Cost-Saving Analysis of Screening Colonoscopy in Germany
Kosten-Nutzen-Analyse der präventiven Koloskopie in Deutschland

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Abstract
Background: Screening colonoscopy was introduced into the National Cancer Prevention Program in Germany in 2002. We have explored costs and savings of screening and surveillance colonoscopy to investigate whether the induced savings may compensate for the costs of screening.

Methods: The study design was a model calculation based on data of a large-scale documentation of screening colonoscopy. The costs and savings of screening colonoscopy were evaluated over a defined period of 10 years. Basic data about findings, adverse effects and costs of screening colonoscopy were obtained from a large-scale online registry of 109989 procedures and from the actual payments of procedures in Germany. Plausible baseline parameter values of the characteristics of screening and surveillance colonoscopy, of adenoma progression and recurrence, and of costs for diagnosis and treatment of colorectal cancer were based on available data. The impact of major model assumptions was evaluated by sensitivity analyses.

Results: A programme based on one-time screening colonoscopy could result in net savings over a period of 10 years in Germany due to avoidance of cancer treatment costs compensating for the costs of screening, surveillance and adverse effects. Average net savings from €121 to €623 per screenee could be achieved according to our model assuming different progression and recurrence rates of adenomas and carcinoma costs from €21820 to €40000.

Limitations: For some major model parameters assumptions had to be derived from the literature.

Conclusions: This analysis based on empirical data from the nationwide screening colonoscopy programme in Germany suggests net savings re-
Schlussfolgerungen: Die Analyse der empirisch erhobenen Daten aus einem deutschlandweiten Screening-Koloskopie-Programm zeigt Netto-Einsparungen durch die Prävention kolorektaler Karzinome, die die gesamten Kosten von Screening und Nachsorge kompensieren. Limitationen des Modells ergeben sich aus der Tatsache, dass die Annahmen für einzelne Modellparameter aus der Literatur entnommen werden mussten.

Introduction

Germany is one of the countries with the highest incidence (73/100 000 in men and 50/100 000 in women with 71400 new cases per year) and mortality (30 000 deaths per year) of colorectal cancer (CRC) [1, 2], which constitutes a major public health burden. Screening colonoscopy was introduced into the National Cancer Prevention Programme in Germany in 2002 [3] even though results from randomised controlled studies on its effect on incidence and mortality of colorectal cancer are not strongly available. However, evidence from observational studies strongly suggests that this screening tool may in fact be very effective. Colonoscopy is the definitive diagnostic method of all studies with the fecal-occult blood test [4–7]. Sigmoidoscopy studies were effective [8–10] and it is reasonable to anticipate that colonoscopy is more sensitive than sigmoidoscopy [11]. In case-control studies in the U.S.A. [12] and Germany [13] colonoscopy was associated with a strongly reduced probability to develop colorectal cancer. Furthermore, the results from the National Polyp Study in the U.S.A. showed that polypectomy reduced the incidence of CRC between 76 to 90% [14]. In Germany, screening colonoscopy is offered to every person from 55 years. A second colonoscopy will be offered after 10 years if no neoplasms are found and the screenee is below the age of 65 years at first screening colonoscopy. A first evaluation of the results of screening colonoscopy showed high prevalence of adenomas and colorectal cancer [15]. Cost-effectiveness analyses in the U.S.A. showed that CRC screening is cost-effective compared with no screening at ratios between $10 000 and $25 000 per live-year saved [16]. The aim of this analysis was to evaluate the costs of screening colonoscopy and surveillance after polypectomy using data from a nationwide large-scale online-registry in comparison with savings by prevention of colorectal cancers and by removal of early cancer stages at screening. A comparison with other screening methods (FOBT, screening sigmoidoscopy) was not intended.

Methods

Basic model of cost saving analysis

The costs and savings of screening colonoscopy were evaluated over a defined period of 10 years. Direct costs of screening and surveillance colonoscopies, the latter scheduled according to national guidelines, were considered, taking complications into account. Savings were calculated from the estimated numbers of CRC immediately removed at colonoscopy or prevented by removal of adenomas, multiplied by average treatment costs of CRC in Germany. The baseline assumptions are shown in Table 1 and explained in the following paragraphs. The perspective of the analysis was that of a third party payer.

Analysis of costs

Costs of screening colonoscopy, polypectomy and histopathological evaluation are based on payments of the insurance companies according to the actual contract with the association of physicians (EBM 2000 plus). Around 90% of the Germans are members of general insurance companies and 10% are enrolled in a private insurance; the latter are neglected in this analysis. The payment of the physicians follows a rather complicated system with procedures credited in points with floating values. A point value of 4.5 cents is the actual value in most parts of Germany for preventive medicine. The total salaries for screening colonoscopy contain physician, pathology and nursing fees, endoscope repair/depreciation and cleaning expenses, room costs, laboratory costs and costs of medication for analgo-sedation and for bowel preparation and amount to €197 for colonoscopies without histology, €209 with histology but without polypectomy (performed as forceps biopsy in polyps smaller than 5 mm and in pathological findings other than polyps) and €245 with polypectomy.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline findings and assumptions forming the model</th>
</tr>
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<tbody>
<tr>
<td>findings at screening colonoscopy (n = 109 989)</td>
<td>6728 advanced (6.1%), 15 245 non-advanced (13.9%) adenomas, 281 pT1-CRC removed by polypectomy (0.3%), 5 bleedings (0.004%), 23 perforations requiring surgery (0.02%)</td>
</tr>
<tr>
<td>surveillance colonoscopy</td>
<td>3 years after removal of an adenoma, 5 years after a negative surveillance colonoscopy</td>
</tr>
<tr>
<td>10-year conversion rate of non-advanced adenomas into CRC</td>
<td>2.5%</td>
</tr>
<tr>
<td>10-year conversion rate of advanced adenomas into CRC</td>
<td>40%</td>
</tr>
<tr>
<td>adenoma recurrence 3 years after polypectomy</td>
<td>30%</td>
</tr>
<tr>
<td>adenoma recurrence 5 years after a first negative surveillance colonoscopy</td>
<td>20%</td>
</tr>
<tr>
<td>costs of diagnosis and treatment of CRC</td>
<td>€ 21 820</td>
</tr>
<tr>
<td>discount rate of costs and benefits occurring in the future</td>
<td>3% per year</td>
</tr>
</tbody>
</table>
Basic findings at screening colonoscopy

In contrast to cost-effectiveness analyses published earlier we obtained the basic data in our cost-saving analysis from a large-scale online registry of 109,989 screening colonoscopies in Germany [15]. Screening colonoscopies were performed in 295 practices of gastroenterology and/or internal medicine in Germany from October 2003 until July 2005 [15]. Tubular and villous adenomas were found in 17,792 (16.2%) and 4,181 (3.8%) screenees, respectively, hyperplastic polyps in 9,873 (9.0%), adenomas with high-grade dysplasia in 733 (0.7%), and invasive cancer was detected in 757 (0.7%) screenees. Advanced adenomas, defined as adenomas ≥10 mm in diameter, villous in histology, or the presence of high-grade dysplasia, were detected in 6,728 (6.1%) screenees. The mean age of patients with non-advanced adenomas was 65 years and of patients with advanced adenomas 66 years. Colorectal cancers were staged according to the UICC classification. UICC stage was I in 48%, II in 22%, III in 20% and IV in 10% of the carcinomas.

Costs of adverse effects at screening colonoscopy

Adverse effects were documented by the endoscopists immediately following the examinations. Therefore some of the delayed complications such as perforation and bleeding may not have been captured although every severe complication was validated by contacting the practices concerned. Cardiopulmonary complications occurred in 0.09% of screening colonoscopies, bleedings in 0.16% of colonoscopies and in 0.77% of polypectomies and perforations in 0.02% of colonoscopies and in 0.10% of polypectomies. Surgery due to bleeding following polypectomy was necessary in 5 patients and due to perforation in 23 patients. In the online registry of screening colonoscopy no fatalities were registered. All severe complications and carcinoma stages were validated by contacting the practices concerned. The average inpatient costs in Germany were €3,400 in 2002 [17] at an average duration of inpatient treatment of 10 days [18]. As most of the complications leading to inpatient admission were perforations, we assumed this sum for the overall costs including ICU costs to treat complications like bleedings or perforations requiring surgery. We further assumed a complication rate of surveillance colonoscopy identical to that described for screening colonoscopy.

Surveillance guidelines

According to the guidelines of the German Gastroenterological Association [1] the endoscopic removal of an adenoma should...
result in a surveillance colonoscopy after 3 years. This is in contrast to the guidelines of the AGA suggesting a 5-year surveillance interval for non-advanced adenomas (1–2 small tubular adenomas) [19]. The surveillance interval is extended to 5 years after a negative surveillance colonoscopy. The expected proportion of surveillance colonoscopies was reduced according to the expected 5-year total mortality which was estimated from the 2002/2004 life tables for the German population. An overview on the necessary number of surveillance colonoscopies is given in Fig. 1.

Assumptions on sensitivity of optical colonoscopy

The sensitivity of screening and surveillance colonoscopy was assumed to be 80% in adenomas less than 10 mm and 95% in adenomas larger than or equal 10 mm and cancers [20, 21]. In a recent study comparing computed tomographic virtual colonoscopy with optical colonoscopy, a sensitivity of around 90% for optical colonoscopy in colorectal neoplasms was described [22]. An average detection rate of 90% for colorectal neoplasms was therefore assumed.

Assumptions on adenoma progression and recurrence

Based on long-term surveillance studies [23–25], an average conversion rate of 40% of advanced adenomas into carcinomas and a 2.5% conversion rate for non-advanced adenomas within a 10-year period is expected. Together with 281 pT1 carcinomas removed at screening colonoscopy, 2816 cancers would be prevented (Table 3), i.e., cancer would be prevented in 2.56% of the cohort. This proportion is in accordance with CRC incidence data from Germany before the introduction of colonoscopy screening: The average age of our screenee was 65 years. In 2002, the cumulative incidence of CRC in Germany between 65 and 75 years of age was 3.7% in males and 2.2% in females. Eide described a conversion rate of 30% for large adenomas irrespective of histopathology [23]. In a recently published paper about the impact of CRC screening on clinical and economic outcomes, Ladabaum and Song assumed an annual transition rate from large polyps to CRC of 5% [26]. The expected number of carcinomas was reduced according to the expected 5-year total mortality which was estimated from the 2002/2004 life tables for the German population. According to published data [27] a recurrence rate of adenomas 3 years after polypectomy of 30% and a recurrence rate of 20% five years after a first negative surveillance colonoscopy were assumed.

Analysis of benefit

In 1994 the Central Institute of the Registered Physicians in Germany (Zentralinstitut für die kassenärztliche Versorgung) calculated average direct costs for diagnosis and treatment of colorectal carcinomas of €20,000 dependent on the UICC stage (I/II: €11,000, III: €22,000 and IV: €29,000). In 2002, €1558 million were spent to treat 71,400 CRC detected in Germany, which is on average €21820 per CRC [28]. We used this amount as an average benefit per prevented case. Currently no actual calculation of CRC costs in Germany is available. For the future a dramatic increase of treatment costs by chemotherapy with newly developed medication is expected. We also assumed that curative removal of low risk UICC stage I colorectal cancers by endoscopic polypectomy would save €21820 of carcinoma costs per case, taking into account that a substantial proportion of these cancers would have progressed to more advanced cases without screening colonoscopy (the proportion of early stage carcinomas was 25% units above the proportion described in an epidemiological study in Germany [29]).

We calculated overall costs and benefits in all 109,989 screenees as well as average costs per screenee. All costs and benefits occurring in the future were discounted using the formula:

\[
D = \frac{K}{(1 + r)^N}
\]

where D are the discounted values, K are the values occurring in the future, r the discount rate and N the number of years after which the costs occur. We used 0.03 as a generally accepted discount rate [30] in the base-case analysis. Assuming that the carcinomas prevented during 10 years would on average occur after 5 years, this value was used for N.

Model variants

In a sensitivity analysis the impact of changes of major assumptions was assessed (Table 1). The number of surveillance colonoscopies depends on the recurrence rate of adenomas 3 years after polypectomy which was varied between 20 and 40%. The conversion rate of advanced adenomas into carcinomas and the costs of CRC largely determine the savings of screening colonoscopy. The basic conversion rate of 40% for advanced adenomas was varied between 30 and 50%. We did not perform model variants for the 10-year conversion rate of non-advanced adenomas and for adenoma recurrence 5 years after a first negative surveillance colonoscopy as these parameters contributed to less than 10% to the costs. For the costs of CRC, alternative variants with €30000 or €40000 per case were calculated to evaluate the impact of increased costs, e.g., by novel chemotherapy regimens. Finally, the discount rate was varied between 2% and 5%.

<table>
<thead>
<tr>
<th>n</th>
<th>costs (€)</th>
<th>benefits (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefits from polypectomy of pT1Carcinomas removed at screening</td>
<td>281</td>
<td>6131420</td>
</tr>
<tr>
<td>Discounted benefits from preventing incident CRC within 10 years</td>
<td>2535</td>
<td>47713016</td>
</tr>
<tr>
<td>Total discounted benefits from screening and surveillance</td>
<td>53844436</td>
<td></td>
</tr>
<tr>
<td>Total benefits per screenee</td>
<td>490</td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Costs of screening and surveillance colonoscopies in 109,989 individuals over a period of 10 years

Table 3 Benefits from preventing incident CRC by screening and surveillance within 10 years

1 CRC = colorectal cancer; we assumed a detection rate of 90% for colorectal neoplasia, average carcinoma costs of €21820 and a discount rate of 3%.

Results

Based on data from the online registry of screening colonoscopy we calculated direct screening costs of €22598138 in 109989 screening colonoscopies. 77381 colonoscopies were performed without histology (normal colon), 16053 colonoscopies with histology (small polyyps and non-polyloid lesions) and 16555 colonoscopies with polypectomy (Table 2). The expected number of surveillance colonoscopies with and without adenomas are shown in Fig. 1. Adenomas were detected in a total of 21978 patients at screening colonoscopy (year 0), of whom 95.8%, 90.4%, 85.9% and 83.5% were assumed to be alive at potential dates of surveillance colonoscopy 3, 6, 8, or 9 years after screening colonoscopy. Based on the assumptions shown in Table 1, a total of 41881 surveillance colonoscopies within 10 years (30639 colonoscopies without histology and 11242 colonoscopies with histology/polypectomy) are expected, raising discounted costs of €7401692 (Table 2).

At screening colonoscopy five bleedings requiring surgery and 23 perforations occurred. The respective numbers of complications in surveillance colonoscopy were expected to be two bleedings and 10 perforations. All complications occurring at screening and surveillance colonoscopy (n = 40) therefore induced costs of €136000.

The benefits from polypectomy of 281 pT1-carcinomas amounted to €6131420. The base case model, assuming a 40% conversion rate of 6728 advanced adenomas and a 2.5% conversion rate of 15250 non-advanced adenomas into carcinomas within a period of 10 years and taking reductions of case numbers according to the expected general mortality into account, would result in 2465 + 352 = 2817 carcinomas of which 2535 (90%) would be prevented by transendoscopic detection and removal of colorectal neoplasias at surveillance and screening colonoscopies. The overall savings by removal of early carcinomas (€ 6131420) and prevention of CRC by polypectomy at screening colonoscopy (€ 47713016) discounted at 3% amount to €53844436 (Table 3).

Total costs of screening and surveillance colonoscopy and of complications are balanced against benefits from screening and surveillance per person in Table 4. In the base case model, average savings of €216 per screening colonoscopy were calculated. In a sensitivity analysis we further investigated the influence of different key variables like adenoma recurrence and progression, colorectal cancer costs and discount rates on the net costs. Clearly, the most influential variables were the transition rate of advanced adenomas to CRC and the cost of CRC treatment. Higher costs than assumed in the base case analysis would lead to much higher savings. Within a period of 10 years net savings induced by screening colonoscopy ranged between €121 and €623 per person.

Discussion

To our knowledge, this is the first cost-savings analysis of screening colonoscopy for a country where colonoscopy is offered as a primary screening method. Many important parameters could be directly obtained from a large-scale nationwide online registry of screening colonoscopy [15]. In our base case analysis, we find that screening colonoscopy will on average save €216 for each individual undergoing screening colonoscopy and surveillance according to the guidelines of the gastroenterological associations [1, 19]. Savings could even be much higher with less conservative assumptions regarding costs of CRC treatment. The introduction of novel biologicals for chemotherapy will inflate the treatment costs and cost-saving preventive methods are mandatory.

We did not intend to compare different screening models like FOBT, virtual colonoscopy or sigmoidoscopy but rather tried to determine the value of screening colonoscopy. Several model calculations of cost-effectiveness, all pertaining to the United States of America, showed incremental costs per live-year saved of screening colonoscopy every 10 years between $10000 and $25000 compared with no screening [16, 31 – 35]. Compared with colonoscopy, annual screening with fecal occult-blood testing costs less but saves fewer live-years. In a cost-saving analysis with a programme based on every 5-year sigmoidoscopy screenings net savings of direct health-care costs due to prevention of cancer were reported [30]. A recently published model on the National impact of CRC screening in the U.S.A. did not show net savings for any of the methods evaluated (FOBT, fecal DNA tests, flexible sigmoidoscopy, colonoscopy and virtual colonoscopy) as the screening expenditures surmounted the decrease of CRC-related expenditures caused by a decrease of CRC incidence and mortality [26]. The difference between the U.S.A. models with lower or missing net savings [26, 30] and our model can be explained by different costs of endoscopy, different kinds of calculating treatment costs, a generally higher assumption of screening-related morbidity and mortality in the U.S.A. compared to surveys in Germany [15, 36] and to the lower sensitivity of screening sigmoidoscopy compared to colonoscopy [11].

According to our study, about 70% of costs are caused by screening colonoscopies, and another 30% are caused by surveillance colonoscopy. Obviously, costs of complications play a minor role in screening colonoscopy. The rate of complications in screening colonoscopy [15] is similar to the low rate described earlier for ambulatory endoscopy in Germany [36] and the U.S.A. [37]. The high frequency of examinations and the expertise of colonoscopists underlying strict quality control may contribute to the results. A recently published study from Japan came to similar results in diagnostic colonoscopy [38]. These complication rates are lower than those reported in earlier studies [39 – 43]. Some of the delayed complications such as perforation and bleeding may not have been captured since adverse effects were documented by the endoscopists immediately following the examinations. A recent polypectomy study from Germany showed that complication rates

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**Table 4** Comparison of costs and benefits in screening and surveillance colonoscopy during 10 years per screenee

<table>
<thead>
<tr>
<th>A. base case model</th>
<th>net costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>total induced costs by screening and surveillance colonoscopy including complications</td>
<td>€ 274</td>
</tr>
<tr>
<td>total benefits from prevention of incident CRC by screening and surveillance within 10 years</td>
<td>€ 490</td>
</tr>
<tr>
<td>net costs of screening and surveillance colonoscopy</td>
<td>€ – 216</td>
</tr>
</tbody>
</table>

| B. model variant/varied parameter (range) | net costs |
| base case model | € – 216 |
| adenoma recurrence (20 – 40%) | € – 214 to – 220 |
| advanced adenoma progression to CRC (10 – 50%) | € – 121 to – 310 |
| CRC costs (€ 30 000)/€ 40 000 | € – 399 to – 623 |
| discount rate (2 to 5%) | € – 175 to – 237 |
may rise three-fold within a 30-day period [44]. However, this would not change our results because of the minor contribution of complications to the total costs.

The overwhelming share of benefits results from preventing CRC within the 10-year interval, about 7%, are due to removal of pT1 cancers by polypectomy at screening. Obviously, the total direct costs for diagnosis and treatment of CRC are the most decisive factor for calculating the absolute amounts of benefits. In a conservative approach, direct costs for diagnosis and treatment of CRC were assumed to be €21,820 in the base-case analysis based on a comprehensive evaluation of CRC costs in Germany in 2002, and varied up to €40,000 owing to the high costs of newly developed chemotherapeutics. With increasing costs of CRC treatment, prevention of CRC by polypectomy of advanced adenomas will become an increasingly important issue for insurance companies.

In the interpretation of our data, a number of caveats have to be kept in mind. Our calculations pertain to a situation where expert recommendations regarding surveillance colonoscopy are perfectly followed. In practice, the compliance with surveillance colonoscopy is not 100% as assumed in our study. Thus, both the costs for surveillance colonoscopy as well as the benefits from prevented CRC are likely to be somewhat smaller.

For some major parameters, assumptions had to be derived from the literature. The biological behaviour of colorectal adenomas and carcinomas was derived from long-term follow-up studies [22, 23, 44]. The numbers of prevented cases estimated on the basis of these assumptions are in accordance with epidemiological data from Germany before introduction of colonoscopy screening. Assumptions about the proportion of cancer arising from adenomas are particularly important in screening models that work mostly by preventing cancer through the removal of polyps. However, prospective studies on the natural history of untreated polyps with the knowledge of results from the National Polyp Study [14] are unethic. The shortcomings of using assumptions that carry some uncertainty as base for our calculations were partly overcome by a sensitivity analysis with variations of the recurrence rate of adenomas after polypectomy and of the conversion rate of adenomas into carcinomas.

We neglected indirect costs (loss of productivity) for individuals undergoing screening and surveillance colonoscopies amounting to about one-seventh of the costs of screening colonoscopies. We also neglected indirect costs of CRC treatment, since the vast majority of CRC would have occurred after retirement in this population with a mean age of 64.4 years at screening colonoscopy. Germany is the first country worldwide with a national colorectal cancer screening programme including colonoscopy. With this programme we have a large-scale data base with results from a “real-world setting”. Despite its limitations, our study strongly suggests that screening colonoscopy in Germany is likely to be cost-saving. The amount saved per screenee during a 10-year period may range between €121 and €623. These data are a strong argument to continue with, and to attempt to maximise participation in, screening colonoscopy in Germany.

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