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Colorectal cancer screening within colonoscopy capacity constraints: can FIT-based programmes save more lives by trading-off more sensitive test cut-offs against longer screening intervals?

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ABSTRACT (250 words)

Introduction: Colorectal cancer (CRC) prevention programmes using faecal immunochemical testing (FIT) as the primary screen typically rely on colonoscopy for secondary and surveillance testing. Colonoscopy capacity is an important constraint, limiting the number of primary tests offered. Many European programmes lack sufficient colonoscopy capacity to provide optimal screening intensity regarding screening age ranges, intervals and FIT cut-offs. It is currently unclear how to optimise programmes within colonoscopy capacity constraints.

Design: The MISCAN-Colon microsimulation model was used to determine if more effective CRC screening programmes can be identified within existing colonoscopy capacity. The model assessed

29 525 strategies of varying screening intervals, age ranges and FIT cut-offs, including previously
30 unevaluated 4 and 5 year screening intervals. These strategies were compared with policy
31 decisions taken in Ireland to provide CRC screening within available colonoscopy capacity.
32 Outcomes estimated net costs, quality-adjusted-life-years and required colonoscopy numbers. The
33 optimal strategies within finite colonoscopy capacity constraints were identified.

34 **Results:** Combining a reduced FIT cut-off of 10 µg Hb/g, an extended screening interval of 4 years
35 and an age range of 60-72 years requires 6% fewer colonoscopies, reduces net costs by 23% while
36 preventing 15% more CRC deaths and saving 16% more QALYs relative to current policy.

37 **Conclusion:** Previously overlooked longer screening intervals may balance optimal cancer
38 prevention with finite colonoscopy capacity constraints. Simple changes to screening
39 configurations could save lives, reduce costs, and relieve colonoscopy capacity pressures. These
40 findings are directly relevant to CRC screening programmes across Europe that employ FIT-based
41 testing and face colonoscopy capacity constraints.

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INTRODUCTION

Colorectal cancer (CRC) is a common malignancy that kills approximately 800 000 people globally each year[1]. Early detection improves survival, with survival rates of 90% for locally detected disease versus 13% when metastasized[2]. Screening for CRC has been shown to reduce both incidence and mortality[3]. CRC screening is cost-effective when offered at an appropriate intensity[4,5].

The advent of population-based CRC screening is relatively recent, with 14 EU states only adopting screening after 2009. Organised CRC screening programmes in Europe commonly use faecal-based tests such as the guaiac faecal occult blood tests (gFOBT) or faecal immunochemical testing (FIT)[6]. As of 2015, 20 out of 28 EU member states were in various stages of implementing population-based CRC screening (Table 1)[7]. Recent reports show that more than half of these use FIT[8]. The most common screening interval was every two years, but there are significant differences in FIT thresholds in use, ranging from 6-180 micrograms of haemoglobin per gram of faeces ($\mu\text{g Hb/g}$).

Programmes using faecal-based primary screening typically use colonoscopy for secondary diagnostic testing of those with positive screening tests, as well as within alternative routes of referrals and for post-treatment surveillance. Insufficient colonoscopy capacity can constrain what intensity and population coverage of CRC screening is feasible[9,10]. Consequently, colonoscopy capacity imposes limits on how many lives can be saved through CRC screening.

The effectiveness and cost-effectiveness of population CRC screening varies with the breadth of the screening age range and length of the screening interval. In the case of FIT-based testing, effectiveness and cost-effectiveness also vary with the test cut-off used to determine positivity[11]. Reducing the FIT cut-off improves sensitivity at the cost of reduced specificity. Shorter screening intervals, wider screening age ranges and lower FIT cut-offs all lead to increased colonoscopy requirements. Despite the increase in colonoscopies, lower FIT cut-offs are generally more cost-effective[12].

Most cost-effectiveness analyses (CEAs) of CRC screening do not consider the binding colonoscopy capacity constraints. Some studies have, however, shown how finite capacity might be best used in the Dutch context[9,13]. The objective of this study is to further explore the potential for improved effectiveness and cost-effectiveness within a capacity-constrained system. In particular, while most existing CRC screening CEAs have explored screening intervals between 1 and 3 years[14–18], this analysis aims to investigate the potential of longer screening intervals to enhance screening effectiveness within colonoscopy constraints. It uses the example of the policy changes made in the Irish CRC screening programme as a case study to investigate what alternative strategies could improve population health outcomes.

Case Study

The challenges facing European CRC screening are demonstrated by the case of the Irish CRC screening programme. It serves as a useful example as the screening strategy was initially specified following a health economic analysis and has been modified since in response to colonoscopy

capacity constraints. The initial health technology assessment (HTA) that informed the establishment of Ireland's CRC screening programme was conducted in 2009[19,20]. It simulated comparisons of FIT, gFOBT and once-off sigmoidoscopy. FIT and gFOBT were considered over a limited selection of age ranges at one screening interval of two years. The FIT test performance characteristics were derived from pooled analyses and employed a single FIT cut-off of 20 µg Hb/g of faeces, equivalent to 100 nano-grams of haemoglobin per millilitre of buffer (ng Hb/ml)[20,21]. The HTA found biennial FIT between ages 55-74 was the optimally effective and cost-effective strategy. However, insufficient colonoscopy capacity prevented the implementation of this strategy and prompted further analyses(26, 27). These suggested narrower age range as one way to operate within existing colonoscopy capacity[23]. These subsequent assessments did not examine varying the screening interval or FIT cut-offs.

The programme was launched in October 2012 with biennial screening offered between ages 60-69 at a cut-off of 20 µg Hb/g (FIT 100ng Hb/ml). The stated intention was to expand to the initially planned 55-74 age range as colonoscopy capacity developed[24]. In practice, colonoscopy capacity constraints persisted, leading to a second policy change in early 2014. The FIT cut-off was increased from 20 to 45 µg Hb/g (100 to 225 ng Hb/ml)[25]. While adopting a higher cut-off would improve specificity and ease colonoscopy demand, the loss of sensitivity would reduce screening effectiveness[26]. Restoring the 55-74 age range was recently restated as a policy objective, but reducing the FIT threshold was not[27].

METHODS

We used a microsimulation model to estimate the costs and effects of a broad range of FIT-based screening strategies. We simulated the policy choices made to date to address colonoscopy capacity constraints and attempted to find alternative policies that are feasible given these constraints but offered greater effectiveness and cost-effectiveness. We used the MISCAN-Colon model to simulate multiple screening strategies in a single birth cohort of average-risk individuals. This established micro-simulation model was developed at the Erasmus University Medical Center[28]. Its underlying structure and parameters have been described elsewhere, alongside comparative evaluations against other CRC screening models[29]. An overview of the model applied in other studies[9,30] is publicly available[28].

MISCAN-Colon simulates the life histories of individuals who may develop one or more adenomas. These adenomas may progress from small (≤ 5 mm) to medium (6 to 9 mm) to large (≥ 10 mm) lesions. Some adenomas will develop into preclinical cancer, which may then progress through stages I to IV. Symptomatic presentation of CRC is possible at any stage. Survival after clinical diagnosis is determined by the stage at diagnosis, the localization of the cancer and the person's age.

Screening alters some of the simulated life histories through the detection and removal of adenomas or the detection of cancer earlier than a clinical presentation, potentially leading to improved prognosis due to earlier treatment[2]. However, screening can also result in serious complications including perforation[31], over-diagnosis and overtreatment of CRC (that is, the detection and treatment of cancer that would not otherwise progress to affect quality of life or life

expectancy)[32]. By comparing all simulated life histories with and without screening, MISCAN-Colon estimates the cost and effectiveness of the alternative screening strategies. Whilst patients were not involved in this study due to the nature of the methods applied, this work seeks to advocate for their interests in the policy practice interface.

Test Characteristics

The FIT test characteristics (Table 2) were taken from published estimates[33]. In the absence of a consistent source of test performance characteristics corresponding to the case study programme cut-off of 45 µg Hb/g (225ng Hb/ml) [20], we used published estimates for 40 µg Hb/g (200 ng Hb/ml) as an approximation. The colonoscopy test characteristics are those applied routinely with MISCAN[34]. The model assumes that 95% of all colonoscopies reach the cecum[35] and that the remaining 5% are distributed uniformly over the colon and rectum.

Diagnostic Testing and Surveillance

The model assumes that a diagnostic colonoscopy is offered after any positive FIT. If no adenomas or CRCs are found, individuals return to routine screening at the interval of the simulated strategy. Adenomas detected at colonoscopy are assumed to be removed by polypectomy and individuals then enter colonoscopy-based surveillance following risk-based guidelines: that is, patients received surveillance colonoscopy in 1 and 3-year intervals, in high risk (all lesions ≥ 10 mm) and intermediate-risk (>2 lesions < 10 mm) respectively[36] to a maximum age of 80 years. Low-risk cases (< 3 adenomas < 10 mm) are returned to routine FIT screening, based on customary

practice[37–39]. The model simulates total colonoscopy requirements for each strategy including those for (secondary) diagnostic testing, surveillance and clinical presentations of the disease.

Screening, Surveillance Strategies and Attendance Assumptions

As our purpose was to broaden the scope for optimising screening within colonoscopy capacity constraints, we simulated 525 screening strategies in addition to no screening. We modelled five FIT cut-offs of 10, 15, 20, 30 and 40 µg Hb/g (equivalent to 50, 75, 100, 150 and 200 ng Hb/ml). We considered intervals of 1, 2, 3, 4 and 5 years. In addition to the current programme start and stop age of 60 and 70 years respectively, we simulated start ages of 45, 50, 55, 60, 65 and 70 years, with stop ages of 70, 75, 80 years or close approximations thereof depending on the screening interval (Table 3).

All strategies were assessed in terms of the net cost and health effects measured in quality-adjusted life-years (QALYs) relative to no screening. Costs and effects were both discounted at 3% in accordance with the previous Dutch analyses on which our model is based[13,40]. The net costs included the costs of screening, diagnostic colonoscopy, surveillance and any net changes in treatment costs due to early intervention.

We estimated the current colonoscopy capacity constraint in the case study programme as the simulated lifetime colonoscopy demand of the current policy. This was the capacity required for a biennial FIT test in those aged 60-69 with a FIT cut-off of 40 µg Hb/g. We also estimated the

implied capacity constraint for the planned expansion of the age range to 55-75 years. We determined the optimally cost-effective strategies within the implied current and future capacity constraints. We used a cost-effectiveness threshold of €20 000/QALY to determine cost-effectiveness[41].

The following results section outlines the overall cost and effect estimates. We give a detailed description of the policy changes taken to date and their estimated outcomes. We then consider what policy alternatives exist within current colonoscopy capacity. Finally, we consider how the programme might be optimally expanded beyond the current colonoscopy capacity.

RESULTS

An overview of all simulated strategies is presented in Appendix 1, including the FIT cut-off, screening interval and age range along with the estimated colonoscopy requirements, costs, effects and total CRC deaths prevented. Figure 1 plots the estimated costs and effects of all 525 strategies according to FIT cut-off and capacity requirements. The current strategy requires 464 colonoscopies over the lifetime of 1000 individuals. While many strategies exceed current colonoscopy capacity (305 strategies), there are 220 that do not. Many strategies feasible within the colonoscopy constraint (n=85) are more effective than the current strategy (those that lie to the right of the status quo in Figure 1). Some (n=5) also lie below the current strategy, indicating they are cost-saving relative to the current programme. This efficient set is exclusively composed of strategies with a FIT cut-off of 10 µg Hb/g (50 ng Hb/ml). This indicates that the lowest cut-off generally yields strategies that are more effective and less costly.

195

196 **Decisions reducing colonoscopy capacity requirements**

197 Figure 2 illustrates previous policy changes and some future policy options are detailed in Table 4.
198 The originally HTA-recommended strategy (Point 1) requires a colonoscopy capacity of more than
199 twice the present strategy (1017 colonoscopies per 1000 persons), which would also incur greater
200 costs and yield greater benefits than the status quo. Narrowing the age range to 60-69 adopted at
201 the programme's introduction in 2012 (Point 2) reduced the colonoscopy requirements by almost
202 half (662 colonoscopies per 1000 persons). The 2014 increase in the FIT cut-off to 45 µg Hb/g
203 further reduces colonoscopy demand, but also reduces effectiveness and modestly increases costs
204 (Point 3: current strategy). The currently planned restoration of the screening age range to 55-75
205 (Point 4) would generate more QALYs relative to the status quo, however, it would still be less
206 effective than the initially recommended strategy employing the FIT cut-off of 20 µg Hb/g (100 ng
207 Hb/ml) shown by Point 1.

208

209 **Potential policy alternatives**

210 Three potential policy alternatives to the status quo are illustrated in Figure 2. Options A and B are
211 both within the current colonoscopy capacity and so are feasible now. Option A uses a FIT cut-off
212 of 10 µg Hb/g (50 ng Hb/ml) with a 4-year screening interval for those aged 60-72. It dominates the
213 current policy, offering 16% more QALYs, 15% more CRC deaths prevented, 23% less costs and
214 requires 6% fewer colonoscopies relative to the current strategy, Strategy 3. Option B is the
215 optimally cost-effective currently feasible strategy. It uses a 10 µg Hb/g (FIT 50 ng Hb/ml) cut-off
216 with a 5-year screening interval between ages 55-75. It provides an approximate 35% gain in

QALYs, 29% more CRC deaths prevented, a modest 2% reduction in colonoscopies relative to the current strategy, but at a 25% cost increase.

The current policy commitment to restore the initially-planned 55-74 age range does not mention plans to change the screening interval or FIT cut-off[27]. Consequently, expanding the age range implies a 59% increase in colonoscopy capacity (Point 4). Strategy C is an alternative policy using the same implied increased capacity. This uses a 10 µg Hb/g (FIT 50 ng Hb/ml) cut-off with a 4-year interval between ages 50-74. It would provide a 13% QALY gain relative to the planned age expansion (Strategy 4), but would also be 2% more costly, it would, however, require 4% fewer colonoscopies than those predicted for the planned age expansion.

Finally, Figure 3 shows the overall optimally cost-effective strategy without any colonoscopy capacity constraint Point D which uses annual screening between ages 50-80 at a FIT cut-off 10 µg Hb/g (50 ng Hb/ml). This would require a considerable increase in colonoscopy capacity of 691% relative to the status quo and would cost 320% more but would yield an estimated 163% more QALYs and 111% more CRC deaths prevented.

DISCUSSION

Our analysis shows that the optimal policy response to limited colonoscopy capacity may not be to raise the FIT cut-off level, or widen the screening age-range, but rather to use longer screening intervals and more sensitive cut-off levels. In our case study, the policy response to limited capacity to date has been to preserve biennial screening while narrowing the screening age range and

raising the FIT cut-off. Modelling indicates that this runs counter to what makes the most effective use of scarce colonoscopy services. We find that by lengthening the screening interval we can maintain a broad screening age range and retain a more sensitive FIT cut-off and deliver greater benefits in terms of CRC deaths prevented. Costs would also be reduced by this approach. The primary explanation for our findings is the diminishing marginal returns of intensifying the frequency of screening: screening more people less often with a more sensitive FIT threshold seems a more efficient way of reducing the colonoscopy requirements than screening fewer people more frequently with a less sensitive FIT threshold.

Our findings are of clear policy relevance to the many countries facing difficulties in implementing CRC screening within constrained colonoscopy capacity, especially following the initial introduction of national programmes[42]. Restricting the screening age range and reducing the positivity threshold sensitivity of FIT appears a common policy response. A recent EU review of cancer screening services noted that “to optimise (limited) resource allocation, by maximising the cost-effectiveness ratio of the intervention, and to match their endoscopy capacity, several EU member states had actually adopted screening policies targeting a stricter age range, usually shifted to the older age groups, showing a higher prevalence of disease, resulting in a lower cost per lesion detected”[7]. Our results raise the possibility that these countries may also be making what seem like logical, but potentially sub-optimal policy responses to capacity constraints.

Our results differ from other studies of CRC screening using the same MISCAN-Colon model to estimate the optimal policy response to scarce colonoscopy capacity[9,13]. They found higher FIT

cut-offs would be optimal under binding colonoscopy constraints. Our results differ from Van Hees et al. as, among other reasons, that analysis addressed a set of alternatives within an already limited screening age range as set out by policymakers [9]. Similarly, our conclusions differ from Wilschut et al. because we simulated a broader range of screening intervals including every 4 and 5 years[13]. As such, our analysis adds a novel finding to the literature on optimal CRC screening within constrained colonoscopy capacity.

Our findings illustrate the general principle that a cancer screening CEA should simulate a broad range of policy alternatives to find the optimal strategy. The initial HTA within the case study assessed only a small range of strategies and was published prior to work showing the benefit of varying FIT cut-offs. This led that analysis to overlook the issue of diminishing marginal returns of shortening the screening interval. Accordingly, it could not identify the benefits of applying longer intervals to more people, rather than retaining short intervals for a narrow age range. Whilst the original HTA was supplemented by additional evaluations, these too did not consider strategies with longer intervals[24].

Within the specific context of Ireland, better CRC prevention will require careful planning. A similar conclusion could, therefore, apply to many other European countries. The Irish Cancer Society has raised concerns regarding colonoscopy capacity constraints and the emergence of inequities of access to colonoscopy between public and private patients[43,44]. The recently renewed National Cancer Strategy restated the plan to expand capacity to permit the restoration of the screening age

range to 55-74 by end-2021[27]. Plans for this ambitious capacity expansion are being managed by Ireland's Health Service Executive National Endoscopy Steering Group[27].

While the currently planned expansion of colonoscopy capacity is welcome, our results indicate that the case study programme will remain unnecessarily inefficient. Modelling suggests that considerable improvements could be achieved if longer intervals of 4 years were adopted instead of the current 2-year interval. An increase in the screening interval could lead decision-makers to worry that the public might become confused and adherence could suffer. While such potential concerns are understandable, there is no evidence that adherence would be compromised, given the use of wider intervals in other disease areas. Conversely, the modelling evidence suggests that persisting with the present policy is likely to save fewer lives than other feasible strategies.

Our results also highlight a broader concern about the sufficiency of CRC screening programmes in Ireland and other European nations. While Ireland plans to expand colonoscopy capacity, the current policy commitment still falls far short of what is ultimately required. Our results indicate that much larger gains could be made if annual screening were adopted, while remaining cost-effective (Strategy D, Figure 3). This again emphasises the need for CEAs to consider a broad range of options. Current recommendations for biennial screening throughout Europe might lead policymakers to accept very considerable under-provision of CRC screening and save too few lives.

Our analysis naturally has some limitations. Firstly, to date, no trial or observational data has examined the long-term effect of varying FIT intervals[45], thus the correlation between multiple

tests and absolute risk, especially in the context of non-bleeding lesions, remains uncertain. Accordingly, the conclusions presented here on both extending the interval and using annual screening depend heavily on the current model assumptions. More data might be required to give decision-makers confidence in varying the screening interval. Despite this, our analysis usefully illustrates what additional studies could be beneficial to undertake. Secondly, the model reflects Dutch disease incidence and healthcare costs and therefore can only give a broad indication of what is likely to apply in an Irish context. Furthermore, in common with many screening HTAs, we assumed 100% screening adherence. Currently, uptake within the national bowel cancer screening programme is approximately 40%[24]. Similarly, the FIT cut-off of 45 µg Hb/g as used in the programme would generate fewer false positives than we inferred by using a 40 µg Hb/g cut-off. Consequently, our analysis may marginally over-estimate current colonoscopy capacity. However, this approximation was necessary given the need for a consistent source for the test performance characteristics of the alternative FIT cut-offs. Finally, the model assumes 95% of colonoscopies reach the caecum. This may overestimate the effectiveness of the procedure as studies have shown that this can be lower[46,47]. Despite these simplifications, we are confident that the analysis valuably illustrates the relevance of considering a broad range of policy alternatives and a clear indication of how a national bowel cancer screening programme could save more lives.

An explicit acknowledgement of the relevance of the COVID-19 pandemic to our study is necessary. Our analysis was conceived before the advent of COVID-19 and does not reflect the additional capacity challenges that population-based CRC screening programmes are now facing as they attempt to mitigate transmission risk. Our study naturally does not reflect these additional constraints, but the principles of our findings remain the same. Indeed, the possibility that capacity

constraints in CRC screening will be exacerbated in the medium term heighten the relevance of our conclusions.

Adopting annual FIT would require very large increases in colonoscopy capacity for many countries. In the Irish context, we suggest that a revision of the HTA evidence supporting the CRC screening programme is now timely, both for the medium-term optimisation of current capacity and the longer-term planning of overall colonoscopy capacity requirements. It is now necessary to revisit and expand previous analyses of CRC screening and consider additional policy alternatives. Such evidence and policy reviews are now required elsewhere in Europe too. Given that trials examining the effectiveness of FIT may not be available for another ten years[48] modelling provides for more timely improvements. Given the interim shortfall in trial data, initiatives such as the EUTOPIA screening modelling project will be useful in assisting member states to inform such reviews[49].

CONCLUSION

Existing CRC screening programmes may be unnecessarily ineffective and inefficient if analyses informing their design do not consider a wide range of strategies. In our case study, more lives and health services costs could be saved within existing colonoscopy capacity constraints if a lengthening of the screening interval was traded-off against an increase in population coverage and the adoption of a more sensitive FIT cut-off. A broader finding is that much larger increases in colorectal cancer screening capacity than is currently planned appears warranted if annual screening were to be adopted. Policymakers must recognise the need to consider all policy alternatives, within both current colonoscopy capacity constraints and future expanded service

349 capacity. Otherwise, many avoidable colorectal cancer deaths will result over the coming decades.
350 The findings from this case study are likely to be highly relevant for all European nations
351 implementing FIT-based CRC screening with biennial intervals in the face of constrained
352 colonoscopy capacity.

ADDITIONAL INFORMATION

The authors declare no conflict of interest.

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Authors' contributions: EMF and JFOM conducted the simulation modelling experiments and wrote the manuscript. SN, LS, FK and AGZ helped review and edit the manuscript. ILV supported MISCAN model access, provided technical advice on study design, and manuscript review.

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- 524

525 TABLES

526 Table 1 Screening programmes across European countries

Country	Programme initiation	Target age range	Screening interval in years (screening modality)	FIT cut-off (where available, converted to µgHb/g)
Austria ¹	2003	40+gFOBT; 50+ Colo ¹ 40-80 (Bergenland)	1 (FIT); 7-10 (Colo) ¹ 1 (gFOBT)	-
Belgium	2009 ² 2013	50-74 (Wallonia/ Brussels) 56-74 (Flanders)	2 FIT 2 (FIT); 10 (Colo)	15µg Hb/g (FIT as of 2016) 15µg Hb/g
Bulgaria	-	-	-	-
Croatia	2008	50-74	2 (gFOBT)	-
Cyprus	2013	50-69	2 (gFOBT)	-
Czech Republic	2000 ³	50/ 55+ ³	1 (FIT;50-54);2 (FIT;55+) 10 (Colo)	15µg Hb/g
Denmark	2014	50-74	2 (FIT)	20 µg Hb/g
Estonia ⁴	2016 ⁴	60-69 ⁴	2 (FIT)	20 µg Hb/g
Finland	2004	60-69	2 (FIT)	FIT as of 2019 25 µg Hb/g for Females 70 µg Hb/g for Males
France ¹⁴	2002	50-74	2 (FIT)	30 µg Hb/g
Germany ⁵	1974 ⁵	50-74	1 (50-54 gFOBT); 2 (55+ gFOBT) 10 ⁵ (55+ Colo)	Conversion to FIT underway (2017)
Greece	-	50-70	2 (gFOBT); 5 (Colo)	-
Hungary	2007	50-70	2 (gFOBT)	-
Ireland	2012	60-69 ⁷	2 (FIT)	40 µg Hb/g [24]
Italy	1982 ⁸	50-69	2 (FIT)	20 µg Hb/g
Latvia	2009	50-74	1 (gFOBT)	-
Lithuania	2009 ⁶	50-74	2 (FIT)	6-40 µg Hb/g
Luxembourg ¹⁰	2016	55-74	2 (FIT)	50 µg Hb/g
Malta	2013	55-66	2 (FIT)	20 µg Hb/g
Netherlands	2014	55-75	2 (FIT)	47 µg Hb/g [18]
Norway	-	-	-	-
Poland	2012	55-64	10+	-
Portugal	2017 2018	50-75 (Algarve) 50-74	2 (FIT)	117 µg Hb/g (preliminary data) 20 µg Hb/g
Romania	-	-	-	-
Slovak Republic	-	-	-	-
Slovenia	2009	50-74	2 (FIT)	67 µg Hb/g
Spain	2000	50-69 50-69 (Basque Country)	2 (gFOBT) 2 (FIT)	- 20 µg Hb/g
Sweden ¹¹	2008	60-69	2 (FIT)	40 and 80 µg Hb/g for women and men, respectively
United Kingdom	2006 ¹²	60-74 (England) 2018 recommendation to lower start age to 50 50-74 (Scotland)	2 gFOBT/ FIT (rolling introduction) 2 FIT	England pilot sites 180 µg Hb/g, 120 µg Hb/g in some areas Scotland 80 ug Hb/g since Nov 2017
		60-74 (Northern Ireland)	2 gFOBT/ FIT (planned introduction)	FIT Introduction planned 2020
Switzerland ¹³	2015	50-59 (*Canton of Vaud)	2 (FIT); 10 (Colo)	15 µg Hb/g

527 ¹**Austria** - population-based FIT screening programme implemented only in Burgenland (2003), in the rest of the country, opportunistic screening where an
528 annual check, a gFOBT is offered, the colonoscopy interval is 10 years. ²**Belgium** - In March 2016 Wallonia-Brussels replaced gFOBT with FIT. ³The
529 population-based programme in the **Czech Republic** started in 2014. ⁴In **Estonia**, the population-based pilot programme started in 2016, intended target
530 group of 60-69 years old; ⁵In **Germany**, opportunistic gFOBT screening activities started in 1974, a population-based programme started 2019.
531 Colonoscopy continues, recommended twice for those older than 55 years. ⁶In **Hungary**, women who have already been screened opportunistically were
532 not invited; ⁷**Ireland** committed to planned age extension to target age to 55-74-year-olds; ⁸In **Italy**, screening started in 1982 in Florence, and between
533 2000 and 2004 in other regions. The majority of programmes employ FIT (apart from Piedmont region which adopted Flexible Sigmoidoscopy and FIT for
534 non-responders) for subjects aged from 50 to 69 or 70 years; ⁹In **Lithuania**, population-based programme started in 2009 in two districts, decentralised
535 national testing available from 2014, with a pilot with two centralised labs due to commence 2021. ¹⁰In **Luxembourg** a population-based programme
536 started in 2016; ¹¹In **Sweden**, only Stockholm Gotland region introduced screening in 2008, and then switched to FIT in 2015 [50]; ¹²Year of programme
537 initiation: gFOBT **England** 2006, gFOBT **Northern Ireland** 2010, gFOBT **Scotland** 2007, gFOBT **Wales** 2008, as of 2016 the UK Screening Committee
538 recommended the adoption of FIT, rolling introduction [16,51] is underway in all areas except Northern Ireland (due 2020). ¹³In **Switzerland**, A 2013 law
539 authorized reimbursement by basic health insurance of either FIT every 2 years or colonoscopy every 10 years for adults aged 50 to 69 years. In 2015, the
540 Canton of Vaud launched the first large-scale, organized CRC screening program in Switzerland. ¹⁴ In **France**, FIT screening replaced gFOBT with FIT in April
541 2015.

542 **Table 2** Test Characteristics

FIT Cut-off Level (µg Hb/g)[33]*	Specificity (Per person, %)	Sensitivity per lesion, %				
		Adenoma			CRC	
		≤5mm	6-9mm	≥10mm	CRC early stage	CRC late-stage
10	95.79	0.0	9.6	16.1	65.0	90.0
15	97.05	0.0	5.7	14.4	58.5	87.0
20	97.76	0.0	4.4	13.1	52.0	83.5
30	98.34	0.0	2.9	12.3	50.5	83.0
40	98.70	0.0	2.5	10.3	50.0	82.5
Colonoscopy [34]		75.0	85.0	95.0	95.0	95.0

543 *according to the manufacturer, the OC-SENSOR delivers 10 mg of faeces into in 2.0 mL of buffer; thus, a test result of 100 ng haemoglobin per mL buffer
544 equals 20 µg haemoglobin per g faeces [21].

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546
547 **Table 3** Simulated Screening Strategy Characteristics

Strategy Characteristics	
Screening interval (Years)	1/2/3/4/5
Start age (Years)	45/50/55/60/65/70
Stop ages (Years)	70/75/80
FIT cut-off levels (µg Hb/g)	10/15/20/30/40

549

550 **Table 4** Summary of Policy Positions

551

Identifier	Strategy	Age range	Interval	FIT Cut off (µg Hb/g)	QALYs per 1000	Cost (€) per 1000	Colonoscopies per 1000	Change in QALYs (%)*	Change in Costs (%)*	Change in Colonoscopies (%)*
1	Initial Recommendation	55-75	2	20	59	85,748	1,017	67	67	119
2	Age restriction	60-70	2	20	41	44,422	662	17	-13	43
3	Approximation of current strategy	60-70	2	40	35	51,201	464	REF	REF	REF
4	Planned age expansion	55-75	2	40	52	93,152	735	47	82	59
A	Max NHB with cost-saving	60-72	4	10	41	39,680	437	16	-23	-6
B	Max NHB within capacity	55-75	5	10	47	63,861	455	35	25	-2
C	Optimised (Max NHB) with expanded capacity	50-74	4	10	58	95,271	707	66	86	52
D	Max overall Net Health Benefit	50-80	1	10	92	215,284	3,669	163	320	691

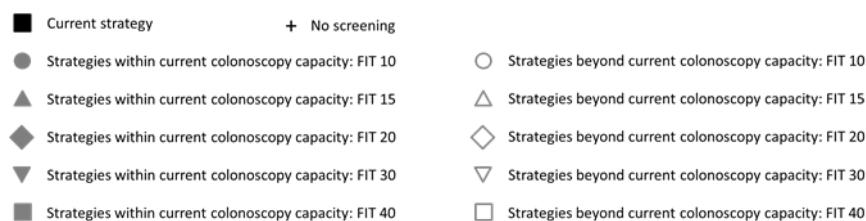
*Percentage change relative to the current strategy (Strategy 3)

552

553 **FIGURES LEGENDS**

554 Strategies with FIT cut-offs of 10, 15, 20, 30 and 40 µg Hb/g are shown with round, triangular,
555 diamond, inverted triangular and square markers respectively. Strategies that are within the
556 colonoscopy capacity of the current strategy are shown with solid markers, whereas those exceeding
557 current capacity are shown with hollow markers. The current strategy is shown as the black square.
558 The black dotted lines correspond to the costs and effects of the status quo. The efficient frontier is
559 shown with the grey dotted line.

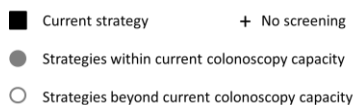
560 **Figure 1 Legend**



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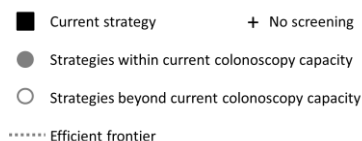
563 **Figure 2 Legend**



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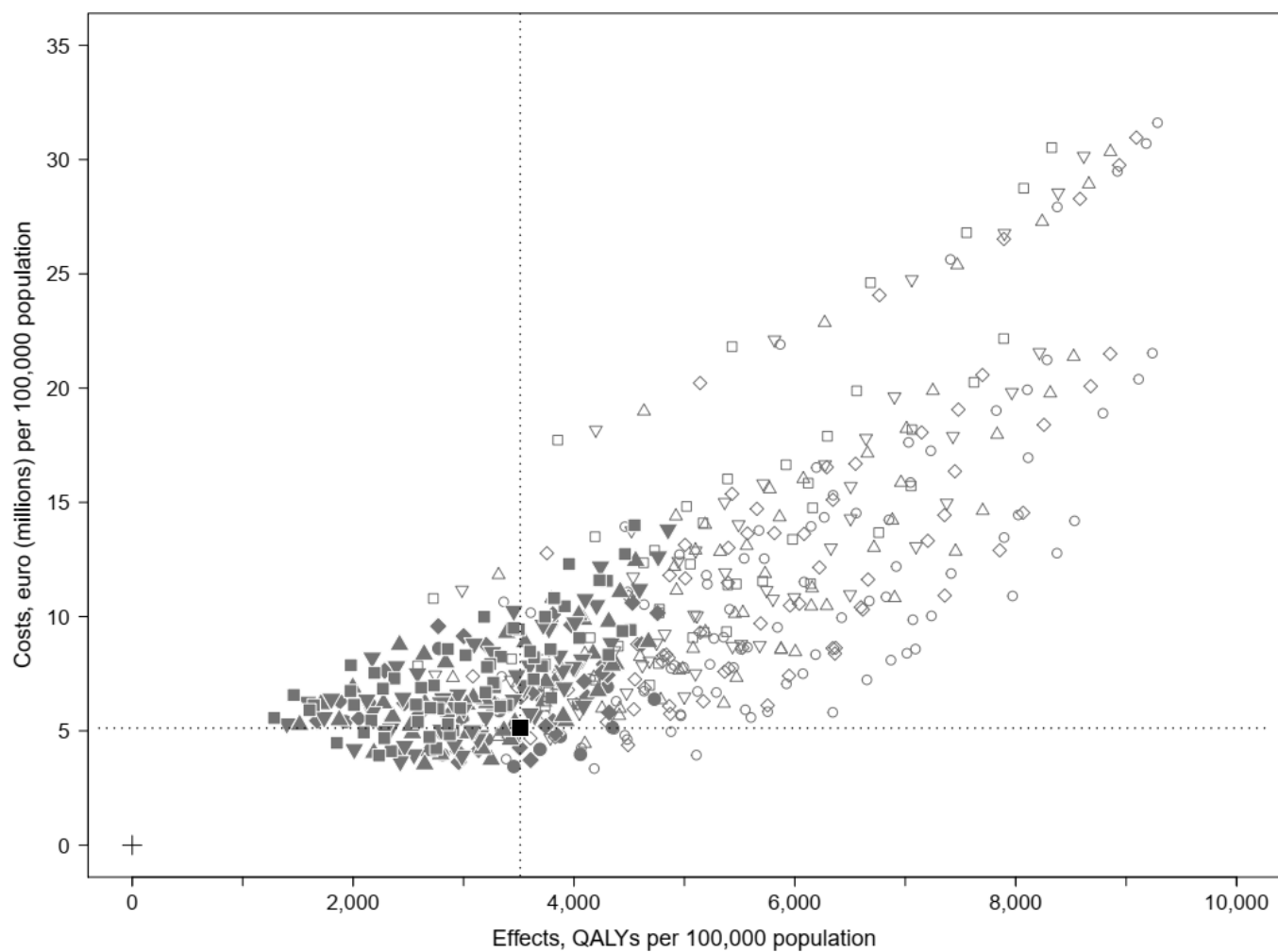
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566 **Figure 3 Legend**

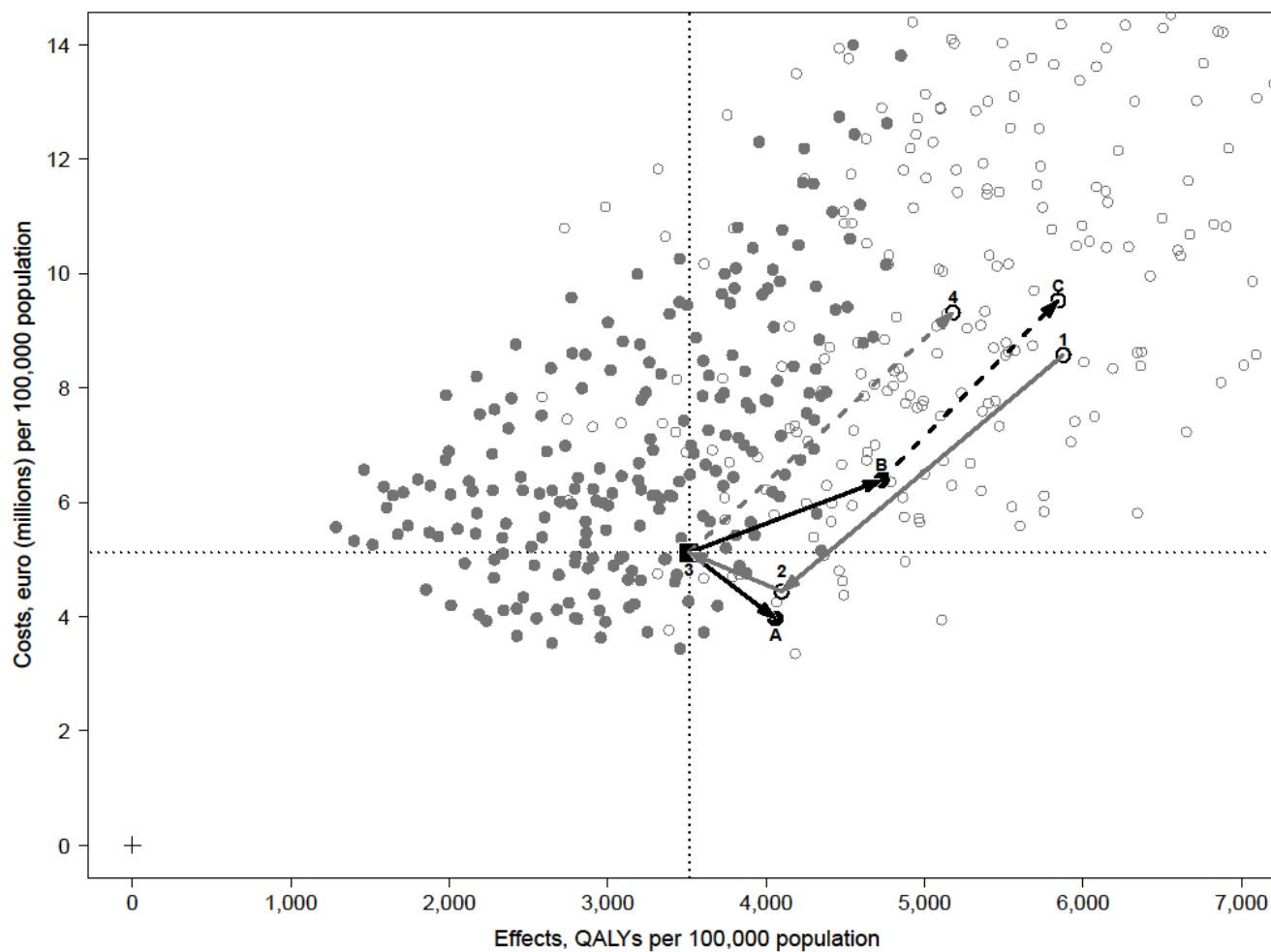


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570 **Figure 1** All Strategies by FIT cut-off and colonoscopy capacity

572 **Figure 2** Past Policy Changes and Future Policy Options

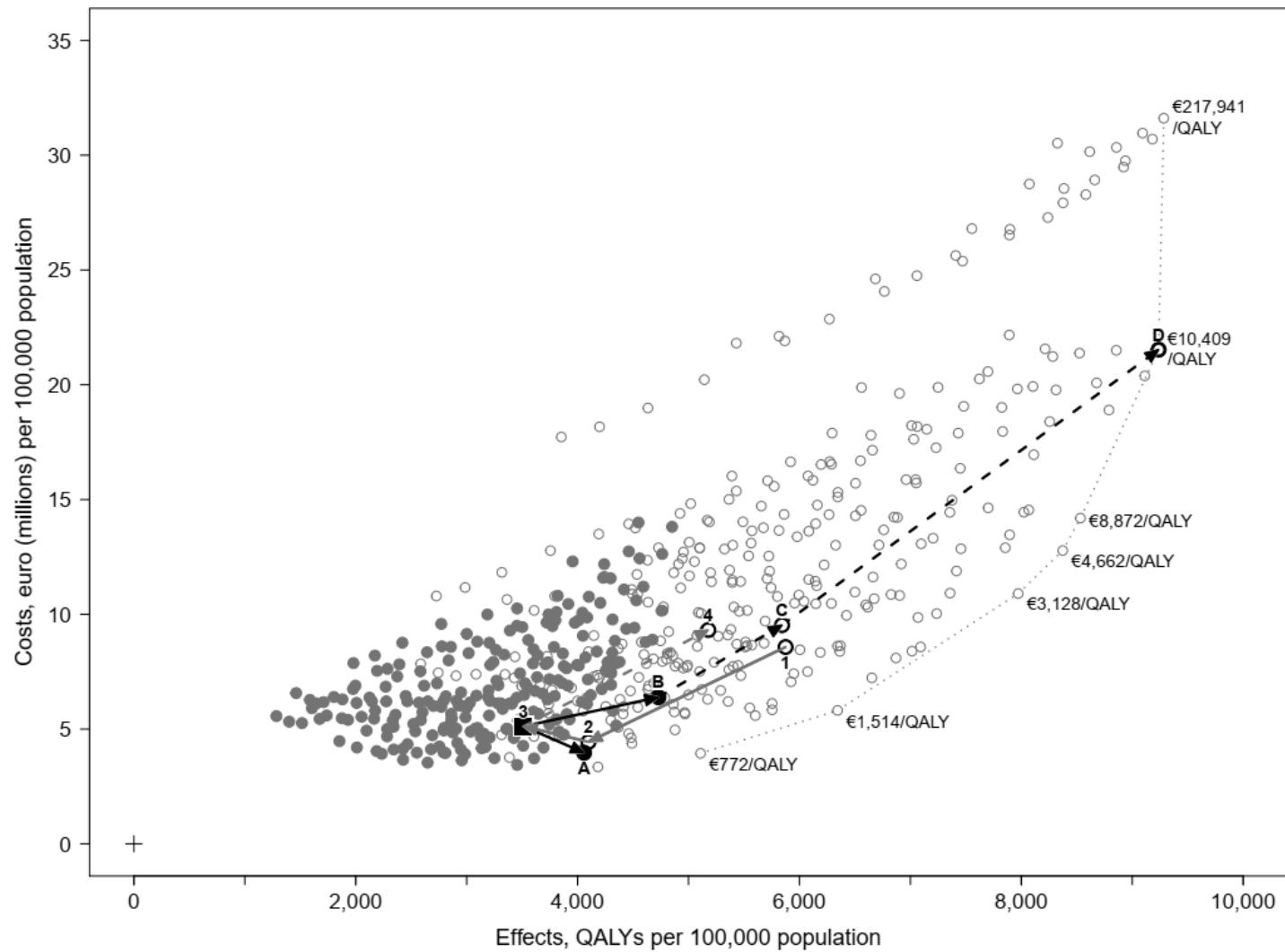


573

574 Figure 2 shows a subset of Figure 1, with the axes rescaled for clarity. This illustrates previous policy changes chronologically, 1 to 2 and 2 to 3. Future policy options are
 575 presented as moves from 3 to A (cost-saving and more effective, requiring 6% fewer colonoscopies.) From 3 to B, providing maximum NHB within capacity. Assuming an
 576 increased capacity, as required to provide the planned age expansion point 4, the maximum NHB at that predicted colonoscopy capacity would be provided by point C.

577

578 **Figure 3** Policy Overview, including overall Max NHB policy (D)



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Appendices

585 **APPENDIX 1** Results of All Strategies Modelled (sorted by FIT cut-off)

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	0	0	0	0	0	0	0	0	0					0	-
Max overall NHB (D)	10	1	50	80	30	923,774	2,152,841,980	962,802	36,690,721	0	163	320	691	91186	10409
	10	1	50	75	25	911,291	2,038,845,024	948,937	36,029,947	0	159	298	677	88557	-
	10	1	50	70	20	878,990	1,889,923,187	914,974	34,438,993	0	150	269	643	83408	-
	10	1	55	80	25	853,279	1,419,041,116	892,270	32,412,179	0	143	177	599	90489	8872
	10	1	55	75	20	837,341	1,277,636,957	874,613	31,587,240	0	138	150	581	87173	4662
	10	1	45	80	35	928,401	3,161,158,158	969,447	38,998,864	0	164	517	741	87349	217941
	10	1	45	75	30	918,185	3,070,154,354	958,158	38,465,302	0	161	500	729	85224	-
	10	1	45	70	25	892,149	2,948,308,364	930,661	37,189,552	0	154	476	702	81081	-
	10	1	55	70	15	797,157	1,090,283,748	832,305	29,563,393	0	127	113	538	80744	3128
	10	1	50	65	15	811,243	1,695,206,231	845,463	31,394,594	0	131	231	577	74679	-
	10	1	45	65	20	837,582	2,792,411,142	874,754	34,789,084	0	138	445	650	74040	-
	10	1	55	65	10	709,224	857,943,179	742,492	25,578,155	0	102	68	452	69389	-
	10	1	60	80	20	706,852	986,260,798	749,691	26,540,438	0	101	93	472	83750	-
	10	1	60	75	15	686,998	809,446,643	727,648	25,490,509	0	96	58	450	79597	-
	10	1	50	60	10	685,214	1,423,396,387	718,065	26,200,406	0	95	178	465	61184	-
	10	1	45	60	15	740,870	2,563,015,440	776,495	30,771,718	0	111	401	564	63639	-
	10	1	60	70	10	634,347	581,066,953	672,429	22,818,047	0	81	13	392	71121	1514
	10	1	65	80	15	523,101	791,176,426	570,808	19,654,061	0	49	55	324	72051	-
	10	1	45	55	10	586,770	2,190,946,536	620,525	24,617,684	0	67	328	431	49193	-
	10	1	65	75	10	496,510	571,947,109	541,520	18,263,474	0	41	12	294	66537	-
	10	1	70	80	10	334,539	738,080,543	385,218	12,362,713	0	-5	44	167	56490	-
	10	2	50	80	15	802,314	1,444,752,482	872,082	17,539,998	0	128	182	278	84887	-
	10	2	45	81	18	828,387	2,123,170,365	900,496	19,368,532	0	136	315	318	84566	-
	10	2	50	76	13	789,494	1,345,952,060	855,800	17,124,596	0	125	163	269	81704	-
	10	2	45	75	15	810,525	1,992,527,265	878,106	18,804,614	0	131	289	306	80251	-
	10	2	45	71	13	782,377	1,901,606,608	845,891	18,089,982	0	123	271	290	75224	-
	10	2	50	70	10	741,534	1,188,515,223	800,689	15,895,718	0	111	132	243	73277	-
	10	2	55	81	13	723,695	1,003,088,247	792,025	15,090,209	0	106	96	225	82307	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	10	2	55	75	10	701,455	839,544,597	764,056	14,372,371	0	100	64	210	76944	-
	10	2	55	71	8	665,232	723,266,647	722,585	13,441,645	0	89	41	190	70506	-
	10	2	50	66	8	682,599	1,086,265,340	736,108	14,526,217	0	94	112	213	65015	-
	10	2	45	65	10	702,995	1,762,301,445	759,134	16,296,739	0	100	244	251	64317	-
	10	2	60	80	10	592,420	705,902,275	658,520	12,035,801	0	69	38	160	74578	-
	10	2	60	76	8	575,371	583,723,782	637,209	11,493,660	0	64	14	148	70415	-
	10	2	45	61	8	619,463	1,652,385,064	670,127	14,509,698	0	76	223	213	54906	-
	10	2	55	65	5	560,257	558,610,770	608,155	11,004,228	0	59	9	137	55976	-
	10	2	60	70	5	510,850	394,125,332	563,686	9,804,082	0	45	-23	111	59017	772
	10	2	50	60	5	535,459	909,694,154	579,400	11,372,549	0	52	78	145	48455	-
	10	2	65	81	8	438,231	629,411,196	502,881	8,984,357	0	25	23	94	64417	-
	10	2	65	75	5	406,673	425,304,283	464,060	7,979,930	0	16	-17	72	56887	-
	10	2	45	55	5	446,112	1,393,734,864	486,162	10,823,546	0	27	172	133	37968	-
	10	2	70	80	5	275,209	603,227,178	334,639	5,650,250	0*	-22	18	22	49100	-
	10	3	45	81	12	723,132	1,725,591,172	807,480	11,959,541	0	106	237	158	77229	-
	10	3	50	80	10	691,806	1,219,123,010	774,726	10,834,242	0	97	138	134	76616	-
	10	3	45	75	10	704,712	1,586,774,580	782,403	11,479,280	0	101	210	148	72326	-
	10	3	50	74	8	667,403	1,068,268,766	742,491	10,245,532	0	90	109	121	70565	-
	10	3	50	71	7	642,359	995,380,953	712,249	9,780,945	0	83	94	111	65894	-
	10	3	45	69	8	655,535	1,452,838,258	723,613	10,624,442	0	87	184	129	63539	-
	10	3	55	79	8	618,771	833,750,463	696,773	9,201,050	0	76	63	98	72665	-
	10	3	55	76	7	607,300	750,310,851	681,183	8,901,165	0	73	47	92	69630	-
	10	3	45	66	7	614,689	1,394,869,637	677,239	10,004,383	0	75	172	116	57774	-
	10	3	55	70	5	555,147	592,314,553	618,020	7,901,249	0	58	16	70	59730	-
	10	3	50	65	5	557,050	865,773,932	614,793	8,406,382	0	59	69	81	53501	-
	10	3	60	81	7	511,883	672,359,371	587,074	7,349,506	0*	46	31	58	67378	-
	10	3	60	75	5	487,855	496,380,554	554,500	6,712,099	0*	39	-3	45	60979	-
	10	3	45	60	5	495,488	1,271,389,179	546,082	8,306,459	0	41	148	79	43868	-
	10	3	55	64	3	448,274	462,275,645	497,758	6,212,031	0*	28	-10	34	44965	-
	10	3	60	69	3	418,359	335,033,755	472,381	5,500,475	0*	19	-35	19	48630	-
	10	3	50	59	3	414,833	728,871,279	459,007	6,349,948	0*	18	42	37	37485	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	10	3	65	80	5	373,947	569,414,230	443,045	5,496,182	0*	6	11	19	56626	-
	10	3	65	74	3	338,594	376,439,372	397,295	4,657,950	0*	-4	-26	0	48047	-
	10	3	45	54	3	336,341	1,064,714,167	373,269	5,983,644	0*	-4	108	29	28372	-
	10	3	70	79	3	233,446	537,708,524	293,457	3,647,597	1*	-34	5	-21	42708	-
	10	4	45	81	9	634,650	1,531,006,698	723,683	8,436,251	0	81	199	82	70096	-
	10	4	45	77	8	626,646	1,434,333,688	710,842	8,176,163	0	78	180	76	67303	-
	10	4	50	82	8	608,340	1,151,702,200	696,295	7,668,753	0	73	125	65	70213	-
Optimised (Max NHB) with expanded capacity (C)	10	4	50	74	6	584,285	952,705,745	661,351	7,065,385	0*	66	86	52	63306	-
	10	4	45	69	6	572,330	1,253,621,886	642,319	7,358,045	0	63	145	59	56515	-
	10	4	50	70	5	551,155	857,413,543	619,985	6,583,323	0*	57	67	42	56997	-
	10	4	55	79	6	544,582	776,942,952	625,176	6,502,716	0*	55	52	40	65848	-
	10	4	55	75	5	528,949	668,137,370	603,165	6,145,744	0*	51	30	33	61562	-
	10	4	55	71	4	496,870	565,688,439	562,802	5,638,202	0*	41	10	22	55137	-
	10	4	45	65	5	519,871	1,181,088,410	581,174	6,735,302	0*	48	131	45	48901	-
	10	4	50	66	4	499,193	777,776,913	558,903	5,939,650	0*	42	52	28	49088	-
	10	4	60	80	5	463,505	673,509,708	540,643	5,576,630	0*	32	32	20	63020	-
	10	4	55	67	3	446,037	480,511,662	502,330	4,955,736	0*	27	-6	7	46886	-
	10	4	60	76	4	436,522	507,372,483	506,403	4,870,522	0*	24	-1	5	56323	-
	10	4	45	61	4	448,757	1,108,387,476	500,926	5,947,920	0*	28	116	28	40349	-
	10	4	50	62	3	426,384	706,498,688	476,562	5,116,824	0*	21	38	10	39950	-
Max NHB with cost saving (A)	10	4	60	72	3	405,847	396,797,580	467,287	4,368,403	1*	16	-23	-6	49801	-
	10	4	45	57	3	360,844	1,016,977,789	403,308	4,981,988	0*	3	99	7	31139	-
	10	4	65	81	4	332,405	587,973,994	403,421	3,962,115	1*	-5	15	-15	52048	-
	10	4	65	77	3	320,785	463,363,110	385,414	3,600,857	1*	-9	-10	-22	48142	-
	10	4	70	82	3	214,632	620,130,770	278,324	2,922,624	1*	-39	21	-37	41424	-
	10	5	45	80	7	567,502	1,377,043,855	655,746	6,461,558	0*	62	169	39	63939	-
	10	5	45	75	6	554,118	1,254,714,856	635,199	6,148,904	0*	58	145	33	59754	-
	10	5	50	80	6	540,902	1,032,069,961	626,544	5,752,420	0*	54	102	24	63240	-
	10	5	50	75	5	526,696	904,318,681	604,872	5,421,222	0*	50	77	17	58823	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	10	5	45	70	5	520,726	1,142,045,189	592,025	5,703,863	0*	48	123	23	52903	-
	10	5	50	70	4	490,702	786,836,047	558,424	4,950,911	0*	40	54	7	51481	-
	10	5	55	80	5	487,965	773,449,220	569,219	4,900,614	0*	39	51	6	60535	-
Max NHB within capacity (B)	10	5	55	75	4	472,789	638,614,456	546,134	4,549,020	1*	35	25	-2	55821	-
	10	5	45	65	4	463,521	1,052,653,478	523,459	5,110,920	0*	32	106	10	44059	-
	10	5	55	70	3	434,759	515,284,785	497,073	4,045,291	1*	24	1	-13	48018	-
	10	5	50	65	3	430,174	692,863,637	485,786	4,316,919	1*	22	35	-7	42091	-
	10	5	60	80	4	403,866	618,230,470	479,923	3,991,031	1*	15	21	-14	55257	-
	10	5	60	75	3	387,639	475,577,032	455,246	3,611,471	1*	10	-7	-22	50212	-
	10	5	55	65	2	369,220	419,017,019	418,820	3,355,957	1*	5	-18	-28	37875	-
	10	5	45	60	3	379,983	974,232,295	428,176	4,348,822	1*	8	90	-6	33938	-
	10	5	60	70	2	345,527	343,881,706	401,089	3,055,984	1*	-2	-33	-34	41599	-
	10	5	50	60	2	340,757	610,099,492	383,614	3,492,848	1*	-3	19	-25	31208	-
	10	5	65	80	3	298,932	551,237,692	367,609	3,067,574	1*	-15	8	-34	47215	-
	10	5	65	75	2	280,903	395,944,154	340,307	2,649,399	1*	-20	-23	-43	41626	-
	10	5	45	55	2	277,658	860,510,920	313,313	3,400,608	1*	-21	68	-27	23507	-
	10	5	70	80	2	193,019	539,979,484	252,102	2,185,244	1*	-45	5	-53	36944	-
	15	1	50	80	30	885,609	2,150,147,793	953,719	33,945,738	0	152	320	632	91214	-
	15	1	50	75	25	867,906	2,008,183,578	933,175	33,209,233	0	147	292	616	87381	-
	15	1	45	80	35	909,275	3,096,192,914	981,570	36,997,989	0	159	505	698	89670	-
	15	1	45	75	30	893,801	2,975,861,303	963,697	36,367,643	0	154	481	684	86358	-
	15	1	55	80	25	806,697	1,454,368,293	871,536	29,286,716	0	130	184	532	88908	-
	15	1	50	70	20	825,582	1,839,383,141	886,891	31,474,667	0	135	259	579	80478	-
	15	1	55	75	20	785,530	1,290,065,772	847,062	28,422,491	0	124	152	513	84364	-
	15	1	45	70	25	858,183	2,828,337,696	924,693	34,884,576	0	144	452	652	80529	-
	15	1	55	70	15	735,743	1,092,206,037	792,666	26,337,881	0	109	113	468	76246	-
	15	1	50	65	15	744,930	1,635,877,295	801,275	28,269,083	0	112	219	510	69977	-
	15	1	45	65	20	789,294	2,652,234,312	851,586	32,203,284	0	125	418	594	71565	-
	15	1	60	80	20	661,581	1,030,873,996	725,098	23,405,975	0	88	101	405	81205	-
	15	1	60	75	15	636,347	838,312,463	695,923	22,365,533	0	81	64	382	75775	-
	15	1	55	65	10	636,977	863,045,712	688,211	22,370,084	0	81	69	382	63363	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	15	1	45	60	15	676,617	2,406,521,360	733,203	27,929,697	0	93	370	502	59346	-
	15	1	60	70	10	575,369	611,537,554	629,627	19,751,682	0	64	19	326	65789	-
	15	1	50	60	10	608,386	1,362,001,589	658,568	23,056,080	0	73	166	397	55258	-
	15	1	65	80	15	485,781	819,627,956	547,921	16,859,864	0	38	60	264	69125	-
	15	1	65	75	10	454,262	594,450,072	511,730	15,551,819	0	29	16	235	62400	-
	15	1	45	55	10	514,212	2,022,129,051	562,876	21,745,446	0	46	295	369	43977	-
	15	1	70	80	10	308,442	738,697,957	367,287	10,255,080	0	-12	44	121	53668	-
	15	2	45	81	18	769,895	2,057,488,235	866,988	16,469,886	0	119	302	255	82096	-
	15	2	50	80	15	735,548	1,444,113,899	828,418	14,659,237	0	109	182	216	80981	-
	15	2	50	76	13	720,404	1,331,638,049	808,151	14,272,441	0	105	160	208	77073	-
	15	2	45	75	15	748,095	1,906,034,325	838,300	15,923,283	0	113	272	243	76607	-
	15	2	45	71	13	714,781	1,805,924,149	798,669	15,240,898	0	103	253	229	70577	-
	15	2	50	70	10	666,327	1,162,201,939	743,307	13,144,397	0	90	127	183	67312	-
	15	2	55	81	13	659,853	1,041,042,150	748,216	12,485,887	0	88	103	169	78057	-
	15	2	55	75	10	634,338	861,730,404	714,472	11,826,790	0	81	68	155	71631	-
	15	2	55	71	8	594,817	741,262,291	667,374	10,988,441	0	69	45	137	64400	-
	15	2	50	66	8	604,039	1,056,495,208	672,376	11,907,407	0	72	106	157	58434	-
	15	2	45	65	10	628,902	1,653,603,954	700,933	13,568,232	0	79	223	193	58487	-
	15	2	60	80	10	536,426	758,965,359	618,290	9,762,195	0	53	48	111	70055	-
	15	2	60	76	8	517,214	629,615,563	593,155	9,284,595	0	47	23	100	65221	-
	15	2	45	61	8	543,137	1,537,128,469	606,097	11,945,313	0	55	200	158	48672	-
	15	2	55	65	5	487,200	574,426,306	545,444	8,849,283	0	39	12	91	49260	-
	15	2	60	70	5	448,983	437,705,016	512,184	7,818,209	0	28	-15	69	52886	-
	15	2	50	60	5	457,516	879,019,251	511,038	9,151,145	0	30	72	97	41763	-
	15	2	65	81	8	394,528	679,425,721	470,680	7,203,415	0*	12	33	55	60278	-
	15	2	65	75	5	360,621	467,362,112	426,770	6,333,236	0*	3	-9	37	51867	-
	15	2	70	80	5	246,441	621,060,326	311,652	4,408,740	1*	-30	21	-5	45548	-
	15	3	45	81	12	654,996	1,668,914,859	758,141	9,672,427	0	86	226	109	72921	-
	15	3	50	80	10	622,256	1,215,320,565	721,865	8,633,988	0	77	137	86	71484	-
	15	3	45	75	10	634,516	1,511,280,937	728,699	9,238,874	0	81	195	99	67204	-
	15	3	50	74	8	595,642	1,048,632,964	684,959	8,122,393	0	70	105	75	64642	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	15	3	50	71	7	569,044	970,156,138	651,535	7,726,530	0	62	89	67	59587	-
	15	3	45	69	8	581,541	1,365,423,262	662,702	8,491,548	0	66	167	83	57518	-
	15	3	55	79	8	552,602	863,361,916	644,772	7,287,037	0*	57	69	57	67280	-
	15	3	55	76	7	540,168	773,172,576	627,024	7,025,457	0*	54	51	52	63851	-
	15	3	45	66	7	539,799	1,301,237,031	613,332	7,958,937	0	54	154	72	51482	-
	15	3	55	70	5	486,313	608,400,875	559,145	6,175,313	0*	38	19	33	53338	-
	15	3	50	65	5	483,671	833,700,767	550,290	6,576,703	0*	38	63	42	46919	-
	15	3	60	81	7	455,233	725,558,064	542,265	5,754,683	0*	30	42	24	62293	-
	15	3	60	75	5	429,959	538,913,629	506,230	5,213,198	0*	22	5	12	55299	-
	15	3	45	60	5	424,329	1,165,742,248	481,554	6,528,285	0*	21	128	41	37810	-
	15	3	60	69	3	360,768	372,266,673	421,118	4,217,763	1*	3	-27	-9	42697	-
	15	3	50	59	3	349,544	687,213,972	398,164	4,895,446	0*	-1	34	6	31661	-
	15	3	65	80	5	330,490	611,984,366	407,183	4,217,313	1*	-6	20	-9	51943	-
	15	3	65	74	3	294,840	410,584,241	358,689	3,531,481	1*	-16	-20	-24	42955	-
	15	3	45	54	3	277,111	958,068,240	316,672	4,626,028	1*	-21	87	0	23437	-
	15	3	70	79	3	205,265	553,679,707	268,574	2,785,162	1*	-42	8	-40	38809	-
	15	4	45	81	9	565,662	1,471,592,383	668,389	6,610,138	0*	61	187	43	65037	-
	15	4	45	77	8	557,114	1,363,847,459	653,778	6,382,786	0*	59	166	38	61887	-
	15	4	50	82	8	539,523	1,148,231,612	640,315	5,979,136	0*	54	124	29	64797	-
	15	4	50	74	6	514,302	930,422,368	601,613	5,461,626	0*	46	82	18	57237	-
	15	4	45	69	6	500,831	1,167,339,795	579,731	5,697,125	0*	43	128	23	50403	-
	15	4	55	79	6	480,199	803,947,912	571,221	5,018,591	0*	37	57	8	60113	-
	15	4	50	70	5	480,940	829,351,044	558,268	5,064,781	0*	37	62	9	50717	-
	15	4	55	75	5	463,990	687,933,364	547,314	4,716,996	0*	32	34	2	55511	-
	15	4	55	71	4	431,832	580,051,619	505,190	4,300,085	1*	23	13	-7	48887	-
	15	4	45	65	5	449,429	1,088,037,055	517,452	5,190,493	0*	28	113	12	42795	-
	15	4	50	66	4	430,390	743,983,212	496,577	4,544,728	1*	23	45	-2	42868	-
	15	4	60	80	5	409,263	716,240,120	495,611	4,262,037	1*	16	40	-8	57888	-
	15	4	55	67	3	383,196	488,753,783	445,081	3,753,314	1*	9	-5	-19	40854	-
	15	4	60	76	4	381,041	542,421,244	457,915	3,668,694	1*	8	6	-21	50628	-
	15	4	45	61	4	380,945	1,009,566,034	437,560	4,554,086	1*	8	97	-2	34476	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	15	4	60	72	3	350,936	427,059,057	417,828	3,268,939	1*	0	-17	-30	44028	-
	15	4	50	62	3	361,793	665,847,270	416,182	3,888,870	1*	3	30	-16	34122	-
	15	4	65	81	4	290,888	623,243,466	367,405	2,992,424	1*	-17	22	-35	47367	-
	15	4	65	77	3	279,325	493,845,071	348,431	2,696,038	1*	-20	-4	-42	43293	-
	15	4	45	57	3	300,105	914,686,502	344,989	3,789,925	1*	-15	79	-18	25950	-
	15	4	70	82	3	188,010	629,273,922	254,155	2,207,244	1*	-46	23	-52	37695	-
	15	5	45	80	7	500,610	1,313,850,021	598,861	4,935,619	0*	42	157	6	58544	-
	15	5	45	75	6	486,677	1,180,942,028	576,383	4,673,051	0*	39	131	1	54020	-
	15	5	50	80	6	475,679	1,015,483,005	570,519	4,357,665	1*	35	98	-6	57598	-
	15	5	50	75	5	461,277	878,718,250	547,342	4,083,026	1*	31	72	-12	52912	-
	15	5	45	70	5	452,904	1,060,740,744	531,053	4,315,689	1*	29	107	-7	46903	-
	15	5	50	70	4	425,468	755,918,185	499,406	3,709,683	1*	21	48	-20	45441	-
	15	5	55	80	5	427,034	791,205,827	516,150	3,678,713	1*	22	55	-21	54882	-
	15	5	55	75	4	411,822	648,100,598	491,754	3,390,299	1*	17	27	-27	49954	-
	15	5	45	65	4	397,544	963,129,558	462,149	3,850,646	1*	13	88	-17	38189	-
	15	5	55	70	3	374,489	519,908,398	441,748	2,996,199	1*	7	2	-35	42111	-
	15	5	50	65	3	368,194	654,927,801	428,023	3,220,490	1*	5	28	-31	36373	-
	15	5	60	80	4	351,784	648,620,717	433,826	2,968,500	1*	0	27	-36	49887	-
	15	5	60	75	3	335,822	500,117,407	408,271	2,661,968	1*	-4	-2	-43	44712	-
	15	5	55	65	2	313,534	416,472,620	366,077	2,467,491	1*	-11	-19	-47	32476	-
	15	5	60	70	2	295,579	363,502,321	354,389	2,231,746	1*	-16	-29	-52	36253	-
	15	5	45	60	3	320,413	876,017,339	371,037	3,261,336	1*	-9	71	-30	28709	-
	15	5	50	60	2	286,035	566,190,578	331,010	2,592,360	1*	-19	11	-44	26281	-
	15	5	65	80	3	260,180	573,602,400	332,360	2,262,391	1*	-26	12	-51	42537	-
	15	5	65	75	2	242,585	414,119,308	304,378	1,928,911	1*	-31	-19	-58	36913	-
	15	5	45	55	2	228,575	762,681,838	265,001	2,533,203	1*	-35	49	-45	19317	-
	15	5	70	80	2	167,463	544,126,708	227,634	1,604,568	1*	-52	6	-65	33141	-
	20	1	50	80	30	852,468	2,137,772,800	936,679	31,270,289	0	143	318	574	90065	-
	20	1	45	80	35	885,735	3,034,168,533	974,716	34,532,939	0	152	493	645	89853	-
	20	1	50	75	25	831,254	1,977,549,582	911,352	30,529,828	0	137	286	558	85376	-
	20	1	45	75	30	866,195	2,892,364,773	951,525	33,874,407	0	147	465	630	85600	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	20	1	55	80	25	770,114	1,463,537,276	848,658	26,629,041	0	119	186	474	86886	-
	20	1	50	70	20	783,162	1,796,565,424	857,576	28,791,947	0	123	251	521	77425	-
	20	1	45	70	25	823,919	2,728,765,832	904,221	32,336,009	0	135	433	597	78605	-
	20	1	55	75	20	745,519	1,285,609,223	819,447	25,791,141	0	112	151	456	81503	-
	20	1	55	70	15	690,314	1,082,003,696	757,769	23,771,829	0	96	111	413	72395	-
	20	1	45	65	20	747,052	2,538,769,756	820,740	29,602,790	0	113	396	538	68491	-
	20	1	50	65	15	696,137	1,586,715,984	763,108	25,638,880	0	98	210	453	65967	-
	20	1	60	80	20	628,827	1,046,992,635	702,983	21,013,052	0	79	104	353	78830	-
	20	1	60	75	15	600,425	845,461,430	669,287	20,034,408	0	71	65	332	72598	-
	20	1	55	65	10	587,417	854,814,872	646,616	19,986,146	0	67	67	331	58873	-
	20	1	45	60	15	626,993	2,286,176,874	692,304	25,371,453	0	78	347	447	55449	-
	20	1	60	70	10	535,732	620,132,854	597,265	17,574,762	0	52	21	279	61865	-
	20	1	50	60	10	556,406	1,310,091,119	613,898	20,631,714	0	58	156	345	50837	-
	20	1	65	80	15	459,805	824,824,424	528,854	14,907,893	0	31	61	221	66734	-
	20	1	65	75	10	425,413	598,496,206	488,396	13,709,428	0	21	17	196	59277	-
	20	1	45	55	10	463,401	1,898,756,805	517,279	19,430,262	0	32	271	319	39932	-
	20	1	70	80	10	290,429	732,131,472	352,853	8,897,294	0	-17	43	92	51494	-
	20	2	45	81	18	724,960	1,988,589,847	831,857	14,389,148	0	106	288	210	79212	-
	20	2	50	80	15	688,245	1,421,745,756	790,096	12,688,793	0	96	178	174	77462	-
	20	2	45	75	15	701,142	1,822,288,770	799,504	13,880,229	0	100	256	199	73080	-
	20	2	50	76	13	671,671	1,301,914,981	767,360	12,337,457	0	91	154	166	73122	-
	20	2	45	71	13	665,798	1,714,704,364	756,367	13,247,347	0	90	235	186	66590	-
	20	2	55	81	13	614,810	1,045,720,282	710,900	10,765,996	0	75	104	132	74397	-
	20	2	50	70	10	615,550	1,124,458,783	698,461	11,314,090	0	75	120	144	62797	-
Initial recommendation Policy (1)	20	2	55	75	10	587,514	857,478,098	673,872	10,169,898	0	67	67	119	67404	-
	20	2	55	71	8	547,167	732,966,124	624,463	9,416,543	0	56	43	103	59881	-
	20	2	50	66	8	552,972	1,016,800,276	625,753	10,204,053	0	57	99	120	53825	-
	20	2	45	65	10	577,236	1,557,853,051	653,501	11,711,980	0	64	204	153	53969	-
	20	2	60	80	10	498,556	769,646,702	585,738	8,330,943	0	42	50	80	66450	-
	20	2	60	76	8	478,611	635,781,678	558,864	7,909,959	0	36	24	71	61314	-
	20	2	45	61	8	492,305	1,439,698,235	557,923	10,246,097	0	40	181	121	44231	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	20	2	55	65	5	441,059	566,241,695	501,764	7,522,059	0	26	11	62	44824	-
Age Restriction (2)	20	2	60	70	5	409,868	444,216,122	475,514	6,624,968	0*	17	-13	43	48722	-
	20	2	50	60	5	409,843	837,441,676	465,066	7,757,511	0	17	64	67	37442	-
	20	2	65	81	8	366,110	691,292,756	445,665	6,114,863	0*	4	35	32	57065	-
	20	2	65	75	5	331,474	474,925,597	399,499	5,353,641	0*	-6	-7	15	48311	-
	20	2	45	55	5	331,722	1,182,725,297	378,856	7,378,623	0	-6	131	59	28389	-
	20	2	70	80	5	227,516	620,666,855	293,741	3,680,243	1*	-35	21	-21	42862	-
	20	3	45	81	12	607,692	1,602,741,230	715,814	8,191,639	0	73	213	77	69124	-
	20	3	45	75	10	586,140	1,435,413,852	684,020	7,802,609	0	67	180	68	63012	-
	20	3	50	80	10	573,034	1,187,605,873	677,014	7,245,190	0*	63	132	56	67280	-
	20	3	50	74	8	545,705	1,012,911,190	638,103	6,797,736	0*	55	98	47	60130	-
	20	3	50	71	7	518,994	932,863,224	603,854	6,455,159	0*	48	82	39	54974	-
	20	3	45	69	8	532,373	1,284,455,158	615,734	7,145,554	0*	52	151	54	53061	-
	20	3	55	79	8	507,917	860,102,287	603,449	6,116,034	0*	45	68	32	62996	-
	20	3	55	76	7	495,267	765,764,419	584,838	5,886,280	0*	41	50	27	59427	-
	20	3	45	66	7	491,009	1,218,944,942	565,913	6,679,975	0*	40	138	44	47027	-
	20	3	55	70	5	441,427	597,831,530	515,566	5,149,904	0*	26	17	11	48819	-
	20	3	50	65	5	435,109	794,212,550	502,525	5,467,080	0*	24	55	18	42417	-
	20	3	60	81	7	417,952	734,013,070	507,384	4,801,017	0*	19	43	4	58364	-
	20	3	60	75	5	392,721	542,333,555	470,338	4,332,590	1*	12	6	-7	51190	-
	20	3	55	64	3	342,454	461,181,246	397,826	3,965,106	1*	-3	-10	-14	34751	-
	20	3	60	69	3	325,039	373,273,737	385,321	3,483,854	1*	-7	-27	-25	38745	-
	20	3	50	59	3	308,809	645,763,766	356,699	4,037,432	1*	-12	26	-13	27960	-
	20	3	65	80	5	302,956	615,758,970	380,449	3,476,636	1*	-14	20	-25	48500	-
	20	3	65	74	3	267,897	412,000,819	331,476	2,894,658	1*	-24	-20	-38	39468	-
	20	3	45	54	3	242,022	876,139,858	280,040	3,813,237	1*	-31	71	-18	20336	-
	20	3	70	79	3	187,467	547,161,952	249,992	2,295,719	1*	-47	7	-50	36030	-
	20	4	45	81	9	518,792	1,402,355,729	623,252	5,478,181	0*	48	174	18	60870	-
	20	4	45	77	8	510,013	1,290,070,987	607,841	5,277,742	0*	45	152	14	57568	-
	20	4	50	82	8	492,892	1,114,880,456	595,250	4,951,755	0*	40	118	7	60489	-
	20	4	50	74	6	467,483	889,451,220	555,250	4,500,392	1*	33	74	-3	52741	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	20	4	45	69	6	454,086	1,087,994,374	532,793	4,690,172	0*	29	112	1	45994	-
	20	4	55	79	6	437,789	792,559,390	529,734	4,139,237	1*	25	55	-11	55772	-
	20	4	50	70	5	434,544	786,324,715	511,679	4,162,676	1*	24	54	-10	46247	-
	20	4	55	75	5	421,753	673,983,811	505,463	3,879,373	1*	20	32	-16	51120	-
	20	4	55	71	4	390,248	564,980,505	463,329	3,525,942	1*	11	10	-24	44543	-
	20	4	45	65	5	404,356	1,006,910,833	471,470	4,261,725	1*	15	97	-8	38577	-
	20	4	50	66	4	385,926	700,220,442	451,316	3,725,365	1*	10	37	-20	38629	-
	20	4	60	80	5	374,464	717,183,825	461,673	3,496,816	1*	7	40	-25	54025	-
	20	4	55	67	3	343,670	473,498,944	404,714	3,066,955	1*	-2	-8	-34	36785	-
	20	4	60	76	4	346,466	537,687,313	422,999	2,985,970	1*	-1	5	-36	46645	-
	20	4	60	72	3	317,008	422,078,644	383,054	2,651,791	1*	-10	-18	-43	40116	-
	20	4	45	61	4	339,054	929,166,460	394,222	3,726,084	1*	-3	81	-20	30612	-
	20	4	50	62	3	321,181	622,274,818	374,224	3,175,748	1*	-9	22	-32	30312	-
	20	4	65	81	4	265,039	620,584,899	340,918	2,440,677	1*	-25	21	-47	43923	-
	20	4	65	77	3	253,707	490,041,966	321,785	2,188,537	1*	-28	-4	-53	39852	-
	20	4	45	57	3	264,302	834,617,702	307,287	3,090,030	1*	-25	63	-33	22711	-
	20	4	70	82	3	170,983	617,294,374	235,626	1,804,350	1*	-51	21	-61	34896	-
	20	5	45	80	7	455,853	1,243,592,264	553,786	4,020,546	1*	30	143	-13	54291	-
	20	5	45	75	6	441,807	1,108,012,569	530,714	3,795,396	1*	26	116	-18	49676	-
	20	5	50	80	6	431,501	977,626,063	525,971	3,538,069	1*	23	91	-24	53195	-
	20	5	50	75	5	417,301	837,930,527	502,525	3,303,644	1*	19	64	-29	48484	-
	20	5	45	70	5	408,630	986,434,727	485,418	3,497,136	1*	16	93	-25	42635	-
	20	5	55	80	5	387,642	773,856,182	476,197	2,975,623	1*	10	51	-36	50665	-
	20	5	50	70	4	382,544	713,081,177	455,132	2,992,787	1*	9	39	-35	41164	-
	20	5	55	75	4	372,872	628,937,138	451,911	2,731,046	1*	6	23	-41	45790	-
	20	5	55	70	3	336,584	501,385,392	402,539	2,406,805	1*	-4	-2	-48	38104	-
	20	5	45	65	4	355,563	887,926,065	418,301	3,114,082	1*	1	73	-33	34222	-
	20	5	50	65	3	328,183	612,000,911	386,348	2,592,142	1*	-7	20	-44	32496	-
	20	5	60	80	4	319,227	638,731,511	400,067	2,392,408	1*	-9	25	-48	46050	-
	20	5	60	75	3	303,575	488,947,559	374,426	2,132,932	1*	-14	-5	-54	40899	-
	20	5	55	65	2	279,206	397,977,075	330,092	1,976,801	1*	-21	-22	-57	28966	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	20	5	60	70	2	264,818	353,748,083	321,707	1,780,406	1*	-25	-31	-62	32688	-
	20	5	45	60	3	283,754	799,465,759	332,116	2,630,256	1*	-19	56	-43	25342	-
	20	5	50	60	2	251,933	522,159,389	294,910	2,083,252	1*	-28	2	-55	23117	-
	20	5	65	80	3	235,818	562,593,335	306,231	1,813,703	1*	-33	10	-61	39163	-
	20	5	65	75	2	218,843	403,992,113	278,602	1,534,452	1*	-38	-21	-67	33645	-
	20	5	45	55	2	199,724	689,374,791	233,929	2,033,822	1*	-43	35	-56	16758	-
	20	5	70	80	2	151,559	526,025,077	209,483	1,284,537	1*	-57	3	-72	30427	-
	30	1	50	80	30	821,429	2,156,508,902	924,037	28,007,745	0	134	321	504	88939	-
	30	1	45	80	35	861,614	3,015,420,600	970,052	31,244,767	0	145	489	574	89680	-
	30	1	50	75	25	796,496	1,981,667,521	893,397	27,296,663	0	127	287	489	83311	-
	30	1	45	75	30	838,437	2,855,198,793	941,664	30,596,676	0	139	458	560	84505	-
	30	1	55	80	25	737,501	1,497,042,428	831,821	23,638,436	0	110	192	410	85153	-
	30	1	45	70	25	789,739	2,677,339,792	885,597	29,083,690	0	125	423	527	76368	-
	30	1	50	70	20	743,143	1,789,477,510	832,059	25,625,686	0	112	249	453	74360	-
	30	1	55	75	20	709,723	1,307,005,465	797,834	22,852,408	0	102	155	393	78904	-
	30	1	55	70	15	649,986	1,096,698,020	729,250	20,961,469	0	85	114	352	68936	-
	30	1	45	65	20	705,865	2,475,340,477	792,134	26,432,829	0	101	383	470	65249	-
	30	1	50	65	15	650,563	1,570,617,520	728,818	22,649,850	0	85	207	388	62086	-
	30	1	60	80	20	599,444	1,083,990,558	686,335	18,470,008	0	71	112	298	76802	-
	30	1	60	75	15	568,154	874,202,124	648,058	17,575,158	0	62	71	279	69788	-
	30	1	55	65	10	543,570	870,248,079	611,577	17,472,616	0	55	70	277	54879	-
	30	1	45	60	15	581,588	2,211,379,444	656,010	22,427,299	0	66	332	384	51667	-
	30	1	60	70	10	499,949	649,146,776	570,158	15,327,192	0	42	27	231	58353	-
	30	1	50	60	10	510,105	1,288,055,672	575,166	18,033,736	0	45	152	289	46774	-
	30	1	65	80	15	436,718	850,829,582	514,628	12,959,958	0	24	66	179	64738	-
	30	1	65	75	10	399,869	622,268,209	470,060	11,886,997	0	14	22	156	56598	-
	30	1	45	55	10	419,789	1,816,904,748	478,951	16,960,210	0	19	255	266	36281	-
	30	1	70	80	10	274,335	745,348,669	342,071	7,626,031	0	-22	46	64	49674	-
	30	2	45	81	18	690,163	1,962,236,298	811,561	12,336,037	0	96	283	166	77354	-
	30	2	50	80	15	650,493	1,429,284,981	765,424	10,781,262	0	85	179	132	75012	-
	30	2	45	75	15	664,462	1,780,535,838	775,328	11,875,157	0	89	248	156	70539	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
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	30	2	50	76	13	632,610	1,301,083,286	740,122	10,470,691	0	80	154	126	70243	-
	30	2	45	71	13	627,306	1,665,398,540	728,625	11,305,367	0	79	225	144	63593	-
	30	2	55	81	13	580,183	1,077,242,242	688,198	9,130,679	0	65	110	97	71934	-
	30	2	50	70	10	574,408	1,115,559,506	666,631	9,572,835	0	64	118	106	59310	-
	30	2	55	75	10	551,440	879,134,937	647,906	8,605,265	0	57	72	86	64381	-
	30	2	55	71	8	509,958	750,754,394	595,739	7,942,711	0	45	47	71	56544	-
	30	2	45	65	10	536,485	1,500,552,285	620,361	9,942,069	0	53	193	114	50523	-
	30	2	50	66	8	511,332	1,003,830,729	591,408	8,602,124	0	46	96	86	50152	-
	30	2	60	80	10	468,365	806,004,709	564,866	6,991,978	0*	33	57	51	63960	-
	30	2	60	76	8	447,648	666,088,528	535,990	6,629,173	0*	27	30	43	58484	-
	30	2	45	61	8	452,061	1,376,256,330	522,945	8,654,539	0	29	169	87	40752	-
	30	2	55	65	5	404,956	578,532,013	471,177	6,302,288	0*	15	13	36	41462	-
	30	2	50	60	5	372,630	816,978,413	431,851	6,488,748	0*	6	60	40	34105	-
	30	2	65	81	8	342,912	723,060,020	429,076	5,128,835	0*	-2	41	11	54791	-
	30	2	65	75	5	307,737	501,663,730	380,702	4,471,702	1*	-12	-2	-4	45682	-
	30	2	45	55	5	298,611	1,116,709,025	347,950	6,172,804	0*	-15	118	33	25527	-
	30	2	70	80	5	212,419	636,935,832	282,176	3,042,105	1*	-40	24	-34	40954	-
	30	3	45	81	12	571,312	1,582,020,522	690,241	6,823,550	0*	63	209	47	66678	-
	30	3	45	75	10	549,025	1,403,093,384	656,199	6,482,618	0*	56	174	40	60176	-
	30	3	50	80	10	536,965	1,192,567,897	650,613	5,978,095	0*	53	133	29	64574	-
	30	3	50	74	8	508,913	1,007,716,600	609,363	5,595,304	0*	45	97	21	57058	-
	30	3	50	71	7	482,100	924,248,271	573,994	5,308,497	0*	37	81	14	51784	-
	30	3	45	69	8	494,506	1,242,906,644	584,924	5,920,596	0*	41	143	28	49881	-
	30	3	55	79	8	474,764	884,232,458	578,626	5,054,431	0*	35	73	9	60163	-
	30	3	55	76	7	461,929	785,594,381	559,063	4,856,016	0*	31	53	5	56423	-
	30	3	45	66	7	453,534	1,173,939,824	534,339	5,525,443	0*	29	129	19	43830	-
	30	3	55	70	5	408,468	609,800,187	488,270	4,231,905	1*	16	19	-9	45708	-
	30	3	50	65	5	399,519	779,488,505	471,727	4,481,907	1*	14	52	-3	39253	-
	30	3	60	81	7	390,015	764,980,767	486,404	3,949,507	1*	11	49	-15	55838	-
	30	3	60	75	5	364,506	566,305,643	447,694	3,550,691	1*	4	11	-23	48410	-
	30	3	45	60	5	345,499	1,025,467,262	405,579	4,477,079	1*	-2	100	-3	30836	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	30	3	55	64	3	312,866	464,666,975	371,498	3,242,014	1*	-11	-9	-30	31960	-
	30	3	60	69	3	298,580	390,857,912	362,529	2,839,486	1*	-15	-24	-39	36044	-
	30	3	65	80	5	281,256	642,805,614	363,337	2,821,533	1*	-20	26	-39	46139	-
	30	3	50	59	3	279,287	623,678,992	329,495	3,294,458	1*	-21	22	-29	25361	-
	30	3	65	74	3	246,693	433,903,412	313,510	2,335,910	1*	-30	-15	-50	37014	-
	30	3	45	54	3	217,246	820,101,090	256,358	3,121,184	1*	-38	60	-33	18203	-
	30	3	70	79	3	173,815	559,350,588	238,515	1,874,455	1*	-51	9	-60	34178	-
	30	4	45	81	9	485,172	1,381,260,612	597,915	4,469,030	1*	38	170	-4	58339	-
	30	4	45	77	8	476,253	1,262,890,869	581,654	4,296,090	1*	36	147	-7	54885	-
	30	4	50	82	8	459,281	1,120,375,479	569,345	4,036,691	1*	31	119	-13	57858	-
	30	4	50	74	6	433,635	884,373,588	527,612	3,649,427	1*	23	73	-21	49815	-
	30	4	45	69	6	420,441	1,049,787,901	504,542	3,805,979	1*	20	105	-18	43107	-
	30	4	55	79	6	407,106	812,411,530	505,463	3,359,131	1*	16	59	-28	53008	-
	30	4	50	70	5	401,079	776,649,891	483,317	3,368,980	1*	14	52	-27	43271	-
	30	4	55	75	5	391,233	689,053,266	480,582	3,138,590	1*	11	35	-32	48273	-
	30	4	55	71	4	360,178	576,293,462	437,959	2,844,056	1*	3	13	-39	41676	-
	30	4	45	65	5	372,120	964,125,641	443,359	3,455,207	1*	6	88	-25	35783	-
	30	4	50	66	4	354,391	685,742,490	423,691	3,010,991	1*	1	34	-35	35802	-
	30	4	60	80	5	348,082	742,918,735	440,888	2,815,030	1*	-1	45	-39	51481	-
	30	4	60	76	4	320,248	558,927,187	401,147	2,380,326	1*	-9	9	-49	43954	-
	30	4	55	67	3	315,330	480,123,014	379,898	2,468,629	1*	-10	-6	-47	34088	-
	30	4	60	72	3	291,599	439,425,170	361,112	2,108,221	1*	-17	-14	-55	37473	-
	30	4	45	61	4	309,549	881,119,968	367,470	3,018,571	1*	-12	72	-35	28060	-
	30	4	50	62	3	292,836	602,755,704	348,512	2,563,145	1*	-17	18	-45	27796	-
	30	4	65	81	4	245,065	644,200,728	324,508	1,961,845	1*	-30	26	-58	41672	-
	30	4	65	77	3	234,121	510,082,611	305,167	1,749,797	1*	-33	0	-62	37576	-
	30	4	45	57	3	239,304	782,081,513	283,727	2,498,539	1*	-32	53	-46	20563	-
	30	4	70	82	3	158,678	627,083,981	225,186	1,459,539	1*	-55	22	-69	33200	-
	30	5	45	80	7	423,989	1,218,571,847	527,834	3,216,893	1*	21	138	-31	51647	-
	30	5	45	75	6	410,155	1,076,287,743	504,159	3,026,385	1*	17	110	-35	46940	-
	30	5	50	80	6	400,903	973,934,503	500,920	2,816,100	1*	14	90	-39	50571	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	30	5	50	75	5	386,707	829,028,988	476,730	2,618,974	1*	10	62	-44	45757	-
	30	5	45	70	5	377,314	948,600,075	458,107	2,784,706	1*	7	85	-40	39857	-
	30	5	55	80	5	359,767	785,705,918	453,168	2,355,481	1*	2	53	-49	48082	-
	30	5	50	70	4	352,598	699,827,827	428,996	2,368,127	1*	0	37	-49	38448	-
	30	5	55	75	4	345,140	636,414,920	428,326	2,150,664	1*	-2	24	-54	43140	-
	30	5	55	70	3	309,785	505,081,924	378,952	1,890,437	1*	-12	-1	-59	35529	-
	30	5	45	65	4	326,293	844,769,628	391,877	2,479,922	1*	-7	65	-47	31648	-
	30	5	50	65	3	300,208	594,348,110	361,032	2,051,402	1*	-15	16	-56	29983	-
	30	5	60	80	4	294,955	659,360,629	379,856	1,884,874	1*	-16	29	-59	43576	-
	30	5	60	75	3	279,756	505,329,246	353,944	1,669,199	1*	-20	-1	-64	38403	-
	30	5	55	65	2	255,084	397,186,354	308,124	1,552,132	1*	-27	-22	-67	26703	-
	30	5	60	70	2	242,720	366,222,290	302,057	1,388,352	1*	-31	-28	-70	30390	-
	30	5	45	60	3	258,297	751,697,612	308,291	2,097,984	1*	-26	47	-55	23149	-
	30	5	50	60	2	228,359	500,061,701	272,793	1,652,114	1*	-35	-2	-64	21052	-
	30	5	65	80	3	217,507	580,727,876	290,659	1,426,017	1*	-38	13	-69	37050	-
	30	5	65	75	2	201,048	419,752,243	262,905	1,195,601	1*	-43	-18	-74	31544	-
	30	5	45	55	2	180,286	639,903,271	215,046	1,622,337	1*	-49	25	-65	15087	-
	30	5	70	80	2	139,987	532,381,713	199,106	1,012,628	1*	-60	4	-78	28792	-
	40	1	45	80	35	832,619	3,052,464,257	960,244	28,435,120	0	137	496	513	88954	-
	40	1	50	80	30	789,126	2,216,660,058	909,514	25,324,635	0	125	333	446	87599	-
	40	1	45	75	30	807,232	2,874,636,200	928,022	27,814,462	0	130	461	500	83132	-
	40	1	50	75	25	762,211	2,025,409,463	875,211	24,654,523	0	117	296	432	81370	-
	40	1	55	80	25	705,222	1,572,008,525	815,670	21,201,956	0	101	207	357	83493	-
	40	1	45	70	25	755,446	2,680,188,126	866,548	26,356,454	0	115	423	468	74261	-
	40	1	50	70	20	706,080	1,818,003,589	808,691	23,064,263	0	101	255	397	71760	-
	40	1	55	75	20	675,961	1,367,749,639	778,528	20,470,100	0	92	167	341	76708	-
	40	1	55	70	15	614,202	1,144,177,410	705,391	18,693,886	0	75	123	303	66189	-
	40	1	45	65	20	668,489	2,461,316,708	766,939	23,816,360	0	90	381	414	62553	-
	40	1	50	65	15	612,124	1,583,786,993	700,862	20,254,665	0	74	209	337	59063	-
	40	1	60	80	20	570,830	1,155,392,724	670,782	16,418,853	0	62	126	254	75007	-
	40	1	60	75	15	538,114	934,065,637	629,371	15,594,848	0	53	82	236	67477	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	40	1	55	65	10	507,610	908,056,444	584,358	15,436,071	0	44	77	233	51834	-
	40	1	45	60	15	543,137	2,181,299,070	626,233	20,025,718	0	55	326	332	48674	-
	40	1	60	70	10	468,577	700,087,152	547,562	13,505,046	0	33	37	191	55595	-
	40	1	50	60	10	472,981	1,289,888,754	545,047	15,949,416	0	35	152	244	43732	-
	40	1	65	80	15	414,622	907,530,530	501,976	11,392,054	0	18	77	146	63027	-
	40	1	70	80	10	258,567	784,410,431	332,341	6,591,084	0*	-26	53	42	48098	-
	40	2	45	81	18	655,958	1,987,993,976	791,885	10,692,841	0	87	288	131	75522	-
	40	2	50	80	15	616,114	1,476,017,951	744,324	9,272,862	0	75	188	100	72889	-
	40	2	45	75	15	629,462	1,789,408,620	752,968	10,275,675	0	79	249	122	68279	-
	40	2	50	76	13	597,929	1,337,974,121	717,519	8,995,656	0	70	161	94	67868	-
	40	2	45	71	13	592,013	1,664,467,966	704,295	9,761,274	0	69	225	110	61069	-
	40	2	55	81	13	546,962	1,142,842,270	667,229	7,823,192	0	56	123	69	69728	-
	40	2	50	70	10	539,402	1,138,526,000	641,262	8,196,846	0	54	122	77	56609	-
Planned age expansion (4)	40	2	55	75	10	517,847	931,519,640	624,837	7,353,689	0	47	82	59	61825	-
	40	2	55	71	8	476,397	794,499,796	571,042	6,765,404	0*	36	55	46	53821	-
	40	2	45	65	10	501,981	1,482,074,552	593,623	8,540,432	0	43	189	84	47830	-
	40	2	50	66	8	477,087	1,016,536,462	564,701	7,336,756	0*	36	99	58	47380	-
	40	2	60	80	10	440,117	870,995,011	546,537	5,921,862	0*	25	70	28	61790	-
	40	2	60	76	8	419,271	722,327,245	516,347	5,603,145	0*	19	41	21	56114	-
	40	2	45	61	8	419,106	1,349,638,689	495,535	7,393,963	0	19	164	59	38075	-
	40	2	55	65	5	373,877	607,865,205	445,859	5,321,750	0*	6	19	15	38812	-
Current Policy (3)	40	2	60	70	5	351,316	512,011,709	428,784	4,637,215	0*	0	0	0	43142	-
	40	2	50	60	5	343,514	814,710,211	406,885	5,486,305	0*	-2	59	18	31679	-
	40	2	65	81	8	321,310	779,250,054	414,845	4,319,051	1*	-9	52	-7	52830	-
	40	2	65	75	5	286,568	546,414,128	365,124	3,740,782	1*	-18	7	-19	43516	-
	40	2	45	55	5	272,661	1,079,412,159	324,500	5,219,934	0*	-22	111	13	23399	-
	40	2	70	80	5	197,579	674,327,031	271,767	2,519,882	1*	-44	32	-46	39255	-
	40	3	45	81	12	539,089	1,602,510,285	669,137	5,729,585	0*	53	213	24	64622	-
	40	3	45	75	10	516,898	1,410,058,606	633,712	5,429,543	0*	47	175	17	57894	-
	40	3	50	80	10	505,343	1,229,592,596	628,931	4,983,826	0*	44	140	7	62327	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	40	3	50	74	8	477,375	1,032,526,491	586,183	4,653,247	0*	36	102	0	54582	-
	40	3	50	71	7	451,192	941,574,874	550,401	4,408,724	1*	28	84	-5	49282	-
	40	3	45	69	8	463,016	1,235,446,436	560,816	4,945,576	0*	32	141	7	47444	-
	40	3	55	79	8	443,903	936,905,948	556,889	4,198,496	1*	26	83	-9	57815	-
	40	3	55	76	7	431,280	832,978,007	536,853	4,025,272	1*	23	63	-13	53997	-
	40	3	45	66	7	423,125	1,159,224,635	510,110	4,609,317	1*	20	126	-1	41430	-
	40	3	55	70	5	379,329	644,186,148	465,584	3,490,004	1*	8	26	-25	43268	-
	40	3	50	65	5	371,057	782,842,969	448,114	3,709,809	1*	6	53	-20	36863	-
	40	3	60	81	7	363,893	821,934,923	467,984	3,249,392	1*	4	61	-30	53621	-
	40	3	60	75	5	339,074	612,208,462	428,583	2,904,858	1*	-3	20	-37	46099	-
	40	3	45	60	5	318,675	999,157,139	382,388	3,717,818	1*	-9	95	-20	28665	-
	40	3	55	64	3	287,464	484,951,501	350,068	2,655,900	1*	-18	-5	-43	29787	-
	40	3	60	69	3	275,394	423,943,758	343,569	2,305,419	1*	-22	-17	-50	33857	-
	40	3	65	80	5	261,622	688,879,418	349,142	2,294,817	1*	-26	35	-51	44194	-
	40	3	50	59	3	256,930	615,085,390	309,518	2,712,412	1*	-27	20	-42	23456	-
	40	3	65	74	3	228,254	468,104,170	299,000	1,882,127	1*	-35	-9	-59	35081	-
	40	3	45	54	3	197,941	787,461,947	238,524	2,578,134	1*	-44	54	-44	16635	-
	40	3	70	79	3	160,501	590,579,766	228,384	1,517,950	1*	-54	15	-67	32544	-
	40	4	45	81	9	454,871	1,399,822,326	576,431	3,666,678	1*	29	173	-21	56230	-
	40	4	45	77	8	446,142	1,274,045,233	559,629	3,515,991	1*	27	149	-24	52677	-
	40	4	50	82	8	429,797	1,156,866,635	548,134	3,302,982	1*	22	126	-29	55628	-
	40	4	50	74	6	404,790	906,502,122	505,491	2,968,012	1*	15	77	-36	47454	-
	40	4	45	69	6	391,619	1,044,827,528	481,638	3,106,093	1*	11	104	-33	40834	-
	40	4	55	79	6	378,738	857,241,491	484,301	2,724,363	1*	8	67	-41	50658	-
	40	4	50	70	5	373,297	790,728,136	461,122	2,735,129	1*	6	54	-41	40946	-
	40	4	55	75	5	363,497	726,111,151	459,209	2,536,331	1*	3	42	-45	45918	-
	40	4	55	71	4	333,297	606,427,033	416,418	2,290,112	1*	-5	18	-51	39331	-
	40	4	45	65	5	345,315	950,079,607	421,098	2,817,972	1*	-2	86	-39	33642	-
	40	4	50	66	4	328,628	691,451,211	402,261	2,442,137	1*	-6	35	-47	33626	-
	40	4	60	80	5	324,078	792,361,179	423,436	2,271,907	1*	-8	55	-51	49378	-
	40	4	60	76	4	296,952	598,975,325	383,099	1,896,691	1*	-15	17	-59	41814	-

Strategy Characteristics						Estimated Outcomes (for 10 million persons simulated)				Comparisons Relative to Current Policy				Total CRC deaths prevented	ICER
Policy Position	Cut off (µg Hb/g)	Interval (Years)	Start Age	Stop Age	Number of Lifetime Screens	ΔQALY	ΔC (€)	ΔLYG	Total Number of Colonoscopies	Within Capacity 0= No 1= Yes	% ΔQALY	% ΔC	%ΔNo. Colonoscopies		
	40	4	55	67	3	290,608	502,059,880	359,287	1,981,724	1*	-17	-2	-57	31916	-
	40	4	60	72	3	269,132	473,091,308	342,921	1,672,010	1*	-23	-8	-64	35353	-
	40	4	45	61	4	285,804	858,098,279	346,857	2,461,120	1*	-19	68	-47	26182	-
	40	4	50	62	3	269,963	600,842,580	328,659	2,076,177	1*	-23	17	-55	25873	-
	40	4	65	81	4	227,009	684,666,986	310,930	1,566,126	1*	-35	34	-66	39810	-
	40	4	65	77	3	216,524	545,092,940	291,432	1,384,721	1*	-38	6	-70	35709	-
	40	4	45	57	3	219,256	753,879,981	265,576	2,035,451	1*	-38	47	-56	18961	-
	40	4	70	82	3	146,274	656,767,988	215,686	1,167,618	1*	-58	28	-75	31655	-
	40	5	45	80	7	395,518	1,230,204,791	506,268	2,585,504	1*	13	140	-44	49495	-
	40	5	45	75	6	382,070	1,080,653,063	482,210	2,423,387	1*	9	111	-48	44749	-
	40	5	50	80	6	373,785	999,592,131	480,185	2,246,826	1*	6	95	-52	48377	-
	40	5	50	75	5	360,307	847,525,345	455,966	2,080,270	1*	3	66	-55	43579	-
	40	5	45	70	5	350,153	944,507,885	435,932	2,226,717	1*	0	84	-52	37694	-
	40	5	55	80	5	333,703	824,410,604	433,204	1,864,114	1*	-5	61	-60	45884	-
	40	5	50	70	4	326,964	710,812,937	407,923	1,876,218	1*	-7	39	-60	36286	-
	40	5	55	75	4	319,785	668,397,221	408,296	1,691,016	1*	-9	31	-64	40948	-
	40	5	45	65	4	301,780	830,958,436	371,026	1,986,417	1*	-14	62	-57	29684	-
	40	5	55	70	3	285,855	528,857,979	359,263	1,481,388	1*	-19	3	-68	33443	-
	40	5	50	65	3	277,105	596,751,993	341,253	1,625,619	1*	-21	17	-65	28041	-
	40	5	60	80	4	273,236	698,814,185	362,956	1,480,334	1*	-22	36	-68	41518	-
	40	5	60	75	3	258,702	539,048,464	337,011	1,298,675	1*	-26	5	-72	36378	-
	40	5	55	65	2	234,236	410,994,541	290,203	1,214,760	1*	-33	-20	-74	24897	-
	40	5	60	70	2	223,496	392,251,527	285,946	1,073,511	1*	-36	-23	-77	28537	-
	40	5	45	60	3	237,425	729,472,599	289,707	1,683,848	1*	-32	42	-64	21477	-
	40	5	50	60	2	209,762	493,166,843	256,132	1,312,452	1*	-40	-4	-72	19507	-
	40	5	65	80	3	200,769	613,901,647	277,464	1,112,573	1*	-43	20	-76	35246	-
	40	5	65	75	2	185,289	447,436,913	250,036	920,320	1*	-47	-13	-80	29815	-
	40	5	45	55	2	164,407	611,938,881	200,307	1,304,021	1*	-53	20	-72	13838	-
	40	5	70	80	2	128,496	556,541,437	189,832	789,794	1*	-63	9	-83	27297	-

586 *= within the future extended capacity

