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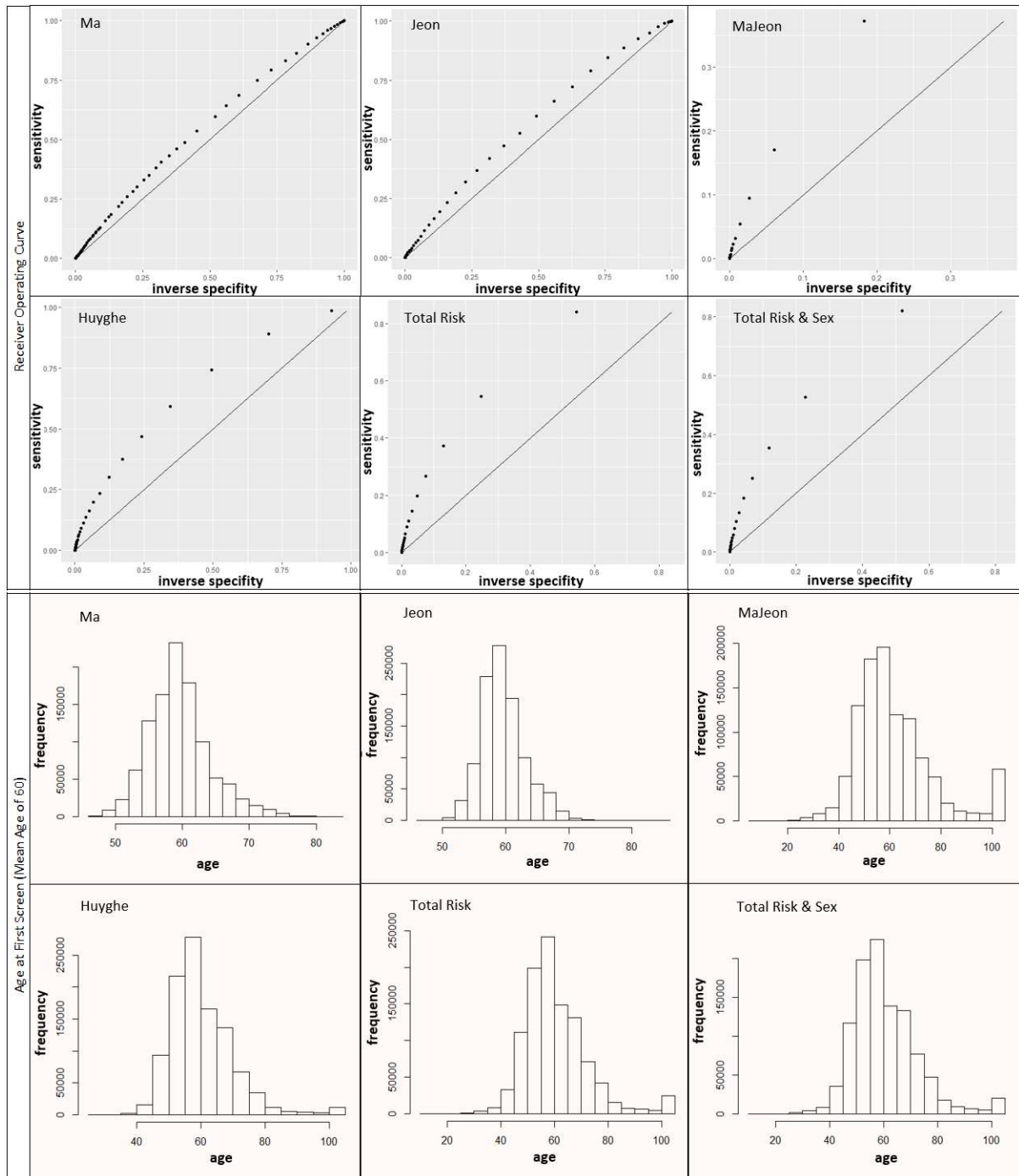
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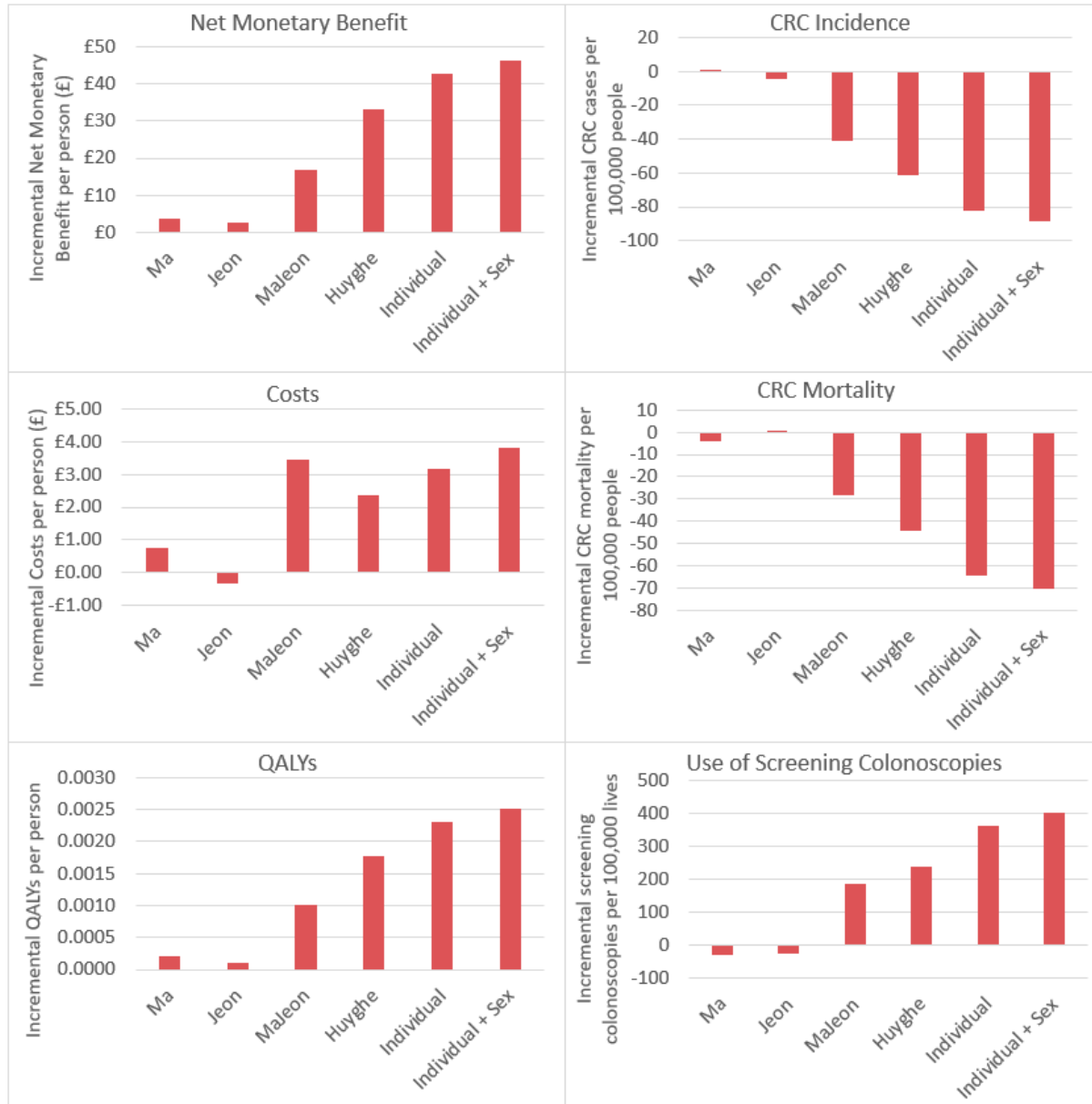


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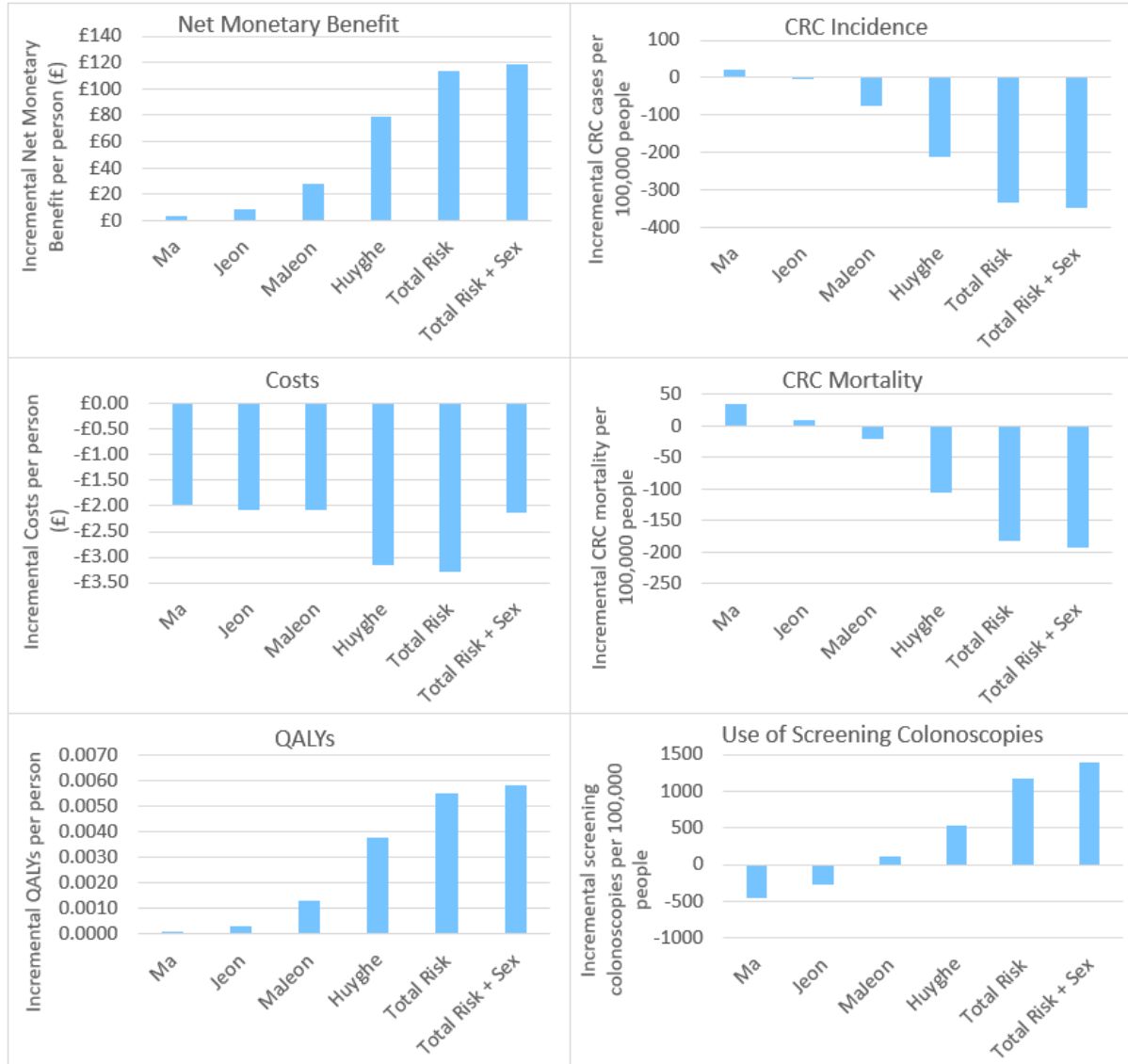
Supplementary Figure 1: Receiver Operating Curves and FIT starting age distribution (based on a mean starting age of 60) for each risk score, based on assessing 10-year risk at age 40.



Supplementary Figure 2: Incremental outcomes for risk-stratification (based on a mean screening start age of 50), compared to screening start age of 50 for the entire population using FIT120. Incremental net monetary benefit is based on a cost-effectiveness threshold of £20,000/QALY.



Supplementary Figure 3: Incremental outcomes for risk-stratification (based on a mean screening start age of 60), compared to screening start age of 60 for the entire population using FIT20. Incremental net monetary benefit is based on a cost-effectiveness threshold of £20,000/QALY.



Supplementary Table 1: Values used in the model for FIT sensitivity and specificity (first round of screening).

FIT Threshold	Age	Sex	Sensitivity to CRC	Sensitivity to High Risk Adenoma	Sensitivity to Low Risk Adenoma	Specificity
FIT120	60	Male	0.354	0.104	0.020	0.996
		Female	0.156	0.085	0.011	0.997
	50	Male	0.356	0.080	0.014	0.998
		Female	0.144	0.074	0.008	0.998
FIT20	60	Male	0.410	0.249	0.080	0.976
		Female	0.211	0.229	0.049	0.979
FIT Faecal Immunochemical Test; CRC Colorectal Cancer						

Supplementary Table 2: Full set of incremental outcomes for risk-stratification based on a mean FIT120 screening start age of 50, compared to screening everyone with FIT120 at age 50.

Risk Score		Ma	Jeon	MaJeon	Huyghe	Total Risk	Total Risk + Sex
Total Costs per person	M	£0.78	-£0.34	£3.46	£2.35	£3.15	£3.82
	L	-£19	-£21	-£16	-£20	-£20	-£20
	U	£20	£19	£26	£26	£27	£27
CRC Treatment Costs per person	M	£0.54	-£0.49	-£1.23	-£1.87	-£2.51	-£2.38
	L	-£20	-£23	-£23	-£26	-£27	-£28
	U	£20	£20	£22	£21	£23	£23
Screen & Surveillance Costs per person	M	£0.23	£0.15	£4.69	£4.22	£5.67	£6.20
	L	-£5	-£5	-£1	-£1	£0	£0
	U	£5	£5	£10	£10	£12	£13
QALYs per person	M	0.0002	0.0001	0.0010	0.0018	0.0023	0.0025
	L	-0.0048	-0.0043	-0.0044	-0.0036	-0.0038	-0.0035
	U	0.0050	0.0045	0.0059	0.0075	0.0087	0.0090
NMB per person (£20,000/QALY Threshold)	M	£3.53	£2.48	£16.91	£33.15	£42.79	£46.32
	L	-£91	-£86	-£88	-£75	-£75	-£68
	U	£96	£90	£112	£140	£171	£180
NMB per person (£30,000/QALY Threshold)	M	£5.68	£3.55	£27.10	£50.90	£65.76	£71.38
	L	-£139	-£129	-£133	-£118	-£110	-£109
	U	£149	£136	£172	£209	£257	£269
MJC per person (£20,000/QALY Threshold)	M	£4.98	£3.50	£23.86	£46.76	£60.36	£65.33
	L	-£129	-£121	-£124	-£106	-£106	-£96
	U	£136	£127	£158	£198	£241	£253
MJC per person (£30,000/QALY Threshold)	M	£8.01	£5.00	£38.23	£71.80	£92.76	£100.69
	L	-£196	-£182	-£187	-£167	-£155	-£153
	U	£210	£192	£243	£295	£363	£380
Prob. cost-effective (£20,000/QALY)		53%	53%	64%	73%	75%	78%
Prob. cost-effective (£30,000/QALY)		53%	52%	66%	74%	75%	78%
CRC Incidence per 100,000 people	M	1	-5	-41	-61	-83	-89
	L	-1106	-1098	-1201	-1242	-1324	-1363
	U	1092	1050	1082	1121	1157	1165
CRC Mortality per 100,000 people	M	-4	0	-28	-44	-64	-70
	L	-483	-462	-518	-560	-616	-611
	U	460	458	450	456	471	460
FIT screening invites per person	M	-0.035	-0.031	0.572	0.044	0.012	0.035
	L	-0.058	-0.055	0.546	0.006	-0.091	-0.072
	U	-0.012	-0.008	0.596	0.082	0.093	0.125
Screening colonoscopies per 100,000 people	M	-28	-26	188	237	360	403
	L	-785	-782	-485	-517	-458	-362
	U	723	728	916	1019	1206	1272
QALY Quality Adjusted Life Year; NMB Net Monetary Benefit; MJC Maximum Justifiable Cost (of risk scoring procedure); CRC Colorectal Cancer; FIT Faecal Immunochemical Test; Prob. Probability; M Mean; L Lower 95% credible interval; U Upper 95% credible interval.							

Supplementary Table 3: Full set of incremental outcomes for risk-stratification based on a mean FIT20 screening start age of 60, compared to screening everyone with FIT20 at age 60.

Risk Score		Ma	Jeon	Maleon	Huyghe	Total Risk	Total Risk + Sex
Total Costs per person	M	-£1.96	-£2.07	-£2.08	-£3.15	-£3.29	-£2.13
	L	-£23	-£20	-£23	-£26	-£25	-£26
	U	£17	£15	£16	£18	£20	£21
CRC Treatment Costs per person	M	-£2.78	-£2.67	-£7.46	-£14.36	-£20.08	-£20.48
	L	-£24	-£22	-£30	-£40	-£44	-£47
	U	£17	£16	£12	£8	£4	£5
Screen & Surveillance Costs per person	M	£0.82	£0.60	£5.37	£11.22	£16.79	£18.36
	L	-£5	-£5	£0	£5	£9	£11
	U	£6	£6	£12	£18	£25	£28
QALYs per person	M	0.0001	0.0003	0.0013	0.0038	0.0055	0.0058
	L	-0.0043	-0.0037	-0.0029	-0.0007	0.0004	0.0007
	U	0.0041	0.0041	0.0057	0.0091	0.0113	0.0118
NMB per person (£20,000/QALY Threshold)	M	£3.77	£8.36	£28.10	£79.03	£113.32	£118.45
	L	-£78	-£73	-£57	-£14	£11	£20
	U	£86	£86	£117	£181	£225	£233
NMB per person (£30,000/QALY Threshold)	M	£4.68	£11.50	£41.11	£116.97	£168.33	£176.60
	L	-£120	-£109	-£87	-£17	£16	£30
	U	£127	£126	£172	£271	£336	£357
MJC per person (£20,000/QALY Threshold)	M	£5.32	£11.79	£39.64	£111.48	£159.85	£167.08
	L	-£110	-£103	-£81	-£20	£16	£28
	U	£121	£121	£165	£256	£317	£329
MJC per person (£30,000/QALY Threshold)	M	£6.59	£16.22	£58.00	£165.00	£237.45	£249.12
	L	-£169	-£154	-£123	-£24	£22	£43
	U	£179	£177	£243	£382	£474	£503
Prob. cost-effective (£20,000/QALY)		54%	57%	74%	95%	99%	99%
Prob. cost-effective (£30,000/QALY)		53%	57%	74%	94%	99%	98%
CRC Incidence per 100,000 people	M	20	-3	-75	-212	-335	-347
	L	-1147	-1104	-1271	-1445	-1614	-1605
	U	1210	1145	1090	984	923	886
CRC Mortality per 100,000 people	M	34	10	-21	-106	-182	-193
	L	-480	-469	-536	-622	-709	-733
	U	582	524	500	420	351	328
FIT screening invites per person	M	0.016	-0.024	0.253	0.020	0.027	0.049
	L	-0.011	-0.050	0.224	-0.022	-0.040	-0.018
	U	0.043	0.002	0.283	0.061	0.088	0.112
Screening colonoscopies per 100,000 people	M	-457	-274	119	526	1166	1397
	L	-1536	-1339	-1006	-762	-107	137
	U	718	858	1302	1798	2448	2722
QALY Quality Adjusted Life Year; NMB Net Monetary Benefit; MJC Maximum Justifiable Cost (of risk scoring procedure); CRC Colorectal Cancer; FIT Faecal Immunochemical Test; Prob. Probability; M Mean; L Lower 95% credible interval; U Upper 95% credible interval.							

Supplementary Table 4: Full set of incremental outcomes for a scenario in which screening uptake is reduced by 25%. Risk-stratification based on a mean FIT120 screening start age of 60 is compared to screening everyone with FIT120 at age 60.

Risk Score		Ma	Jeon	MaJeon	Huyghe	Total Risk	Total Risk + Sex
Total Costs per person	M	-£1.97	-£1.82	-£1.24	-£0.03	£2.00	£2.52
	L	-£17	-£17	-£16	-£16	-£16	-£15
	U	£13	£13	£14	£16	£20	£22
CRC Treatment Costs per person	M	-£2.11	-£1.58	-£2.44	-£4.91	-£5.38	-£5.69
	L	-£18	-£17	-£18	-£22	-£24	-£25
	U	£14	£14	£13	£12	£13	£14
Screen & Surveillance Costs per person	M	£0.14	-£0.24	£1.19	£4.88	£7.38	£8.21
	L	-£3	-£4	-£2	£1	£3	£4
	U	£4	£3	£5	£9	£12	£14
QALYs per person	M	0.0000	0.0001	0.0004	0.0019	0.0028	0.0031
	L	-0.0033	-0.0031	-0.0030	-0.0017	-0.0011	-0.0008
	U	0.0033	0.0033	0.0038	0.0060	0.0077	0.0078
NMB per person (£20,000/QALY Threshold)	M	£1.33	£3.80	£9.74	£37.75	£54.60	£59.20
	L	-£61	-£55	-£56	-£31	-£21	-£14
	U	£68	£68	£77	£119	£146	£150
NMB per person (£30,000/QALY Threshold)	M	£1.01	£4.78	£13.98	£56.61	£82.90	£90.06
	L	-£91	-£86	-£82	-£50	-£31	-£20
	U	£101	£102	£115	£179	£224	£232
MJC per person (£20,000/QALY Threshold)	M	£1.87	£5.36	£13.73	£53.25	£77.02	£83.51
	L	-£86	-£77	-£79	-£43	-£29	-£19
	U	£95	£96	£109	£168	£206	£211
MJC per person (£30,000/QALY Threshold)	M	£1.42	£6.75	£19.72	£79.85	£116.94	£127.04
	L	-£128	-£122	-£116	-£70	-£43	-£28
	U	£142	£144	£162	£252	£315	£327
Prob. cost-effective (£20,000/QALY)		50%	54%	61%	86%	93%	93%
Prob. cost-effective (£30,000/QALY)		50%	54%	61%	87%	93%	93%
CRC Incidence per 100,000 people	M	6	3	-13	-102	-147	-163
	L	-978	-932	-1010	-1121	-1236	-1228
	U	995	971	979	895	909	877
CRC Mortality per 100,000 people	M	30	21	12	-56	-102	-115
	L	-405	-394	-411	-498	-553	-579
	U	458	426	438	384	329	344
FIT screening invites per person	M	-0.176	-0.221	-0.160	-0.139	-0.115	-0.081
	L	-0.200	-0.239	-0.186	-0.173	-0.177	-0.146
	U	-0.154	-0.200	-0.132	-0.103	-0.053	-0.020
Screening colonoscopies per 100,000 people	M	-229	-200	-134	228	489	601
	L	-807	-779	-725	-412	-187	-55
	U	365	357	473	933	1161	1289
QALY Quality Adjusted Life Year; NMB Net Monetary Benefit; MJC Maximum Justifiable Cost (of risk scoring procedure); CRC Colorectal Cancer; FIT Faecal Immunochemical Test; Prob. Probability; M Mean; L Lower 95% credible interval; U Upper 95% credible interval.							

Supplementary Table 5: Incremental cost-effectiveness outcomes for risk-stratification based on a mean FIT120 screening start age of 60, compared to screening everyone with FIT120 at age 60, using a discount rate of 1.5%. Note that clinical and resource use outcomes are not discounted so are identical to those shown in Table 2 of the main results.

Risk Score		Ma	Jeon	MaJeon	Huyghe	Total Risk	Total Risk + Sex
Total Costs per person	M	-£1.42	-£1.24	-£0.68	£1.24	£3.00	£3.64
	L	-£11	-£11	-£10	-£9	-£9	-£8
	U	£8	£8	£9	£12	£15	£16
CRC Treatment Costs per person	M	-£1.79	-£1.27	-£2.01	-£3.26	-£3.73	-£3.82
	L	-£12	-£11	-£12	-£14	-£16	-£16
	U	£8	£9	£8	£8	£9	£8
Screen & Surveillance Costs per person	M	£0.37	£0.03	£1.33	£4.51	£6.72	£7.46
	L	-£2	-£2	-£1	£2	£3	£4
	U	£3	£2	£4	£8	£10	£12
QALYs per person	M	0.0000	0.0001	0.0003	0.0013	0.0020	0.0022
	L	-0.0018	-0.0016	-0.0015	-0.0007	-0.0002	-0.0003
	U	0.0019	0.0019	0.0023	0.0037	0.0048	0.0048
NMB per person (£20,000/QALY Threshold)	M	£1.01	£2.70	£7.00	£25.31	£36.62	£39.69
	L	-£33	-£30	-£29	-£16	-£9	-£5
	U	£39	£37	£49	£69	£91	£91
NMB per person (£30,000/QALY Threshold)	M	£0.81	£3.42	£10.16	£38.59	£56.43	£61.36
	L	-£49	-£45	-£42	-£23	-£10	-£6
	U	£58	£53	£71	£106	£140	£139
MJC per person (£20,000/QALY Threshold)	M	£1.65	£4.39	£11.41	£41.23	£59.66	£64.66
	L	-£54	-£49	-£47	-£27	-£15	-£9
	U	£63	£61	£79	£112	£148	£148
MJC per person (£30,000/QALY Threshold)	M	£1.32	£5.58	£16.56	£62.85	£91.93	£99.95
	L	-£80	-£74	-£68	-£38	-£16	-£10
	U	£94	£87	£115	£173	£229	£226
Prob cost-effective (£20,000/QALY)		50%	56%	63%	88%	95%	95%
Prob cost-effective (£30,000/QALY)		49%	56%	62%	88%	95%	95%
QALY Quality Adjusted Life Year; NMB Net Monetary Benefit; MJC Maximum Justifiable Cost (of risk scoring procedure); CRC Colorectal Cancer; FIT Faecal Immunochemical Test; Prob. Probability; M Mean; L Lower 95% credible interval; U Upper 95% credible interval.							

Supplementary Table 6: Incremental cost-effectiveness outcomes for risk-stratification based on a mean FIT120 screening start age of 60, compared to screening everyone with FIT120 at age 60, using a discount rate of 5%. Note that clinical and resource use outcomes are not discounted so are identical to those shown in Table 2 of the main results.

Risk Score		Ma	Jeon	MaJeon	Huyghe	Total Risk	Total Risk + Sex
Total Costs per person	M	-£8.19	-£6.54	-£8.18	-£10.16	-£10.08	-£9.52
	L	-£45	-£45	-£47	-£48	-£54	-£51
	U	£29	£33	£31	£29	£34	£33
CRC Treatment Costs per person	M	-£6.68	-£4.86	-£9.05	-£18.98	-£24.27	-£25.77
	L	-£46	-£46	-£51	-£59	-£70	-£68
	U	£33	£35	£33	£24	£22	£19
Screen & Surveillance Costs per person	M	-£1.51	-£1.68	£0.87	£8.82	£14.19	£16.25
	L	-£11	-£11	-£9	-£1	£3	£5
	U	£8	£7	£10	£20	£27	£29
QALYs per person	M	-0.0007	0.0000	0.0009	0.0058	0.0087	0.0096
	L	-0.0098	-0.0094	-0.0091	-0.0048	-0.0026	-0.0022
	U	0.0097	0.0097	0.0114	0.0169	0.0212	0.0222
NMB per person (£20,000/QALY Threshold)	M	-£6.23	£6.07	£26.30	£125.93	£184.21	£202.11
	L	-£190	-£179	-£166	-£84	-£47	-£22
	U	£196	£199	£233	£345	£424	£452
NMB per person (£30,000/QALY Threshold)	M	-£13.44	£5.83	£35.36	£183.81	£271.27	£298.41
	L	-£290	-£272	-£255	-£132	-£68	-£52
	U	£296	£301	£344	£517	£639	£675
MJC per person (£20,000/QALY Threshold)	M	-£7.23	£7.04	£30.52	£146.14	£213.78	£234.56
	L	-£220	-£208	-£193	-£97	-£55	-£26
	U	£227	£231	£271	£400	£492	£525
MJC per person (£30,000/QALY Threshold)	M	-£15.59	£6.76	£41.04	£213.32	£314.82	£346.31
	L	-£336	-£316	-£296	-£153	-£79	-£60
	U	£344	£350	£399	£600	£742	£783
Prob cost-effective (£20,000/QALY)		46%	53%	57%	87%	95%	95%
Prob cost-effective (£30,000/QALY)		45%	52%	56%	86%	95%	95%
QALY Quality Adjusted Life Year; NMB Net Monetary Benefit; MJC Maximum Justifiable Cost (of risk scoring procedure); CRC Colorectal Cancer; FIT Faecal Immunochemical Test; Prob. Probability; M Mean; L Lower 95% credible interval; U Upper 95% credible interval.							

Supplementary Table 7: Full set of incremental outcomes by sex for risk-stratification based on a mean FIT120 screening start age of 60, compared to screening everyone with FIT120 at age 60.

Risk Score		Ma	Jeon	Maleon	Huyghe	Total Risk	Total Risk + Sex
Males							
Total Costs per person	M	-£3.40	-£3.23	-£2.76	-£0.42	£1.59	£6.31
	L	-£33	-£31	-£32	-£31	-£33	-£30
	U	£25	£23	£28	£31	£39	£40
CRC Treatment Costs per person	M	-£4.47	-£2.84	-£5.57	-£7.94	-£10.87	-£11.96
	L	-£34	-£32	-£35	-£42	-£49	-£52
	U	£24	£25	£26	£27	£26	£26
Screen & Surveillance Costs per person	M	£1.07	-£0.39	£2.81	£7.53	£12.46	£18.27
	L	-£6	-£7	-£4	£0	£3	£8
	U	£8	£7	£10	£17	£23	£30
QALYs per person	M	0.0002	0.0000	0.0009	0.0029	0.0047	0.0061
	L	-0.0060	-0.0055	-0.0048	-0.0037	-0.0026	-0.0016
	U	0.0062	0.0062	0.0077	0.0101	0.0134	0.0152
NMB per person (£20,000/QALY Threshold)	M	£7.32	£4.03	£20.01	£59.22	£91.56	£114.95
	L	-£115	-£107	-£92	-£66	-£53	-£31
	U	£132	£118	£149	£205	£262	£302
NMB per person (£30,000/QALY Threshold)	M	£9.27	£4.42	£28.64	£88.62	£138.14	£175.58
	L	-£174	-£158	-£141	-£99	-£82	-£45
	U	£197	£179	£218	£304	£391	£456
MJC per person (£20,000/QALY Threshold)	M	M	£5.68	£28.23	£83.53	£129.16	£162.15
	L	-£162	-£151	-£130	-£94	-£74	-£43
	U	£186	£166	£210	£289	£370	£427
MJC per person (£30,000/QALY Threshold)	M	£13.08	£6.24	£40.39	£125.01	£194.86	£247.67
	L	-£245	-£223	-£198	-£140	-£115	-£63
	U	£278	£253	£307	£429	£552	£643
CRC Incidence per 100,000 people	M	-3	19	-29	-132	-229	-321
	L	-1878	-1758	-1879	-2021	-2175	-2310
	U	1867	1837	1878	1728	1734	1625
CRC Mortality per 100,000 people	M	44	41	20	-65	-134	-219
	L	-707	-685	-754	-808	-945	-1039
	U	849	788	822	697	639	555
FIT screening invites per person	M	-0.008	-0.203	0.019	-0.121	0.008	0.930
	L	-0.049	-0.263	-0.040	-0.226	-0.150	0.771
	U	0.032	-0.151	0.076	-0.002	0.166	1.085
Screening colonoscopies per 100,000 people	M	-334	-345	-170	317	820	1455
	L	-1543	-1577	-1308	-873	-413	50
	U	920	856	1141	1565	2226	2856
Females							
Total Costs per person	M	£0.45	£0.41	£0.17	-£2.85	£1.36	-£1.11
	L	-£21	-£18	-£20	£6	-£20	-£23
	U	£20	£19	£19	£7	£23	£21
CRC Treatment Costs per person	M	£0.09	-£0.68	-£1.31	-£4.91	-£6.37	-£5.29
	L	-£22	-£21	-£22	-£28	-£29	-£28
	U	£21	£18	£18	£18	£17	£18

Screen & Surveillance Costs per person	M	£0.36	£1.09	£1.48	£6.15	£7.73	£4.18
	L	-£4	-£3	-£3	£1	£2	-£1
	U	£5	£5	£6	£12	£14	£10
QALYs per person	M	0.0000	0.0003	0.0005	0.0024	0.0031	0.0024
	L	-0.0042	-0.0042	-0.0045	-0.0027	-0.0019	-0.0029
	U	0.0042	0.0049	0.0058	0.0082	0.0093	0.0084
NMB per person (£20,000/QALY Threshold)	M	£0.34	£5.90	£9.94	£45.79	£60.22	£49.59
	L	-£84	-£77	-£87	-£46	-£36	-£48
	U	£81	£92	£109	£158	£182	£169
NMB per person (£30,000/QALY Threshold)	M	£0.74	£9.05	£15.00	£69.30	£91.01	£73.83
	L	-£125	-£119	-£130	-£71	-£51	-£73
	U	£124	£141	£163	£237	£279	£250
MJC per person (£20,000/QALY Threshold)	M	£0.48	£8.32	£14.03	£64.59	£84.95	£69.95
	L	-£119	-£109	-£123	-£65	-£50	-£68
	U	£115	£129	£153	£223	£257	£239
MJC per person (£30,000/QALY Threshold)	M	£1.04	£12.76	£21.16	£97.75	£128.38	£104.14
	L	-£177	-£167	-£184	-£101	-£72	-£103
	U	£174	£199	£230	£334	£394	£353
CRC Incidence per 100,000 people	M	7	-21	-28	-137	-183	-123
	L	-1228	-1281	-1267	-1436	-1522	-1497
	U	1205	1220	1252	1202	1196	1254
CRC Mortality per 100,000 people	M	-7	-21	-25	-108	-145	-98
	L	-559	-575	-600	-712	-774	-731
	U	546	535	569	492	468	542
FIT screening invites per person	M	0.039	0.146	0.049	0.186	0.094	-0.721
	L	0.014	0.095	-0.002	0.082	-0.080	-0.891
	U	0.064	0.192	0.101	0.282	0.262	-0.551
Screening colonoscopies per 100,000 people	M	-8	126	87	493	642	303
	L	-795	-648	-776	-310	-194	-476
	U	778	895	893	1383	1490	1148
<p>QALY Quality Adjusted Life Year; NMB Net Monetary Benefit; MJC Maximum Justifiable Cost (of risk scoring procedure); CRC Colorectal Cancer; FIT Faecal Immunochemical Test; Prob. Probability; M Mean; L Lower 95% credible interval; U Upper 95% credible interval.</p>							