

# Appendices

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## **Appendix 1: Model Description – MISCAN-Colon**

### **General Model Structure**

MISCAN-Colon is a stochastic microsimulation model for colorectal cancer (CRC) programmed in Delphi (Borland Software Corporation, Scotts Valley, California, United States). It can be used to explain and predict trends in CRC incidence and mortality and to quantify the effects and costs of primary prevention of CRC, screening for CRC, and surveillance after polypectomy.

The term 'microsimulation' implies that individuals are moved through the model one at a time, rather than as proportions of a cohort. This allows future state transitions to depend on past transitions, giving the model a 'memory'. Furthermore, unlike most traditional Markov models, MISCAN-Colon does not use yearly transition probabilities; instead it generates durations in states, thereby increasing model flexibility and computational performance. The term 'stochastic' implies that the model simulates sequences of events by drawing from distributions of probabilities/ durations, rather than using fixed values. Hence, the results of the model are subject to random variation.

MISCAN-Colon consists of 3 modules: a demography module, natural history module, and screening module.

#### **a. The Demography Module**

Using birth- and life-tables representative for the population under consideration, MISCAN-Colon draws a date of birth and a date of non-CRC death for each individual simulated. In MISCAN-Colon the maximum age an individual can achieve is exactly 100 years.

#### **b. The Natural History Module**

##### *Transitions*

As each simulated person ages, one or more adenomas may develop (Model Appendix Figure 1). These adenomas can be either progressive or non-progressive. Both progressive and non-progressive adenomas can grow in size from small ( $\leq 5\text{mm}$ ), to medium (6-9mm), to large ( $\geq 10\text{mm}$ ); however, only progressive adenomas can develop into preclinical cancer. A preclinical cancer may

progress through stages I to IV; however, during each stage CRC may be diagnosed because of symptoms. After clinical diagnosis, the survival depends on the stage of the cancer. For individuals with synchronous CRCs at time of diagnosis, the survival of the most advanced cancer is used. The date of death for individuals with CRC is set to the earliest simulated death (either due to CRC or due to another cause (see: 'The demography module')).

### *Transition Probabilities and Durations in States*

An individual's risk of developing adenomas depends on the individual's age and a personal risk index. As a result of the latter most individuals develop no adenomas, whilst some develop many. We assumed that the distribution of adenomas over the colon and rectum equals the distribution of cancers in Norway during the NORCCAP trial, before the introduction of screening (between 1999 and 2011). Data was provided by the Norwegian Cancer Registry. The age-specific onset of adenomas and the dispersion of the personal risk index were calibrated to data on the prevalence and multiplicity distribution of adenomas as observed in autopsy studies (Model Appendix Figure 2).(2-11) The age-specific probability of adenoma-progressivity and the age- and localization-specific transition probabilities between preclinical cancer stages and between preclinical and clinical cancer stages were simultaneously calibrated to data on the age-, stage-, and localization-specific incidence of CRC in Norway during the NORCCAP trial, before the introduction of screening (between 1999 and 2011) (Model Appendix Figure 3). Data was provided by the Norwegian Cancer Registry.

The average durations between the preclinical cancer stages were calibrated to the rates of screen-detected and interval cancers observed in randomized controlled trials evaluating screening using guaiac fecal occult blood tests.(12-14) This exercise has been described extensively in a publication by Lansdorp-Vogelaar and colleagues.(15) The average duration from the emergence of an adenoma (state 2) until progression into preclinical cancer (state 7) (i.e. the adenoma dwell-time) was calibrated to the rates of interval cancers (including surveillance detected cancers) observed in a randomized controlled trial evaluating once-only sigmoidoscopy screening (Model Appendix Figure 4). (16) We assumed an equal overall dwell-time for adenomas developing into CRC from a medium size (30% of all CRCs) and from a large size (70% of all CRCs). All durations in the adenoma and preclinical cancer phase were drawn from exponential distributions. Durations within the adenoma phase and within the preclinical cancer phase were assumed to be perfectly correlated (i.e. if a small

adenoma grows into a medium-sized adenoma rapidly, it will also grow into a large adenoma or develop into CRC rapidly); however, durations in the adenoma phase were assumed to be uncorrelated with durations in the preclinical cancer phase (i.e. a rapidly growing adenoma does not necessarily develop into a rapidly progressing cancer). The proportion of medium sized, non-progressive adenomas growing large and the average duration in duration in the medium size, non-progressive adenoma state (state 5) were calibrated to size-specific adenoma detection rates observed in a Dutch randomized controlled trial on colonoscopy screening (73% small adenomas, 15% medium sized adenomas, 12% large adenomas).(17)

### **c. The Screening Module**

Screening will alter some of the simulated life histories: Some cancers will be prevented by the detection and removal of adenomas; other cancers will be detected in an earlier stage with a more favorable survival. As the stage-specific survival of screen-detected CRC as observed in randomized controlled trials on guaiac fecal occult blood testing was substantially more favorable than that of clinically detected CRC, even after correcting for lead-time bias, we assigned those screen-detected cancers that would have been clinically detected in the same stage the survival corresponding to a one stage less progressive cancer. Hence, a cancer screen-detected in stage II, that would also have been clinically diagnosed in stage II, is assigned the survival of a clinically diagnosed stage I cancer. The only exceptions were screen-detected stage IV cancers. These cancers were always assigned the survival of a clinically diagnosed stage IV cancer.

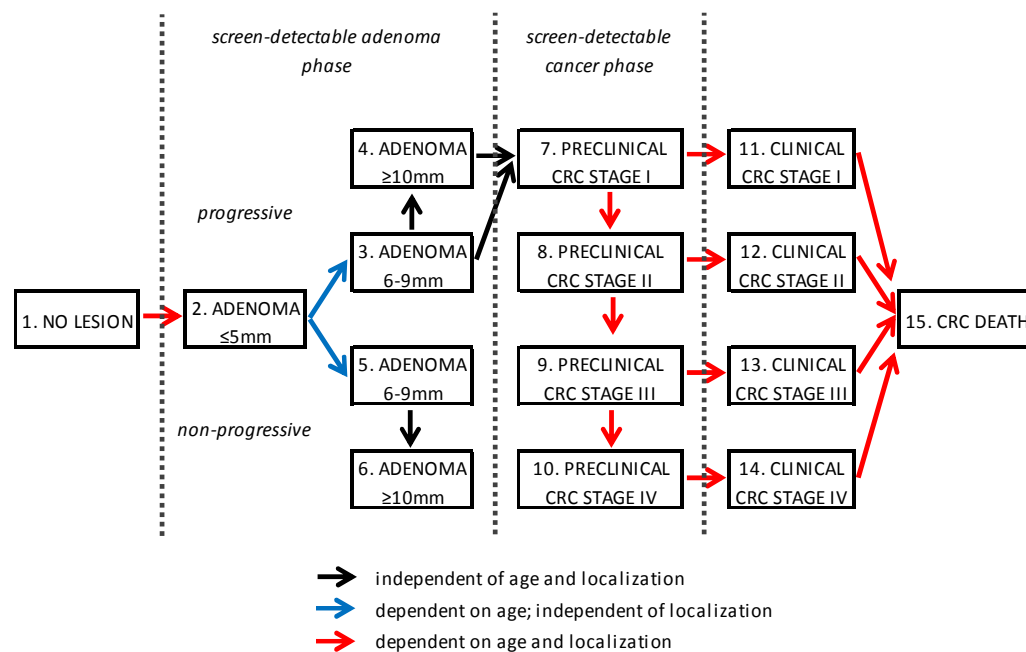
Besides modeling positive health effects of screening, we also model colonoscopy-related complications and over-diagnosis and over-treatment of CRC (i.e. the detection and treatment of cancers that would not have been diagnosed without screening).

### **Integrating Modules**

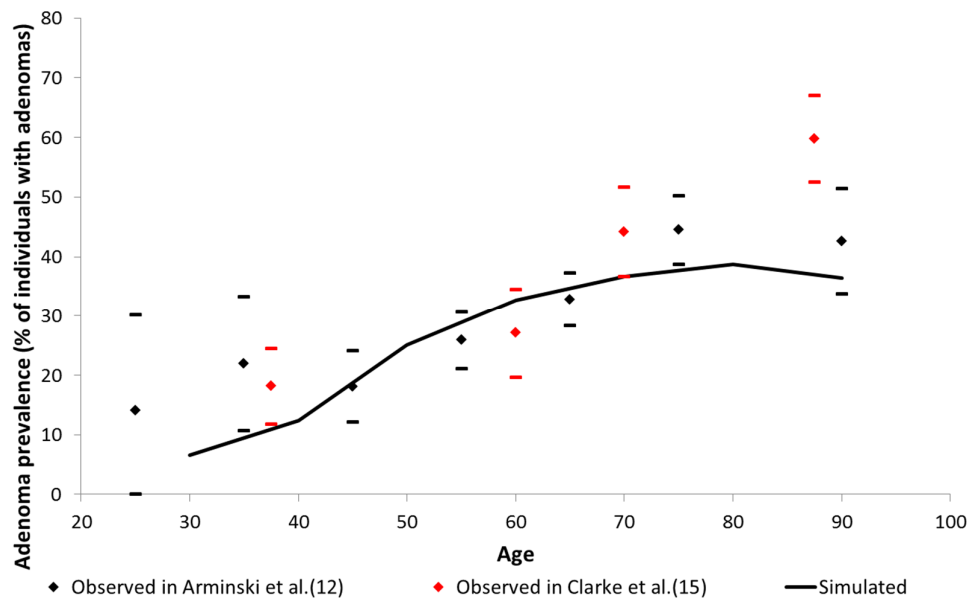
The demography module generates a date of birth and a date of non-CRC death for each individual simulated, creating a life-history without adenomas or CRC. In Patient A in Model Appendix Figure 5, the natural history module generates an adenoma. This adenoma progresses into preclinical cancer, which is diagnosed because of symptoms in stage II and results in CRC death before non-

CRC death would have occurred. In the screening module a screening examination is simulated, indicated by the blue arrow. During this examination the adenoma is detected, and as a result both CRC and CRC death are prevented. Hence, in Patient A, screening prolongs life by the amount indicated by the green arrow. Patient B also develops an adenoma, and although this adenoma does progress into preclinical cancer, Patient B would never have been diagnosed with CRC in a scenario without screening (see life history 2). However, during the screening examination simulated in the screening module, again indicated by the blue arrow, CRC is screen-detected in stage I. Hence, in this patient screening results in over-diagnosis of CRC: It detects a cancer that would never have been diagnosed in a scenario without screening. Hence, screening does not prolong life, but it does result in additional LYs with CRC care (over-treatment) as indicated by the red arrow.

*Model Appendix Figure 1. An Overview of the Natural History Module of MISCAN-Colon.*



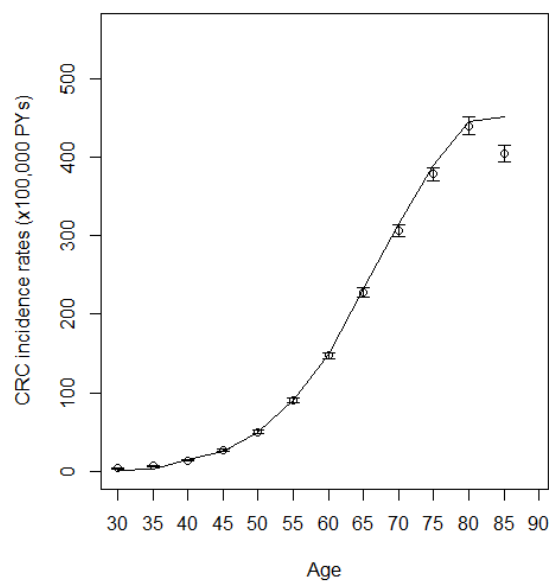
**Model Appendix Figure 2. Adenoma Prevalence Simulated by MISCAN-Colon Versus Observed in Selected Autopsy Studies and corrected for country specific differences in CRC incidence (% of individuals with adenomas).\***



\*Observed results are only shown for the two largest studies on which the model has been calibrated.

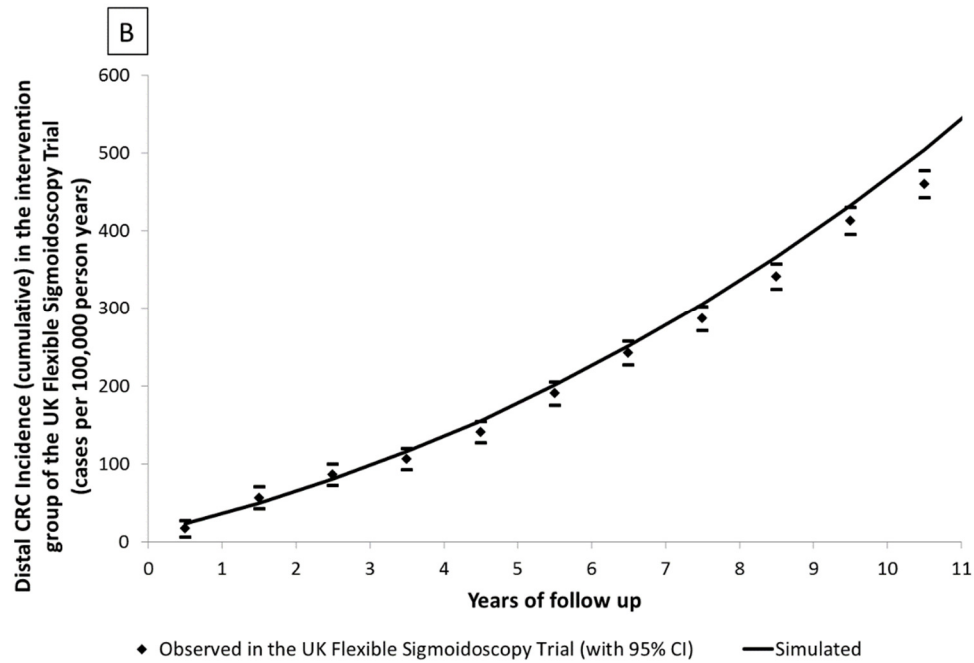
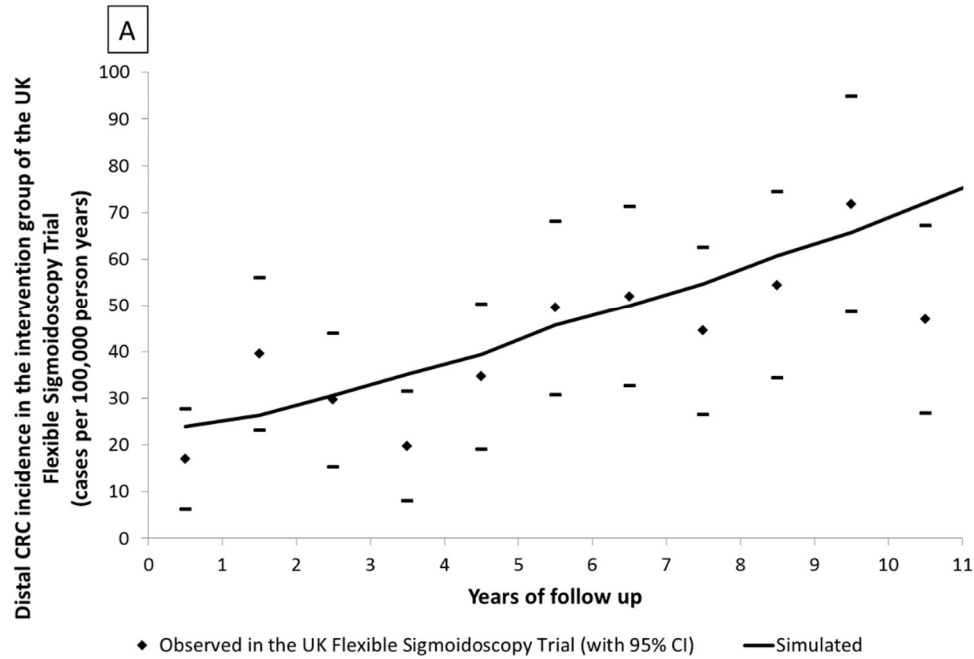
MISCAN-Colon has additionally been calibrated to 8 other autopsy studies.

**Model Appendix Figure 3. Norwegian CRC Incidence Observed during the NORCCAP trial period Versus Simulated by MISCAN-Colon; cases per 100,000 person years)**



Solid line: simulated; error bars and point estimates: observed in Norway 1999-2011 (with 95% CI)

*Model Appendix Figure 4. Distal CRC Incidence Observed in the Intervention Group of the UK Flexible Sigmoidoscopy Trial Versus Simulated by MISCAN-Colon (per year of follow-up (A), cumulative (B); cases per 100,000 person years).*

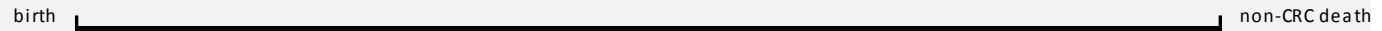


Model Appendix Figure 5. Integrating Modules: Two example Patients.

### PATIENT A: BENEFITTING FROM SCREENING

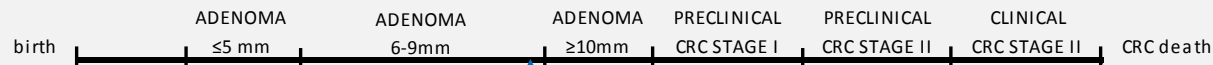
#### DEMOGRAPHY MODULE

*Patient A: life history 1*  
(without adenomas or CRC)



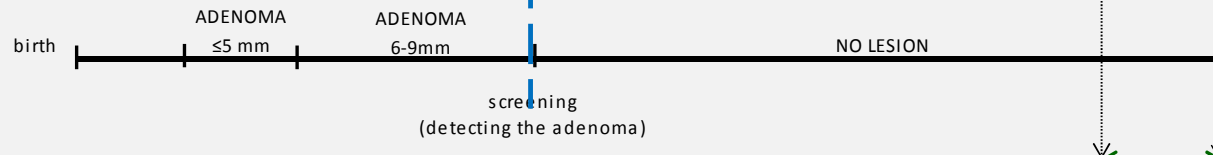
#### NATURAL HISTORY MODULE

*Patient A; life history 2*  
(develops CRC in the natural history module)



#### SCREENING MODULE

*Patient A; life history 3*  
(undergoes screening in the screening module)



### PATIENT B: OVER-DIAGNOSING CRC

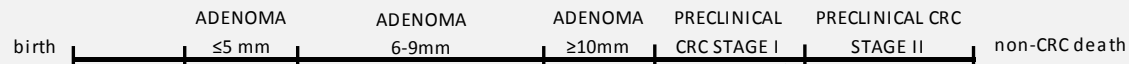
#### DEMOGRAPHY MODULE

*Patient B: life history 1*  
(without adenomas or CRC)



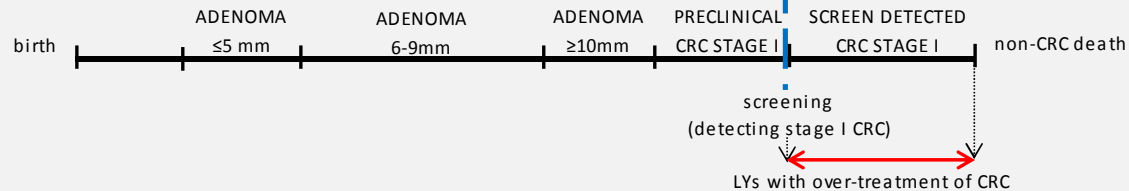
#### NATURAL HISTORY MODULE

*Patient B; life history 2*  
(develops CRC in the natural history module)



#### SCREENING MODULE

*Patient B; life history 3*  
(undergoes screening in the screening module)

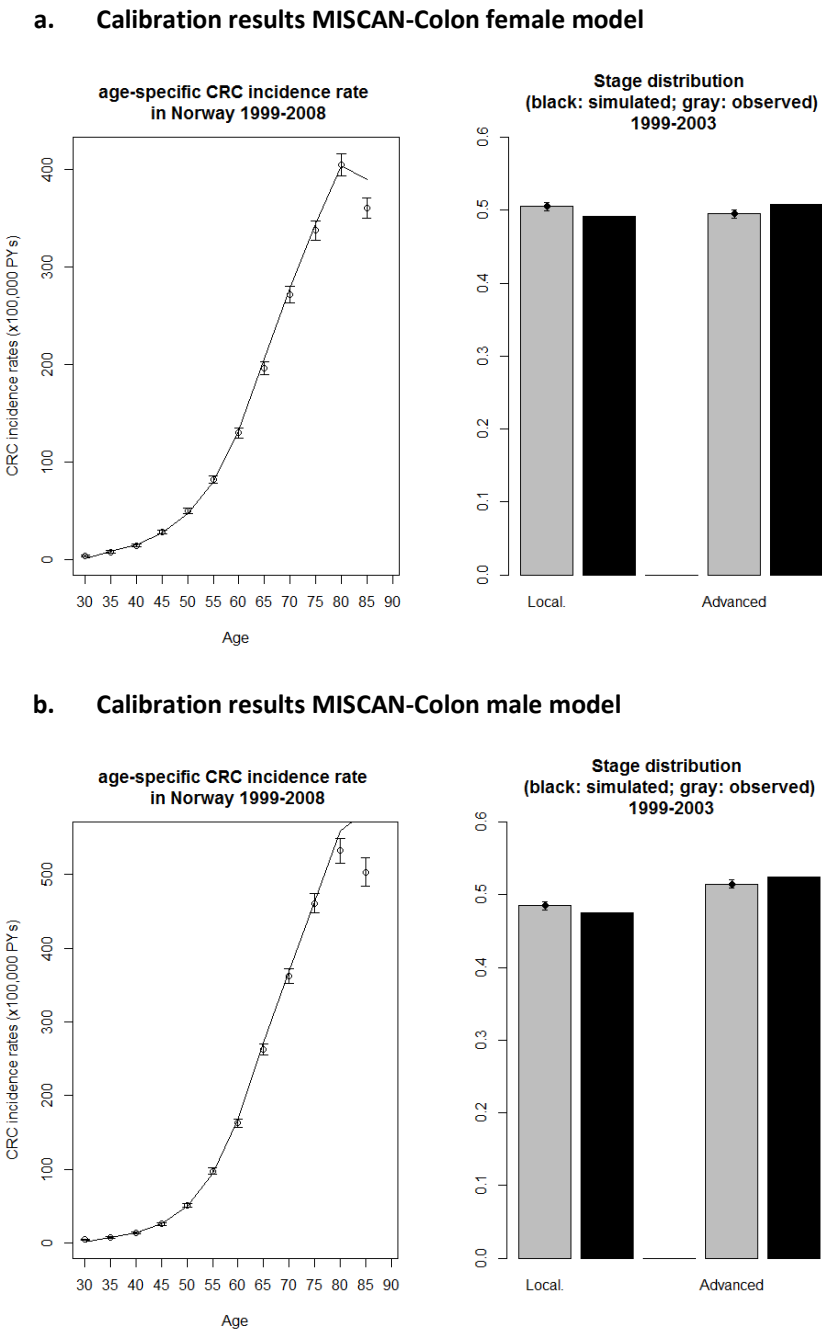


## References

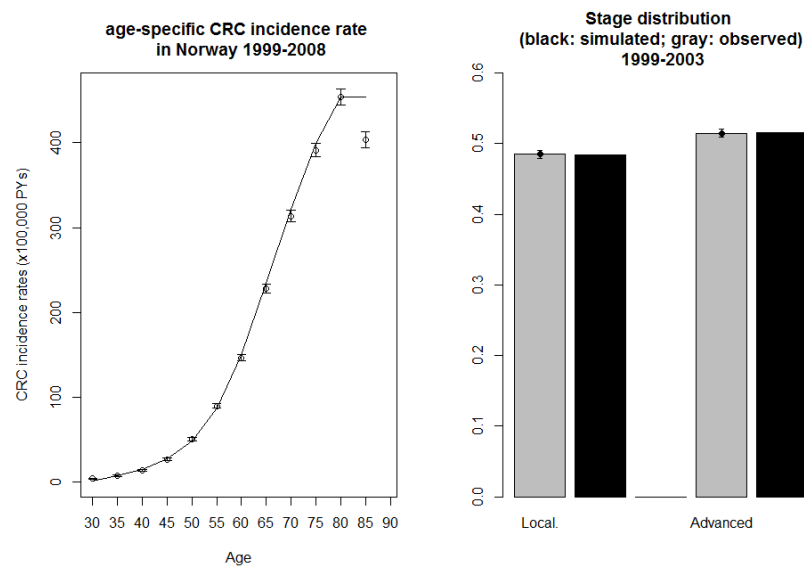
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**Appendix 2: Calibration results of the MISCAN-Colon microsimulation model to the Norwegian setting**

**Figure 1: Calibration results: Observed and model-predicted colorectal cancer incidence rates by age and stage distribution for Norway**



c. Calibration results MISCAN-Colon combined model



### **Appendix 3: Validation of the MISCAN-Colon microsimulation model against the NORCCAP sigmoidoscopy study**

#### **Methods**

We used MISCAN-Colon to simulate NORCCAP trial outcomes and compared predictions with those observed according to the same methodology as previously described.<sup>1</sup> Primary validation targets were relative overall and distal CRC incidence reduction and mortality reduction observed by Holme et al.,<sup>2</sup> who described the 15-year follow-up results of the NORCCAP trial. To simulate the NORCCAP trial, we adjusted MISCAN-Colon to the demography and screening behavior of the NORCCAP trial population.

#### *NORCCAP Trial*

In the NORCCAP trial, individuals between the ages of 50 and 65 years from 2 Norwegian regions were randomly assigned to either a control group (n = 78,220) or an intervention group that consisted of 2 arms (n = 10,283 and n = 10,289). Since there was no screening program in place in Norway during the study period, the control group did not receive routine CRC screening.<sup>3</sup> In the intervention arm, individuals were offered a once-only sigmoidoscopy (arm 1, n = 10,283) or sigmoidoscopy with a qualitative fecal occult blood test (FOBT) (arm 2, n = 10,289).<sup>4</sup>

The trial was carried out in 2 phases; individuals born from 1935 to 1945 were selected and randomized to undergo screening in 1999 and 2000 (i.e., 53–65 years old at time of screening), and individuals born from 1946 to 1950 were selected and randomized to undergo screening in 2001 (i.e., 49–54 years old at the time of screening). Individuals were followed until CRC diagnosis, death, emigration, or 31 December 2015, whichever occurred first.<sup>2</sup> The latest paper on long-term effects of the study made no distinction between the 2 different

intervention arms. Therefore, we compared model outcomes with the overall results of the intervention arms and will use the term intervention group when referring to both intervention arms.

#### *Adjustment of MISCAN-Colon to the NORCCAP Trial*

We used MISCAN-Colon to simulate a population with an age distribution comparable to the NORCCAP trial (personal communication with research leader G. Hoff, 2016). CRC incidence in the NORCCAP control group was 11% lower than incidence in the whole of Norway. We therefore adjusted the model accordingly by lowering the age-specific onset of adenomas by 11% for all ages. Comparing incidence rates observed in the NORCCAP trial, we assumed that nonadherers had a slightly higher age-specific onset of adenomas for all ages than individuals in the control group (relative risk of 1.05). In addition, age-specific onset in adherers was lowered for all ages to ensure that the overall CRC risk in the intervention group did not differ from the CRC risk in the control group, taking participation rate into account (relative risk of 0.97).

Control group and intervention group were simulated for 16 years according to trial design. For the intervention group, we assumed age-specific participation rates for sigmoidoscopy, FOBT and diagnostic colonoscopy as observed in the NORCCAP trial. Adherence for surveillance colonoscopies was not reported in trial publications and was assumed to be 80%. Test sensitivity of FS and follow-up colonoscopy and specificity of follow-up colonoscopy were based on literature.<sup>5</sup> Test specificity of FS, FOBT test characteristics and reach of sigmoidoscopy and colonoscopy were based on observations in the NORCCAP study.

### *Validation Targets*

Our primary validation targets were the overall and distal CRC incidence and mortality rate and HRs of overall and distal CRC incidence and mortality at 14- to 16-year follow-up (depending on the year of trial inclusion) in the intervention group relative to the control group. Model outcomes were considered consistent when predicted within 95% confidence intervals (CIs) of the corresponding NORCCAP trial targets.

### **Validation results**

Overall, the MISCAN-Colon predictions for 15-year incidence and mortality reduction from a once-only sigmoidoscopy in the NORCCAP trial were consistent with the trial results. The simulated HR for incidence was 0.84 compared to an observed HR of 0.78 (95% CI: 0.70-0.87) (Supplement 2, table 2), while simulated and observed HR for mortality reduction were 0.72 and 0.79 (95% CI: 0.65-0.96), respectively.

For males, MISCAN-Colon underestimated the impact of screening on CRC incidence compared to the NORCCAP trial results (observed HR: 0.66, 95% CI: 0.57-0.78; simulated HR: 0.81), but MISCAN-Colon predictions of CRC mortality reduction were consistent (observed HR: 0.63, 95% CI: 0.47-0.83; simulated HR: 0.70). For females, MISCAN-Colon predictions for CRC incidence reduction were in line with the trial results (observed HR: 0.92, 95% CI: 0.79-1.07; simulated HR: 0.85), but CRC mortality reduction was overestimated (observed HR: 1.01, 95% CI: 0.77-1.33; simulated HR: 0.76).

**Table 1. Hazard ratios: 14-16 years follow-up interventions effects of the NORCCAP trial including 95% confidence intervals for these effects and MISCAN- Colon predictions of these effects.<sup>a</sup> NORCCAP trial results were derived from Holme et al. 2018<sup>2</sup>**

| Gender            | Outcome   | CRC location | Observed HR | Confidence interval | Simulated HR | Cases per 100,000 person-years  |                     |                                  |                               |                     |   |
|-------------------|-----------|--------------|-------------|---------------------|--------------|---------------------------------|---------------------|----------------------------------|-------------------------------|---------------------|---|
|                   |           |              |             |                     |              | Observed (control) <sup>b</sup> | Confidence Interval | Simulated (control) <sup>c</sup> | Observed (intervention group) | Confidence Interval | Simulated (intervention group) <sup>d</sup> |
| Both <sup>e</sup> | Incidence | Overall      | 0.78        | (0.70-0.87)         | 0.84         | 174.5                           | (166.9-182.1)       | 174.5                            | 135.9                         | (122.5-149.3)       | 146.5                                       |
| Both <sup>e</sup> | Mortality | Overall      | 0.79        | (0.65-0.96)         | 0.72         | 52.9                            | (48.8-57)           | 51.2                             | 41.9                          | (34.5-49.3)         | 36.7  |
| Male              | Incidence | Overall      | 0.66        | (0.57-0.78)         | 0.81         | 196.9                           | (185.4-208.4)       | 195.4                            | 131.4                         | (112.5-150.3)       | 158.9                                       |
| Male              | Mortality | Overall      | 0.63        | (0.47-0.83)         | 0.70         | 63.3                            | (57-69.6)           | 61.6                             | 40.0                          | (29.6-50.4)         | 43.0  |
| Female            | Incidence | Overall      | 0.92        | (0.79-1.07)         | 0.85         | 153.1                           | (143.2-163)         | 152.7                            | 140.1                         | (121.0-159.2)       | 130.4                                       |
| Female            | Mortality | Overall      | 1.01        | (0.77-1.33)         | 0.76         | 43.3                            | (38.2-48.4)         | 39.0                             | 43.7                          | (33.1-54.3)         | 29.5  |
| Both <sup>e</sup> | Incidence | Distal       | 0.68        | (0.58-0.79)         | 0.80         | 98.5                            | (92.8-104.2)        | 96.2                             | 67.1                          | (57.7-76.5)         | 77.3  |
| Both <sup>e</sup> | Mortality | Distal       | 0.83        | (0.64-0.87)         | 0.65         | 27.8                            | (24.8-30.8)         | 28.5                             | 23.4                          | (17.8-29.0)         | 19.0  |
| Male              | Incidence | Distal       | 0.59        | (0.48-0.73)         | 0.80         | 124.3                           | (115.1-133.5)       | 119.7                            | 74.3                          | (60.1-88.5)         | 95.4  |
| Male              | Mortality | Distal       | 0.65        | (0.45-0.93)         | 0.66         | 37.3                            | (32.4-42.2)         | 35.6                             | 24.6                          | (16.5-32.7)         | 23.5  |
| Female            | Incidence | Distal       | 0.81        | (0.64-1.02)         | 0.81         | 74.3                            | (67.4-81.2)         | 74.8                             | 60.1                          | (47.6-72.6)         | 60.8  |
| Female            | Mortality | Distal       | 1.17        | (0.79-1.73)         | 0.69         | 18.8                            | (15.4-22.2)         | 18.0                             | 22.2                          | (14.6-29.8)         | 12.4  |
| Both <sup>e</sup> | Incidence | Proximal     | 0.92        | (0.78-1.08)         | 0.88         | 72.0                            | (67.2-76.8)         | 78.3                             | 66.1                          | (56.7-75.5)         | 69.2  |
| Both <sup>e</sup> | Mortality | Proximal     | 0.71        | (0.52-0.98)         | 0.78         | 22.7                            | (20-25.4)           | 22.7                             | 16.2                          | (11.6-20.8)         | 17.7  |
| Male              | Incidence | Proximal     | 0.81        | (0.63-1.04)         | 0.84         | 67.6                            | (60.9-74.3)         | 76.3                             | 55.1                          | (42.9-67.3)         | 63.8  |
| Male              | Mortality | Proximal     | 0.60        | (0.37-0.96)         | 0.75         | 23.3                            | (19.5-27.1)         | 26.2                             | 14.1                          | (7.9-20.3)          | 19.7  |
| Female            | Incidence | Proximal     | 1.01        | (0.82-1.25)         | 0.89         | 76.1                            | (69.2-83)           | 77.9                             | 76.5                          | (62.4-90.6)         | 69.6  |
| Female            | Mortality | Proximal     | 0.83        | (0.54-1.26)         | 0.81         | 22.2                            | (18.6-25.8)         | 21.0                             | 18.2                          | (11.4-25.0)         | 17.1  |

Shading indicates model predictions outside confidence intervals of the trial. Blu shading indicates underestimation by the model, while orange shading indicates overestimation.

Abbreviations: HR, hazard ratio; CRC, colorectal cancer.; NORCCAP trial, Norwegian Colorectal Cancer Prevention trial.

- NORCCAP is screening trial comparing effectiveness reducing CRC mortality of once-only flexible sigmoidoscopy to no screening. Validation has been performed as described previously.<sup>1</sup>
- For observed values, the number of distal and proximal CRC cases and deaths are less than the total number of overall CRC cases and deaths. This is due to some unclassified cancers in the NORCCAP trial. For simulated values, the number of distal and proximal CRC cases are equal to the total number of overall CRC cases and deaths, since there is no correction for unclassified cancers. MISCAN-Colon is therefore more likely to overestimate proximal and distal CRC cases and deaths compared to the NORCCAP trial results.
- Adenoma onset for all ages was adjusted to match overall CRC incidence in control group
- Adenoma onset for all ages was adjusted to match the risk difference between CRC incidence in the control group versus non adherers
- For the results of both genders, aggregated data was used.

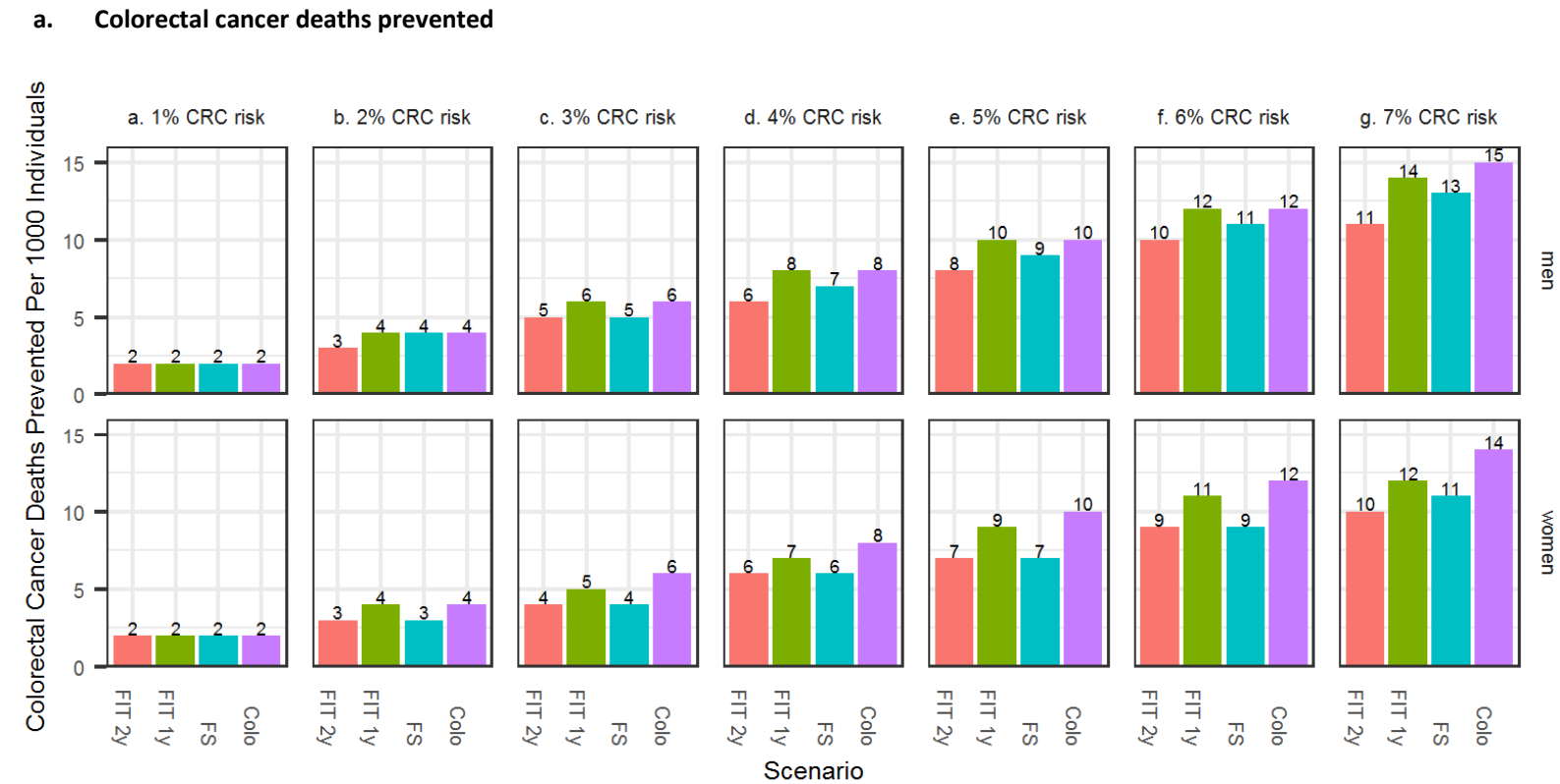
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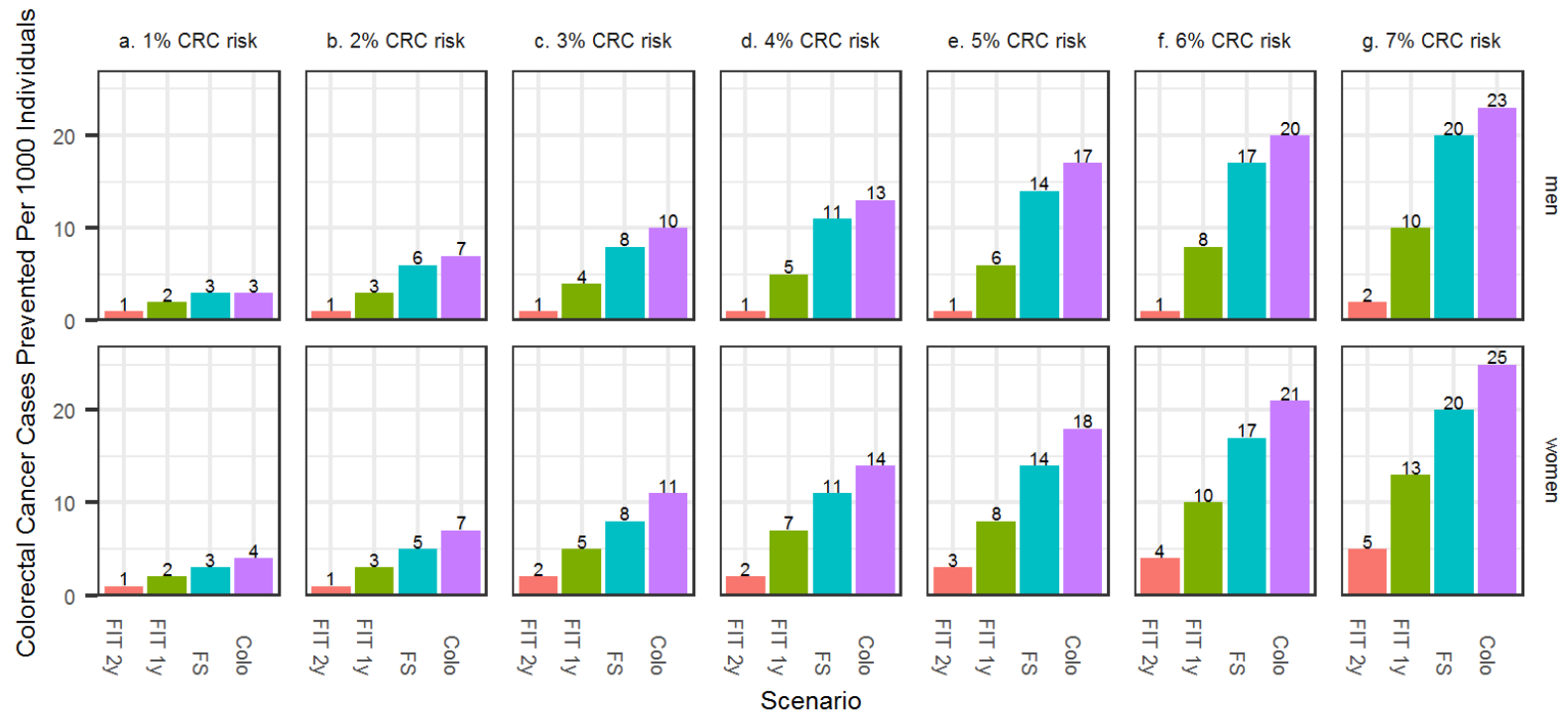
#### **Appendix 4: MISCAN-Colon predictions with 15 year follow-up stratified for colorectal cancer risk, age and gender**

Note: For consistency and completeness, we present outcomes for all combinations of colorectal cancer risk, age and gender. However, with current discriminatory performance of risk calculators, many of these combinations will be obsolete or very rare. For example according to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 50 years varies between 0.9% without risk factors and 2.2% (22 per 1000). with all risk factors. Similarly, 15-year colorectal cancer risk in men aged 75 years varies between 6.4% without any risk factors and 18.6% with all risk factors. Thus results presented for 50-54y old women with a 7% colorectal cancer risk and 75-79y old men with 3% colorectal cancer risk (and many other combinations) are currently not applicable.

**Figure 1: MISCAN-Colon predictions of colorectal cancer mortality and incidence reduction per 1000 individuals, using FIT, flexible sigmoidoscopy or colonoscopy. Results are stratified by CRC risk and sex. Individuals were followed-up during 15 years.**



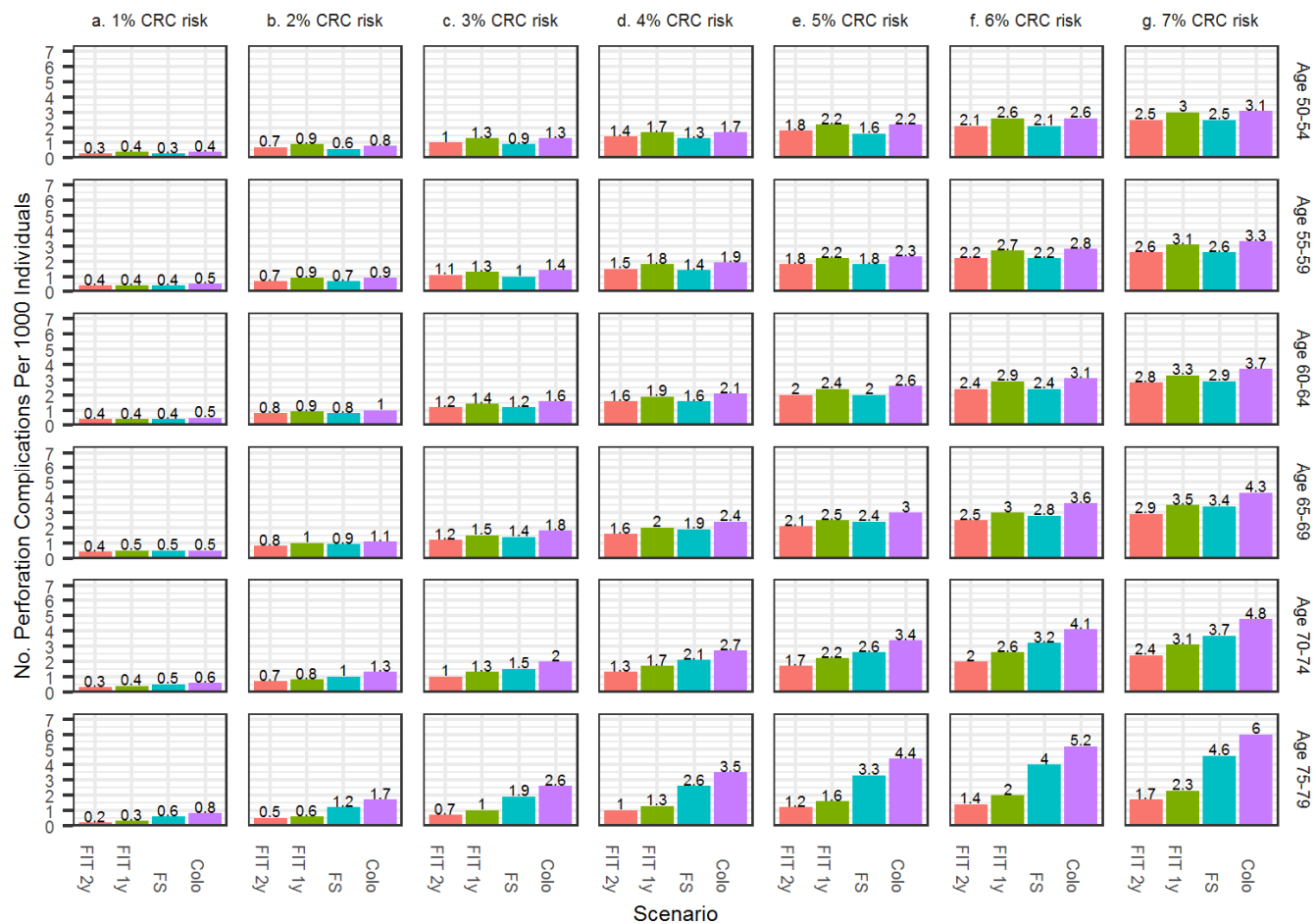
**b. Colorectal cancer cases prevented**



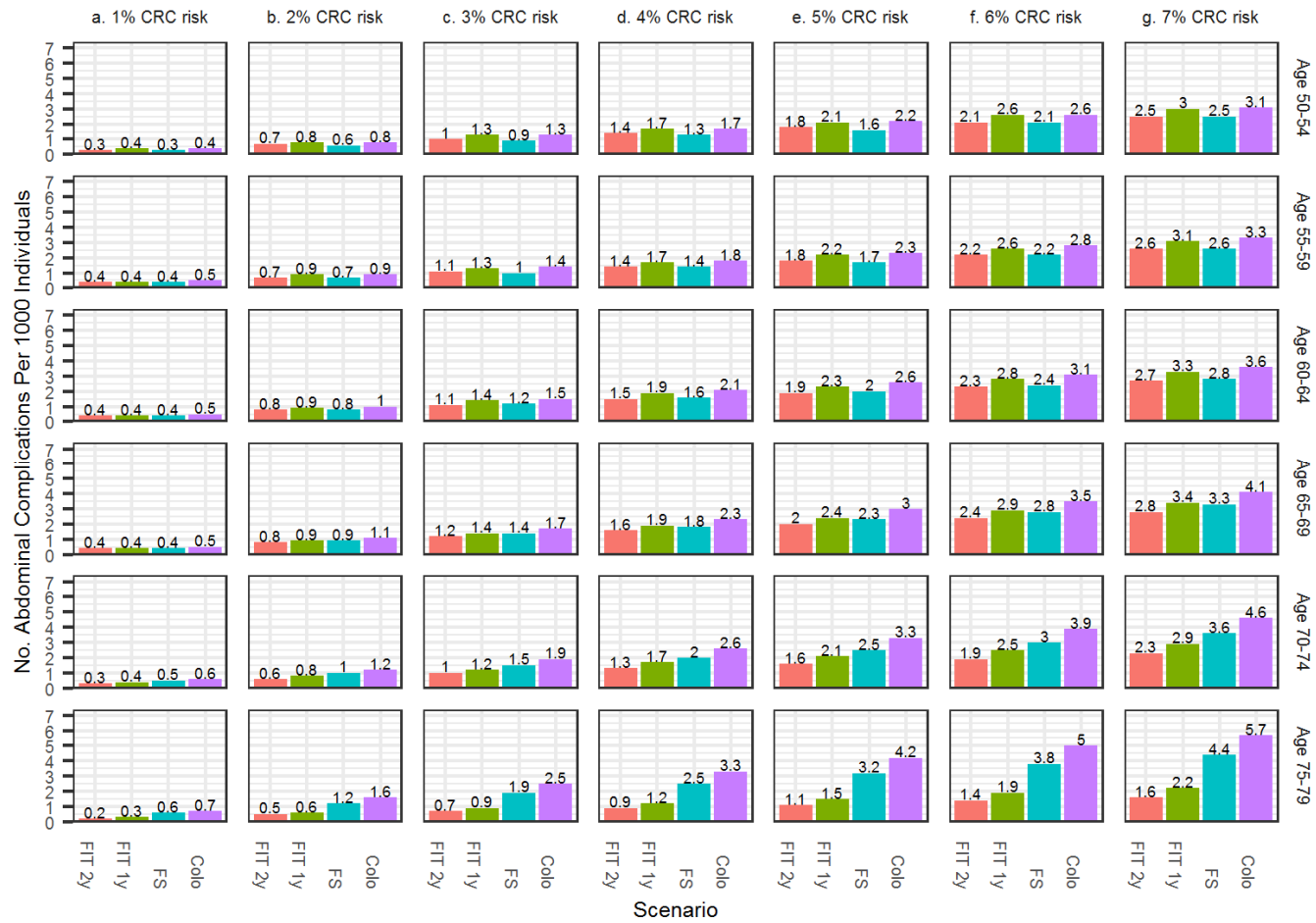
Abbreviations: Colo, colonoscopy; CRC, colorectal cancer; FIT, faecal immunochemical test; FS, flexible sigmoidoscopy.

**Figure 2: MISCAN-Colon predictions of complications per 1000 individuals, using FIT, flexible sigmoidoscopy or colonoscopy. Results are stratified by CRC risk and age. Individuals were followed-up during 15 years.**

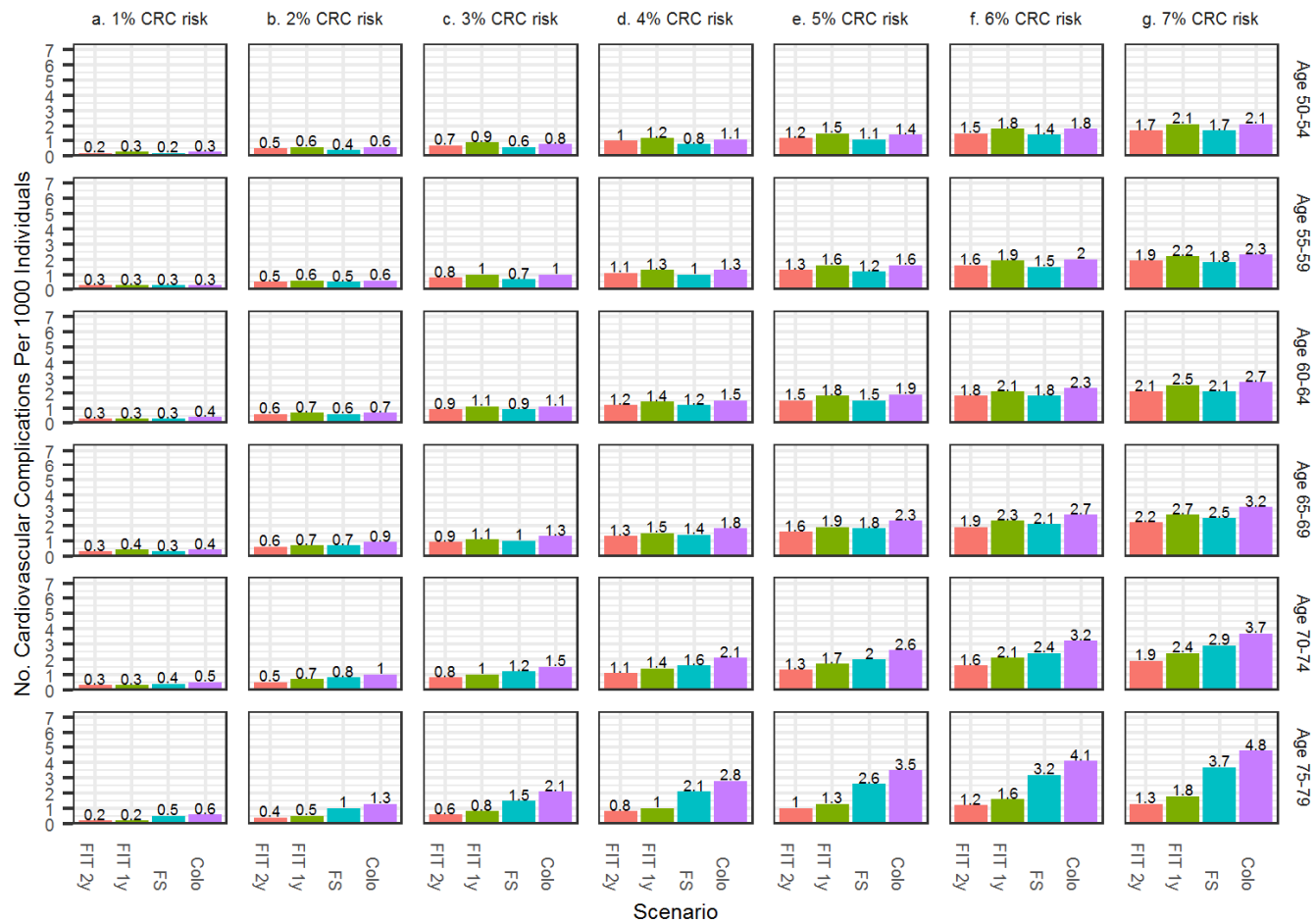
**a. Number of perforation complications**



**b. Number of abdominal complications**



**c. Number of cardiovascular complications**



Abbreviations: Colo, colonoscopy; CRC, colorectal cancer; FIT, faecal immunochemical test; FS, flexible sigmoidoscopy.

**Tables: MISCAN-Colon predictions stratified for colorectal cancer risk, age and sex.**

Note: For consistency and completeness, we present outcomes for all combinations of colorectal cancer risk, age and gender. However, with current discriminatory performance of risk calculators, many of these combinations will be obsolete or very rare. For example according to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 50 years varies between 0.9% without risk factors and 2.2% with all risk factors. Similarly, 15-year colorectal cancer risk in men aged 75 years varies between 6.4% without any risk factors and 18.6% with all risk factors. Thus results presented for 50-54y old women with a 7% colorectal cancer risk and 75-79y old men with 3% colorectal cancer risk (and many other combinations) are currently not applicable.

**Table 1: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for men, aged 50-54, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in men aged 52 years varies between 1.2% without risk factors and 4.3% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -5  | -1  | 53  | 2  | 1.4                               | 6893            | 211                                       | 39  | 0.4                      | 0.6                     | 0.9                   | 0.03                               |
| Annual FIT              | 9   | 1   | 63  | 2  | 1.6                               | 11882           | 329                                       | 48  | 0.5                      | 0.7                     | 1.1                   | 0.03                               |
| Sigmoidoscopy once-only | 25  | 3   | 47  | 1  | 1.2                               | 1000            | 113                                       | 36  | 0.4                      | 0.6                     | 0.9                   | 0.02                               |
| Colonoscopy once-only   | 32  | 3   | 58  | 2  | 1.5                               | 1000            | 1000                                      | 42  | 0.5                      | 0.8                     | 1.1                   | 0.03                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -7  | -1  | 51  | 3  | 2.5                               | 6641            | 274                                       | 80  | 0.9                      | 1.2                     | 1.8                   | 0.05                               |
| Annual FIT              | 7   | 1   | 62  | 4  | 3                                 | 11276           | 395                                       | 98  | 1.1                      | 1.5                     | 2.3                   | 0.06                               |
| Sigmoidoscopy once-only | 24  | 5   | 44  | 3  | 2.1                               | 1000            | 226                                       | 68  | 0.8                      | 1.1                     | 1.6                   | 0.05                               |
| Colonoscopy once-only   | 30  | 6   | 55  | 3  | 2.7                               | 1000            | 1000                                      | 82  | 1.1                      | 1.5                     | 2.2                   | 0.06                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.6% (6 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -7  | -2  | 52  | 5  | 3.7                               | 6405            | 332                                       | 121   | 1.3                      | 1.8                     | 2.8                   | 0.08                               |
| Annual FIT              | 7   | 2   | 62  | 6  | 4.5                               | 10716           | 456                                       | 149   | 1.6                      | 2.2                     | 3.4                   | 0.09                               |
| Sigmoidoscopy once-only | 23  | 7   | 44  | 4  | 3.1                               | 1000            | 328                                       | 103   | 1.2                      | 1.7                     | 2.4                   | 0.07                               |
| Colonoscopy once-only   | 30  | 9   | 55  | 5  | 3.9                               | 1000            | 1000                                      | 124   | 1.6                      | 2.2                     | 3.2                   | 0.09                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 0.9% (9 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -7  | -3  | 52  | 6  | 4.8                               | 6160            | 390                                       | 165   | 1.8                      | 2.5                     | 3.7                   | 0.1                                |
| Annual FIT              | 8   | 3   | 63  | 7  | 5.8                               | 10133           | 515                                       | 205   | 2.2                      | 3                       | 4.6                   | 0.13                               |
| Sigmoidoscopy once-only | 24  | 10  | 46  | 5  | 4.2                               | 1000            | 426                                       | 147   | 1.6                      | 2.3                     | 3.4                   | 0.1                                |
| Colonoscopy once-only   | 31  | 12  | 57  | 7  | 5.2                               | 1000            | 1000                                      | 174   | 2.1                      | 3                       | 4.4                   | 0.13                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.2% (12 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -6  | -3  | 52  | 8  | 5.9                               | 5930            | 443                                       | 209   | 2.2                      | 3.1                     | 4.7                   | 0.13                               |
| Annual FIT              | 9   | 5   | 64  | 9  | 7.3                               | 9608            | 567                                       | 260   | 2.7                      | 3.8                     | 5.7                   | 0.16                               |
| Sigmoidoscopy once-only | 25  | 12  | 47  | 7  | 5.3                               | 1000            | 508                                       | 195   | 2.1                      | 3                       | 4.4                   | 0.13                               |
| Colonoscopy once-only   | 30  | 15  | 57  | 8  | 6.5                               | 1000            | 1000                                      | 226   | 2.7                      | 3.8                     | 5.5                   | 0.16                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.5% (15 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -4  | -2  | 53  | 9  | 7.1                               | 5727            | 488                                       | 252   | 2.6                      | 3.7                     | 5.6                   | 0.16                               |
| Annual FIT              | 10  | 6   | 64  | 11   | 8.5                               | 9146            | 611                                       | 312   | 3.2                      | 4.5                     | 6.8                   | 0.19                               |
| Sigmoidoscopy once-only | 26  | 16  | 49  | 9  | 6.6                               | 1000            | 576                                       | 245   | 2.7                      | 3.8                     | 5.5                   | 0.16                               |
| Colonoscopy once-only   | 31  | 19  | 58  | 10   | 7.8                               | 1000            | 1000                                      | 280   | 3.3                      | 4.6                     | 6.7                   | 0.19                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.8% (18 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -2  | -2  | 55  | 11   | 8.4                               | 5525            | 530                                       | 294   | 3.1                      | 4.3                     | 6.6                   | 0.18                               |
| Annual FIT              | 12  | 8   | 65  | 13   | 9.9                               | 8693            | 652                                       | 365   | 3.7                      | 5.3                     | 8                     | 0.22                               |
| Sigmoidoscopy once-only | 27  | 19  | 52  | 11   | 8                                 | 1000            | 636                                       | 298   | 3.3                      | 4.6                     | 6.8                   | 0.19                               |
| Colonoscopy once-only   | 32  | 22  | 60  | 12   | 9.2                               | 1000            | 1000                                      | 336   | 3.9                      | 5.5                     | 8                     | 0.23                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.0% (20 per 1000).

**Table 2: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for men, aged 55-59, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in men aged 57 years varies between 2.0% without risk factors and 6.1% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 5   | 1   | 56  | 2  | 0.9                               | 6757            | 192                                       | 30  | 0.4                      | 0.6                     | 1                     | 0.03                               |
| Annual FIT              | 17  | 2   | 66  | 2  | 1.1                               | 11703           | 307                                       | 36  | 0.5                      | 0.7                     | 1.2                   | 0.03                               |
| Sigmoidoscopy once-only | 31  | 3   | 58  | 2  | 0.9                               | 1000            | 86  | 31  | 0.5                      | 0.7                     | 1                     | 0.03                               |
| Colonoscopy once-only   | 35  | 3   | 65  | 2  | 1.1                               | 1000            | 1000                                      | 35  | 0.6                      | 0.8                     | 1.2                   | 0.03                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 0   | 0   | 52  | 3  | 1.7                               | 6561            | 239                                       | 62  | 0.9                      | 1.2                     | 2                     | 0.05                               |
| Annual FIT              | 13  | 3   | 63  | 4  | 2                                 | 11236           | 356                                       | 76  | 1.1                      | 1.5                     | 2.4                   | 0.06                               |
| Sigmoidoscopy once-only | 29  | 6   | 52  | 3  | 1.6                               | 1000            | 174                                       | 63  | 0.9                      | 1.3                     | 2                     | 0.06                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 35  | 7   | 62  | 4  | 2                                 | 1000            | 1000                                      | 72  | 1.2                      | 1.6                     | 2.5                   | 0.07                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.6% (6 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -1  | 0   | 51  | 5  | 2.4                               | 6360            | 287                                       | 95  | 1.3                      | 1.9                     | 3                     | 0.08                               |
| Annual FIT              | 12  | 4   | 61  | 6  | 2.9                               | 10764           | 405                                       | 116   | 1.6                      | 2.3                     | 3.7                   | 0.1                                |
| Sigmoidoscopy once-only | 28  | 8   | 50  | 5  | 2.3                               | 1000            | 262                                       | 94  | 1.4                      | 1.9                     | 3                     | 0.08                               |
| Colonoscopy once-only   | 34  | 10  | 60  | 6  | 2.8                               | 1000            | 1000                                      | 109   | 1.8                      | 2.5                     | 3.8                   | 0.1                                |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 0.9% (9 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -1  | -1  | 52  | 6  | 3.1                               | 6163            | 333                                       | 128   | 1.8                      | 2.5                     | 4                     | 0.11                               |
| Annual FIT              | 12  | 5   | 62  | 7  | 3.7                               | 10305           | 453                                       | 158   | 2.2                      | 3.1                     | 4.9                   | 0.13                               |
| Sigmoidoscopy once-only | 27  | 11  | 49  | 6  | 2.9                               | 1000            | 346                                       | 127   | 1.9                      | 2.6                     | 4                     | 0.11                               |
| Colonoscopy once-only   | 34  | 13  | 59  | 7  | 3.5                               | 1000            | 1000                                      | 148   | 2.3                      | 3.3                     | 5                     | 0.14                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.2% (12 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -2  | -1  | 52  | 8  | 3.9                               | 5973            | 377                                       | 161   | 2.3                      | 3.2                     | 5                     | 0.13                               |
| Annual FIT              | 12  | 6   | 62  | 10   | 4.7                               | 9858            | 498                                       | 198   | 2.8                      | 3.9                     | 6.1                   | 0.16                               |
| Sigmoidoscopy once-only | 28  | 14  | 51  | 8  | 3.8                               | 1000            | 421                                       | 163   | 2.3                      | 3.3                     | 5.1                   | 0.14                               |
| Colonoscopy once-only   | 34  | 17  | 61  | 9  | 4.6                               | 1000            | 1000                                      | 188   | 2.9                      | 4.1                     | 6.3                   | 0.17                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.5% (15 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -1  | -1  | 53  | 10   | 4.7                               | 5781            | 421                                       | 197   | 2.8                      | 3.8                     | 6.1                   | 0.16                               |
| Annual FIT              | 12  | 7   | 63  | 12   | 5.6                               | 9418            | 542                                       | 243   | 3.3                      | 4.7                     | 7.4                   | 0.2                                |
| Sigmoidoscopy once-only | 28  | 17  | 51  | 9  | 4.6                               | 1000            | 494                                       | 204   | 2.9                      | 4.1                     | 6.3                   | 0.17                               |
| Colonoscopy once-only   | 34  | 20  | 61  | 11   | 5.4                               | 1000            | 1000                                      | 233   | 3.6                      | 5                       | 7.7                   | 0.21                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.8% (18 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -1  | 0   | 53  | 11   | 5.4                               | 5601            | 461                                       | 231   | 3.2                      | 4.5                     | 7.2                   | 0.19                               |
| Annual FIT              | 13  | 9   | 63  | 14   | 6.5                               | 9008            | 581                                       | 285   | 3.9                      | 5.4                     | 8.7                   | 0.23                               |
| Sigmoidoscopy once-only | 29  | 20  | 53  | 11   | 5.4                               | 1000            | 556                                       | 246   | 3.5                      | 4.9                     | 7.5                   | 0.21                               |
| Colonoscopy once-only   | 34  | 24  | 62  | 13   | 6.3                               | 1000            | 1000                                      | 278   | 4.2                      | 5.9                     | 9                     | 0.25                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.2% (22 per 1000).

**Table 3: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for men, aged 60-64, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in men aged 62 years varies between 3.0% without risk factors and 8.6% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 11  | 1   | 60  | 2  | 0.6                               | 6500            | 177                                       | 23  | 0.5                      | 0.6                     | 1.1                   | 0.03                               |
| Annual FIT              | 21  | 2   | 67  | 2  | 0.7                               | 11303           | 287                                       | 28  | 0.5                      | 0.7                     | 1.2                   | 0.03                               |
| Sigmoidoscopy once-only | 33  | 3   | 62  | 2  | 0.6                               | 1000            | 72  | 27  | 0.5                      | 0.7                     | 1.2                   | 0.03                               |
| Colonoscopy once-only   | 38  | 4   | 69  | 2  | 0.7                               | 1000            | 1000                                      | 29  | 0.6                      | 0.8                     | 1.4                   | 0.04                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 6   | 1   | 56  | 4  | 1.1                               | 6341            | 213                                       | 49  | 0.9                      | 1.3                     | 2.2                   | 0.06                               |
| Annual FIT              | 18  | 4   | 65  | 4  | 1.3                               | 10934           | 325                                       | 60  | 1.1                      | 1.5                     | 2.6                   | 0.07                               |
| Sigmoidoscopy once-only | 32  | 6   | 59  | 4  | 1.2                               | 1000            | 140                                       | 55  | 1.1                      | 1.5                     | 2.4                   | 0.06                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 37  | 7   | 68  | 4  | 1.4                               | 1000            | 1000                                      | 62  | 1.3                      | 1.8                     | 2.8                   | 0.07                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.6% (6 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 5   | 1   | 53  | 5  | 1.6                               | 6170            | 254                                       | 77  | 1.4                      | 2                       | 3.3                   | 0.08                               |
| Annual FIT              | 17  | 5   | 63  | 6  | 1.9                               | 10531           | 367                                       | 94  | 1.7                      | 2.4                     | 4                     | 0.1                                |
| Sigmoidoscopy once-only | 31  | 9   | 55  | 5  | 1.6                               | 1000            | 215                                       | 85  | 1.6                      | 2.2                     | 3.6                   | 0.09                               |
| Colonoscopy once-only   | 37  | 11  | 65  | 6  | 1.9                               | 1000            | 1000                                      | 96  | 2                        | 2.7                     | 4.4                   | 0.12                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 1.0% (10 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 4   | 1   | 52  | 7  | 2                                 | 6000            | 293                                       | 104   | 1.9                      | 2.7                     | 4.5                   | 0.11                               |
| Annual FIT              | 16  | 6   | 63  | 8  | 2.4                               | 10137           | 407                                       | 128   | 2.3                      | 3.2                     | 5.4                   | 0.14                               |
| Sigmoidoscopy once-only | 31  | 12  | 56  | 7  | 2.1                               | 1000            | 289                                       | 114   | 2.1                      | 3                       | 4.8                   | 0.13                               |
| Colonoscopy once-only   | 37  | 15  | 65  | 8  | 2.5                               | 1000            | 1000                                      | 131   | 2.6                      | 3.7                     | 5.9                   | 0.16                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.3% (13 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 3   | 1   | 53  | 8  | 2.5                               | 5838            | 331                                       | 132   | 2.4                      | 3.3                     | 5.6                   | 0.14                               |
| Annual FIT              | 16  | 8   | 63  | 10   | 3                                 | 9757            | 446                                       | 162   | 2.9                      | 4.1                     | 6.8                   | 0.17                               |
| Sigmoidoscopy once-only | 30  | 15  | 55  | 9  | 2.6                               | 1000            | 359                                       | 145   | 2.7                      | 3.7                     | 6                     | 0.16                               |
| Colonoscopy once-only   | 36  | 18  | 65  | 10   | 3.1                               | 1000            | 1000                                      | 165   | 3.3                      | 4.6                     | 7.4                   | 0.2                                |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.6% (16 per 1000). (16 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 3   | 2   | 52  | 10   | 3                                 | 5676            | 367                                       | 159   | 2.9                      | 4                       | 6.8                   | 0.17                               |
| Annual FIT              | 16  | 9   | 63  | 12   | 3.6                               | 9389            | 484                                       | 196   | 3.5                      | 4.9                     | 8.2                   | 0.21                               |
| Sigmoidoscopy once-only | 31  | 18  | 56  | 11   | 3.1                               | 1000            | 425                                       | 177   | 3.3                      | 4.5                     | 7.3                   | 0.19                               |
| Colonoscopy once-only   | 36  | 22  | 64  | 12   | 3.6                               | 1000            | 1000                                      | 202   | 4                        | 5.5                     | 8.9                   | 0.23                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.9% (19 per 1000). (19 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 4   | 3   | 52  | 12   | 3.5                               | 5517            | 404                                       | 187   | 3.4                      | 4.7                     | 7.9                   | 0.2                                |
| Annual FIT              | 16  | 12  | 63  | 14   | 4.2                               | 9018            | 520                                       | 231   | 4.1                      | 5.7                     | 9.6                   | 0.24                               |
| Sigmoidoscopy once-only | 31  | 22  | 55  | 12   | 3.6                               | 1000            | 485                                       | 212   | 3.9                      | 5.4                     | 8.7                   | 0.23                               |
| Colonoscopy once-only   | 37  | 26  | 64  | 15   | 4.3                               | 1000            | 1000                                      | 239   | 4.7                      | 6.5                     | 10.5                  | 0.27                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.3% (23 per 1000).

**Table 4: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for men, aged 65-69, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in men aged 67 years varies between 4.2% without risk factors and 11.8% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 13  | 1   | 58  | 2  | 0.3                               | 5488            | 149                                       | 19  | 0.5                      | 0.6                     | 1.1                   | 0.03                               |
| Annual FIT              | 22  | 2   | 66  | 2  | 0.4                               | 9751            | 247                                       | 23  | 0.6                      | 0.8                     | 1.3                   | 0.03                               |
| Sigmoidoscopy once-only | 33  | 3   | 65  | 2  | 0.4                               | 1000            | 66  | 24  | 0.6                      | 0.8                     | 1.4                   | 0.04                               |
| Colonoscopy once-only   | 37  | 4   | 70  | 2  | 0.4                               | 1000            | 1000                                      | 26  | 0.7                      | 0.9                     | 1.6                   | 0.04                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 12  | 2   | 54  | 4  | 0.7                               | 5377            | 180                                       | 42  | 1                        | 1.3                     | 2.3                   | 0.06                               |
| Annual FIT              | 21  | 4   | 63  | 4  | 0.8                               | 9479            | 280                                       | 51  | 1.2                      | 1.6                     | 2.8                   | 0.07                               |
| Sigmoidoscopy once-only | 34  | 7   | 61  | 4  | 0.7                               | 1000            | 127                                       | 51  | 1.2                      | 1.7                     | 2.9                   | 0.07                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 38  | 8   | 68  | 5  | 0.8                               | 1000            | 1000                                      | 57  | 1.5                      | 2                       | 3.4                   | 0.09                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.7% (7 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 10  | 3   | 52  | 5  | 0.9                               | 5260            | 212                                       | 66  | 1.5                      | 2                       | 3.5                   | 0.09                               |
| Annual FIT              | 20  | 6   | 61  | 6  | 1.1                               | 9191            | 315                                       | 80  | 1.8                      | 2.5                     | 4.3                   | 0.11                               |
| Sigmoidoscopy once-only | 33  | 10  | 59  | 6  | 1                                 | 1000            | 194                                       | 79  | 1.9                      | 2.6                     | 4.4                   | 0.11                               |
| Colonoscopy once-only   | 38  | 11  | 66  | 7  | 1.1                               | 1000            | 1000                                      | 89  | 2.3                      | 3.1                     | 5.3                   | 0.13                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 1.0% (10 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 9   | 3   | 52  | 7  | 1.2                               | 5140            | 246                                       | 90  | 2                        | 2.7                     | 4.8                   | 0.12                               |
| Annual FIT              | 19  | 7   | 61  | 8  | 1.4                               | 8893            | 352                                       | 110   | 2.5                      | 3.4                     | 5.9                   | 0.15                               |
| Sigmoidoscopy once-only | 32  | 13  | 58  | 8  | 1.3                               | 1000            | 262                                       | 108   | 2.5                      | 3.5                     | 5.9                   | 0.15                               |
| Colonoscopy once-only   | 37  | 15  | 66  | 9  | 1.5                               | 1000            | 1000                                      | 121   | 3.1                      | 4.2                     | 7.1                   | 0.18                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.3% (13 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 8   | 4   | 51  | 8  | 1.5                               | 5024            | 278                                       | 114   | 2.5                      | 3.5                     | 6                     | 0.15                               |
| Annual FIT              | 18  | 9   | 60  | 10   | 1.7                               | 8607            | 386                                       | 139   | 3.1                      | 4.3                     | 7.4                   | 0.18                               |
| Sigmoidoscopy once-only | 32  | 16  | 57  | 9  | 1.6                               | 1000            | 328                                       | 138   | 3.2                      | 4.4                     | 7.5                   | 0.19                               |
| Colonoscopy once-only   | 38  | 19  | 65  | 11   | 1.8                               | 1000            | 1000                                      | 155   | 3.9                      | 5.3                     | 9                     | 0.23                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.7% (17 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 8   | 5   | 51  | 10   | 1.7                               | 4910            | 310                                       | 137   | 3                        | 4.1                     | 7.3                   | 0.18                               |
| Annual FIT              | 18  | 11  | 60  | 12   | 2                                 | 8326            | 420                                       | 168   | 3.7                      | 5.1                     | 8.9                   | 0.22                               |
| Sigmoidoscopy once-only | 32  | 19  | 57  | 11   | 1.9                               | 1000            | 390                                       | 167   | 3.8                      | 5.3                     | 9                     | 0.23                               |
| Colonoscopy once-only   | 37  | 22  | 65  | 13   | 2.2                               | 1000            | 1000                                      | 188   | 4.6                      | 6.4                     | 10.8                  | 0.27                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 2.0% (20 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 8   | 6   | 51  | 12   | 2                                 | 4797            | 341                                       | 162   | 3.6                      | 4.9                     | 8.5                   | 0.21                               |
| Annual FIT              | 19  | 13  | 60  | 14   | 2.4                               | 8051            | 453                                       | 199   | 4.4                      | 6                       | 10.5                  | 0.26                               |
| Sigmoidoscopy once-only | 33  | 23  | 57  | 13   | 2.2                               | 1000            | 450                                       | 199   | 4.5                      | 6.3                     | 10.6                  | 0.27                               |
| Colonoscopy once-only   | 37  | 26  | 65  | 15   | 2.5                               | 1000            | 1000                                      | 223   | 5.5                      | 7.5                     | 12.7                  | 0.32                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.3% (23 per 1000).

**Table 5: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for men, aged 70-74, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in men aged 72 years varies between 5.6% without risk factors and 16.1% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 12  | 1   | 56  | 2  | 0.2                               | 3617            | 104                                       | 16  | 0.4                      | 0.5                     | 1                     | 0.02                               |
| Annual FIT              | 18  | 2   | 62  | 2  | 0.2                               | 6509            | 173                                       | 20  | 0.5                      | 0.7                     | 1.2                   | 0.03                               |
| Sigmoidoscopy once-only | 29  | 3   | 64  | 2  | 0.2                               | 1000            | 69  | 24  | 0.6                      | 0.9                     | 1.5                   | 0.04                               |
| Colonoscopy once-only   | 33  | 3   | 69  | 2  | 0.2                               | 1000            | 1000                                      | 26  | 0.7                      | 1                       | 1.8                   | 0.04                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 10  | 2   | 53  | 4  | 0.3                               | 3564            | 130                                       | 35  | 0.8                      | 1.1                     | 2                     | 0.05                               |
| Annual FIT              | 17  | 3   | 61  | 4  | 0.4                               | 6362            | 204                                       | 44  | 1                        | 1.4                     | 2.5                   | 0.06                               |
| Sigmoidoscopy once-only | 29  | 6   | 62  | 4  | 0.4                               | 1000            | 132                                       | 52  | 1.3                      | 1.8                     | 3.2                   | 0.08                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 34  | 7   | 69  | 5  | 0.4                               | 1000            | 1000                                      | 57  | 1.6                      | 2.2                     | 3.9                   | 0.1                                |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.7% (7 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 10  | 3   | 51  | 5  | 0.5                               | 3509            | 158                                       | 54  | 1.2                      | 1.7                     | 3                     | 0.07                               |
| Annual FIT              | 17  | 5   | 59  | 6  | 0.6                               | 6208            | 236                                       | 68  | 1.6                      | 2.2                     | 3.9                   | 0.09                               |
| Sigmoidoscopy once-only | 30  | 9   | 60  | 6  | 0.6                               | 1000            | 199                                       | 80  | 2.1                      | 2.8                     | 5                     | 0.12                               |
| Colonoscopy once-only   | 35  | 10  | 68  | 7  | 0.7                               | 1000            | 1000                                      | 89  | 2.5                      | 3.5                     | 6.1                   | 0.15                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 1.1% (11 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 9   | 4   | 50  | 7  | 0.6                               | 3452            | 186                                       | 74  | 1.7                      | 2.3                     | 4.1                   | 0.1                                |
| Annual FIT              | 16  | 6   | 59  | 8  | 0.7                               | 6049            | 270                                       | 94  | 2.2                      | 2.9                     | 5.3                   | 0.13                               |
| Sigmoidoscopy once-only | 30  | 12  | 60  | 8  | 0.8                               | 1000            | 268                                       | 110   | 2.8                      | 3.9                     | 6.8                   | 0.17                               |
| Colonoscopy once-only   | 34  | 14  | 67  | 9  | 0.8                               | 1000            | 1000                                      | 123   | 3.5                      | 4.8                     | 8.4                   | 0.21                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.4% (14 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 9   | 4   | 50  | 9  | 0.8                               | 3398            | 214                                       | 93  | 2.1                      | 2.9                     | 5.1                   | 0.12                               |
| Annual FIT              | 16  | 8   | 59  | 10   | 0.9                               | 5898            | 302                                       | 119   | 2.7                      | 3.7                     | 6.6                   | 0.16                               |
| Sigmoidoscopy once-only | 30  | 15  | 60  | 10   | 0.9                               | 1000            | 333                                       | 140   | 3.6                      | 4.9                     | 8.6                   | 0.21                               |
| Colonoscopy once-only   | 34  | 17  | 67  | 12   | 1.1                               | 1000            | 1000                                      | 157   | 4.4                      | 6                       | 10.5                  | 0.26                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.7% (17 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 9   | 5   | 49  | 10   | 0.9                               | 3345            | 241                                       | 113   | 2.5                      | 3.4                     | 6.1                   | 0.15                               |
| Annual FIT              | 16  | 10  | 59  | 12   | 1.1                               | 5748            | 334                                       | 144   | 3.3                      | 4.5                     | 8                     | 0.19                               |
| Sigmoidoscopy once-only | 31  | 18  | 60  | 12   | 1.1                               | 1000            | 397                                       | 171   | 4.3                      | 5.9                     | 10.4                  | 0.26                               |
| Colonoscopy once-only   | 35  | 21  | 67  | 14   | 1.2                               | 1000            | 1000                                      | 191   | 5.3                      | 7.2                     | 12.7                  | 0.31                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 2.1% (21 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 9   | 6   | 49  | 12   | 1.1                               | 3291            | 267                                       | 132   | 2.9                      | 4                       | 7.2                   | 0.17                               |
| Annual FIT              | 16  | 11  | 59  | 14   | 1.3                               | 5599            | 365                                       | 169   | 3.8                      | 5.2                     | 9.3                   | 0.23                               |
| Sigmoidoscopy once-only | 31  | 21  | 60  | 14   | 1.3                               | 1000            | 457                                       | 203   | 5.1                      | 6.9                     | 12.2                  | 0.3                                |
| Colonoscopy once-only   | 35  | 24  | 67  | 16   | 1.5                               | 1000            | 1000                                      | 226   | 6.1                      | 8.4                     | 14.8                  | 0.36                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.4% (24 per 1000).

**Table 6: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for men, aged 75-79, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in men aged 77 years varies between 6.7% without risk factors and 21.4% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 3   | 0   | 43  | 2  | 0.1                               | 1723            | 58  | 12  | 0.3                      | 0.4                     | 0.7                   | 0.02                               |
| Annual FIT              | 6   | 1   | 51  | 2  | 0.1                               | 2792            | 86  | 16  | 0.4                      | 0.5                     | 1                     | 0.02                               |
| Sigmoidoscopy once-only | 21  | 2   | 65  | 2  | 0.1                               | 1000            | 81  | 27  | 0.8                      | 1.1                     | 2                     | 0.05                               |
| Colonoscopy once-only   | 23  | 2   | 69  | 3  | 0.1                               | 1000            | 1000                                      | 30  | 1                        | 1.3                     | 2.5                   | 0.06                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.4% (4 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 0   | 40  | 3  | 0.1                               | 1712            | 78  | 25  | 0.6                      | 0.8                     | 1.5                   | 0.04                               |
| Annual FIT              | 4   | 1   | 48  | 4  | 0.2                               | 2754            | 112                                       | 32  | 0.8                      | 1.1                     | 2                     | 0.05                               |
| Sigmoidoscopy once-only | 19  | 4   | 61  | 5  | 0.2                               | 1000            | 155                                       | 57  | 1.7                      | 2.3                     | 4.2                   | 0.1                                |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 23  | 5   | 68  | 5  | 0.2                               | 1000            | 1000                                      | 63  | 2.1                      | 2.9                     | 5.3                   | 0.13                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.7% (7 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 0   | 39  | 4  | 0.2                               | 1699            | 100                                       | 38  | 0.9                      | 1.2                     | 2.3                   | 0.05                               |
| Annual FIT              | 4   | 1   | 47  | 5  | 0.2                               | 2713            | 140                                       | 50  | 1.2                      | 1.7                     | 3.1                   | 0.07                               |
| Sigmoidoscopy once-only | 20  | 6   | 61  | 7  | 0.3                               | 1000            | 234                                       | 90  | 2.7                      | 3.6                     | 6.7                   | 0.16                               |
| Colonoscopy once-only   | 23  | 7   | 68  | 7  | 0.3                               | 1000            | 1000                                      | 100   | 3.4                      | 4.6                     | 8.4                   | 0.2                                |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 1.1% (11 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 0   | 40  | 6  | 0.3                               | 1687            | 120                                       | 50  | 1.2                      | 1.6                     | 3                     | 0.07                               |
| Annual FIT              | 4   | 2   | 48  | 7  | 0.3                               | 2674            | 165                                       | 66  | 1.6                      | 2.2                     | 4                     | 0.1                                |
| Sigmoidoscopy once-only | 21  | 8   | 62  | 9  | 0.4                               | 1000            | 305                                       | 120   | 3.6                      | 4.8                     | 8.9                   | 0.21                               |
| Colonoscopy once-only   | 24  | 10  | 69  | 10   | 0.5                               | 1000            | 1000                                      | 133   | 4.5                      | 6.1                     | 11.1                  | 0.27                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.5% (15 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 0   | 0   | 38  | 7  | 0.3                               | 1676            | 141                                       | 64  | 1.5                      | 2.1                     | 3.8                   | 0.09                               |
| Annual FIT              | 3   | 2   | 47  | 9  | 0.4                               | 2635            | 192                                       | 85  | 2                        | 2.8                     | 5.1                   | 0.12                               |
| Sigmoidoscopy once-only | 21  | 10  | 61  | 11   | 0.5                               | 1000            | 381                                       | 154   | 4.5                      | 6.2                     | 11.3                  | 0.27                               |
| Colonoscopy once-only   | 24  | 12  | 68  | 12   | 0.6                               | 1000            | 1000                                      | 171   | 5.7                      | 7.7                     | 14.1                  | 0.34                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.8% (18 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 1   | 38  | 8  | 0.4                               | 1664            | 162                                       | 77  | 1.8                      | 2.5                     | 4.5                   | 0.11                               |
| Annual FIT              | 4   | 2   | 47  | 10   | 0.5                               | 2596            | 217                                       | 102   | 2.5                      | 3.3                     | 6.1                   | 0.15                               |
| Sigmoidoscopy once-only | 21  | 13  | 61  | 13   | 0.6                               | 1000            | 450                                       | 188   | 5.5                      | 7.4                     | 13.5                  | 0.32                               |
| Colonoscopy once-only   | 24  | 14  | 68  | 15   | 0.7                               | 1000            | 1000                                      | 208   | 6.7                      | 9.2                     | 16.7                  | 0.4                                |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 2.2% (22 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 1   | 39  | 10   | 0.4                               | 1652            | 182                                       | 90  | 2.1                      | 2.9                     | 5.3                   | 0.13                               |
| Annual FIT              | 4   | 3   | 47  | 12   | 0.5                               | 2557            | 244                                       | 120   | 2.9                      | 3.9                     | 7.1                   | 0.17                               |
| Sigmoidoscopy once-only | 21  | 15  | 62  | 16   | 0.7                               | 1000            | 516                                       | 223   | 6.4                      | 8.6                     | 15.8                  | 0.38                               |
| Colonoscopy once-only   | 24  | 17  | 69  | 18   | 0.8                               | 1000            | 1000                                      | 246   | 7.8                      | 10.5                    | 19.3                  | 0.46                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.6% (26 per 1000).

**Table 7: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for women, aged 50-54, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 52 years varies between 1.0% without risk factors and 2.6% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 0   | 0   | 50  | 1  | 1.8                               | 6929            | 224                                       | 44  | 0.5                      | 0.6                     | 1                     | 0.03                               |
| Annual FIT              | 12  | 1   | 60  | 2  | 2.2                               | 11898           | 345                                       | 52  | 0.6                      | 0.8                     | 1.2                   | 0.03                               |
| Sigmoidoscopy once-only | 24  | 2   | 42  | 1  | 1.5                               | 1000            | 113                                       | 35  | 0.4                      | 0.5                     | 0.8                   | 0.02                               |
| Colonoscopy once-only   | 33  | 3   | 55  | 2  | 2                                 | 1000            | 1000                                      | 46  | 0.6                      | 0.8                     | 1.1                   | 0.03                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -3  | -1  | 50  | 3  | 3.4                               | 6613            | 299                                       | 89  | 0.9                      | 1.3                     | 2                     | 0.06                               |
| Annual FIT              | 11  | 2   | 60  | 3  | 4.1                               | 11143           | 422                                       | 108   | 1.1                      | 1.6                     | 2.4                   | 0.07                               |
| Sigmoidoscopy once-only | 21  | 4   | 39  | 2  | 2.7                               | 1000            | 221                                       | 67  | 0.7                      | 1                       | 1.5                   | 0.04                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 32  | 6   | 56  | 3  | 3.8                               | 1000            | 1000                                      | 91  | 1.1                      | 1.6                     | 2.3                   | 0.07                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.5% (5 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -3  | -1  | 50  | 4  | 5                                 | 6311            | 368                                       | 136   | 1.4                      | 2                       | 3                     | 0.08                               |
| Annual FIT              | 10  | 3   | 59  | 5  | 5.9                               | 10431           | 493                                       | 164   | 1.7                      | 2.4                     | 3.6                   | 0.1                                |
| Sigmoidoscopy once-only | 21  | 6   | 40  | 3  | 4                                 | 1000            | 319                                       | 104   | 1.1                      | 1.6                     | 2.3                   | 0.07                               |
| Colonoscopy once-only   | 31  | 9   | 55  | 4  | 5.5                               | 1000            | 1000                                      | 140   | 1.7                      | 2.4                     | 3.4                   | 0.1                                |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 0.8% (8 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | -2  | -1  | 51  | 5  | 6.6                               | 6017            | 434                                       | 185   | 1.9                      | 2.7                     | 4.1                   | 0.11                               |
| Annual FIT              | 11  | 4   | 61  | 6  | 7.8                               | 9751            | 558                                       | 224   | 2.3                      | 3.2                     | 4.8                   | 0.13                               |
| Sigmoidoscopy once-only | 23  | 9   | 42  | 4  | 5.3                               | 1000            | 410                                       | 149   | 1.6                      | 2.2                     | 3.3                   | 0.09                               |
| Colonoscopy once-only   | 31  | 13  | 57  | 6  | 7.3                               | 1000            | 1000                                      | 196   | 2.3                      | 3.2                     | 4.7                   | 0.13                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.1% (11 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 0   | 0   | 51  | 7  | 8                                 | 5756            | 490                                       | 233   | 2.4                      | 3.4                     | 5.1                   | 0.14                               |
| Annual FIT              | 12  | 6   | 60  | 8  | 9.5                               | 9159            | 612                                       | 282   | 2.8                      | 4                       | 6                     | 0.17                               |
| Sigmoidoscopy once-only | 24  | 12  | 43  | 6  | 6.8                               | 1000            | 487                                       | 197   | 2.1                      | 2.9                     | 4.3                   | 0.12                               |
| Colonoscopy once-only   | 32  | 16  | 58  | 8  | 9.1                               | 1000            | 1000                                      | 253   | 2.9                      | 4.1                     | 5.9                   | 0.17                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.3% (13 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 1   | 53  | 8  | 9.5                               | 5507            | 540                                       | 280   | 2.9                      | 4                       | 6.1                   | 0.17                               |
| Annual FIT              | 14  | 9   | 62  | 10   | 11.2                              | 8604            | 660                                       | 340   | 3.4                      | 4.8                     | 7.2                   | 0.2                                |
| Sigmoidoscopy once-only | 25  | 15  | 46  | 7  | 8.4                               | 1000            | 554                                       | 251   | 2.6                      | 3.7                     | 5.5                   | 0.16                               |
| Colonoscopy once-only   | 32  | 19  | 59  | 9  | 10.7                              | 1000            | 1000                                      | 313   | 3.5                      | 4.9                     | 7.2                   | 0.21                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.6% (16 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 3   | 2   | 54  | 10   | 11.1                              | 5271            | 586                                       | 326   | 3.3                      | 4.7                     | 7.1                   | 0.2                                |
| Annual FIT              | 16  | 11  | 63  | 12   | 13                                | 8094            | 703                                       | 396   | 4                        | 5.6                     | 8.4                   | 0.23                               |
| Sigmoidoscopy once-only | 27  | 19  | 50  | 9  | 10.2                              | 1000            | 612                                       | 307   | 3.2                      | 4.6                     | 6.7                   | 0.19                               |
| Colonoscopy once-only   | 33  | 23  | 61  | 11   | 12.4                              | 1000            | 1000                                      | 374   | 4.1                      | 5.8                     | 8.5                   | 0.24                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 1.9% (19 per 1000).

**Table 8: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for women, aged 55-59, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 57 years varies between 1.6% without risk factors and 3.6% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 6   | 1   | 56  | 2  | 1.4                               | 6884            | 205                                       | 35  | 0.5                      | 0.7                     | 1.1                   | 0.03                               |
| Annual FIT              | 19  | 2   | 66  | 2  | 1.6                               | 11878           | 323                                       | 41  | 0.6                      | 0.8                     | 1.3                   | 0.03                               |
| Sigmoidoscopy once-only | 28  | 3   | 52  | 1  | 1.2                               | 1000            | 89  | 31  | 0.4                      | 0.6                     | 1                     | 0.03                               |
| Colonoscopy once-only   | 36  | 4   | 65  | 2  | 1.6                               | 1000            | 1000                                      | 39  | 0.6                      | 0.8                     | 1.3                   | 0.04                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 3   | 1   | 51  | 3  | 2.4                               | 6626            | 264                                       | 72  | 1                        | 1.4                     | 2.2                   | 0.06                               |
| Annual FIT              | 15  | 3   | 61  | 3  | 2.8                               | 11271           | 383                                       | 86  | 1.2                      | 1.6                     | 2.6                   | 0.07                               |
| Sigmoidoscopy once-only | 25  | 5   | 46  | 3  | 2.1                               | 1000            | 174                                       | 60  | 0.9                      | 1.2                     | 1.8                   | 0.05                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 34  | 7   | 60  | 3  | 2.8                               | 1000            | 1000                                      | 79  | 1.2                      | 1.7                     | 2.6                   | 0.07                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.5% (5 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 1   | 0   | 52  | 4  | 3.5                               | 6373            | 321                                       | 110   | 1.5                      | 2.1                     | 3.3                   | 0.09                               |
| Annual FIT              | 15  | 4   | 61  | 5  | 4.1                               | 10670           | 442                                       | 132   | 1.8                      | 2.5                     | 3.9                   | 0.11                               |
| Sigmoidoscopy once-only | 25  | 7   | 44  | 4  | 3                                 | 1000            | 259                                       | 91  | 1.3                      | 1.8                     | 2.7                   | 0.07                               |
| Colonoscopy once-only   | 34  | 10  | 60  | 5  | 4                                 | 1000            | 1000                                      | 120   | 1.8                      | 2.6                     | 3.9                   | 0.11                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 0.8% (8 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 2   | 1   | 51  | 6  | 4.6                               | 6132            | 375                                       | 147   | 2                        | 2.7                     | 4.4                   | 0.12                               |
| Annual FIT              | 15  | 6   | 61  | 7  | 5.4                               | 10112           | 496                                       | 176   | 2.4                      | 3.3                     | 5.2                   | 0.14                               |
| Sigmoidoscopy once-only | 25  | 10  | 44  | 5  | 3.9                               | 1000            | 335                                       | 124   | 1.7                      | 2.4                     | 3.6                   | 0.1                                |
| Colonoscopy once-only   | 34  | 14  | 59  | 7  | 5.3                               | 1000            | 1000                                      | 161   | 2.4                      | 3.4                     | 5.2                   | 0.14                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.1% (11 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 2   | 1   | 52  | 7  | 5.7                               | 5893            | 427                                       | 185   | 2.5                      | 3.5                     | 5.5                   | 0.15                               |
| Annual FIT              | 15  | 7   | 61  | 8  | 6.7                               | 9565            | 547                                       | 223   | 3                        | 4.1                     | 6.6                   | 0.17                               |
| Sigmoidoscopy once-only | 25  | 13  | 45  | 6  | 5                                 | 1000            | 407                                       | 161   | 2.2                      | 3.1                     | 4.7                   | 0.13                               |
| Colonoscopy once-only   | 34  | 17  | 60  | 8  | 6.5                               | 1000            | 1000                                      | 208   | 3.1                      | 4.3                     | 6.6                   | 0.18                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.4% (14 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 3   | 2   | 52  | 9  | 6.8                               | 5670            | 473                                       | 223   | 3                        | 4.2                     | 6.6                   | 0.18                               |
| Annual FIT              | 16  | 10  | 62  | 10   | 8                                 | 9063            | 593                                       | 269   | 3.5                      | 4.9                     | 7.8                   | 0.21                               |
| Sigmoidoscopy once-only | 26  | 16  | 47  | 8  | 6.0                               | 1000            | 472                                       | 200   | 2.7                      | 3.8                     | 5.8                   | 0.16                               |
| Colonoscopy once-only   | 35  | 21  | 61  | 10   | 7.9                               | 1000            | 1000                                      | 255   | 3.7                      | 5.2                     | 7.9                   | 0.22                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.7% (17 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 4   | 3   | 53  | 10   | 7.8                               | 5462            | 515                                       | 261   | 3.5                      | 4.9                     | 7.7                   | 0.21                               |
| Annual FIT              | 17  | 12  | 62  | 12   | 9.1                               | 8600            | 633                                       | 315   | 4.1                      | 5.7                     | 9.1                   | 0.24                               |
| Sigmoidoscopy once-only | 27  | 19  | 49  | 9  | 7.2                               | 1000            | 529                                       | 243   | 3.3                      | 4.6                     | 7                     | 0.19                               |
| Colonoscopy once-only   | 35  | 24  | 62  | 12   | 9                                 | 1000            | 1000                                      | 303   | 4.3                      | 6                       | 9.3                   | 0.25                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 1.9% (19 per 1000).

**Table 9: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for women, aged 60-64, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 62 years varies between 2.2% without risk factors and 4.8% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 11  | 1   | 57  | 2  | 0.9                               | 6760            | 28  | 62  | 0.5                      | 0.7                     | 1.2                   | 0.03                               |
| Annual FIT              | 21  | 2   | 66  | 2  | 1                                 | 11710           | 33  | 77  | 0.6                      | 0.8                     | 1.4                   | 0.04                               |
| Sigmoidoscopy once-only | 31  | 3   | 56  | 2  | 0.9                               | 1000            | 28  | 81  | 0.5                      | 0.7                     | 1.2                   | 0.03                               |
| Colonoscopy once-only   | 38  | 4   | 68  | 2  | 1                                 | 1000            | 33  | 98  | 0.7                      | 0.9                     | 1.5                   | 0.04                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 8   | 2   | 54  | 3  | 1.6                               | 6551            | 238                                       | 59  | 1.1                      | 1.5                     | 2.5                   | 0.06                               |
| Annual FIT              | 20  | 4   | 63  | 4  | 1.9                               | 11220           | 354                                       | 70  | 1.3                      | 1.7                     | 2.9                   | 0.07                               |
| Sigmoidoscopy once-only | 30  | 6   | 51  | 3  | 1.5                               | 1000            | 143                                       | 55  | 1                        | 1.4                     | 2.2                   | 0.06                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 37  | 7   | 64  | 4  | 1.9                               | 1000            | 1000                                      | 69  | 1.3                      | 1.9                     | 3                     | 0.08                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.6% (6 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 6   | 2   | 52  | 4  | 2.3                               | 6335            | 286                                       | 90  | 1.6                      | 2.2                     | 3.7                   | 0.09                               |
| Annual FIT              | 18  | 5   | 62  | 5  | 2.7                               | 10713           | 403                                       | 108   | 1.9                      | 2.6                     | 4.4                   | 0.11                               |
| Sigmoidoscopy once-only | 28  | 8   | 49  | 4  | 2.1                               | 1000            | 215                                       | 83  | 1.5                      | 2                       | 3.3                   | 0.09                               |
| Colonoscopy once-only   | 37  | 11  | 64  | 5  | 2.7                               | 1000            | 1000                                      | 106   | 2                        | 2.9                     | 4.6                   | 0.12                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 0.8% (8 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 5   | 2   | 52  | 6  | 3                                 | 6123            | 332                                       | 122   | 2.1                      | 3                       | 5                     | 0.13                               |
| Annual FIT              | 18  | 7   | 62  | 7  | 3.6                               | 10230           | 449                                       | 146   | 2.6                      | 3.5                     | 5.9                   | 0.15                               |
| Sigmoidoscopy once-only | 28  | 11  | 48  | 6  | 2.8                               | 1000            | 283                                       | 111   | 2                        | 2.7                     | 4.4                   | 0.12                               |
| Colonoscopy once-only   | 37  | 15  | 64  | 7  | 3.7                               | 1000            | 1000                                      | 143   | 2.7                      | 3.8                     | 6.1                   | 0.16                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.2% (12 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 5   | 3   | 52  | 7  | 3.7                               | 5918            | 377                                       | 153   | 2.7                      | 3.7                     | 6.3                   | 0.16                               |
| Annual FIT              | 18  | 9   | 62  | 9  | 4.4                               | 9750            | 495                                       | 184   | 3.2                      | 4.4                     | 7.4                   | 0.19                               |
| Sigmoidoscopy once-only | 27  | 14  | 48  | 7  | 3.4                               | 1000            | 349                                       | 142   | 2.5                      | 3.4                     | 5.6                   | 0.15                               |
| Colonoscopy once-only   | 37  | 18  | 63  | 9  | 4.4                               | 1000            | 1000                                      | 182   | 3.4                      | 4.8                     | 7.7                   | 0.2                                |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.4% (14 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 7   | 4   | 52  | 9  | 4.4                               | 5722            | 419                                       | 184   | 3.2                      | 4.4                     | 7.5                   | 0.19                               |
| Annual FIT              | 19  | 11  | 62  | 11   | 5.2                               | 9307            | 537                                       | 221   | 3.8                      | 5.3                     | 8.8                   | 0.23                               |
| Sigmoidoscopy once-only | 28  | 17  | 49  | 9  | 4.1                               | 1000            | 407                                       | 174   | 3                        | 4.2                     | 6.7                   | 0.18                               |
| Colonoscopy once-only   | 37  | 22  | 63  | 11   | 5.3                               | 1000            | 1000                                      | 220   | 4.1                      | 5.7                     | 9.2                   | 0.24                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.7% (17 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 7   | 5   | 52  | 11   | 5.1                               | 5528            | 459                                       | 216   | 3.8                      | 5.2                     | 8.7                   | 0.22                               |
| Annual FIT              | 19  | 13  | 62  | 12   | 6.0                               | 8866            | 577                                       | 260   | 4.5                      | 6.2                     | 10.3                  | 0.26                               |
| Sigmoidoscopy once-only | 29  | 20  | 50  | 10   | 4.9                               | 1000            | 464                                       | 209   | 3.6                      | 5                       | 8.1                   | 0.21                               |
| Colonoscopy once-only   | 37  | 26  | 64  | 13   | 6.2                               | 1000            | 1000                                      | 260   | 4.8                      | 6.7                     | 10.7                  | 0.28                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.0% (20 per 1000).

**Table 10: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for women, aged 65-69, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 67 years varies between 3.0% without risk factors and 6.2% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 17  | 2   | 56  | 2  | 0.5                               | 5769            | 161                                       | 23  | 0.5                      | 0.7                     | 1.3                   | 0.03                               |
| Annual FIT              | 26  | 3   | 62  | 2  | 0.6                               | 10241           | 264                                       | 27  | 0.6                      | 0.8                     | 1.5                   | 0.04                               |
| Sigmoidoscopy once-only | 33  | 3   | 58  | 2  | 0.5                               | 1000            | 66  | 24  | 0.6                      | 0.8                     | 1.3                   | 0.03                               |
| Colonoscopy once-only   | 39  | 4   | 66  | 2  | 0.6                               | 1000            | 1000                                      | 29  | 0.7                      | 1                       | 1.7                   | 0.04                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 14  | 3   | 52  | 3  | 0.9                               | 5628            | 198                                       | 49  | 1.1                      | 1.5                     | 2.6                   | 0.06                               |
| Annual FIT              | 23  | 5   | 60  | 4  | 1.1                               | 9895            | 304                                       | 58  | 1.3                      | 1.8                     | 3.1                   | 0.08                               |
| Sigmoidoscopy once-only | 31  | 6   | 53  | 3  | 1                                 | 1000            | 125                                       | 50  | 1.1                      | 1.6                     | 2.7                   | 0.07                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 38  | 8   | 64  | 4  | 1.2                               | 1000            | 1000                                      | 62  | 1.5                      | 2.1                     | 3.5                   | 0.09                               |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.6% (6 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 13  | 4   | 51  | 5  | 1.3                               | 5480            | 238                                       | 77  | 1.6                      | 2.2                     | 3.9                   | 0.1                                |
| Annual FIT              | 22  | 7   | 59  | 5  | 1.6                               | 9527            | 347                                       | 91  | 2                        | 2.7                     | 4.7                   | 0.12                               |
| Sigmoidoscopy once-only | 30  | 9   | 51  | 5  | 1.4                               | 1000            | 189                                       | 77  | 1.7                      | 2.4                     | 4                     | 0.1                                |
| Colonoscopy once-only   | 39  | 12  | 63  | 6  | 1.7                               | 1000            | 1000                                      | 96  | 2.3                      | 3.2                     | 5.4                   | 0.14                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 0.9% (9 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 12  | 5   | 51  | 6  | 1.8                               | 5332            | 278                                       | 104   | 2.2                      | 3                       | 5.3                   | 0.13                               |
| Annual FIT              | 22  | 9   | 60  | 7  | 2.1                               | 9159            | 389                                       | 125   | 2.7                      | 3.6                     | 6.3                   | 0.16                               |
| Sigmoidoscopy once-only | 30  | 12  | 50  | 6  | 1.8                               | 1000            | 253                                       | 104   | 2.3                      | 3.1                     | 5.3                   | 0.13                               |
| Colonoscopy once-only   | 39  | 15  | 64  | 8  | 2.2                               | 1000            | 1000                                      | 131   | 3.1                      | 4.3                     | 7.3                   | 0.18                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.2% (12 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 11  | 6   | 51  | 8  | 2.2                               | 5186            | 317                                       | 132   | 2.8                      | 3.8                     | 6.6                   | 0.16                               |
| Annual FIT              | 22  | 11  | 59  | 9  | 2.6                               | 8800            | 429                                       | 158   | 3.3                      | 4.6                     | 8                     | 0.2                                |
| Sigmoidoscopy once-only | 30  | 15  | 50  | 8  | 2.2                               | 1000            | 315                                       | 132   | 2.9                      | 4                       | 6.7                   | 0.17                               |
| Colonoscopy once-only   | 39  | 19  | 64  | 10   | 2.8                               | 1000            | 1000                                      | 166   | 3.9                      | 5.4                     | 9.2                   | 0.23                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.5% (15 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 12  | 7   | 50  | 9  | 2.6                               | 5043            | 353                                       | 159   | 3.3                      | 4.6                     | 8                     | 0.2                                |
| Annual FIT              | 22  | 13  | 58  | 11   | 3                                 | 8452            | 468                                       | 191   | 4                        | 5.5                     | 9.6                   | 0.24                               |
| Sigmoidoscopy once-only | 31  | 18  | 50  | 9  | 2.6                               | 1000            | 372                                       | 161   | 3.5                      | 4.8                     | 8.2                   | 0.21                               |
| Colonoscopy once-only   | 39  | 23  | 63  | 11   | 3.3                               | 1000            | 1000                                      | 202   | 4.7                      | 6.5                     | 11                    | 0.28                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 1.8% (18 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 12  | 8   | 50  | 11   | 3                                 | 4905            | 389                                       | 186   | 3.9                      | 5.3                     | 9.4                   | 0.23                               |
| Annual FIT              | 22  | 16  | 59  | 13   | 3.6                               | 8112            | 506                                       | 224   | 4.7                      | 6.5                     | 11.3                  | 0.28                               |
| Sigmoidoscopy once-only | 30  | 21  | 50  | 11   | 3                                 | 1000            | 426                                       | 192   | 4.1                      | 5.7                     | 9.6                   | 0.24                               |
| Colonoscopy once-only   | 39  | 27  | 63  | 13   | 3.8                               | 1000            | 1000                                      | 238   | 5.5                      | 7.6                     | 12.8                  | 0.33                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.1% (21 per 1000)

**Table 11: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for women, aged 70-74, stratified by risk**

Note: According to the Qcancer risk calculator, the 15-year colorectal cancer risk in women aged 72 years varies between 3.8% without risk factors and 7.7% with all risk factors.

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 0.18                                      | 2   | 0.53                                      | 2  | 0.997                             | 3754            | 111                                       | 19  | 0.4                      | 0.6                     | 1.1                   | 0.03                               |
| Annual FIT              | 0.24                                      | 2   | 0.61                                      | 2  | 0.997                             | 6771            | 183                                       | 23  | 0.5                      | 0.7                     | 1.3                   | 0.03                               |
| Sigmoidoscopy once-only | 0.33                                      | 3   | 0.58                                      | 2  | 0.997                             | 1000            | 67  | 24  | 0.6                      | 0.8                     | 1.4                   | 0.04                               |
| Colonoscopy once-only   | 0.38                                      | 4   | 0.67                                      | 2  | 0.997                             | 1000            | 1000                                      | 29  | 0.8                      | 1.1                     | 1.9                   | 0.05                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.3% (3 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 16  | 3   | 52  | 3  | 0.5                               | 3691            | 141                                       | 39  | 0.9                      | 1.2                     | 2.1                   | 0.05                               |
| Annual FIT              | 22  | 4   | 60  | 4  | 0.6                               | 6596            | 218                                       | 49  | 1.1                      | 1.5                     | 2.7                   | 0.07                               |
| Sigmoidoscopy once-only | 31  | 6   | 56  | 4  | 0.6                               | 1000            | 124                                       | 50  | 1.2                      | 1.7                     | 2.9                   | 0.07                               |

| Screening strategy    | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-----------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                       |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Colonoscopy once-only | 38  | 8   | 67  | 4  | 0.7                               | 1000            | 1000                                      | 61  | 1.7                      | 2.3                     | 4                     | 0.1                                |

Without screening these individuals would have a 1% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.7% (7 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 15  | 4   | 51  | 5  | 0.81                              | 3626            | 173                                       | 61  | 1.3                      | 1.8                     | 3.3                   | 0.08                               |
| Annual FIT              | 22  | 7   | 59  | 6  | 0.9                               | 6409            | 257                                       | 76  | 1.7                      | 2.3                     | 4.2                   | 0.1                                |
| Sigmoidoscopy once-only | 31  | 9   | 54  | 5  | 0.8                               | 1000            | 187                                       | 77  | 1.9                      | 2.6                     | 4.5                   | 0.11                               |
| Colonoscopy once-only   | 39  | 12  | 67  | 7  | 1                                 | 1000            | 1000                                      | 96  | 2.6                      | 3.6                     | 6.2                   | 0.15                               |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 1.0% (10 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 14  | 6   | 50  | 7  | 1                                 | 3561            | 205                                       | 160   | 1.8                      | 2.4                     | 4.4                   | 0.11                               |
| Annual FIT              | 21  | 8   | 59  | 8  | 1.2                               | 6225            | 295                                       | 204   | 2.3                      | 3.2                     | 5.6                   | 0.14                               |
| Sigmoidoscopy once-only | 30  | 12  | 53  | 7  | 1.1                               | 1000            | 249                                       | 231   | 2.5                      | 3.5                     | 6.1                   | 0.15                               |
| Colonoscopy once-only   | 38  | 15  | 66  | 9  | 1.3                               | 1000            | 1000                                      | 287   | 3.5                      | 4.8                     | 8.4                   | 0.21                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.3% (13 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 14  | 7   | 49  | 8  | 1.2                               | 3496            | 236                                       | 82  | 2.3                      | 3.1                     | 5.5                   | 0.13                               |
| Annual FIT              | 21  | 10  | 58  | 10   | 1.4                               | 6043            | 332                                       | 103   | 2.9                      | 4                       | 7.1                   | 0.17                               |
| Sigmoidoscopy once-only | 30  | 15  | 53  | 9  | 1.3                               | 1000            | 310                                       | 104   | 3.2                      | 4.4                     | 7.7                   | 0.19                               |
| Colonoscopy once-only   | 38  | 19  | 66  | 11   | 1.6                               | 1000            | 1000                                      | 129   | 4.4                      | 6                       | 10.6                  | 0.26                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.7% (17 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 14  | 8   | 49  | 10   | 1.5                               | 3432            | 267                                       | 103   | 2.7                      | 3.7                     | 6.6                   | 0.16                               |
| Annual FIT              | 21  | 13  | 59  | 12   | 1.7                               | 5865            | 367                                       | 130   | 3.5                      | 4.7                     | 8.5                   | 0.21                               |
| Sigmoidoscopy once-only | 30  | 18  | 53  | 11   | 1.6                               | 1000            | 366                                       | 132   | 3.8                      | 5.3                     | 9.2                   | 0.23                               |
| Colonoscopy once-only   | 38  | 23  | 66  | 13   | 1.9                               | 1000            | 1000                                      | 164   | 5.3                      | 7.2                     | 12.6                  | 0.31                               |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 2.0% (20 per 1000).

**g. 7% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 14  | 10  | 49  | 11   | 1.7                               | 3370            | 297                                       | 124   | 3.2                      | 4.3                     | 7.7                   | 0.19                               |
| Annual FIT              | 22  | 15  | 58  | 14   | 2                                 | 5690            | 402                                       | 157   | 4.1                      | 5.5                     | 9.9                   | 0.24                               |
| Sigmoidoscopy once-only | 31  | 22  | 54  | 13   | 1.9                               | 1000            | 419                                       | 161   | 4.5                      | 6.2                     | 10.8                  | 0.27                               |
| Colonoscopy once-only   | 39  | 27  | 66  | 15   | 2.3                               | 1000            | 1000                                      | 199   | 6.1                      | 8.3                     | 14.6                  | 0.36                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.3% (23 per 1000).

**Table 12: MISCAN-Colon predictions of benefits and harms of various screening strategies during a follow-up period of 15 years for women, aged 75-79, stratified by risk**

**a. 1% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 10  | 1   | 42  | 2  | 0.1                               | 1741            | 60  | 10  | 0.3                      | 0.4                     | 0.8                   | 0.02                               |
| Annual FIT              | 14  | 1   | 49  | 2  | 0.1                               | 2825            | 89  | 13  | 0.4                      | 0.5                     | 1                     | 0.02                               |
| Sigmoidoscopy once-only | 27  | 3   | 58  | 2  | 0.2                               | 1000            | 74  | 22  | 0.7                      | 1                       | 1.8                   | 0.04                               |
| Colonoscopy once-only   | 33  | 3   | 69  | 3  | 0.2                               | 1000            | 1000                                      | 26  | 1                        | 1.3                     | 2.4                   | 0.06                               |

Without screening these individuals would have a 1% colorectal cancer risk (10 cases per 1000) and a risk of dying of colorectal cancer of 0.4% (4 per 1000).

**b. 2% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 8   | 2   | 40  | 3  | 0.2                               | 1728            | 81  | 21  | 0.6                      | 0.8                     | 1.5                   | 0.04                               |
| Annual FIT              | 12  | 2   | 48  | 4  | 0.3                               | 2782            | 117                                       | 27  | 0.8                      | 1.1                     | 2.1                   | 0.05                               |
| Sigmoidoscopy once-only | 26  | 5   | 57  | 4  | 0.3                               | 1000            | 139                                       | 45  | 1.5                      | 2.1                     | 3.8                   | 0.09                               |
| Colonoscopy once-only   | 32  | 6   | 68  | 5  | 0.4                               | 1000            | 1000                                      | 55  | 2.1                      | 2.9                     | 5.3                   | 0.13                               |

Without screening these individuals would have a 2% colorectal cancer risk (20 cases per 1000) and a risk of dying of colorectal cancer of 0.7% (7 per 1000).

**c. 3% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 8   | 2   | 39  | 4  | 0.3                               | 1715            | 104                                       | 31  | 0.9                      | 1.3                     | 2.3                   | 0.06                               |
| Annual FIT              | 11  | 3   | 48  | 5  | 0.4                               | 2738            | 146                                       | 42  | 1.3                      | 1.7                     | 3.1                   | 0.07                               |
| Sigmoidoscopy once-only | 26  | 8   | 56  | 6  | 0.4                               | 1000            | 209                                       | 69  | 2.3                      | 3.2                     | 5.8                   | 0.14                               |
| Colonoscopy once-only   | 33  | 10  | 69  | 7  | 0.5                               | 1000            | 1000                                      | 85  | 3.3                      | 4.5                     | 8.3                   | 0.2                                |

Without screening these individuals would have a 3% colorectal cancer risk (30 cases per 1000) and risk of dying of colorectal cancer of 1.1% (11 per 1000).

**d. 4% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 7   | 3   | 38  | 6  | 0.4                               | 1701            | 127                                       | 42  | 1.3                      | 1.7                     | 3.1                   | 0.07                               |
| Annual FIT              | 11  | 4   | 46  | 7  | 0.5                               | 2694            | 175                                       | 56  | 1.7                      | 2.3                     | 4.2                   | 0.1                                |
| Sigmoidoscopy once-only | 25  | 10  | 55  | 8  | 0.6                               | 1000            | 278                                       | 94  | 3.2                      | 4.3                     | 7.9                   | 0.19                               |
| Colonoscopy once-only   | 32  | 13  | 68  | 10   | 0.7                               | 1000            | 1000                                      | 116   | 4.5                      | 6.1                     | 11.2                  | 0.27                               |

Without screening these individuals would have a 4% colorectal cancer risk (40 cases per 1000) and a risk of dying of colorectal cancer of 1.5% (15 per 1000).

**e. 5% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 7   | 4   | 38  | 7  | 0.5                               | 1688            | 150                                       | 53  | 1.6                      | 2.1                     | 3.9                   | 0.09                               |
| Annual FIT              | 11  | 5   | 46  | 9  | 0.6                               | 2650            | 204                                       | 71  | 2.1                      | 2.9                     | 5.3                   | 0.13                               |
| Sigmoidoscopy once-only | 26  | 13  | 55  | 10   | 0.7                               | 1000            | 343                                       | 119   | 4                        | 5.4                     | 9.9                   | 0.24                               |
| Colonoscopy once-only   | 33  | 16  | 68  | 13   | 0.9                               | 1000            | 1000                                      | 147   | 5.6                      | 7.7                     | 14                    | 0.33                               |

Without screening these individuals would have a 5% colorectal cancer risk (50 cases per 1000) and a risk of dying of colorectal cancer of 1.9% (19 per 1000).

**f. 6% colorectal cancer risk**

| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Risk of complications    |                         |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   | Perforation and bleeding | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 7   | 4   | 37  | 8  | 0.6                               | 1674            | 172                                       | 64  | 1.9                      | 2.6                     | 4.7                   | 0.11                               |
| Annual FIT              | 11  | 7   | 46  | 10   | 0.7                               | 2606            | 233                                       | 86  | 2.6                      | 3.5                     | 6.4                   | 0.15                               |
| Sigmoidoscopy once-only | 26  | 15  | 55  | 12   | 0.9                               | 1000            | 406                                       | 146   | 4.8                      | 6.6                     | 12                    | 0.29                               |
| Colonoscopy once-only   | 33  | 20  | 68  | 15   | 1.1                               | 1000            | 1000                                      | 178   | 6.7                      | 9.1                     | 16.6                  | 0.4                                |

Without screening these individuals would have a 6% colorectal cancer risk (60 cases per 1000) and a risk of dying of colorectal cancer of 2.2% (22 per 1000).

**g. 7% colorectal cancer risk**

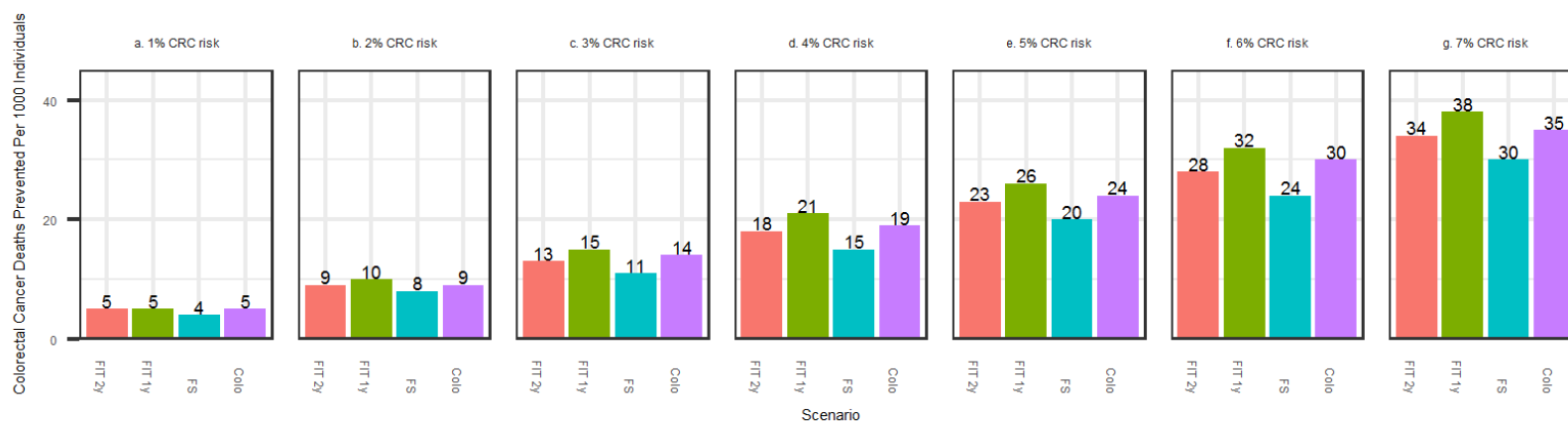
| Screening strategy      | Colorectal cancer incidence reduction (%) | Number of prevented colorectal cancer cases | Colorectal cancer mortality reduction (%) | Number of prevented colorectal cancer deaths | All-cause mortality reduction (%) | Screening tests | Individuals with at least one colonoscopy | Individuals with at least two colonoscopies | Perforation and bleeding | Risk of complications   |                       |                                    |
|-------------------------|---|---|---|--|-----------------------------------|-----------------|---|---|--------------------------|-------------------------|-----------------------|------------------------------------|
|                         |   |   |   |  |                                   |                 |   |   |                          | Other adverse GI events | Cardiovascular events | Screen procedure related mortality |
| Biennial FIT            | 7   | 5   | 38  | 10   | 0.7                               | 1661            | 194                                       | 75  | 2.2                      | 3                       | 5.5                   | 0.13                               |
| Annual FIT              | 11  | 8   | 46  | 12   | 0.9                               | 2564            | 260                                       | 100   | 3                        | 4.1                     | 7.5                   | 0.18                               |
| Sigmoidoscopy once-only | 26  | 19  | 56  | 15   | 1                                 | 1000            | 464                                       | 173   | 5.6                      | 7.6                     | 14                    | 0.33                               |
| Colonoscopy once-only   | 33  | 23  | 69  | 18   | 1.3                               | 1000            | 1000                                      | 210   | 7.7                      | 10.4                    | 19                    | 0.45                               |

Without screening these individuals would have a 7% colorectal cancer risk (70 cases per 1000) and a risk of dying of colorectal cancer of 2.6% (26 per 1000).

## Appendix 5: MISCAN-Colon predictions with lifetime year follow-up stratified for colorectal cancer risk, age and gender

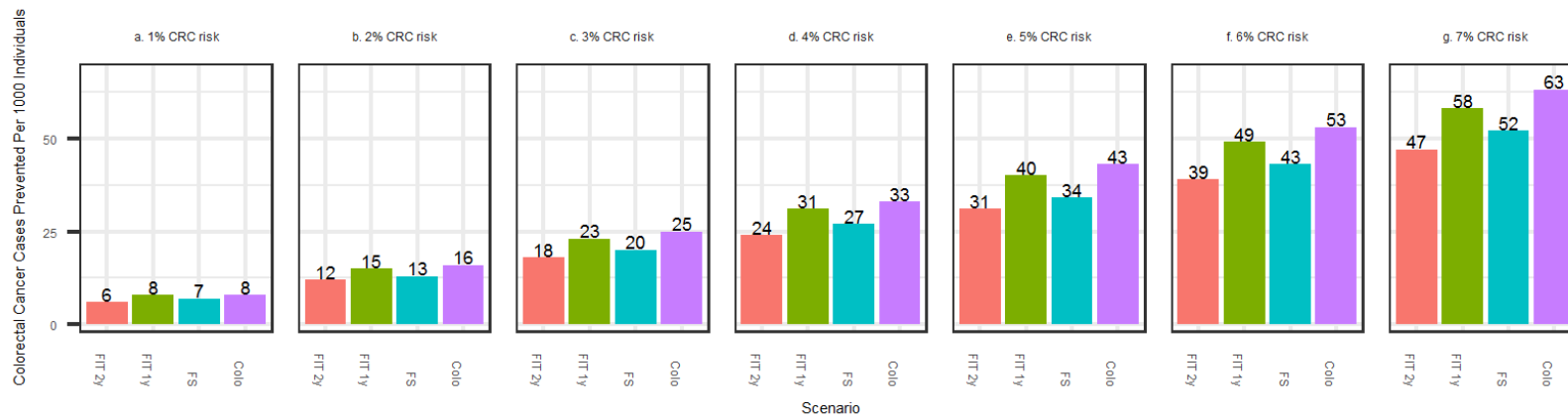
**Figure 1: MISCAN-Colon predictions of colorectal cancer mortality reduction, colorectal cancer incidence reduction per 1000 individuals, using FIT, flexible sigmoidoscopy or colonoscopy. Results were stratified for CRC risk. Individuals were followed for a lifetime.**

### a. Colorectal cancer deaths prevented



## b. Colorectal cancer cases prevented

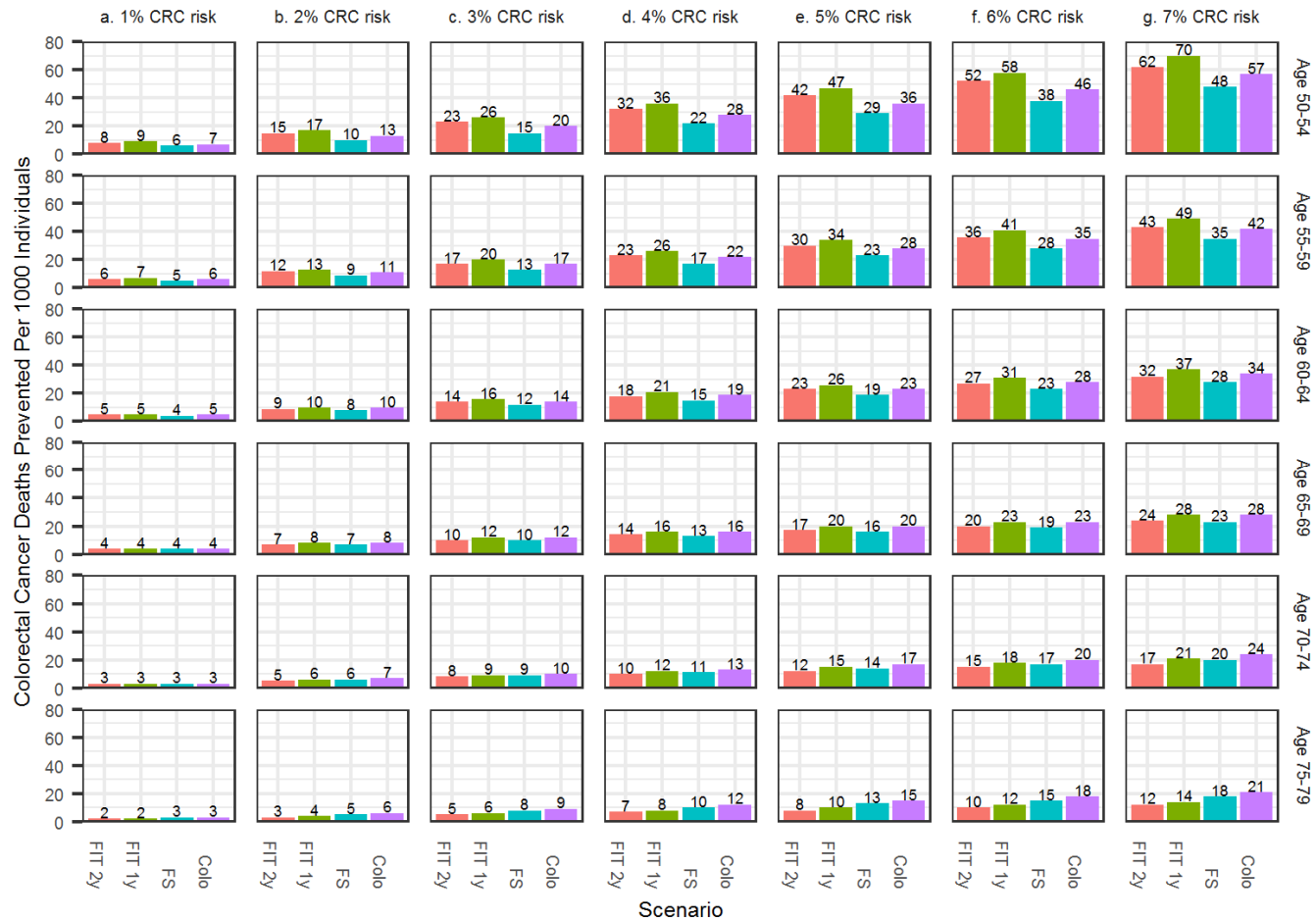
b. Colorectal Cancer Cases Prevented Per 1000 Individuals



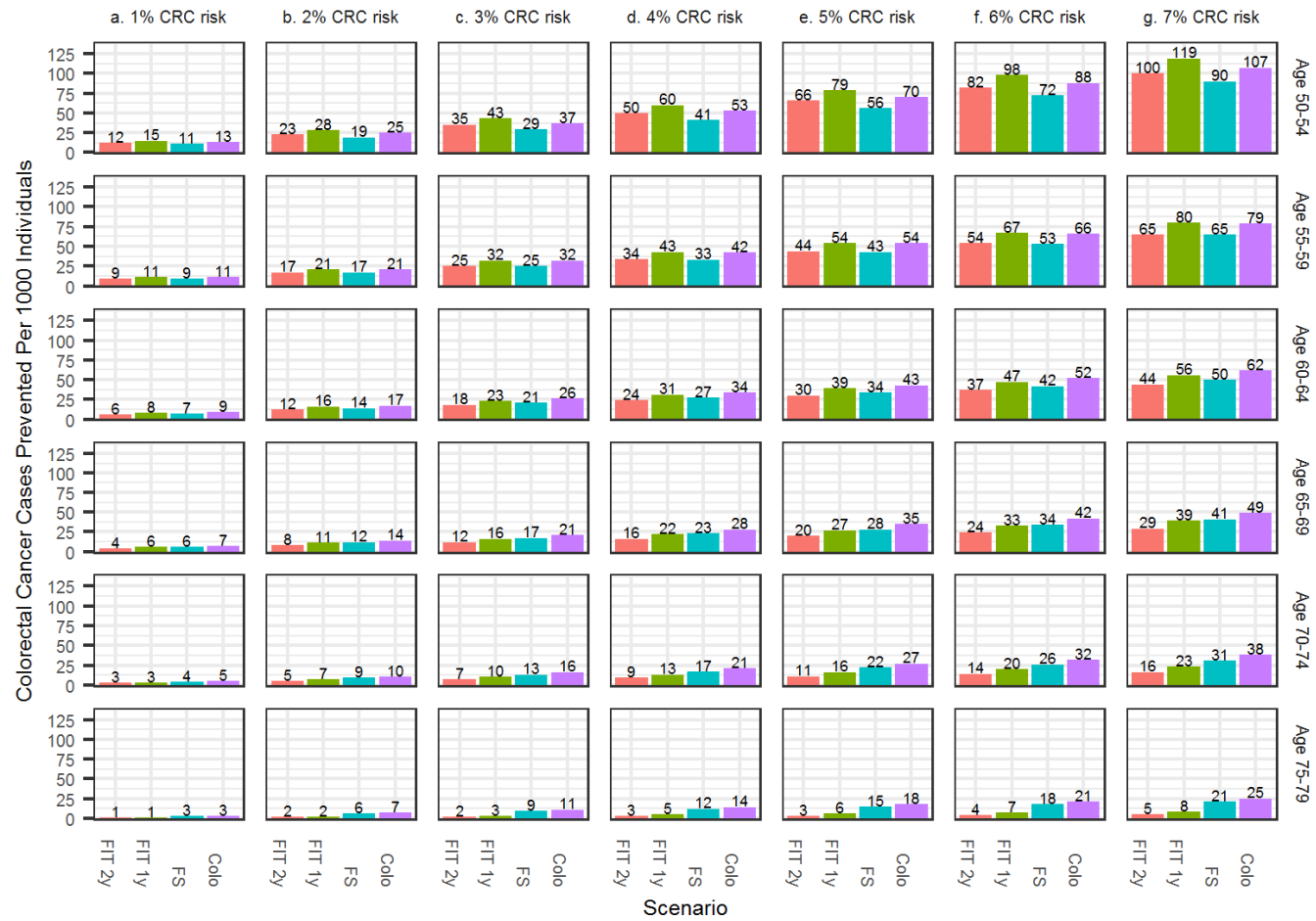
Abbreviations: Colo, colonoscopy; CRC, colorectal cancer; FIT, faecal immunochemical test; FS, flexible sigmoidoscopy.

**Figure 2: MISCAN-Colon predictions of colorectal cancer mortality reduction, colorectal cancer incidence reduction per 1000 individuals, using FIT, flexible sigmoidoscopy or colonoscopy. Results were stratified for CRC risk and age. Individuals were followed for a lifetime.**

**a. Colorectal cancer deaths prevented**



**b. Colorectal cancer cases prevented**



Abbreviations: Colo, colonoscopy; CRC, colorectal cancer; FIT, faecal immunochemical test; FS, flexible sigmoidoscopy.