The Economic and Clinical Utility of Fecal Calprotectin Use by Family Physicians

Author: Eric Sigmund, post-graduate year 2 family medicine resident, UBC

Principal Supervisor: Dr. Audrey Campbell

Key Stakeholders: Patients with symptoms of irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD); family physicians; gastroenterologists; and the tax-paying population of British Columbia (BC).

Abstract:

Introduction: There is extensive literature on the sensitivity and specificity of fecal calprotectin (FC) to differentiate between IBS and IBD. Moreover, there has been some work done with models in measuring and predicting the effectiveness and cost-effectiveness of using FC in this way.\textsuperscript{1,2} However, there is no readily available analysis of this type applied to the BC medical system. Moreover, the models used above are so complex as to preclude simple modifications to incorporate population-specific data in a different region.\textsuperscript{1,2}

Objective: To conduct an economic analysis to explore whether it would be economically advantageous (while maintaining superior diagnostic outcomes) if the MSP of BC paid for the use of FC by family physicians to differentiate between IBS and IBD in the patient population with a low to moderate pre-test probability of having IBD, and consider clinical implications.

Model Derivation and Analysis: A basic mathematical model was created to approximate the immediate potential cost-savings if the Medical Services Plan (MSP) of BC paid for the use of FC by family physicians to differentiate between IBS and IBD in the patient population with a low to moderate pre-test probability of having IBD. This model also incorporated the demand (in the form of a mathematical constraint) of reducing the number of missed diagnoses of IBD. The parameters used in the model were derived from data in pre-existing medical literature. More specifically, a rapid review was conducted on literature pertaining to the sensitivity and specificity of fecal calprotectin; the pathophysiology of fecal calprotectin; and the pre-existing models for the estimated economic effectiveness of fecal calprotectin use. In addition, the official MSP billing documents were reviewed to gather information on the costs of colonoscopies and gastroenterologist referrals.

Results: Of course, the specific values generated by the model depend on the predicted parameter values that are not entirely known. However, using an evidence-based and systematic approach to estimate these parameters, the model suggests that the use of FC by family
physicians to differentiate between IBS and IBD in the patient population with a low to moderate pre-test probability of having IBD would result in cost savings of over $100 to $190 per patient in this population. Moreover, to prevent one missed or significantly delayed diagnosis of IBD in the population with a low pre-test probability of having IBD, 54 patients from this population would need to be tested with the FC protocol.

**Conclusion:** Analysis with this model suggests that the use of FC by family physicians in BC to differentiate between IBS and IBD (in the patient population with a low to moderate pre-test probability of having IBD) would result in significant cost-savings to the BC health care system while reducing the number of missed and significantly delayed diagnoses of IBD. Coverage of this test by the provincial health insurance plan should be considered.

**Introduction:**

Fecal calprotectin (FC) is a small protein that is especially abundant in neutrophils, in which it likely has an anti-microbial function. Accordingly, with the intestinal inflammation of IBD, as neutrophils move into the damaged intestinal mucosa, some of the neutrophils end up in the stool. Consequently, the abundant fecal calprotectin is also released into the stool. FC has a sensitivity of 0.93 (95% confidence interval 0.85 to 0.97) and a specificity of 0.96 (0.79 to 0.99) for differentiating between IBS and IBD.

Thus, FC is a simple non-invasive test with both a high sensitivity and a high specificity to differentiate IBS from IBD. Such differentiation is very important, given that the treatments and monitoring requirements for IBD are dramatically distinct from those for IBS. Yet a family physician is often challenged to differentiate early or mild IBD from IBS clinically, thus resulting in reliance on observation over time or specialist referrals for colonoscopies. Given that such referrals for mild symptoms often involve waiting months, both strategies ultimately result in the delayed diagnosis and treatment of IBD, as well as unnecessary colonoscopies for some IBS patients. Given the risk of IBD-related complications (including both short-term complications, such as severe exacerbations requiring surgery, as well as longer-term issues like cancer) and the general impairment to quality of life, minimizing such delayed diagnoses can offer the potential for dramatic clinical improvements. Indeed, if the family doctor can be nearly certain that a patient has mild IBD based on a non-invasive test like FC, then this can empower the primary care physician to start basic treatments such as 5-ASA while the patient waits for the specialist appointment (while being cautious not to interfere with the diagnostic accuracy of the colonoscopy with prior treatments). Further, colonoscopies involve small but not completely negligible risks for morbidity or mortality, so many patients with IBS would appreciate avoiding unnecessary colonoscopies if a non-invasive test can effectively rule out IBD. Moreover, the potential cost savings with avoiding such unnecessary referrals can be quite significant, as will be shown later in this paper.
So what is preventing more widespread utilization of fecal calprotectin in the primary care setting of BC? There are a couple of possible reasons. Firstly, the test is relatively new (it only became more widely used around year 2000) so many family physicians in BC may still be unaware of the test. Secondly, the test is not covered under the Medical Services Plan (MSP) of BC, so patients have to pay approximately $150 for the test.

**Objective:**

Therefore, the purpose is to conduct an economic analysis to explore whether it would be economically advantageous (while maintaining superior diagnostic outcomes) if the MSP of BC paid for the use of FC by family physicians to differentiate between IBS and IBD in the patient population with a low to moderate pre-test probability of having IBD, and consider clinical implications.

**Model Derivation:**

The following mathematical model was derived.

Let $VL =$ Population with a *very low* pre-test probability of having IBD,

$W =$ Population with a *low* pre-test probability of having IBD,

$N =$ Population with a *moderate* pre-test probability of having IBD,

and

$VH =$ Population with a *high* pre-test probability of having IBD.

For now, we do not need to assign numerical values to these definitions; that said, this issue will be further discussed later.

Then in the absence of utilizing the FC test, by our definition of the $N$ and $VH$ populations, family physicians would tend to send the $N$ and $VH$ populations to specialists for probable colonoscopies. Similarly, from our definitions of the $VL$ and $W$ populations, family physicians would not be sending the $VL$ and $W$ populations to the specialists in the absence of FC use.

Now suppose the FC test were to be utilized by family physicians only on the $N$ and $W$ populations to provide additional information on whom to send to specialists. This would be a reasonable approach, given that a negative FC test would not avoid a referral in the case of the $VH$ population, since patients with such a high pre-test probability should be sent for a colonoscopy regardless of the FC test results. Furthermore, it is reasonable for the analysis in this paper to be limited to the case of not applying the FC test to patients with a very low pre-test
probability of having IBD, as the false positive rate would likely be unacceptably high and the
costs of ordering the expensive test on all patients with IBS-type symptoms would be very
significant. Thus, with this model of proposed FC test implementation, family physicians would
only order the FC test on the N and W populations; if it is negative, then no referral is required
and simple observation and treatment for presumed IBS would take place. Otherwise, if the FC is
positive, these patients would be referred to specialists for colonoscopies.

Thus, in summary, the model constructed so far consists of the following:
(Total population of primary care patients with IBS or IBD symptoms) = VL + W + N + VH

*Before* implementation of FC:
(Patients sent to specialists for colonoscopies) = N + VH

*After* implementation of FC:
(Patients sent to specialists for colonoscopies) = W_{4FC} + N_{4FC} + VH
where
W_{4FC} = patients from W population with a positive FC test result, and
N_{4FC} = patients from N population with a positive FC test result.

Using this construction, the cost savings from implementing FC testing in this way would be
approximated by
(current costs) – (new costs)
= (current number of referrals)(RF) – (new number of referrals)(RF) –(number of FC tests)($150)
where RF = referral cost = specialist consult fee + colonoscopy fee,
and the $150 is the current cost of FC testing.

But from above, we have
current number of referrals = N + VH,
new number of referrals = W_{4FC} + N_{4FC} + VH,
and
number of FC tests = W + N.

Therefore,
Cost savings
= (N + VH)(RF) – (W_{4FC} + N_{4FC} + VH)(RF) – (W+N)($150)
= (N)(RF) –(N_{4FC })(RF) –(N)($150) – (W_{4FC })(RF) –(W)($150).

But N = N_{4FC} + N_{-FC} ,
where N_{-FC} = patients from population N with a negative FC test result,
so N_{4FC} = N – N_{-FC} , and therefore
Cost savings =
(N)(RF) –(N – N_{-FC} (RF) –(N)($150) – (W_{4FC})(RF) –(W)($150)
= (N_{4FC})(RF) –(N)($150) – (W_{4FC})(RF) –(W)($150).
By the definition of true negatives (TN) and false negatives (FN),
\[ N_{FC} = TN_N + FN_N. \]

Similarly, by the definition of true positives (TP) and false positives (FP),
\[ W_{+FC} = TP_W + FP_W. \]

Thus,
\[
\text{Cost savings} = (TN_N + FN_N)(RF) - (N)(\$150) - (TP_W + FP_W)(RF) - (W)(\$150).
\]

Now, let
\[ \text{No} = \text{number of patients from population N without IBD}, \]
\[ \text{Np} = \text{number of patients from population N with IBD}, \]
\[ \text{Pn} = \text{prevalence of IBD in population N}, \]
\[ \text{Spec} = \text{specificity of the FC test}, \]
and
\[ \text{Sens} = \text{sensitivity of the FC test}. \]

Then,
\[ (TN_N + FN_N) = \text{No}(\text{Spec}) + \text{Np}(1-\text{Sens}) = N(1-Pn)(\text{Spec}) + N(Pn)(1-\text{Sens}). \]

Therefore,
\[
\text{Cost savings} = [N(1-Pn)(\text{spec}) + N(Pn)(1-\text{Sens})](RF) - (N)(\$150) - (TP_W + FP_W)(RF) - (W)(\$150).
\]

Using a similar approach with \((TP_W + FP_W)\), letting
\[ \text{Pw} = \text{prevalence of IBD in population W}, \]
then we have
\[ (TP_W + FP_W) = (\text{Sens})(\text{Pw})(W) + (1-\text{Spec})(1-Pw)(W), \]
and thus
\[
\text{Cost savings} = [N(1-Pn)(\text{spec}) + N(Pn)(1-\text{Sens})](RF) - (N)(\$150) - [(\text{Sens})(\text{Pw})(W) + (1-\text{Spec})(1-Pw)(W)](RF) - (W)(\$150).
\]

As already mentioned,
\[ \text{Sens} = 0.93 \ (95\% \ \text{confidence interval 0.85 to 0.97}) \]
and
\[ \text{Spec} = 0.96 \ (0.79 \ to \ 0.99). \]

Furthermore, using the data from the British Columbia Ministry of Health Medical Services Commission Payment Schedule, we see that a colonoscopy fee is $230, while a gastroenterologist consultation fee is $158. Therefore, RF can be approximated by $388.

Inputting these specific values, we have
\[
\text{Cost savings}
\]
\[ N(1-P_n)(0.96) + N(P_n)(1-0.93) \times (\$388 - (N)(\$150)) - [(0.93)(P_w)(W) + (1-0.96)(1-P_w)(W)] \times (\$388 - (W)(\$150)). \]

An obvious weakness of this model is that it fails to take into account the costs associated with missed or delayed diagnoses of IBD. Admittedly, it is very difficult to quantify such costs. However, we can work around this difficulty by introducing a constraint into the model such that we demand that the implementation of FC testing result in a decrease of missed diagnoses of IBD (which, of course, includes significantly delayed diagnoses).

Thus, we now have two demands:
1. Cost savings > 0
and
2. (Missed diagnoses of IBD with FC) < (Missed diagnoses of IBD without FC).

We will now construct a model for the second demand. Let \( X = \) number of missed diagnoses of IBD (which we will simply refer to as “misses”) in population \( VL \).

Now, we will assume that a colonoscopy (with biopsies) is 100% sensitive at detecting IBD (this is reasonable, given that it is the gold standard that we use to define sensitivity and specificity data for FC testing). Therefore, the number of misses in the populations \( N \) or \( VH \) would be 0 before FC implementation, as all of these patients are being sent for a colonoscopy. Thus, 
\[ \text{(Missed diagnoses of IBD without FC)} = W_p + X, \]
where \( W_p = \) number of patients from population \( W \) with IBD. This follows from the fact that, from our definition of population \( W \), none of the patients in this group are being sent for colonoscopy in the present state before FC use in the primary care setting.

But \( W_p \) can be approximated by \( (W)(P_w) \).

Thus, 
\[ \text{(Missed diagnoses of IBD without FC)} = (W)(P_w) + X. \]

Now, with use of FC, we have
\[ \text{(Missed diagnoses of IBD with FC)} = FN_w + FN_n + X \]
\[ = (W_p)(1-\text{Sens}) + (N_p)(1-\text{Sens}) + X \]
\[ = (W)(P_w)(1-\text{Sens}) + (N)(P_n)(1-\text{Sens}) + X \]
\[ = (W)(P_w)(0.07) + (N)(P_n)(0.07) + X. \]

Combining all of the above, we have that the demand
\[ \text{(Missed diagnoses of IBD with FC)} < \text{(Missed diagnoses of IBD without FC)} \]
equates to
\[ (W)(P_w)(0.07) + (N)(P_n)(0.07) + X < (W)(P_w) + X \]
\[ \Rightarrow 0.07(WP_w + NP_n) < (W)(P_w) \]
\[ \Rightarrow 0.07NP_n < 0.93WP_w \]
\[ N/W < (0.93/0.07)(Pw/Pn) \]
\[ N/W < (13.3)(Pw/Pn). \]

Therefore, our two demands are

\[
[ N(1-Pn)(0.96) + N(Pn)(1-0.93)](\$388) - (N)(\$150) - [(0.93)(Pw)(W) + (1-0.96)(1-Pw)(W)](\$388) - (W)(\$150) > 0
\]

and

\[
N/W < (13.3)(Pw/Pn).
\]

\[ N/W < (13.3)(Pw/Pn) \]
and

\[ (N/W)[(388)[(1-Pn)(0.96) + (Pn)(1-0.93)] - (150)] > 0 \]

For ease of notation, we will now omit the dollar sign.

Claim:

\[
(388)[(1-Pn)(0.96) + (Pn)(1-0.93)] - (150) > 0 \quad \text{(this is relevant so that we can divide both sides by of the above expression without changing inequality sign)}.
\]

Proof:

By our chose of the definition of “very high pre-test probability,” we can have \( Pn < 64.4\% \).

Thus,

\[
Pn < 222.48/345.32 = 0.644
\]

\[ 222.48 > (388)0.89Pn = 345.32Pn \]

\[ 372.48 - (388)0.89Pn > 150 \]

\[ 388(0.96 - 0.96Pn + 0.07Pn) > 150 \]

\[ 388[(1-Pn)(0.96) + (Pn)(1-0.93)] - (150)] > 0. \]

Q.E.D.

Thus, we can divide the inequality

\[ (N/W)[(388)[(1-Pn)(0.96) + (Pn)(1-0.93)] - (150)] > [150+(388)((0.93)(Pw)+(1-0.96)(1-Pw))]} \]

by

\[ (388)[(1-Pn)(0.96) + (Pn)(1-0.93)] - (150)]

and

\[ (N/W)[(388)[(1-Pn)(0.96) + (Pn)(1-0.93)] - (150)] > [150+(388)((0.93)(Pw)+(1-0.96)(1-Pw))].

Therefore, our two demands can be combined into a single expression of the form
To simplify this, note  

\[
150 + (388)(0.93P_w + (1-0.96)(1-P_W)) = 150 + (388)(0.93P_w + 0.04 - 0.04P_w) = 150 + 388(0.89P_w + 0.04) = 165.52 + 345.32P_w 
\]

and

\[
(388)[(1-P_n)(0.96) + (P_n)(1-0.93)] - 150 = 388[0.96 - 0.96P_n + 0.07P_n] - 150 = 222.48 - 388(0.89P_n) = 224.48 - 335.32P_n. 
\]

Hence, our two demands amount to

\[
(165.52 + 345.32P_w)/(224.48 - 335.32P_n) < N/W < (13.3)(P_w/P_n). 
\]

In other words, the above inequality needs to be satisfied in order for the implementation of FC testing in the primary care setting to result in a net cost savings while simultaneously reducing the number of missed (or significantly delayed) diagnoses of IBD.

**Model Analysis:**

Conceptually, the above inequality makes a lot of sense. Indeed, the left side of the inequality is saying that, for there to be cost savings (using the limited model that does not take into account the costs associated with missed or significantly delayed diagnoses of IBD), N has to be relatively large compared to W. In other words, since implementation of FC testing would involve using the test on all of the patients in the W population, all of whom were not going to be sent for a colonoscopy in the absence of FC testing, a cost savings would only result if W is relatively small compared to N. Similarly, the larger the population N, the greater the absolute number of patients in this group with negative FC results who will end up avoiding a gastroenterology referral that they would otherwise have in the absence of FC use. In terms of the Pw and Pn dependence on the left side, note that, the higher the prevalence of IBD in population W (i.e., the higher the Pw), the greater the number of expected positive FC results in W, and hence the higher the costs associated with referring these patients who would otherwise not have been referred in the absence of FC testing. On the other hand, the greater the prevalence in population N (i.e., the higher the Pn), the lower the number of expected negative FC results in this population, and hence the lower the number of unnecessary colonoscopies being avoided in this population by use of FC; of course, this contributes to reduced cost savings. Putting all of this together, for maximal cost savings (not taking into account costs due to missed or significantly delayed diagnoses), we want a high N, and a low W, Pw, and Pn. This conceptual conclusion fits with the mathematical expression above.
Turning our attention to the right side of the expression, we see that, for there to be a decrease in the number of missed (or significantly delayed) diagnoses of IBD after FC testing implementation, we want N to be relatively small compared to W. This makes conceptual sense, given that a larger N would result in a greater absolute number of expected false negatives in population N when FC is utilized, and hence a greater number of patients with IBD not receiving the colonoscopy they otherwise would have if FC were not utilized. Applying a similar logic to population W, we see that the smaller the population W, the smaller the absolute number of expected true positives in W with application of FC testing, and hence the smaller the value of the corresponding reduction in missed diagnoses of IBD that would otherwise have occurred if FC testing were not utilized. Looking at the far right part of the expression, the dependence on Pw and Pn makes sense for similar reasons. More specifically, the higher the Pw, the greater the prevalence of IBD in W, and hence the greater the number of expected true positives in W when using FC testing, resulting in fewer missed diagnoses of IBD as explained above. Similarly, with a lower Pn, we anticipate a lower number of false negatives with FC testing in population N, and this translates to fewer missed diagnoses by applying FC testing to population N.

So we now have a model to show the relationships among N, W, Pn, and Pw that need to be considered when deciding if and how FC testing implementation in British Columbia would result in cost savings while reducing missed and significantly delayed diagnoses of IBD. Naturally, we would like to input actual province-specific data for N, W, Pn, and Pw to determine whether FC implementation would achieve the stated goals. Unfortunately, such data is not readily available. Moreover, Pn and Pw actually depend on how we exactly define (in terms of precise numbers) “very low, low, moderate, and high” pre-test probabilities. Ultimately, such definitions reflect the suggested guidelines for when family physicians should order FC testing in a patient with IBD or IBS symptoms. Of course, N and W also depend on such definitions, since they are clearly a function of Pn and Pw, respectively.

Accordingly, while we are limited by the lack of data, we are also empowered by the flexibility in considering the different choices for the pre-test probabilities we feel are appropriate for FC testing. With this in mind, we will now explore the range of outcomes when considering a spectrum of possible parameter values.

For example, suppose we define “very low, low, moderate, and high” pre-test probabilities such that Pn = 20% and Pw = 5%. This is a reasonable consideration, since a meta-analysis (involving patients from many regions outside of BC) showed a prevalence of IBD in the total population of patients suspected of having IBD (as demonstrated via referrals for colonoscopies for this reason) of 32%. Therefore, since this population corresponds to the combined populations of N and VH in our model, this meta-analysis would suggest that Pn < 32% while Pvh > 32% (where Pvh is the prevalence of IBD in our VH population).

Furthermore, the total prevalence of IBD in BC is 323 per 100,000 i.e. 0.323/100 or 0.323%.7
Then, using $P_n = 20\%$ and $P_w = 5\%$, we have

Cost savings

\[
= [N(1-0.2)(0.96) + N(0.2)(1-0.93)](S388) - (N)(S150) - [(0.93)(0.05)(W) + (1-0.96)(1-0.05)(W)](S388) - (W)(S150)) = N(153.416) - W(117.21).
\]

Further, our demand

\[
\frac{N}{W} < (13.3)(P_w/P_n)
\]

becomes

\[
\frac{N}{W} < (13.3)(0.05/0.2)
\]

\[
\Rightarrow \frac{N}{W} < 3.325
\]

\[
\Rightarrow N < 3.325W.
\]

Applying all of the above results, we get that, for $P_n = 20\%$ and $P_w = 5\%$, our demands

(Misses with FC) < (Misses without FC)

and

(Cost savings) > 0

correspond to

\[
\frac{N}{W} < 3.325
\]

and

\[
N(153.416) - W(117.21) > 0 \Rightarrow \frac{N}{W} > (117.21)/(153.416) = 0.764.
\]

Combining the above two inequalities, we get

\[
0.764 < \frac{N}{W} < 3.325.
\]

In other words, for $P_n = 20\%$ and $P_w = 5\%$, in order for FC testing implementation to reduce costs while simultaneously decreasing missed or significantly delayed IBD diagnoses, $N$ would need to be between 0.764 and 3.325 times the size of $W$.

Suppose we choose a value approximately midway in this range, such that $N = 2W$. Then

Cost savings

\[
= 2W(S153.416) - W(S117.21).
\]

\[
= W(S189.62)
\]

\[
= (N/2)(S189.62)
\]

\[
= N( S94.81).
\]

This means that, for each patient in population $W$ being tested with FC, $189.62$ would be saved when not considering the costs associated with missed or significantly delayed IBD diagnoses. Similarly, $94.81$ would be saved for each patient in population $N$. Since we know that FC testing would reduce the number of such missed diagnoses for our parameters in this situation, the true cost savings (when taking into account the costs associated with missed or severely delayed diagnoses) should exceed $189$ per patient in population $W$ and $94$ per patient in
For $N = 2W$, we can use our previous results to calculate the expected number of reduced missed (or severely delayed) IBD diagnoses as

$$(W)(P_w) + X - [(W)(P_w)(0.07) + (N)(P_n)(0.07) + X] = 0.93WP_w - 0.07NP_n = 0.93W(0.05) - 0.07(2W)(0.2) = W(0.0185).$$

Therefore, since $1/0.0185 = 54$, this means that you would need to order FC for 54 patients from population W in order to prevent 1 missed or significantly delayed diagnosis of IBD. Recall that this value takes into account the missed diagnoses resulting from false negative FC results in population N.

An obvious and major weakness from the above analysis is that the $P_w$ value used was not derived in any rigorous way from available prevalence data. As such, we should explore constraints in a more rigorous way using the following approach. First, recall that the meta-analysis data can be used to approximate the prevalence of IBD in the combined populations of N and VH to be around 32%, and so $P_w < P_n < 0.32$.

Therefore,

$$(224.48 - 335.32P_n) > (224.48 - 335.32*0.32) = 117.48$$

and

$$(165.52 + 345.32P_w) < (165.52 + 345.32*0.32) = 276.$$

Thus,

$$(165.52 + 345.32P_w)/(224.48 - 335.32P_n) < 276/117.48 = 2.35.$$ 

Therefore, if $N/W > 2.35$, then our demand

$$(165.52 +345.32P_w)/(224.48 -335.32P_n) < N/W$$

is satisfied.

Next, note that,

$P_n < 0.32$

$P_w/P_n > P_w/0.32 = 3.1P_w$

$$(13.3)(P_w/P_n) > (13.3)(3.1P_w) = 41.23P_w.$$ 

Thus, if $N/W < 41.23P_w$, then the number of missed/delayed diagnoses will be reduced.

So, if $2.35 < N/W < 41.23P_w$, then we will also satisfy our two original demands, namely
\[(165.52 + 345.32Pw)/(224.48 - 335.32Pn) < N/W < (13.3)(Pw/Pn).\]

Clearly, a necessary (but not sufficient) condition for the above is

\[2.35 < 41.23Pw \Rightarrow Pw > 2.35/41.23 = 5.7\%.

In other words, with only the assumption (based of the meta-analysis data) that the prevalence of populations N and VH collectively is 32%, then we need to choose the FC protocol such that the average pre-test probability of patients in W (i.e., the prevalence, Pw) exceeds 5.7%. However, we know that Pw < Pn < 32%.

Consequently, Pw must be chosen to be somewhere in the 5.7% to 31% range if the simplified constraint were to be fulfilled.

Of course, practically speaking, a guideline for FC use would not specify a prevalence number, but instead reference a chosen pre-test probability range in which FC should be utilized. With this in mind, let wL be the pre-test probability above which FC testing should be ordered, and let wH be the pre-test probability above which patients are currently being sent for colonoscopy in the absence of FC use. Then wH is not something we choose; rather, it is a fixed value in our model that reflects the current pattern of practice. In contrast, wL is something we can choose. In fact, our population W is defined as those patients with a pre-test probability between wL and wH. Accordingly, Pw can be viewed as the weighted average of such pre-test probabilities in W (with Pw between wL and wH). Similarly, N represents those patients with a pre-test probabilities above wH but below those of population VH. As such, unlike W, N does not depend on wL or Pw.

Applying the above observations, note that if wL is chosen to be a lower value within the range of 5.7% to 31%, then W becomes larger, and so N/W becomes smaller. However, from the above explanations, we also know that a smaller wL would result in a lower Pw value, and hence 41.23Pw also would decrease. This relationship between wL, Pw, and W can more readily be used to help guide the choice of wL for the BC population when considering the simplified constraint

\[2.35 < N/W < 41.23Pw.

Not only is this simpler to use, but this revised version of our model also has the added strength of having incorporated prevalence data from a meta-analysis.

In this way, one could quickly get an idea of how to create guidelines on the appropriate use of FC in the primary care setting.

**Discussion:**
This paper has presented an economic analysis exploring the use of FC by family physicians to differentiate between IBS and IBD in the patient population with a low to moderate pre-test probability of having IBD.

The main strengths of this paper include the use of a simple yet apparently novel model to analyze the expected financial consequences of using FC while incorporating the demand of superior diagnostic outcomes. Furthermore, the parameters utilized in this model are derived from very high-quality data in the medical literature (including that collected from a meta-analysis).

The major limitations of this paper include the inability to more precisely consider the economics associated with unnecessary colonoscopies and the impact of early or delayed diagnoses of IBD. In addition, the overall results heavily depend on some parameters with limited associated data.

It is highly probable that the pre-test probability thresholds could be chosen (with the guidance from models like those derived in this paper) such that FC testing by family physicians in BC for patients with low to moderate pre-test probabilities of IBD could be fully covered by MSP to reduce total health care costs while also decreasing missed and significantly delayed diagnoses of IBD. The expected clinical implications of this were explored, with emphasis on the potential for earlier treatment (via family doctors while waiting for the specialist appointments, or by the possibility of shorter wait times for gastroenterologists by reducing the number of IBS patients being sent). Moreover, there is the closely-related potential benefit of a more rapid recognition and surveillance of IBD-related complications. Of course, patients certainly also tend to appreciate avoiding the discomfort and risks associated with colonoscopies whenever possible.

Lastly, it is important to note that there are additional potential benefits of FC use that were not discussed in this paper as they are less directly relevant to family physicians. For example, gastroenterologists are now finding utility in using serial FC testing to monitor disease activity and response to treatment.

**Conclusions:**

In conclusion, analysis with this model suggests that the use of FC by family physicians in BC to differentiate between IBS and IBD (in the patient population with a low to moderate pre-test probability of having IBD) would result in significant cost-savings to the BC health care system while reducing the number of missed and significantly delayed diagnoses of IBD. Coverage of this test by the provincial health insurance plan should be considered.

**Authorship Statement:**

I conceived of this project idea on my own and completed the project on my own (including development of the mathematical model, collecting data to use in the model, and interpreting the
model) with general guidance from Dr. Audrey Campbell (as described below).

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**References:**


