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# Expected reduction of colorectal cancer incidence within 8 years after introduction of the German screening colonoscopy programme: Estimates based on 1,875,708 screening colonoscopies

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## ABSTRACT

In late 2002, colonoscopy was introduced as a primary screening tool for colorectal cancer (CRC) in Germany. We aimed to estimate the expected reduction in case numbers and incidence of CRC between 2003 and 2010 by detection and removal of advanced adenomas. Data from 1,875,708 women and men included in the national screening colonoscopy database were combined with estimates of transition rates of advanced adenomas and with national population projections. Despite relatively low screening participation, incident CRC cases are expected to be reduced by more than 15,000 between 2003 and 2010. The impact is expected to be largest in age groups 55–59, 60–64 and 65–69 in whom total case numbers in 2010 are expected to be reduced by 13%, 19% and 14% among women, and by 11%, 15% and 12%, respectively, among men. Our results forecast a major rapid reduction of the CRC burden in Germany by screening colonoscopy.

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## 1. Introduction

Colonoscopy is thought to be a powerful tool for early detection of colorectal cancer (CRC) and its precursors.<sup>1–3</sup> Starting in late 2002, Germany was the first country in the world where colonoscopy was offered nationwide as a primary screening tool for CRC.<sup>4</sup> For evidence-based decisions about continuation of this screening programme, it is crucial to timely estimate its effects on the population level. The aim of this study was to estimate the reduction in case numbers and incidence of CRC by detection and removal of advanced adenomas at first round screening colonoscopy between 2003 and 2010, i.e. within the initial 8 years after implementation of the screening programme.

## 2. Material and methods

### 2.1. The German colonoscopy screening programme

Since October 2002, people covered by the statutory health insurance system in Germany are entitled to have a first screening colonoscopy from age 55 on, and a second screening colonoscopy after 10 or more years, provided the first screening colonoscopy was performed before the age of 65 (sigmoidoscopy is not utilised for colorectal cancer screening in Germany; faecal occult blood testing has been offered before introduction of screening colonoscopy and continues to be offered, but participation has always been low). Along with introduction of the colonoscopy screening offer, a national

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registry was set up to document participation rates and reports of screening colonoscopies in a standardised manner. Only experienced endoscopists (internists/gastroenterologists or surgeons with pertinent certified specialisations), having conducted at least 200 colonoscopies and at least 50 polypectomies under supervision in the preceding two calendar years, become eligible to conduct screening colonoscopies. Requirements for maintenance of eligibility in subsequent years include conduction of at least 200 colonoscopies and at least 10 polypectomies per year. Histopathological examination is performed decentrally by certified pathological labs.

The statutory health insurance system covers approximately 90% of the German population. With few exceptions, the remaining people are covered by private health insurance which provides equivalent screening offers. Screening examinations of privately insured patients are though not included in the national registry.

## 2.2. Parameters and data sources

The reduction in numbers of CRC cases attributable to screening colonoscopy with detection and removal of advanced adenomas was estimated by age and sex from the following parameters:

- age and sex-specific population figures;
- age and sex-specific participation rates in screening colonoscopy;
- age and sex-specific detection rates of advanced adenomas;
- age and sex-specific transition rates of advanced adenomas to preclinical CRC and of preclinical CRC to clinically manifest CRC.

In a conservative approach, only advanced adenomas were considered, as progression of other adenomas to CRC seems to be more than 10-fold lower.<sup>5</sup> Data sources for estimating the various parameters are described in the following:

### 2.2.1. Population figures

Estimates of the German population in calendar years 2003 to 2006, and population projections for calendar years 2007 to 2010 were obtained from the German Federal Statistical Office.<sup>6</sup>

### 2.2.2. Participation in screening colonoscopy

Participation rates in screening colonoscopy were obtained from the German nationwide registry. For patients covered by the statutory health insurance system, this registry can be considered complete, since reporting is a prerequisite for endoscopists' reimbursement of screening colonoscopies. The agency in charge of the registry also maintains the database of people covered by the statutory health insurance system whose number is needed as denominator to calculate participation rates. At the time of this analysis, registration was complete up to and including the year 2006, and participation rates were obtained for calendar years 2003–2006. Equivalent screening participation rates were assumed for the minority of the German population with other forms of health insurance. Participation rates were assumed to remain stable in 2007–2010 at the levels observed in 2006.

### 2.2.3. Detection rates of advanced adenomas

Detection rates of advanced adenomas were likewise obtained from the nationwide registry. The registry documents findings at colonoscopy, using a standardised reporting form to be completed by the endoscopists. The reporting form includes information about presence, number, size and type of hyperplastic polyps, adenomas and CRCs. In case of multiple adenomas, details regarding size and type are to be recorded only for the largest adenoma. The reporting forms are scanned, processed and checked for completeness and plausibility using standardised algorithms at regional data centres before electronic transmission to the national data centre for analysis. For this analysis, detection rates of advanced adenomas (defined as presence of at least one adenoma with at least one of the following features: >1 cm in size, tubulovillous or villous components, high grade dysplasia) were derived by age, sex and calendar year. Equivalent detection rates of advanced adenomas were assumed for the minority of the German population with other forms of health insurance. Detection rates were assumed to remain stable in 2007–2010 at the levels observed in 2006.

### 2.2.4. Transition rates of advanced adenomas

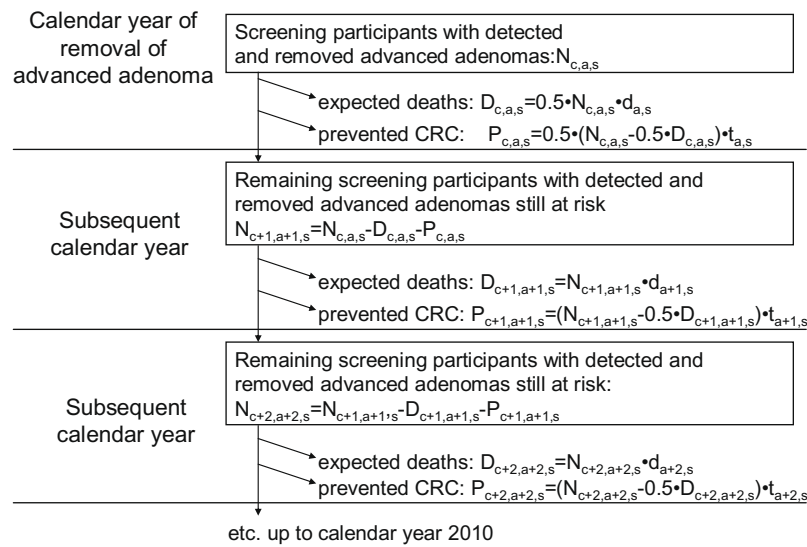
Transition rates of advanced adenomas to preclinical CRC by age and sex were obtained from a previous study as described in detail elsewhere.<sup>7</sup> Estimated annual transition rates were similar in women and men and increased from 2.6% in age group 55–59 to more than 5% in the oldest age groups. In additional sensitivity analyses, 20% higher or lower progression rates were assumed. Transition rates of preclinical to clinical CRCs were derived assuming a median sojourn time of 3.6 years (sensitivity analyses: 2–5 years), corresponding to an annual transition rate of 17.5% (sensitivity analyses: 12.9–29.3%), as previously suggested.<sup>7,8</sup>

## 2.3. Statistical analysis

Total numbers of people with detected and removed advanced adenomas among participants of screening colonoscopy in Germany were estimated (stratified by sex and 5-year age groups) by multiplying respective population figures with the participation rates in screening colonoscopy and the observed detection rates of advanced adenomas.

Starting from screening participants with detected and removed advanced adenomas, the numbers of CRC cases prevented due to screening colonoscopy were estimated as follows: First, cohorts of patients were defined on the basis of the calendar year in which advanced adenomas were detected and removed at screening colonoscopy. For each cohort, the number of CRC cases prevented in each calendar year up to 2010 was estimated (stratified by sex and age) in a stepwise Markov-type manner as illustrated in Fig. 1 and described in more detail below.

Within each calendar year, we first determined the initial numbers of screening participants with detected and removed adenomas still at risk, i.e. those expected to be still alive and without CRC prevented due to screening in preceding years. For calculation of prevented CRC within the calendar year, these numbers of people at risk were reduced by half of those expected to die within the calendar year, assuming



Parameter definitions:

$c$  = calendar year of detection and removal of advanced adenoma

$a$  = age at detection and removal of advanced adenoma

$s$  = sex of screening participants

$N_{i,j,k}$  = screening participants at risk of CRC in calendar year  $i$  at age  $j$  with sex  $k$

$D_{i,j,k}$  = expected deaths in calendar year  $i$  at age  $j$  with sex  $k$

$P_{i,j,k}$  = expected number of preclinical CRC cases in calendar year  $i$  at age  $j$  with sex  $k$  that would have developed from advanced adenomas if the latter had not been removed at screening colonoscopy (i.e., prevented preclinical CRC cases)

$d_{j,k}$  = death rate at age  $j$  in sex  $k$

$t_{j,k}$  = transition rate from advanced adenoma to preclinical CRC at age  $j$  in sex  $k$

**Fig. 1 – Stepwise calculation of expected numbers of preclinical colorectal cancer cases prevented by detection and removal of advanced adenomas. All analyses were done separately by sex, age and calendar year of adenoma detection and removal.**

that such deaths are on average equally spread over the year, and then multiplied with the estimated age and sex-specific transition rates from advanced adenomas to CRC. In the initial year of screening participation with adenoma removal, these numbers of prevented CRC cases were additionally multiplied by 0.5, assuming that screening with adenoma removal on average occurred in the middle of the calendar year.

At the beginning of each subsequent calendar year, numbers of the remaining women and men still at risk of CRC were obtained by subtracting the numbers of women and men expected to have died or to have been prevented from CRC in the preceding calendar year from the numbers of women and men at risk at the beginning of the preceding year. In addition the age of the cohort was increased by 1.

The aforementioned procedure yielded estimates of prevented preclinical CRCs. An analogous Markov-type procedure was subsequently applied to age and sex-specific

numbers of preclinical CRCs to estimate prevented clinically manifest CRCs.

To estimate the relative impact of detection and removal of advanced adenomas on observed CRC incidence, expected reductions in the numbers of CRC cases due to screening colonoscopy between 2003 and 2010 were compared to CRC cases expected in the absence of screening colonoscopy. Latter were estimated by multiplying age- and sex-specific population figures for each calendar year between 2003 and 2010 with the respective age and sex-specific CRC incidence rates in Germany in 2002, the year preceding introduction of screening colonoscopy.

### 3. Results

Table 1 (left-hand block) shows numbers of men and women aged 55 years and older in Germany estimated for calendar

**Table 1 – Population estimates and projections for the male and female population in Germany according to age in 2006 and 2010 (source: Ref. 4), and percentage covered by statutory health insurance in 2006.**

Sex/age	Population estimates and projections (in thousands)		Covered by statutory health insurance (in%)
	2006	2010	2006
<i>Men</i>			
55–59	2478.6	2724.8	80.9
60–64	2204.7	2298.3	77.9
65–69	2590.3	2102.4	87.1
70–74	1759.2	2226.3	92.7
75–79	1254.5	1361.9	92.0
80+	1074.2	1335.3	90.2
Total	11,361.4	12,049.0	85.7
<i>Women</i>			
55–59	2501.2	2764.3	90.7
60–64	2281.6	2377.8	86.0
65–69	2825.4	2285.6	93.0
70–74	2105.7	2616.8	96.6
75–79	1803.9	1815.7	94.0
80+	2667.6	2844.6	97.3
Total	14,185.3	14,704.8	92.9

year 2006 and projected for calendar year 2010. In addition, the table shows the proportions of people covered by the statutory health care system in 2006, which were 86% and 93% in men and women overall, with pertinent proportions increasing with age.

Participation rates in screening colonoscopy and detection rates of advanced adenomas are given in Table 2. Overall, 1,875,708 colonoscopy reports were available for this analysis. Among ages 55–69, annual participation averaged 3% in men and 4% in women (corresponding to programme participation of 30% and 40%, respectively, given the 10 year interval for participation). Above age 70, participation rates were lower and decreased with age. Detection rates of advanced adenomas and CRCs were much higher among men than among women and increased with age in both sexes.

Despite increasing detection rates with age, the majority of advanced adenomas and CRCs were detected in the younger age groups (below 70 years), due to the much higher numbers of screening participants in these groups (Table 3). Overall, more than 150,000 advanced adenomas were estimated to have been detected and removed by screening colonoscopy in Germany between 2003 and 2006, respectively.

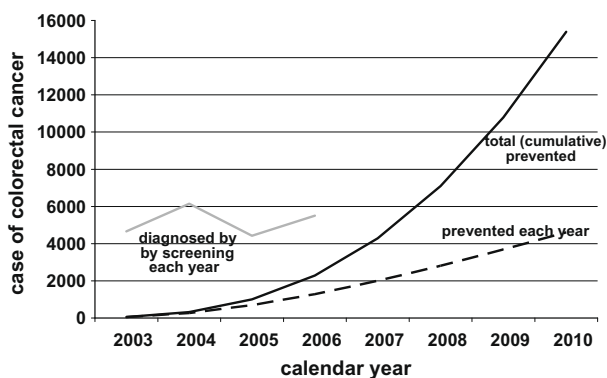
Fig. 2 shows expected numbers of CRC cases prevented due to detection and removal of advanced adenomas up to the year 2010. Given that many of the CRCs would have been expected to occur and become clinically manifest only years after removal of advanced adenomas at screening colonoscopy, the expected yearly number of prevented CRC cases continuously increases over the entire period of investigation, despite essentially stable numbers of removed advanced ade-

**Table 2 – Participation rate in screening colonoscopy, availability of colonoscopy records from participants in national database and detection of advanced adenomas and colorectal cancers among participants with available records. German statutory health insurance, 2003–2006.**

	Participation rate in screening colonoscopy (%)				Detection of at least one advanced adenoma (%)			
	2003	2004	2005	2006	2003	2004	2005	2006
<i>Men</i>								
55–59	2.2	3.0	2.8	3.1	6.0	6.2	6.6	6.7
60–64	3.0	4.0	3.5	3.3	7.0	7.6	8.3	8.2
65–69	2.7	3.5	3.0	3.0	8.1	8.4	8.9	9.4
70–74	1.9	2.5	2.3	2.3	8.7	9.1	9.7	10.0
75–79	1.2	1.6	1.5	1.6	9.1	9.5	9.8	10.6
80+	0.4	0.6	0.6	0.7	8.4	9.2	9.0	9.8
Total	2.2	2.9	2.5	2.6	7.5	7.9	8.4	8.6
<i>Women</i>								
55–59	3.5	4.4	3.7	3.9	3.4	3.4	3.5	3.5
60–64	4.1	5.0	3.8	3.5	4.1	4.2	4.6	4.6
65–69	3.1	3.8	3.0	2.9	4.6	4.8	5.3	5.3
70–74	1.8	2.3	2.0	2.0	5.4	5.9	6.1	6.0
75–79	0.9	1.3	1.2	1.2	6.2	6.4	6.8	6.9
80+	0.2	0.3	0.3	0.3	6.6	7.2	6.8	7.3
Total	2.3	2.9	2.3	2.3	4.4	4.5	4.9	4.9

**Table 3 – Estimated numbers of participants in screening colonoscopy in Germany in whom advanced adenomas and colorectal cancers have been detected and removed in 2003–2006.**

Sex/age	Advanced adenoma			
	2003	2004	2005	2006
<b>Men</b>				
55–59	2931	4105	4262	5113
60–64	5783	7946	6945	6022
65–69	4980	7195	6675	7276
70–74	2623	3641	3653	4105
75–79	1155	1745	1808	2162
80+	341	554	550	700
Total	17,813	25,187	23,892	25,378
<b>Women</b>				
55–59	2621	3310	3000	3382
60–64	4814	5668	4345	3650
65–69	3586	4888	4341	4290
70–74	1896	2685	2413	2521
75–79	1055	1464	1434	1516
80+	351	569	552	673
Total	14,323	18,583	16,085	16,032

**Fig. 2 – Expected numbers of clinically manifest cases of colorectal cancer prevented by detection and removal of advanced adenomas in Germany, 2003–2010. In addition, cases early detected by screening in 2003–2006 are given.**

nomas estimated for 2004–2006 (after an initial rise from 2003 to 2004, see Table 3) and projected for 2007–2010. The annual number of prevented CRC is expected to approach 5000, and the cumulative number over years is expected to surpass 15000 in 2010 (Fig. 2). The latter estimate ranged from 12,480 to 18,227 in sensitivity analyses in which advanced adenoma progression rates were varied by  $\pm 20\%$ , and from 22,068 to 12,121 in sensitivity analyses in which sojourn time of CRC was varied from 2 to 5 years. Fig. 2 additionally provides the numbers of CRCs detected by screening colonoscopy from 2003 to 2006.

To estimate the relative impact of prevention of CRCs by detection and removal of advanced adenomas on CRC incidence, numbers of thus prevented cases were put into perspective by comparison with the numbers of CRCs expected in the absence of screening colonoscopy, which are close to 70,000 and 75,000 cases in 2006 and 2010, respectively, under the assumptions stated in the methods section. This implies an expected reduction of CRC incidence due to detection

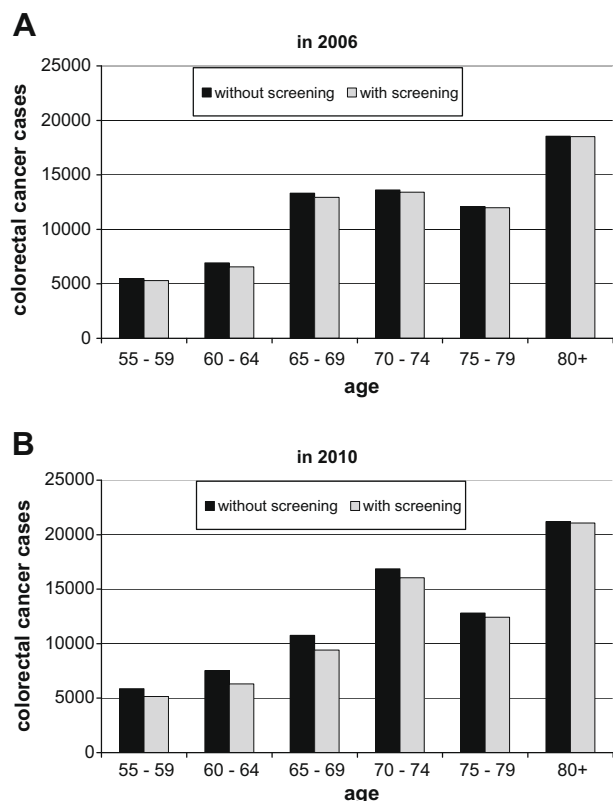
and removal of advanced adenomas of 1.8% and 6.1% in 2006 and 2010, respectively. However, as Fig. 3 shows, this reduction strongly varies by age. Expected reduction of CRC incidence due to detection and removal of advanced adenomas for age groups 55–59, 60–64 and 65–69 is 3.0%, 5.2% and 2.9%, respectively, in 2006 and 12.1%, 16.2% and 12.5%, respectively, in 2010.

The expected reduction in numbers of CRC cases further varies by sex, which is illustrated for the year 2010 in Fig. 4. In relative terms, the reduction is stronger among women than among men in all of the younger age groups, due to the higher screening participation of women. In detail, expected reductions of CRC incidence among women amount to 13.4%, 18.9% and 13.7% in age groups 55–59, 60–64 and 65–69 in 2010. The corresponding proportions for men are 11.3%, 14.7% and 11.8%.

#### 4. Discussion

Introduction of screening colonoscopy in Germany in late 2002 has opened an entirely new avenue for CRC prevention. Close monitoring of this programme and its expected effects is a crucial basis for decisions whether and how this screening offer shall be maintained, modified or extended. The distribution of findings at screening colonoscopy in Germany as well as complications rates (which were generally very low) has been reported previously.<sup>9</sup> Here, we provide first estimates of the expected numbers of CRC cases prevented by removal of advanced adenomas at screening colonoscopy up to the year 2010. Our analyses reveal that, despite relatively low participation rates, more than 15,000 manifest CRC cases are expected to be prevented between 2003 and 2010, and that close to 5000 CRC cases are expected to be prevented in 2010 alone. Within the first 8 years after introduction of screening colonoscopy, reduction in CRC incidence by detection and removal of advanced adenomas are expected to be largest in age groups between 55 and 69 years. In relative terms, the impact is higher in women, due to their higher par-





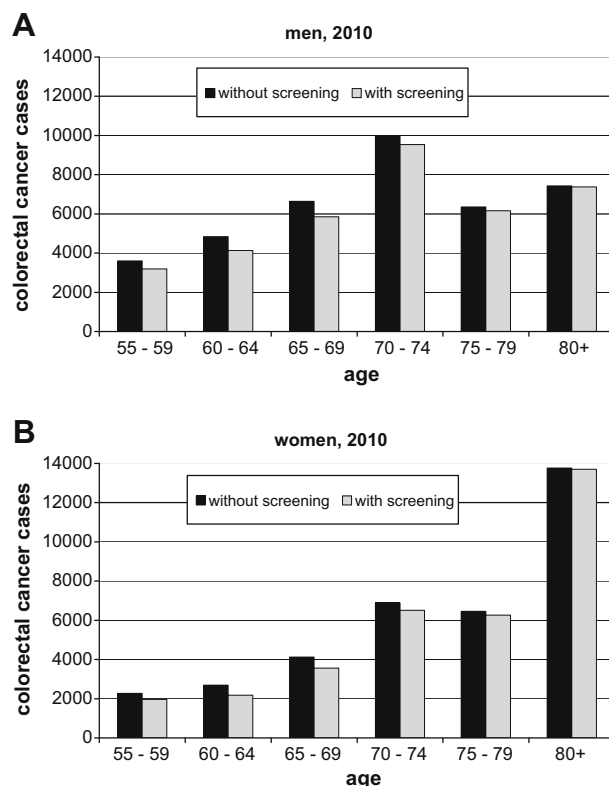
**Fig. 3 – Numbers of clinically manifest colorectal cancer cases by age group expected in Germany in 2006 (A) and in 2010 (B) without and with removal of advanced adenomas at screening colonoscopy (both sexes).**

ticipation rate in screening colonoscopy. In particular, removal of advanced adenomas at screening colonoscopy is estimated to prevent 13–19% of otherwise expected CRC cases in 2010 among women aged 55–69 years.

Despite major improvement in recent years, about 40% of patients with CRC still die from their disease within 5 years following diagnosis,<sup>10</sup> and there are further disease related deaths even in the longer run. Therefore, the prevention of more than 15,000 incident cases by 2010 is expected to be followed by prevention of about half that number of deaths due to CRC, even though not all of these deaths would be expected to occur by 2010. Furthermore, our analyses focused on prevented CRC cases that, in the absence of screening colonoscopy, would have occurred by 2010. The long-term benefit of removal of screening-detected advanced adenomas in 2003–2010 will be much larger due to prevention of many additional CRC cases otherwise expected to occur after 2010.

In the interpretation of our results, specific strengths and limitations of this study require careful consideration. Strengths include the unique nationwide registry with more than 1.8 million screening colonoscopy records. On the other hand, the degree of standardisation of colonoscopy and histology information is likely to be less perfect in such a nationwide database than it could be achieved in a trial by a few specialised centres with centralised review of all adenomas.

Our estimates are based on several simplifying assumptions. These include, in particular, the assumptions that



**Fig. 4 – Numbers of clinically manifest colorectal cancer cases by age group expected among men (A) and among women (B) in Germany in 2010 without and with removal of advanced adenomas at screening colonoscopy.**

sex- and age specific participation rates in screening colonoscopy and sex- and age specific detection rates of advanced adenomas remain constant from 2006 to 2010. Although these assumptions seem justified, given the high stability of these parameters over calendar years 2003–2006, major efforts need to be made to enhance those participation rates which would then lead to larger numbers of prevented CRCs. Furthermore, no distinction was made with respect to location of neoplasms. There is increasing evidence that protection from CRC by endoscopy is less pronounced for the right colon than for the left colorectum.<sup>11–13</sup>

Our analysis intentionally focused on prevention of CRC by detection and removal of advanced adenomas, which is a very important, but not the sole way by which screening colonoscopy can reduce CRC incidence and mortality. As regard to incidence, CRC may also develop from other ('non-advanced') adenomas, but their progression to CRC seems to be more than ten times lower than progression of advanced adenomas.<sup>5</sup> While detailed estimates on transition rates from advanced adenomas to CRC in the German population by sex and age are available from a preceding study,<sup>7</sup> no such estimates are available for other adenomas. Considering the effect of detecting and removing non-advanced adenomas would further increase the estimated benefit of screening colonoscopy.

Whereas screening colonoscopy is expected to avert incident CRC cases due to detection and removal of advanced

adenomas right from the beginning, detection of prevalent CRCs at screening colonoscopy is expected to have led to an apparent, transient increase in CRC incidence in the early years of the screening programme. Among participants with documented colonoscopy records in the national database, 15,820 cases of CRC have been detected from 2003 to 2006, suggesting that, overall (and taking non-registered cases into account), approximately 4500 cases have been detected in Germany per year. In the long run, the apparent increase in incidence by screening detected CRC is expected to be compensated to a large extent by lower occurrence of CRC in subsequent years, when most screening detected cases would have become clinically manifest. Furthermore, earlier detection of prevalent CRC through screening colonoscopy is expected to lead to an additional reduction in CRC mortality.

On the other hand, the numbers of prevented CRC cases may have been overestimated to some extent in our analyses, given that some proportion of advanced adenomas detected by screening colonoscopy could have become clinically manifest (e.g. through bleeding) and removed even in the absence of screening. Furthermore, detection and removal of advanced adenomas will not always entirely eliminate the occurrence of CRC from these lesions. First, there is a risk of recurrence of removed advanced adenomas, even though this risk seems to be very small within 5 years after polypectomy.<sup>14</sup> Second, carriers of advanced adenomas may be at increased risk of developing another advanced adenoma or CRC at a different site. Risks of CRC after removal of advanced adenomas can be minimised by surveillance colonoscopy, which is recommended three years after polypectomy in the German colonoscopy screening programme. It is unclear, however, to what extent this recommendation is followed. Our analyses should at best be marginally affected, however, by the well known fact that not all adenomas are detected and removed at colonoscopy,<sup>15,16</sup> as undetected adenomas were not included in the estimates of prevented CRC.

In summary, our study suggests major reductions in CRC incidence to be expected from detection and removal of advanced adenomas in Germany in ages 55–69 already by 2010. This benefit is expected to further increase in subsequent years. Even larger reductions could be achieved if participation rates, which are still at relatively low levels, can be increased. According to consistent experience from other countries and other cancer screening programmes, this would probably be achieved best by implementation of a more organised structure of the screening programme that includes a well-defined schedule of personal invitations and reminders,<sup>17–19</sup> and goes along with preceding and accompanying measures to ensure adequate capacity and best possible quality of endoscopic examinations.<sup>20</sup>

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### Conflict of interest statement

None declared.

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