

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Report for Guidance Executive

Review of DG11: Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel

This guidance was issued in October 2013.

The review date for this guidance is October 2016.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Recommendation

Transfer the guidance to the 'static guidance list' with a post publication update to reflect the publication of the updated NICE guideline on [suspected cancer](#).

That we should consult on the proposal.

A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper.

2. Original objective of guidance

To assess the clinical and cost effectiveness of faecal calprotectin diagnostic tests for inflammatory diseases of the bowel.

3. Current guidance

Adoption recommendations

1.1 Faecal calprotectin testing is recommended as an option to support clinicians with the differential diagnosis of inflammatory bowel disease (IBD) or irritable bowel syndrome (IBS) in adults with recent onset lower gastrointestinal symptoms for whom specialist assessment is being considered, if:

- cancer is not suspected, having considered the risk factors (for example, age) described in [Referral guidelines for suspected cancer](#) (NICE clinical guideline 27), **and**

- appropriate quality assurance processes and locally agreed care pathways are in place for the testing.

1.2 Faecal calprotectin testing is recommended as an option to support clinicians with the differential diagnosis of IBD or non-IBD (including IBS) in children with suspected IBD who have been referred for specialist assessment, if:

- appropriate quality assurance processes and locally agreed care pathways are in place for the testing.

Research recommendations

7.1 Further research is needed on the use and clinical utility of faecal calprotectin testing, and support pathways for the long-term management of these conditions in the community should be developed.

7.2 Further research is needed on the impact of faecal calprotectin testing on clinical decision-making when added to current practice. This includes research into optimal cut-off values for tests and the investigation of repeat testing strategies in people with intermediate levels of faecal calprotectin. Development of a consistent definition for the 'intermediate range' is encouraged.

7.3 Robust evidence is needed on the comparative performance of different faecal calprotectin tests, including the performance of POCTs compared with laboratory-based tests.

4. Rationale

Changes in clinical practice, technology costs or evidence that would lead to a change in the recommendations of the original guidance have not been identified. It is therefore proposed that the guidance is placed on the static list.

5. Implications for other guidance producing programmes

No overlaps have been identified.

6. New evidence

The search strategy from the original diagnostics assessment report was re-run on the Cochrane Library (Wiley) (CDSR, DARE, HTA and CENTRAL, NHS EED and HTA), MEDLINE, MEDLINE in Process and EMBASE (all via Ovid) and Science Citation Index and Conference Proceedings Citation Index via Web of Science. References from September 2012 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. Companies were asked to submit all

new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. Specialist Committee Members for this guidance topic were also consulted and asked to submit any information regarding changes to the technologies, the evidence base and clinical practice. The results of the literature search are discussed in the ‘Summary of evidence and implications for review’ section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies

Several technologies that measure the level of calprotectin in stool samples (faecal calprotectin) were evaluated in the original assessment. These included fully quantitative laboratory-based tests, fully quantitative rapid tests and semi-quantitative point-of-care tests.

Any identified changes to technologies included in the guidance are summarised in table 1.

Table 1 Changes to technologies included in guidance

Technology	Summary of changes
EK-CAL calprotectin ELISA test (Range: 10–600 micrograms/g; Bühlmann)	No changes reported.
EK-CAL calprotectin ELISA test (Range: 30–1800 micrograms/g; Bühlmann)	No changes reported. The company commented that many laboratories are now using the CALEX sample extraction device to obtain stool samples for use with this test.
LF-CAL25 Quantum Blue calprotectin test (Bühlmann)	No changes reported.
LF-CHR 25 Quantum Blue calprotectin test (Bühlmann)	No changes reported. A new BÜHLMANN Quantum Blue ® fCAL extended (LF-CALE25) which has a range of 30 - 1000µg/g to complement the existing Quantum Blue ® fCAL (LF-CAL25) and Quantum Blue ® fCAL high range (LF-CHR25) is now available.
CALPRO CALPROTECTIN ELISA TEST (ALP) CAL0100 (Calpro, formerly known as the Phical test CAL0100)	No changes reported. PhiCal Calprotectin ELISA has been renamed as IDK Calprotectin ELISA.

CALPROLAB CALPROTECTIN ELISA (ALP) CALP0170 (Calpro, formerly known as the Phical test CALP0170)	No changes reported.
Calprest (Eurospital)	No changes identified.
Calfast (Eurospital)	No changes identified.
ELISA (K6927) (Immundiagnostik)	No changes identified
EliA Calprotectin (Phadia AB, part of ThermoFisher Scientific)	No changes reported. A new version (the EliA Calprotectin 2) is now available. This version differs in the reagents used and is suggested to improve sample stability.
KST11005 CalDetect Calprotectin Rapid test (version 1 – Caldetect; Preventis)	No changes identified.
Preventis (sister company to Immundiagnostik) CalDetect Calprotectin Rapid test (version 3 – CalScreen)	No changes identified.
CalDetect Calprotectin Rapid test (version 3 – CalScreen; Preventis)	No changes identified.

6.1.2 Additional technologies

Several alternative technologies with a similar purpose to those included in the original guidance were identified, although the availability of the devices to the NHS is not known:

- BÜHLMANN fCAL turbo (CE mark status unknown)
- DiaSorin LIAISON Calprotectin Assay (CE mark status unknown)
- Calprosmart – Office Testkit, manufacturer CalPro (CE mark status unknown)
- EpiTuub Calprotectin/i-FOB DUO Test, manufacturer Concile GmbH (CE mark status unknown)
- EDI Quantitative Fecal Calprotectin ELISA, manufacturer EpiTope Diagnostics Inc (CE marked)
- EpiTuub Fecal Calprotectin Rapid Test Kit (CE mark status unknown)
- Cerfast Biotec Calprotectin Turbilatex (CE mark status unknown)
- Sol particle immunoassay (in-house test)

- Proflow Calprotectin, ProLab Diagnostics (CE mark status unknown)

Other faecal calprotectin tests that are intended for home-use were also identified. The CE marking status and availability of these tests is not known.

6.2 Clinical practice

No changes to the diagnostic and care pathways that have occurred since the publication of DG11 have been identified. A UK National External Quality Assessment Service (UK NEQAS) scheme referenced in DG11 remains in place.

The NICE guideline on [irritable bowel syndrome in adults](#) includes recommendations on the diagnosis of irritable bowel syndrome (IBS). This guideline has been updated since DG11 published; however no changes were made to recommendations relating to IBS diagnosis. A [surveillance review proposal](#) is currently underway which proposes not to update this guideline. The NICE guideline on [suspected cancer](#) has been updated but the changes do not have an impact on DG11. The cross references to NICE clinical guideline 27 in DG11 will need to be updated to NICE guideline 12.

The British Society of Gastroenterology (BSG) have released [guidance on the use of faecal calprotectin](#) (October 2016). Selected summary recommendations are:

- It is recommended that faecal calprotectin is used to discriminate between functional gastrointestinal symptoms and inflammatory bowel disease in primary and secondary care in adults with recent onset lower gastrointestinal symptoms, where cancer is not suspected and for whom specialist assessment is being considered. It should not be used in patients with acute diarrhoea, bloody diarrhoea, or in older patients where the need to rule out polyps or cancer mandates colonoscopy anyway.
- It is recommended that threshold values regarded to be raised significantly are determined on the basis of local audit data, and assay used.
- It is suggested that faecal calprotectin measurement is useful in IBD patients in whom it is unclear whether symptoms are due to active inflammation, or other causes such as coexisting irritable bowel syndrome or bile salt malabsorption.

Since DG11 was published, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition has published revised criteria for the diagnosis of inflammatory bowel disease in children and adolescents (Levine et al. 2014). This document comments that “*Faecal calprotectin is superior to any blood marker for detection of intestinal inflammation.*”

6.3 New studies

6.3.1. Systematic review

Four systematic reviews were identified that have been produced since diagnostics guidance 11 published:

- Menees et al. (2015) included 8 studies that reported faecal calprotectin testing results (however only 2 of these studies were not included in the original diagnostics assessment report). These studies all included adults whose faecal calprotectin levels were assessed using ELISA-based assays. All studies were in secondary or tertiary care. The review reported that the maximal positive predictive value for faecal calprotectin testing for IBD was 78%, which occurred at a cut off of 1,000 µg/g. Of the people with <40 µg/g faecal calprotectin, ≤1% had IBD.
- Kopylov et al. (2016) included 7 studies that investigated the accuracy of faecal calprotectin tests to detect active small bowel disease (Crohn's disease). Three of studies were included in the original diagnostics assessment report. The review does not report if the included studies enrolled people presenting to primary or secondary care. At a cut-off of 50 µg/g, pooled sensitivity was 83% and specificity was 53%. At a cut-off of 100 µg/g, pooled sensitivity was 68% and specificity was 71%. At a cut-off of 200 µg/g, pooled sensitivity was 42% and specificity was 94%.
- An unpublished systematic review provided by ThermoFisher reported summary test statistics of a number of different faecal calprotectin tests, using the manufacturer's recommended cut-off values. The majority of the studies included in this review were in the original diagnostics assessment report, or are described below. Pooled sensitivity values for different faecal calprotectin tests ranged between [REDACTED] and specificity values between [REDACTED]

A further systematic review included studies that assessed the use of faecal calprotectin testing only in children:

- Holtman et al. (2016) included 10 studies involving children with gastrointestinal symptoms suggestive of IBD who were assessed using faecal calprotectin testing (using the PhiCal ELISA-based test). Reported pooled sensitivity was 99% (95% CI 92 to 100%), and specificity was 65% (95% CI 54 to 74%).

6.3.2 Primary care

Four studies that published since diagnostics guidance 11 was issued were identified that reported on the diagnostic accuracy of faecal calprotectin tests to distinguish

people with IBD from people with IBS or non-IBD conditions in a primary care setting.

A cohort study set in general practice in England (Pavlidis et al. 2013) considered faecal calprotectin use within an IBS diagnostic pathway including patients aged 18-45 (N=962). Samples were tested in a pathology laboratory using a Buhlmann ELISA-based test. At a cut-off of 50µg/g, sensitivity was 82%, specificity 77%, negative predictive value (NPV) was 98% and positive predictive value (PPV) was 28%. Using a cut-off of 150µg/g reduced the NPV by 1% while increasing PPV to 71%.

Turvill et al. (2016) reported an evaluation of a care pathway produced by the York Hospital and Vale of York Clinical Commissioning Group which incorporated faecal calprotectin testing as a triage tool to facilitate initial clinical assessment of patients with lower GI symptoms without suspected cancer (N=262). The care pathway including faecal calprotectin testing (using the Buhlmann EK-CAL ELISA-based test) was reported to have a higher NPV and PPV (97% and 40%) compared to GP clinical judgement alone (93% and 35%). The pathway used the following cut-offs: faecal calprotectin less than 100µg/g - IBS presumed likely; faecal calprotectin levels 100-250µg/g - test repeated at 6 weeks; faecal calprotectin more than 250µg/g - urgent colonoscopy. When a cut-off of 50µg/g was used, NPV was 93% and PPV was 20%.

A primary care study in children in the Netherlands (Holtman et al. 2016; N=114) reported on the accuracy of faecal calprotectin testing (using the PhiCal ELISA-based test) to rule-out IBD in children with chronic gastrointestinal symptoms. Using a cut-off of 50µg/g, faecal calprotectin testing had a sensitivity of 99% (95% CI 81 to 100) and a specificity of 84% (95% CI 74 to 91). PPV at this cut-off was 59% and NPV was 100%. Using a cut-off of 100µg/g, sensitivity was 87% (95% CI 65 to 96), specificity was 93% (95% CI 84 to 97), PPV was 74% (95% CI 53 to 88) and NPV was 97% (95% CI 89 to 99).

A Canadian multicentre prospective cohort study (Rosenfeld et al. 2016) reported that faecal calprotectin testing (using the Buhlmann Quantum Blue; a point-of-care test) resulting in a change in patient management 51.3% of the time, which included a significant reduction in the number of colonoscopies performed. A New Zealand audit (Bai and Boswell, 2016) reported that of the included faecal calprotectin tests ordered to distinguish IBD from IBS (n=85), the mean faecal calprotectin level in patients diagnosed with IBS was 27 µg/g (n=30; range 14 to 41 µg/g).

Additional studies also reported on the diagnostic accuracy of faecal calprotectin tests to identify IBD in addition to other bowel conditions.

A cohort study of patients in Scotland who were referred to secondary care for investigation of bowel symptoms (Mowat et al. 2015; N=1043) reported that faecal

calprotectin testing (using the Buhlmann Calprotectin EK-CAL ELISA-based test) used with a cut-off of 50 µg/g had a positive predictive value of 17% for significant bowel disease (cancer, high-risk adenoma or IBD) and 6% for IBD alone. The negative predictive value for IBD was 99%. Older patients with a higher risk of colorectal cancer were included in this study.

6.3.3. Secondary care

Nine identified studies reported on faecal calprotectin testing in secondary care.

A retrospective cohort study from 2 Scottish hospitals (Kennedy et al. 2015; N=895) considered faecal calprotectin testing (using the PhiCal Calpro ALP ELISA-based test) at thresholds of 20, 50, 70 and 100µg/g to distinguish IBD from functional gastrointestinal disease. Using a cut-off of 50µg/g, faecal calprotectin testing for IBD had a sensitivity of 97%, specificity of 74%, PPV of 37% and NPV of 99%.

Alternatively, using a cut-off of 100µg/g, faecal calprotectin testing for IBD had a sensitivity of 96%, specificity of 87%, PPV of 54% and NPV of 99%.

Test characteristics at faecal calprotectin cut-offs between 8 and 150 µg/g were considered in an English hospital gastroenterology clinic (using the Immunodiagnostik ELISA-based test; Bannerjee et al. 2015; N=121). This study reported sensitivity of 90% and specificity of 60% (at a cut-off of 50µg/g) in distinguishing IBD from IBS. At a cut-off of 100µg/g, sensitivity was 68% and specificity 82%. The authors concluded that IBS can be distinguished from IBD in newly referred patients with diarrhoea at a cut-off of 50µg/g; however this study only included 12 patients with IBD.

A study from Italy (Caviglia et al. 2014; N=66) reported faecal calprotectin diagnostic test characteristics to distinguish between people with IBS and IBD at 50, 100 and 150 µg/g cut-offs (using the Eurospital Calprest ELISA-based test). Using 50µg/g as a cut-off for the diagnosis of IBD produced a sensitivity of 100%, specificity of 52%, PPV of 71% and NPV of 100%. Using 150 µg/g as a cut-off resulted in a sensitivity of 88%, specificity of 91%, PPV of 91% and NPV of 86%.

A study in Egypt (Elsaadany et al. 2016; N=96) reported that faecal calprotectin testing, using an Immunodiagnostik ELISA-based test at a cut-off of 140µg/g, had 100% sensitivity and specificity for distinguishing ulcerative colitis from IBS. At a cut-off of 223 µg/g, sensitivity was 90% and specificity was 97%.

A hospital based cohort study in Iran (Kalantari et al. 2016; N=109) reported that, at a faecal calprotectin cut-off of 164µg/g (using an unspecified commercial faecal calprotectin enzyme linked immunoassay kit), sensitivity of faecal calprotectin testing to distinguish ulcerative colitis from IBS was 56%, specificity was 75%, PPV was 80% and NPV was 93%.

A case-control study which was a subset of a multicentre North America study (Minar et al. 2014; 32 cases and 14 controls) reported that, at a cut off of 50 µg/g, faecal calprotectin (test not specified) was 100% sensitive, 29% specific, and had a PPV of 64% and a NPV of 100% for the diagnosis of Crohn's disease in children. At a cut-off of 250 µg/g, faecal calprotectin was 94% sensitive, 64% specific, and had a PPV of 77% and a NPV of 90%.

A US study (Emmanuel et al. 2016; N=2667) reported that in 11% of patients with abdominal pain meeting the IBS Rome III criteria (that is, with symptoms of irritable bowel syndrome), faecal calprotectin levels (measured using the PhiCal ELISA-based test) were above 50 µg/g.

In a cohort of patients from an English hospital (McFarlane et al. 2016; N=208) with a 'normal' faecal calprotectin result (less than 50µg/g; measured using an Immunodiagnostik ELISA-based test), 46% underwent CT, MRI and/or colonoscopy. In this group, 2 new cases (1%) of IBD were identified.

A retrospective study in Scottish clinics (Seenan et al. 2016; N=161) reported that in adults under 50 years old that the NPV of a cut-off 100-200 µg/g (measured using the Buhlmann Calprotectin ELSIA-based test) was 86.7% for any pathology and 97.5% for significant luminal pathologies (IBD, advanced adenoma or colorectal carcinoma).

6.3.4. Comparisons of faecal calprotectin tests

Ten studies comparing faecal calprotectin tests were identified in this review. Summary details are provided in table 2.

Table 2 Overview of identified studies comparing faecal calprotectin tests

Study	Setting	Inclusion criteria	Interventions compared	Results
Oyaert et al. (2014)	Clinical laboratory, Belgium	<u>Included</u> : consecutive in- and outpatients with suspicion of IBD, measurement of faecal calprotectin and undergoing ileocolonoscopy. <u>Excluded</u> : unclear diagnosis, inability to collect sufficient sample, aged <14 years.	EliA calprotectin assay Buhlmann POCT calprotectin (Quantum Blue Calprotectin)	The AUC for the EliA calprotectin assay was 0.96 (95% CI 0.92-0.99), and for the Buhlmann POCT AUC was 0.96 (95% CI 0.91-0.96). At faecal calprotectin cut-off of 50µg/g, sensitivity for EliA and the Quantum blue test were 94.1% and 100%, and specificity was 87.1% and 72.0%.
Dhaliwal et al. (2015)	Hospital, England	Patients where IBD or IBS was suspected.	ELISA kits: Buhlmann, PhiCal v1 and PhiCal v2	Authors stated that faecal calprotectin levels measured by the 3 ELISA tests were broadly comparable. Correlation between the Buhlmann ELISA and PhiCal v2 ELISA was r2=0.95 (for FC samples >250 µg/g) and r2=0.72 (for FC samples <250 µg/g).
Mirsepasi-Lauridsen et al. (2016)	Hospital, Denmark	<u>Included</u> : previously confirmed IBD diagnosis/healthy control	EK-CAL, CALPRO and HK325	The CALPRO calprotectin ELISA test was shown to have the best specificity at 96%, compared to the HK325 (28%) and the EK-CAL calprotectin (74%) ELISA tests.
Puolanne et al. (2016)	Hospital, Finland	Patients with colonic IBD referred to ileocolonoscopy between January 2013 and September 2013 were invited to participate in the study.	CerTest Calprotectin 50 (Biotec SL, Spain), Prevent ID CalDetect (Immundiagnostik, Germany), PhiCal Test (Calpro AS, Norway) (ELISA)	Sensitivity values (for tests using a cut off of 50µg/g) were reported for PhiCal: 88%, CerTest: 88% and CalDetect: 93%. Specificity values were PhiCal: 50%, CerTest: 64% and CalDetect: 34%.

Schulz (2015)	Tertiary centre, Germany	Included: aged > 18 years and histologically proven diagnosis of Crohn disease, ulcerative colitis and irritable disease according to Rome III criteria.	Quantum Blue, Prevent ID Cal Detect, PhiCal ELISA	Ability to differentiate IBS and IBD: <u>Sensitivity</u> : Prevent ID Cal Detect (79.3%), Quantum Blue (79.3%), PhiCal (73.7%) <u>Specificity</u> : Prevent ID Cal Detect (70%), Quantum Blue (60%), PhiCal (99.5%)
Labaere et al. (2014)	Hospital gastroenterology department, Belgium	Included: referred to gastroenterology department for colonoscopy. Excluded: colonoscopy inconclusive, stool extremely watery.	Buhlmann Quantum Blue, Eurospital Calfast, Biotec Certest (rapid immunochromatographic assays), Eurospital and Calprolab ELISAs and Phadia Elia (automated immunoassay).	Ability to differentiate IBD and non-IBD: <u>Sensitivity</u> : Calprolab (83%), Quantum Blue (83%), Calfast (82%), Calprest (82%), Phadia EliA (75%), Certest (83%). <u>Specificity</u> : Calprolab (89%), Quantum Blue (68%), Calfast (88%), Calprest (88%), Phadia EliA (95%), Certest (84%). All tests using a cut-off of 50µg/g – except Calfast (70 µg/g).
Delefortrie (2015)	Belgium	Stool specimens were collected January to June 2015. Every stool sample received for laboratory testing where general practitioner or gastroenterologist requested FC tests.	Liaison Calprotectin (Diasorin) Quantum Blue point of care test	Higher levels of FC were measured with Quantum Blue than with Liaison: mean difference with weighing extraction protocol -99µg/g (95% CI -157 to -41); mean difference with extraction device -70µg/g (95% CI -130 to -11).
Prell (2014)	Tertiary referral	Outpatients or inpatients Paediatric patients	EliA Calprotectin, Phadia AB, Sweden) and two ELISA tests	Sensitivity to diagnose IBD (cut-off 50µg/g): EliA Calprotectin (97.7%), PhiCal (97.7%), EK-Cal (98.4%).

	centre, Germany		(PhiCal, Calpro AS, Norway; EK-Cal, Bühlmann Laboratories, Switzerland	Specificity: EliA Calprotectin (82.1%), PhiCal (85.1%), EK-Cal (62.7%).
Kolho (2012)	Multicentre study, single laboratory, Europe	Children newly diagnosed with Crohn disease meeting GROWTH study inclusion criteria	Quantum Blue (Bühlmann Laboratories) Tecan ELISA health analysis using Magellan software (Männendoft, Switzerland)/	Authors commented that the ELISA and Quantum Blue tests correlated well with each other (Spearman $r=0.94$, $p<0.001$). When using a cut off of $100\mu\text{g/g}$, percentage agreement was 87% with moderate κ of 0.72 (95% CI 0.60-0.84). The corresponding values were identical for a cut-off value of $150\mu\text{g/g}$.
Okuyama et al. (2016)	IBD hospital centre, Japan	Patients with endoscopically confirmed IBD	Hycult (research use only), PhiCal Calprotectin. Compared to a newly developed assay by this group.	Reported correlation between results produced by the Hycult kit and the PhiCal kit was 0.89 (95% CI 0.88– 0.91).

6.3.5. Cost effectiveness studies

One published study relevant to the scope of this guidance was identified. Yang et al. (2014) reported a decision analytic model from a third party payer perspective. The authors of this study concluded that the use of faecal calprotectin prior to endoscopy in the diagnosis of inflammatory bowel disease is cost effective for both adults and children.

7. Summary of new evidence and implications for review

The majority of the studies that have completed since diagnostics guidance 11 was published reported sensitivity and specificity estimates which are similar to those reported in the studies from the original review. Several studies were identified that compared the diagnostic accuracy of different faecal calprotectin tests. The identified studies vary considerably in terms of the tests they assess, their clinical setting, the cut-off values used, and the baseline characteristics of the population. These new data are unlikely to have any material effect on the existing guidance recommendations. No studies were identified which report the impact of faecal calprotectin testing on clinical decision making when added to current practice.

No substantive changes to the care pathway that have occurred since diagnostics guidance 11 published have been identified. Faecal calprotectin tests are increasingly being used in the NHS to help diagnose IBD, and the British Society of Gastroenterology (BSG) have recently released guidance on the use of these tests. The recommendations made by the BSG support those in diagnostics guidance 11. The NICE guideline on [suspected cancer](#) has been updated since diagnostics guidance 11 was published, and references to NICE clinical guideline 27 will therefore be updated to reflect NICE guideline 12.

In conclusion, the evidence base and clinical environment has not changed to an extent that is likely to have a material effect on the adoption recommendations in the existing guidance; it is therefore suggested that the guidance is transferred to the static list.

8. Implementation

Specialist committee members reported that they were beginning to see uptake of faecal calprotectin testing in the NHS. Several companies reported that their tests were in use in the NHS. Identified guidelines also support the use of faecal calprotectin testing.

9. Equality issues

No new equality issues have been identified since the publication of the guidance.

GE paper sign off: Mirella Marlow, Programme Director, 17 January 2017

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Appendix 1 – explanation of options

If the published Diagnostics Guidance needs updating NICE must select one of the options in the table below:

Options	Consequence	Selected – ‘Yes/No’
Standard update of the guidance	A standard update of the Diagnostics Guidance will be planned into NICE’s work programme.	No
Accelerated update of the guidance	An accelerated update of the Diagnostics Guidance will be planned into NICE’s work programme. Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Diagnostics Guidance does not need updating NICE must select one of the options in the table below:

Options	Consequences	Selected – ‘Yes/No’
Transfer the guidance to the ‘static guidance list’	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Diagnostics Guidance on the static list should be flagged for review.	Yes
Produce a technical supplement	A technical supplement describing newer versions of the technologies is planned into NICE’s work programme.	No
Defer the decision to review the guidance to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Diagnostics Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

Published

[Irritable bowel syndrome in adults: diagnosis and management](#) (2008) NICE guidance CG61. Updated February 2015.

[Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy](#) (2015) NICE technology appraisal 329

[Extracorporeal photopheresis for Crohn's disease](#) (2009) NICE interventional procedures IPG288

[Leukapheresis for inflammatory bowel disease](#) (2005) NICE interventional procedures IPG126

[Colorectal cancer prevention: colonoscopic surveillance in adults with ulcerative colitis, Crohn's disease or adenomas](#) (2011) NICE guidance CG118

[Therapeutic monitoring of TNF-alpha inhibitors in Crohn's disease \(LISA-TRACKER ELISA kits, IDKmonitor ELISA kits, and Promonitor ELISA kits\)](#) (2016) NICE guidance DG22

[Crohn's Disease: management](#) (2012) NICE guidance CG152. Updated May 2016

[Vedolizumab for treating moderately to severe active Crohn's disease after prior therapy](#) (2015) NICE technology appraisal 352

[Infliximab and adalimumab for the treatment of Crohn's disease](#) (2010) NICE technology appraisal 187

[Vedolizumab for treating moderately to severely active ulcerative colitis](#) (2015) Technology appraisal 342

[Faecal incontinence in adults: management](#) (2007) NICE guidance CG49

[Ulcerative colitis: management](#) (2013) NICE guidance CG166

[SeHCAT \(tauroselcholic \[75 selenium\] acid\) for the investigation of diarrhoea due to bile acid malabsorption in people with diarrhoea-predominant irritable bowel syndrome \(IBS-D\) or Crohn's disease without ileal resection](#) (2012) NICE guidance DG7

[Infliximab for acute exacerbations of ulcerative colitis](#) (2008) NICE technology appraisal 163

[Leukapheresis for inflammatory bowel disease](#) (2005) NICE Interventional procedures guidance 126

In progress

[Irritable bowel syndrome \(diarrhoea\) – eluxadoline](#). NICE technology appraisal, publication expected June 2017.

[Short bowel syndrome – teduglutide](#) NICE technology appraisal, publication expected September 2017.

[Ustekinumab for previously treated moderate to severe active Crohn's disease](#) NICE technology appraisal, publication expected July 2017

Referred - QSs and CGs

None identified.

Suspended/terminated

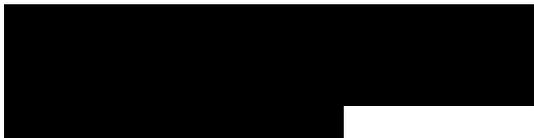
None identified

Details of new technologies

See section 6.1.2.

Registered and unpublished trials

Trial name and registration number	Details
BÜHLMANN fCAL™ ELISA - Aid in Differentiation of IBD From IBS NCT02351635	Aims to confirm the sensitivity and specificity of the BÜHLMANN fCAL™ ELISA as an aid in diagnosis to differentiate between Inflammatory Bowel Disease (IBD; Crohn's Disease (CD), Ulcerative Colitis (UC), or indeterminate colitis) and Irritable Bowel Syndrome (IBS).
ALERT: VALIDation of an 8-item questionnaire predictive for a positive CaLprotectin tEst and Real-life implemenTation in primary care to reduce diagnostic delay in inflammatory bowel disease ISRCTN66310845	Aims to test an 8-item-questionnaire, the CalproQuest, which aims to identify those patients most likely to have IBD and therefore in need of a faecal Calprotectin test and assess its feasibility in primary care setting. The study is described as completed and retrospectively registered.

Trial name and registration number	Details
	
<p>EliA Calprotectin 2: Cut off values for young healthy children</p>	<p>Objective: To determine the optimal fecal calprotectin (EliA Calprotectin 2) cut off levels in young healthy children.</p> <p>Expected completion date: Dec 2016</p> <p>Test: EliA Calprotectin 2</p>
<p>Evaluation of EliA Calprotectin 2 in patients with gastrointestinal disorders</p>	<p>Objective: To evaluate the technical performance (precision, linearity) of EliA Calprotectin 2. To evaluate the correlation between EliA Calprotectin 2 and Calprest (Eurospital) used as a reference method in clinically characterized patients with gastrointestinal disorders.</p> <p>Test: EliA Calprotectin 2</p>
<p>Evaluation of the new EliA Calprotectin 2 Test (wider measurement range)</p>	<p>Objective: To evaluate the performance of the EliA Calprotectin 2 test on patients suffering from Crohn disease and ulcerative colitis.</p> <p>Test: EliA Calprotectin 2</p>
<p>Clinical usefulness of Calprotectin for the diagnosis in children with recurrent gastrointestinal symptoms</p>	<p>Objective: To evaluate F-Calprotectin levels in healthy children.</p> <p>Test: EliA Calprotectin</p>
<p>Determination of nominal values in healthy children</p>	<p>Objective: To evaluate F-Calprotectin levels in healthy children.</p> <p>Test: EliA Calprotectin</p>

Trial name and registration number	Details
Factors affecting the fecal calprotectin level in Neonates	Objective: To find the factors affecting the fecal calprotectin level in newborns through checking the level of fecal calprotectin longitudinally in the same newborn and to determine fecal calprotectin levels in neonatal period. Test: EliA Calprotectin
The clinical effects and adherence of asacol comparing 2.4g once daily with 800mg three times daily for maintain therapy in the ulcerative colitis: A prospective multicenter randomized study	Objective: To confirm the usefulness of calprotectin to monitor the management of UC patients. Test: EliA Calprotectin
Validation of an 8-item-questionnaire predictive for a positive calprotectin test and Real-life implementation in primary care to reduce diagnostic delay in inflammatory bowel disease (ALERT): protocol for a prospective diagnostic study	Objective: To investigate the role of an eight-item questionnaire for general practitioners to assure appropriate use of the calprotectin test. We hypothesize that with the combination of questionnaire and calprotectin test the proportion of patients with a diagnostic delay of more than 18 months in CD and 5 months in UC, respectively, can be reduced from 25% to 10% Test: EliA Calprotectin
	

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