

Appendix 1: Search strategy

We followed a Cochrane Collaboration recommended iterative process to design our search strategy.¹ As recommended, we avoided routine use of methodology search filters to identify diagnostic test accuracy studies.² First of all, we conducted a series of preliminary searches in PubMed to identify already known key articles or published search strategies in related reviews. We noted common text words and their variants as well as search terms or subject headings that database indexers have assigned to those articles. Additional relevant articles and subject headings were identified using the “Related Articles” and “MeSH Database” options, respectively. Thus, we identified the range of terminology (synonyms, abbreviations) likely to be used to denote:

- Index test being evaluated
 1. ("Immunologic Tests/analysis"[Mesh] OR "Immunologic Tests/diagnosis"[Mesh] OR "Immunologic Tests/utilization"[Mesh]) (962)
 2. ("Faeces/abnormalities"[Mesh] OR "Faeces/blood"[Mesh] OR "Faeces/diagnosis"[Mesh] OR "Faeces/immunology"[Mesh] OR "Faeces/prevention and control"[Mesh]) (855)
 3. Fit test colon (138)
 4. Fit test colon cancer (140)
 5. Fecal occult blood test (2325)
 6. Faecal occult blood test (1290)
 7. Fecal occult blood tests (1431)
 8. Faecal occult blood tests (833)
 9. Fecal occult blood testing (1198)
 10. Faecal occult blood testing (630)
 11. Fecal immunochemical test (715)
 12. Fecal immunochemical tests (500)
 13. Fobt (1219)
 14. Ifobt (113)
 15. Ifobt sensitivity (71)
 16. Hemosure (4)

¹ De Vet HCW, Eisinga A, Riphagen IL, Aertgeerts B, Pewsner D. Chapter 7: Searching for Studies. In: Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Version 0.4 The Cochrane Collaboration, 2008. [updated September 2008; Last cited 2018 July 8]. Available from: <http://methods.cochrane.org/sites/methods.cochrane.org.sdt/files/public/uploads/Chapter07-Searching-%28September-2008%29.pdf>

² Whiting P, Westwood M, Beynon R, Burke M, Sterne JA, Glanville J. Inclusion of methodological filters in searches for diagnostic test accuracy studies misses relevant studies. *J Clin Epidemiol* 2011;**64**:602-607. [PMID: 21075596 DOI: 10.1016/j.jclinepi.2010.07.006]

17. OC-Sensor (52)
18. OC-Hemodia (19)
19. "OC light" (6)
20. OC-micro (9)
21. "FOB Gold" (20)
22. Hem-SP (5)
23. "MagStream HT" (1)
24. Hemocult (563)
25. Immudia (6)
26. Hemoquant (47)
27. Occultech (1)
28. Immocare (3)
29. Flexsure (30)
30. HM-JACK (2)
31. HM-JACKarc (7)
32. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 (6576)
 - Patient population under study
33. abdominal pain [tiab] (49258)
34. abdominal discomfort [tiab] (2366)
35. chronic diarrhoea or diarrhea [tiab] (11092)
36. Constipation [tiab] (21321)
37. Digestive bleeding [tiab] (301)
38. painless rectal bleeding (154)
39. rectorrhagia (85)
40. abdominal distension [tiab] (3534)
41. constitutional syndrome [tiab] or constitutional symptoms [tiab] (2242)
42. weight loss [tiab] (74997)
43. #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 (154880)
44. ("Signs and Symptoms, Digestive/diagnosis"[Mesh]) AND #43 (5796)
45. "Signs and Symptoms, Digestive/prevention and control"[Mesh] AND #43 (1009)

46. #44 OR #45 (6722)
 - Reference standard being used against which the accuracy of the index test is to be measured
47. Colonoscopy screening (24940)
48. "Colonoscopy"[Mesh] (27020)
49. #47 OR #48 (33552)
 - Combining concepts
50. #46 AND #49 (249)
51. (fecal [tiab] or faecal [tiab] or fobt [tiab] or fit [tiab] or ifobt [tiab]) AND colonoscopy [tiab] AND (symptom* [tiab] OR pain [tiab] OR discomfort [tiab] OR constipat*[tiab] OR syndr*[tiab] OR bleed*[tiab] OR diarrhea [tiab] OR diarrhoea [tiab]) (662)
52. #32 OR #50 OR #51 (7122)

In order to repeat the previously reported search in EMBASE, we used MEDLINE subject headings (MeSH) in EMBASE format (EMTREE):

- Index test being evaluated
1. Occult blood test/ (3908)
 2. Fit test.mp (1638)
 3. Fecal occult blood test.mp (2100)
 4. Faecal occult blood test.mp (841)
 5. Fecal occult blood tests.mp (511)
 6. Faecal occult blood tests.mp (245)
 7. Fecal occult blood testing.mp (1090)
 8. Faecal occult blood testing.mp (405)
 9. Fecal occult blood test screening.mp (41)
 10. Faecal occult blood test screening.mp (42)
 11. Fecal occult blood test sensitivity.mp (2)
 12. Fecal occult blood test false positive.mp (0)
 13. Immunochemical faecal occult blood test.mp (101)
 14. Fecal immunochemical tests.mp. or occult blood test/ (4040)
 15. Fobt.mp (2267)
 16. Ifobt.mp (205)

17. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 (8656)
18. Hemosure.mp (12)
19. OC-Sensor.mp (258)
20. OC-Hemodia.mp (24)
21. "OC light".mp (16)
22. OC-micro.mp (20)
23. "FOB Gold".mp (52)
24. Hem-SP.mp (10)
25. "MagStream HT".mp (2)
26. Hemoccult.mp (830)
27. Immudia.mp (9)
28. Hemoquant.mp (57)
29. Occultech.mp (1)
30. Immocare.mp (10)
31. Flexsure.mp (49)
32. HM JACK.mp (12)
33. HM JACKarc.mp (17)
34. #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 (1226)
 - Target condition being detected
35. Colorectal tumor.mp. or colon cancer/or rectum carcinoma/or colorectal tumour/or rectum cancer/or *cancer diagnosis/or colon carcinoma/(155816)
36. Colon cancer.mp (88125)
37. Colorectal cancer.mp. or rectum tumor/or colorectal cancer/or colon tumour/(195171)
38. advanced colorectal cancer.mp (4384)
39. colon adenoma/ or advanced adenoma.mp. (6168)
40. #35 OR #36 OR #37 OR #38 OR #39 (329320)
 - Patient population under study
41. diarrhoea/or Diarrhea.mp (249881)
42. (Nausea and vomiting).mp (202)
43. constipation/or Constipation.mp (86189)

44. abdominal pain.mp. or abdominal pain/(164227)
45. abdominal discomfort.mp. or abdominal discomfort/or weight reduction/(158911)
46. digestive system haemorrhage/or gastrointestinal hemorrhage/or Digestive bleeding.mp (60733)
47. painless rectal bleeding.mp (77)
48. rectorrhagia.mp. or rectum haemorrhage/(15015)
49. (constitutional syndrome or constitutional symptoms).mp (3966)
50. weight loss.mp (122192)
51. #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 (651849)
 - Reference standard being used against which the accuracy of the index test is to be measured
52. colonoscopy/or Colonoscopy screening.mp (67259)
 - Combining concepts
53. #40 AND #51 (22892)
54. #52 AND #53 (3641)
55. #17 AND #53 (268)
56. #17 AND #54 (393)
57. #34 OR #54 OR #55 OR #56 (4951)

Total selected: 7122 (MEDLINE) & 4951 (EMBASE)

Once we had reviewed the previous results, we also designed a filter to complete our search and simplify the future identification of FIT-related studies in PubMed by combining the first and corresponding authors of each potentially interesting article via the Boolean operator "OR"

("Atef SH" [au]) OR ("Bachir NM" [au]) OR ("Barber MD" [au]) OR ("Biondi A" [au]) OR ("Boereboom CL" [au]) OR ("Calogero A" [au]) OR ("Ferraris R" [au]) OR ("Hata K" [au]) OR ("Adelstein BA" [au]) OR ("Ahlquist DA" [au]) OR ("Ahmed S" [au]) OR ("Akbari A" [au]) OR ("Allameh Z" [au]) OR ("Allard J" [au]) OR ("Allison JE" [au]) OR ("Alvarez-Urturi C" [au]) OR ("Annibale B" [au]) OR ("Armitage N" [au]) OR ("Ashraf I" [au]) OR ("Astin M" [au]) OR ("Auge JM" [au]) OR ("Azlie S" [au]) OR ("Ballal MS" [au]) OR ("Ballantyne GH" [au]) OR ("Bampton PA" [au]) OR ("Barrett P" [au]) OR ("Barrison IG" [au]) OR ("Bassett ML" [au]) OR ("Bates T" [au]) OR ("Bernardini S" [au]) OR ("Bessa X" [au]) OR ("Bhargava A" [au]) OR ("Bini EJ" [au]) OR ("Bjerregaard NC" [au]) OR ("Bjornsson ES" [au]) OR ("Bosch LJ" [au]) OR ("Brault J" [au]) OR ("Brenner H" [au]) OR ("Brodersen J" [au]) OR ("Burch JA" [au]) OR ("Cade D" [au]) OR ("Cai QC" [au]) OR ("Capurso G" [au]) OR

("Carlsson L" [au]) OR ("Carroll M" [au]) OR ("Castells A" [au]) OR ("Castiglione G" [au]) OR ("Celestino A" [au]) OR ("Chang HJ" [au]) OR ("Chen HH" [au]) OR ("Chen LS" [au]) OR ("Chiang TH" [au]) OR ("Chiu HM" [au]) OR ("Church JM" [au]) OR ("Ciatto S" [au]) OR ("Cilona A" [au]) OR ("Clarke N" [au]) OR ("Collins JF" [au]) OR ("Corley DA" [au]) OR ("Corte C" [au]) OR ("Crotta S" [au]) OR ("Cubiella J" [au]) OR ("Dancourt V" [au]) OR ("Daveson AJ" [au]) OR ("de Vet HC" [au]) OR ("Dent OF" [au]) OR ("Diaz-Ondina M" [au]) OR ("Dilshad AT" [au]) OR ("Doi Y" [au]) OR ("Dominitz JA" [au]) OR ("Dutta AK" [au]) OR ("Eckardt VF" [au]) OR ("Elsafi SH" [au]) OR ("Eskeland SL" [au]) OR ("Ewald N" [au]) OR ("Faivre J" [au]) OR ("Falkson CB" [au]) OR ("Farkouh M" [au]) OR ("Farrands PA" [au]) OR ("Fauzi A" [au]) OR ("Favre H" [au]) OR ("Fenocchi E" [au]) OR ("Fisher DA" [au]) OR ("Flashman K" [au]) OR ("Fletcher RH" [au]) OR ("Fraser CG" [au]) OR ("Freedman A" [au]) OR ("Freitas BR" [au]) OR ("Friedman A" [au]) OR ("Fu R" [au]) OR ("Gandhi S" [au]) OR ("Garman KS" [au]) OR ("Gibson P" [au]) OR ("Gillberg A" [au]) OR ("Godber IM" [au]) OR ("Godos J" [au]) OR ("Gopalswamy N" [au]) OR ("Goulston KJ" [au]) OR ("Greenberg PD" [au]) OR ("Grosso G" [au]) OR ("Guardiola J" [au]) OR ("Guittet L" [au]) OR ("Haddy RI" [au]) OR ("Hamilton W" [au]) OR ("Han DS" [au]) OR ("Harmston C" [au]) OR ("Harrison AJ" [au]) OR ("Hatch QM" [au]) OR ("Haug U" [au]) OR ("Hazazi R" [au]) OR ("Heresbach D" [au]) OR ("Herrero J" [au]) OR ("Hewett DG" [au]) OR ("Hewitson P" [au]) OR ("Hill AG" [au]) OR ("Hippisley-cox J" [au]) OR ("Hirai HW" [au]) OR ("Hirayama Y" [au]) OR ("Hirobe K" [au]) OR ("Hoepffner N" [au]) OR ("Hogberg C" [au]) OR ("Hol L" [au]) OR ("Holden DJ" [au]) OR ("Holloway RH" [au]) OR ("Hope RL" [au]) OR ("Howden CW" [au]) OR ("Hreinsson JP" [au]) OR ("HU H-" [au]) OR ("Huang G" [au]) OR ("Hundt S" [au]) OR ("Hunt RH" [au]) OR ("Imperiale TF" [au]) OR ("Ioannidis JP" [au]) OR ("Ioannou GN" [au]) OR ("Ip S" [au]) OR ("Iwase N" [au]) OR ("Jamil S" [au]) OR ("Jeanson A" [au]) OR ("Jellema P" [au]) OR ("Jimbo M" [au]) OR ("Jin P" [au]) OR ("Kadakia SC" [au]) OR ("Kalimutho M" [au]) OR ("Kalra L" [au]) OR ("Kato J" [au]) OR ("Kaul A" [au]) OR ("Kemppainen M" [au]) OR ("Kepczyk MT" [au]) OR ("Khakimov N" [au]) OR ("Khasanova G" [au]) OR ("kim BC" [au]) OR ("Klewandrowski K" [au]) OR ("Ko CW" [au]) OR ("Koga Y" [au]) OR ("Kok L" [au]) OR ("Kolligs F" [au]) OR ("Konrad C" [au]) OR ("Koo JH" [au]) OR ("Kovarova JT" [au]) OR ("Kozlowski T" [au]) OR ("Krivec S" [au]) OR ("Kubisch H" [au]) OR ("Lanoy G" [au]) OR ("Lansdorp-Vogelaar I" [au]) OR ("Launois R" [au]) OR ("Lawson N" [au]) OR ("Lee FI" [au]) OR ("Lee JK" [au]) OR ("Lee TJ" [au]) OR ("Lee YC" [au]) OR ("Leicester RJ" [au]) OR ("Leis VM" [au]) OR ("Letsou G" [au]) OR ("Levi Z" [au]) OR ("Levy BT" [au]) OR ("Li R" [au]) OR ("Li ZC" [au]) OR ("Lieberman DA" [au]) OR ("Macrae FA" [au]) OR ("Mansouri D" [au]) OR ("Mansson J" [au]) OR ("Manus B" [au]) OR ("Marshall JK" [au]) OR ("Marshall TP" [au]) OR

("Matsumura Y" [au]) OR ("Maw A" [au]) OR ("McDonald CA" [au]) OR ("McDonald PJ" [au]) OR ("McDonald R" [au]) OR ("McDonald RL" [au]) OR ("Meijer GA" [au]) OR ("Mesquita MA" [au]) OR ("Miyoshi H" [au]) OR ("Moran A" [au]) OR ("Morikawa T" [au]) OR ("Morini S" [au]) OR ("Mowat C" [au]) OR ("Murakami R" [au]) OR ("Murphy J" [au]) OR ("Nagaoka S" [au]) OR ("Nakama H" [au]) OR ("Narula N" [au]) OR ("Niedermaier T" [au]) OR ("Niv Y" [au]) OR ("Olsson L" [au]) OR ("Oono Y" [au]) OR ("Oort FA" [au]) OR ("Ostrow JD" [au]) OR ("Ou C-" [au]) OR ("Parente FR" [au]) OR ("Park DD" [au]) OR ("Park JG" [au]) OR ("Park Y" [au]) OR ("Paz-Valiñas L" [au]) OR ("Peacock O" [au]) OR ("Petty MT" [au]) OR ("Pfeifer RM" [au]) OR ("Piperno A" [au]) OR ("Pochapin MB" [au]) OR ("Pongprasobchai S" [au]) OR ("Pye G" [au]) OR ("Quintero E" [au]) OR ("Rae AJ" [au]) OR ("Rai S" [au]) OR ("Rajasekhar PT" [au]) OR ("Ransohoff DF" [au]) OR ("Rao J" [au]) OR ("Rao SK" [au]) OR ("Rees CJ" [au]) OR ("Rentier B" [au]) OR ("Riboe DG" [au]) OR ("Rigas B" [au]) OR ("Ritchie MC" [au]) OR ("Robertson R" [au]) OR ("Robinson MH" [au]) OR ("Rockey DC" [au]) OR ("Rodriguez-Alonso L" [au]) OR ("Rodriguez-Moranta F" [au]) OR ("Rosman AS" [au]) OR ("Rozen P" [au]) OR ("Rubeca T" [au]) OR ("Saccomanno S" [au]) OR ("Saito H" [au]) OR ("Saldanha JD" [au]) OR ("Saquib N" [au]) OR ("Saratzis A" [au]) OR ("Scales CD" [au]) OR ("Schwartz S" [au]) OR ("Scriven AJ" [au]) OR ("Segal WN" [au]) OR ("Selinger RR" [au]) OR ("Selvachandran SN" [au]) OR ("Sequist TD" [au]) OR ("Shah R" [au]) OR ("Sharma VK" [au]) OR ("Shashideep S" [au]) OR ("Shastri YM" [au]) OR ("Shaw AG" [au]) OR ("Sheng J" [au]) OR ("Sieg A" [au]) OR ("Singh H" [au]) OR ("Singhal S" [au]) OR ("Skaife P" [au]) OR ("Smith A" [au]) OR ("Sohn DK" [au]) OR ("Songster CL" [au]) OR ("Sontag SJ" [au]) OR ("St John DJ" [au]) OR ("Stapley S" [au]) OR ("Steele RJ" [au]) OR ("Stegeman I" [au]) OR ("Stein J" [au]) OR ("Stelling HP" [au]) OR ("Stockbrugger RW" [au]) OR ("Stray N" [au]) OR ("Stubbs RS" [au]) OR ("Subramanian S" [au]) OR ("Sung JJ" [au]) OR ("Symonds EL" [au]) OR ("Tan V" [au]) OR ("Tannous B" [au]) OR ("Tao S" [au]) OR ("Tarpay Ad" [au]) OR ("Tate JJ" [au]) OR ("Thompson M" [au]) OR ("Tsoi KK" [au]) OR ("van Turenhout ST" [au]) OR ("Vega P" [au]) OR ("Weller D" [au]) OR ("Whitlock EP" [au]) OR ("Wu MS" [au]) OR ("Yansong J" [au]) OR ("Young GP" [au]) OR ("Zullo A" [au]) OR ("Terhaar sive Droste JS" [au]) OR ("Thomas WM" [au]) OR ("Thompson MR" [au]) OR ("Thomson AD" [au]) OR ("Tibble J" [au]) OR ("Tonus C" [au]) OR ("Trickett JP" [au]) OR ("Donaldson DR" [au]) OR ("Trojan J" [au]) OR ("Turunen MJ" [au]) OR ("Adlercreutz H" [au]) OR ("van Rijn AF" [au]) OR ("Vacante M" [au]) OR ("van Rossum LG" [au]) OR ("Vandvik P" [au]) OR ("van Roon AH" [au]) OR ("Vart G" [au]) OR ("Vasilyev S" [au]) OR ("Syrjanen K" [au]) OR ("Vaughan-Shaw PG" [au]) OR ("Wheeler JM" [au]) OR ("Vilkin A" [au]) OR ("Vironen J" [au]) OR ("Kellokumpu I" [au]) OR ("Wanebo HJ" [au]) OR ("de Wijkerslooth TR" [au]) OR ("Williams JA" [au]) OR ("Winawer SJ" [au])

OR ("Wong WM" [au]) OR ("Wong BC" [au]) OR ("Wong CK" [au]) OR ("Sadowski DC" [au]) OR ("Dube C" [au]) OR ("Wong MC" [au]) OR ("Woo HY" [au]) OR ("Park H" [au]) OR ("Wu D" [au]) OR ("Li JN" [au]) OR ("Guoxiang L" [au]) OR ("Jufang S" [au]) OR ("Yoshinaga M" [au]) OR ("Zhu MM" [au]) OR ("Widlak MM" [au]) OR ("Arasaradnam R" [au]) OR ("Ran ZH" [au]) OR ("Wen-xian Z" [au])

AND

((((((((((ifobt) OR fobt) OR Faecal occult blood) OR Fecal occult blood) OR Fit test colon cancer) OR Fit test colon) OR Fit test) OR "Occult Blood"[Mesh]) OR ("Immunological Tests/analysis"[Mesh] OR "Immunological Tests/diagnosis"[Mesh] OR "Immunological Tests/utilisation"[Mesh])))) (1539)

Appendix 2. Characteristics of the studies included in the systematic review

Author & Objective	Design & Setting	Inclusion criteria	Exclusion criteria	Study population	Index and reference test
Rozen P, 2010^[17] Evaluate accuracy for CRC and advanced adenomatous polyps by the faecal threshold used to determine a positive test and the number of FITs prepared per test, to determine the least number of colonoscopies required to detect a CRC.	Cohort study; Sampling procedure: Mixed (consecutive plus patients included in previous study); Planning data collection: prospective. Setting: Primary care, Colonoscopy setting, Tel Aviv, Israel (Multicentre, Unknown recruitment period).	Patients with symptoms scheduled for colonoscopy plus high-risk patients (personal or family history of CRC) plus positive guaiac-based FOBT result (Hemoccult SENSEA)	Hospitalization, visible rectal bleeding, known diagnosis of IBD, haematuria, menstruation, non-cooperation with preparing a faecal test or failure to reach the caecum	Enrolled: 2352; Included in 2x2 table: n=1682; Mean age: 63.7 years; Sex: 49.6% women. Prevalence CRC: 1.2% Prevalence AN: 8.9% Prevalence SCL: no info Symptomatic: 23% Asymptomatic: 77%	Index test: OC-Micro/Sensor. Three samples. They specify that patients observed no dietary or medication restrictions other than stopping aspirin and anticoagulant therapy before endoscopy. Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology.
Van Turenhout ST, 2014^[18] Compare sensitivity and specificity of a FIT between males and females, and	Cohort study; Sampling procedure: 'all ambulatory patients	Patients > 17 years old, scheduled for colonoscopy regardless of the	Documented history of IBD, incomplete colonoscopy or	Enrolled: 4704; Included in 2x2 table: n=3022; Mean age: 59.7 years; Sex: 55%	Index test: OC-Micro/Sensor Reference standard: colonoscopy and

study potential explanatory variables.	scheduled'; Planning data collection: prospective. Setting: secondary care, Colonoscopy setting, Amsterdam, Netherlands (Multicentre-five hospitals, two rural areas & Two large teaching hospitals-, June 2006-October 2010).	indication for colonoscopy	inadequate bowel cleansing, failure in completing one of the tests or subjects in whom no written informed consent was obtained, visible rectal bleeding or anaemia	women. Prevalence CRC: 2.3% Prevalence AN: 12.3% Prevalence SCL: no info. Symptomatic: 44% (Weight loss 2.9%; Abdominal pain 11.7%; Altered bowel habit 18.1%; constipation 3.0%, diarrhoea 4.2%). Asymptomatic: 46.7% Unknown: 9.3%	histopathology. If a barium enema, virtual colonography or second colonoscopy was performed within six months after completing FIT and a first incomplete colonoscopy, evaluation of the colon was considered complete.
Woo HY, 2005^[19] Evaluate the diagnostic validity of HM- Jack for detecting CRC in patients undergoing colonoscopy and compared its results with qualitative FITs Instant-View and	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective. Setting:	Patients scheduled for colonoscopy regardless of the indication for colonoscopy	Refusal to participate or no submission of faecal samples or poor bowel preparation	Enrolled: unreported; Included in 2x2 table: n=85; Median age: 56 years; Sex: 52.9% women. prevalence CRC: 7.1% AN/SCL: no info. Symptomatic 49.4%	Index test: HM-JACK Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology

OcculTech	Ambulatory patients, Colonoscopy setting, Seoul, South Korea, February 2004.			(Pain 15.3%; Altered bowel habit 1.2%; dyspepsia 10.6%; haematochezia 5.9%, melena 4.7%; anaemia 4.7%, diarrhoea 17.6%). Asymptomatic 40%	
McDonald PJ, 2012^[20] Determine whether faecal haemoglobin concentration can assist in deciding which patient with lower abdominal symptoms will benefit from endoscopy.	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective. Setting: Primary care Colonoscopy setting, NHS Tayside, UK, February 2010-March 2012.	Patients scheduled for colonoscopy regardless of the indication for colonoscopy	Patients under 16 years old, unable to understand instructions or to consent	Enrolled: 739; Included in 2x2 table: n=280; Median age: 63 years; Sex: 59.6% women. Prevalence CRC: 2.1% Prevalence AN: no info Prevalence significant neoplasia (CRC + High risk adenoma): 20.4 Prevalence SCL (CRC + HRA + IBD): 19.6% Unknown percentage of symptomatic patients	Index test: OC-Micro/Sensor Reference standard: colonoscopy and flexible sigmoidoscopy
Ou CH, 2013^[21]	Cohort study;	Patients scheduled	Patients who had	Enrolled: 784;	Index test: OC-

Evaluate the performance of FIT for the screening of CRC.	Sampling procedure: consecutive; Planning data collection: prospective. Setting: Ambulatory patients, Colonoscopy setting, Taiwan, China, November 2009-June 2011.	for colonoscopy regardless of the indication for colonoscopy	overt gastrointestinal bleeding symptoms, IBD, repeated rectal bleeding or other causes of rectal bleeding such as angiodysplasia	Included in 2x2 table: n=697; Median age: 60 years; Sex: 55.9% women. Prevalence CRC: 0.4% Prevalence AN: 6.0% Prevalence SCL: no info Unknown percentage of symptomatic patients	Micro/Sensor Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology
Auge JM, 2016^[22] Evaluate the diagnostic yield for advanced CRC in symptomatic patients using the first of two samples and the higher concentration of two samples.	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective. Setting: ‘Patients who attended Hospital Clinic’,	Patients who required colonoscopy for the investigation of lower abdominal symptoms or colonic polyp surveillance	Patients undergoing CRC screening or with a history of gastrointestinal bleeding, active rectal bleeding, menstruation, haematuria or known ulcerative	Enrolled: no info; Included in 2x2 table: n=208; Median age: 63 years; Sex: 55.8% women. Prevalence CRC: 1.0% Prevalence AN: no info Prevalence SCL: no info Prevalence advanced	Index test: HM-JACKarc. Two samples. They specify that medications, such as aspirin and non-steroidal anti-inflammatory drugs (NSAID), were withdrawn 1 week before preparation for

	Barcelona, Spain, December 2013- March 2014.		colitis	colorectal neoplasia (CRC + HRA): 14% Unknown percentage of symptomatic patients	colonoscopy. Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology
Auge JM, 2018^[30] Assess the analytical and diagnostic capabilities of SENTIFIT® 20 using SENTIFIT®-FOB Gold® latex reagent and SENTIFIT® pierce tube (Sentinel Diagnostics, Italy; Sysmex, Spain). As a secondary aim, to study the diagnostic yield for advanced CRC in symptomatic patients using the first of two samples vs. the mean and the higher concentration of two samples.	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective. Setting: 'Patients who attended Hospital Clinic', Barcelona, Spain, June to October 2015.	Patients who required colonoscopy for the investigation of lower abdominal symptoms or colonic polyp surveillance	Not reported	Enrolled: no info; Included in 2x2 table: n=487; Average age: 62 years (range: 22-94 years); Sex: 51.2% women. Prevalence CRC: 2.5% Prevalence AN: 14.6% Prevalence any colonoscopy finding: 47.2% (AN 14.6%; hyperplastic or inflammatory polyps 5.7%; diverticular disease 23.4%; haemorrhoids 30.6% angiodysplasia 1.4%;	Index test: FOB Gold. Two samples. They specify that medications, such as aspirin and non- steroidal anti- inflammatory drugs (NSAID), were withdrawn 1 week before preparation for colonoscopy. Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology

				<p>IBD 1.6%; minor irrelevant lesions 1.2%)</p> <p>Symptomatic: 54.2%</p> <p>Asymptomatic: 45.8%</p>	
<p>Symonds EL, 2016^[23]</p> <p>Compare performance of a new blood test for CRC (methylated BCAT1 and IKZF1 DNA) to OC Sensor in a study population with the full range of pathologies encountered in the colon and rectum.</p>	<p>Cohort study;</p> <p>Sampling procedure: consecutive;</p> <p>Planning data collection: prospective.</p> <p>Setting: Ambulatory patients.</p> <p>Multicentre, South Australia</p>	<p>Any adults (40-85 years) scheduled for colonoscopy for standard indications (Symptoms, positive FOBT, surveillance (personal or family history), screening, surveillance for IBD, diverticular disease and radiation proctitis).</p>	<p>Not reported</p>	<p>Enrolled: 4657;</p> <p>Included in 2x2 table: n=1381; Median age: 64.1 years; Sex: 50.6% women.</p> <p>Prevalence CRC: 4.8%</p> <p>Prevalence AN: 17.1%</p> <p>Prevalence SCL: no info</p> <p>Symptomatic: 34.8%</p> <p>Asymptomatic: 57.7%</p> <p>Unknown: 7.5%</p>	<p>Index test: OC-Micro/Sensor</p> <p>Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology</p>
<p>Parente F, 2012^[24]</p> <p>Test a combination of faecal tests (HM-Jack® calprotectin and M2-PK) as</p>	<p>Cohort study;</p> <p>Sampling procedure: consecutive;</p>	<p>Any adults (50-80 years) scheduled for colonoscopy in suspicion of an</p>	<p>Patients who had undergone colonoscopy in the previous five years,</p>	<p>Enrolled: 299;</p> <p>Included in 2x2 table: n=280; Mean age: 67 years; Sex: 43.9%</p>	<p>Index test: HM-JACK</p> <p>Reference standard: colonoscopy up to the caecum or obstructing</p>

<p>markers for advanced neoplasia in a selected series of patients requiring colonoscopy for the suspicion of CRC.</p>	<p>Planning data collection: prospective.</p> <p>Setting: Secondary care, Multicentre (Rome, Lecco, Bologna), Italy.</p>	<p>organic bowel disease due to symptoms for at least three weeks.</p>	<p>IBD, coexisting serious illness or were on medication known to be associated with intestinal inflammation or intestinal infection, incomplete colonoscopy or inadequate cleansing</p>	<p>women.</p> <p>Prevalence CRC: 16.8%</p> <p>Prevalence AN: 47.1%</p> <p>Prevalence SCL: no info</p> <p>100% Symptomatic (Weight loss 11.0%; Pain 17.9%; Altered bowel habit 23.1%; haematochezia 26.1%, anaemia 15%).</p>	<p>carcinoma plus histopathology</p>
<p>Rodríguez-Alonso L, 2015^[25]</p> <p>Evaluate whether quantitative FIT performs better than NICE and SIGN referral criteria</p>	<p>Cohort study; Sampling procedure: consecutive;</p> <p>Planning data collection: prospective.</p> <p>Setting: Primary and secondary care, Barcelona, Spain, September 2011-</p>	<p>Patients scheduled for colonoscopy due to gastrointestinal symptoms</p>	<p>Patients referred for adenoma surveillance and postoperative surveillance of CRC, Hospitalized, Previous colectomy, IBD and polyp syndromes, incomplete colonoscopies.</p>	<p>Enrolled: 1054;</p> <p>Included in 2x2 table: n=1003; Age: < 40 years 7.1%;41-50 yea 13%; 51-60 years 22.4%; 61-70 years 29.1%; > 70 years 28.4%; Sex: 46.8% women. Prevalence CRC: 3.0%; Prevalence AN: 13.3%; Prevalence SCL: no info. 100%</p>	<p>Index test: OC-Micro/Sensor</p> <p>Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology</p>

	October 2012.			Symptomatic (Weight loss 19.0%; Pain 36.4%; haematochezia 34.2%, anaemia 8.9%; constipation 12.1%; diarrhoea 23.5%).	
Mowat C, 2016^[26] Study the diagnostic accuracies of faecal haemoglobin and faecal calprotectin in a cohort of symptomatic patients	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective. Setting: Primary care, NHS Tayside, UK, October 2013-March 2014.	All adult patients referred for investigation of bowel symptoms (if patients had more than one symptom, they were attributed only one in order of decreasing importance: rectal bleeding, anaemia, diarrhoea, altered bowel habit, abdominal pain and weight loss)	Not reported	Enrolled:2189; Included in 2x2 table: n=750; Median Age 64; Sex: 54.7% women. Prevalence CRC: 3.7% Prevalence SCL (CRC + HRA + IBD) 10.0%.100% Symptomatic (Weight loss 0.9%; Pain 11.0%; haematochezia 34.2%, anaemia 8.9%; change in bowel habit 42.8%; diarrhoea 16.8%).	Index test: OC-Micro/Sensor Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology
Godber IM, 2016^[27]	Cohort study;	Patients referred for	Patients under 16	Enrolled: 909;	Index test: HM-JACKarc

Determine whether patients with lower abdominal symptoms can be investigated quickly using results of FIT, and whether this test could form part of a diagnostic pathway for significant colorectal disease	Sampling procedure: consecutive; Planning data collection: prospective. Setting: Primary care, NHS Lanarkshire, UK, June 2013-December 2013.	colonoscopy examination	years old, unable to understand instructions or to consent	Included in 2x2 table: n=484; Median Age 59; Sex: 60.1% women. Prevalence CRC: 2.3% Prevalence AN: no info Prevalence SCL (CRC + HRA + IBD + colitis) 9.3% 100% Symptomatic (Weight loss 1.7%; Pain 18.8%; haematochezia 15.9%, anaemia 4.8%; change in bowel habits 39.7%).	Reference standard: colonoscopy
Widlak MM 2017^[28] Assess using FIT or faecal calprotectin to detect CRC and adenoma in symptomatic patients referred from primary care	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective. Setting: Secondary care, Multicentre,	Referral as per national two week wait guidance - bowel symptoms suggestive of colorectal cancer	Patients who declined to participate, were deemed physically unfit for further investigation or unable to provide valid consent due to language barrier,	Enrolled: 2822; Included in 2x2 table: n=430; Median Age 67; Sex: 51% women. Prevalence CRC: no info (CRC + High grade dysplasia) 5.7% Prevalence AN: no info Prevalence SCL: no	Index test: HM-JACKarc Reference standard: colonoscopy and histopathology / CT colonography or CT abdomen/pelvis with contrast plus flexible sigmoidoscopy (CT = computed

	UK, January 2015-March 2016.		visual impairment or illness (i.e. dementia)	info 100% Symptomatic (Weight loss 15.8%; Pain 30%; haematochezia 43.0%, anaemia 17.2%; change in bowel habit 64.2%)	tomography)
Cubiella, 2014^[29] Primary and secondary care, Multicentre (2 Hospitals), Spain, Derivation cohort: Ourense March 2012-September 2013	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective	Patients scheduled for colonoscopy due to gastrointestinal symptoms	Age under 18, pregnancy, asymptomatic individuals who were undergoing surveillance colonoscopy, hospitalised, patients whose symptoms had ceased within 3 months before evaluation or who declined participation	Derivation cohort: Enrolled: 2381; Included in 2x2 table: n=1567; Mean age: 66.9 years; Sex: 48.6% women. Prevalence CRC: 13.7% Prevalence AN: 26.7% Prevalence SCL (CRC, AN, polyposis (>10 polyps of any histology, including serrated lesions), histologically confirmed colitis, polyps ≥10 mm,	Index test: OC-Micro/Sensor They were specifically instructed to sample a stool where no blood was visible. Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology

				complicated diverticular disease, colonic ulcer, bleeding angiodysplasia): 29.5	
Cubiella, 2017^[31] Primary and secondary care, Multicentre (11 Hospitals), Spain, Validation cohort: Multicentre, March 2014- March 2015	Cohort study; Sampling procedure: consecutive; Planning data collection: prospective	Patients scheduled for colonoscopy due to gastrointestinal symptoms	Age under 18, pregnancy, asymptomatic individuals who were undergoing surveillance colonoscopy, hospitalised, patients whose symptoms had ceased within 3 months before evaluation or who declined participation	Validation cohort: 1481; Included in 2x2 table: n=715; Mean age: 64.4 years; Sex: 53.3% women. Prevalence CRC: 9.4% Prevalence AN: 21.1% Prevalence SCL: 25.3%	Index test: OC- Micro/Sensor They were specifically instructed to sample a stool where no blood was visible. Reference standard: colonoscopy up to the caecum or obstructing carcinoma plus histopathology