.0	0.44 – 2.5
11 or more	1.5	0.57 – 4.1
Type of Practice		
Community	1.0	-
Academic	0.74	0.33 – 1.7

Appendix Table C6-0-5: Multivariable Logistic Regression Models for Estimating the Effect of IBD-specific Reproductive Knowledge (measured by the CCPKnow Score) on Appropriate Use of Biologics during Pregnancy and Breastfeeding among 183 Practicing Canadian Physicians

	OR	95% CI
Model for the effect of CCPKnow score on continuing IFX during pregnancy		
CCPKnow score (per unit increase)	1.7	1.3 – 2.1
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.69	0.20 – 2.3
11 to 20 years	1.2	0.36 – 3.8
>20 years	1.0	0.36 – 3.0
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.4	0.92 – 6.4
11 or more	1.3	0.45 – 3.9
Type of Practice		
Community	1.0	-
Academic	1.7	1.3 – 2.1
Model for the effect of CCPKnow score on continuing ADA during pregnancy		
CCPKnow score (per unit increase)	1.6	1.3 – 2.0
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.92	0.27 – 3.2
11 to 20 years	1.6	0.50 – 5.4
>20 years		
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.1	1.2 – 8.2
11 or more	1.8	0.59 – 5.3
Type of Practice		
Community	1.0	-
Academic	1.1	0.50 – 2.6
Model for the effect of CCPKnow score on continuing IFX during breastfeeding		
CCPKnow score (per unit increase)	1.8	1.4 – 2.3
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	0.84	0.20 – 3.5
11 to 20 years	0.51	0.14 – 1.9
>20 years		
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.3	1.2 – 9.1
11 or more	5.5	1.7 - 18
Type of Practice		
Community	1.0	-
Academic	0.83	0.32 – 2.2

	OR	95% CI
Model for the effect of CCPKnow score on continuing ADA during breastfeeding		
CCPKnow score (per unit increase)	1.7	1.4 – 2.2
Years in practice		
0 to 4 years	1.0	-
5 to 10 years	1.0	0.25 – 4.2
11 to 20 years	0.63	0.17 – 2.3
>20 years	0.74	0.40 – 2.6
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.6	1.3 – 9.8
11 or more	6.1	1.9 – 20
Type of Practice		
Community	1.0	-
Academic	1.0	0.40 – 2.6

Appendix C-7: Appendix for Chapter 9

Appendix Table C7-0-1: Free Text Responses for Other Sources of Information Regarding Reproduction and IBD among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

Comment	Number of responses
Internet type	
Mother Risk	1
Chatrooms internet	1
Google.forums	1
Physician	
Endocrinologist	1
Gynaecologist	2
High risk pregnancy physician at Royal Alex	1
Internist	1
Obstetrician (and fertility expert – 1 response)	3
Other	
Just recently started	1
n/a children born before diagnosis	1
School	1
By discussing family planning I mean discussing future (how many kids) as well as birth control, no discussion in relation to IBD	1
The whole PE thing kinda did me in for getting pregnant and that happened prior to my CD diag. So I chose not to biologically have children because of my clotting risk not because of IBD	1

Appendix Table C7-0-2: Multivariable Logistic Regression Models for Estimating the Effects of Information Sources on Having Poor CCPKnow Scores among 248 Women with IBD from the IBD Consultation and Research Clinic, University of Alberta Hospital, 2010-2013

	OR	95% CI
Model for effect of patient obtaining information from Gastroenterologist		
Obtain from Gastroenterologist		
No	1.00	-
Yes	0.52	0.30 – 0.91
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.20	0.088 – 0.44
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.56	0.28 – 1.1
Graduate degree	0.070	0.012 – 0.43
Professional school degree	0.16	0.015 – 1.6
Other	0.55	0.18 – 1.7
Model for effect of patient obtaining information from General Practitioner		
Obtain from General Practitioner		
No	1.0	-
Yes	0.34	0.19 – 0.62
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.21	0.094 – 0.47
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.52	0.26 – 1.1
Graduate degree	0.062	0.010 – 0.38
Professional school degree	0.16	0.015 – 1.6
Other	0.42	0.13 – 1.3
Model for effect of patient obtaining information from IBD nurse		
Obtain from IBD nurse		
No	1.00	-
Yes	0.40	0.18 – 0.89
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.18	0.080 – 0.39
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.52	0.26 – 1.0
Graduate degree	0.069	0.011 – 0.42
Professional school degree	0.14	0.014 – 1.4
Other	0.49	0.16 – 1.5

	OR	95% CI
Model for effect of patient obtaining information from Pharmacist		
Obtain from Pharmacist		
No	1.00	-
Yes	0.22	0.060 – 0.79
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.15	0.067 – 0.344
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.56	0.28 – 1.1
Graduate degree	0.064	0.011 – 0.38
Professional school degree	0.16	0.017 – 1.6
Other	0.49	0.16 – 1.6
Model for effect of patient obtaining information from Internet		
Obtain information from Internet		
No	1.00	-
Yes	0.46	0.26 – 0.84
Current Age (years)	1.1	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.18	0.082 – 0.41
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.55	0.27 – 1.1
Graduate degree	0.084	0.014 – 0.48
Professional school degree	0.16	0.018 – 1.8
Other	0.53	0.17 – 1.7
Model for effect of patient obtaining information from Pamphlets		
Obtain information from pamphlets		
No	1.00	-
Yes	0.34	0.17 – 0.70
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.18	0.080 – 0.40
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.50	0.25 – 1.0
Graduate degree	0.067	0.012 – 0.39
Professional school degree	0.13	0.013 – 1.3
Other	0.54	0.17 – 1.8

	OR	95% CI
Model for effect of patient obtaining information from Books		
Obtain information from books		
No	1.00	-
Yes	0.36	0.14 – 0.88
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.17	0.078 – 0.38
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.53	0.26 – 1.1
Graduate degree	0.078	0.013 – 0.46
Professional school degree	0.18	0.018 – 1.8
Other	0.46	0.15 – 1.4
Model for effect of patient obtaining information from Support Groups		
Obtain information from support groups		
No	1.00	-
Yes	2.2	0.46 – 11
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.18	0.080 – 0.40
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.50	0.25 – 1.0
Graduate degree	0.066	0.012 – 0.38
Professional school degree	0.17	0.017 – 1.6
Other	0.49	0.16 – 1.5
Model for effect of patient obtaining information from Family and Friends		
Obtain information from family/friends		
No	1.00	-
Yes	0.45	0.21 – 0.94
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.17	0.075 – 0.37
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.52	0.26 – 1.0
Graduate degree	0.060	0.010 – 0.35
Professional school degree	0.20	0.019 – 2.0
Other	0.55	0.17 – 1.8

	OR	95% CI
Model for effect of patient obtaining information from Other sources		
Obtain information from Other		
No	1.00	-
Yes	0.58	0.21 – 1.6
Current Age (years)	1.0	0.98 – 1.1
Marital Status		
Single	1.0	-
Partnered	0.18	0.079 – 0.39
Education level		
Grade 1 to Grade 12	1.0	-
College/university	0.52	0.26 – 1.0
Graduate degree	0.067	0.012 – 0.39
Professional school degree	0.16	0.016 – 1.6
Other	0.54	0.17 – 1.7

Appendix Table C7-0-3: Multivariable Logistic Regression Models for Estimating the Effects of Information Sources on Having Very Good CCPKnow Scores among 183 Practicing Canadian Physicians

	OR	95% CI
Model for effect of physician information obtaining behavior on having Very Good CCPKnow		
Obtain information		
No	1.00	-
Yes	5.4	9.5 - 30
Years in practice (years)		
0 to 4 years	1.0	-
5-10 years	0.47	0.055 – 4.0
11-20 years	0.18	0.032 – 0.97
>20 years	0.17	0.44 – 7.3
Type of practice		
Community	1.0	-
Academic	1.8	0.44 – 7.3
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.4	0.74 – 15
11 or more	4.2	1.3 – 14
Training Status		
GI	1.0	-
GP	0.063	0.013 – 0.29
Other	0.23	0.038 – 1.4
Model for effect of physician information source of GI conferences		
Obtain information from GI conferences		
No	1.00	-
Yes	0.36	1.1 – 12
Years in practice (years)		
0 to 4 years	1.0	-
5-10 years	0.72	0.081 – 6.5
11-20 years	0.20	0.038 – 1.0
>20 years	0.17	0.036 – 0.81
Type of practice		
Community	1.0	-
Academic	2.1	0.48 – 9.0
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.2	0.69 – 15
11 or more	5.4	1.7 – 18
Training Status		
GI	1.0	-
GP	0.10	0.019 – 0.53
Other	0.23	0.039 – 1.4

	OR	95% CI
Model for effect of physician information source of IBD conferences		
Obtain information from IBD conferences		
No	1.00	-
Yes	2.1	0.69 – 6.2
Years in practice (years)		
0 to 4 years	1.0	-
5-10 years	0.73	0.083 – 6.4
11-20 years	0.19	0.037 – 0.98
>20 years	0.17	0.036 – 0.80
Type of practice		
Community	1.0	-
Academic	2.0	0.46 – 8.5
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.9	0.62 – 13
11 or more	5.0	1.6 – 16
Training Status		
GI	1.0	-
GP	0.058	0.012 – 0.28
Other	0.15	0.027 – 0.82
Model for effect of physician information source of medical journals		
Obtain information from medical journals		
No	1.00	-
Yes	1.9	0.54 – 6.5
Years in practice (years)		
0 to 4 years	1.0	-
5-10 years	0.71	0.084 – 6.0
11-20 years	0.20	0.038 – 1.0
>20 years	0.19	0.040 – 0.91
Type of practice		
Community	1.0	-
Academic	1.7	0.39 – 7.0
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	2.8	0.58 – 13
11 or more	5.2	1.6 – 17
Training Status		
GI	1.0	-
GP	0.046	0.010 – 0.21
Other	0.13	0.024 – 0.69
Model for effect of physician information source of Internet		
Obtain information from Internet		
No	1.00	-
Yes	1.0	0.37 – 2.9

	OR	95% CI
Years in practice (years)		
0 to 4 years	1.0	-
5-10 years	0.64	0.075 – 5.4
11-20 years	0.19	0.037 – 0.98
>20 years	0.18	0.038 – 0.83
Type of practice		
Community	1.0	-
Academic	1.7	0.43 – 7.0
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.5	0.80 – 16
11 or more	5.1	1.6 – 17
Training Status		
GI	1.0	-
GP	0.045	0.010 – 0.20
Other	0.13	0.022 – 0.73
Model for effect of physician information source of Literature Reviews		
Obtain information from Literature Reviews		
No	1.00	-
Yes	1.3	0.43 – 3.9
Years in practice (years)		
0-4 years	1.0	-
5-10 years	0.67	0.079 – 5.6
11-20 years	0.20	0.038 – 1.1
>20 year	0.19	0.039 – 0.90
Type of practice		
Community	1.0	-
Academic	1.6	0.39 – 6.8
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.3	0.72 – 15
11 or more	5.1	1.6 – 16
Training Status		
GI	1.0	-
GP	0.046	0.010 – 0.21
Other	0.13	0.024 – 0.67
Model for effect of physician information source of Textbooks		
Obtain information from Textbooks		
No	1.00	-
Yes	1.9	0.50 – 7.5
Years in practice (years)		
0-4 years	1.0	-
5-10 years	0.74	0.086 – 6.4
11-20 years	0.21	0.041 – 1.0
>20 years	0.18	0.040 – 0.84

	OR	95% CI
Type of practice		
Community	1.0	-
Academic	1.7	0.42 – 6.9
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.4	0.77 – 15
11 or more	5.2	1.6 – 16
Training Status		
GI	1.0	-
GP	0.040	0.009 – 0.19
Other	0.133	0.025 – 0.71
Model for effect of physician information source of specialist consults		
Obtain information from specialists		
No	1.00	-
Yes	1.5	0.57 – 3.9
Years in practice (years)		
0-4 years	1.0	-
5-10 years	0.54	0.061 – 4.8
11-20 years	0.19	0.035 – 0.97
>20 years	0.17	0.035 – 0.81
Type of practice		
Community	1.0	-
Academic	1.7	0.41 – 6.8
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.1	0.68 – 14
11 or more	4.9	1.5 - 16
Training Status		
GI	1.0	-
GP	0.040	0.008 – 0.19
Other	0.12	0.021 – 0.63
Model for effect of physician information source of Other source		
Obtain information from Other sources		
No	1.00	-
Yes	1.2	0.22 – 6.1
Years in practice (years)		
0-4 years	1.0	-
5-10 years	0.61	0.068 – 5.5
11-20 years	0.19	0.037 – 0.98
>20 years	0.18	0.037 – 0.83
Type of practice		
Community	1.0	-
Academic	1.7	0.43 – 7.1
Number of pregnant IBD patients managed in past year		
None	1.0	-
1 to 10	3.44	0.77 – 15
11 or more	5.1	1.6 – 16

	OR	95% CI
Training Status		
GI	1.0	-
GP	0.044	0.010 - 0.20
Other	0.13	0.024 – 0.68