

APPENDIX 1. Details of the cost computation for (a) sigmoidoscopy (FS) and (b) FIT at first and subsequent rounds, respectively.

(a)

Programme organization and evaluation	
Patients invitable in 1 year	12,350
Yearly cost per 1 epidemiologist, €	115,084
Yearly cost per 1 administrative, €	38,278
Total cost Epidemiologist, €	28,771
Total cost Administrative, €	76,556
Cost per 1 FS letter, €	0.5
Total number of letter	12,350
Total cost Letter x 1° FS, €	6,175
Total cost invitation, €	111,502
<i>Cost invitation per adherent, €</i>	30
Endoscopy staff, €	
Theoretical adherence to 1° FS	30%
1° FS	3,705
Theoretical FS repeated rate	6%
1°FS repeated	225
Total FS	3,930
Session for FS	164
Post-FS OC theoretical rate	8%
1° OC	295
1° OC theoret. repeated rate	10%
1° OC repeated	29
Total 1°OC	324
OC per session	8
Session for OC	41
Endoscopy session per year	204
Yearly cost per 1 endoscopist, €	115,084
Yearly cost per 1 nurse, €	45,914
Yearly cost per 1 administrative, €	38,278
Endoscopy sessions per year, €	204
Total cost Endoscopist, €	126,769
Total cost Nurse, €	101,151
Total cost Administrative, €	38,331
Total cost endoscopy staff, €	266,251
<i>Cost End. Staff/adherent, €</i>	72
Endoscopy equipment, €	
Cost 1 Colonoscope	15,151
Cost 1 Video processor and light source, €	21,606
Cost 1 Monitor, €	3,209
Cost 1 Dual-scope reprocessing, €	29,257
Cost 1 Electrosurgical generator, €	6,817

Cost 1 Not reusable snare, €	99
N° Colonoscope	6
N° Video processor and light source	1
N° Monitor	1
N° Dual-scope reprocessing	2
N° Electrosurgical generator	1
N° Not reusable snare	1
Duration 1 Colonoscope	3
Duration 1 Video processor and light source	5
Duration 1 Monitor	10
Duration 1 Dual-scope reprocessing	10
Duration 1 Electrosurgical generator	4
Duration 1 Not reusable snare	4
Maintenance cost 1 Colonoscope per year, €	516
Maintenance cost 1 Video processor and lig, €ht source per year	4,105
Maintenance cost 1 Monitor per year, €	
Maintenance cost 1 Dual-scope reprocessing per year, €	1,980
Maintenance cost 1 Electrosurgical generator per year, €	103
Maintenance cost 1 Not reusable snare per year, €	
Yearly cost Colonoscope, €	38,063
Yearly cost Video processor and light source, €	8,426
Yearly cost Monitor, €	321
Yearly cost Dual-scope reprocessing, €	9,811
Yearly cost Electrosurgical generator, €	1,808
Yearly cost Not reusable snare, €	
Total yearly cost equipment, €	58,428
Total cost equipment, €	58,510
<i>Cost End. Staff/adherent, €</i>	<i>15.8</i>
Endoscope accessories	
Cost of 1 single-use biopsy forceps, €	11
Cost of 1 single-use biopsy snare, €	26
Cost of 1 cleaning brush long, €	6
Cost of 1 cleaning brush short, €	6
Cost of 1 biopsy valve, €	2
Cost of 1 water bottle, €	165
Cost of 1 electric plate, €	1
Cost of 1 silicon, €	7
Theor. rate of polyp removed by biopsy forceps	50%
Theor. rate of polyp removed with diathermy	17%
Theoret. prevalence of polyps at FS+post-FS OC	31%
Total number of polypectomies with biopsy forceps	583
Total number of polypectomies with snare	583
Total number of polypectomies with diathermy	192
Total cost of polypectomies with biopsy forceps, €	6,281

Total cost of polypectomies with snare, €	14,868
Total cost of polypectomies with diathermy, €	209
Total cost polypectomy, €	21,358
Theoretical number of end. with 1 clean brusher long	20
Theoretical number of end. with 1 clean brusher short	50
Theoretical number of end. with 1 biopsy valve	60
Theoretical number of end. with 1 water bottle	4,254
Theoretical number of end. with 1 silicon	150
Total number of clean brusher long	213
Total number of clean brusher short	85
Total number of biopsy valve	71
Total number of water bottle	1
Total number of silicon	28
Total cost of clean brusher long, €	1,366
Total cost of clean brusher short, €	547
Total cost of biopsy valve, €	165
Total cost of water bottle, €	165
Total cost of silicon, €	187
Total cost accessories, €	2,431
Total cost endoscopy accessories, €	23,789
<i>Cost End. accessories/adherent, €</i>	<i>6.4</i>
Disposable material	
Cost of 1 Anallergic gloves, €	0.03
Cost of 1 Polhyethylene gloves, €	0.01
Cost of 1 Latex gloves, €	0.02
Cost of 1 Syringe 2.5 ml, €	0.09
Cost of 1 Syringe 60 ml, €	0.20
Cost of 1 Lubrificant, €	0.17
Cost of 1 Gauze, €	0.04
Cost of 1 Disposable bed linen, €	0.45
Cost of 1 Buscopan, €	0.25
Cost of 1 Midazolam, €	2.42
Cost of 1 Pethidine, €	0.77
VAT, €	20%
Theoretical number of end. with 1 Anallergic gloves	1.25
Theoretical number of end. with 1 Polhyethylene gloves	1.25
Theoretical number of end. with 1 Latex gloves	1.25
Theoretical number of end. with 1 Syringe 2.5 ml	2%
Theoretical number of end. with 1 Syringe 60 ml	7%
Theoretical number of end. with 1 Lubrificant	0.50
Theoretical number of end. with 1 Gauze	1.00
Theoretical number of end. with 1 Disposable bed linen	1.00
Theoretical number of end. with 1 Buscopan	7%
Theoretical number of end. with 1 Midazolam	8%

Theoretical number of end. with 1 Pethidine	0.4%
Total number of Anallergic gloves	3,403
Total number of Polhyethylene gloves	3,403
Total number of Latex gloves	3,403
Total number of Syringe 2.5 ml	101
Total number of Syringe 60 ml	277
Total number of Lubrificant	8,509
Total number of Gauze	4,254
Total number of Disposable bed linen	4,254
Total number of Buscopan	288
Total number of Midazolam	328
Total number of Pethidine	16
Total cost of Anallergic gloves, €	112
Total cost of Polhyethylene gloves, €	19
Total cost of Latex gloves, €	75
Total cost of Syringe 2.5 ml, €	9
Total cost of Syringe 60 ml, €	55
Total cost of Lubrificant, €	1,404
Total cost of Gauze, €	187
Total cost of Disposable bed linen, €	1,919
Total cost of Buscopan, €	73
Total cost of Midazolam, €	794
Total cost of Pethidine, €	12
Total cost disposable material, €	4,658
VAT, €	932
Total cost disposable material+VAT, €	5,590
<i>Cost End. accessories/adherent, €</i>	<i>1.5</i>
Hospital furniture	
Cost of 1 Bed, €	11,362
Cost of 1 PC+printer, €	2,840
Cost of 1 Seats, €	109
Cost of 1 Desk, €	233
Cost of 1 Stool, €	327
Cost of 1 Aspiration system, €	28,405
Duration of 1 Bed	10
Duration of 1 PC+printer	5
Duration of 1 Seats	10
Duration of 1 Desk	10
Duration of 1 Stool	10
Duration of 1 Aspiration system	10
Theoretical number of Bed	1
Theoretical number of PC+printer	2
Theoretical number of Seats	3
Theoretical number of Desk	2

Theoretical number of Stool	2
Theoretical number of Aspiration system	1
Total cost of Bed, €	1,136
Total cost of PC+printer, €	1,136
Total cost of Seats, €	33
Total cost of Desk, €	47
Total cost of Stool, €	65
Total cost of Aspiration system, €	2,841
Tota yearly cost of furniture, €	5,257
Total cost of furniture, €	5,265
<i>Cost furniture/adherent, €</i>	<i>1.4</i>
Endoscopic surveillance	
PPV advanced adenomas	5%
N° advanced adenomas	177
Cost each surveillance OC, €	213
N° surveillance OC	2
Yearly cost surveillance, €	75,340
<i>Cost surveillance/adherent, €</i>	<i>20.3</i>
Other costs	
Cost of 1 histological examination, €	35
Cost of 1 CTC, €	165
Cost of Prep for 1 FS, €	0.6
Cost of Prep for 1 OC, €	1.0
Cost yearly informatic system, €	61,325
Polyps retrieved for histology	95%
Incomplete OC	7%
Number of histological examination	1,107
Number of CTC	23
Number of Prep for FS	3,705
Number of Prep for OC	549
Number of informatic system	1.0
Cost of histological examination, €	39,209
Cost of CTC, €	3,745
Cost of Prep for FS, €	2,242
Cost of Prep for OC, €	568
Cost of informatic system, €	61,410
Total cost of other, €	107,173
<i>Cost furniture/adherent, €</i>	<i>28.9</i>

(b)

	1° round	≥2° round
Programme organization and evaluation		
Patients invitable	63,000	77,200
Yearly cost per 1 epidemiologist, €	115,084	115,084
Yearly cost per 1 administrative, €	38,278	38,278
Total cost Epidemiologist, €	28,771	28,771
Total cost Administrative, €	76,556	76,556
Cost per 1 FIT letter, €	0.5	0.5
Total number of letter	63,000.0	77,200.0
Total cost Letter x 1° FIT, €	31,500	38,600
Total cost invitation, €	136,827	143,927
<i>cost invitation per adherent, €</i>	<i>5</i>	<i>3</i>
Endoscopy staff+ cost FIT		
Theoretical adherence to 1° FIT	42%	60%
Total N° FIT	26,460	46,320
Post-FIT OC rate	7%	4%
OC compliance	80%	80%
1° OC theoret. repeated rate	10%	10%
1° OC repeated	148	148
Total 1°OC	1,630	1,630
OC per session	8	8
Yearly cost per 1 endoscopist, €	115,084	115,084
Yearly cost per 1 nurse, €	45,914	45,914
Yearly cost per 1 administrative, €	38,278	38,277
Endoscopy sessions per year	204	204
Total cost Endoscopist, €	126,432	126,473
Total cost Nurse, €	100,883	100,916
Cost 1 FIT, €	4.2	4.2
Total cost FIT, €	111,132	194,544
Total cost Administrative, €	38,229	38,242
Total cost endoscopy staff and FIT, €	376,681	460,179
<i>Cost End. Staff and FIT/adherent, €</i>	<i>14</i>	<i>10</i>
Endoscopy equipment		
Cost 1 Colonoscope, €	15,151	15,151
Cost 1 Video processor and light source, €	21,606	21,606
Cost 1 Monitor, €	3,209	3,209
Cost 1 Dual-scope reprocessing, €	29,257	29,257
Cost 1 Electrosurgical generator, €	6,817	6,817
Cost 1 Not reusable snare, €	99	99
N° Colonoscope	3	3
N° Video processor and light source	1	1
N° Monitor	1	1

N° Dual-scope reprocessing	1	1
N° Electrosurgical generator	1	1
N° Not reusable snare	1	1
Duration 1 Colonoscope	3	3
Duration 1 Video processor and light source	5	5
Duration 1 Monitor	10	10
Duration 1 Dual-scope reprocessing	10	10
Duration 1 Electrosurgical generator	4	4
Duration 1 Not reusable snare	4	4
Maintenance cost 1 Colonoscope per year, €	516	516
Maintenance cost 1 Video processor + light source per year, €	4,105	4,105
Maintenance cost 1 Monitor per year, €		
Maintenance cost 1 Dual-scope reprocessing per year, €	1,980	1,980
Maintenance cost 1 Electrosurgical generator per year, €	103	103
Maintenance cost 1 Not reusable snare per year, €		
Yearly cost Colonoscope, €	19,031	19,031
Yearly cost Video processor and light source, €	8,426	8,426
Yearly cost Monitor, €	321	321
Yearly cost Dual-scope reprocessing, €	6,885	6,885
Yearly cost Electrosurgical generator, €	1,808	1,808
Yearly cost Not reusable snare, €		
Total yearly cost equipment, €	36,471	36,471
Total cost equipment, €	36,425	36,437
<i>Cost End. Staff/adherent, €</i>	<i>1.4</i>	<i>0.8</i>
Endoscope accessories		
Cost of 1 single-use biopsy forceps, €	11	10.8
Cost of 1 single-use biopsy snare, €	26	25.5
Cost of 1 cleaning brush long, €	6	6.4
Cost of 1 cleaning brush short, €	6	6.4
Cost of 1 biopsy valve, €	2	2.3
Cost of 1 water bottle, €	165	165.0
Cost of 1 electric plate, €	1	1.1
Cost of 1 silicon, €	7	6.6
Theor. rate of polyp removed by biopsy forceps	50%	50%
Theor. rate of polyp removed with diathermy	17%	17%
Theoret. prevalence of polyps at FIT+post-FS OC	50%	50%
Total number of polypectomies with biopsy forceps	6,615	11,580
Total number of polypectomies with snare	6,615	11,580
Total number of polypectomies with diathermy	2,183	3,821
Total cost of polypectomies with biopsy forceps, €	71,310	124,832
Total cost of polypectomies with snare, €	168,815	295,522
Total cost of polypectomies with diathermy, €	2,377	4,162
Total cost polypectomy, €	242,502	424,516
Theoretical number of end. with 1 clean brush long	20	20

Theoretical number of end. with 1 clean brusher short	50	50
Theoretical number of end. with 1 biopsy valve	60	60
Theoretical number of end. with 1 water bottle	28,090	47,950
Theoretical number of end. with 1 silicon	150	150
Total number of clean brusher long	1,404	2,398
Total number of clean brusher short	562	959
Total number of biopsy valve	468	799
Total number of water bottle	1	1
Total number of silicon	187	320
Total cost of clean brusher long, €	9,022	15,402
Total cost of clean brusher short, €	3,609	6,161
Total cost of biopsy valve, €	1,092	1,864
Total cost of water bottle, €	165	165
Total cost of silicon, €	1,236	2,110
Total cost accessories, €	15,124	25,701
Total cost endoscopy accessories, €	257,626	450,216
<i>Cost End. accessories/adherent, €</i>	<i>9.7</i>	<i>9.7</i>
Disposable material		
Cost of 1 Anallergic gloves, €	0.03	0.03
Cost of 1 Polhyethylene gloves, €	0.01	0.01
Cost of 1 Latex gloves, €	0.02	0.02
Cost of 1 Syringe 2.5 ml, €	0.09	0.09
Cost of 1 Syringe 60 ml, €	0.20	0.20
Cost of 1 Lubrificant, €	0.17	0.17
Cost of 1 Gauze, €	0.04	0.04
Cost of 1 Disposable bed linen, €	0.45	0.45
Cost of 1 Buscopan, €	0.25	0.25
Cost of 1 Midazolam, €	2.42	2.42
Cost of 1 Pethidine, €	0.77	0.77
VAT	20%	20%
Theoretical number of end. with 1 Anallergic gloves	1.25	1.25
Theoretical number of end. with 1 Polhyethylene gloves	1.25	1.25
Theoretical number of end. with 1 Latex gloves	1.25	1.25
Theoretical number of end. with 1 Syringe 2.5 ml	0%	0%
Theoretical number of end. with 1 Syringe 60 ml	1%	1%
Theoretical number of end. with 1 Lubrificant	0.50	0.50
Theoretical number of end. with 1 Gauze	1.00	1.00
Theoretical number of end. with 1 Disposable bed linen	1.00	1.00
Theoretical number of end. with 1 Buscopan	1%	1%
Theoretical number of end. with 1 Midazolam	1%	1%
Theoretical number of end. with 1 Pethidine	0.1%	0.0%
Total number of Anallergic gloves	22,472	38,360
Total number of Polhyethylene gloves	22,472	38,360
Total number of Latex gloves	22,472	38,360

Total number of Syringe 2.5 ml	101	101
Total number of Syringe 60 ml	277	277
Total number of Lubrificant	56,180	95,901
Total number of Gauze	28,090	47,950
Total number of Disposable bed linen	28,090	47,950
Total number of Buscopan	288	288
Total number of Midazolam	328	328
Total number of Pethidine	16	16
Total cost of Anallergic gloves, €	742	1,266
Total cost of Polhyethilene gloves, €	124	211
Total cost of Latex gloves, €	494	844
Total cost of Syringe 2.5 ml, €	9	9
Total cost of Syringe 60 ml, €	55	55
Total cost of Lubrificant, €	9,270	15,824
Total cost of Gauze, €	1,236	2,110
Total cost of Disposable bed linen, €	12,669	21,626
Total cost of Buscopan, €	73	73
Total cost of Midazolam, €	794	794
Total cost of Pethidine, €	12	12
Total cost disposable material, €	25,476	42,823
VAT	5,095	8,565
Total cost disposable material+VAT, €	30,572	51,387
<i>Cost End. accessories/adherent, €</i>	<i>1.2</i>	<i>1.1</i>
Hospital furniture		
Cost of 1 Bed, €	11,361	11,361
Cost of 1 PC+printer, €	2,840	2,840
Cost of 1 Seats, €	108.90	108.90
Cost of 1 Desk, €	233.20	233.20
Cost of 1 Stool, €	326.70	326.70
Cost of 1 Aspiration system, €	28,405	28,405
Duration of 1 Bed	10	10
Duration of 1 PC+printer	5	5
Duration of 1 Seats	10	10
Duration of 1 Desk	10	10
Duration of 1 Stool	10	10
Duration of 1 Aspiration system	10	10
Theoretical number of Bed	1	1
Theoretical number of PC+printer	2	2
Theoretical number of Seats	3	3
Theoretical number of Desk	2	2
Theoretical number of Stool	2	2
Theoretical number of Aspiration system	1	1
Total cost of Bed, €	1,136	1,136
Total cost of PC+printer, €	1,136	1,136

Total cost of Seats, €	33	33
Total cost of Desk, €	47	47
Total cost of Stool, €	65	65
Total cost of Aspiration system, €	2,841	2,841
Tota yearly cost of furniture, €	5,257	5,257
Total cost of furniture, €	5,251	5,253
<i>Cost furniture/adherent, €</i>	<i>0.2</i>	<i>0.1</i>
Endoscopic surveillance		
PPV advanced adenomas	35%	28%
N° advanced adenomas	570	457
Cost each surveillance OC, €	213	213
N° surveillance OC	2	2
Yearly cost surveillance, €	243,023	194,482
<i>Cost surveillance/adherent</i>	<i>9.2</i>	<i>4.2</i>
Other costs		
Cost of 1 histological examination, €	35.42	35.42
Cost of 1 CTC, €	165	165
Cost of Prep for 1 OC, €	1.03	1.03
Cost yearly informatic system, €	61,325	61,325
Polyps retrieved for histology	95%	95%
Incomplete OC	7%	7%
Number of histological examination	774	774
Number of CTC	114	114
Number of Prep for FS		
Number of Prep for OC	1,630	1,630
Number of informatic system	1.0	1.0
Cost of histological examination, €	27,423	27,432
Cost of CTC, €	18,826	18,832
Cost of Prep for FS, €	0	0
Cost of Prep for OC, €	1,685	1,686
Cost of informatic system, €	61,247	61,267
Total cost of other, €	109,181	109,217
<i>Cost other/adherent, €</i>	<i>4.1</i>	<i>2.4</i>

APPENDIX 2

Assumptions concerning screening parameters.

1) FS

Attendance rate. A 30% compliance to FS in the Piedmont CRC screening programme has been recently reported.¹⁰ This data already incorporated the additional effect due to subsequent remainders sent to non-adherent screenees.

Efficacy. In two large RCT on the efficacy of FS for CRC screening, CRC incidence and mortality reduction at per protocol analysis (i.e. those needed for our model) were 33% and 31%, and 43% and 38%, respectively, after a mean follow up of 11.2 years.^{7,8} The slight discrepancy in mortality estimate was referred to the different length of the studies (12 vs. 11 years) and to a lower colorectal cancer mortality in the trial control arm compared to the source population in one study, thus the highest estimate was included in the model.

Costs. To assess the cumulative cost of a single FS procedure, we firstly computed the cumulative 1-year direct cost of a FS organized screening programme, by dividing it in six main chapters, namely endoscopy staff, endoscopic equipment, endoscopy accessories, disposable material, hospital furniture, and general administrative costs. Secondly, we divided this 1-year cost estimate by the expected number of subjects to be examined with FS within 1 year in order to fill in the endoscopic sessions planned in the same time frame (i.e. 204), when including both FS and FS-induced TCs. The cost of FS- and TC-related polypectomies (including histology) was based on the polyp detection rate assessed within the Piedmont region FS programme. Thus, although *polyps* were not considered for the efficacy assessment in our model, they were included in the cost analysis. Of note, the detection rates measured within the regional programme was an adequate and certain source of information, so that the inclusion of this information did not weak the reliability of the model, since no simulation of the adenoma-carcinoma sequence was needed for estimating the polypectomy cost. This also applies to FIT-strategy

(see below). No post-polypectomy surveillance was simulated in the reference case scenario, given the uncertainty concerning the impact of surveillance on CRC risk and the wide variability in the surveillance protocols adopted by different programmes, which would limit the generalisability of estimates based on the active surveillance protocol adopted in the Piedmont organized screening programme. However, in the sensitivity analysis, post-polypectomy surveillance was simulated only for advanced adenomas, as recommended by the *European guidelines for quality assurance in colorectal cancer screening and diagnosis*.³ The downstaging efficacy of FS on prevalent cancer was also included in the cost analysis, because of the lower cost of treatment in the earlier than in the later stages. For this purpose, the stage distribution of FS-screen detected CRC was extracted by the Piedmont regional screening programme.

2) **FIT**

Attendance rate. A 42% compliance to initial invitation of FIT has been shown during the ongoing programme in Piedmont where 307,600 eligible subjects has been invited in the period 2010-2011. In a recent study based on a sequence of 4 FIT performed in a Piedmont-adjacent region¹⁷, an additional 15% adherence was shown for non-adherent subjects at each of the biennially re-invitations. Thus, the cumulative adherence simulated in the model was the sum of the initial adherence and that to repeated invitation in the five subsequent rounds. In the same study, adherent subjects showed a 85% compliance at each of the biennially repeated invitations, whilst non-compliant in any round showed a 15% compliance to any of the subsequent invitations. These rates were also included in the model.

Efficacy. One cohort study based on an Italian biennial FIT programme and including 6,961 attendees and 26,285 non-attendees subjects, respectively, showed a 22% and 26% reduction in colorectal cancer incidence and mortality, respectively, for a 12-year period.⁹ These data of efficacy were applied to the adherent-screenees of the simulated cohort. Thus, the simulated effect would start at the beginning of the simulation for those who were adherent to the initial invitation, and from the following years to

those who accepted the invitation only at the subsequent rounds (see adherence section above). On the other hand, these data also incorporated a suboptimal compliance to repeated FIT invitations, so that no adjustment for compliance was needed.

3) FS+FIT for non-adherent to FS

It is routine policy in the Piedmont region to re-invite subjects non-adherent to FS to FIT. This has been recently reported in a North-Italy cohort (Turin, Verona).¹⁰ Briefly in an initial FS-screening cohort of 63,718 subjects, 19.3% of those non-responders to FIT underwent a FIT, when re-invited. This value was used as baseline value in our analysis. All the remaining inputs in this simulation were entirely taken from what already reported separately for FS and FIT in the above sections.

APPENDIX 3.

To estimate the distribution of expected costs and efficacy of the screening strategies dependent on the uncertainty in the input parameters, Monte Carlo (MC) simulation was used to repeatedly sample from the distributions assigned to all the uncertain parameters shown in Table 3. For each MC iteration, the NB for each strategy was computed, in order to represent the possible values of NB for all the possible realizations of the uncertain parameters. For each MC iteration, the maximum NB among all the strategies was also calculated in order to estimate the total expected value of perfect information (EVPI) per subject. The expected value of a decision taken with perfect information (i.e. the identification of the optimal test) was found by averaging the maximum net benefit over the joint distribution of the included parameters (i.e. average of the maximum NBs of all the 10,000 iterations). The difference between the maximum NB with perfect information and the maximum NB with current information corresponds to the total EVPI per subject.

An analysis of the EVPI associated with particular subsets of model parameters was also conducted (partial EVPI) to indicate what type of additional evidence would be most valuable. Partial EVPI was calculated as the difference between the expected net benefit with perfect information about the parameters of interest and the expected value with current information. Subsequently, we estimated the expected value for the entire population that can potentially benefit from more research (population EVPI).

APPENDIX 4.

Cost, effect and net benefit for all the included strategies for a cohort of 100,000 subjects invited for screening, when assuming equal adherence among all the strategies.

	No screening	FS	FIT	FS + FIT
CRC cases, n	1,517	1,313	1,312	1,224
CRC deaths, n	528	432	442	395
CRC prevented, %	-	13%	14%	19%
CRC deaths prevented, %	-	18%	16%	25%
Life-years lost, n	19,431	17,463	17,700	16,712
Life-years saved, n[§]	-	1,969	1,731	2,719
Life-years saved discounted, n	-	1,689	1,460	2,312
Cost CRC care, €[§]	44,294,628	34,393,357	38,503,258	32,716,202
Cost screening, €[§]	-	6,450,886	6,146,373	5,884,306
Total cost, €[§]	44,294,628	40,844,243	44,649,631	38,600,508
Total cost discounted, €	37,884,430	35,866,930	38,400,217	36,832,184
ICER vs no screening, € per life-year saved	-	€20 saving per person	353	€11 saving per person
MNB*,€	-	48,591,072	34,599,573	78,790,042

CRC: colorectal cancer; FS: flexible sigmoidoscopy; FIT: immunochemical faecal test;

MNB: mean net benefit;

ICER: Incremental cost-effectiveness ratio;

[§]Not discounted;

* Mean net benefit was calculated by multiplying effect by willingness to pay and subtracting cost.

Willingness to pay was assumed to be €50,000 per life-year saved.

APPENDIX 5.

Cost-effectiveness among the different strategies, according to the reference case scenario, when simulating screening between 50 and 75 years of age (sensitivity analysis). Non-dominated strategies are connected by a continuous line. Differently from the reference case scenario, we simulated a 10% additional increase in the attendance to FS related with a re-invitation at 65 years in the FS only strategy. FS cost-effectiveness improved, but was still not competitive with the sequential strategies.

