

# YORKSHIRE AND HUMBER ACADEMIC HEALTH SCIENCE NETWORK

## Faecal Calprotectin Screening in Primary Care

### Final Report

HAYDEN HOLMES, Senior Research Consultant

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# Executive Summary

## INTRODUCTION

Patients often see their GPs with lower gastrointestinal symptoms. These are challenging to deal with because different diseases can cause similar symptoms. Many patients will have irritable bowel syndrome (IBS). More rarely the symptoms are caused by inflammatory bowel disease (IBD). This disease affects one in 250 and urgent specialist investigation and treatment is required.

Calprotectin is a stable protein released from white blood cells during inflammation. When the lower gastrointestinal tract is inflamed elevated levels of calprotectin are detected in the stool. A normal faecal calprotectin (FC) strongly predicts for IBS and a raised FC increases the likelihood of IBD<sup>1</sup>.

NICE have assessed FC testing in various scenarios and have published formal guidance for its use<sup>2</sup>. However, most studies investigated FC testing in secondary care, not primary care. In primary care, a raised calprotectin test result is less accurate at predicting IBD than a normal test result is for predicting IBS.

In the Yorkshire and Humber region, the NICE guidelines are not widely implemented. This is because FC testing is not available in some areas and other local guidelines have been introduced. A new FC pathway has been developed with the intention that it could be universally adopted to reduce the number of unnecessary referrals to secondary care and unnecessary colonoscopies.

This report describes the modelling approach used to assess the new pathway and the results of the economic model.

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<sup>1</sup> Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technology Assessment, No. 17.55*. N Waugh, E Cummins, P Royle, N-B Kandala, D Shyangdan, R Arasaradnam, C Clar, and R Johnston.

<sup>2</sup> National Institute for Health and Care Excellence (NICE), Clinical Guideline [CG61], irritable bowel syndrome in adults: diagnosis and management <https://www.nice.org.uk/guidance/cg61>.

## METHODS

York Health Economics Consortium (YHEC) and the Yorkshire and Humber Academic Health Science Network (YHAHSN) came together to develop the framework for an economic model and agreed on the development of a cost-consequence model to measure the following clinically meaningful outputs:

- Total cost for cohort;
- Correctly diagnosed IBS cases;
- Correctly diagnosed IBD cases;
- Unnecessary colonoscopies (false positives);
- Outpatient gastroenterology appointments.

YHEC staff undertook a targeted literature search to determine the effectiveness of the current patient pathway. Two key evidence sources were identified. The first was data from Tibble et al (2002)<sup>3</sup> which was used to inform a 2010 report for the NHS Centre for Evidence-based Purchasing (CEP) report; *Value of calprotectin in screening out irritable bowel syndrome*<sup>4</sup>. The second key evidence source was a systematic review of faecal calprotectin testing for differentiating between IBS and IBD by Waugh et al (2003)<sup>5</sup>. The Waugh et al systematic review was used by NICE to inform its diagnostic guidance for faecal calprotectin<sup>6</sup>.

The YHAHSN provided observational data from a pilot of the new pathway conducted by a selection of general practices in the York region. The York data included both, the sensitivity and specificity of the observed patients from the new pathway and a projected sensitivity and specificity of the observed cohort if they had followed the NICE guidance (using a referral cut-off of >50ug/g to a single stool sample).

This enabled us to develop a model for the following comparators:

1. Non FC pathway informed by Tibble et al
2. Non FC pathway informed by Waugh et al
3. Projected results of the York cohort following the >50ug/g cut-off
4. >50 ug/g cut-off informed by Tibble et al
5. >50 ug/g cut-off informed by Waugh et al

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<sup>3</sup> Tibble JA, Sigthorsson G, Foster R, Forgacs I, Bjarnason I. Use of surrogate markers of inflammation and Rome criteria to distinguish organic from nonorganic intestinal disease. *Gastroenterology*. 2002 Aug;123(2):450-60. PubMed PMID: 12145798.

<sup>4</sup> Department of Health, Centre for Evidence-base Purchasing, CEP09041 <http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx>

<sup>5</sup> Waugh N, Cummins E, Royle P, Kandala NB, Shyangdan D, Arasaradnam R, Clar C, Johnston R. Faecal Calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technol Assess*. 2013 Nov;17(55):xv-xix, 1-211. doi: 10.3310/hta17550. Review. PubMed PMID: 24286461; PubMed Central PMCID: PMC4781415.

<sup>6</sup> NICE diagnostic guidance 11: Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel. 2013. [www.nice.org.uk/guidance/dg11](http://www.nice.org.uk/guidance/dg11).

A decision tree model was developed with a separate tree for the intervention and the five comparator pathways. Costs and outcomes were calculated for each of the decision trees and incremental costs were calculated and reported on separate results sheets.

## **RESULTS**

### **Tibble et al – No FC**

For the new pathway, the model estimates a saving of over £100,000 per 1,000 patients, while diagnosing an additional 175 IBS cases, (therefore, avoiding 175 unnecessary colonoscopies) and avoiding 162 gastroenterology outpatient visits.

### **Waugh et al – No FC**

For the new pathway, the model estimates a cost saving of approximately £67,000 per 1,000 patients. The intervention arm also correctly diagnoses more IBS and avoids over 100 colonoscopies and gastroenterology outpatient appointments. However, there is a trade off with diagnosing 4-5 fewer cases of IBD due to the higher referral rates in the comparator arm.

### **York projected data**

When comparing the new pathway with projected data for the >50ug/g cut-off used on a single stool sample, the model returns the most dominant result of all the comparators with a £160,000 saving and greater than 250 more correctly diagnosed IBS cases. The intervention arm avoids an unnecessary colonoscopy and gastroenterology outpatient referral for every four patients seen in primary care.

### **Tibble >50ug/g cut-off**

When compared to Tibble et al published data for >50ug/g cut-off, the intervention arm dominates with both a saving and clinical benefit. The intervention arm diagnoses more than 100 additional IBS cases in primary care and an additional 3-4 IBD cases. The intervention arm avoids >100 gastroenterology outpatient referrals and unnecessary colonoscopies

### **Waugh et al >50ug/g cut-off**

When comparing the intervention pathway with the Waugh et al published data for the >50ug/g cut-off, the model estimates that the intervention arm is more costly incurring an additional £25,000 it is also less effective at diagnosing IBS cases but does diagnose slightly more IBD cases per 1,000 patients at a cost of £20,937 per diagnosed IBD case. The intervention pathway does have slightly fewer gastroenterology referrals but higher unnecessary colonoscopies.

## **DISCUSSION**

When compared to four of the five comparators used in the model, the model predicts the intervention arm is a cost-saving strategy. It is dominant when compared to Tibble et al in both the no FC and >50ug/g cut-off strategies. It is cost saving but diagnoses fewer cases of IBD when compared with the Waugh et al data for the no FC pathway.

The one comparator that the intervention arm did not have dominance was from the >50ug/g cut-off from the Waugh et al systematic review. Nearly all studies used in the Waugh et al systematic review came from secondary care studies<sup>7</sup>. This could be interpreted that the sensitivity and specificity from that pooled analysis is reflective of FC testing in an optimum environment as it essentially uses a population that has already undergone primary care screening. It is noted in the text of Waugh that Jellema et al<sup>8</sup> had reservations about applying results from specialist care to primary care.

We also ran a separate scenario comparing the published data from Waugh et al for the >50 ug/g cut-off, which was used by NICE, with the projected data for the >50ug/g cut-off from the York data. The model predicted the Waugh et al arm would be £170,000 less expensive per 1,000 patients and would diagnose 300 more cases of IBS in primary care than the York projections using the same pathway.

This comparison shows the vast gulf between using FC in an optimal environment and using FC in primary care for low risk patients who exhibit no red flags upon presentation. There is the potential that using the current NICE guidelines and assuming the optimal sensitivity and specificity data could actually be costing the NHS significantly in terms of patient outcomes, wait times for treatment and longer waitlists for gastroenterology outpatient appointments that are being taken up by unnecessary referrals. We would recommend that there needs to be further study on FC in a primary care environment using a range of FC cut-offs.

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<sup>7</sup> Waugh N, Cummins E, Royle P, et al. Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. Southampton (UK): NIHR Journals Library; 2013 Nov. (Health Technology Assessment, No. 17.55.) Chapter 2, Results of clinical effectiveness review.

<sup>8</sup> Jellema P, van Tulder MW, van der Horst HE, Florie J, Mulder CJ, van der Windt DA. Inflammatory bowel disease: a systematic review on the value of diagnostic testing in primary care. *Colorectal Dis* 2011;13:239–54. 10.1111/j.1463-1318.2009.02131.x.

# Section 1: Introduction

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## 1.1 CONTEXT

Patients often see their GPs with lower gastrointestinal symptoms. These are challenging to deal with because different diseases can cause similar symptoms. Many patients will have irritable bowel syndrome (IBS). IBS affects 10-20% of the population and is a condition characterised by disordered function in the absence of inflammation<sup>9</sup><sup>10</sup>. NICE guidance exists to help GPs manage patients with IBS<sup>11</sup>. Therefore, if the GP can make the diagnosis positively, then the patient will not need to be referred to secondary care for expensive, invasive investigations (colonoscopy and CT scans)<sup>12</sup>. More rarely the symptoms are caused by inflammatory bowel disease (IBD). This disease affects one in 250 and urgent specialist investigation and treatment is required.

Calprotectin is a stable protein released from white blood cells during inflammation. When the lower gastrointestinal tract is inflamed elevated levels of calprotectin are detected in the stool. A normal faecal calprotectin (FC) strongly predicts for IBS and a raised FC increases the likelihood of IBD<sup>13</sup>.

Because it is difficult to distinguish the one from the other, unnecessary referrals to specialist care for patients with IBS and late referrals for patients with IBD are made. Calprotectin tests have been developed to help distinguish between IBD and non-inflammatory bowel diseases. NICE have assessed FC testing in various scenarios and have published formal guidance for its use<sup>14</sup>. However, most studies investigated FC testing in secondary care, not primary care. In primary care, a raised calprotectin test result is less accurate at predicting IBS than a normal test result is for predicting IBD. Often the FC is falsely raised and so there is a risk of inundating secondary care with inappropriate referrals at increased cost and risk for patients.

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<sup>9</sup> Stone et al, Prevalence and management of IBD: a cross-sectional study from central England, *Eur J Gastroenterol Hepatol* 2003.

<sup>10</sup> National Institute for Health and Care Excellence (NICE), Clinical Guideline [CG61], irritable bowel syndrome in adults: diagnosis and management <https://www.nice.org.uk/guidance/cg61>.

<sup>11</sup> National Institute for Health and Care Excellence (NICE), Clinical Guideline [CG61], irritable bowel syndrome in adults: diagnosis and management <https://www.nice.org.uk/guidance/cg61>.

<sup>12</sup> National Institute for Health and Care Excellence (NICE), Clinical Guideline [CG61], irritable bowel syndrome in adults: diagnosis and management <https://www.nice.org.uk/guidance/cg61>.

<sup>13</sup> Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technology Assessment, No. 17.55*. N Waugh, E Cummins, P Royle, N-B Kandala, D Shyangdan, R Arasaradnam, C Clar, and R Johnston.

<sup>14</sup> NICE diagnostic guidance 11: Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel. 2013. [www.nice.org.uk/guidance/dg11](http://www.nice.org.uk/guidance/dg11).

Clinical advice indicates that in addition to the reduced accuracy in the real world setting, there is also poor uptake of the NICE guidance for the use of FC testing. Clinical experts consider this is because uncertainties exist at primary care level about its implementation and because GPs consider they are already effective at distinguishing between IBS and IBD.

## **1.2 METHODOLOGIES**

The Yorkshire and Humber Academic Health Science Network (YHAHSN) has asked YHEC to construct an economic model to test the cost effectiveness of the use of faecal calprotectin testing as a risk assessment tool for use in primary care for patients presenting with lower gastrointestinal symptoms in line with NICE DG11.

The project was broken down into stages:

1. A project initiation stage;
2. Model development stage;
3. Literature search stage;
4. Model population stage.

### **Project Initiation**

We had an initial project initiation meeting between the YHAHSN and YHEC to discuss the project and potential ways to show the data. It was agreed that a cost-consequence model should be developed. The model should compare costs and outcomes for the new intervention patient pathway (the intervention) when compared with current practice. It was noted that in 2010, YHEC had developed a cost-consequence model for the Department of Health, NHS Purchasing and Supply Agency, Centre for Evidence-based Purchasing (CEP)<sup>15</sup>. It was agreed that this would make a good foundation for future models.

### **Model Development Stage**

A cost-consequence model framework was developed. The YHAHSN then tested the model to determine if it was fit for purpose to display the information required by the YHAHSN. A follow up meeting between the YHAHSN and YHEC was used to go through the model in more detail and for YHEC to receive feedback on its functionality. We also used this session to gain expert clinical advice from Dr James Turvill on patient pathways and treatments.

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<sup>15</sup> Department of Health, Centre for Evidence-base Purchasing, CEP09041  
<http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx>

## Literature Search Stage

We undertook a targeted literature search to identify what the most appropriate comparators were for evaluation. We used published data to inform appropriate sensitivity and specificity data for the comparator arms used in the model. The York Faecal Calprotectin Care Pathway (YFCCP) provided data to inform the sensitivity and specificity of the intervention arm. A range of resources were used to inform the costs used in the model. We noted that NICE had undertaken a review of its FC guidance (DG11)<sup>16</sup> in May 2017 and had decided to move this guidance to the static list, indicating that there had been no significant new evidence since it was last reviewed by NICE in 2013. Taking this into consideration we were generally satisfied that the NICE evidence review of 2013 was still a good source for the most up to date evidence.

## Model Population Stage

We then updated the model inputs for user testing. The model was again reviewed by the YHAHSN with the updated data. YHEC and the YHAHSN had a follow up meeting to discuss the capabilities of the model. The range of comparisons was agreed and the preliminary results of the model discussed. 6-month follow up data from the YFCCP was used to populate the model. Sensitivity analysis was built into the model to test different scenarios. YHEC then ran an internal quality assurance process of the model whereby a senior consultant who had not been involved in the development of the model pressure tested the model using model validation checklists. The model was then finalised.

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<sup>16</sup> NICE diagnostic guidance11: Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel, Evidence, review decision <https://www.nice.org.uk/guidance/dg11/evidence/review-decision-may-2017-4474871533?tab=evidence>

## Section 2: The Model

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### 2.1 MODEL OUTLINE

The patient population used in the model is patients presenting in primary care with lower gastrointestinal symptoms suggestive of IBS and who are exhibiting no red flag symptoms or signs for suspected cancer. Patients exhibiting red flag symptoms would go down a different patient pathway and are not included in this analysis. Some people with IBS may not present at the GP and may opt for over the counter treatments. The prevalence data for the model comes from observed data from the YFCCP; therefore, patients who do not present at their GP are not included in this model.

We developed a decision tree model to determine the cost-effectiveness of different evidence pathways with different sensitivity and specificity in the diagnosis of IBS and IBD. We used a simplifying assumption that all patients entering the model will have either IBS or IBD. IBS is used as a proxy for all non-IBD outcomes and IBD is the only organic disease outcome used in the model. This is consistent with other similar models used to assess the cost effectiveness of FC as a risk assessment tool for IBD and IBS<sup>1718</sup>. The prevalence of IBD in the model is informed by observed prevalence of IBD in the YFCCP. Each pathway of the decision tree leads to different costs as a result of different patient experience, for example; patients will have a different number of GP visits, specialist referrals or different medication.

The probabilities of moving down different pathways are determined by the prevalence of IBD in the cohort and the sensitivity and specificity of each of the evidence pathways. The model then calculates the total costs and total patient outcomes for each of the evidence pathways. The model compares the different pathways and calculates the incremental change in costs and outcomes, which are reported on separate results sheets.

The model was developed in Excel and used a cohort of 1,000 hypothetical patients. This cohort number can be varied by the user to simulate an estimated local patient cohort. This analysis was taken from the perspective of the payer, in this case, the NHS and as such only costs that would be incurred by the NHS are included. The model does not have an explicit time horizon, the time horizon is the time taken to reach a defined clinical endpoint of positive IBS or positive IBD. There is no discounting used in the model due to the short time horizon.

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<sup>17</sup> NICE, Diagnostic Guidance 11, evidence overview DAP12, <https://www.nice.org.uk/guidance/dg11/documents/faecal-calprotectin-diagnostic-tests-for-inflammatory-diseases-of-the-bowel-evidence-overview-dap122>

<sup>18</sup> Department of Health, Centre for Evidence-base Purchasing, CEP09041 <http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx>

## 2.2 DESCRIPTION OF INTERVENTION AND INTERVENTION PATHWAY

Each of the pathways used in the model are risk assessment pathways essentially used to screen for IBD. Clinical expert advice is that the current NICE guidance for FC screening are not widely implemented across Yorkshire and Humber. This is because in some areas there is no access to FC testing and in others, a local guideline has been introduced. The intervention care pathway has been developed using a higher FC cut-off than the current NICE guidance and includes a follow-up FC test to confirm the next steps for primary care. The intervention pathway is described as follows (a model schematic illustrating this pathway is provided below; Figure 2.1, Section 2.4):

1. Patient presents to GP with lower gastrointestinal symptoms suggestive of IBS or IBD but there is diagnostic uncertainty; cancer is not suspected. After appropriate baseline investigations patient receives diagnostic FC test to detect inflammation in conjunction with assessment of patient history and physical examination;
2. Patients return to GP, those with an FC >100 receive a second FC test to detect inflammation. Those with an FC <100 are treated for IBS;
3. Patients with a second FC test of >100 are then referred on to gastroenterology. Those with an FC >250 are referred urgently. Those with an FC <100 on the second FC test treated for IBS;
4. Those referred to gastroenterology are either confirmed as having IBD (IBD true positive) or confirmed as not having IBD (IBD false positive) and are treated for IBS;
5. Those treated for IBS will either have their symptoms adequately controlled (IBD true negative) or will remain symptomatic;
6. Those that remain symptomatic will have further testing by their GP and may be started on second-line IBS medication. These patients will either have their symptoms adequately controlled (IBD true negative) or will remain symptomatic;
7. Those that continue to have unresolved symptoms will be referred on to gastroenterology for further assessment;
8. Patients referred to gastroenterology are either confirmed as having IBD (IBD false negative) or confirmed as not having IBD (IBD true negative) and continue treatment for IBS.

The intervention pathway uses prevalence, sensitivity and specificity data from the YFCCP. Clinical advice was used to form assumptions for the proportion of patients being prescribed medication and second-line medication for IBS.

There is functionality built into the model that not all GPs will adhere with the intervention pathway. Data from the YFCCP indicates that approximately 90% of GPs are adhering with the intervention pathway. We have used 100% adherence in our base-case estimates to illustrate the potential benefits of this pathway when fully utilised. This is consistent with other published studies used in the NICE guidance where GP adherence was not considered, therefore, implicitly using a 100% adherence rate. We have also reported results using a conservative estimate that 85% of GPs will adhere with the pathway in the results section. The 15% that do not adhere to the pathway are assumed to have the same sensitivity and specificity as the non-FC testing comparator pathway.

## 2.3 DESCRIPTION OF COMPARATORS AND COMPARATOR PATHWAYS

### Comparator 1: Non-FC Testing Pathway

The model includes a drop-down function here to select between two sets of published data for the Non-FC testing pathway. The first is the published data Tibble et al (2002)<sup>19</sup> which gives the sensitivity and specificity for ESR and CRP testing to identify IBD in a low-risk patient population. This is the reference which was used for the NHS Centre for Evidence-based Purchasing (CEP) report in 2010<sup>20</sup>. We did not use the high-risk patient population data from the Tibble paper, as we have assumed the high-risk cohort would follow a different patient pathway. The alternative set of published data is from a systematic review by Waugh et al (2013)<sup>21</sup> which was used in the NICE guidance for Faecal Calprotectin testing (DG11)<sup>22</sup>. The sensitivity and specificity data for primary care with no FC testing are much higher in the Waugh data. This may be because GPs are good at diagnosing IBS and use ESR and CRP testing as part of the complete diagnostic toolkit. This means they may be more accurate at referring patients than if they had relied on ESR and CRP testing alone<sup>23</sup>.

The treatment pathway for Comparator 1 is detailed below (a model schematic illustrating this pathway is provided below; Figure 2.2 Section 2.4):

1. Patient presents to GP with lower gastrointestinal symptoms suggestive of IBS or IBD but there is diagnostic uncertainty; cancer is not suspected. Patient receives diagnostic ESR and CRP tests in conjunction with assessment of patient history and physical examination;
2. Patients return to their GP where the GP will make an assessment as to whether to refer to gastroenterology or treat for IBS;
3. Those referred to gastroenterology are either confirmed as having IBD (IBD true positive) or confirmed as not having IBD (IBD false positive) and are treated for IBS;
4. Those treated for IBS will either have their symptoms adequately controlled (IBD true negative) or will remain symptomatic;
5. Those that remain symptomatic will have further testing by their GP and may be started on second-line IBS medication. These patients will either have their symptoms adequately controlled (IBD true negative) or will remain symptomatic;

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<sup>19</sup> Tibble JA, Sigthorsson G, Foster R, Forgacs I, Bjarnason I. Use of surrogate markers of inflammation and Rome criteria to distinguish organic from nonorganic intestinal disease. *Gastroenterology*. 2002 Aug;123(2):450-60. PubMed PMID: 12145798.

<sup>20</sup> Department of Health, Centre for Evidence-based Purchasing, CEP09041 <http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx>

<sup>21</sup> Waugh N, Cummins E, Royle P, Kandala NB, Shyangdan D, Arasaradnam R, Clar C, Johnston R. Faecal Calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technol Assess*. 2013 Nov;17(55):xv-xix, 1-211. doi: 10.3310/hta17550. Review. PubMed PMID: 24286461; PubMed Central PMCID: PMC4781415.

<sup>22</sup> NICE, Diagnostic Guidance 11, evidence overview DAP12, <https://www.nice.org.uk/guidance/dg11/documents/faecal-calprotectin-diagnostic-tests-for-inflammatory-diseases-of-the-bowel-evidence-overview-dap122>

<sup>23</sup> Waugh N, Cummins E, Royle P, Kandala NB, Shyangdan D, Arasaradnam R, Clar C, Johnston R. Faecal Calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technol Assess*. 2013 Nov;17(55):xv-xix, 1-211. doi: 10.3310/hta17550. Review. PubMed PMID: 24286461; PubMed Central PMCID: PMC4781415.

6. Those that continue to have unresolved symptoms will be referred on to gastroenterology for further assessment;
7. Patients referred to gastroenterology are either confirmed as having IBD (IBD false negative) or confirmed as not having IBD (IBD true negative) and continue treatment for IBS.

Sensitivity and specificity data for this pathway is informed by Tibble et al or Waugh et al as described above. All pathways use the prevalence data from the YFCCP.

### **Comparator 2 – NICE Pathway Cut-Off**

This pathway assumes the GP has assessed the patient using the suggested FC cut-off in the current NICE guidance DG11<sup>24</sup>. The observed patient data from the YFCCP has been analysed and the sensitivity and specificity has been calculated based on what *would* have happened, had this cohort been referred according to the NICE pathway instead of using the intervention pathway. The NICE pathway is detailed below:

1. Patient presents to GP with lower gastrointestinal symptoms suggestive of IBS or IBD but there is diagnostic uncertainty; cancer is not suspected. After appropriate baseline investigations patient receives diagnostic FC test to detect inflammation in conjunction with assessment of patient history and physical examination;
2. Patients return to their GP, those with an FC >50 are referred on to gastroenterology and those with an FC <50 are treated for IBS;
3. Those referred to gastroenterology are either confirmed as having IBD (IBD true positive) or confirmed as not having IBD (IBD false positive) and are treated for IBS;
4. Those treated for IBS will either have their symptoms adequately controlled (IBD true negative) or will remain symptomatic;
5. Those that remain symptomatic will have further testing by their GP and may be started on second-line IBS medication. These patients will either have their symptoms adequately controlled (IBD true negative) or will remain symptomatic;
6. Those that continue to have unresolved symptoms will be referred on to gastroenterology for further assessment;
7. Patients referred to gastroenterology are either confirmed as having IBD (IBD false negative) or confirmed as not having IBD (IBD true negative) and continue treatment for IBS.

Sensitivity and specificity data for this pathway is derived from the YFCCP data. All pathways use the prevalence data from the YFCCP.

This is an important data set as it models the potential real world sensitivity and specificity of the NICE pathway that is experienced in the York region. It will be interesting to investigate the region specific sensitivity and specificity data as this care pathway is up-scaled beyond York.

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<sup>24</sup> NICE Diagnostic Guidance DG11, Faecal Calprotectin diagnostic tests for inflammatory diseases of the bowel. Published October 2013, updated May 2017. <https://www.nice.org.uk/guidance/dg11>

The data from the YFCCP returns a much lower sensitivity and specificity than what the published data shows. This indicates that there may be some comparability issues with the data used by NICE which was taken from studies in secondary care and applying it to the primary care setting.

### **Comparator 3 – Published Data for >50ug/g Pathway Cut-Off**

This pathway uses the NICE pathway as described in Comparator 2. There is a drop-down feature in this part of the model that allows the user to select between two sets of published data. To ensure consistency we have used the Tibble et al data from the CEP review (2002) and the Waugh et al data used in the NICE Guidelines (2013). The prevalence data for all pathways is from the YFCCP.

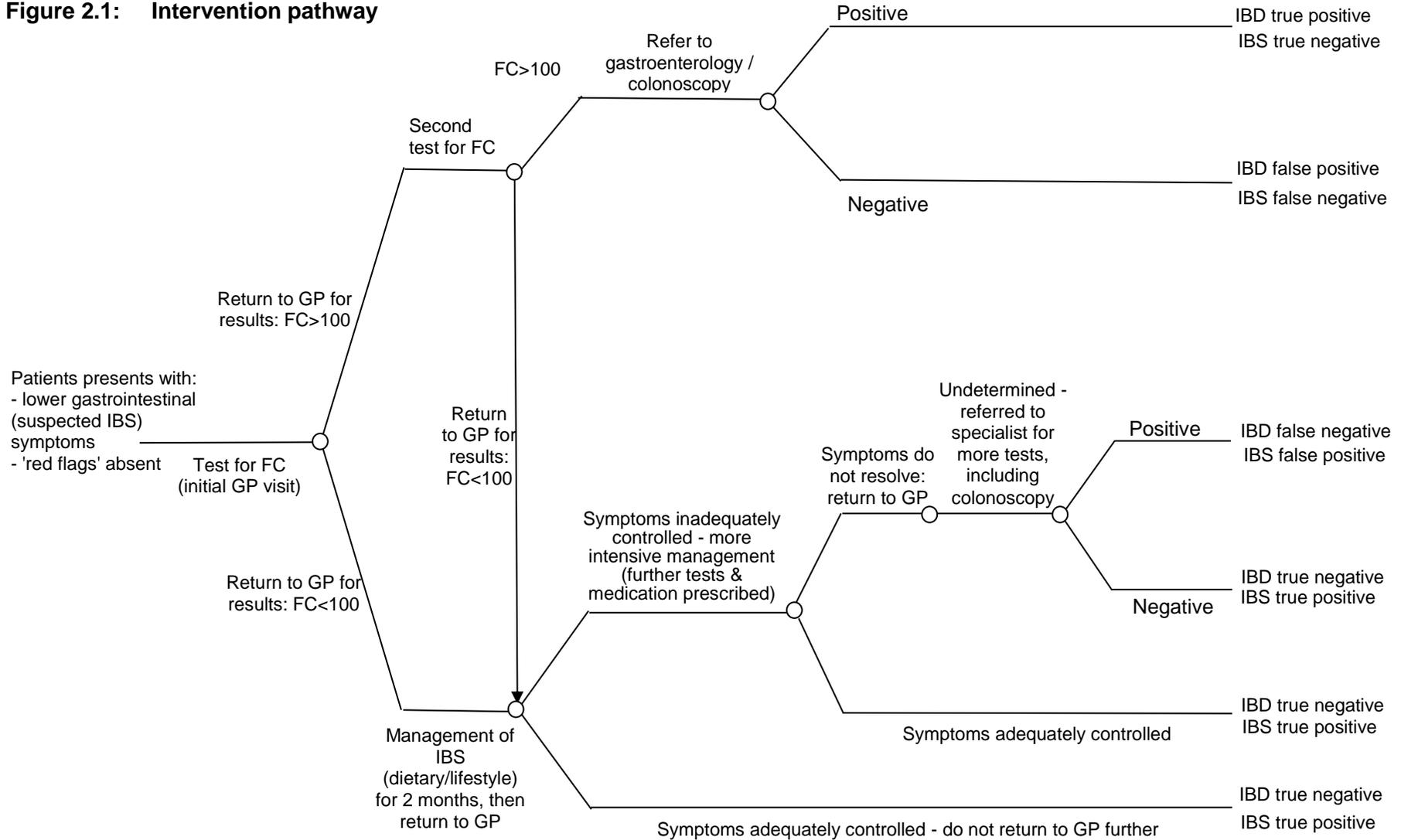
## **2.4 MODEL SCHEMATIC OF PATIENT PATHWAYS**

The model structure for the intervention arm and comparator arms are depicted in Figure 2.1 and Figure 2.2. The model schematics are amended versions of the schematic used for the CEP report (2010)<sup>25</sup>.

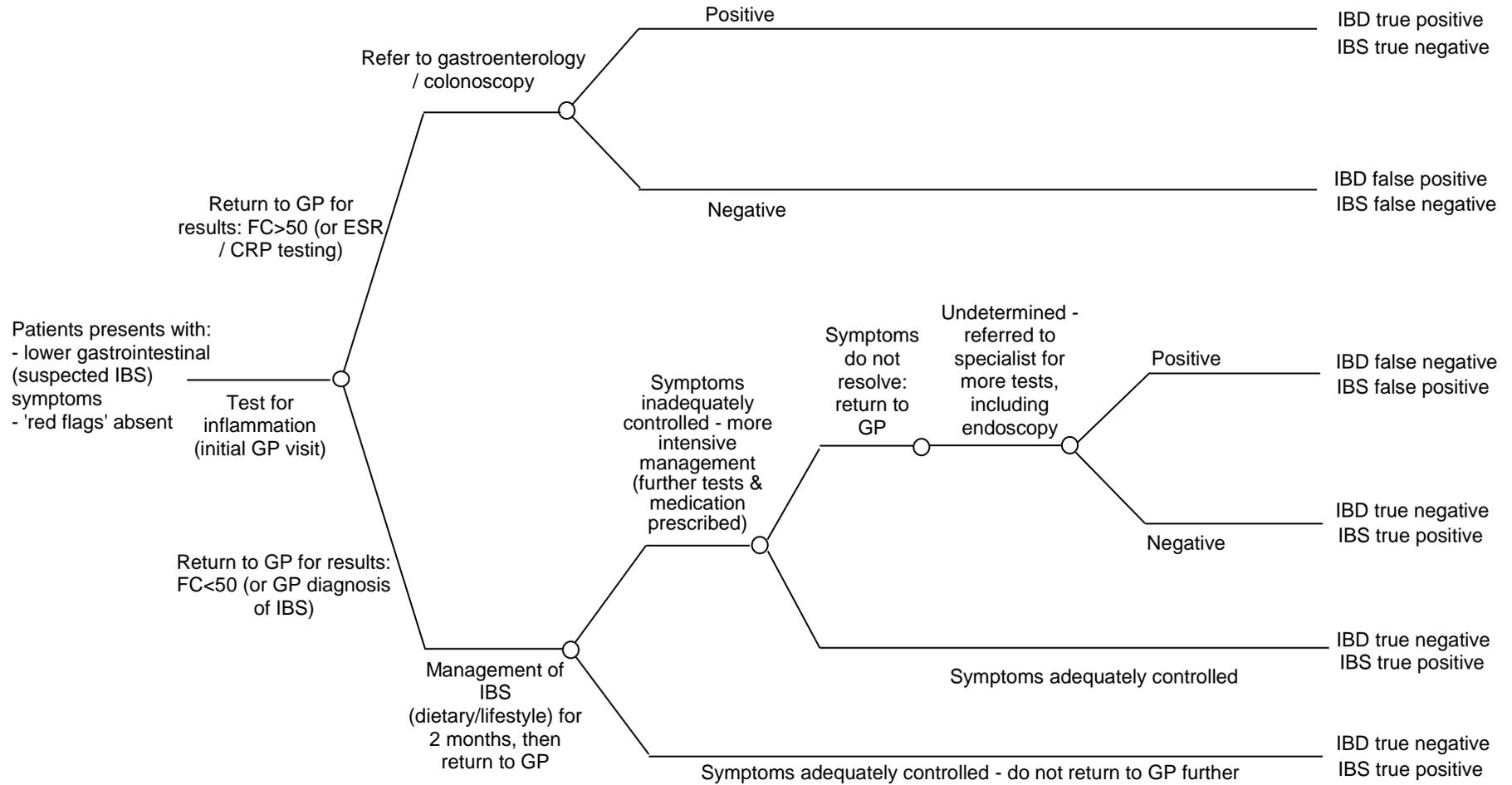
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<sup>25</sup> Department of Health, Centre for Evidence-based Purchasing, CEP09041  
<http://nhscep.useconnect.co.uk/CEPProducts/Catalogue.aspx>

**Figure 2.1: Intervention pathway**



**Figure 2.2: Comparator pathway**



## 2.5 EFFECTIVENESS

The effectiveness data used in the modelling is displayed in Table 2.1.

**Table 2.1: Effectiveness data used in model**

Test	Sensitivity	Specificity
Intervention (YFCCP data)	94%	92%
No FC testing (ESR + CRP) (Tibble et al) <sup>26</sup>	35%	73%
GP Pathway (Waugh et al) <sup>27</sup>	100%	79%
Standard cut-off (YFCCP data)	94%	61%
Published FC testing (Tibble et al) <sup>28</sup>	90%	80%
Published FC testing (Waugh et al) <sup>29</sup>	93%	94%

## 2.6 COSTS

The costs used in the model are displayed in Table 2.2.

**Table 2.2: Costs used in model**

Description of event	Unit Cost	Source
GP Visit	£65	Personal Social Services Research Unit <sup>30</sup>
ESR + CRP test	£9.28	NICE Faecal Calprotectin costing template <sup>31</sup>
Faecal Calprotectin test	£23	NICE Faecal Calprotectin costing template <sup>32</sup>
IBS medication 1 <sup>st</sup> line	£26	Drug tariff July 2017 <sup>33</sup>
IBS second line	£76	Drug tariff July 2017 <sup>34</sup>
Outpatient gastroenterology	£141	NHS reference costs <sup>35</sup>
Colonoscopy	£499	NHS reference costs <sup>36</sup>

<sup>26</sup> Tibble JA, Sigthorsson G, Foster R, Forgacs I, Bjarnason I. Use of surrogate markers of inflammation and Rome criteria to distinguish organic from nonorganic intestinal disease. *Gastroenterology*. 2002 Aug;123(2):450-60. PubMed PMID: 12145798.

<sup>27</sup> NICE, Diagnostic Guidance 11, evidence overview DAP12, <https://www.nice.org.uk/guidance/dg11/documents/faecal-calprotectin-diagnostic-tests-for-inflammatory-diseases-of-the-bowel-evidence-overview-dap122>

<sup>28</sup> Tibble JA, Sigthorsson G, Foster R, Forgacs I, Bjarnason I. Use of surrogate markers of inflammation and Rome criteria to distinguish organic from nonorganic intestinal disease. *Gastroenterology*. 2002 Aug;123(2):450-60. PubMed PMID: 12145798.

<sup>29</sup> NICE, Diagnostic Guidance 11, evidence overview DAP12, <https://www.nice.org.uk/guidance/dg11/documents/faecal-calprotectin-diagnostic-tests-for-inflammatory-diseases-of-the-bowel-evidence-overview-dap122>

<sup>30</sup> PSSRU unit costs, <http://www.pssru.ac.uk/project-pages/unit-costs/>

<sup>31</sup> NICE DG11, Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel, resources, costing template. <https://www.nice.org.uk/guidance/dg11/resources>

<sup>32</sup> NICE DG11, Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel, resources, costing template. <https://www.nice.org.uk/guidance/dg11/resources>

<sup>33</sup> Drug Tariff, [http://www.drugtariff.nhsbsa.nhs.uk/#/00462733-DA\\_1/DA00462451/Part\\_VIIIA\\_products\\_L](http://www.drugtariff.nhsbsa.nhs.uk/#/00462733-DA_1/DA00462451/Part_VIIIA_products_L)

<sup>34</sup> Drug Tariff, [http://www.drugtariff.nhsbsa.nhs.uk/#/00462733-DA\\_1/DA00462451/Part\\_VIIIA\\_products\\_L](http://www.drugtariff.nhsbsa.nhs.uk/#/00462733-DA_1/DA00462451/Part_VIIIA_products_L)

<sup>35</sup> National schedule of reference costs: the main schedule, <https://www.gov.uk/government/publications/nhs-reference-costs-2015-to-2016>

<sup>36</sup> National schedule of reference costs: the main schedule, <https://www.gov.uk/government/publications/nhs-reference-costs-2015-to-2016>

The costs for first line IBS medication were made up of two month's supply of loperamide, mebeverine and ispaghula husk<sup>37</sup>. The cost for second line IBS medication were made up of 2 month's supply of amitriptyline hydrochloride and linaclotide<sup>38</sup>.

The following assumptions were used to calculate the proportion of patients receiving each treatment. These assumptions were informed by expert clinical advice.

### **Assumptions:**

- For patients screened positive for IBD 100% will have a specialist visit and colonoscopy. Therefore, false positives incur the same system costs as true positives;
- For patients screened negative for IBD and do not have IBD:
  - 20% will have further testing (either FC or ESR + CRP);
  - 50% will be prescribed first line IBS treatment;
  - 20% will have unresolved symptoms after first line IBS treatment and will visit their GP;
  - 65% of those patients who had unresolved symptoms from first line treatment will have second line IBS treatment;
  - 7.5% of all patients screened negative for IBD will be referred to gastroenterology
  - 38% of those screened negatively and referred to gastroenterology will have a colonoscopy.
- For patients screened negative for IBD but actually have IBD:
  - 100% will return to their GP, 50% will be started on first line IBS medication;
  - 100% of patients will remain symptomatic and will return to their GP, 65% of those patients that started first line IBS treatment will be prescribed second line IBS treatment;
  - 100% will have further testing (either FC or ESR + CRP);
  - 100% will remain symptomatic and be referred to gastroenterology;
  - 100% will have a colonoscopy.

## **2.7 OUTPUTS**

The model reported the following outputs:

- Total cost for cohort;
- Correctly diagnosed IBS cases;
- Correctly diagnosed IBD cases;
- Unnecessary colonoscopies (false positives);
- Outpatient gastroenterology appointments.

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<sup>37</sup> NICE Diagnostic Guidance DG11, Faecal Calprotectin diagnostic tests for inflammatory diseases of the bowel. Published October 2013, updated May 2017. <https://www.nice.org.uk/guidance/dg11>

<sup>38</sup> NICE Diagnostic Guidance DG11, Faecal Calprotectin diagnostic tests for inflammatory diseases of the bowel. Published October 2013, updated May 2017. <https://www.nice.org.uk/guidance/dg11>

Using the above data, the model calculates the following:

- Incremental cost;
- Incremental correctly diagnosed IBS cases;
- Incremental correctly diagnosed IBD cases;
- Incremental unnecessary colonoscopies (false positives);
- Incremental outpatient gastroenterology appointments;
- Number needed to treat (NNT) to avoid an unnecessary colonoscopy;
- NNT to avoid an outpatient gastroenterology referral.

## Section 3: Results

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### 3.1 SUMMARY

Using data from the first 950 patients with up to 9 months follow up for the YFCCP the IBD prevalence is predicted at 8.1% and the sensitivity and specificity for the intervention cohort was 94% and 92%.

When compared to four of the five comparators used in the model, the model predicts the intervention arm is a cost-saving strategy. It is dominant when compared to Tibble et al in both the no FC and >50ug/g cut-off strategies. It is cost saving but diagnoses fewer cases of IBD when compared with the Waugh et al data for the no FC pathway.

The YFCCP pathway achieves very similar clinical outcomes when compared with the Waugh et al systematic review for the >50ug/g cut-off. This indicates that the intervention pathway is approaching parity with the secondary care published data that was used by NICE in their assessment of the FC pathway using the Waugh et al<sup>39</sup> systematic review. However, the YFCCP pathway was cost incurring due to the second round of FC testing.

Clinical experts consider the Waugh et al data may not be comparable because the studies used to inform the data were from a secondary care setting and in ideal clinical conditions. This means the patients are potentially quite different from the population we would expect to see in primary care in the UK<sup>40</sup>.

The results of the model are displayed in Tables 3.1 to 3.11. We have presented the data in separate tables for the intervention arm assuming 100% and 85% GP adherence with the pathway.

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<sup>39</sup> Waugh N, Cummins E, Royle P, Kandala NB, Shyangdan D, Arasaradnam R, Clar C, Johnston R. Faecal Calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. *Health Technol Assess*. 2013 Nov;17(55):xv-xix, 1-211. doi: 10.3310/hta17550. Review. PubMed PMID: 24286461; PubMed Central PMCID: PMC4781415

<sup>40</sup> Jellema P, van Tulder MW, van der Horst HE, Florie J, Mulder CJ, van der Windt DA. Inflammatory bowel disease: a systematic review on the value of diagnostic testing in primary care. *Colorectal Dis* 2011;13:239–54. 10.1111/j.1463-1318.2009.02131.x.

### 3.2 INTERVENTION COMPARED WITH ESR AND CRP

**Table 3.1: Summary results for intervention compared to no FC assuming 100% GP adherence with the intervention pathway and using Tibble et al as the evidence source for the comparator**

	<b>Intervention</b>	<b>No FC (ESR + CRP)</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£311,159</b>	<b>£421,642</b>	<b>-£110,483</b>	
Correctly diagnosed IBS cases	845	671	175	
Correctly diagnosed IBD cases	76	28	47	
Unnecessary colonoscopies (i.e. false +ves)	74	248	-175	5.7
Outpatient appointments	218	379	-162	6.2

**Table 3.2: Summary results for intervention compared to no FC assuming 85% GP adherence with the intervention pathway and using Tibble et al as the evidence source for the comparator**

	<b>Intervention</b>	<b>No FC (ESR + CRP)</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£324,298</b>	<b>£421,642</b>	<b>-£97,223</b>	
Correctly diagnosed IBS cases	819	671	148	
Correctly diagnosed IBD cases	69	28	40	
Unnecessary colonoscopies (i.e. false +ves)	100	248	-148	6.7
Outpatient appointments	185	379	-194	5.1

The data in the tables above shows that the intervention is cost saving and of clinical benefit when compared to the published data for ESR and CRP testing. When we assume a lower level of GP adherence with the pathway, the model still returns a dominant result.

### 3.3 INTERVENTION COMPARED WITH NICE GP PATHWAY

**Table 3.3: Summary results for intervention compared to no FC assuming 100% GP adherence with the intervention pathway and using the NICE pathway as the evidence source for the comparator**

	<b>Intervention</b>	<b>No FC (ESR + CRP)</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£311,159</b>	<b>£378,881</b>	<b>-£67,723</b>	
Correctly diagnosed IBS cases	845	726	119	
Correctly diagnosed IBD cases	76	81	-5	
Unnecessary colonoscopies (i.e. false +ves)	74	193	-119	8.4
Outpatient appointments	218	328	-111	9.0

**Table 3.4: Summary results for intervention compared to no FC assuming 85% GP adherence with the intervention pathway and using the NICE pathway as the evidence source for the comparator**

	<b>Intervention</b>	<b>No FC (ESR + CRP)</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£318,298</b>	<b>£378,881</b>	<b>-£60,583</b>	
Correctly diagnosed IBS cases	828	726	102	
Correctly diagnosed IBD cases	77	81	-4	
Unnecessary colonoscopies (i.e. false +ves)	91	193	-102	9.8
Outpatient appointments	185	328	-143	7.0

When compared to the GP pathway using the pooled data from the NICE commissioned analysis the intervention arm is cost saving by approximately £67,000 per 1,000 patients. The intervention arm also correctly diagnoses more IBS and avoids over 100 colonoscopies and gastroenterology outpatient appointments. However, there is a trade off with the NICE GP pathway diagnosing an additional 4-5 case of IBD due to the 100% sensitivity in the comparator arm. The results are very similar when we assume a reduced GP adherence with the intervention pathway.

### 3.4 INTERVENTION COMPARED WITH STANDARD CUT-OFF

**Table 3.5: Summary results for intervention compared to FC >50ug/g cut-off in a single stool sample using YFCCP data projections and assuming 100% GP adherence with the intervention pathway**

	<b>Intervention</b>	<b>Standard cut-off</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£311,159</b>	<b>£471,158</b>	<b>-£159,999</b>	
Correctly diagnosed IBS cases	845	557	289	
Correctly diagnosed IBD cases	76	76	0	
Unnecessary colonoscopies (i.e. false +ves)	74	362	-289	3.5
Outpatient appointments	218	485	-267	3.7

**Table 3.6: Summary results for intervention compared to FC >50ug/g cut-off in a single stool sample using YFCCP data projections and assuming 85% GP adherence with the intervention pathway**

	<b>Intervention</b>	<b>Standard cut-off</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£318,298</b>	<b>£471,158</b>	<b>-£152,859</b>	
Correctly diagnosed IBS cases	828	557	271	
Correctly diagnosed IBD cases	77	76	1	
Unnecessary colonoscopies (i.e. false +ves)	91	362	-271	3.7
Outpatient appointments	185	485	-300	3.3

When comparing the YFCCP data from the intervention arm with the projected data where the >50ug/g cut-off has been used, the model returns the most dominant result of all the comparators with a £160,000 saving and greater than 250 more correctly diagnosed IBS cases. The intervention arm avoids an unnecessary colonoscopy and gastroenterology outpatient referral for every four patients seen in primary care.

### 3.5 INTERVENTION COMPARED WITH PUBLISHED DATA 1

**Table 3.7: Summary results for intervention compared to FC >50ug/g cut-off in a single stool sample using published data when assuming 100% GP adherence and using Tibble et al as the evidence source for the comparator**

	<b>Intervention</b>	<b>Published data</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£311,159</b>	<b>£368,298</b>	<b>-£50,140</b>	
Correctly diagnosed IBS cases	845	735	110	
Correctly diagnosed IBD cases	76	73	3	
Unnecessary colonoscopies (i.e. false +ves)	74	184	-110	9.1
Outpatient appointments	218	320	-102	9.8

**Table 3.8: Summary results for intervention compared to FC >50ug/g cut-off in a single stool sample using published data when assuming 85% GP adherence and using Tibble et al as the evidence source for the comparator**

	<b>Intervention</b>	<b>Published data</b>	<b>Incremental</b>	<b>NNT</b>
<b>Total costs</b>	<b>£318,298</b>	<b>£368,298</b>	<b>-£50,000</b>	
Correctly diagnosed IBS cases	828	735	92	
Correctly diagnosed IBD cases	77	73	4	
Unnecessary colonoscopies (i.e. false +ves)	91	184	-92	10.8
Outpatient appointments	185	320	-135	7.4

In this scenario with the intervention compared to the published data for >50ug/g cut-off, the intervention arm dominates with both a saving and clinical benefit. The intervention arm diagnoses more than 100 additional IBS cases in primary care and an additional 3-4 IBD cases. The intervention arm avoids >100 gastroenterology outpatient referrals and unnecessary colonoscopies. The result remains dominant when a reduced GP adherence of 85% is assumed.

### 3.6 INTERVENTION COMPARED WITH PUBLISHED DATA 2

**Table 3.9: Summary results for intervention compared to FC >50ug/g cut-off in a single stool sample using published data when assuming 100% GP adherence and using the NICE pathway as the evidence source for the comparator**

	Intervention	Published data	Incremental	NNT
<b>Total costs</b>	<b>£311,159</b>	<b>£293,290</b>	<b>£17,869</b>	
Correctly diagnosed IBS cases	845	864	-18	
Correctly diagnosed IBD cases	76	75	0	
Unnecessary colonoscopies (i.e. false +ves)	74	55	18	-54.4
Outpatient appointments	218	201	-16	-58.8

**Table 3.10: Summary results for intervention compared to FC >50ug/g cut-off in a single stool sample using published data when assuming 85% GP adherence and using the NICE pathway as the evidence source for the comparator**

	Intervention	Published data	Incremental	NNT
<b>Total costs</b>	<b>£318,298</b>	<b>£293,290</b>	<b>£25,014</b>	
Correctly diagnosed IBS cases	828	864	-36	
Correctly diagnosed IBD cases	77	75	1	
Unnecessary colonoscopies (i.e. false +ves)	91	55	36	-27.5
Outpatient appointments	185	201	-16	-63.7

When comparing the intervention pathway with the NICE published data for the >50ug/g cut-off, the model estimates that the intervention arm is more costly incurring an additional £18,000. It is also less effective at diagnosing IBS cases but does diagnose slightly more IBD cases per 1,000 patients at a cost of £20,937 per diagnosed IBD case. The intervention pathway does have slightly fewer gastroenterology referrals but higher unnecessary colonoscopies.

The difference in sensitivity and specificity for these two arms is not statistically significant. This means we could expect clinically similar outcomes in each arm. However, there would be an additional cost in the intervention arm due to the second round of FC testing.

This report has previously discussed some of the potential issues when using the data from the NICE pathway as a comparator. The main issue being that the NICE pathway uses evidence from secondary care and applies it to a primary care setting.

### 3.7 PUBLISHED DATA USED BY NICE COMPARED WITH STANDARD CUT-OFF

**Table 3.11: Summary results for published data (NICE) compared to FC >50ug/g cut-off in a single stool sample using YFCCP data projections**

	<b>Published data</b>	<b>Standard cut-off</b>	<b>Incremental published data -v- standard cut-off</b>	<b>Standard cut-off -v- published data</b>
<b>Total costs</b>	<b>£293,164</b>	<b>£471,076</b>	<b>-£177,912</b>	<b>£177,912</b>
Correctly diagnosed IBS cases	864	557	307	-307
Correctly diagnosed IBD cases	75	76	-1	1
Unnecessary colonoscopies (i.e. false +ves)	55	362	-307	307

This scenario compares the published data for the >50ug/g cut-off in a single stool sample using the NICE published data with the YFCCP projected data for the >50ug/g cut-off. This shows the NICE published data estimates a saving of £180,000 per 1,000 patients mainly through the greater than 300 false positives that are referred on from primary care which actually have IBS. This shows a significant gap in what is being experienced in the NHS system at York for gastrointestinal presentations when compared with those predicted in the NICE guidelines.

## Section 4: Sensitivity Analysis

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### 4.1 SENSITIVITY ANALYSIS

We developed the model with the main comparator being published data for primary care in a setting where FC is not being used. This is the most similar scenario to what is being experienced in primary care across Yorkshire and Humber. The sensitivity analysis only looks at the intervention arm when compared to the no FC arm (which can be toggled between Tibble et al and NICE data). All sensitivity analysis was univariate (we changed one variable at a time and held all others at their base-case value) and deterministic (the model variable we were adjusting are manually changed rather than through probabilistic computer generation).

We set up sensitivity analysis to assess the impact of the prevalence of IBD, the GP uptake of the intervention and the effectiveness of the intervention arm. The results are reported using a format of incremental cost per correctly diagnosed IBD, incremental cost per correctly diagnosed IBS and incremental cost per unnecessary colonoscopy avoided.

#### Prevalence of IBD

For the prevalence of IBD, we varied the range from 0% to 20%. The intervention arm was dominant (cost saving and better health benefits) across all outcomes except at a prevalence of 0% for the incremental cost per IBD patient where at this setting there would be no IBD. In a scenario where IBD did not exist in the patient population the intervention would still be cost saving but there would be no IBD to detect so it would save money due to its greater efficacy at predicting IBS. It is important to note that the 95% confidence interval for prevalence from the YFCCP data is 6.5% - 10%. The intervention arm is dominant across all outcomes within the 95% confidence interval range.

#### GP Adherence

We varied GP adherence with the intervention arm between 0 and 100%. At 0%, we assume that all GPs are ignoring the new pathway and using current practice as determined by the NICE published data to predict IBD and IBS. This means that at 0% adherence both arms are identical. As soon as we reach 1% the intervention arm dominates (cost saving with better health benefits) the comparator. The intervention arm remains dominant from 1% to 100% meaning that as soon as one GP starts to use the intervention pathway, the model predicts a saving and more accurate diagnosis.

## Effectiveness

We varied sensitivity and specificity in the intervention arm between 50% and 100% to test a range of scenarios. It is important to note that the 95% confidence interval for the intervention arm based on the YFCCP data is sensitivity 85%-98% and specificity 90%-94%.

The intervention arm is dominant at all levels of specificity above 75% if specificity drops below 75% then the intervention arm starts to incur cost due to the increase in false positives being treated in secondary care. For IBS and unnecessary colonoscopies avoided, the comparator arm would dominate the intervention arm (the intervention arm incurs more cost and is less effective). However, the intervention arm would still be more effective at diagnosing IBD. At a sensitivity and specificity of 70% and 70%, the cost per IBD correctly diagnosed would be £469. As stated earlier when the 95% confidence intervals are used as our sensitivity ranges, the intervention arm is dominant for all outcome measures when compared to the projected data from the YFCCP.

## Section 5: Discussion

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### 5.1 SUMMARY

When compared to four of the five comparators used in the model, the model predicts the intervention arm is a cost-saving strategy. It is dominant when compared to Tibble et al in both the no FC and >50ug/g cut-off strategies. It is cost saving but diagnoses fewer cases of IBD when compared with the NICE data for the no FC pathway. The one comparator that the intervention arm did not have dominance was in the NICE data from the Waugh et al systematic review, which had a sensitivity and specificity of 93% and 94% respectively. Nearly all studies used in the Waugh et al systematic review came from secondary care studies<sup>41</sup>. This could be interpreted that the sensitivity and specificity from that pooled analysis is reflective of FC testing in an optimum environment as it essentially uses a population that has already undergone primary care screening. It is noted in the text of Waugh et al that Jellema et al<sup>42</sup> had reservations about applying results from specialist care to primary care.

It is important to note that the 95% confidence intervals for the YFCCP pathway and the Waugh et al systematic review overlap enormously as displayed in Table 5.1:

**Table 5.1: 95% confidence intervals for YFCCP and Waugh et al**

Source	Sensitivity	Lower	Upper	Specificity	Lower	Upper
YFCCP	94%	85%	98%	92%	90%	94%
Waugh et al	93%	83%	97%	94%	73%	99%

The above table illustrates that there is no statistical significance between the two pathways although there would be an additional cost in the YFCCP arm due to the second round of FC testing. The additional cost is illustrated in Table 3.9 above.

We also ran a separate scenario comparing the published data from Waugh et al for the >50 ug/g cut-off, which was used by NICE, with the projected data for the >50ug/g cut-off single stool sample from the YFCCP. The model predicted the Waugh et al arm would be £170,000 less expensive per 1,000 patients and would diagnose 300 more cases of IBS in primary care than the YFCCP real world observational data predicts.

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<sup>41</sup> Waugh N, Cummins E, Royle P, et al. Faecal calprotectin testing for differentiating amongst inflammatory and non-inflammatory bowel diseases: systematic review and economic evaluation. Southampton (UK): NIHR Journals Library; 2013 Nov. (Health Technology Assessment, No. 17.55.) Chapter 2, Results of clinical effectiveness review.

<sup>42</sup> Jellema P, van Tulder MW, van der Horst HE, Florie J, Mulder CJ, van der Windt DA. Inflammatory bowel disease: a systematic review on the value of diagnostic testing in primary care. *Colorectal Dis* 2011;13:239–54. 10.1111/j.1463-1318.2009.02131.x.

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This comparison shows the vast gulf between using FC in an optimal environment and using FC in primary care for low risk patients who exhibit no red flags upon presentation. There is the potential that using the current NICE guidelines and assuming the optimal sensitivity and specificity data could actually be costing the NHS significantly in terms of patient outcomes, wait times for treatment and longer waitlists for gastroenterology outpatient appointments that are being taken up by unnecessary referrals. We would recommend that there needs to be further study on FC in a primary care environment using a range of FC cut-offs.