

Title

Modeling costs and benefits of the organized colorectal cancer screening programme and its potential future improvements in Hungary

Abstract

Objective: The national population-based colorectal cancer (CRC) screening programme in Hungary was initiated in December 2018. We aimed to evaluate the current programme and investigate the costs and benefits of potential future changes to overcome the low coverage of the target population.

Methods: We performed an economic evaluation from a healthcare payer perspective using an established micro-simulation model (Microsimulation Screening Analysis-Colon). We simulated costs and benefits of screening with fecal immunochemical test in the Hungarian population aged 50-100 years, investigating also the impact of potential future scenarios which were assumed to increase invitation coverage: improvement of the IT platform currently used by GPs or distributing the tests through pharmacies instead of GPs.

Results: The model predicted that the current screening programme could lead to 6.2% CRC mortality reduction between 2018 and 2050 compared to no screening. Even higher reductions, up to 16.6%, were estimated when tests were distributed through pharmacies and higher coverage was assumed. This change in the programme was estimated to require up to 26 million performed fecal immunochemical tests and 1 million colonoscopies for the simulated period. These future scenarios have acceptable cost-benefit ratios of €8,000-€8,700 per life-years gained depending on the assumed adherence of invited individuals.

Conclusions: With its limitations, the current CRC screening programme in Hungary will have a modest impact on CRC mortality. Significant improvements in mortality reduction could be made at acceptable costs, if the tests were to be distributed by pharmacies allowing the entire target population to be invited.

Keywords

colorectal cancer screening; national screening programme; economic evaluation; costs and benefits

1 **Introduction**

2 Colorectal cancer (CRC) is a major health problem in Hungary, where mortality rates are among the
3 highest in Europe and an increasing trend in incidence was projected due to the aging population.(1-3)
4 CRC screening can reduce cancer-specific mortality significantly and might also lead to a reduction in all-
5 cause mortality.(4, 5) However, screening could also result in certain harms (6) and, therefore, expected
6 net benefit should be assessed before implementing CRC screening at population level.(7) In Hungary,
7 multiple pilot screening programmes were conducted with moderate success, considering screening and
8 follow-up participation rates.(8) After these pilots, the national population-based organized CRC screening
9 programme was initiated in December 2018, offering biennial fecal immunochemical test (FIT) screening
10 to individuals aged 50-70 years (positivity cut-off: 20 µg/g).(9) The invitation process for the target
11 population is centrally coordinated by the National Public Health Institute. This involves sending
12 invitations to all individuals associated with GPs who are participating in the programme. GPs volunteered
13 to participate in the programme for extra funding, which is a fixed fee per screened individual. The invited
14 individuals can collect the FIT kit from their GP.

15 Some organizational barriers might limit the performance of the current screening programme as shown
16 by the EU-TOPIA project framework.(10) GPs are generally overwhelmed in Hungary as the country has
17 been suffering from a significant workforce crisis in primary care in the past two decades, which is
18 indicated by the decreased inflow of GPs and by the fact that almost half of GPs are aged over 55 years.(11)
19 Hence, not all GPs have decided to have an active part in the organized CRC screening programme for
20 reasons including the additional workload and the user-unfriendly IT platform of the programme. Thus,
21 only eligible individuals whose GPs had volunteered to participate were invited in the first implementation
22 of the screening programme. This resulted in a situation where a substantial part of the target population
23 was not invited (invitation coverage approximatively 50%). Moreover, among the invited population the
24 willingness to perform the test and participate in diagnostic colonoscopy after a positive result was low.(8)
25 Considering these major limitations, the short- and long-term outcomes of the current screening
26 programme should be systematically evaluated in order to provide input for strategic health policy
27 decisions.(12)

28 In this study, we performed an economic evaluation of the Hungarian national CRC screening programme
29 using an established micro-simulation model, investigating also the costs and benefits of potential future
30 changes to the programme that may help to overcome the abovementioned barriers, including
31 improvement of the IT platform currently used by GPs and distributing the FIT kits through pharmacies

32 instead of GPs.

33 **Materials and methods**

34 MISCAN-Colon model

35 We used the Microsimulation Screening Analysis-Colon (MISCAN-Colon) model (Erasmus University
36 Medical Center, Rotterdam, The Netherlands) to simulate future outcomes of CRC screening in Hungary.
37 MISCAN-Colon is a well-established microsimulation model which has been used to inform public health
38 policies in the US, Canada, Australia and Europe.(6, 13-15) The structure and underlying assumptions of
39 the model are reported in the **Supplementary Materials**.

40 Study population

41 The model simulated the Hungarian population from 2015 to 2050. The age distribution was based on the
42 observed age distribution in Hungary in 2018.(16) **Supplementary Table 1** provides an overview of the
43 main model assumptions. In this analysis, our model was specifically calibrated to replicate the age-
44 specific CRC incidence observed in Hungary in 2008-2012 (period before introduction of screening,
45 **Supplementary Figure 1**).(17) Incidence and age-specific CRC mortality data were obtained from the
46 National Screening Registry. As data on CRC stage distribution was not available in Hungary, those model
47 parameters were calibrated using pre-screening data from a neighboring country (Slovenia, period 2004-
48 2008).(18) The model used all-cause mortality estimates from the 2014 Hungarian life tables.(19) Because
49 age- and stage-specific information on CRC relative survival was not available in Hungary, we informed
50 our model with the age- and stage-specific survival observed in The Netherlands during 1999-2003 (5-year
51 CRC relative survival: 59%). Under these assumptions, the predicted CRC mortality rates showed a
52 reasonable fit with the Hungarian CRC mortality rates during the period 2008-2012 (**Supplementary**
53 **Figure 1**).(20)

54 Simulated screening scenarios

55 In order to evaluate potential future improvements to the programme, we modelled the 2015-2050
56 Hungarian population under 17 specific screening scenarios as described in **Table 1**. First, we simulated
57 no screening (as reference for computing all screening benefits; “No screening”). Second, we simulated
58 the current screening scenario assuming biennial FIT screening from age 50 to 70 (starting in 2018), with
59 the FIT kit collected from the GP, in which 50% of target population is invited to FIT screening, and of
60 those 40% participate (“Current screening strategy”).(8)

61 Then, we investigated the impact of updating the IT platform of the organized screening programme used
62 by GPs. We assumed such an improvement would increase GP participation. Specifically, we simulated
63 three specific scenarios (see **Table 1**) where we assumed that this policy would result in a direct increase
64 in invitation coverage because those individuals of the target population whose GPs would newly join the
65 programme could now be invited for screening. In all these three scenarios, the other characteristics of
66 the screening programme were simulated as in the current screening scenario.(8)

67 Finally, we simulated 12 specific screening scenarios to investigate the potential impact of involving
68 pharmacies instead of GPs in the distribution of the FIT kit. For all these scenarios, biennial FIT screening
69 starting in 2018 was simulated assuming the entire target population aged from 50 to 70 years was invited
70 (100% invitation coverage). Full invitation coverage was assumed because it is expected that pharmacies
71 would collectively join the screening programme under the lead of their advocacy organization, instead
72 of joining individually as the GPs did. We assumed that the impact of this policy relates to: i) the proportion
73 of invited individuals who collect the test from the pharmacies; and ii) the proportion of individuals that
74 perform the test once collected. Specific assumptions for these parameters are listed in **Table 1**.

75 All screening scenarios (except for no screening) were simulated assuming 60% adherence in diagnostic
76 colonoscopy.(8) For individuals with adenomas detected during a diagnostic colonoscopy, surveillance
77 colonoscopy was offered. Surveillance was simulated every one to five years depending on the number
78 and size of adenomas, in line with the European guidelines, assuming an adherence of 60%. Assumptions
79 for test characteristics for FIT and colonoscopy were based on scientific literature (**Supplementary Table**
80 **1**).

81 CRC screening costs

82 We performed a cost-effectiveness analysis from a healthcare payer perspective. Costs for CRC screening
83 were obtained from the National Screening Coordination Department and costs for CRC treatment were
84 extracted from a study that estimated the net cost of CRC patients' care at patient-level in Hungary.(21)
85 All costs were converted to Euro (**Supplementary Table 1**). Simulating FIT screening, screening costs were
86 accounted differently according to the simulated screening policy. Simulating current screening, we
87 accounted a FIT organizational cost (€9.6) for each invited individual, as well as a laboratory cost (€8.9)
88 and GP reimbursement cost (€4.8) for each FIT performed. When we simulated scenarios with the
89 updated IT platform, we accounted the same FIT cost as in the current screening. When we simulated the
90 FIT kit distributed by pharmacies, we accounted a FIT organizational cost (€9.6) for each invited individual,

91 a pharmacy reimbursement (€2.1) for each FIT kit collected, and a laboratory cost (€8.9) for each FIT
92 performed. Finally, we included for each screening scenario (except 'No screening') two organizational
93 public investments (€1.85Million in 2018 and €1.9Million in 2020) made by the Hungarian government to
94 improve the facilities of health service providers performing colonoscopies.

95 Model outcomes

96 For each simulated scenario, we computed the effectiveness, i.e. prevented CRC deaths and life-years
97 gained from screening (LYG), and costs of screening. LYG and costs were discounted by 3.7% annually, as
98 indicated by the Hungarian guideline of performing economic evaluations.(22) In addition, we computed
99 the cumulative reduction in CRC mortality due to screening over time and the total undiscounted net costs
100 (compared to the current screening strategy) per calendar year during the period 2018-2050.

101 Cost-effectiveness analysis

102 Cost-effectiveness was evaluated comparing each simulated screening scenario with no screening.
103 However, incremental cost-effectiveness ratios (ICERs) were estimated as ratio of additional costs and
104 additional LYG in comparison with the current screening scenario. Cost-effectiveness results were
105 computed specifically among individuals aged 50 or older during the period 2018-2050 (cost-effectiveness
106 outcomes in period 2018-2030 were also computed and reported in **Supplementary Table 2**).

107 Sensitivity Analyses

108 We investigated the model parameter uncertainty by performing specific sensitivity analyses. In these, we
109 assumed: i) a higher participation in the follow-up diagnostic colonoscopy (80%); ii) lower organizational
110 costs for the FIT test (-10%, -20%, or -50%); iii) higher or lower GP reimbursement costs (variations in the
111 actual reimbursement assumed as follows: 50%/20% lower; or 20%/50% higher); and iv) higher or lower
112 pharmacy reimbursement costs (variations in the actual reimbursement assumed as follows: 50%/20%
113 lower; or 20%/50% higher). We summarized the results of those analyses in **Supplementary Table 3**.

114 Results

115 In the absence of screening, the model predicted up to 189,600 CRC deaths in Hungary between 2018 and
116 2050. The current screening strategy was estimated to avoid 2.9% of CRC deaths in the 2018-2030 period
117 and up to 6.2% in the period 2018-2050 (**Table 2, Supplementary Table 2**). Up to 7.9 million performed
118 FITs and 0.3 million colonoscopies were required by the current screening scenario (**Table 2**).

119 Updating the IT platform for the GPs reduced CRC mortality in the 2018-2050 period up to 7.7% in the
120 case of 65% invitation coverage (compared to No screening) (**Figure 1**), requiring up to 10.2 million
121 performed FITs and 0.4 million colonoscopies. Screening related costs of the programme increased from
122 €179 million to €223 million in this scenario. Moreover, annual net costs were estimated to potentially
123 reach €6.2 million in the period 2018-2030 (**Figure 2**). Compared to current screening the incremental
124 costs for every additional life-year (ICER) were €9,701, €10,953 and €10,659 per LYG for the invitation
125 coverages of 55%, 60% and 65%, respectively.

126 The model predicted higher reductions in CRC mortality when pharmacies distributed the FIT test (**Figure**
127 **1**). During 2018-2050, the estimated mortality reduction ranged from 11.2% to 16.6% depending on
128 expected rates of FIT collection and adherence. The highest reduction was observed when 70% of the
129 invited individuals collected the test with 95% performing the test after picking it up. Distributing the test
130 through pharmacies was also estimated to avert slightly more CRC deaths in the first decade (2018-2030)
131 compared to the current screening scenario (**Figure 1, Supplementary Table 2**).

132 When 50% of the individuals were simulated to collect the FIT through pharmacies, the model estimated
133 that up to 18.7 million FITs and 0.7 million colonoscopies were required by the programme, with predicted
134 ICERs ranging from €9,700 (95% adherence rate) to €11,500 (80% adherence rate) per LYG. When more
135 individuals collected the FIT from pharmacies, the resources needed for the programme and the costs
136 increased (**Table 2**). When 70% of invited individuals collected the test, up to 26 million performed FIT
137 and 1 million colonoscopies were needed by the programme, with predicted ICERs ranging from €8,000
138 (95% adherence rate) to €8,700 (80% adherence rate) per LYG. The screening related costs for this
139 scenario were estimated to be €471 million. Annually, total net costs of the pharmacy scenarios (screening
140 costs + CRC care costs) ranged from €13 to €37 million, with the highest annual net costs estimated in the
141 first years after the introduction of the policy (2018-2025; **Figure 2**).

142 Compared to the scenarios of updating the IT platform, the scenarios of distributing the FIT tests through
143 pharmacies resulted in more benefits and lower ICERs when at least 60% of invited individuals collected
144 the tests. Therefore, these alternatives are more cost-effective options to improve the current system.

145 Sensitivity analyses

146 The impact of model parameter uncertainty was investigated for a selected number of scenarios in **Figure**
147 **2** and for all simulated scenarios in **Supplementary Table 3**. ICERs were reduced by between €1,000 and
148 €3,000 per LYG when we assumed a higher participation in diagnostic colonoscopy (i.e. 80%) or a 50%
149 reduction in the cost of the FIT. Varying the GP reimbursement costs, pharmacy reimbursement costs, or
150 reducing the FIT costs (by up to 10% or 20%) did not substantially increase or decrease the ICERs.

151 Discussion

152 This study provides the first comprehensive evaluation of the newly implemented CRC screening
153 programme in Hungary, using a widely validated simulation model. We show that even with its important
154 limitations the current screening programme can ensure a modest mortality reduction in the long term
155 for the Hungarian population aged 50-100 years. However, we also investigated a number of alternative
156 scenarios in which the major barriers of the screening programme could (at least partly) be overcome,
157 leading to even better outcomes: e.g. over 15% mortality reduction with ICERs estimated between €8,000
158 and €8,400 per LYG in some scenarios. These ICERs are well below the current Hungarian threshold for
159 cost-effectiveness in drug reimbursement (health technologies with an ICER above 3 times the GDP per
160 capita [\sim €40 000] / quality-adjusted life years are considered not cost-effective).(22) The national
161 guideline for health technology assessment does not define cost-effectiveness thresholds for other health
162 technologies such as public health programmes.

163 Our study presumed that different invitation strategies lead to a variation in participation rate (i.e.
164 different % of attenders among annual target population shown in **Table 1**). The key benefit of the
165 pharmacy scenario would not necessarily be the increased attendance rate of the invited individuals, but
166 the higher coverage, which could lead to the invitation of the full target population for the screening. An
167 interesting trade-off was investigated in this respect, where we assumed a lower unit cost per FIT test for
168 pharmacies compared to GPs, with a more frequent occurrence as pharmacies would receive the funding
169 for every distributed KIT whereas GPs received it after every performed test. The ICERs showed that most
170 scenarios of distributing the FIT tests through pharmacies were more favorable, indicating that the costs
171 of reimbursing more tests (even some unused) would be outweighed by the higher benefits expressed in
172 LYG.

173 As the effectiveness of screening is directly associated with the level of screening participation, it is also
174 reasonable to expect that screening costs (i.e. test and following investigation costs) increase as well.
175 However, our model also estimated elevated costs due to CRC care (both in the short and long term). This
176 is counterintuitive as detecting CRC at an earlier stage should be associated with less expensive
177 treatments and hospitalization costs, as shown in previous cost-effectiveness analyses (also carried out
178 with MISCAN-Colon).(23-25) This result can be explained by the fact that costs did not vary substantially
179 according to CRC care phase: costs accounted in the last year before death (from CRC or other causes)
180 were in line with those for ongoing/continuous care. In previous cost-effectiveness analyses, terminal care
181 costs were from 10- to 50-fold higher than those assumed for continuous care.(23-25) Thus, when a CRC

182 case was detected early at a lower stage in our analysis, the model accounted lower CRC terminal care
183 costs (death averted) than in the previous analyses but higher costs for CRC ongoing care (because
184 accounted for each LYG for those with a screen-detected CRC).

185 Besides the results concerning the cost-benefit ratio of the investigated scenarios, other estimations of
186 our economic evaluation, such as number of tests performed or number of follow-up examinations
187 executed, are important for capacity planning purposes (e.g. human resources, organizational capacities).
188 Scenarios in our study also indicated an increasing number of colonoscopies to be performed in the future.
189 These estimations could help healthcare policymakers to judge whether the two public investments made
190 in 2018 and 2020 to improve the facilities for performing colonoscopies were sufficient, or whether
191 further investment is required in the future.

192 In the literature, CRC screening programmes have been proven to be highly cost effective, ensuring major
193 health gains at acceptable costs.(7, 26, 27) However, it is not clear which screening strategy is preferable
194 for a population-based CRC screening programme, as costs of screening, screening adherence, test
195 sensitivity, and costs of CRC treatment have a substantial impact on overall cost-effectiveness and are
196 highly dependent on country settings.(28) For example in a previous economic evaluation, Arrospe et al
197 found that, in the first years of the CRC FIT screening programme in the Basque country (64.3% screening
198 adherence), €69.2 million were necessary (on average) to annually fund the programme.(26) In our budget
199 analysis, we found that in Hungary the current FIT screening programme would need from €14 to €20
200 million of annual funds (Supplementary Table 4) during its first years assuming that 20% of the individuals
201 in the target population participated in screening.

202 In the scenarios where pharmacies would distribute the tests, we projected a relatively large total net cost
203 compared to the current screening strategy (ranging from an extra €13 to €37 million, see **Figure 2**).
204 However, these estimates include not only the screening-related costs but also the increased costs in CRC
205 care. Still, such an increase in costs would require a significant investment considering the Hungarian
206 public health perspective. To put this amount into a local context, about €85-90 million were nominated
207 for public health in the annual national budget in Hungary (not counting the less centralized regional or
208 local-level spending on public health). This amount covered mainly national-level public health
209 programmes, interventions and initiatives.

210 Our study has a number of limitations. First, some of the input data for the modelling were not available
211 for Hungary, and therefore data from other countries were used. Second, our screening scenarios are

212 based on the experience and knowledge of experts from Hungary, and it is difficult to judge whether they
213 are realistic to achieve in real life. However, we performed extensive analysis with multiple scenarios and
214 sensitivity analyses, so the results should be useful under a wide range of circumstances. Third, there were
215 certain cost elements which were not possible to estimate and include in the calculations (i.e. additional
216 costs of pharmacies to implement screening-related tasks or additional investments needed to improve
217 the current IT platform used by the GPs), and therefore future screening scenarios might underestimate
218 costs. Moreover, our analysis did not include additional alternative options of invitation, such as sending
219 the FIT kit by post. However, with the low participation in CRC screening currently observed in Hungary,
220 introducing this last option may not be opportune. Fourth, the benefits of screening in economic
221 evaluations are frequently expressed in quality-adjusted life years. (29, 30) However, quality-of-life data
222 were not available in our case and, therefore, LYGs were used. Finally, the MISCAN-Colon model simulates
223 the natural history of CRC through the adenoma-carcinoma sequence and does not consider adenoma
224 histology (villous histology or advanced atypia) or sessile serrated polyps.

225 The results of our study should serve as the basis for further improvement of the current CRC screening
226 programme in Hungary. Switching to the distribution of FIT kits through pharmacies instead of GPs in the
227 organized screening programme seems to be a justifiable and important step towards achieving higher
228 invitation coverage. However, it should be noted that such a change might be difficult to achieve without
229 the collaboration and support of GPs who are currently the key stakeholders. Although the test kits would
230 not be distributed by the GPs in this scenario, their role in the screening process would still be crucial as
231 they would still be responsible for the coordination of the patient pathway from the screening to patient
232 care. Thus, appropriate communication with the GPs is an important initial element for implementing
233 future changes in the screening programme. On the other hand, pharmacies should also be prepared to
234 implement screening-related activities into their current practice.

235 **Conclusions**

236 Despite the important organizational limitations, the current national CRC screening programme in
237 Hungary can ensure modest mortality reduction in the long-term for the population aged between 50 and
238 100. However, this study shows that in order to fully exploit the benefits of the programme further
239 improvements are required; for instance, changes to the current IT platform or involving pharmacies in
240 the test distribution mechanism. We estimated that alternative scenarios reflecting these changes have
241 favorable cost-benefit ratios.

242 **Table 1.** Overview of the assumptions for each simulated screening strategy.

| Scenario number\Health policy implemented | Invitation coverage (% of invited among annual target population) | Adherence to screening (% of attenders in screening among invited) | | | %* | % of attenders among annual target population |
|---|---|--|---|-------|-------|---|
| | | Distribution through pharmacies | | | | |
| | | % collecting FIT kit (among invited) | % performing FIT (among those who collected the test) | | | |
| <i>No screening</i> | - | - | - | - | - | |
| <i>Current screening</i> (Biennial FIT, age 50-70) | 50% | - | - | 40% | 20% | |
| a. Strategies improving IT platform for GPs (40% of adherence in screening): | | | | | | |
| <i>GP1.</i> Invitation coverage: 55% | 55% | - | - | 40% | 22% | |
| <i>GP2.</i> Invitation coverage: 60% | 60% | - | - | 40% | 24% | |
| <i>GP3.</i> Invitation coverage: 65% | 65% | - | - | 40% | 26% | |
| b. Strategies of distributing FIT tests through pharmacies (100% invitation coverage): | | | | | | |
| - 50% collected the FIT:* | | | | | | |
| 80% performed the test | 100% | 50% | 80% | 40% | 40% | |
| 85% performed the test | 100% | 50% | 85% | 42.5% | 42.5% | |
| 90% performed the test | 100% | 50% | 90% | 45% | 45% | |
| 95% performed the test | 100% | 50% | 95% | 47.5% | 47.5% | |
| - 60% collected the FIT:* | | | | | | |
| 80% performed the test | 100% | 60% | 80% | 48% | 48% | |
| 85% performed the test | 100% | 60% | 85% | 51% | 51% | |
| 90% performed the test | 100% | 60% | 90% | 54% | 54% | |
| 95% performed the test | 100% | 60% | 95% | 57% | 57% | |
| - 70% collected the FIT:* | | | | | | |
| 80% performed the test | 100% | 70% | 80% | 56% | 56% | |
| 85% performed the test | 100% | 70% | 85% | 59.5% | 59.5% | |
| 90% performed the test | 100% | 70% | 90% | 63% | 63% | |
| 95% performed the test | 100% | 70% | 95% | 66.5% | 66.5% | |

243 + All policies were simulated in 2018;

244 * We assumed a 40% adherence in screening among invited simulating scenarios where the FIT kit was collected through GPs; when we simulated scenarios
 245 of distributing the FIT kits through pharmacies, adherence in screening was the result of the multiplication between proportion of invited individuals that
 246 collected the test from pharmacies and proportion of individuals that performed the test among those that collected the kit.

Table 2. Colorectal cancer screening simulated outcomes (x10,000, for individuals in the total Hungarian population aged 50-100 years-old in 2018-2050) per policy implemented.

| Strategy / Policy | CRC mortality | | | No. FITs | No. COLs | Total Screening Costs (€) | Total CRC Care Costs (€) | Total Costs** (€) | ICER† |
|---|---------------|------------|-------|----------|----------|---------------------------|--------------------------|-------------------|-----------|
| | No. Deaths‡ | Red. (%)‡, | LYG | | | | | | |
| No screening | 18.96 | - | - | - | - | 0.00 | 585339.0 | 588170.4 | - |
| Current screening (Biennial FIT, age 50-70) | 17.79 | 6.17 | 4.80 | 786.77 | 32.10 | 17890.45 | 597437.0 | 620968.1 | Reference |
| a. Strategies improving IT platform for GPs (40% of adherence in screening): | | | | | | | | | |
| GP1. Invitation coverage: 55% | 17.68 | 6.75 | 5.17 | 866.15 | 35.35 | 19390.03 | 599274.7 | 624557.4 | 9701 |
| GP2. Invitation coverage: 60% | 17.59 | 7.23 | 5.46 | 946.02 | 38.64 | 20859.73 | 601191.6 | 628197.2 | 10953 |
| GP3. Invitation coverage: 65% | 17.50 | 7.70 | 5.80 | 1025.83 | 41.89 | 22289.17 | 602941.8 | 631626.9 | 10659 |
| b. Strategies of distributing FIT tests through pharmacies (100% invitation coverage): | | | | | | | | | |
| - 50% collected the FIT:* | | | | | | | | | |
| 80% performed the test | 16.83 | 11.23 | 7.99 | 1589.26 | 64.85 | 33425.28 | 616183.2 | 657783.6 | 11541 |
| 85% performed the test | 16.72 | 11.81 | 8.45 | 1684.98 | 68.24 | 34812.52 | 617079.3 | 660323.2 | 10782 |
| 90% performed the test | 16.62 | 12.34 | 8.87 | 1780.10 | 71.58 | 36148.35 | 617922.7 | 662755.9 | 10267 |
| 95% performed the test | 16.52 | 12.87 | 9.34 | 1874.78 | 74.95 | 37436.91 | 618740.3 | 665115.3 | 9724 |
| - 60% collected the FIT:* | | | | | | | | | |
| 80% performed the test | 16.50 | 12.97 | 9.43 | 1893.72 | 75.59 | 37734.23 | 618898.4 | 665619.5 | 9644 |
| 85% performed the test | 16.37 | 13.66 | 9.96 | 2006.85 | 79.52 | 39357.19 | 619850.1 | 668490.4 | 9210 |
| 90% performed the test | 16.27 | 14.19 | 10.43 | 2120.12 | 83.19 | 40938.67 | 620664.9 | 671162.6 | 8916 |
| 95% performed the test | 16.15 | 14.82 | 10.90 | 2232.05 | 86.98 | 42456.27 | 621443.8 | 673742.4 | 8652 |
| - 70% collected the FIT:* | | | | | | | | | |
| 80% performed the test | 16.18 | 14.66 | 10.75 | 2194.67 | 85.72 | 41699.91 | 621176.1 | 672624 | 8682 |
| 85% performed the test | 16.05 | 15.35 | 11.31 | 2325.00 | 90.11 | 43547.29 | 622219.7 | 675841.8 | 8429 |
| 90% performed the test | 15.93 | 15.98 | 11.87 | 2454.36 | 94.38 | 45332.74 | 622897.1 | 678626.7 | 8155 |
| 95% performed the test | 15.81 | 16.61 | 12.38 | 2582.72 | 98.64 | 47059.05 | 623723.7 | 681499.5 | 7986 |

CRC = Colorectal cancer; FIT = Fecal Immunochemical Test; LYG = Life-years gained from screening; ICER = Incremental Cost-Effectiveness Ratio; COL = Colonoscopy; Scr. Participation = participation rate in FIT screening; FIT screening was simulated assuming a biennial screening interval between age 50 and 70 years.

* percentage of invited individuals that collected the FIT kit through the pharmacies, the proportion of performed test is meant as the proportion of individuals that performed the test among those who collected the FIT kit through pharmacies;

† ICER were computed as ratio between incremental costs and benefits (LYG) compared to current screening; ICER values are not expressed in x10,000 in this table

‡ CRC deaths were not discounted;

|| Compared to no screening;

** Total costs included costs for primary screening, for CRC care and treatment, for CRC diagnosis due to symptoms (no screen-detected CRCs), for diagnostic follow-up investigations, and for colonoscopy surveillance.

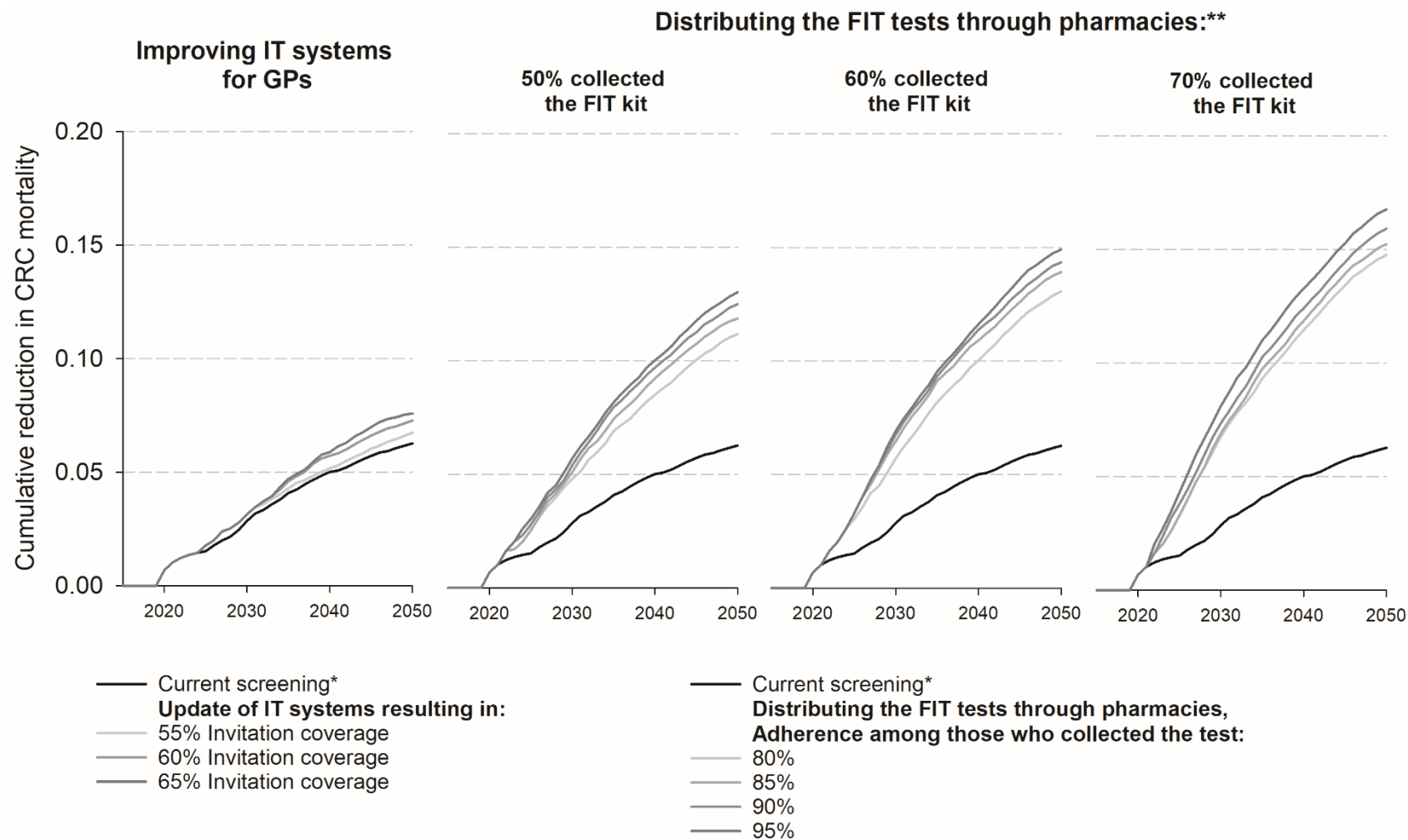


Figure 1. Cumulative colorectal cancer mortality reduction due to screening in Hungary for individuals aged 50 years or older and per simulated screening scenario. Note: *current screening: biennial FIT, 50-70, invitation coverage = 50% and screening adherence among invited = 40%; ** we assumed full invitation coverage in scenarios where the FIT kits were distributed through pharmacies

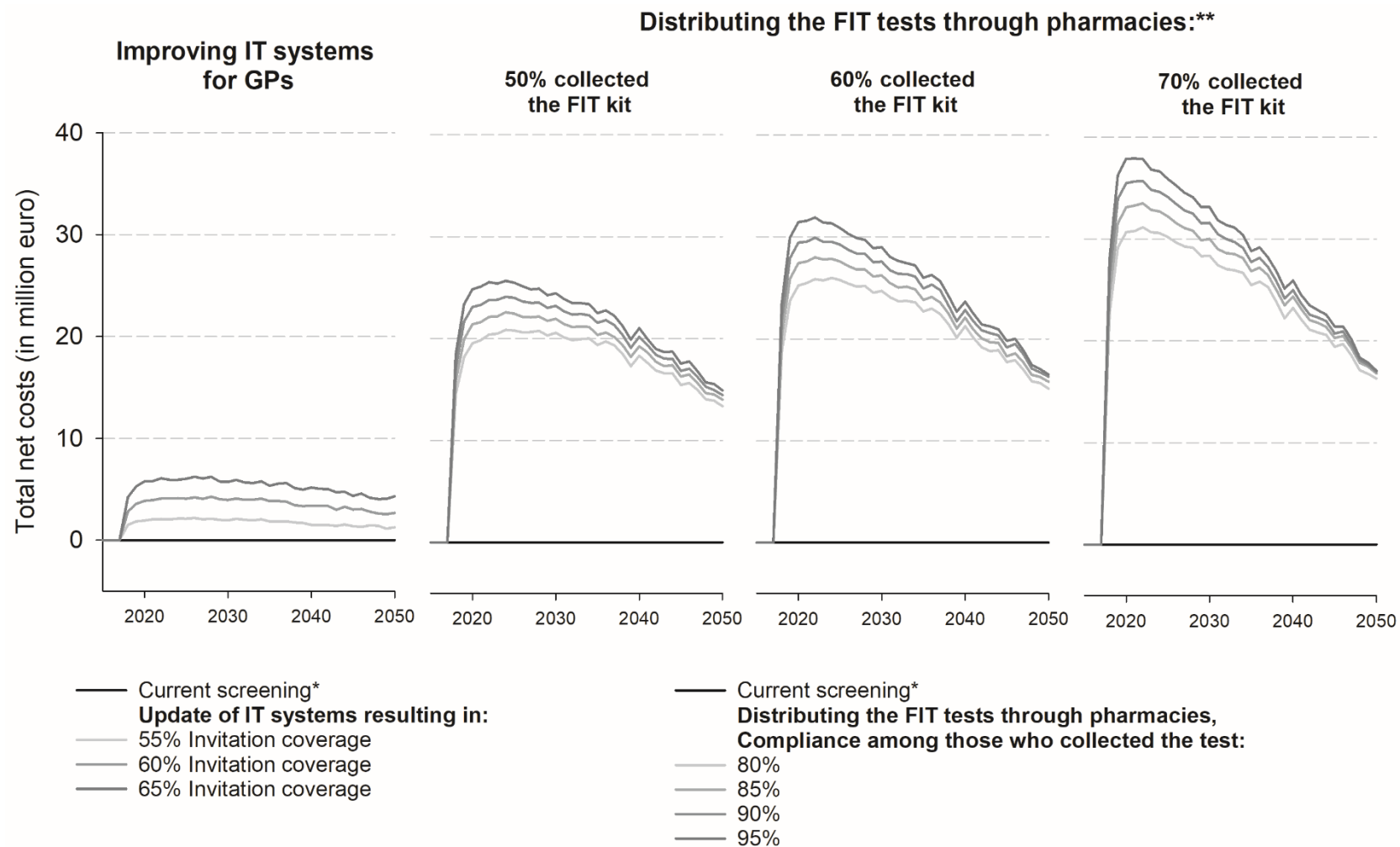


Figure 2. Estimated total annual net costs in Hungary among individuals aged 50 years or older and per simulated screening scenario (net costs compared to the current screening scenario). Note: *current screening: biennial FIT, 50-70, invitation coverage = 50% and screening adherence among invited = 40%; ** we assumed full invitation coverage in scenarios where the FIT kits were distributed through pharmacies

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