

Report Supplementary Material 12

Table 9. Faecal immunochemical test sensitivity, specificity, PPV, and NPV for ACN at various thresholds in participants who completed 1-3 tests and had at least one colonic examination performed, by age at invite

Age at invite (years)	FIT threshold (µg/g)	Test	Completed FIT ^a	Tested +ve		ACN ^b		Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
						Total cases	FIT +ve cases				
≤ 65	40	1 st	n	n	%	n	n	%	%	%	%
		2 nd ^d	2532	136	5.4	211 ^c	36	17.1 (12.2 to 22.8)	95.7 (94.8 to 96.5)	26.5 (19.3 to 34.7)	92.7 (91.6 to 93.7)
		3 rd ^e	2376	107	4.5	174	17	9.8 (5.8 to 15.2)	95.9 (95.0 to 96.7)	15.9 (9.5 to 24.2)	93.1 (92.0 to 94.1)
		Cumulative 2 tests ^f	2173	84	3.9	147	17	11.6 (6.9 to 17.9)	96.7 (95.8 to 97.4)	20.2 (12.3 to 30.4)	93.8 (92.7 to 94.8)
		test analysis 3 tests ^g	2512	243	9.7	210	53	25.2 (19.5 to 31.7)	91.7 (90.5 to 92.8)	21.8 (16.8 to 27.5)	93.1 (92.0 to 94.1)
		Programme 2 tests ^h	2416	327	13.5	200	70	35.0 (28.4 to 42.0)	88.4 (87.0 to 89.7)	21.4 (17.1 to 26.3)	93.8 (92.7 to 94.8)
	analysis 3 tests ⁱ	2532	243	9.6	211	53	25.1 (19.4 to 31.5)	91.8 (90.6 to 92.9)	21.8 (16.8 to 27.5)	93.1 (92.0 to 94.1)	
	30	1 st	2532	160	6.3	211	41	19.4 (14.3 to 25.4)	94.9 (93.9 to 95.7)	25.6 (19.1 to 33.1)	92.8 (91.7 to 93.8)
	2 nd ^d	2353	119	5.1	169	18	10.7 (6.4 to 16.3)	95.4 (94.4 to 96.2)	15.1 (9.2 to 22.8)	93.2 (92.1 to 94.2)	
	3 rd ^e	2139	105	4.9	141	22	15.6 (10.0 to 22.7)	95.8 (94.9 to 96.7)	21.0 (13.6 to 30.0)	94.1 (93.0 to 95.1)	
	Cumulative 2 tests ^f	2513	279	11.1	210	59	28.1 (22.1 to 34.7)	90.4 (89.2 to 91.6)	21.1 (16.5 to 26.4)	93.2 (92.1 to 94.2)	
	test analysis 3 tests ^g	2418	384	15.9	200	81	40.5 (33.6 to 47.7)	86.3 (84.8 to 87.7)	21.1 (17.1 to 25.5)	94.1 (93.0 to 95.1)	
	Programme 2 tests ^h	2532	279	11.0	211	59	28.0 (22.0 to 34.5)	90.5 (89.3 to 91.7)	21.1 (16.5 to 26.4)	93.3 (92.1 to 94.3)	
	analysis 3 tests ⁱ	2532	384	15.2	211	81	38.4 (31.8 to 45.3)	86.9 (85.5 to 88.3)	21.1 (17.1 to 25.5)	93.9 (92.9 to 94.9)	
	20	1 st	2532	206	8.1	211	50	23.7 (18.1 to 30.0)	93.3 (92.2 to 94.3)	24.3 (18.6 to 30.7)	93.1 (92.0 to 94.1)

		2 nd ^d	2310	154	6.7	160	18	11.3 (6.8 to 17.2)	93.7 (92.6 to 94.7)	11.7 (7.1 to 17.8)	93.4 (92.3 to 94.4)	
		3 rd ^e	2067	129	6.2	132	21	15.9 (10.1 to 23.3)	94.4 (93.3 to 95.4)	16.3 (10.4 to 23.8)	94.3 (93.1 to 95.3)	
		Cumulative	2 tests ^f	2516	360	14.3	210	68	32.4 (26.1 to 39.2)	87.3 (85.9 to 88.7)	18.9 (15.0 to 23.3)	93.4 (92.3 to 94.4)
		test analysis	3 tests ^g	2427	489	20.1	200	89	44.5 (37.5 to 51.7)	82.0 (80.4 to 83.6)	18.2 (14.9 to 21.9)	94.3 (93.1 to 95.3)
		Programme	2 tests ^h	2532	360	14.2	211	68	32.2 (26.0 to 39.0)	87.4 (86.0 to 88.7)	18.9 (15.0 to 23.3)	93.4 (92.3 to 94.4)
		analysis	3 tests ⁱ	2532	489	19.3	211	89	42.2 (35.4 to 49.2)	82.8 (81.2 to 84.3)	18.2 (14.9 to 21.9)	94.0 (92.9 to 95.0)
	10	1st	2532	321	12.7	211	69	32.7 (26.4 to 39.5)	89.1 (87.8 to 90.4)	21.5 (17.1 to 26.4)	93.6 (92.5 to 94.6)	
		2 nd ^d	2197	212	9.6	142	22	15.5 (10.0 to 22.5)	90.8 (89.4 to 92.0)	10.4 (6.6 to 15.3)	94.0 (92.8 to 95.0)	
		3 rd ^e	1904	177	9.3	112	18	16.1 (9.8 to 24.2)	91.1 (89.7 to 92.4)	10.2 (6.1 to 15.6)	94.6 (93.4 to 95.6)	
		Cumulative	2 tests ^f	2518	533	21.2	211	91	43.1 (36.3 to 50.1)	80.8 (79.2 to 82.4)	17.1 (14.0 to 20.5)	94.0 (92.8 to 95.0)
		test analysis	3 tests ^g	2437	710	29.1	203	109	53.7 (46.6 to 60.7)	73.1 (71.2 to 74.9)	15.4 (12.8 to 18.2)	94.6 (93.4 to 95.6)
		Programme	2 tests ^h	2532	533	21.1	211	91	43.1 (36.3 to 50.1)	81.0 (79.3 to 82.5)	17.1 (14.0 to 20.5)	94.0 (92.9 to 95.0)
		analysis	3 tests ⁱ	2532	710	28.0	211	109	51.7 (44.7 to 58.6)	74.1 (72.3 to 75.9)	15.4 (12.8 to 18.2)	94.4 (93.2 to 95.4)
> 65	40	1st	2667	190	7.1	252 ^c	47	18.7 (14.0 to 24.0)	94.1 (93.1 to 95.0)	24.7 (18.8 to 31.5)	91.7 (90.6 to 92.8)	
		2 nd ^d	2461	126	5.1	202	27	13.4 (9.0 to 18.8)	95.6 (94.7 to 96.4)	21.4 (14.6 to 29.6)	92.5 (91.4 to 93.5)	
		3 rd ^e	2256	98	4.3	166	21	12.7 (8.0 to 18.7)	96.3 (95.4 to 97.1)	21.4 (13.8 to 30.9)	93.3 (92.1 to 94.3)	
		Cumulative	2 tests ^f	2651	316	11.9	249	74	29.7 (24.1 to 35.8)	89.9 (88.7 to 91.1)	23.4 (18.9 to 28.5)	92.5 (91.4 to 93.5)
		test analysis	3 tests ^g	2572	414	16.1	240	95	39.6 (33.4 to 46.1)	86.3 (84.9 to 87.7)	22.9 (19.0 to 27.3)	93.3 (92.1 to 94.3)
		Programme	2 tests ^h	2667	316	11.8	252	74	29.4 (23.8 to 35.4)	90.0 (88.7 to 91.1)	23.4 (18.9 to 28.5)	92.4 (91.3 to 93.5)
		analysis	3 tests ⁱ	2667	414	15.5	252	95	37.7 (31.7 to 44.0)	86.8 (85.4 to 88.1)	22.9 (19.0 to 27.3)	93.0 (91.9 to 94.0)
	30	1st	2667	226	8.5	252	54	21.4 (16.5 to 27.0)	92.9 (91.8 to 93.9)	23.9 (18.5 to 30.0)	91.9 (90.7 to 92.9)	
		2 nd ^d	2425	157	6.5	195	36	18.5 (13.3 to 24.6)	94.6 (93.6 to 95.5)	22.9 (16.6 to 30.3)	93.0 (91.9 to 94.0)	
		3 rd ^e	2191	115	5.2	151	24	15.9 (10.5 to 22.7)	95.5 (94.6 to 96.4)	20.9 (13.9 to 29.4)	93.9 (92.8 to 94.9)	
		Cumulative	2 tests ^f	2651	383	14.4	249	90	36.1 (30.2 to 42.4)	87.8 (86.4 to 89.1)	23.5 (19.3 to 28.1)	93.0 (91.9 to 94.0)
		test analysis	3 tests ^g	2574	498	19.3	241	114	47.3 (40.9 to 53.8)	83.5 (82.0 to 85.0)	22.9 (19.3 to 26.8)	93.9 (92.8 to 94.9)

	Programme analysis	2 tests^h	2667	383	14.4	252	90	35.7 (29.8 to 42.0)	87.9 (86.5 to 89.1)	23.5 (19.3 to 28.1)	92.9 (91.8 to 93.9)	
	analysis	3 testsⁱ	2667	498	18.7	252	114	45.2 (39.0 to 51.6)	84.1 (82.6 to 85.5)	22.9 (19.3 to 26.8)	93.6 (92.5 to 94.6)	
20		1st	2667	286	10.7	252	69	27.4 (22.0 to 33.3)	91.0 (89.8 to 92.1)	24.1 (19.3 to 29.5)	92.3 (91.2 to 93.4)	
		2nd^d	2367	177	7.5	181	41	22.7 (16.8 to 29.4)	93.8 (92.7 to 94.8)	23.2 (17.2 to 30.1)	93.6 (92.5 to 94.6)	
		3rd^e	2115	138	6.5	132	21	15.9 (10.1 to 23.3)	94.1 (93.0 to 95.1)	15.2 (9.7 to 22.3)	94.4 (93.3 to 95.4)	
		Cumulative test analysis	2 tests^f	2653	463	17.5	250	110	44.0 (37.8 to 50.4)	85.3 (83.8 to 86.7)	23.8 (20.0 to 27.9)	93.6 (92.5 to 94.6)
		analysis	3 tests^g	2578	601	23.3	242	131	54.1 (47.6 to 60.5)	79.9 (78.2 to 81.5)	21.8 (18.6 to 25.3)	94.4 (93.3 to 95.4)
		Programme analysis	2 tests^h	2667	463	17.4	252	110	43.7 (37.4 to 50.0)	85.4 (83.9 to 86.8)	23.8 (20.0 to 27.9)	93.6 (92.5 to 94.5)
	analysis	3 testsⁱ	2667	601	22.5	252	131	52.0 (45.6 to 58.3)	80.5 (78.9 to 82.1)	21.8 (18.6 to 25.3)	94.1 (93.0 to 95.1)	
10		1st	2667	421	15.8	252	90	35.7 (29.8 to 42.0)	86.3 (84.9 to 87.6)	21.4 (17.6 to 25.6)	92.8 (91.6 to 93.8)	
		2nd^d	2232	229	10.3	160	46	28.8 (21.9 to 36.4)	91.2 (89.9 to 92.4)	20.1 (15.1 to 25.9)	94.3 (93.2 to 95.3)	
		3rd^e	1933	170	8.8	107	25	23.4 (15.7 to 32.5)	92.1 (90.7 to 93.3)	14.7 (9.7 to 20.9)	95.3 (94.3 to 96.3)	
		Cumulative test analysis	2 tests^f	2653	650	24.5	250	136	54.4 (48.0 to 60.7)	78.6 (76.9 to 80.2)	20.9 (17.9 to 24.3)	94.3 (93.2 to 95.3)
		analysis	3 tests^g	2583	820	31.7	243	161	66.3 (59.9 to 72.2)	71.8 (70.0 to 73.7)	19.6 (17.0 to 22.5)	95.3 (94.3 to 96.3)
		Programme analysis	2 tests^h	2667	650	24.4	252	136	54.0 (47.6 to 60.2)	78.7 (77.0 to 80.3)	20.9 (17.9 to 24.3)	94.2 (93.1 to 95.2)
	analysis	3 testsⁱ	2667	820	30.7	252	161	63.9 (57.6 to 69.8)	72.7 (70.9 to 74.5)	19.6 (17.0 to 22.5)	95.1 (94.0 to 96.0)	

PPV, positive predictive value; NPV, negative predictive value; ACN, advanced colorectal neoplasia; FIT, faecal immunochemical test; +ve, positive; CI, confidence interval.

- Participants were not included as invited to any subsequent tests following a FIT positive test at the specified threshold.
- ACN was defined as CRC or AA. AAs were defined as adenomas (namely an adenoma, serrated adenoma, or mixed hyperplastic/dysplastic adenoma) which satisfied at least one of the following criteria: (1) ≥ 10 mm in size or (2) tubulovillous or villous histology or (3) high grade dysplasia.
- A total of 463 participants had advanced neoplasia: 20 participants had CRC but no AAs, 437 participants had AAs but not CRC, and six participants had both CRC and AAs.
- The round at which a participant completes their second FIT; for a particular participant this could be round 2 or round 3.
- The round at which a participant completes their third FIT; equivalent to round 3 in participants who completed FIT at both prior rounds.

- f. Includes participants who completed at least two rounds of FIT or who were FIT positive at round 1; participants were classed as positive if FIT was positive at either of the first two rounds at which they completed FIT.
- g. Includes participants who completed all three rounds of FIT or who were FIT positive at any round; participants were classed as positive if FIT was positive at any of the three rounds.
- h. Includes participants who completed at least one round of FIT; participants were classed as positive if FIT was positive at either of the first two rounds at which they completed FIT.
- i. Includes participants who completed at least one round of FIT; participants were classed as positive if FIT was positive at any of the three rounds.