Supplement 1: Methodology

- GDG and extended-Delphi Group
- PICOs
- Systematic review flowchart
- GRADE tables

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PICOs

PICO 1: Diagnostic utility of FIT in patients with a suspicion of CRC

Population	**Intervention**	**Comparisons**	**Outcome**
Patients with signs or symptoms of suspected CRC (CRC) Subgroups: a. Patient factors: i. Age ii. Ethnicity iii. Gender iv. Deprivation v. Geography vi. Smoking	Pathways including FIT testing in **primary care** to: a. triage patients for referral to secondary care (2WW / urgent / routine / safety netting / none) Subgroups: a. FIT Threshold i. Value (ug/g) ii. Single or multiple (e.g. for population subgroup) b. FIT Interpretation	Pathways not including FIT testing in **primary care**. Specialist investigation: i. Direct colonoscopy ii. CT Colonography iii. Flexible sigmoidoscopy iv. Colon Capsule v. Composite of specialist investigations vi. Other Clinical records follow-up: i.6 months ii.12 months	Patient reported outcomes: a. **Critical** for decision making i. Overall survival ii. Disease free survival iii. Progression free survival iv. Morbidity related to tests in those without bowel disease v. Quality of Life b. **Important** for decision making i. Serious adverse effects ii. Time intervals to diagnosis (consultation -> FIT -> referral -> diagnosis -> treatment)

vii. BMI viii. Anticoagulants/antiplatelets ix. Family history x. Previous whole colon investigation xi. Other b. Specific symptoms/signs: i. PR Bleeding ii. Change in bowel habit i. Overall ii. Constipation iii. Diarrhoea iii. Abdominal mass iv. Abdominal pain v. Unexplained Weight loss	i. alone ii. plus clinical assessment iii. plus simple biomarkers iv. plus safety netting protocol v. incorporated into a prediction model c. FIT laboratory platform: i. Individually (OC-Sensor, HM-JACKarc, FOB Gold, other) ii. Combined	iii. 18 months iv. 24 months v. Other	iii. Complications – e,g, physical functioning / incontinence / stoma iv. Recurrence Surrogate/Intermediate outcomes: a. **Critical** for decision making i. Diagnostic accuracy ii. Changes in treatment offered iii. Stage at diagnosis (% stage I & II) iv. Route to diagnosis (all categories) - 2WW referral - Urgent referral

vi. Palpable Rectal mass vii. Anal mass / anal ulceration viii. Other c. Specific blood abnormalities i. IDA ii. Broad anaemia iii. Thrombocytosis iv. Hyper-ferritinaemia v. Other d. Clinically stratified i. Any symptoms/signs of concern ii. High-risk (e.g. NG12 criteria) iii. Low-risk (e.g. DG30 criteria)	Pathways including FIT testing in **secondary care** to: a. counsel patient on decision/need to investigate b. determine choice of investigation (urgent / convert to routine with GP consent) c. select patients for one-stop investigation (endoscopy with dedicated radiology staging slots) Subgroups: a. FIT Threshold i. Value (ug/g)	Pathways not including FIT testing in **secondary care**. Specialist investigation: i. Direct colonoscopy ii. CT Colonography iii. Flexible sigmoidoscopy iv. Colon capsule v. Composite of specialist investigations vi. Other Clinical records follow-up: i. 6 months ii. 12 months iii. 18 months iv. 24 months v. Other	- Routine referral - Emergency presentation v. Number needed to (scope / CTC) to detect one cancer vi. Patient acceptability / reassurance b. **Important** for decision making i. Improved diagnostic pathway elements ii. Length of stay in hospital iii. Clinician acceptability iv. Number of tests performed per patient

	ii. Single or multiple (e.g. for population subgroup) b. FIT Interpretation i. alone ii. plus clinical assessment iii. plus simple biomarkers vi. plus safety netting protocol iv. incorporated into a prediction model c. FIT laboratory platform: i. Individually (OC-Sensor, HM-JACKarc, FOB Gold, other)		

	ii. Combined		

PICO 2: What mechanisms may be employed to avoid delayed diagnosis in patients with FIT negative CRC?

Population	**Intervention**	**Comparison**	**Outcome**
Patients with a negative FIT Patients who do not return FIT Subgroups: a. Patient factors: i. Age ii. Ethnicity iii. Gender iv. Deprivation v. Geography vi. Previous whole colon investigation b. Ongoing / no ongoing symptoms c. Referred / not referred.	Referral (urgent / routine) in selected subgroups (demographics / symptoms /blood results). Repeat FIT testing (frequency and interval) Safety netting (as defined by study) Clinical assessment Use of other simple tests i. Platelets ii. Haemoglobin iii. MCV iv. Ferritin	Watch and wait in primary care No safety netting Single FIT test An alternative intervention	Patient reported outcomes: a. **Critical** for decision making i. Overall survival ii. Disease free survival iii. Progression free survival iv. Morbidity related to tests in those without bowel disease v. Quality of Life b. **Important** for decision making i. Serious adverse effects ii. Time to diagnosis (consultation -> FIT -> referral -> diagnosis -> treatment) iii. Complications – e,g, physical functioning / incontinence / stoma iv. Recurrence Surrogate/Intermediate Outcomes:

	v. CRP vi. Other		c. **Critical** for decision making i. Diagnostic accuracy ii. Changes in treatment offered iii. Stage at diagnosis iv. Route to diagnosis (all categories) - 2WW referral - Urgent referral - Routine referral - Emergency presentation v. Number needed to (scope / CTC) to detect one cancer vi. Patient acceptability / reassurance d. **Important** for decision making i. Improved diagnostic pathway elements ii. Length of stay in hospital iii. Clinician acceptability iv. Number of tests performed per patient

PICO 3: FIT and equality and access to care

1) What is the acceptability of FIT in patients with suspected CRC symptoms and their treating clinicians?
2) How can we avoid discriminating against certain populations in this guideline?
3) What lessons may be learned from implementation programmes of FIT in symptomatic populations?

May need to develop non-PICO model for this topic

Population	**Intervention**	**Comparison**	**Outcome**
Patients with symptoms of suspected CRC ○ Subgroups: - Patient - Age, ethnicity, gender, language, deprivation - Learning disability - Hearing or sight impaired	FIT testing ○ Qualitative outcomes ○ Uptake in subgroup populations ○ Implementation	Direct – Specialist investigation: i. Direct colonoscopy ii. CT Colonography iii. Flexible sigmoidoscopy iv. Colon Capsule v. Composite of specialist investigations vi. Other	PRO • Critical for decision making i. Overall survival ii. Disease free survival iii. Progression free survival iv. Morbidity (to be decided what is included) **v. Quality of Life** • Important for decision making i. Serious adverse effects ii. Time to diagnosis

- Accessibility other e.g. housebound, travel - Other physical conditons - Symptoms: High vs low-risk			iii. Physical functioning / incontinence / stoma iv. Recurrence Unimportant for decision making v. Costs, # of colonoscopies vi. Adverse effects including psychological vii. Satisfaction Intermediates • Critical for decision making • Diagnostic accuracy • Changes in treatment offered • Stage at diagnosis • Route to diagnosis (all categories) • Number needed to (colono)scope / CTC

			• Patient acceptability (combine with reassurance) • Important for decision making • Improved diagnostic pathway elements • Length of stay in hospital • Reassurance / time to reassurance / time to diagnostic resolution • Clinician acceptability • Number of tests performed Critical: • CRC diagnostic accuracy • Time to diagnosis • Earlier diagnosis (stage shift) Important:

			• Prioritising investigations • Morbidity of interventions • Reduced CRC Morbidity • Develop patient pathway to diagnosis Lower importance • Predicted resource impact • SBD: Polyps – advanced / non-advanced • Other SBD

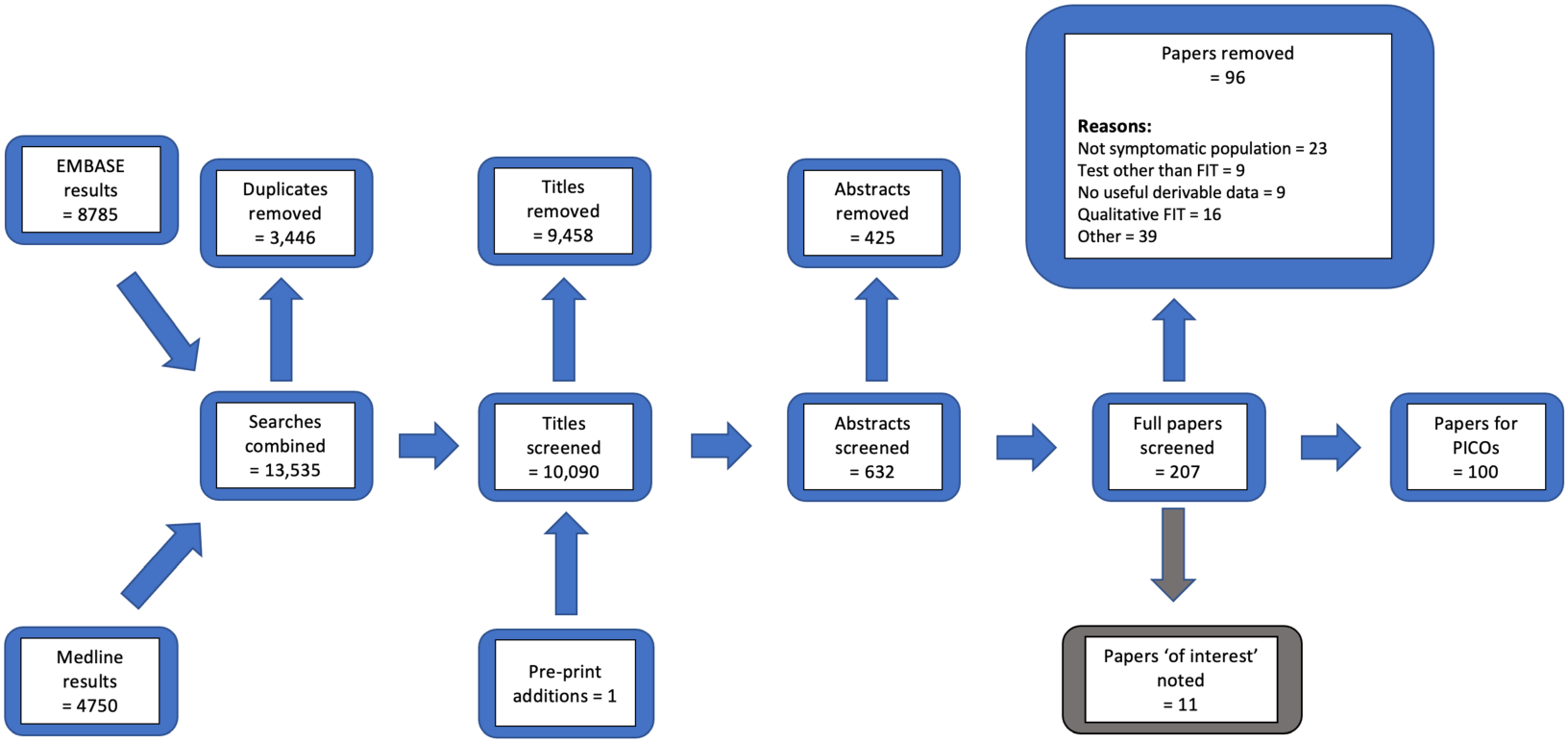

Figure S1: Flowchart of systematic review of evidence

GRADE Tables

Table 1: Should Faecal immunochemical test be used to diagnose colorectal cancer in patients with all symptoms (NG12, DG30 or NC)?

Sensitivity	0.90 (95% CI: 0.88 to 0.92)
Specificity	0.76 (95% CI: 0.71 to 0.80)

Prevalences			
	4.2%	1.1%	13.6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of4.2%	pre-test probability of1.1%	pre-test probability of13.6%	
True positives (patients with colorectal cancer)	15 studies 35782 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	none	38 (37 to 39)	10 (10 to 10)	122 (120 to 125)	⊕◯◯◯ Very low[1,2,3,4,5,6,7,8,9,10,11,12,13,14,15]
False negatives (patients incorrectly classified as not								4 (3 to 5)	1 (1 to 1)	14 (11 to 16)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of4.2%	pre-test probability of1.1%	pre-test probability of13.6%	
having colorectal cancer)											
True negatives (patients without colorectal cancer)	15 studies 35782 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	none	728 (680 to 766)	752 (702 to 791)	657 (613 to 691)	⊕◯◯◯ Very low
False positives (patients incorrectly classified as having colorect								230 (192 to 278)	237 (198 to 287)	207 (173 to 251)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of4.2%	pre-test probability of1.1%	pre-test probability of13.6%	
al cancer)											

Explanations:

a. Studies were judged at a high risk of bias in patient selection.

b. Results based on indirect comparisons from different studies; direct evidence about impact on patient-important outcomes

c. Significant heterogeneity detected

Footnote: CoE = certainty of evidence

References

1.Chapman, C, Thomas, C, Morling, J, Tangri, A, Oliver, S, Simpson, J A, Humes, D J, Banerjea, A. Early clinical outcomes of a rapid colorectal cancer diagnosis pathway using faecal immunochemical testing in Nottingham. Colorectal Disease; 2020.

2.D'Souza, N, Delisle, T G, Chen, M, Benton, S C, Abulafi, M, Committee, Nice Fit Steering. Faecal immunochemical testing in symptomatic patients to prioritize investigation: diagnostic accuracy from NICE FIT Study. British Journal of Surgery; 2021.

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14.Navarro, M, Hijos, G, Sostres, C, Lue, A, Puente-Lanzarote, J J, Carrera-Lasfuentes, P, Lanas, A. Reducing the Cut-Off Value of the Fecal Immunochemical Test for Symptomatic Patients Does Not Improve Diagnostic Performance. Frontiers in Medicine; 2020.
15.Tsapournas, G, Hellstrom, P M, Cao, Y, Olsson, L I. Diagnostic accuracy of a quantitative faecal immunochemical test vs. symptoms suspected for colorectal cancer in patients referred for colonoscopy. Scandinavian Journal of Gastroenterology; 2020.

Table 2: Flexible sigmoidoscopy compared to FIT (if negative) for referral of patients with persistent / recurrent rectal bleeding
Setting: Secondary care

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
Under-detection of CRC (assessed with: FIT)									

Certainty assessment							Impact	Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**			
1	observational studies	serious[a]	not serious	serious[b]	serious[c]	strong association all plausible residual confounding would reduce the demonstrated effect	We recommend referral of patients with persistent / recurrent rectal bleeding for flexible sigmoidoscopy if FIT is negative. In patients with rectal bleeding and undetectable f-Hb the use of flexible sigmoidoscopy can reduce the probability of undetected CRC to 0.03%.	⨁◯◯◯ Very low[1]	CRITICAL

CI: confidence interval

Explanations

a. D'Souza was judged at a high risk of bias in patient selection.

b. Direct evidence about impact on patient-important outcomes was missing

c. Wide confidence intervals for sensitivity in NRB for >10

References

1.Hicks, G, D'Souza, N, Georgiou Delisle, T, Chen, M, Benton, S C, Abulafi, M. Using the faecal immunochemical test in patients with rectal bleeding: evidence from the NICE FIT study. Colorectal Disease; 2021.

2.D'Souza, N., Monahan, K., Benton, S. C., Wilde, L., Abulafi, M., Group, Nice Fit Steering. Finding the needle in the haystack: the diagnostic accuracy of the faecal immunochemical test for colorectal cancer in younger symptomatic patients. Colorectal Disease; 2021.

Table 3: Should FIT threshold of ≥10µg vs. be used for be used to diagnose in referral for CRC investigation?

Sensitivity	0.91 (95% CI: 0.85 to 0.94)
Specificity	0.71 (95% CI: 0.57 to 0.82)

Prevalences	1.1%	0.8%	1.8%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of1.1%	pre-test probability of0.8%	pre-test probability of1.8%	
True positives (patients with)	4 studies 12141 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious[b]	serious[c]	not serious	none	10 (9 to 10)	7 (7 to 8)	16 (15 to 17)	⊕◯◯◯ Very low[1,2,3,4]
False negatives (patients incorrectly classified as not having)								1 (1 to 2)	1 (0 to 1)	2 (1 to 3)	
True negatives (patients without)	4 studies 12141 patients	cross-sectional (cohort type	serious [a]	serious[b]	serious[c]	not serious	none	702 (564 to 811)	704 (565 to 813)	697 (560 to 805)	⊕◯◯◯ Very low

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of1.1%	pre-test probability of0.8%	pre-test probability of1.8%	
False positives (patients incorrectly classified as having)		accuracy study)						287 (178 to 425)	288 (179 to 427)	285 (177 to 422)	

Explanations

a. Studies were judged at a high risk of bias in patient selection.

b. Results based on indirect comparisons from different studies; direct evidence about impact on patient-important outcomes

c. Significant heterogeneity detected

Footnote: CoE = certainty of evidence

References

1.Chapman, C, Bunce, J, Oliver, S, Ng, O, Tangri, A, Rogers, R, Logan, R F, Humes, D J, Banerjea, A. Service evaluation of faecal immunochemical testing and anaemia for risk stratification in the 2-week-wait pathway for colorectal cancer. BJS Open; 2019.

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Table 4: Should OC-sensor vs. HM JACK-arc be used to diagnose CRC in patients with all symptoms (NG12, DG30 or NC)?

OC-sensor		HM JACK-arc	
Sensitivity	0.90 (95% CI: 0.86 to 0.93)	Sensitivity	0.90 (95% CI: 0.87 to 0.92)
Specificity	0.74 (95% CI: 0.68 to 0.79)	Specificity	0.78 (95% CI: 0.69 to 0.85)

Prevalences	4.2%	1.1%	13.6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of4.2%		pre-test probability of1.1%		pre-test probability of13.6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	OC-sensor	HM JACK-arc	OC-sensor	HM JACK-arc	OC-sensor	HM JACK-arc	
True positives (patients with CRC)	13 studies 34813 patients	cross-sectional (cohort type accura	not serious	serious[a]	serious[b]	not serious	none	38 (36 to 39)	38 (37 to 39)	10 (9 to 10)	10 (10 to 10)	122 (117 to 126)	122 (118 to 125)	⊕⊕◯◯ Low[1,2,3,4,5,6,7,8,9,10,11,12,13]
								0 fewer TP in OC-sensor		**0 fewer TP in OC-sensor**		**0 fewer TP in OC-sensor**		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of4.2%		pre-test probability of1.1%		pre-test probability of13.6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	OC-sensor	HMJACK-arc	OC-sensor	HMJACK-arc	OC-sensor	HMJACK-arc	
False negatives (patients incorrectly classified as not having CRC)		cy study)						4 (3 to 6)	4 (3 to 5)	1 (1 to 2)	1 (1 to 1)	14 (10 to 19)	14 (11 to 18)	
								0 fewer FN in OC-sensor		**0 fewer FN in OC-sensor**		**0 fewer FN in OC-sensor**		
True negatives (patients without CRC)	13 studies 34813 patients	cross-sectional (cohort type accura	not serious	serious[a]	serious[b]	not serious	none	709 (651 to 757)	747 (661 to 814)	732 (673 to 781)	771 (682 to 841)	639 (588 to 683)	674 (596 to 734)	⨁⨁◯◯ Low
								38 fewer TN in OC-sensor		**39 fewer TN in OC-sensor**		**35 fewer TN in OC-sensor**		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of4.2%		pre-test probability of1.1%		pre-test probability of13.6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	OC-sensor	HMJAK-arc	OC-sensor	HMJAK-arc	OC-sensor	HMJAK-arc	
False positives (patients incorrectly classified as having CRC)		cy study)						249 (201 to 307)	211 (144 to 297)	257 (208 to 316)	218 (148 to 307)	225 (181 to 276)	190 (130 to 268)	
								38 more FP in OC-sensor		**39 more FP in OC-sensor**		**35 more FP in OC-sensor**		

Explanations

a. Results based on indirect comparisons from different studies

b. There was high amount of heterogeneity detected.

Footnote: CoE = certainty of evidence

References

1.Chapman, C, Thomas, C, Morling, J, Tangri, A, Oliver, S, Simpson, J A, Humes, D J, Banerjea, A. Early clinical outcomes of a rapid colorectal cancer diagnosis pathway using faecal immunochemical testing in Nottingham. Colorectal Disease; 2020.

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Table 5: Should FOB Gold vs. QuikRead go be used to diagnose CRC in in patients with all symptoms (NG12, DG30 or NC)?

FOB Gold		QuikRead go	
Sensitivity	0.94 (95% CI: 0.81 to 0.99)	Sensitivity	0.92 (95% CI: 0.64 to 0.99)
Specificity	0.75 (95% CI: 0.71 to 0.78)	Specificity	0.77 (95% CI: 0.71 to 0.82)

Prevalences	5.1%	5%	5.3%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of5.1%		pre-test probability of5%		pre-test probability of5.3%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FOB Gold	QuikRead go	FOB Gold	QuikRead go	FOB Gold	QuikRead go	
True positives (patients with CRC)	1 studies 727 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	none	48 (41 to 50)	47 (33 to 50)	47 (41 to 50)	46 (32 to 50)	50 (43 to 52)	49 (34 to 52)	⊕◯◯◯ Very low[1]
								1 more TP in FOB Gold		**1 more TP in FOB Gold**		**1 more TP in FOB Gold**		
False negatives								3 (1 to 10)	4 (1 to 18)	3 (0 to 9)	4 (0 to 18)	3 (1 to 10)	4 (1 to 19)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of5.1%		pre-test probability of5%		pre-test probability of5.3%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FOB Gold	QuikRead go	FOB Gold	QuikRead go	FOB Gold	QuikRead go	
(patients incorrectly classified as not having CRC)								**1 fewer FN in FOB Gold**		**1 fewer FN in FOB Gold**		**1 fewer FN in FOB Gold**		
True negatives (patients without CRC)	1 studies 727 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	serious	none	712 (674 to 740)	731 (674 to 778)	712 (675 to 741)	731 (675 to 779)	710 (672 to 739)	729 (672 to 777)	⊕◯◯◯ Very low
								19 fewer TN in FOB Gold		**19 fewer TN in FOB Gold**		**19 fewer TN in FOB Gold**		
False positives (patients								237 (209 to	218 (171 to 275)	238 (209 to	219 (171 to 275)	237 (208 to	218 (170 to 275)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of5.1%		pre-test probability of5%		pre-test probability of5.3%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FOB Gold	QuikRead go	FOB Gold	QuikRead go	FOB Gold	QuikRead go	
incorrectly classified as having CRC)								275)		275)		275)		
								19 more FP in FOB Gold		**19 more FP in FOB Gold**		**19 more FP in FOB Gold**		

Explanations

a. Tsapournas 2020 was judged at a high risk of bias in patient selection.

b. Results based on indirect comparisons from different studies

c. There was high amount of heterogeneity detected.

Footnote: CoE = certainty of evidence

References

1.Navarro, M, Hijos, G, Sostres, C, Lue, A, Puente-Lanzarote, J J, Carrera-Lasfuentes, P, Lanas, A. Reducing the Cut-Off Value of the Fecal Immunochemical Test for Symptomatic Patients Does Not Improve Diagnostic Performance. Frontiers in Medicine; 2020.

Table 6: Should CT colonography be preferred over colonoscopy for patients with non-specific symptoms including abdominal pain or weight loss?

Patient or population: patients with non-specific symptoms including abdominal pain or weight loss
Setting: 2WW CRC pathway
Intervention: Is CT colonography preferred
Comparison: colonoscopy

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Patients' preference (Preference)	For patients recommended whole colon investigation as part of a 2WW CRC pathway, CTC is equivalent to colonoscopy for detection of CRC; and use of CTC can be determined by local teams according to audited performance, capacity and experience	9822 (1 observational study)	⨁⨁◯◯ Low[1,2,a]

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. Study was judged to be at a high risk of bias.

References

1.D'Souza N, Delisle TG,Chen M,Benton S,Abulafi M,NICE FIT Steering Committee. Faecal immunochemical test is superior to symptoms in predicting pathology in patients with suspected colorectal cancer symptoms referred on a 2WW pathway; a diagnostic accuracy study. Gut; 2020.

2.Delisle, T G, D'Souza, N, Davies, B, Ward, H, Abulafi, M. Patient acceptability of a home colorectal cancer rule out test. British Journal of Surgery; 2020.

Table 7: Should FIT be used to diagnose CRC in younger patients (<50)?

Sensitivity	0.81 to 0.93
Specificity	0.83 to 0.88

Prevalences	2.7%	1.5%	3.9%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2.7%	pre-test probability of1.5%	pre-test probability of3.9%	
True positives (patients with CRC)	2 studies 9969 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious[b]	not serious	not serious	none	22 to 25	12 to 14	32 to 36	⊕⊕◯◯ Low[1,2]
False negatives (patients incorrectl								2 to 5	1 to 3	3 to 7	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2.7%	pre-test probability of1.5%	pre-test probability of3.9%	
y classified as not having CRC)											
True negatives (patients without CRC)	2 studies 9969 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious[b]	not serious	not serious	none	808 to 856	818 to 867	798 to 846	⨁⨁◯◯ Low
False positives (patients incorrectly classified as having CRC)								117 to 165	118 to 167	115 to 163	

Explanations

a. High risk of bias in patient selection

b. Results based on indirect comparisons from different studies

Footnote: CoE = certainty of evidence

References

1.Lue, A, Hijos, G, Sostres, C, Perales, A, Navarro, M, Barra, M V, Mascialino, B, Andalucia, C, Puente, J J, Lanas, A, Gomollon, F. The combination of quantitative faecal occult blood test and faecal calprotectin is a cost-effective strategy to avoid colonoscopies in symptomatic patients without relevant pathology. Therapeutic Advances in Gastroenterology; 2020.

2.D'Souza, N, Monahan, K, Benton, S C, Wilde, L, Abulafi, M, Group, Nice Fit Steering. Finding the needle in the haystack: the diagnostic accuracy of the faecal immunochemical test for colorectal cancer in younger symptomatic patients. Colorectal Disease; 2021.

Table 8: FIT compared to no test or no-return for risk of CRC
Patient or population: risk of CRC
Setting: Various
Intervention: FIT
Comparison: no test or no-return

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)
Adherence (Adherence) assessed with: Questionnaire/survey	We recommend that GPs should be advised that in a symptomatic patient with no recent FIT result (through lack of return of the kit or sample failure) evaluation of CRC risk is likely to be suboptimal. This is likely to be of an order greater than failing to consider well known “alarm” symptoms such as rectal bleeding or change in bowel habit. We recommend that patients who refuse to return a FIT test should be counselled that the absence of a result may impair their responsible clinician’s ability to correctly assess their risk of CRC and take appropriate action to address this.	(0 studies)	-

Table 8: FIT compared to no test or no-return for risk of CRC
Patient or population: risk of CRC
Setting: Various
Intervention: FIT
Comparison: no test or no-return

Outcomes	Impact	№ of participants (studies)	Certainty of the evidence (GRADE)

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Table 9: Should FIT (HM-JACKarc) be used to diagnose CRC in similar in both high (NG12) and low risk (DG30) symptomatic patients (in any setting at the >10 cut-off, Tier 1)?

FIT (HM-JACKarc) DG30		FIT (HM-JACKarc) NG12	
Sensitivity	0.88 (95% CI: 0.78 to 0.95)	Sensitivity	0.89 (95% CI: 0.82 to 0.93)
Specificity	0.88 (95% CI: 0.87 to 0.89)	Specificity	0.81 (95% CI: 0.79 to 0.82)

Prevalences	4.6%	3.3%	6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of4.6%		pre-test probability of3.3%		pre-test probability of6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	
True positives (patients with CRC)	4 studies 11464 patients	cross-sectional (cohort type accuracy study)	serious[1,2,3,4,a]	serious[b]	serious[c]	not serious	none	40 (36 to 44)	41 (38 to 43)	29 (26 to 31)	29 (27 to 31)	53 (47 to 57)	53 (49 to 56)	⊕◯◯◯ Very low
								1 fewer TP in FIT (HM-JACKarc) DG30		**0 fewer TP in FIT (HM-JACKarc) DG30**		**0 fewer TP in FIT (HM-JACKarc) DG30**		
False negatives (patients incorrec								6 (2 to 10)	5 (3 to 8)	4 (2 to 7)	4 (2 to 6)	7 (3 to 13)	7 (4 to 11)	
								1 more FN in FIT (HM-JACKarc) DG30		**0 fewer FN in FIT (HM-JACKarc) DG30**		**0 fewer FN in FIT (HM-JACKarc) DG30**		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of4.6%		pre-test probability of3.3%		pre-test probability of6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	
tly classified as not having CRC)														
True negatives (patients without CRC)	4 studies 11464 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	none	840 (830 to 849)	773 (754 to 782)	851 (841 to 861)	783 (764 to 793)	827 (818 to 837)	761 (743 to 771)	⊕◯◯◯ Very low
								67 more TN in FIT (HM-JACKarc) DG30		**68 more TN in FIT (HM-JACKarc) DG30**		**66 more TN in FIT (HM-JACKarc) DG30**		
False positives (patient								114 (105 to 124)	181 (172 to 200)	116 (106 to 126)	184 (174 to 203)	113 (103 to 122)	179 (169 to 197)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of4.6%		pre-test probability of3.3%		pre-test probability of6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	FIT (HM-JACKarc) DG30	FIT (HM-JACKarc) NG12	
s incorrectly classified as having CRC)								**67 fewer FP in FIT (HM-JACKarc) DG30**		**68 fewer FP in FIT (HM-JACKarc) DG30**		**66 fewer FP in FIT (HM-JACKarc) DG30**		

Explanations

a. Farrugia 2020 was judged to be at a high risk of bias for flow and timing; D'Souza 2020 was judged to be at a high risk of bias for patient selection.

b. Results based on indirect comparisons from different studies; direct evidence about impact on patient-important outcomes missing.

c. Significant heterogeneity for sensitivity detected.

Footnote: CoE = certainty of evidence

References

1.D'Souza, N., Georgiou Delisle, T., Chen, M., Benton, S., Abulafi, M.. Faecal immunochemical test is superior to symptoms in predicting pathology in patients with suspected colorectal cancer symptoms referred on a 2WW pathway: A diagnostic accuracy study. Gut; 2021.

2.Chapman, C. J., Banerjea, A., Humes, D. J., Allen, J., Oliver, S., Ford, A., Hardy, K., Djedovic, N., Logan, R. F., Morling, J. R.. Choice of faecal immunochemical test matters: comparison of OC-Sensor and HM-JACKarc, in the assessment of patients at high risk of colorectal cancer. Clin Chem Lab Med; Oct 29 2020.

3.D'Souza N, Delisle TG,Chen M,Benton S,Abulafi M,NICE FIT Steering Committee. Faecal immunochemical test is superior to symptoms in predicting pathology in patients with suspected colorectal cancer symptoms referred on a 2WW pathway; a diagnostic accuracy study. Gut; 2020.
4.Farrugia, A, Widlak, M, Evans, C, Smith, S C, Arasaradnam, R. Faecal immunochemical testing (FIT) in symptomatic patients: What are we missing?. Frontline Gastroenterology; 2020.

Table 10: Should FIT (OC-sensor) be used to diagnose CRC in in patients with rectal bleeding (in primary care at >10 cut-off)?

Sensitivity	0.96 (95% CI: 0.80 to 0.99)
Specificity	0.38 (95% CI: 0.33 to 0.43)

Prevalences	5.6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of5.6%	
True positives (patients with CRC)	1 studies 462 patients	cross-sectional (cohort type accuracy study)	serious[1,a]	serious[b]	not serious	serious[c]	none	54 (45 to 55)	⨁◯◯◯ Very low
False negatives (patients incorrectly classified as not having CRC)								2 (1 to 11)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of5.6%	
True negatives (patients without CRC)	1 studies 462 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	serious[c]	none	359 (312 to 406)	⨁◯◯◯ Very low
False positives (patients incorrectly classified as having CRC)								585 (538 to 632)	

Explanations

a. Mowat/Digby was judged to be at a high risk of bias for flow and timing; and a high risk of bias for patient selection.

b. direct evidence about impact on patient-important outcomes is missing.

c. Wide confidence intervals

Footnote: CoE = certainty of evidence

References

1.Mowat, C., Digby, J., Strachan, J. A., Wilson, R., Carey, F. A., Fraser, C. G., Steele, R. J.. Faecal haemoglobin and faecal calprotectin as indicators of bowel disease in patients presenting to primary care with bowel symptoms. Gut; Sep 2016.

Table 11: Should FIT (HM-JACKarc) be used to diagnose CRC in iron deficiency anaemia?

Sensitivity	1.00 (95% CI: 0.89 to 1.00)
Specificity	0.81 (95% CI: 0.77 to 0.85)

Prevalences	3.3%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of3.3%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with CRC)	1 studies 479 patients	cross-sectional (cohort type accuracy study)	serious[1, a]	serious[b]	not serious	serious[c]	none	33 (29 to 33)	0 (0 to 0)	0 (0 to 0)	⨁◯◯◯ Very low
False negatives (patients incorrectly classified as not having CRC)								0 (0 to 4)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without CRC)	1 studies 479 patients	cross-sectional (cohort type	serious[a]	serious[b]	not serious	serious[c]	none	783 (745 to 822)	810 (770 to 850)	810 (770 to 850)	⨁◯◯◯ Very low

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of3.3%	pre-test probability of0%	pre-test probability of0%	
False positives (patients incorrectly classified as having CRC)		accuracy study)						184 (145 to 222)	190 (150 to 230)	190 (150 to 230)	

Explanations

a. D'Souza 2021 was judged to be at a high risk of bias for patient selection.

b. direct evidence about impact on patient-important outcomes is missing

c. Wide confidence intervals for sensitivity and specificity

Footnote: CoE = certainty of evidence

References

1.D'Souza, N, Delisle, T G, Chen, M, Benton, S C, Abulafi, M, Committee, Nice Fit Steering. Faecal immunochemical testing in symptomatic patients to prioritize investigation: diagnostic accuracy from NICE FIT Study. British Journal of Surgery; 2021.

Table 12: Should FIT (OC-sensor) be used to diagnose CRC in in those with isolated change in bowel habits?

Sensitivity	0.88 (95% CI: 0.79 to 0.95)
Specificity	0.80 (95% CI: 0.79 to 0.81)

Prevalences	1.2%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of1.2%	
True positives (patients with CRC)	1 study 5818 patients	cross-sectional (cohort type accuracy study)	serious[1,a]	serious[b]	not serious	serious[c]	publication bias strongly suspected[d]	11 (9 to 11)	⊕◯◯◯ Very low
False negatives (patients incorrectly classified as not having CRC)								1 (1 to 3)	
True negatives (patients without CRC)	1 study 5818 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	serious[c]	publication bias strongly suspected[d]	790 (781 to 800)	⊕◯◯◯ Very low
False positives (patients incorrectly classified as having CRC)								198 (188 to 207)	

Explanations

a. Khasawneh 2020 was judged to be at an unclear risk of bias.

b. direct evidence about impact on patient-important outcomes is missing.

c. Wide confidence intervals for sensitivity

d. Results based on a single study
Footnote: CoE = certainty of evidence

References
1.Khasawneh, F, Osborne, T, Stephenson, J, Barnes, D, Seehra, J, Danaher, P, Jones, J, Singh, B. Faecal immunochemical testing is a cost-effective way to stratify symptomatic patients for urgent straight to test investigation. Colorectal Disease; 2020.

Table 13: Should FIT (OC-sensor) be used to diagnose CRC in in patients with CIBH or RB at thresholds >4 to >10 in primary care?

Sensitivity	0.91 to 0.96
Specificity	0.38 to 0.69

Prevalences	0%	1.2%	5.6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of0%	pre-test probability of1.2%	pre-test probability of5.6%	
True positives (patients with CRC)	2 studies 6280 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	none	0 to 0	11 to 12	51 to 54	⊕◯◯◯ Very low[1,2]
False negatives (patients incorrectl								0 to 0	0 to 1	2 to 5	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of0%	pre-test probability of1.2%	pre-test probability of5.6%	
y classified as not having CRC)											
True negatives (patients without CRC)	2 studies 6280 patients	cross-sectional (cohort type accuracy study)	serious [a]	serious[b]	serious[c]	not serious	none	380 to 690	375 to 682	359 to 651	⊕◯◯◯ Very low
False positives (patients incorrectly classified as having CRC)								310 to 620	306 to 613	293 to 585	

Explanations

a. Khasawneh 2020 was judged to be at an unclear risk of bias in all domains.

b. Results based on indirect comparisons from different studies; direct evidence about impact on patient-important outcomes is missing

c. Significant heterogeneity detected for both sensitivity and specificity

Footnote: CoE = certainty of evidence

References
1.Khasawneh, F, Osborne, T, Stephenson, J, Barnes, D, Seehra, J, Danaher, P, Jones, J, Singh, B. Faecal immunochemical testing is a cost-effective way to stratify symptomatic patients for urgent straight to test investigation. Colorectal Disease; 2020.
2.Digby, J, Strachan, J A, McCann, R, Steele, R J C, Fraser, C G, Mowat, C. Measurement of faecal haemoglobin with a faecal immunochemical test can assist in defining which patients attending primary care with rectal bleeding require urgent referral. Annals of Clinical Biochemistry; 2020.

Table 14: Should FIT in primary care vs. FIT in secondary care be used to diagnose CRC in adults with lower gastrointestinal signs or symptoms (at >10) and in all symptoms (NG12, DG30 and NC)?

FIT in primary care		FIT in secondary care	
Sensitivity	0.91 (95% CI: 0.85 to 0.94)	Sensitivity	0.91 (95% CI: 0.88 to 0.93)
Specificity	0.71 (95% CI: 0.57 to 0.82)	Specificity	0.79 (95% CI: 0.74 to 0.83)

Prevalences	5.2%	1.2%	13.6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of5.2%		pre-test probability of1.2%		pre-test probability of13.6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FIT in primary care	FIT in secondary care	FIT in primary care	FIT in secondary care	FIT in primary care	FIT in secondary care	
True positives (patients with CRC)	13 studies 34357 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	strong association	47 (44 to 49)	47 (46 to 48)	11 (10 to 11)	11 (11 to 11)	124 (116 to 128)	124 (120 to 126)	⊕⊕◯◯ Low[1,2,3,4,5,6,7,8,9,10,11,12,13]
								0 fewer TP in FIT in primary care		**0 fewer TP in FIT in primary care**		**0 fewer TP in FIT in primary care**		
False negatives (patients incorrectly classified as not having CRC)								5 (3 to 8)	5 (4 to 6)	1 (1 to 2)	1 (1 to 1)	12 (8 to 20)	12 (10 to 16)	
								0 fewer FN in FIT in primary care		**0 fewer FN in FIT in primary care**		**0 fewer FN in FIT in primary care**		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested						Test accuracy CoE
								pre-test probability of5.2%		pre-test probability of1.2%		pre-test probability of13.6%		
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	FIT in primary care	FIT in secondary care	FIT in primary care	FIT in secondary care	FIT in primary care	FIT in secondary care	
True negatives (patients without CRC)	13 studies 34357 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	serious[c]	not serious	strong association	673 (540 to 777)	749 (702 to 787)	701 (563 to 810)	781 (731 to 820)	613 (492 to 708)	683 (639 to 717)	⊕⊕◯◯ Low
								76 fewer TN in FIT in primary care		**80 fewer TN in FIT in primary care**		**70 fewer TN in FIT in primary care**		
False positives (patients incorrectly classified as having CRC)								275 (171 to 408)	199 (161 to 246)	287 (178 to 425)	207 (168 to 257)	251 (156 to 372)	181 (147 to 225)	
								76 more FP in FIT in primary care		**80 more FP in FIT in primary care**		**70 more FP in FIT in primary care**		

Explanations

a. Studies were judged at a high risk of bias in patient selection e.g., McSorley 2020, Mowat 2016.

b. Results based on indirect comparisons from different studies; direct evidence about impact on patient-important outcomes is missing

c. Significant heterogeneity detected for specificity

Footnote: CoE = certainty of evidence

References

1.Chapman, C, Thomas, C, Morling, J, Tangri, A, Oliver, S, Simpson, J A, Humes, D J, Banerjea, A. Early clinical outcomes of a rapid colorectal cancer diagnosis pathway using faecal immunochemical testing in Nottingham. Colorectal Disease; 2020.

2.D'Souza, N, Delisle, T G, Chen, M, Benton, S C, Abulafi, M, Committee, Nice Fit Steering. Faecal immunochemical testing in symptomatic patients to prioritize investigation: diagnostic accuracy from NICE FIT Study. British Journal of Surgery; 2021.

3.D'Souza, N, Hicks, G, Benton, S C, Abulafi, M. The diagnostic accuracy of the faecal immunochemical test for colorectal cancer in risk-stratified symptomatic patients. Annals of the Royal College of Surgeons of England; 2020.

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Question: Should FIT be used to diagnose CRC in aspirin users ?

Sensitivity	0.88 (95% CI: 0.75 to 0.95)
Specificity	0.66 (95% CI: 0.62 to 0.71)

Prevalence	10.5%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10.5%	
True positives (patients with CRC)	1 study 485 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious	serious[b]	publication bias strongly suspected[c]	92 (79 to 100)	⊕◯◯◯ Very low
False negatives (patients incorrectly								13 (5 to 26)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10.5%	
classified as not having CRC)									
True negatives (patients without CRC)	1 study 485 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious	serious[b]	publication bias strongly suspected[c]	591 (555 to 635)	⨁◯◯◯ Very low
False positives (patients incorrectly classified as having CRC)								304 (260 to 340)	

Explanations

a. Poor representativeness of the population.

b. Wide confidence intervals; small sample <500 participants

c. Results based on a single study

References:

[1] Bujanda L, Sarasqueta C, Vega P, Salve M, Quintero E, Alvarez-Sanchez V, et al. Effect of aspirin on the diagnostic accuracy of the faecal immunochemical test for colorectal advanced neoplasia. *United European Gastroenterol J* 2018;6(1):123-130.

Question: Should FIT be used to diagnose CRC in females in secondary care (threshold: ≥10 µg Hb/g)?

Sensitivity	0.76 to 0.88
Specificity	0.82 to 0.85

Prevalences	1.1%	4.5%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 1.1%	pre-test probability of 4.5%	
True positives (patients with CRC)	2 studies 21435 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	not serious	none	8 to 10	34 to 40	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having CRC)								1 to 3	5 to 11	
True negatives (patients without CRC)	2 studies 21435 patients	cross-sectional (cohort type	serious[a]	serious[b]	not serious	not serious	none	811 to 841	783 to 812	⨁⨁◯◯ Low

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 1.1%	pre-test probability of 4.5%	
False positives (patients incorrectly classified as having CRC)		accuracy study)						148 to 178	143 to 172	

Explanations

a. High risk of bias in patient selection and index test in Khan 2020.

b. Results based on indirect comparisons from different studies

References

[1] Pin-Vieito N, Garcia Nimo L, Bujanda L, Roman Alonso B, Gutierrez-Stampa MA, Aguilar-Gama V, et al. Optimal diagnostic accuracy of quantitative faecal immunochemical test positivity thresholds for colorectal cancer detection in primary health care: A community-based cohort study. *United European Gastroenterology Journal* 2021;9(2):256-267.

[2] Khan AA, Klimovskij M, Harshen R. Accuracy of faecal immunochemical testing in patients with symptomatic colorectal cancer. *BJS Open* 2020;4(6):1180-1188.

Question: Should FIT be used to diagnose CRC in males in secondary care (threshold: ≥10 µg Hb/g)?

Sensitivity	0.91 to 0.95
Specificity	0.79 to 0.80

Prevalences	2.3%	5.9%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2.3%	
True positives (patients with CRC)	2 studies 18168 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	not serious	none	21 to 22	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having CRC)								1 to 2	
True negatives (patients without CRC)	2 studies 18168 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	not serious	none	772 to 782	⊕⊕◯◯ Low
False positives (patients incorrectly classified as having CRC)								195 to 205	

Explanations

a. High risk of bias in patient selection and index test in Khan 2020.

b. Results based on indirect comparisons from different studies.

References

[1] Pin-Vieito N, Garcia Nimo L, Bujanda L, Roman Alonso B, Gutierrez-Stampa MA, Aguilar-Gama V, et al. Optimal diagnostic accuracy of quantitative faecal immunochemical test positivity thresholds for colorectal cancer detection in primary health care: A community-based cohort study. *United European Gastroenterology Journal* 2021;9(2):256-267.

[2] Khan AA, Klimovskij M, Harshen R. Accuracy of faecal immunochemical testing in patients with symptomatic colorectal cancer. *BJS Open* 2020;4(6):1180-1188.

Question: Should FIT be used to diagnose CRS in aspirin non-users?

Sensitivity	0.92 (95% CI: 0.88 to 0.95)
Specificity	0.71 (95% CI: 0.69 to 0.73)

Prevalence	11.6%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of11.6%	
True positives (patients with CRS)	1 study 2567 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious	not serious	publication bias strongly suspected[b]	107 (102 to 110)	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having CRS)								9 (6 to 14)	
True negatives (patients without CRS)	1 study 2567 patients	cross-sectional (cohort type accuracy study)	serious[a]	not serious	not serious	not serious	publication bias strongly suspected[b]	628 (610 to 645)	⊕⊕◯◯ Low
False positives (patients incorrectly classified as having CRS)								256 (239 to 274)	

Explanations

a. Poor representativeness of the population.

b. Results based on a single study.

References:

[1] Bujanda L, Sarasqueta C, Vega P, Salve M, Quintero E, Alvarez-Sanchez V, et al. Effect of aspirin on the diagnostic accuracy of the faecal immunochemical test for colorectal advanced neoplasia. *United European Gastroenterol J* 2018;6(1):123-130.

GRADE Tables