Supplementary Material 1 Search strategy

Embase

('large intestine tumor'/exp OR ((colorect* or colon* or rect* or anal* or anus* or intestin* or bowel*) NEAR/3 (carcinom* or neoplas* or adenocarcinom* or cancer* or tumor* or tumour* or sarcom* or polyp* or adenom*)):de,ab,ti) AND ((((('occult blood'/exp OR 'occult blood':de,ab,ti) AND (faecal or fecal or feces or faeces or stool*):de,ab,ti) OR (FOBT* or FIT* or gFOBT*):de,ab,ti) AND ((immunohistochem* or immunochem* or immunol* or guaiac*):de,ab,ti OR immunochemistry/exp OR guaiac/exp) OR (('fecal immunochemical' NEXT/1 test* or 'faecal immunochemical' NEXT/1 test* or 'fecal immunochemistry' NEXT/1 test* or 'faecal immunochemistry' NEXT/1 test* or ColoScreen or Hema-Screen or Hemdetect or Hemoccult or SENSA or Hema-Check or HemaCheck or hemoCARE or Peroheme or ColoCare or Lifeguard or Fecatwin or HemaWipe or Instaccult or Monohaem or Okokit or Seracult or Dencoccult or Early-detector or Earlydetector or Fe-Cult or Fecult or Feca-EIA or FecaEIA or Hemo-FEC or HemoFEC or Hexagon or SureScreen or Hemaprompt or Hemdetect or Camco-PAK or CamcoPAK or Colocheck or Cecogenics or Hematest or Dencocult or Fecatest or Hemofecia or Quick-CULT or QuickCULT)):de,ab,ti)

Medline Ovid

(exp Colorectal Neoplasms/ OR ((colorect* or colon* or rect* or anal* or anus* or intestin* or bowel*) adj3 (carcinom* or neoplas* or adenocarcinom* or cancer* or tumor* or tumour* or sarcom* or polyp* or adenom*)).mp.) AND ((((exp Occult Blood/ OR occult blood.mp.) AND (faecal or fecal or feces or faeces or stool*).mp.) OR (FOBT* or FIT* or gFOBT*).mp.) AND ((immunohistochem* or immunochem* or immunol* or guaiac*).mp. OR exp Immunochemistry/ OR exp Guaiac/) OR ((fecal immunochemical test* or faecal immunochemical test* or fecal immunochemistry test* or faecal immunochemistry test* or ColoScreen or Hema-Screen or HemaScreen or Hemdetect or Hemoccult or SENSA or Hema-Check or HemaCheck or hemoCARE or Peroheme or ColoCare or Lifeguard or Fecatwin or HemaWipe or Instaccult or Monohaem or Okokit or Seracult or Dencoccult or Early detector or Earlydetector or Fe Cult or Fecult or Feca EIA or FecaEIA or Hemo FEC or HemoFEC or Hexagon or SureScreen or Hemaprompt or Hemdetect or Camco PAK or CamcoPAK or Colocheck or Cecogenics or Hematest or Dencocult or Fecatest or Hemofecia or Quick-CULT or QuickCULT)).mp.)

Cochrane Library

(((colorect* or colon* or rect* or anal* or anus* or intestin* or bowel*) NEAR/3 (carcinom* or neoplas* or adenocarcinom* or cancer* or tumor* or tumour* or sarcom* or polyp* or adenom*)):kw,ab,ti) AND ((((('occult blood':kw,ab,ti) AND (faecal or fecal or feces or faeces or stool*):kw,ab,ti) OR (FOBT* or FIT* or gFOBT*):kw,ab,ti) AND ((immunohistochem* or immunochem* or immunol* or guaiac*):kw,ab,ti) OR (('fecal immunochemical' NEAR/1 test* or 'faecal immunochemical' NEAR/1 test* or 'fecal immunochemistry' NEAR/1 test* or 'faecal immunochemistry' NEAR/1 test* or ColoScreen or Hema-Screen or Hemdetect or Hemoccult or SENSA or Hema-Check or HemaCheck or hemoCARE or Peroheme or ColoCare or Lifeguard or Fecatwin or HemaWipe or Instaccult or Monohaem or Okokit or Seracult or Dencoccult or Early-detector or Earlydetector or Fe-Cult or Fecult or Feca-EIA or FecaEIA or Hemo-FEC or HemoFEC or Hexagon or SureScreen or Hemaprompt or Hemdetect or Camco-PAK or CamcoPAK or Colocheck or Cecogenics or Hematest or Dencocult or Fecatest or Hemofecia or Quick-CULT or QuickCULT)):kw,ab,ti)

Science Citation Index

TS=((((colorect* or colon* or rect* or anal* or anus* or intestin* or bowel*) NEAR/3 (carcinom* or neoplas* or adenocarcinom* or cancer* or tumor* or tumour* or sarcom* or polyp* or adenom*))) AND ((((“occult blood”) AND (faecal or fecal or feces or faeces or stool*)) OR (FOBT* or FIT* or gFOBT*)) AND ((immunohistochem* or immunochem* or immunol* or guaiac*)) OR (("fecal immunochemical" NEAR/1 test* or "faecal immunochemical" NEAR/1 test* or "fecal immunochemistry" NEAR/1 test* or "faecal immunochemistry" NEAR/1 test* or ColoScreen or Hema-Screen or Hemdetect or Hemoccult or SENSA or Hema-Check or HemaCheck or hemoCARE or Peroheme or ColoCare or Lifeguard or Fecatwin or HemaWipe or Instaccult or Monohaem or Okokit or Seracult or Dencoccult or Early-detector or Earlydetector or Fe-Cult or Fecult or Feca-EIA or FecaEIA or Hemo-FEC or HemoFEC or Hexagon or SureScreen or Hemaprompt or Hemdetect or Camco-PAK or CamcoPAK or Colocheck or Cecogenics or Hematest or Dencocult or Fecatest or Hemofecia or Quick-CULT or QuickCULT))))

Google scholar

"colorectal|colon|colonic|rectal|anal|anus carcinoma|neoplasm|neoplasms|adenocarcinoma|cancer|tumor|tumors" "occult blood" faecal|fecal|feces|faeces|stool|FOBT|FIT|gFOBT

Supplementary Material 2 Variables for which data were extracted

The following data were abstracted when applicable: (i) study characteristics - primary author, journal of publication, year of publication, geographic location of study population, study design (prospective/retrospective), time period of study enrollment, patient selection (inclusion- and exclusion criteria); (ii) FOBT characteristics - type of FOBT used (FIT or gFOBT), brand of FOBT, referral criteria for positive test (i.e. cut-off or number of positive panels), diagnostic test used, diet restrictions; (iii) study cohort characteristics - cohort size, total number of eligible invitees, total number of participants, total tests analyzed, total participants with a positive test, participants demographics (mean age and range, percentage male), reference standard uptake (percentage); (iv) CRC characteristics - total number diagnosed with CRC after negative FOBT, total number diagnosed with CRC after positive FOBT, location of CRC (proximal/distal), CRC stage (I/>I); (v) patient characteristics - gender, age <59 /≥60 years, time of follow-up in years/months (mean, median, min, max), completeness of follow-up (percentage), findings at index diagnostic test.

Supplementary Table 1 Quality assessment of included studies

a) FIT observational studies*

Study	Selection	Comparability	Outcome
Chen[1]	****	*	***
Chiu[2]	****	*	***
Crotta[3]	***	*	**
Digby[4]	****	*	**
Giorgi Rossi[5]	***	*	**
Itoh[6]	***	*	**
Jensen[7]	***	*	***
Launoy[8]	***	*	**
McNamara[9]	***	*	*
Nakama[10]	***	*	***
Parente[11]	***	*	*
Portillo[12]	****	*	***
Shin[13]	***	*	***
van der Vlugt[14]	****	*	***
Zappa[15]	****	*	***

b) gFOBT observational studies*

Study	Selection	Comparability	Outcome
Blom[16]	****	*	***
Bouvier[17]	***	*	***
Cummings[18]	***	*	**
Faivre[19]	****	*	***
Hardcastle[20]	***	*	***
Kewenter[21]	****	*	***
Kronborg[22]	****	*	***
Mandel[23]	****	*	*
Paimela[24]	****	*	**
Rennert[25]	***	*	***
Souques[26]	***	*	*
Steele[27]	****	*	***
Zappa[15]	****	*	***

c) Randomised controlled trials**

Study	Selection bias		Performance bias	Reporting bias	Detection bias	Attrition bias	Other bias
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Selective reporting	Blinding of outcome assessment	Incomplete outcome data	Anything else, ideally prespecified
Denters[28]	+	+	+	+	+	?	+
Levi[29]	+	+	+	+	+	?	+

* using the Ottawa Newcastle criteria of Wells *et al*.[30]

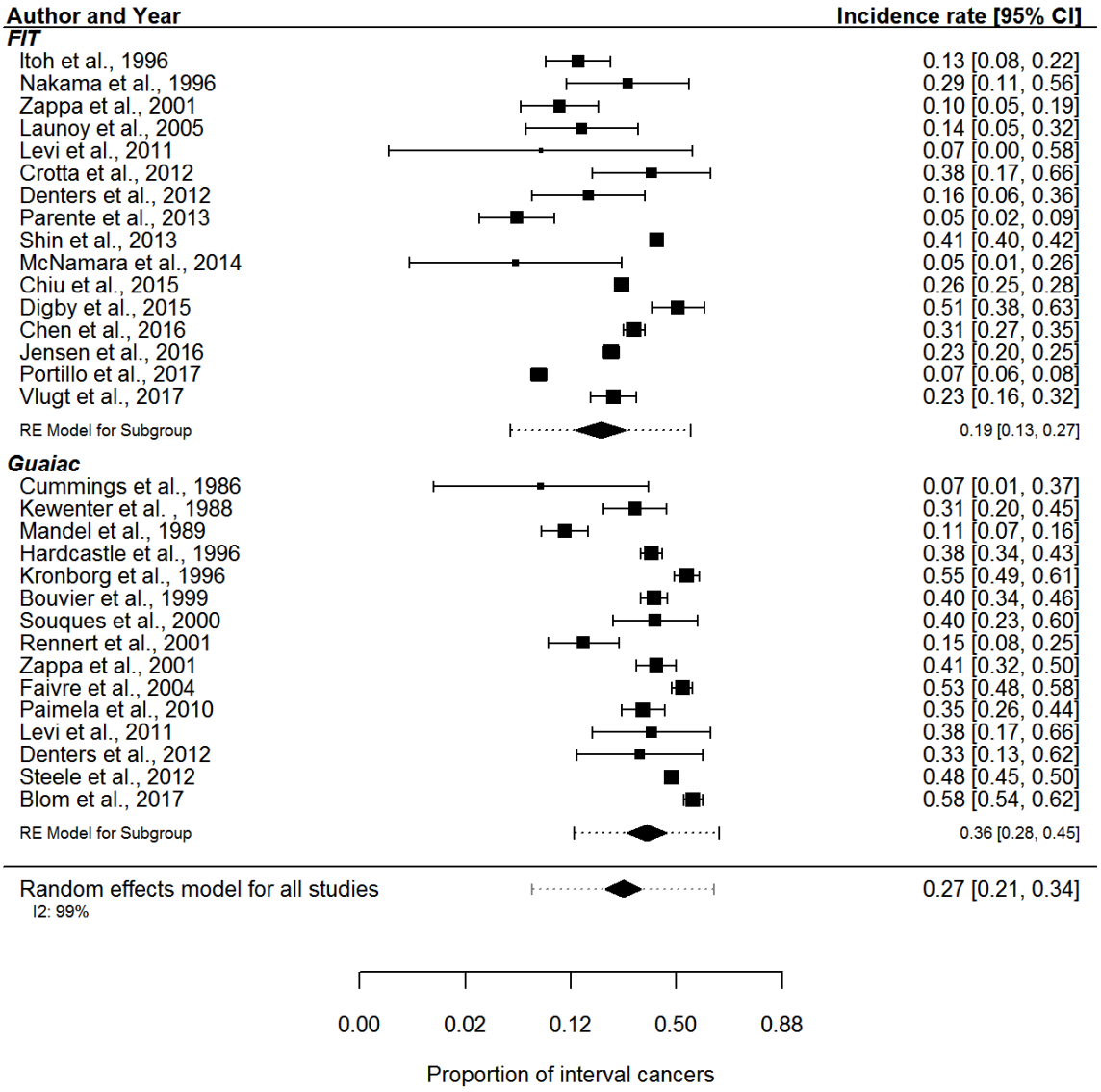
** Both randomised trials were scored as good quality by the Cochrane risk of bias tool.[31] Both studies did not describe handling of incomplete outcome data such as screenees loss to follow-up or missing data when cross-linking the screening pilot database with the cancer registry, therefore, this item was scored as 'unclear risk'. However, this was unlikely to have biased the outcome.

Supplementary Table 2 Quality assessment of the standard and sensitivity analysis of the pooled IRR of FIT iCRC relative to gFOBT iCRC[25]

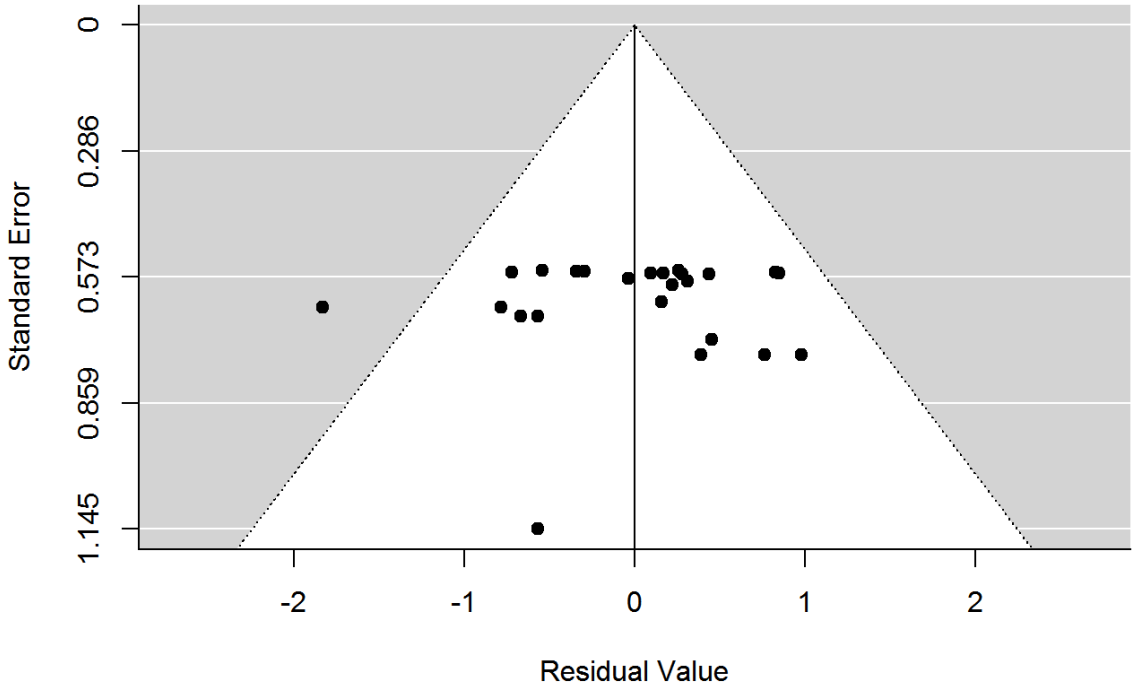
Comparison	Standard pooled IRR		Sensitivity analysis	
	IRR (95% CI)	Quality of evidence	IRR (95% CI)	Quality of evidence
FIT iCRC versus gFOBT iCRC	0.58 (0.32-1.07)	Very low	0.36 (0·17-0·75)	High

IRR: incidence rate ratio; FIT: faecal immunochemical test; gFOBT guaiac faecal occult blood test; iCRC: interval colorectal cancer

Supplementary Figure 1 Forest plot of FOBT iCRC to screen-detected CRC ratio



Supplementary Figure 2 Funnel plot



Visual inspection of the funnel plot did not show asymmetry and the rank correlation test for asymmetry was not significant (Kendall's tau = -0.0768, p=0.6018).

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