Original Article

Cancers Due to Smoking and High Alcohol Consumption

Estimation of the Attributable Cancer Burden in Germany

Ute Mons*, Thomas Gredner*, Gundula Behrens, Christian Stock, Hermann Brenner

Summary

Background: Tobacco and alcohol consumption are known causes of cancer. We set out to estimate the absolute numbers and proportions of cancer attributable to smoking and high alcohol consumption in Germany in 2018.

Methods: Numbers and proportions (population-attributable fractions, PAF) were calculated by sex and age group for ages 35 to 84 years based on population projections, national cancer incidence and exposure data, and published relative risks.

Results: For the year 2018 we estimated the smoking-attributable cancer burden to be 85 072 cases (men 58 760, women 26 312), corresponding to 19% of all incident cancers. The highest PAF was seen for lung cancer: 89% of male and 83% of female lung cancer cases are attributable to smoking. The cancer burden attributable to high alcohol consumption was estimated to be 9588 (men 8117, women 1471) cases (2% of all incident cancers). The highest PAF were observed for cancer of the oral cavity and pharynx (men 34%, women 6%) and squamous cell carcinoma of the esophagus (men 30%; women 5%).

Conclusions: A considerable proportion of cancer cases are attributable to smoking and high alcohol consumption. More rigorous prevention efforts are required to achieve significant reductions in the prevalence of these risk factors and the attributable cancer burden.

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Health authorities in the USA recognized smoking as a cause of lung cancer and laryngeal cancer as early as in 1964. Since then, evidence of a causal link between smoking and several other cancer sites has accumulated, and today smoking is known as the leading avoidable cancer risk factor, causally associated with 12 different types of cancer (1).

Alcohol consumption was first concluded to be carcinogenic to humans by the International Agency for Research on Cancer (IARC) in 1988 (2). According to the Continuous Update Project (CUP) of the World Cancer Research Fund (WCRF), alcohol consumption increases the risk for six types of cancer (3).

Our aim in carrying out this study was to provide projections of the cancer burden attributable to the risk factors smoking and high alcohol consumption in Germany for the year 2018. Due to a lack of epidemiological data on the role of lifestyle cancer risk factors at young and very old ages, we restricted our estimates to the age range of 35 to 84 years.

Methods

Projection of cancer cases

We estimated the number of site-specific cancers for each age and sex group for the year 2018 by multiplying the most recent age- and sex-specific incidence rates available from the German cancer registries (for the year 2014 [4]), by age- and sex-specific population projections for Germany for the year 2018 (5) (*eTables 1 and 2*).

Estimation of the smoking-attributable cancer burden

The strong association between smoking and lung cancer allows estimating the smoking-attributable fraction of lung cancer by means of an established indirect method (6), without having to make assumptions about latency periods. This method requires knowledge of lung cancer rates in never smokers and of relative risks (RR) of cancers causally linked to smoking, for smokers compared to never smokers. Such data were not available for Germany, so we used published pooled data from large contemporary cohorts provided by the American Cancer Society for the period 2000 to 2010: age- and sex-specific lung cancer mortality rates per 100 000 persons were reported by Thun et al. (14), and multivariably adjusted age- and sex-specific

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BOX

Population-attributable fraction (PAF)

This concept was developed in the early 1950s and is widely used in epidemiological studies (7, 8). A PAF expresses by what proportion the prevalence or incidence of a disease could be reduced if the whole population were shifted to a more favorable level of a risk factor for that disease. In a seminal article series, Parkin et al. used the PAF concept to estimate the fraction of cancers occurring in the United Kingdom that are attributable to lifestyle and environmental risk factors (9). This was followed by similar work in other countries (e.g., [10, 11]), and we present here for the first time such estimates for Germany.

The limitations and pitfalls in the interpretation of PAF estimates have been described in detail elsewhere (7, 12). One important aspect of this concept is that while the PAF for a single causal risk factor cannot be more than 100%, in the event of shared responsibility of several causes for a disease—as is usually the case for cancer—the PAF of these causes can add up to more than 100% (7, 13). Thus, PAF cannot be simply added up across causes, but can, however, be combined to estimate a joint PAF assuming independence of risk factors (13), as was done for the estimates presented in the article by Gredner et al. in this issue of *Deutsches Ärzteblatt International*. Even though it would unarguably take several years before reductions in cancer risk factors would lead to reduced cancer incidence, the PAF is nevertheless considered a valuable quantitative appraisal of their population impact (9).

As with all epidemiological models, our PAF estimations are based on assumptions, which may not hold true in all cases. Here, for instance, this applies to the assumption of a 10-year latency period between exposure and cancer incidence, or the assumption of independence of risk factors. However, while all presented results need to be understood as estimates, we are confident that our projections regarding the potential for prevention at population level are reasonably conservative and reflect the best of current knowledge.

relative mortality risks for lung cancer and other smoking-caused cancers combined, derived from the same cohorts, were published in a recent report by US health authorities (1).

By applying the age- and sex-specific lung cancer rates in never smokers to the age- and sex-specific population projections for Germany for the year 2018, we calculated the number of cancer cases that would be expected in the absence of smoking as a risk factor. The number of lung cancer cases attributable to smoking was then calculated by subtracting these cases from the overall number projected for 2018. For other cancers caused by smoking, data on rates among never smokers were not available, so we used the commonly applied Levin's formula for the calculation of population-attributable fractions (PAF) (5):

$$PAF = \frac{\sum(p_x \cdot ERR_x)}{1 + \sum(p_x \cdot ERR_x)}$$

where p_x is the proportion of the population at exposure level x (here: prevalence of ever smokers) and ERR_x is the excess relative risk associated with exposure level x calculated as $(RR - 1)$. Here, we used not the observed smoking prevalence from a population survey, but rather a notional (theoretical) prevalence of ever smoking in the German population that was derived by inserting the calculated attributable fractions of lung cancer and the relative risks for lung cancer in smokers in the above formula and solving it for p_x separately for each sex and age group. This notional prevalence can be regarded as the ever smoking prevalence that would be necessary in the German population to produce the cancer incidence in 2018 if the relative risks of the American cohorts pertained (15).

Estimation of the alcohol-attributable cancer burden

To provide estimates of cancer cases caused by excess alcohol intake, PAF were calculated considering cancers determined as causally related to consumption of alcohol by the IARC (16). Data on the prevalence of alcohol consumption in Germany were obtained from the German Health Interview and Examination Survey for Adults for the period 2008 to 2011 (DEGS1 2008–2011) (17).

Estimation of the average alcohol consumption in the population was based on a validated food frequency questionnaire (18). Self-reported information on amount and frequency of alcohol consumption was combined and converted into average grams of pure alcohol per day (*eSupplement A*). For PAF estimation, alcohol consumption was categorized into “below recommended limits” (<10 g pure alcohol per day in women or <20 g pure alcohol per day in men) and “above recommended limits” (≥ 10 g/d in women or ≥ 20 g/d in men) (19).

RR estimates concerning the association between alcohol consumption and site-specific cancer incidence were taken from meta-analyses of cohort studies, conducted by the WCRF, when available. The mean amount of pure alcohol consumed in grams per day (g/d) by those who stayed within the recommended limits was defined as the optimum exposure level.

For each age and sex group, we computed the PAF associated with the absolute difference of the mean exposure level for those with alcohol consumption above versus those with alcohol consumption at or below recommended limits using the above-mentioned Levin's formula (*eSupplement B*).

As in similar previous studies, we assumed a 10-year latency period between exposure and cancer

FIGURE

Estimated number and population-attributable fraction (PAF) of site-specific incident cancer cases attributable to smoking and high alcohol consumption among men and women in Germany for the year 2018.

TABLE 1

Lung cancer cases attributable to smoking by sex and age group, Germany, 2018

Age (years)	Lung cancer cases projected for 2018	Lung cancer cases expected in absence of smoking in 2018	Smoking-attributable lung cancer cases	PAF (%)
Men				
35–54	2890	434	2456	85
55–64	9136	775	8361	92
65–74	11 492	926	10 566	92
75–84	10 982	1827	9065	83
Total	34 410	3962	30 448	88
Women				
35–54	2268	423	1845	81
55–64	5358	478	4880	91
65–74	6000	785	5215	87
75–84	4878	1409	3469	71
Total	18 504	3095	15 409	83

PAF, population-attributable fraction

incidence. By applying the age- and sex-specific PAF to the projected cancer incidences for Germany for the year 2018, we calculated the number of cancer cases that would be expected if individuals with alcohol consumption above recommended limits reduced their alcohol intake to the levels of those who adhere to recommended limits.

Sensitivity analyses

Methods of sensitivity analyses are described in *eSupplement C*.

Results

Smoking-attributable cancer burden

In most age groups the risk for lung cancer in smokers is around 20 or more times higher than in never smokers, and for other cancers about twice as high (*eTable 3*). While we projected 52 914 lung cancer cases in 2018 in the German population aged 35 to 84 (men 34 410, women 18 504), only 7056 cases were projected to occur in the absence of smoking (men 3962, women 3094) (*Table 1*). Accordingly, 89% of lung cancer cases among men and 83% among women would be attributable to smoking (overall 45 858 cases; men 30 448, women 15 410).

For all other cancers, the PAF was around 30% in men and 20% in women, which translated to 39 214 cancer cases (men 28 312, women 10 902) (*Figure, eTables 4 and 5*). Overall, according to our estimates for 2018, 85 072 out of 440 373 projected cancer cases (*eTables 4 and 5*), i.e., 19.3%, would be attributable to smoking (men 58 760 cases, 24.7%; women 26 312 cases, 13.0%).

The sensitivity analysis based on empirical smoking prevalence from DEGS1 2008–2011 (*eTable 6*) yielded a very similar estimate of 86 000 smoking-attributable cancer cases (*eTable 7*).

Alcohol-attributable cancer burden

According to DEGS1 2008–2011, 18.7% of men and 12.9% of women aged 25 to 74 years were estimated to drink alcohol at levels above the recommended limits, with an average intake of 44.6 g/d for men and 20.2 g/d for women (*Table 2*). Dose–response meta-analyses of alcohol consumption and site-specific cancer risk found risk increases of 7–29% per 10 g/d (for the larynx, per 12.5 g/d) increase in pure alcohol intake (*eFigure*).

The greatest PAF for alcohol consumption were estimated for cancer of the oral cavity and pharynx (men 34%, women 6%) and squamous cell carcinoma of the esophagus (men 30%, women 5%). The attributable cancer burden was greater among men than women, with much higher PAF for all cancer sites. Overall, PAF ranged from 8% to 34% in men and from 1% to 6% in women, which in sum translated to 9588 cancer cases (men 8177, women 1471), corresponding to 2.2% (men 3.4%, women 0.7%) of all cancer cases (*eTables 8 and 9*). The cancer sites contributing most to this excess were cancer of the oral cavity and pharynx in men, with 3191 cancer cases, and breast cancer in women, with 870 cases.

Sensitivity analyses using the 95% confidence limits of risk estimates on the association of alcohol and cancer indicated a potential range of 7000 to 12 300 cancer cases attributable to alcohol (*eTable 10*).

TABLE 2

Prevalence of alcohol consumption below and above recommended limits according to the DEGS1 survey (2008–2011): mean pure alcohol intake in grams per day among men and women aged 25–74 years

	Prevalence (%) and mean (m) for alcohol consumption below and above recommended limits											
	25–34 years		35–44 years		45–54 years		55–64 years		65–74 years		Total	
Exposure	%	m	%	m	%	m	%	m	%	m	%	m
Men												
Below recommended limits (<20 g/d)	86	6.8	85	5.6	78	6.2	81	6.3	76	5.7	81	6.1
Above recommended limits (≥ 20 g/d)	14	57.7	15	38.4	22	47.3	19	38.0	24	43.2	19	44.6
Women												
Below recommended limits (<10 g/d)	89	2.3	86	2.3	88	2.4	83	2.2	90	1.9	87	2.2
Above recommended limits (≥ 10 g/d)	11	16.9	14	23.3	12	18.8	17	20.8	10	19.8	13	20.2

Discussion

Of around 440 000 cancer cases expected in 2018, about 85 000 and 9500 cases are estimated to be attributable to smoking and alcohol consumption, respectively, which corresponds to 19% and 2% of cancers. Especially lung cancer is largely attributable to smoking, with a PAF of 80 to 90%. Generally, the attributable cancer burden was estimated to be considerably greater among men, both in relative and in absolute terms.

Smoking-attributable cancer burden

Tobacco smoke is a complex mixture of more than 5000 chemicals, including carcinogenic substances, with no risk-free level of exposure (20). The health consequences of the cumulative exposure to carcinogens of tobacco smoke are enormous, particularly for the lung but also for other organs (1). Our estimations of the smoking-attributable cancer burden are based on expected cancer incidence in the complete absence of smoking. It is, however, important to keep in mind that even if smoking were eliminated today, it would take decades until no further cancer caused by smoking occurred. Former smokers still have an increased risk of cancer, even though the excess risk declines with increasing time since smoking cessation (21).

The total number of smoking-attributable cancer cases was estimated to be more than twice as high in men than in women, which mostly reflects the higher prevalence of smoking among men, especially in recent decades (22, 23). Our results are quite consistent with a previous study for Germany, which estimated 72 208 cancer cases to be attributable to smoking in 2008; 55 057 cases in men and 17 151 cases in women. Our estimates are slightly higher for men (58 760 vs. 55 057), and markedly higher for women (26 312 vs. 17 151) (24). This might be due to our use of more recent risk estimates, as sex differences in relative risks of smoking have been decreasing over time and are now rather negligible (14).

We found that overall, 19% of cancer cases are attributable to smoking, which is substantially higher than comparable estimates for England (14.7%, [10]) or Australia (13.4%, [11]), two countries that have achieved strong declines in smoking in recent years through comprehensive tobacco control strategies (25, 26).

For Germany, a modeling study demonstrated that significant reductions in smoking prevalence and the attributable disease burden could be achieved by strengthening tobacco control policies in line with recommendations of the World Health Organization, such as raising taxes, banning tobacco advertising, and enhancing cessation support (27).

Alcohol-attributable cancer burden

The major constituent of alcoholic beverages, ethanol, and its metabolite acetaldehyde have been classified as carcinogenic to humans (28). While there are more cancer sites causally associated with alcohol consumption in women, the total number of alcohol-attributable cancer cases was estimated to be more than five times higher in men than in women. In addition to a higher prevalence of alcohol consumption above the recommended limits among men, the greater average amount of alcohol consumed by men in each age group contributes to this inequality.

Instead of an unrealistic zero exposure (total absence of alcohol consumption), we sought to arrive at an achievable target value by setting the reference exposure level to the mean amount of alcohol consumed by those who adhere to recommended limits. However, it is important to note that there is no safe level of alcohol consumption with regard to cancer risk (29).

Overall, our projections of cancer site-specific PAF and corresponding excess cases are lower than those from a previous study (30), which estimated that approximately 8700 cancer cases among men and 4900 cases among women were attributable to alcohol in Germany in 2010. Our lower estimates can be

Key messages

- We used population-attributable fractions (PAF) to estimate the proportion of cancer incidence attributable to the risk factors smoking and high alcohol consumption.
- According to our estimates, around one in five cancer cases is due to smoking and around one in 50 cases is due to high alcohol consumption, pointing to a large potential for prevention.
- Although our projections are based on assumptions and epidemiological data that entail some uncertainties, we are confident that they are the best estimates possible on the basis of current knowledge and are reasonably conservative.
- Public health policies and factors such as pricing and taxation can play an important role in reducing smoking and high alcohol consumption, and thus in cancer prevention.
- Healthcare professionals can contribute to cancer prevention by advising and supporting their patients to quit smoking and reduce alcohol consumption.

explained by the fact that we did not consider the cancer burden due to light drinking and used more recent risk estimates from prospective studies.

A study estimating the alcohol-attributable burden of cancer incidence in eight European countries found that PAF varied across countries because of differences in alcohol exposure (31). Results from modeling studies demonstrate that alcohol consumption could be influenced by public health policies and interventions such as pricing and taxation (32).

Strengths and limitations

We provide up-to-date estimates of the cancer burden attributable to smoking and alcohol consumption in Germany, based on the latest relative risk estimates from cohort studies as well as the most recent population projections and cancer registry data. Sensitivity analyses revealed substantial numbers of attributable cancer cases across all scenarios in a comparable range.

Due to a lack of up-to-date risk estimates from prospective cohort studies, we did not consider synergistic interactions between smoking and alcohol consumption, although there is some evidence of such an effect for head and neck cancer (33). For the estimation of the smoking-attributable cancer burden we had to rely on lung cancer rates in never smokers and relative risk estimates from a US population. We also had to use relative risk estimates for cancer mortality from the same population, but these tend to be similar to those for cancer incidence (21).

Furthermore, with respect to the estimation of the alcohol-attributable cancer burden, PAF depend on the reliability of self-reported alcohol drinking and the definition of exposure categories. Potential changes in prevalence of smoking or alcohol consumption over the past 10 years in the considered age groups should be small and therefore not affect our estimates substantially.

When calculating PAF, we restricted our estimates to cancer types with currently sufficient or convincing evidence as stated by pertinent authorities, but new evidence might confirm other causal links in the future. For example, there is evidence that the risk of gastric cancer is associated with increased alcohol consumption, but this association was observed only for high alcohol intakes (≥ 45 g/d) (34). A causal association between smoking and breast cancer has also been postulated (35). Given these limitations, our PAF and cancer burden projections are likely to be underestimates and can thus be considered conservative.

Conclusion

Of around 440 000 cancer cases to be expected in Germany in 2018, approximately 85 000 and 9500 cases are estimated to be attributable to smoking and alcohol consumption, respectively, corresponding to 19% and 2% of all cancer cases. Given the still significant prevalence of smoking and alcohol consumption in this country, there is huge potential for cancer prevention by intensifying efforts to reduce smoking rates and alcohol use.

Two other articles in this issue of *Deutsches Ärzteblatt International* present the topics “Cancers Due to Infection and Selected Environmental Factors” and “Cancers Due to Excess Weight, Low Physical Activity and Unhealthy Diet”, respectively (36, 37).

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Conflict of interest statement

The authors declare that no conflict of interest exists.

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► Supplementary material

For eReferences please refer to:
www.aerzteblatt-international.de/ref3518

eSupplement, eTables, eFigure:
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Supplementary material to:

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eSupplement

A. Estimation of alcohol consumption

Data on the prevalence of alcohol drinking were obtained from the German Health Interview and Examination Survey for Adults (DEGS1). The first wave of this nationally representative survey was conducted from 2008 to 2011 and covered the German population aged 18 to 79 years (17). Estimation of the consumption of pure alcohol (g/day) was based on a validated food frequency questionnaire (18). Data on frequency and quantity (average amount consumed in liters) for each major alcoholic beverage (i.e., beer, non-alcoholic beer, wine, distilled spirits, cocktails/alcoholic mixed drinks) were collected for the 4-week period prior to interview and combined using the following formula (e1)

Alcohol per type of beverage (g/d)

$$= \frac{\text{Frequency in 4 weeks} \times \text{average amount (l)} \times \text{alcoholic content (g/l)}}{28}$$

where default values for the average alcohol contents (beer=38.11 g/l, non-alcoholic beer=3.97 g/l, wine=87.34 g/l, distilled spirits=262.02 g/l, cocktails/alcoholic mixed drinks=75 g/l) and standard sizes for each type of beverage were used (e1). The average daily alcohol consumption was estimated by adding the amounts consumed across the different types of alcoholic beverages,. Pure alcohol consumption was then categorized into “below recommended limits” (less than 10 g/day in women or 20 g/day in men) and “above recommended limits” (≥ 10 g/day in women or ≥ 20 g/day in men) (19).

B. Statistical methods

We estimated the mean exposure (daily average alcohol consumption) among individuals with at-risk drinking and in those with low-risk alcohol consumption in strata defined by age (25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years) and sex (men, women) using the data and the sample weights of the DEGS1 survey and the survey procedures in SAS, version 9.4.

We defined the corresponding mean excess exposure level by the difference between the mean exposure in those with at-risk drinking and those with low-risk alcohol consumption.

For each age and sex group, we computed the relative risk (RR) of cancer associated with the mean level of excess by multiplying the mean level of excess by the log RR of cancer for a 1-g increase in alcohol consumption using

$$RR_{\text{mean excess}} = \exp(\log(RR \text{ per unit}) \times \text{mean excess})$$

We calculated the population-attributable fraction (PAF) for the mean level of excess for each age and sex group combining the prevalence (P) of at-risk drinking and the relative risk (RR) of cancer associated with the mean level of excess by

$$PAF_{\text{mean excess}} = \frac{P_{\text{at-risk drinking}} \times (RR_{\text{mean excess}} - 1)}{[1 + P_{\text{at-risk drinking}} \times (RR_{\text{mean excess}} - 1)]}$$

Assuming a 10-year latency period, we estimated the number of incident cancers attributable to the mean excess alcohol consumption by multiplying the PAF by the expected cancer incidence for each age and sex group for the year 2018 (i.e., we assumed that those aged 25-34 years, 35-44 years, 45-54 years, 55-64 years, and 65-74 years at exposure were at risk of cancer 10 years later, at ages 35-44 years, 45-54 years, 55-64 years, 65-74 years, and 75-84 years respectively).

C. Sensitivity analyses

As sensitivity analysis for the estimation of the smoking-attributable cancer burden we used an alternative modeling approach based on empirical prevalence of current and former smoking, which we obtained from the DEGS1 survey 2008–2011 (17). We used the same RRs as in the main analyses (1). We then used Levin's formula to calculate PAF for each age and sex group combining the prevalence of current smoking (P_{CS}) and former smoking (P_{FS}), respectively, with the relative risk of cancer associated with current smoking (RR_{CS}) and former smoking (RR_{FS}):

$$PAF = \frac{(P_{CS} \times RR_{CS}) + (P_{FS} \times RR_{FS}) + (1 - P_{CS} - P_{FS}) - 1}{(P_{CS} \times RR_{CS}) + (P_{FS} \times RR_{FS}) + (1 - P_{CS} - P_{FS})}$$

Assuming a 10-year latency period, we estimated the number of incident cancers attributable to smoking by multiplying the PAF by the expected cancer incidence for each age and sex group for the year 2018.

Sensitivity analyses for the estimation of the alcohol-attributable cancer burden were accomplished using the same methods as for the main analyses, but we calculated two different scenarios by using the lower and the upper confidence limit, respectively, of the relative risk estimates, which gave us a potential range of estimation for the PAFs.

eFigure 1. Relative risks of site-specific cancer for increases in intake of pure alcohol per day, summary results from meta-analyses (e2-e7).

eTable 1. Estimated numbers of cancer cases for selected cancer sites and for all cancer sites combined (except non-melanoma skin cancer) among men in 2018 in Germany by age[#]

Cancer site (ICD-10)	35–54 years	55–59 years	60–64 years	65–69 years	70–74 years	75–79 years	80–84 years	All ages combined
<i>Men</i>								
Lip, pharynx and oral cavity (C00-C14)	1,798	1,786	1,798	1,502	982	877	525	9,268
Esophagus (C15)	729	766	873	864	810	779	552	5,373
Squamous cell carcinoma ^a	401	421	480	475	445	428	304	2,954
Stomach (C16)	959	934	1,133	1,267	1,268	1,756	1,596	8,913
Colon and rectum (C18-C20)	2,996	2,955	3,886	4,790	4,686	6,410	5,397	31,120
Liver (C22)	424	568	987	1,101	1,038	1,251	947	6,316
Pancreas (C25)	738	872	1,046	1,382	1,270	1,682	1,329	8,319
Larynx (C32)	421	449	573	541	409	381	229	3,003
Trachea, bronchus, and lung (C33-C34)	2,890	3,844	5,292	6,066	5,426	6,233	4,659	34,410
Kidney and renal pelvis (C64-C65)	1,535	1,275	1,417	1,508	1,392	1,703	1,246	10,076
Bladder (C67)	730	812	1,149	1,614	1,645	2,493	2,356	10,799
Acute myeloid leukemia (C92)	354	195	230	290	343	461	437	2,310
All cancer sites	26,412	24,841	32,462	39,248	36,913	44,430	33,871	238,176

[#] Based on age- and sex-specific cancer incidence rates from 2014 (source: German Center for Cancer Registry Data) and age- and sex-specific population projections (scenario 1) for Germany for the year 2018 (source: Federal Statistical Office)

^a We assumed that 55% of all esophageal cancers are squamous cell carcinomas, as recently reported (e6)

eTable 2. Estimated numbers of cancer cases for selected cancer sites and for all cancer sites combined (except non-melanoma skin cancer) among women in 2018 in Germany by age[#]

Cancer site (ICD-10)	35–54 years	55–59 years	60–64 years	65–69 years	70–74 years	75–79 years	80–84 years	All ages combined
<i>Women</i>								
Lip, pharynx and oral cavity (C00-C14)	608	561	560	548	386	430	341	3,434
Esophagus (C15)	146	162	202	242	203	227	205	1,387
Squamous cell carcinoma ^a	80	89	111	133	112	125	113	763
Stomach (C16)	611	389	544	575	684	1,035	1,159	4,997
Colon and rectum (C18-C20)	2,267	1,891	2,261	2,973	3,070	4,858	5,008	22,328
Liver (C22)	194	172	289	341	321	550	488	2,355
Pancreas (C25)	526	551	726	1,022	1,095	1,755	1,617	7,292
Larynx (C32)	75	73	109	86	71	50	33	497
Trachea, bronchus, and lung (C33-C34)	2,268	2,492	2,866	3,372	2,628	2,679	2,199	18,504
Kidney and renal pelvis (C64-C65)	624	551	628	828	825	1,203	937	5,596
Bladder (C67)	261	267	305	432	516	777	823	3,381
Acute myeloid leukemia (C92)	346	188	196	268	282	371	390	2,041
All cancer sites	39,613	22,503	25,084	28,617	23,885	33,216	29,280	202,197

[#] Based on age- and sex-specific cancer incidence rates from 2014 (source: German Center for Cancer Registry Data) and age- and sex-specific population projections (scenario 1) for Germany for the year 2018 (source: Federal Statistical Office)

^a We assumed that 55% of all esophageal cancer cases are squamous cell carcinomas, as recently reported (e6)

eTable 3. Relative risks for smokers versus never smokers for smoking-caused cancers^a, by sex and age group

Cancer site (ICD-10)	35–54 years	55–64 years	65–74 years	≥74 years
<i>Men</i>				
Trachea, bronchus, and lung (C33-C34)	14.33	19.03	28.29	22.51
Other smoking-caused cancers ^b	1.74	1.86	2.35	2.18
<i>Women</i>				
Trachea, bronchus, and lung (C33-C34)	13.3	18.95	23.65	23.08
Other smoking-caused cancers ^b	1.28	2.08	2.06	1.93

^a Taken from the U.S. Surgeon General's Report, 2014 (e5)

^b Other smoking-caused cancers include cancers of the lip, pharynx, and oral cavity (C00-C14), esophagus (C15), stomach (C16), colon and rectum (C18-C20), liver (C22), pancreas (C25), larynx (C32), cervix uteri (only among women; C53), kidney and renal pelvis (C64-C65), bladder (C67), and acute myeloid leukemia (C92)

eTable 4. Estimated numbers of cancer cases attributable to smoking and population-attributable fractions (PAF) among men in 2018 in Germany by age

Cancer site (ICD-10)	35–54 years	55–64 years	65–74 years	75–84 years	All ages combined	PAF (%)
<i>Men</i>						
Trachea, bronchus, and lung (C33-C34)	2,456	8,361	10,566	9,065	30,448	88.5
Lip, pharynx, and oral cavity (C00-C14)	430	1,212	947	311	2,900	31.3
Esophagus (C15)	174	559	618	292	1,643	30.6
Stomach (C16)	229	707	931	721	2,589	29.0
Colon and rectum (C18-C20)	716	2,353	3,489	2,554	9,112	29.3
Liver (C22)	101	544	790	479	1,915	30.3
Pancreas (C25)	176	656	982	655	2,469	29.7
Larynx (C32)	101	351	357	135	945	31.5
Kidney and renal pelvis (C64-C65)	367	916	1,074	645	3,001	29.8
Bladder (C67)	175	677	1,196	1,040	3,087	28.6
Acute myeloid leukemia (C92)	85	145	229	192	651	28.2

eTable 5. Estimated numbers of cancer cases attributable to smoking and population-attributable fractions (PAF) among women in 2018 in Germany by age

Cancer site (ICD-10)	35–54 years	55–64 years	65–74 years	75–84 years	All ages combined	PAF (%)
<i>Women</i>						
Trachea, bronchus, and lung (C33-C34)	1,845	4,880	5,216	3,469	15,410	83.3
Lip, pharynx, and oral cavity (C00-C14)	55	430	227	72	785	22.8
Esophagus (C15)	13	139	106	41	299	21.6
Stomach (C16)	55	354	295	207	912	18.2
Colon and rectum (C18-C20)	205	1,584	1,430	932	4,150	18.6
Liver (C22)	18	174	158	98	447	19.0
Pancreas (C25)	48	485	500	318	1,350	18.5
Larynx (C32)	7	69	37	8	121	24.4
Cervix uteri (C53)	162	382	150	50	743	19.0
Kidney and renal pelvis (C64-C65)	56	450	392	201	1,100	19.7
Bladder (C67)	24	219	222	151	615	18.2
Acute myeloid leukemia (C92)	31	147	130	72	380	18.6

eTable 6. Prevalence of current and former smoking among men and women aged 25 to 74 years in the DEGS1 survey (2008–2011)

Exposure	25–44 years	45–54 years	55–64 years	65–74 years	All ages combined
	%	%	%	%	%
<i>Men</i>					
Current smokers	42.8	36.8	21.4	11.7	32.1
Former smokers	22.2	37.3	50.8	50.2	35.9
<i>Women</i>					
Current smokers	34.0	32.2	22.3	10.5	27.0
Former smokers	19.3	30.6	29.8	20.4	24.2

eTable 7. Sensitivity analysis of the estimated number of incident cancer cases attributable to smoking in Germany for the year 2018, stratified by gender

	Total and relative number of preventable cancer site-specific cases for all ages combined			
	Main analysis		Sensitivity analysis: based on DEGS1 data for smoking prevalence using Levin's formula	
	N	%	N	%
Tobacco smoking				
<i>Men and women combined</i>	85,072	19.3	85,760	19.5
<i>Men</i>	58,759	24.7	59,080	24.8
<i>Women</i>	26,313	13.0	26,680	13.2

eTable 8. Estimated numbers of cancer cases attributable to alcohol and population-attributable fractions (PAF) among men in 2018 in Germany by age

Cancer site (ICD-10)	35–44 years		45–54 years		55–64 years		65–74 years		75–84 years		All ages combined	
	N	%	N	%	N	%	N	%	N	%	N	%
<i>Men</i>												
Lip, pharynx, and oral cavity (C00-C14)	63	27.1	440	28.1	1,309	36.5	840	33.8	539	38.4	3,191	34.4
Esophagus (C15), squamous cell carcinoma	10	22.8	85	23.7	283	31.4	266	28.9	243	33.2	887	30.0
Colon and rectum (C18-C20)	31	5.8	151	6.1	596	8.7	734	7.8	1,089	9.2	2,601	8.4
Liver (C22)	5	9.9	39	10.3	225	14.5	280	13.1	341	15.5	890	14.1
Larynx (C32)	5	13.4	54	13.9	197	19.3	166	17.5	126	20.6	548	18.2

eTable 9. Estimated numbers of cancer cases attributable to alcohol and population-attributable fractions (PAF) among women in 2018 in Germany by age

Cancer site (ICD-10)	35–44 years		45–54 years		55–64 years		65–74 years		75–84 years		All ages combined	
	N	%	N	%	N	%	N	%	N	%	N	%
<i>Women</i>												
Lip, pharynx, and oral cavity (C00-C14)	5	4.6	31	5.2	58	5.2	66	7.1	34	4.4	194	5.7
Esophagus (C15), squamous cell carcinoma	0	4.0	4	4.4	9	4.4	15	6.1	9	3.8	37	4.9
Colon and rectum (C18-C20)	5	1.2	28	1.5	54	1.3	108	1.8	107	1.1	302	1.4
Liver (C22)	1	1.9	4	2.1	10	2.1	19	2.9	19	1.8	53	2.3
Larynx (C32)	0	2.5	2	2.8	5	2.8	6	3.8	2	2.4	15	3.0
Breast (C50)	49	1.1	198	1.2	204	1.2	266	1.7	153	1.0	870	1.3

eTable 10. Sensitivity analyses of the estimated number of incident cancer cases attributable to alcohol consumption above recommended levels in Germany for the year 2018, stratified by gender

Alcohol consumption	Total and relative number of preventable cancer site-specific cases for all ages combined					
	Main analysis		Sensitivity analysis: lower confidence limits of relative risks		Sensitivity analysis: upper confidence limits of relative risks	
	N	%	N	%	N	%
Men and women combined	9,588	2.2	6,967	1.6	12,262	2.8
Men	8,117	3.4	5,895	2.5	10,387	4.4
Women	1,471	0.7	1,072	0.5	1,875	0.9