Incidence of Colorectal Adenomas: Birth Cohort Analysis among 4.3 Million Participants of Screening Colonoscopy

Hermann Brenner1,2, Lutz Altenhofen3, Christian Stock1,4, and Michael Hoffmeister1

Abstract

Background: Most colorectal cancers develop from adenomas. We aimed to estimate sex- and age-specific incidence rates of colorectal adenomas and to assess their potential implications for colorectal cancer screening strategies.

Methods: Sex- and age-specific incidence rates of colorectal adenomas were derived by a birth cohort analysis using data from 4,322,085 screening colonoscopies conducted in Germany and recorded in a national database in 2003–2012. In addition, cumulative risks of colorectal cancer among colonoscopically neoplasm-free men and women were estimated by combining adenoma incidence rates with previously derived adenoma-colorectal cancer transition rates.

Results: Estimated annual incidence in percentage (95% confidence interval) in age groups 55–59, 60–64, 65–69, 70–74, and 75–79 was 2.4 (2.2–2.6), 2.3 (2.1–2.6), 2.4 (2.1–2.6), 2.2 (1.8–2.5), and 1.8 (1.2–2.3) among men, and 1.4 (1.3–1.5), 1.5 (1.4–1.7), 1.6 (1.4–1.8), 1.6 (1.3–1.8), and 1.2 (0.8–1.6) among women. Estimated 10- and 15-year risks of clinically manifest colorectal cancer were 0.1% and 0.5% or lower, respectively, in all groups assessed.

Conclusions: Annual incidence rates of colorectal adenomas are below 2.5% and 2% among men and women, respectively, and show little variation by age.

Impact: Risk of clinically manifest colorectal cancer is expected to be very small within 10 years and beyond after negative colonoscopy for men and women at all ages. The use of rescreening after a negative screening colonoscopy above 60 years of age may be very limited.

Introduction

Most colorectal cancers are thought to develop over many years through the adenoma-carcinoma sequence (1), and the slowness of this process, along with the existence of effective methods to detect and remove adenomas, offers great opportunities for colorectal cancer prevention by screening (2). Various screening methods have been proposed and shown to be effective in randomized trials and observational studies, including fecal occult blood testing, sigmoidoscopy, and colonoscopy (3–7). However, there is an ongoing debate about the most effective screening programs in terms of important screening features, such as type of screening test, age at first screening, screening, and surveillance intervals.

The effectiveness and cost-effectiveness of various colorectal cancer screening strategies are commonly evaluated by microsimulation models based on the natural history of the disease. For these models, incidence rates of colorectal adenomas as well as transition rates between adenomas of various size, preclinical, and clinical colorectal cancer are critical parameters. Because estimating these parameters by direct observation would require very long-term, ethically unacceptable studies, estimation is commonly done by model calibration to prevalence data from autopsy studies (see refs. 8, 9) or incidence data from cancer registries. However, autopsy studies are often very small in size and entirely cross-sectional, and they may have limited representativeness. Because of small size, deriving sex- and age-specific estimates is usually not possible. Cancer incidence data, on the other hand, do not allow disentangling incidence rates of adenomas and adenoma transition rates, and estimates of these parameters have varied strongly (10, 11). We recently developed a method to estimate adenoma transition rates from screening colonoscopy data using a birth cohort analysis approach (12), and we used this method to estimate adenoma transition rates by sex and age at high levels of precision from the German screening colonoscopy registry. Here, we aim to extend these analyses by estimating sex- and age-specific adenoma incidence, and to assess the potential implications of our results for colorectal cancer screening strategies.
Materials and Methods

Database

Our analysis is based on data of the German screening colonoscopy registry (13). Screening colonoscopy has been offered in Germany as a primary screening examination for early detection and prevention of colorectal cancer since October 2002. Women and men of ages 55 years or older are eligible for a first screening colonoscopy. If this first screening colonoscopy is conducted before 65 years of age, a second screening colonoscopy is offered 10 years later. Certification to conduct screening colonoscopy is tightly regulated on the basis of extensive previous training and experience, and its maintenance is subject to rigorous quality control. Histopathologic examination is performed decentrally by certified pathologic laboratories.

Along with introduction of screening colonoscopy, a national screening colonoscopy registry was built up. Details of its operation have been reported elsewhere (13). Briefly, all screening colonoscopies are reported anonymously on a standardized form. Reporting is virtually complete, as it is a prerequisite for physicians’ reimbursement by the health insurance funds. The registry includes only primary screening examinations (i.e., colonoscopies conducted for surveillance, work-up of symptoms, or other screening tests are not included). Items reported include basic sociodemographic variables as well as information on findings at colonoscopy, including number, size, and histologic characteristics of polyps. In case of multiple neoplasms, only the most advanced one is recorded. The reporting forms are processed and checked for completeness and plausibility using standardized algorithms at regional data centers before anonymized transfer to the national data center. Approximately 20% to 30% of eligible people have had a screening colonoscopy within the initial 10 years from the introduction of this screening offer. For this analysis, we used data from 4,322,085 first-time screening colonoscopies in 2003–2012 among participants 55 to 80 years of age.

Statistical analysis

A birth cohort analysis was performed to assess sex- and age-specific incidence of adenomas. The principle of this approach has been previously described in the context of estimating adenoma transition rates (12). Briefly, sex- and age-specific annual incidence rates, denoted \( I_{sex,age} \) (age = 55–59, 60–64, 65–69, 70–74, and 75–79), were estimated from sex- and age-specific prevalences of nonadvanced adenomas among screening participants from the same birth cohorts in 2003–2011 and 2004–2012, denoted \( P_{2003–2011,sex,age} \) and \( P_{2004–2012,sex,age} \), respectively, sex- and age-specific annual transition rates from nonadvanced adenomas to advanced adenomas, denoted \( T_{sex,age} \), and sex- and age-specific proportions of screening participants free of neoplasms in 2003–2011, denoted \( F_{2003–2011,sex,age} \).

\[
I_{sex,age} = \left( P_{2003–2011,sex,age} × (1 - T_{sex,age}) \times P_{2003–2011,sex,age} \right) / \left( F_{2003–2011,sex,age} \right)
\]

Estimates of \( P_{2003–2011,sex,age} \) and \( P_{2004–2012,sex,age} \) were directly obtained from the national screening colonoscopy registry. Estimates of \( T_{sex,age} \) had been obtained in our previous analyses from the same database using an analogous birth cohort approach (12).

As previously outlined and discussed in detail (12), this approach is based on the assumption that members of the birth cohort having their first screening colonoscopy in a given year are representative of all eligible members of that birth cohort with respect to sex- and age-specific adenoma prevalences. It assesses the annual increase in prevalence of nonadvanced adenoma, taking into account annual progression from nonadvanced adenoma to advanced adenoma. It should be noted that, although the calendar years are overlapping, there is no overlap in the study populations undergoing screening colonoscopy at defined ages in 2003–2011 and 2004–2012 from whom the age-specific adenoma prevalences are estimated. This is because a screening colonoscopy can be repeated after 10 years only. Our specific birth cohort approach therefore ensures maximum efficient use of data from nonoverlapping cohorts of screening colonoscopy participants obtained from overlapping calendar years.

To assess the sensitivity of our estimates against violations of the assumption of representative prevalences of colorectal neoplasms in men and women having screening colonoscopy, we repeated all analyses assuming true sex- and age-specific prevalences in each birth cohort to be 20% higher or lower than observed prevalences, respectively. Furthermore, to assess the sensitivity of the incidence estimates against shifts in the representativeness of screening colonoscopy participants over time, we repeated all analyses assuming true sex- and age-specific prevalences in the later birth cohort (2004–2012) but not in the earlier birth cohort (2003–2011) to be 2% higher or lower than those observed. This 1-year shift in representativeness of screening colonoscopy participants would correspond to a shift in representativeness of observed prevalences by approximately 20% over 10 years.

Monte Carlo simulations were used to derive 95% confidence intervals (CI) of sex- and age-specific incidence rates and for statistical testing of differences in sex-specific incidence rates by age and in age-specific incidence rates by sex. 95% CIs were determined as 2.5th and 97.5th percentiles of incidence rate estimates obtained in 100,000 runs. Statistical tests were two-sided with \( \alpha = 0.05 \).

In addition, multistate Markov models (states: no neoplasm, nonadvanced adenoma, advanced adenoma, preclinical colorectal cancer, and clinically manifest colorectal cancer) were run to estimate age-specific 10-year risks of developing any neoplasm, any advanced neoplasm (advanced adenoma or cancer), any colorectal cancer (preclinical or clinical), and clinically manifest colorectal cancer within 10 years for men and women with no neoplasms detected at screening colonoscopy. The rationale behind this analysis was that 10-year screening...
The analyses were done with the SAS statistical software, version 9.2 (SAS Institute Inc.).

**Results**

Table 1 shows the prevalences of various types of colorectal neoplasms according to sex and age, based on 4,322,085 screening colonoscopies conducted between 2003 and 2012. At all ages, men had substantially higher prevalences of all types of colorectal neoplasms than women. Among both men and women, prevalences were lowest at ages 55–59 years, with 16.8%, 6.7%, and 0.6% of men, and 10.1%, 3.6%, and 0.3% of women screened in 2003–2011 carrying at least one nonadvanced adenoma (but no advanced adenoma), at least one advanced adenoma and cancer, respectively. For advanced adenoma and cancer, prevalences monotonically increased with age, reaching levels of 10.5% and 2.6% in age group 75–79 years among men, and 6.8% and 1.6% among women. In relative terms, the increase was steepest for cancer, with sex-specific prevalences being 4- to 5-fold higher in age group 75–79 years than in age group 55–59 years. Prevalences of nonadvanced adenomas also gradually increased with age between age groups 55–59 and 70–74 years in both sexes, but the increase was rather modest in relative terms, and no increase was seen between age groups 70–74 and 75–79 years. Participants

### Table 1. Numbers and distribution of participants of screening colonoscopy by sex, age, and most advanced finding; summary data from the German national registry, 2003–2012

<table>
<thead>
<tr>
<th>Sex</th>
<th>Calendar years</th>
<th>Age</th>
<th>No neoplasm (n (%))</th>
<th>Nonadvanced adenoma (n (%))</th>
<th>Advanced adenoma (n (%))</th>
<th>Cancer (n (%))</th>
<th>Total (n (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td>2003–2011</td>
<td>55–59</td>
<td>381,155 (75.9)</td>
<td>84,520 (16.8)</td>
<td>33,514 (6.7)</td>
<td>3,044 (0.6)</td>
<td>502,233 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60–64</td>
<td>313,582 (72.6)</td>
<td>78,234 (18.1)</td>
<td>36,086 (8.3)</td>
<td>4,308 (1.0)</td>
<td>432,210 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65–69</td>
<td>307,933 (70.1)</td>
<td>84,417 (19.2)</td>
<td>40,881 (9.3)</td>
<td>5,869 (1.3)</td>
<td>439,100 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>70–74</td>
<td>186,229 (68.1)</td>
<td>54,463 (19.9)</td>
<td>27,508 (10.1)</td>
<td>5,366 (2.0)</td>
<td>273,666 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75–79</td>
<td>86,028 (67.8)</td>
<td>24,203 (19.1)</td>
<td>13,347 (10.5)</td>
<td>3,258 (2.6)</td>
<td>126,836 100</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>2003–2011</td>
<td>55–59</td>
<td>308,101 (71.1)</td>
<td>82,571 (19.1)</td>
<td>37,886 (8.7)</td>
<td>4,780 (1.1)</td>
<td>433,338 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60–64</td>
<td>281,863 (68.7)</td>
<td>82,492 (20.1)</td>
<td>39,857 (9.7)</td>
<td>6,119 (1.5)</td>
<td>410,131 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>65–69</td>
<td>166,786 (67.0)</td>
<td>51,227 (20.6)</td>
<td>25,609 (10.3)</td>
<td>5,312 (2.1)</td>
<td>248,934 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>70–74</td>
<td>72,613 (67.1)</td>
<td>21,187 (19.6)</td>
<td>11,525 (10.6)</td>
<td>2,942 (2.7)</td>
<td>108,267 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>75–79</td>
<td>406,734 (61.3)</td>
<td>63,057 (12.6)</td>
<td>26,786 (4.9)</td>
<td>3,698 (0.7)</td>
<td>500,275 100</td>
</tr>
</tbody>
</table>

The analyses were done with the SAS statistical software, version 9.2 (SAS Institute Inc.).
in screening colonoscopy from the same 5-year birth cohorts, who were screened at ages 56–60, 61–65, 66–70, 71–75, and 76–80 in 2004–2012, had slightly higher prevalences of all kinds of neoplasms.

Estimated annual incidence in percent of nonadvanced adenomas by sex and age is shown in Table 2. It was in a narrow range, from 2.2% to 2.4% per year, for age groups 55–59 to 70–74 years for men. For women, estimated incidences were much lower, ranging from 1.4% to 1.6% per year in the same age groups. For age group 75–79 years, somewhat lower incidences than in younger age groups were estimated. Because of the very large sample size, CIs for all estimates were rather narrow. Sex differences were highly statistically significant for all age groups except the oldest one, whereas the much smaller age differences mostly failed to reach statistical significance, despite the very large sample size. The only exception is the significantly lower incidence in age group 75–79 years compared with the age group 55–59 years among men.

Sensitivity analyses assuming true sex- and age-specific neoplasm prevalences to be 20% higher or lower than those observed in participants of screening colonoscopy yielded estimates of incidence rates that were approximately 20% to 30% higher or lower than those estimated in our base case analyses. Variations in incidence estimates in the same order of magnitude were seen when true prevalences were assumed to be 2% higher or lower than those observed in 2004–2012, but not in 2003–2011, to assess potential implications of a shift in representativeness of screening colonoscopy participants over time (data not shown).

Table 3 provides estimates of 10-year risk (in %) of colorectal neoplasms for men and women free of neoplasm at screening colonoscopy by age. With estimates around 0.1% for men and even lower estimates for women, the estimated 10-year risk of clinically manifest colorectal cancer was very small, regardless of age at negative colonoscopy. Even the risk of any cancer (including preclinical cancers) was below 0.5% in all age groups in both sexes, and less than 4% of men and less than 3% of women are expected to develop any advanced neoplasm within 10 years. Variation of sex- and age-specific mortality by 20% in sensitivity analyses did not alter the estimates to any relevant extent (data not shown).

After a negative screening colonoscopy at the age of 65 years or older, the risk of developing a clinically manifest cancer before the age of 80 years was estimated to be very small even in the absence of any further colorectal cancer screening (around 0.5% or lower; Table 4). After a negative screening colonoscopy at 60 or 55 years of age, cumulative risk up to the age of 80 years would be approximately 1.3% and 2.5%.

Table 2. Estimated annual incidence in % of nonadvanced adenomas by sex and age; on the basis of data from the German national screening colonoscopy registry, 2003–2012

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PE</td>
<td>95% CI</td>
<td>P*</td>
<td>PE</td>
</tr>
<tr>
<td>55–59</td>
<td>2.4</td>
<td>2.2–2.6</td>
<td>0.72</td>
<td>1.4</td>
</tr>
<tr>
<td>60–64</td>
<td>2.3</td>
<td>2.1–2.6</td>
<td>0.97</td>
<td>1.5</td>
</tr>
<tr>
<td>65–69</td>
<td>2.4</td>
<td>2.1–2.6</td>
<td>0.37</td>
<td>1.6</td>
</tr>
<tr>
<td>70–74</td>
<td>2.2</td>
<td>1.8–2.5</td>
<td>0.03</td>
<td>1.6</td>
</tr>
<tr>
<td>75–79</td>
<td>1.8</td>
<td>1.2–2.3</td>
<td>0.04</td>
<td>1.2</td>
</tr>
</tbody>
</table>

Abbreviation: PE, point estimate.
*P value for difference from reference group 55–59 years.
#P value for difference between men and women within age group.

Table 3. 10-year risk (%) of colorectal neoplasms for men and women free of neoplasm at screening colonoscopy (and not undergoing any further colorectal cancer screening) by age

<table>
<thead>
<tr>
<th>Age at negative colonoscopy</th>
<th>Men</th>
<th>Women</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any neoplasm</td>
<td>Advanced neoplasm</td>
<td>Cancer</td>
</tr>
<tr>
<td>55</td>
<td>20.4</td>
<td>3.4</td>
<td>0.28</td>
</tr>
<tr>
<td>60</td>
<td>19.9</td>
<td>3.2</td>
<td>0.31</td>
</tr>
<tr>
<td>65</td>
<td>19.1</td>
<td>3.2</td>
<td>0.40</td>
</tr>
<tr>
<td>70</td>
<td>16.0</td>
<td>2.5</td>
<td>0.33</td>
</tr>
</tbody>
</table>
among men, and 1.0% and 1.9% among women if no further colorectal cancer screening was done in the meantime. The cumulative risks of colorectal cancer up to the age of 80 years among people with a negative screening colonoscopy at ages 55, 60, 65, and 70 years correspond to approximately half, one quarter, one tenth, or 2% of the cumulative risks between 55 and 80 years of age of people with no screening colonoscopy (Fig. 1).

Discussion

In this article, we derived estimates of sex- and age-specific incidence rates of colorectal adenomas from the national screening colonoscopy registry in Germany using a birth cohort approach. Because of the large sample size, estimates were obtained at very high levels of precision. Annual incidence rates around 2.0% to 2.4% and 1.5% were estimated for men and women, respectively, with little variation by age, except for a lower incidence rate in the oldest age group (75–79 years) among men. When combined with previously derived estimates of transition rates of nonadvanced to advanced adenomas, advanced adenoma to preclinical colorectal cancer and preclinical to clinically manifest colorectal cancer, our results suggest a very low 10- and 15-year risk of clinically manifest cancer in the order of 0.1% and 0.5% or even lower after a negative screening colonoscopy for both sexes and all age groups.

The major and statistically significant sex differences in estimates of adenoma incidence in all age groups up to the age of 75 years are consistent with well-known sex differences in adenoma prevalences (13, 16–18) as well as with well-known sex differences in colorectal cancer incidence and mortality (19). Given that no such sex differences were found for transition rates of nonadvanced adenoma to advanced adenoma and from advanced adenoma to colorectal cancer (12), sex differences in colorectal cancer incidence and mortality seem to be mainly, if not exclusively, due to sex differences in adenoma incidence. Potential mechanisms underlying these differences might include, among other factors, higher exposure to cigarette smoking and higher consumption of red meat among men, which have been related to increased prevalence of adenomas and colorectal cancer risk (20–22), as well as hormonal factors. The vast majority of women included in our analysis presumably were postmenopausal. Therefore, hormone replacement therapy (HRT) rather than natural hormone production might have been the main source of sex differences in hormone exposure in our study population. HRT has been consistently related to reduced adenoma prevalence in epidemiologic studies (23–26).

Table 4. Risk of clinically manifest colorectal cancer up to various ages for men and women free of neoplasm at screening colonoscopy (and not undergoing any further colorectal cancer screening) by age.

<table>
<thead>
<tr>
<th>Age at negative colonoscopy</th>
<th>Men Risk of clinically manifest cancer (%) up to age</th>
<th>Women Risk of clinically manifest cancer (%) up to age</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>65</td>
<td>70</td>
</tr>
<tr>
<td>55</td>
<td>0.09</td>
<td>0.44</td>
</tr>
<tr>
<td>60</td>
<td>0.09</td>
<td>0.44</td>
</tr>
<tr>
<td>65</td>
<td>0.11</td>
<td>0.51</td>
</tr>
<tr>
<td>70</td>
<td>0.10</td>
<td>0.44</td>
</tr>
</tbody>
</table>

The Markov model estimates of very low risk of colorectal cancer within 10 or even 15 years after negative colonoscopy are consistent with findings from cohort and case–control studies (27–29). These results therefore further strengthen the evidence that 10-year screening intervals after negative screening colonoscopy are sufficient or may even be prolonged. Given the very low cumulative risk of colorectal cancer up to the age of 80 years among men and women with a negative screening colonoscopy at 60 years or older, the use of repeat screening colonoscopies in these people might be very limited. More comprehensive modeling of effectiveness and cost-effectiveness of various screening and rescreening strategies, which also takes additional factors such as colonoscopy miss rates and complications, availability and costs of high-quality colonoscopy, or alternative rescreening options into account (30), should be done to weigh the benefits versus potential risks and costs for rescreening after a negative screening colonoscopy above 60 years of age. We hope that the very detailed age- and sex-specific adenoma incidence rates derived in our study may be helpful to inform such modeling.

Our analysis has specific strengths and limitations. A major strength is the very large database of a complete national screening colonoscopy registry, including data from more than 4.3 million screening colonoscopies. A further strength is the use of a birth cohort approach rather than a cross-sectional approach for deriving age-specific incidence from age-specific prevalence data, which helped to prevent potential bias by previously identified major birth cohort effects (18). Increasing age-specific adenoma prevalences in younger birth cohorts might have led to underestimation of age-specific adenoma incidences in a cross-sectional approach.
development of more than one colonoscopically detected adenoma during the 1 year interval assessed in our study to be rather small. A further limitation of our database is that no distinction between proximal and distal adenomas could be made. Given the well-known differences in the biology and epidemiology of proximal and distal adenomas (32, 33), major differences in their incidence might be expected. Variation of adenoma incidence would likewise be expected by colorectal cancer risk factors, such as family history of colorectal cancer or lifestyle habits, information on which was not available in the database.

Despite the use of a birth cohort approach, we cannot rule out possible differences in representativeness of members of the same birth cohort who participated in screening colonoscopy 1 year apart. As illustrated in our sensitivity analyses, potential shifts in representativeness of screening colonoscopy participants could have led to some over- or underestimation of incidence rates.

Our analyses from the initial 10 years of the German screening colonoscopy program strictly refer to first-time screening colonoscopies. The estimated incidence rates should therefore not be generalized to people with previous positive or negative screening colonoscopies. The former are likely to have higher incidence rates, whereas even lower incidence rates might be expected for people who were free of neoplasms at a preceding screening colonoscopy.

Finally, our analyses of cumulative risks of clinically manifest colorectal cancer pertain to colorectal cancers developing through the adenoma-colorectal cancer sequence. Although the vast majority of colorectal cancers develop this way, approximately 15% of sporadic colorectal cancers are thought to develop through fundamentally different routes. These include cancers originating from serrated precursor lesions, which are typical premalignant precursor lesions in the proximal colon and are often characterized by the CpG island methylator phenotype (CIMP) and activating BRAF oncogene mutations (34). Identifying these lesions during colonoscopy is particularly difficult because of their flat inconspicuous nature, and these lesions are likely to be responsible for higher 10-year overall colorectal cancer risks than those estimated in our analysis and to contribute to the occurrence of interval cancers (35).

Despite its limitations, our analysis enhances the empirical basis for sex- and age-specific incidence rates of colorectal adenomas, for modeling the effectiveness and cost-effectiveness of various colorectal cancer screening strategies, for screening and rescreening recommendations, and for individual patient decisions. In particular, our results support suggestions that 10-year screening intervals after negative screening colonoscopy are sufficient or may even be prolonged and that rescreening after a negative screening colonoscopy above 60 years of age may often not be warranted. Further research is required, however, to elucidate the natural history of colorectal cancers not developing through the adenoma-carcinoma sequence and its potential implications for screening and screening intervals.
Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Disclaimer

The sponsors did not have any role in this study.

Authors’ Contributions

Conception and design: H. Brenner

Development of methodology: H. Brenner

Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): L. Altenhofen

Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): H. Brenner, L. Altenhofen

Writing, review, and/or revision of the manuscript: H. Brenner, L. Altenhofen, C. Stock, M. Hoffmeister

Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): L. Altenhofen

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References


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For more information, visit the article's page on the Cancer Epidemiology Biomarkers Prev website. You can access the most recent version of the article at doi:10.1158/1055-9965.EPI-14-0367. Additionally, the article cites 34 articles, 7 of which are freely accessible. To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.