Original Article

Cancers Due to Infection and Selected Environmental Factors

Estimation of the Attributable Cancer Burden in Germany

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

Summary

Background: Causal relationships with the occurrence of cancer have been established for a number of infections and environmental risk factors.

Methods: Numbers and proportions (population-attributable fractions, PAF) of cancer cases attributable to these factors in Germany were calculated by sex and age groups for ages 35 to 84 years based on population projections, national cancer incidence, exposure data, and published risk estimates.

Results: For 2018, more than 17 600 cancer cases (4.0% of all incident cancers) were estimated to be attributable to infections. The largest contributions come from *Helicobacter pylori* (n = 8764) and human papillomavirus (n = 7669) infections. Infection with hepatitis B and C, human immunodeficiency virus, and human herpesvirus 8 were estimated to cause 983 cases, 144 cases, and 116 cases, respectively. More than 5400 cancer cases (1.2% of all incident cancers) were estimated to be attributable to selected environmental factors, of which the largest contributor is indoor radon (n = 3185), followed by particulate matter (n = 1049), sunbed use (n = 892), and secondhand smoke (n = 309).

Conclusion: Of all cancers expected in 2018 in Germany, at least 5% are attributable to potentially avoidable infections and environmental factors. Further research should be directed towards more comprehensive identification and quantification of environmental risks as a basis for targeted cancer prevention.

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In a broad sense, people are exposed to a wide range of carcinogenic agents from different sources in their environment. A causal relationship with the occurrence of cancer has been established between exposure to numerous infections and environmental factors (1, 2). This study provides estimates of the burden of incident cancer cases attributable to infections (*Helicobacter pylori*, human papillomavirus, hepatitis B, hepatitis C, human immunodeficiency virus, human herpesvirus 8) and major environmental factors (secondhand smoke, indoor radon, particulate matter, sunbed use) in Germany in 2018.

Methods

To provide estimates of cancer cases attributable to infectious and environmental agents, we calculated population-attributable fractions (PAF; for details see the *Box* in Mons et al., this issue). In this study, we considered six infectious and four environmental agents that fulfilled the following criteria (*Table*):

- The risk factor has been classified as carcinogenic to humans by the International Agency for Research on Cancer (IARC);
- The exposure is potentially modifiable, i.e., a decrease of risk factor exposure can be deemed effective in reducing the risk of cancer; and
- Suitable data on the distribution of risk factors could be obtained for Germany.

Statistical methods

As described in Mons et al. in this issue, we calculated PAF by sex and age groups for ages 35 to 84 years combining the prevalence of exposure and the cancer site–specific relative risk (RR). For infection with human papillomavirus, PAF estimates are based on the proportion of tumors in which viral DNA was prevalent. To estimate the number of cancer cases attributable to each risk factor, we multiplied the PAFs by the projected cancer incidence for the year 2018 (*eTables 1–3*). The methods are reported in detail in the supplement to this article (*eSupplement A and B*).

Data sources and assumptions—infectious agents

Helicobacter pylori

Helicobacter pylori infection is typically acquired in childhood; in the absence of specific treatment, it

TABLE

Infectious agents and environmental factors with corresponding cancer sites, reference exposure level, and prevalence

Exposure	Cancer site (ICD-10)	Reference exposure level	Prevalence (%)		
			of exposure in population	of DNA in tumor cells	Reference
Infections					
Helicobacter pylori (*H. pylori*)	Stomach (C16), non-cardia	No infection	40.0		(26)
	Gastric MALT lymphoma (C88.4)				
Human papillomavirus (HPV)	Oral cavity (C02–C04)	No infection		3.7	(6)
	Oropharynx (C01, C05, C09, C10)			19.9	(6)
	Anus and anal canal (C21)			87.6	(7)
	Vulva (C51)			18.3	(8)
	Vagina (C52)			71.0	(9)
	Cervix (C53)			100.0	(11)
	Penis (C60)			32.2	(10)
Hepatitis B virus (HBV)	Liver (C22), hepatocellular carcinoma	No infection	0.3		(27)
Hepatitis C virus (HCV)	Liver (C22), hepatocellular carcinoma	No infection	0.3		(27)
	Non-Hodgkin lymphoma (C82–C88)				
Human immunodeficiency virus (HIV)	Non-Hodgkin lymphoma (C82–C88)	No infection	0.1		(15)
Human herpesvirus 8 (HHV-8)	Kaposi sarcoma (C46)	No infection		100.0	(5)
Environmental factors					
Secondhand smoke (SHS)	Lung (C33–C34)	No exposure to SHS	25.9*		(12)
Particulate matter (PM_{10})	Lung (C33–C34)	Mean annual exposure to PM_{10} below the WHO guideline value	23.0		(22)
Indoor radon	Lung (C33–C34)	Natural outdoor radon concentration	100.0		(19)
Sunbed use	Skin melanoma (C43)	Never use of sunbeds	28.0		(24)

* For secondhand smoke, the population refers to all never smokers
MALT, mucosa-associated lymphoid tissue

typically persists throughout adulthood. National prevalence data on *H. pylori* infection were available from the German National Health Interview and Examination Survey 1998 (GNHIES98; *eSupplement C, eTable 4)*. For the association between *H. pylori* infection and risk of non-cardia stomach cancer and low-malignant mucosa-associated lymphoid tissue (MALT) gastric lymphoma, we used pooled risk estimates from prospective studies (3, 4) (*eFigure 1*).

Human papillomavirus (HPV)

In order to estimate the PAF for infection with HPV, the prevalence of viral DNA in tumor material is sufficient to infer that HPV caused the cancer (5). The PAF for malignancies of the oral cavity or oropharynx were estimated using the combination of positivity for HPV-DNA and for either E6*I mRNA expression or $p16^{INK4a}$ (6). For cancers of the anus (7), vulva (8), vagina (9), and penis (10), the PAF were derived from HPV-DNA prevalence in invasive cancers. For cancer of the cervix uteri all cases were assumed to be attributable to HPV (11) (*Table*).

Hepatitis B (HBV) and hepatitis C (HCV)

Assuming that combined infection by both HBV and HCV is very rare, and assuming a latency period of 10 years between ascertainment of infection status and cancer diagnosis, we used seroprevalence from the

nationally representative German Health Interview and Examination Survey for Adults for the period 2008 to 2011 (DEGS1) (12). In the process, seropositivity for HBsAG and the prevalence of HCV antibodies were used as indicators for chronic infection with HBV or HCV (*eTable 4*). We used the relative risks for hepatocellular carcinoma reported in a meta-analysis of HBV and HCV mono-infection comprising studies from low-endemic countries (13). Summary relative risks for non-Hodgkin lymphoma associated with HCV were taken from a meta-analysis of epidemiological studies (14) (*eFigure 1*).

Human immunodeficiency virus (HIV) and human herpesvirus 8 (HHV-8)

Based on the absolute number of people living with HIV in Germany in 2016, the relative prevalence in Germany in 2018 was calculated (15) (*eSupplement C*, *eTable 4*).

For uterine cervix and Kaposi sarcoma the PAF were not calculated separately, as both HPV and HHV-8 are considered necessary causal factors (5, 11). The PAF were also not estimated for anal cancer and Hodgkin lymphoma, because it is assumed that these cancers occur due to co-infection with HPV and Epstein–Barr virus. Due to the absence of information on incidence, conjunctival cancer was not considered in the analysis. To estimate the number of cases of HIV-attributable non-Hogkin lymphoma, relative risk estimates were taken from a population-based registry-linkage study (16) (*eFigure 1*).

Data sources and assumptions—environmental factors

Secondhand smoke (SHS)

Assuming a latency period of 10 years between SHS exposure and cancer incidence, we used prevalence of self-reported exposure to SHS at home, at the workplace, and in leisure time from DEGS1 2008–2011 (12) (*eTable 5*). A meta-analysis of the relative risk of lung cancer due to SHS among never smokers provided a lung cancer risk associated with workplace exposure (17), which we assumed to apply to home and leisure time exposure as well (*eFigure 2*). The estimated numbers of lung cancers occurring among never smokers were taken from the study by Mons et al. in this issue.

Indoor radon

For exposure to indoor radon, the mean annual indoor radon concentration for Germany was used (18, 19). Concentrations below the estimated outdoor air concentration were not considered for the calculation of attributable cases (*eSupplement C*). The results from a collaborative analysis of individual data from 13 European studies (20) showed a linear dose–response association between radon exposure and lung cancer risk without a threshold below which an exposure would carry no risk (*eFigure 2*). As most of the radon-induced cancer cases arise from a synergistic effect of radon and smoking (21), we also estimated the attributable cancer cases caused by indoor radon exposure combined with smoking (*eSupplement A*).

Particulate matter (PM_{10})

The proportions of the population at different PM exposure levels for the years 2007–2011 were obtained from the Federal Environmental Agency (22). Based on these, we calculated the mean prevalence of the population exposed to PM_{10} concentrations (particles with aerodynamic diameter $\leq$ 10 µm) exceeding the WHO mean annual guideline value (>20 µg/m^3) and the corresponding population-weighted mean PM_{10}-concentrations. We defined the excess exposure level by the difference between the mean exposure in those exceeding the guideline value and those who are within the limit (*eSupplement A, eTable 6*). Risk estimates were taken from a meta-analysis of nine studies examining the risk for lung cancer associated with particulate matter (23) (*eFigure 2*).

Sunbed use

Sunbeds are a source of artificial ultraviolet (UV) radiation. Assuming a latency period of 10 years between sunbed use and cancer incidence, we used lifetime prevalence from a representative population-based telephone survey from 2007 (24) (*eTables 7, 8*). We used risk estimates from a meta-analysis of sunbed use and risk of developing malignant melanoma (25) (*eFigure 2*).

Sensitivity analyses

The methods used for sensitivity analyses are described in *eSupplement D*.

Results

Infections

Helicobacter pylori

According to GNHIES98, the overall seroprevalence of *H. pylori* antibodies in the German population in 1998 was 40% (26). We estimated that a total of 8299 (86%) non-cardia stomach cancers (men 4833, women 3466) and 465 (67%) gastric MALT lymphomas (men 208, women 257) are attributable to *H. pylori* infection (*Figure 1, eTables 9–11*).

Human papillomavirus (HPV)

A total of 7669 cancers of the oral cavity (n=134), oropharynx (n=983), anus (n=1592), vulva (n=498), vagina (n=292), cervix (n=3913), and penis (n=257) were estimated to be attributable to HPV (men 1691, women 5978) (*Figure 1, eTables 9–11*).

Hepatitis B (HBV) and hepatitis C (HCV)

The overall prevalence of both HBV and HCV infection in Germany in the period 2008 to 2011 was about 0.3% (27). A total of 903 cases (16%) of hepatocellular carcinoma were estimated to be attributable to HBV and HCV infection (men 732, women 171), and a total of 80 non-Hodgkin lymphomas (<1%) to HCV infection (men 37, women 43) (*Figure 1, eTables 9–11*).

Human immunodeficiency virus (HIV) and human herpesvirus 8 (HHV-8)

We estimated that 0.1% of the German population aged 35 to 84 years is infected with HIV in 2018. A total of 144 non-Hodgkin lymphomas (<1%) and 116 cases (100%) of Kaposi sarcoma were estimated to be attributable to HIV and HHV-8 infection (men 224, women 36) (*Figure 1, eTables 9–11)*.

Sensitivity analyses

Sensitivity analyses using the 95% confidence limits of risk estimates and of HPV prevalences respectively indicated a potential range of 16 000 to 18 800 cancer cases attributable to infections (*eTables 12–13*).

Environmental factors

Secondhand smoke

In the period 2008 to 2011, 26% of never smokers aged 25 to 74 years living in Germany were exposed to secondhand smoke. Overall, 309 lung cancer cases were estimated to be attributable to SHS exposure, 212 among men and 97 among women. This corresponds to a PAF of 5% among never-smoking men aged 35 to 84, and a PAF of 3% among never-smoking women (*Figure 2, eTable 14*).

Indoor radon

After subtraction of the mean radon outdoor air concentration, the mean annual excess indoor radon concentration was 40 Bq/m³ for Germany. A total of 3185 (6%) lung cancer cases were estimated to be attributable to residential radon (men 2071, women 1114), of which 425 cases (1%) were estimated to be caused by radon alone and 2760 cases (5%) by the combination of smoking and radon (*Figure 2, eTable 15*).

Particulate matter (PM_{10})

According to the data of the Federal Environmental Agency, 23% of the German population were exposed to PM_{10} concentrations exceeding the WHO mean annual guideline value for PM_{10} in the period 2007 to 2011. Based on this, a total of 1049 (2%) lung cancer cases were estimated to be attributable to PM_{10} exposure at concentrations above the WHO guideline value (men 682, women 367) (*Figure 2*).

Sunbed use

According to a national representative population-based survey on sunbed use in Germany in 2007, 28% of the German population have used sunbeds at some time in their life (24). We estimated that a total of 892 (5%) malignant melanomas are attributable to ever use of sunbeds (men 360, women 532) (*Figure 2, eTable 16*). Additional analyses indicated that the vast majority of these cases could be due to highly frequent sunbed use (*eTable 17*).

Sensitivity analyses

In sensitivity analyses using the 95% confidence limits of risk estimates, estimated numbers of cancer cases attributable to the selected environmental factors ranged from 1500 to 9500 (*eTable 18*).

Summary of results

To estimate the total proportion of cancer cases in Germany in 2018 that could be attributed to all modifiable cancer risk factors considered in this article and in the articles by Mons et al. and Behrens et al. in this issue, we combined the single PAF to estimate a joint PAF assuming independence of risk factors (28). We estimated that of all cancer cases to be expected at ages 35 to 84 years in Germany in 2018 (about 440 000 cases), 37.4% of incident cancer cases are attributable to the considered modifiable risk factors and thus are potentially avoidable (*Figure 3*). The lifestyle-related factors, in particular smoking, but also dietary factors, overweight, and physical inactivity, contribute most to this cancer burden. More than 17 600 cases (4.0%) are attributable to infections and more than 5400 cases (1.2%) are attributable to selected environmental factors. Reducing the prevalence of these risk factors in the German population has the potential to substantially reduce the cancer burden.

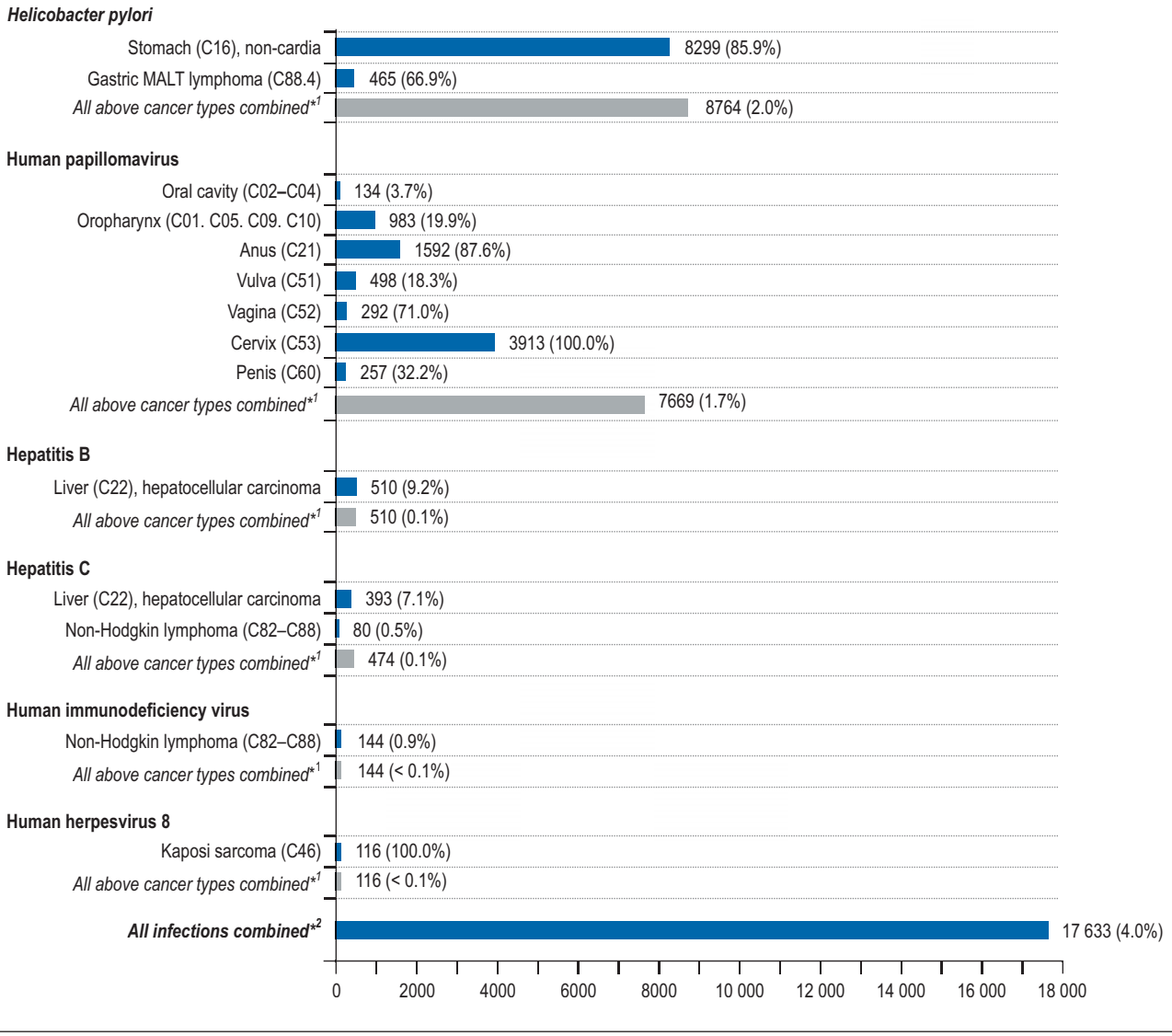
Discussion

Cancer burden attributable to infections

Our analyses indicate that about 4.9% (ca. 9900) of all cancer cases in women and about 3.2% (ca. 7700) of cases in men are due to infections. The cancer burden attributable to infections was estimated to be greater in women than in men, largely because all cervical cancer cases (ca. 3700 cases) are counted as due to HPV infection, as it is considered a necessary causal factor. Among infections, the largest contributors to the cancer burden in the German population were estimated to be *H. pylori* and HPV infection, with about 8700 and 7600 attributable cancer cases, respectively. In total, they account for about 90% of all cancer cases estimated to be attributable to infectious agents. Overall, our cancer burden estimates for infections were slightly greater than those from previous studies in other countries with comparable income levels, which found proportions of cancer cases attributable to infections in the range of 3.3% to 3.6%. The differences can be explained by a higher prevalence of *H. pylori* infection in Germany and the use of more recent risk estimates for the association between *H. pylori* infection and gastric MALT lymphoma.

Effective strategies to reduce the cancer burden attributable to infectious agents include infection control and vaccination promotion. While prevalence of *H. pylori* infection seems to decline substantially in younger birth cohorts even without specific intervention, enhanced promotion of and adherence to HPV vaccination could reduce the burden of HPV-related cancers. For example, Australia has achieved a considerable fall in the prevalence of the most common high-risk HPV types among 18- to 35-year old women in recent years through the implementation of

FIGURE 1



Estimated number and proportion of site-specific incident cancer cases attributable to infections among men and women aged 35 to 84 years in Germany for the year 2018.

*1 The population-attributable fraction (PAF) for the category "All above cancer types combined" was computed with respect to total cancer incidence (ICD-10 C00–C99 without C44).

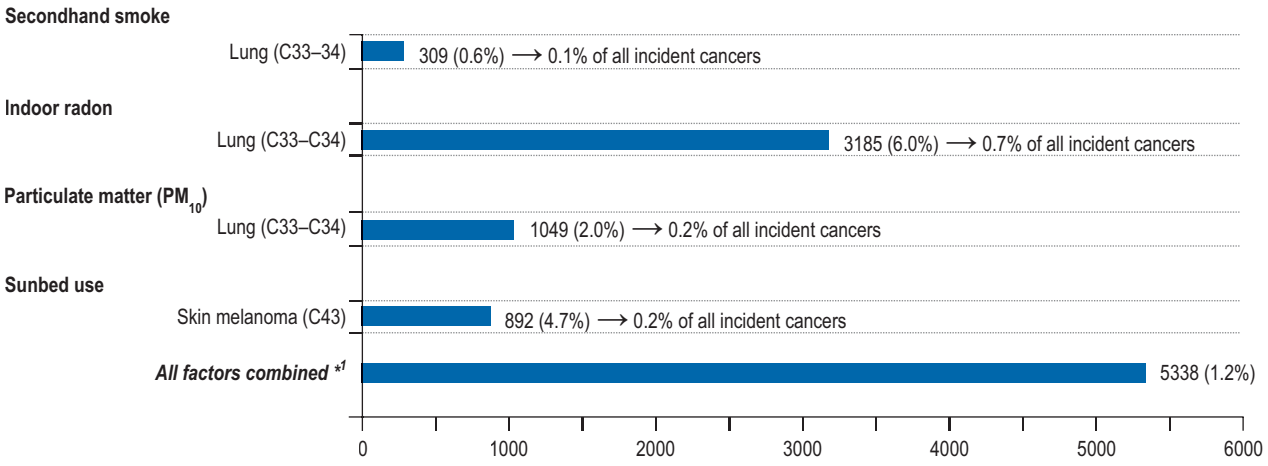
*2 A joint PAF of all infections was calculated assuming independence of infections (28)

a comprehensive government-funded national school-based vaccination program (29).

Cancer burden attributable to selected environmental factors

About 1.4% (ca. 3300) of all cancer cases in men and 1.0% (ca. 2000) of cases in women were estimated to be attributable to selected environmental risk factors. Of all these factors, indoor radon accounted for the highest proportion and number of cancer cases (ca. 3100). Overall, the estimated PAF are roughly in line with previous studies (30–32). With respect to air pollution, a recent study (32) estimated the number of lung cancer cases attributable to fine particles ($PM_{2.5}$) in the UK to be considerably greater (1.0% of all incident cancer cases) than those in this study, which likely reflects the differences in particle size and reference exposure levels. Generally, it is important to keep in mind that the assumptions that were made to estimate the number of PM_{10}-attributable cancers are quite conservative, as a guideline-based reference level was chosen, even though an increased risk for lung cancer has also been reported for exposure levels below current guidelines (1, 31). All of the considered environmental factors are potentially avoidable and there is evidence that exposure could be reduced by policy measures,

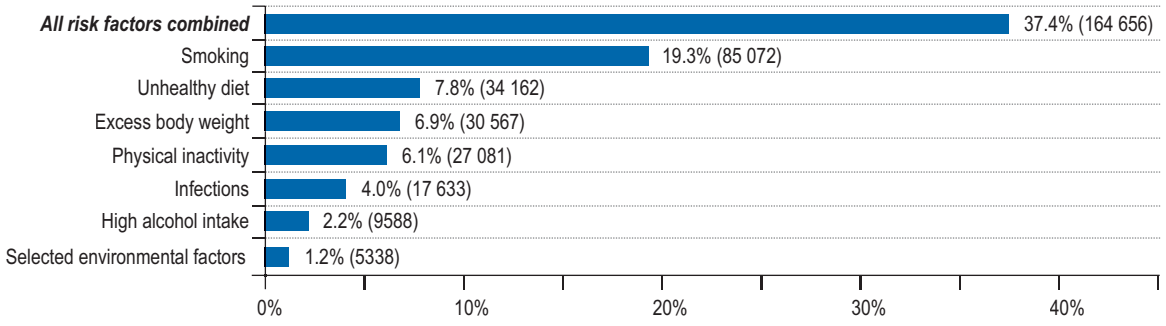
FIGURE 2



Estimated number and proportion of site-specific incident cancer cases attributable to selected environmental factors among men and women aged 35 to 84 years in Germany for the year 2018.

*1A joint PAF of all selected environmental factors was calculated assuming independence of the selected risk factors (28)

FIGURE 3



Estimated number and proportion of all incident cancer cases (ICD-10 C00-C99 without C44) attributable to the reported lifestyle-related factors, environmental factors and infections among men and women aged 35 to 84 years in Germany for the year 2018

such as comprehensive smoke-free legislation (34), building regulations for radon prevention and mitigation (35), road traffic-related emission control interventions to improve air quality (36), and restriction of access to sunbeds (37).

Strengths and limitations

This is the first study to provide estimates of the cancer burden attributable to infections and selected environmental factors in Germany in 2018. Our estimates are based on the latest population projections and cancer registry information and—for most of the considered risk factors—nationally representative survey data on seroprevalence of infections and prevalence of exposure to environmental factors. In agreement with previous studies from other countries, we assumed latency periods for most risk factors, taking into account that current cancer cases were caused by past exposure (38). We were not able to quantify the combined impact of different risk factors due to lack of appropriate data. Generally, we may have underestimated the cancer burden attributable to environmental factors because reliable population-based prevalence estimates were not available for some established risk factors, including exposure to natural solar radiation, which is considered the most important environmental cause of skin cancer (25). In addition, we could not consider numerous potentially carcinogenic environmental factors because they have not yet been sufficiently examined in epidemiological studies.

Conclusion

Our findings suggest that of all cancers expected in 2018 in Germany, at least 5% are attributable to infections and selected environmental factors. Although the estimates rely on several assumptions and not all risk

Key messages

- We used population-attributable fractions (PAF) to estimate the proportion of cancer incidence attributable to exposure to infectious agents and selected environmental factors in 2018.
- Of all incident cancer cases expected to occur at ages 35 to 84 years in Germany in 2018 (ca. 440 000 cases), an estimated 4% (ca. 17 600 cases) are caused by infections and at least 1.2% (5400 cases) are caused by excess levels of selected environmental factors.
- About 90% of cancer cases estimated to be attributable to infections are caused by infection with *Helicobacter pylori* and human papillomavirus.
- Both national vaccination programs and individual vaccination advice delivered by health professionals could be effective in reducing the incidence of infection-related cancer cases.
- Given our exclusive focus on environmental factors for which both reliable exposure data and reliable risk estimates for specific cancers are available and the lack of such data for many other environmental factors, the total numbers and proportions of cancers attributable to environmental factors are likely to be much higher.

factors could be considered, the results indicate that many thousand cancer cases could be avoided if exposure to these risk factors were reduced or eliminated through effective prevention measures. Further research should be directed towards more comprehensive identification and quantification of environmental risks as a basis for targeted cancer prevention.

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Conflict of interest statement
The authors declare that no conflict of interest exists.

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References

1. Espina C, Straif K, Friis S, et al.: European Code against Cancer 4th edition: environment, occupation and cancer. Cancer Epidemiol 2015; 39 (Suppl 1): 84–92.
2. Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S: Global burden of cancers attributable to infections in 2012: a synthetic analysis. Lancet Glob Health 2016; 4: e609–16.
3. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C: Global burden of gastric cancer attributable to Helicobacter pylori. Int J Cancer 2015; 136: 487–90.
4. Parsonnet J, Hansen S, Rodriguez L, et al.: Helicobacter pylori infection and gastric lymphoma. N Engl J Med 1994; 330: 1267–71.
5. De Martel C, Ferlay J, Franceschi S, et al.: Global burden of cancers attributable to infections in 2008: a review and synthetic analysis. Lancet Oncol 2012; 13: 607–15.
6. Castellsagué X, Alemany L, Quer M, et al.: HPV involvement in head and neck cancers: comprehensive assessment of biomarkers in 3680 patients. J Natl Cancer Inst. 2016; 108: djv403.
7. Alemany L, Saunier M, Alvarado-Cabrero I, et al.: Human papillomavirus DNA prevalence and type distribution in anal carcinomas worldwide. Int J Cancer 2015; 136: 98–107.
8. de Sanjosé S, Alemany L, Ordi J, et al.: Worldwide human papillomavirus genotype attribution in over 2000 cases of intraepithelial and invasive lesions of the vulva. Eur J Cancer 2013; 49: 3450–61.
9. Alemany L, Saunier M, Tinoco L, et al.: Large contribution of human papillomavirus in vaginal neoplastic lesions: a worldwide study in 597 samples. Eur J Cancer 2014; 50: 2846–54.
10. Alemany L, Cubilla A, Halec G, et al.: Role of human papillomavirus in penile carcinomas worldwide. Eur Urol 2016; 69: 953–61.
11. Walboomers JM, Jacobs MV, Manos MM, et al.: Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. Pathol 1999; 189: 12–9.
12. Scheidt-Nave C, Kamtsiuris P, Gößwald A, et al.: German health interview and examination survey for adults (DEGS)-design, objectives and implementation of the first data collection wave. BMC Public Health 2012; 12: 730.
13. Cho LY, Yang JJ, Ko KP, et al.: Coinfection of hepatitis B and C viruses and risk of hepatocellular carcinoma: systematic review and meta-analysis. Int J Cancer 2011; 128: 176–84.
14. Dal Maso L, Franceschi S: Hepatitis C virus and risk of lymphoma and other lymphoid neoplasms: a meta-analysis of epidemiologic studies. Cancer Epidemiol Biomarkers Prev 2006; 15: 2078–85.
15. an der Heiden M, Marcus U, Kollan C, et al.: Schätzung der Zahl der HIV-Neuinfektionen und der Gesamtzahl von Menschen mit HIV in Deutschland, Stand Ende 2016. Epid Bull 2017; 47: 531–45.
16. Hernandez-Ramirez RU, Shiels MS, Dubrow R, Engels EA: Cancer risk in HIV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. Lancet HIV 2017; 4: e495–e504.
17. US Department of Health Human Services: The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. US Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta 2006. www.surgeongeneral.gov/library/reports/secondhandsmoke/fullreport.pdf (last accessed on 22 July 2018).
18. Menzler S, Piller G, Gruson M, Rosario AS, Wichmann H-E, Kreienbrock L: Population attributable fraction for lung cancer due to residential radon in Switzerland and Germany. Health Phys 2008; 95: 179–89.
19. Schmid K, Kuwert T, Drexler H: Radon in indoor spaces: an underestimated risk factor for lung cancer in environmental medicine. Dtsch Arztebl Int 2010; 107: 181.
20. Darby S, Hill D, Auvinen A, et al.: Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ 2005; 330: 223.
21. McColl N, Auvinen A, Kesminiene A, et al.: European Code against Cancer 4th edition: ionising and non-ionising radiation and cancer. Cancer Epidemiol 2015; 39: 93–100.
22. Kallweit D, Wintermeyer D: Berechnung der gesundheitlichen Belastung der Bevölkerung in Deutschland durch Feinstaub (PM10). UMID: Umwelt und Mensch–Informationsdienst 2013; 4: 18–24.
23. Hamra GB, Guha N, Cohen A, et al.: Outdoor particulate matter exposure and lung cancer: a systematic review and meta-analysis. Environ Health Perspect 2014; 122: 906.
24. Borner FU, Schutz H, Wiedemann P: A population-based survey on tanning bed use in Germany. BMC Dermatol 2009; 9: 6.
25. Boniol M, Autier P, Boyle P, Gandini S: Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ 2012; 345: e4757.
26. Bornemann R, Gaber E: Themenheft 55 „Gastritis, Magen-und Zwölffingerdarmgeschwüre". Berlin: Robert Koch-Institut, 2013 www.rki.de/DE/Content/Gesundheitsmonitoring/Gesundheitsberichterstattung/GBEDownloadsT/gastritis.pdf?__blob=publicationFile (last accessed on 30 July 2018).
27. Poethko-Muller C, Zimmermann R, Hamouda O, et al.: [Epidemiology of hepatitis A, B, and C among adults in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2013; 56: 707–15.
28. Ezzati M, Vander Hoorn S, Rodgers A, et al.: Estimates of global and regional potentil health gains from reducing muliple major risk factors. Lancet 2003; 362: 271–80.
29. Machalek DA, Garland SM, Brotherton JML, et al.: Very low prevalence of vaccine human papillomavirus (HPV) types among 18 to 35 year old Australian women, nine years following implementation of vaccination. J Infect Dis 2018; 217: 1590–1600.
30. Wilson LF, Antonsson A, Green AC, et al.: How many cancer cases and deaths are potentially preventable? Estimates for Australia in 2013. Int J Cancer 2018; 142: 691–701.

31. Islami F, Goding Sauer A, Miller KD, et al.: Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin 2018; 68: 31–54.
32. Brown KF, Rumgay H, Dunlop C, et al.: The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. 2018; 118: 1130–41.
33. Raaschou-Nielsen O, Andersen ZJ, Beelen R, et al.: Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE). Lancet Oncol 2013; 14: 813–22.
34. Frazer K, Callinan JE, McHugh J, et al.: Legislative smoking bans for reducing harms from secondhand smoke exposure, smoking prevalence and tobacco consumption. Cochrane Database Syst Rev 2016; 2: CD005992.
35. Coskeran T, Denman A, Phillips P, Tornberg R: A critical evaluation of the cost-effectiveness of radon protection methods in new homes in a radon affected area of England. Environ Int 2009; 35: 943–51.
36. Wang L, Zhong B, Vardoulakis S, et al.: Air quality strategies on public health and health equity in Europe-a systematic review. Int J Environ Res Public Health 2016;13: pii: E1196.
37. Watson M, Holman DM, Fox KA, et al.: Preventing skin cancer through reduction of indoor tanning: current evidence. Am J Prev Med 2013; 44: 682–9.
38. Parkin D: 1. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. Br J Cancer 2011; 105: 2

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► **Supplementary material**
For eReferences please refer to:
www.aerzteblatt-international.de/ref3518

eSupplements, eTables, eFigures:
www.aerzteblatt-international.de/18m0586

Supplementary material to:

Cancers Due to Infection and Selected Environmental Factors

Estimation of the Attributable Cancer Burden in Germany

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eReferences

e1. Levin ML: The occurrence of lung cancer in man. Acta Unio Int Contra Cancrum 1953; 9: 531–41.

e2. US Department of Health Human Services: The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. US Department of Health and Human Services, Centers for Disease Control and Prevention, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, Atlanta 2006.

e3. Darby S, Hill D, Auvinen A, et al.: Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ 2005; 330: 223.

e4. Hamra GB, Guha N, Cohen A, et al.: Outdoor particulate matter exposure and lung cancer: a systematic review and meta-analysis. Environ Health Perspect 2014; 122: 906.

e5. Boniol M, Autier P, Boyle P, Gandini S: Cutaneous melanoma attributable to sunbed use: systematic review and meta-analysis. BMJ 2012; 345: e4757.

e6. Cho LY, Yang JJ, Ko KP, et al.: Coinfection of hepatitis B and C viruses and risk of hepatocellular carcinoma: systematic review and meta-analysis. Int J Cancer 2011; 128: 176–84.

e7. Dal Maso L, Franceschi S: Hepatitis C virus and risk of lymphoma and other lymphoid neoplasms: a meta-analysis of epidemiologic studies. Cancer Epidemiol Biomarkers Prev 2006; 15: 2078–85.

e8. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C: Global burden of gastric cancer attributable to Helicobacter pylori. Int J Cancer 2015; 136: 487–90.

e9. Parsonnet J, Hansen S, Rodriguez L, et al.: Helicobacter pylori-infection and gastric lymphoma. N Engl J Med 1994; 330: 1267–71.

e10. Hernandez-Ramirez RU, Shiels MS, Dubrow R, Engels EA: Cancer risk in HIV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. Lancet HIV 2017; 4: 495–504.

e11. Schmid K, Kuwert T, Drexler H: Radon in indoor spaces: an underestimated risk factor for lung cancer in environmental medicine. Dtsch Arztebl Int 2010; 107: 181.

e12. Ezzati M, Vander Hoorn S, Rodgers A, et al.: Estimates of global and regional potentil health gains from reducing muliple major risk factors. Lancet 2003; 362: 271–80.

e13. Statistisches Bundesamt: Bevölkerung Deutschlands bis 2060 – Ergebnisse der 13. koordinierten Bevölkerungsvorausberechnung. Wiesbaden, Germany. www.destatis.de/DE/Publikationen/Thematisch/Bevoelkerung/VorausberechnungBevoelkerung/BevoelkerungDeutschland2060_5124202159004.pdf;jsessionid=D06F3A9634A843F70E6D0D907E659818.InternetLive1?__blob=publicationFile: Statistisches Bundesamt 2015 (last accessed on14 December 2017).

e14. Robert Koch Institute: German Centre for Cancer Registry Data. Database Query 2017. www.krebsdaten.de/Krebs/DE/Datenbankabfrage/datenbankabfrage_stufe1_node.html (last accessed 12 December 2017).

e15. Robert Koch Institute: Bericht zum Krebsgeschehen. Berlin: Robert Koch Institute 2016; www.krebsdaten.de/Krebs/DE/Content/Publikationen/Krebsgeschehen/Krebsgeschehen_download.pdf?__blob=publicationFile (last accessed 14 February 2018).

e16. Robert Koch Institute: Krebs in Deutschland für 2013/2014. Berlin: Robert Koch Institute 2017; www.krebsdaten.de/Krebs/DE/Content/Publikationen/Krebs_in_Deutschland/kid_7/krebs_in_deutschland_7.pdf?__blob=publicationFile (last accessed on 14 February 2018).

e17. Wu X-C, Andrews P, Chen VW, Groves FD: Incidence of extranodal non-Hodgkin lymphomas among whites, blacks, and Asians/Pacific Islanders in the United States: anatomic site and histology differences. Cancer Epidemiol 2009; 33: 337–46.

e18. Feller A: Klassifikation der Non-Hodgkin-Lymphome. Kompendium Internistische Onkologie. Berlin Heidelberg: Springer 2006; 2829–44.

e19. Scheidt-Nave C, Kamtsiuris P, Gößwald A, et al.: German health interview and examination survey for adults (DEGS)-design, objectives and implementation of the first data collection wave. BMC public health 2012; 12: 730.

e20. Poethko-Muller C, Zimmermann R, Hamouda O, et al.: [Epidemiology of hepatitis A, B, and C among adults in Germany: results of the German Health Interview and Examination Survey for Adults (DEGS1)]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2013; 56: 707–15.

e21. Bornemann R, Gaber E: Themenheft 55“ Gastritis, Magen-und Zwölffingerdarmgeschwüre“. 2013.

e22. Statistisches Bundesamt: Bevölkerung und Erwerbstätigkeit – Rückgerechnete und fortgeschriebene Bevölkerung auf Grundlage des Zensus 2011. Wiesbaden, Germany. www.destatis.de/DE/Publikationen/Thematisch/Bevoelkerung/Bevoelkerungsstand/RueckgerechneteBevoelkerung5124105119004.pdf?__blob=publicationFile: Statistisches Bundesamt 2016 (last accessed 22 February 2018).

e23. an der Heiden M, Marcus U, Kollan C, et al.: Schätzung der Zahl der HIV-Neuinfektionen und der Gesamtzahl von Menschen mit HIV in Deutschland, Stand Ende 2016. Epid Bull 2017; 47: 531–45.

e24. McColl N, Auvinen A, Kesminiene A, et al.: European Code against Cancer 4th Edition: ionising and non-ionising radiation and cancer. Cancer Epidemiol 2015; 39: 93–100.

e25. Kummel M, Dushe C, Muller S, Gehrcke K: Outdoor (222)Rn-concentrations in Germany – part 1 – natural background. J Environ Radioact 2014; 132: 123–30.

e26. Borner FU, Schutz H, Wiedemann P: A population-based survey on tanning bed use in Germany. BMC Dermatol 2009; 9: 6.

e27. Castellsagué X, Alemany L, Quer M, et al.: HPV involvement in head and neck cancers: comprehensive assessment of biomarkers in 3680 patients. J Natl Cancer Inst 2016; 108.

e28. Ndiaye C, Mena M, Alemany L, et al.: HPV DNA, E6/E7 mRNA, and p16INK4a detection in head and neck cancers: a systematic review and meta-analysis. Lancet Oncol 2014; 15: 1319–31.

e29. Umweltbundesamt: Gesundheitsrisiken der Bevölkerung durch Feinstaub. Berlin: Umweltbundesamt 2017; www.umweltbundesamt.de/daten/umwelt-gesundheit/gesundheitsrisiken-der-bevoelkerung-durch-feinstaub (last accessed on 14 December 2017).

eSupplement A

Statistical methods

The estimates are based on the concept of population-attributable fraction (PAF), which indicates the proportion of incident cancer cases that would be prevented if exposure to a risk factor were reduced to an alternative exposure level.

The selection of risk factors and corresponding cancer sites followed the IARC evaluations of carcinogenicity, considering only cancer types determined as causally related with environmental factors or infections.

For all risk factors except human papillomavirus (HPV) and human herpesvirus 8 (HHV-8), we calculated the PAF, combining the prevalence of exposure and the relative cancer risk associated with exposure using Levin's formula (e1)

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

where p_x is the proportion of the population at exposure level x and ERR_x is the excess relative risk associated with exposure level x, calculated as $(RR - 1)$.

With respect to human papillomavirus, estimations of the PAF were based on prevalence of the infectious agent in tumor tissue among cases, assuming that the presence of viral DNA is sufficient for causality. For the detection of cancer of the oral cavity and oropharynx attributed to HPV, additionally overexpression of the p16 protein or expression of E6 mRNA was selected to allow for the possibility that HPV was present but had not yet led to cancer.

The reference category against which the excess risk was evaluated differed between risk factors. It referred to the absence of exposure in the case of infections and sunbed use, the presence of natural background exposure for indoor radon, and the mean annual exposure

concentration of the proportion of the population below a specific threshold for particulate matter.

Risk estimates for the association of relevant risk factors with site-specific cancer incidence were derived from published systematic reviews and meta-analyses, where available (eFigures 1, 2) (e2–e10).

For radon, the relative risk was obtained from a collaborative analysis of individual data from 13 European studies (e3), involving 7148 lung cancer cases. The dose–response analysis showed a linear increase in relative risk (RR) of 16% per 100 Bq per cubic meter of air (Bq/m³; RR=1.16, 95% CI 1.05 to 1.31). For our calculations we computed the RR for 40 Bq/m³, because the nationwide mean indoor concentration of radon was estimated at 49 Bq/m³ (e11) and the outdoor air concentration at 9 Bq/m³. The estimations of attributable cases caused by indoor radon exposure were made for radon alone and combined with smoking. We therefore used the estimated numbers of lung cancers occurring among never smokers and smokers (current and former smokers combined). These were taken from the study by Mons et al. in this issue.

For particulate matter, we assumed a log-linear relationship between exposure and risk. We computed the log RR of lung cancer associated with the mean level of excess by multiplying the mean level of excess by the log RR of lung cancer for a one-unit increase in PM_{10}. Using the exponential transformation RR=exp(log RR), we calculated the PAF for the mean level of excess.

The relative risk used for the calculation of the fractions of malignant melanomas attributable to sunbed use was taken from a meta-analysis of 27 studies comparing people who had used sunbeds at least once in their lifetime with people who had never used sunbeds. However, it is important to keep in mind that there is evidence for a dose–response relationship of sunbed use and cancer risk. Dose–response analysis showed an increase of 1.8% (RR=1.018, 95% CI 0.998

to 1.038) in risk of melanoma per additional sunbed use per year. High use of sunbeds was associated with an 42% increased cancer risk (RR=1.42, 95% CI 1.15-1.74) (e5). Using this risk estimate, we additionally estimated the cases of malignant melanoma attributable to frequent use of sunbeds (>10 times/year).

To estimate the number of incident cancers attributable to the excess in each risk factor, we multiplied the PAF by the expected cancer incidence for 2018 (Supplementary Material B). Since prevalence estimates were selected for different years, we assumed latency periods for each risk factor, considering that current cancer burden was caused by past exposure. Where possible, we calculated the PAF separately for each sex and age group (eTables 9 to 11, 14 to 17).

To estimate the total proportion of cancer cases that could be attributed to all considered risk factors, we combined the single PAFs (PAF_i) to estimate a joint PAF assuming independence of risk factors. The joint PAF of the n risk factors was calculated using the following equation proposed by Ezzati et al. (e12):

$$Joint\ PAF\ = 1 - \prod_{i=1}^{n}(1 - PAF_i)$$

eSupplement B

Cancer incidence projections

The estimated number of site-specific cancers among men and women in Germany in 2018 by age were based on the population projections for the year 2018 and the most recent cancer incidence rates, which were those for the year 2014. For each sex and age group, we estimated the number of site-specific cancers by multiplying the most recent sex- and age-specific cancer incidence rates available from the German cancer registries by the sex- and age-specific population projections for Germany for the year 2018 (e13, e14). The estimate of cancer incidence was a conservative one using population projections based on the assumption that the increase in population due to immigration is low (scenario 1).

We used the information that the proportion of gastric non-cardia cancer cases among all gastric cancers is 63% for men and 81% for women (e15) and that 64% of all liver cancer are hepatocellular carcinoma (e16). With respect to low-grade B-cell mucosa-associated lymphoid tissue (MALT) gastric lymphoma, we assumed that the proportion among all non-Hodgkin´s lymphoma is 3.7% for men and 5.4% for women. These calculations were based on the assumptions that gastric MALT lymphoma represents 12.2% of the extranodal non-Hodgkin lymphomas in men and 17.9% in women (e17) and that 30% of all non-Hodgkin´s lymphomas are extranodal (e18) (eTables 1 to 3).

eSupplement C

Infections, environmental factors and their prevalence estimates

To estimate the prevalence of exposure to the selected infections and environmental factors in Germany, we used data from nationwide representative population-based surveys and federal agencies.

We estimated the prevalence of exposure to second-hand smoke among never-smoking men and women using data on 1,028 men and 1,714 women aged 25-74 years from the nationwide representative DEGS1 survey conducted in Germany in 2008-2011 (e19) (eTable 5).

The seroprevalences of hepatitis B and C are based on data on 7,047 men and women from the same survey (e20). For our calculations, we assumed the seroprevalence in the age groups 20 to 29 and 70 to 79 years to be equal to that in age groups 25 to 29 and 70 to 74 years, respectively (eTable 4).

Data on prevalence of *Helicobacter pylori* were obtained from the German National Health Interview and Examination Survey 1998 (GNHIES98) (e21). Since the seroprevalence was reported separately for the former East and West Germany, we combined the two estimates by weighting on basis of the proportion of persons living in East and West Germany in 1998. For this, we used the recalculated population sizes of the federal states based on the microcensus 2011 (e22). For our calculations, we assumed the seroprevalence in age groups 18 to 29 and 50 to 59 years to be equal to that in age groups 20 to 29 and 50 to 54 years, respectively (Supplementary Table S4).

For human immunodeficiency virus (HIV), the estimation of prevalence was based on the total age- and sex-specific number of people living with HIV in Germany in 2016 obtained from the Robert Koch Institute (e23). We calculated the sex-specific prevalence for each age group (35 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, and 80 to 84 years)

using the population projections for Germany for the year 2016 and applied these to the population projections for Germany for the year 2018 (e13) (scenario 1; eTable 4).

Depending on a number of factors, indoor radon levels can vary considerably even within a small geographical area (e24). Concentrations are typically low (approximately 9 Bq/m³) in outdoor air in Germany (e25), but can reach very high levels in buildings. The national average indoor radon concentration was estimated at 49 Bq/m³ (e11), which is under the recommended reference levels of 100 Bq/m³ of the World Health Organization (WHO). For the calculations, concentrations below the estimated outdoor air concentration were not taken into account.

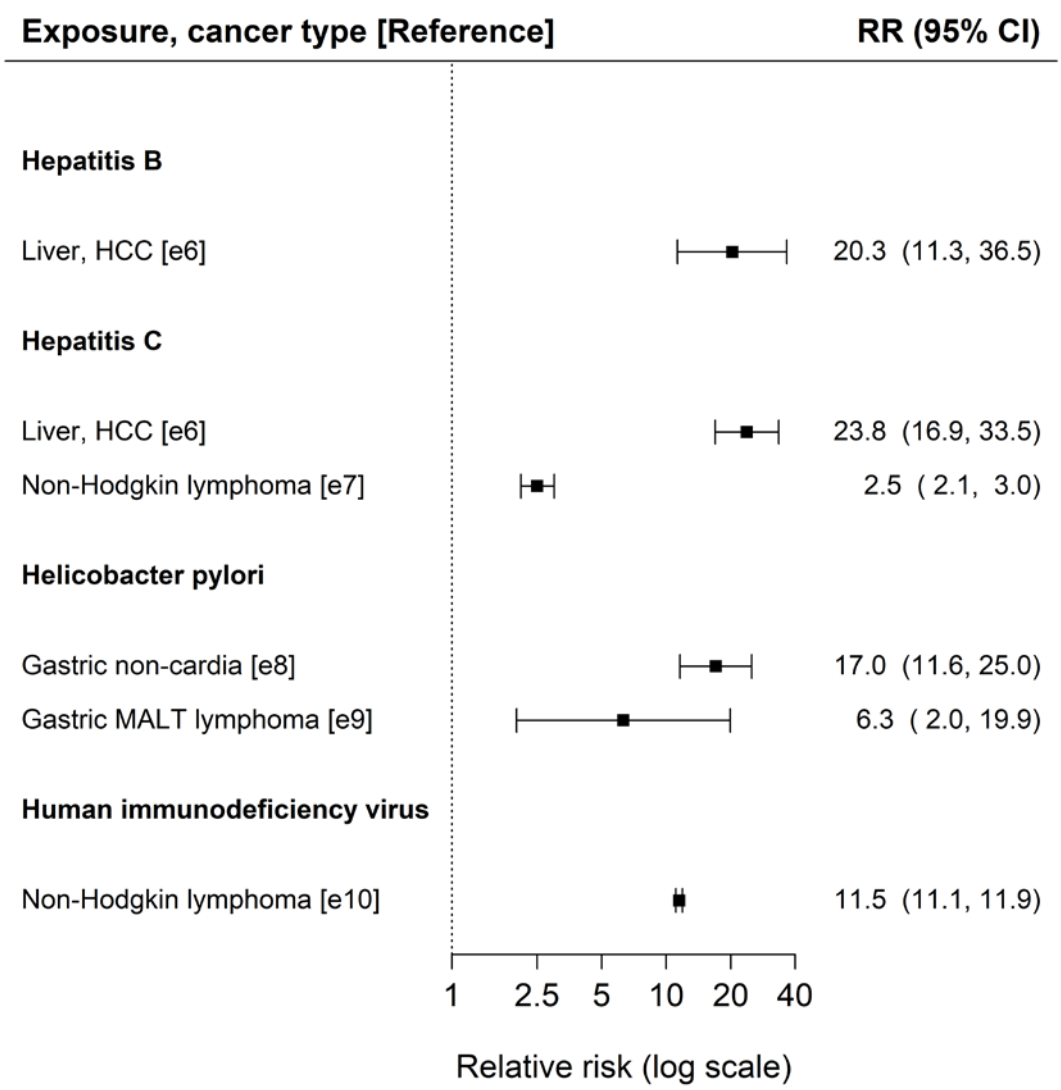
Currently, particulate matter pollution in Germany cannot be determined at an individual level. In order to estimate the burden of lung cancer attributable to particulate matter, we used annual population-weighted average PM_{10} concentrations to approximately indicate the exposure of the population. As exposure levels can vary considerably over time, we calculated the mean concentration for the years 2007 to 2011, assuming a 10-year latency period between exposure and development of cancer. Data were obtained from the Federal Environmental Agency and were categorized into seven exposure levels. For the calculation, we used the proportion of the population exposed to PM_{10}-concentrations exceeding the WHO mean annual guideline value (>20 $\mu g/m^3$) (eTable 6).

Data on the prevalence of sunbed use was obtained from a representative population-based telephone survey of 1501 men and women aged 14 years and older (e26). For the calculations, all respondents who reported having used sunbeds at least once in their lifetime were considered exposed (eTable 7). The prevalence of highly frequent use of sunbeds (>10 times/year) was used for additional analyses (eTable 8). We assumed the prevalence in the age groups 18 to 29 and 60+ years to be equal to that in age groups 25 to 29 and 60 to 74 years, respectively.

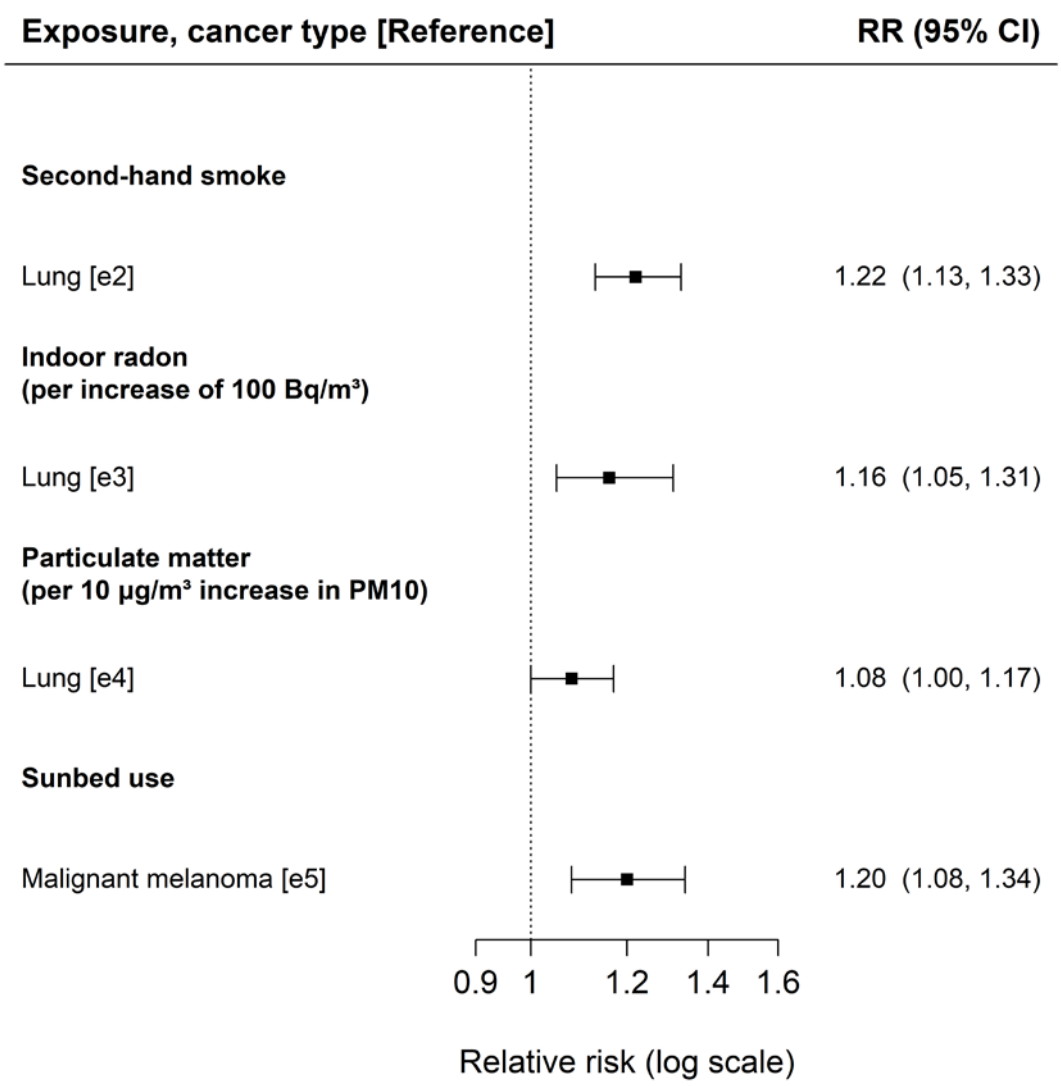
eSupplement D

Sensitivity analyses

In sensitivity analyses, we examined the impact of the uncertainty in the cancer-specific relative risk estimates by comparing the total number of attributable cancer cases when using the point estimate (main analysis), the lower limit of the corresponding 95% confidence interval, and the upper limit, respectively, of the relative risk estimates (eTables 12 to 13, 18). For the sensitivity analyses of human papillomavirus, we used the lower and upper limits of the cancer-site specific prevalence estimates. In the case of oropharyngeal cancer and cancer of the oral cavity, the estimates are based on simultaneous positivity of three markers (HPV-DNA+, HPV E6*I mRNA+, and $p16^{INK4a}$+), as no confidence limits were reported for the prevalence estimates of the main analysis. However, in contrast to the main analysis the geographical origin of the patients was not restricted to Europe due to a lack of appropriate data (eTable 13). In general, it is important to note that the estimates of head and neck cancers attributable to HPV used in our main analysis are conservative because we defined the estimate of the HPV-attributable fraction by the presence of at least two different markers (HPV-DNA+ and HPV E6*I mRNA+ or $p16^{INK4a}$+). A recent meta-analysis reported estimates of attributable fractions of human papillomavirus in head and neck cancers that are substantially higher than those used in our analysis (e27, e28). With respect to cancer of the vulva, the crude prevalence of HPV-DNA and $p16^{INK4a}$ in invasive vulvar cancer was used in the main analysis. In the corresponding sensitivity analysis, we used confidence limits of the adjusted prevalence, because no confidence limits were reported for the crude prevalence estimate of the main analysis. However, it is important to note that both the lower and the upper confidence limit of the crude prevalence are slightly lower than the point estimate used in the main analysis.

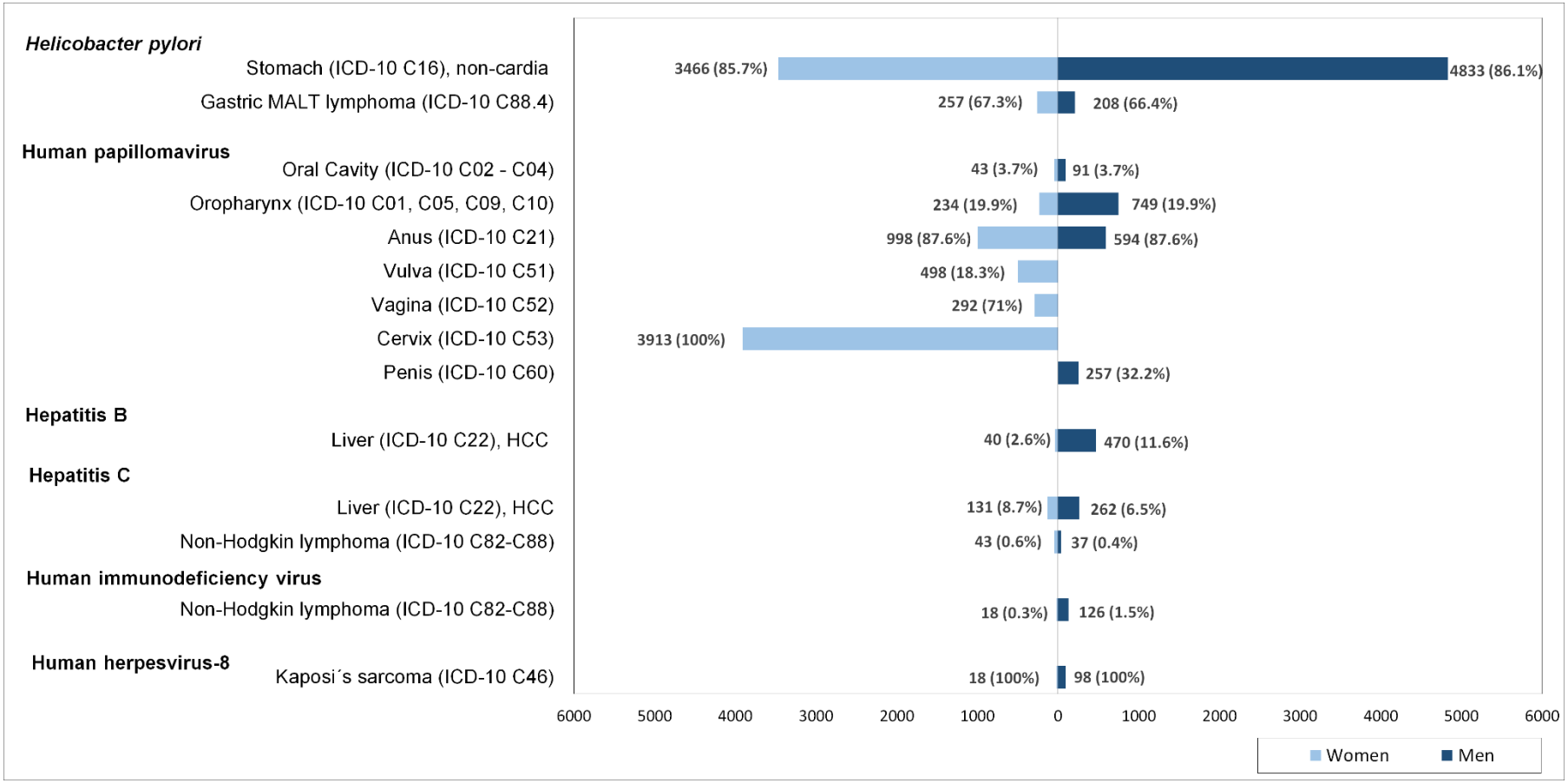


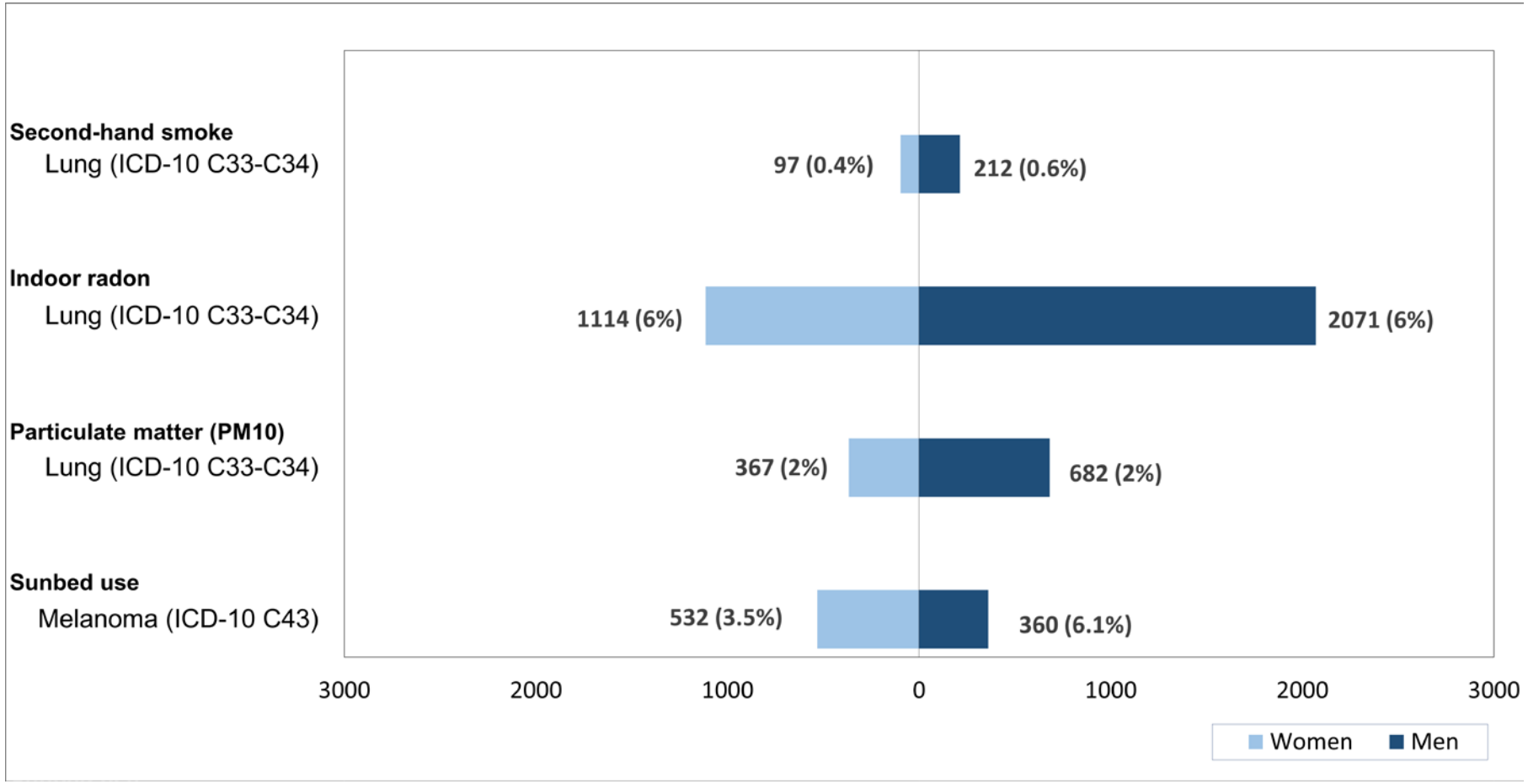
eFigure 1. Relative risks of site-specific cancer for different infections. RR, relative risk; CI, confidence interval; HCC, hepatocellular carcinoma



eFigure 2. Relative risks of site-specific cancer for different environmental factors. RR, Relative risk; CI, confidence interval

eFigure 3. Estimated number of site-specific incident cancer cases attributable to infections among men and women aged 35-84 years in Germany for the year 2018





eFigure 4. Estimated number of site-specific incident cancer cases attributable to environmental factors among men and women aged 35-84 years in Germany for the year 2018

eTable 1. Estimated number of cancers at selected sites in 2018 in Germany by age, based on the population projections for the year 2018 (Federal Office of Statistics, 2015) and the most recent cancer incidence rates (German cancer registry data, 2014)

Cancer site (ICD-10)	35–39 years	40–49 years	50–59 years	60–69 years	70–79 years	80–84 years	All ages combined
Men and women combined							
Oral cavity (C02–C04)	31	262	1,121	1,237	753	254	3,658
Oropharynx (C05, C09, C10)	21	319	1,685	1,834	883	194	4,936
Stomach (C16)	111	603	2,180	3,519	4,743	2,755	13,911
Gastric non-cardia[a]	81	423	1,499	2,418	3,297	1,943	9,661
Anus (C21)	31	209	513	456	435	172	1,816
Liver (C22)	31	191	1,136	2,717	3,160	1,435	8,670
Hepatocellular carcinoma[b]	19	123	727	1,739	2,022	918	5,548
Lung (C33–C34)	150	1,552	9,791	17,597	16,967	6,858	52,915
Melanoma (C43)	771	2,488	4,007	4,624	5,175	1,942	19,007
Kaposi's sarcoma (C46)	11	16	20	18	38	13	116
Vulva (C51)	48	210	501	597	856	506	2,718
Vagina (C52)	5	26	87	101	116	76	411
Cervix (C53)	427	826	1,074	840	501	245	3,913
Penis (C60)	11	54	138	233	254	109	799
Non-Hodgkin lymphoma (C82–C88)	249	923	2,609	3,900	5,253	2,628	15,562
Gastric MALT lymphoma[c] (C88.4)	11	40	116	174	235	119	695

[a] We assumed that the proportion of gastric non-cardia adenocarcinomas among all gastric cancers is 63% for men and 81% for women, based on published data (e15).

[b] We assumed that 64% of all liver cancers are hepatocellular carcinomas, based on the recent cancer report (e16).

[c] We assumed that the proportion of gastric MALT lymphomas among all non-Hodgkin lymphomas is 3.7% for men and 5.4% for women. According to Wu et al. (e17), gastric MALT lymphomas represent 12.2% of the extranodal non-Hodgkin lymphomas in men and 17.9% in women. We assumed that 30% of all non-Hodgkin lymphomas are extranodal (e18).

eTable 2. Estimated number of cancers at selected sites among men in 2018 in Germany by age, based on the population projections for the year 2018 (Federal Office of Statistics, 2015) and the most recent cancer incidence rates (German cancer registry data, 2014)

Cancer site (ICD-10)	35–39 years	40–49 years	50–59 years	60–69 years	70–79 years	80–84 years	All ages combined
Men							
Oral cavity (C02–C04)	21	199	818	841	457	133	2,469
Oropharynx (C01, C05, C09, C10)	18	236	1,318	1,413	660	120	3,765
Stomach (C16)	47	364	1,482	2,400	3,024	1,596	8,913
Gastric non-cardia[a]	30	229	934	1,512	1,905	1,005	5,615
Anus (C21)	16	79	189	165	170	58	677
Liver (C22)	13	123	856	2,088	2,289	947	6,316
Hepatocellular carcinoma[b]	8	79	548	1,336	1,465	606	4,042
Lung (C33–C34)	66	827	5,841	11,358	11,659	4,659	34,410
Melanoma (C43)	306	1,000	2,026	2,562	3,194	1,153	10,241
Kaposi's sarcoma (C46)	11	16	17	15	28	11	98
Penis (C60)	11	54	138	233	254	109	799
Non-Hodgkin lymphoma (C82–C88)	155	570	1,440	2,154	2,839	1,332	8,490
Gastric MALT lymphoma[c] (C88.4)	6	21	53	80	105	49	314

[a] We assumed that the proportion of gastric non-cardia adenocarcinomas among all gastric cancers is 63% for men and 81% for women, based on recently published data (e15).

[b] We assumed that 64% of all liver cancers are hepatocellular carcinomas, based on the recent cancer report (e16).

[c] We assumed that the proportion of gastric MALT lymphomas among all non-Hodgkin lymphomas is 3.7% for men and 5.4% for women. According to Wu et al. (e17), gastric MALT lymphomas represent 12.2% of the extranodal non-Hodgkin lymphomas in men and 17.9% in women. We assumed that 30% of all non-Hodgkin lymphomas are extranodal (e18).

eTable 3. Estimated number of cancers at selected sites among women in 2018 in Germany by age, based on the population projections for the year 2018 (Federal Office of Statistics, 2015) and the most recent cancer incidence rates (German cancer registry data, 2014)

Cancer site (ICD-10)	35–39 years	40–49 years	50–59 years	60–69 years	70–79 years	80–84 years	All ages combined
Women							
Oral cavity (C02–C04)	10	63	303	396	296	121	1,189
Oropharynx (C01, C05, C09, C10)	3	83	367	421	223	74	1,171
Stomach (C16)	64	239	698	1,119	1,719	1,159	4,998
Gastric non-cardia[a]	51	194	565	906	1,392	938	4,046
Anus (C21)	15	130	324	291	265	114	1,139
Liver (C22)	18	68	280	629	871	488	2,354
Hepatocellular carcinoma[b]	11	44	179	403	557	312	1,506
Lung (C33–C34)	84	725	3,950	6,239	5,308	2,199	18,505
Melanoma (C43)	465	1,488	1,981	2,062	1,981	789	8,766
Kaposi's sarcoma (C46)	0	0	3	3	10	2	18
Vulva (C51)	48	210	501	597	856	506	2,718
Vagina (C52)	5	26	87	101	116	76	411
Cervix (C53)	427	826	1,074	840	501	245	3,913
Non-Hodgkin lymphoma (C82–C88)	94	353	1,169	1,746	2,414	1,296	7,072
Gastric MALT lymphoma[c] (C88.4)	5	19	63	94	130	70	381

[a] We assumed that the proportion of gastric non-cardia adenocarcinomas among all gastric cancers is 63% for men and 81% for women, based on recently published data (e15).

[b] We assumed that 64% of all liver cancer are hepatocellular carcinoma, based on the recent cancer report (e16).

[c] We assumed that the proportion of gastric MALT lymphomas among all non-Hodgkin lymphomas is 3.7% for men and 5.4% for women. According to Wu et al. (e17), gastric MALT lymphomas represent 12.2% of the extranodal non-Hodgkin lymphomas in men and 17.9% in women. We assumed that 30% of all non-Hodgkin lymphomas are extranodal (e18).

eTable 4. Prevalence of selected infections among men and women aged 20 to 84 years in Germany

	Prevalence (%) of infection at exposure								
Exposure	**20–29 years[a]**	**30–39 years**	**40–49 years**	**50–59 years**	**60–69 years**	**70–79 years**	**80–84 years**	**All ages combined**	**Reference**
Men and women combined									
Hepatitis B	0.2	0.6	0.1	0.5	0.5	0.1	-	0.3	(e14)
Hepatitis C	0.0	0.0	0.4	0.3	0.3	0.7	-	0.3	(e14)
Helicobacter pylori	21.5	29.4	39.8	45.0	56.6	60.0	-	40.0	(e15)
Human immunodeficiency virus	0.1	0.2	0.2	0.2	0.1	<0.1	<0.1	0.1	(e17)
Men									
Hepatitis B	0.2	0.8	0.2	0.8	1	0.2	-	0.5	(e14)
Hepatitis C	0.0	0.0	0.6	0.5	0.2	0.0	-	0.3	(e14)
Helicobacter pylori	21.5	29.4	39.8	45.0	56.6	60.0	-	40.0	(e15)
Human immunodeficiency virus	0.1	0.3	0.4	0.3	0.1	0.1	<0.1	0.2	(e17)
Women									
Hepatitis B	0.3	0.4	0.0	0.2	0.2	0.0	-	0.2	(e14)
Hepatitis C	0.0	0.0	0.2	0.1	0.4	1.2	-	0.3	(e14)
Helicobacter pylori	21.5	29.4	39.8	45.0	56.6	60.0	-	40.0	(e15)
Human immunodeficiency virus	<0.1	0.1	0.1	0.1	<0.1	<0.1	<0.1	0.1	(e17)

[a] For *Helicobacter pylori*, this age group includes the 18to 29-year-olds.

eTable 5. Prevalence of exposure to second-hand smoke among 1,028 never-smoking men and 325 never-smoking women aged 25 to 74 years, data from of the nationwide representative DEGS1 survey, 2008-2011, Germany

	Prevalence (%) of exposure to second-hand smoke among never smokers				
	25–44 years	**45–54 years**	**55–64 years**	**65–74 years**	**All ages combined**
Men and women combined	35.8	31.0	18.8	10.3	25.9
Men	47.1	38.4	24.5	16.5	35.5
Women	27.3	25.6	15.5	7.2	19.7

eTable 6. Proportion of the German population in different exposure categories of particulate matter (PM_{10}) with mean annual concentration levels in Germany; data from the Federal Environmental Agency (e29)

		Proportion (%) and mean (m) annual concentration for exposure categories by year											
		2007		2008		2009		2010		2011		All years combined	
Exposure category		**%**	**m**	**%**	**m**	**%**	**m**	**%**	**m**	**%**	**m**	**%**	**m**
Particulate matter (PM_{10})													
Level 1	≤ 10 µg/m³	0.0	10	0.0	10	0.0	10	0.0	10	0.1	10	0.0	10.0
Level 2	≥ 10 < 15 µg/m³	1.4	12.5	10	12.5	14.9	12.5	10.4	12.5	7.1	12.5	8.8	12.5
Level 3	≥ 15 < 20 µg/m³	37.4	17.5	59.4	17.5	50.3	17.5	54.4	17.5	48.5	17.5	50.0	17.5
Levels 1–3	**< 20 µg/m³**	38.8	17.3	69.4	16.8	65.2	16.4	64.8	16.7	55.7	16.8	58.8	16.8
Level 4	≥ 20 < 25 µg/m³	56.8	22.5	27.9	22.5	29.9	22.5	31.3	22.5	40.1	22.5	37.2	22.5
Level 5	≥ 25 < 30 µg/m³	4.1	27.5	2.5	27.5	4.7	27.5	3.8	27.5	4.1	27.5	3.8	27.5
Level 6	≥ 30 < 35 µg/m³	0.2	32.5	0.2	32.5	0.2	32.5	0.1	32.5	0.1	32.5	0.2	32.5
Level 7	≥ 35 < 40 µg/m³	0.0	37.5	0.0	37.5	0.0	37.5	0.0	37.5	0.0	37.5	0.0	37.5
Levels 4–7	**≥ 20 µg/m³**	61.1	22.9	30.6	23.0	34.8	23.2	35.2	23.1	44.3	23.0	41.2	23.0

eTable 7. Lifetime prevalence of sunbed use among 1,501 men and women aged 14 to 60+ years; data from a nationwide representative, population-based telephone survey, 2007, Germany (e26)

	Lifetime prevalence (%) of sunbed use					
	14–17 years	**18–29 years**	**30–44 years**	**45–49 years**	**60+ years**	**All**
Men and women combined	18.5	39.1	43.2	22.0	14.8	28.0
Men	4.0	35.0	36.0	14.0	13.0	22.8
Women	34.0	44.0	51.0	31.0	16.0	33.6

eTable 8. Prevalence of high-frequency sunbed use (>10 times/year) among 1501 men and women aged 14 to 60+ years; data from a nationwide representative, population-based telephone survey, 2007, Germany (e26)

	Prevalence (%) of high-frequency (>10 times/year) sunbed use				
	14–17 years	**18–29 years**	**30–44 years**	**45–49 years**	**60+ years**
Men	2.0	19.0	14.0	5.0	7.0
Women	31.0	16.0	16.0	11.0	6.0

eTable 9. Estimated number of site-specific incident cancer cases attributable to infections among men and women combined in Germany for the year 2018, stratified by age

	Total (N) and relative number (%) of attributable cancer site-specific cases by age at outcome													
	35–39 years		40–49 years		50–59 years		60–69 years		70–79 years		80–84 years		All ages combined	
Cancer site (ICD-10)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men and women combined														
Hepatitis B virus														
Liver (C22), HCC	1	5.3	14	11.5	20	2.8	194	11.2	258	12.8	23	2.5	510	9.2
Hepatitis C virus														
Liver (C22), HCC	-	0.0	-	0.0	73	10.0	143	8.2	110	5.4	67	7.3	393	7.1
Non-Hodgkin lymphoma (C82-C88)	-	0.0	-	0.0	16	0.6	19	0.5	22	0.4	23	0.9	80	0.5
Helicobacter pylori														
Stomach (C16), non-cardia	-	-	327	77.3	1,236	82.5	2,090	86.4	2,895	87.8	1,751	90.1	8,299	85.9
Gastric MALT lymphoma (C88.4)	-	-	21	52.5	70	60.3	118	67.8	166	70.6	90	75.6	465	66.9
Human immunodeficiency virus														
Non-Hodgkin lymphoma (C82-C88)	6	2.4	24	2.6	51	2.0	36	0.9	23	0.4	4	0.2	144	0.9
Human herpesvirus 8														
Kaposi's sarcoma (C46)	11	100.0	16	100.0	20	100.0	18	100.0	38	100.0	13	100.0	116	100.0
Human papillomavirus														
Oral cavity (C02–C04)	1	3.7	9	3.7	41	3.7	46	3.7	28	3.7	9	3.7	134	3.7
Oropharynx (C01, C05, C09, C10)	5	19.9	64	19.9	335	19.9	365	19.9	175	19.9	39	19.9	983	19.9
Anus (C21)	27	87.6	183	87.6	450	87.6	400	87.6	381	87.6	151	87.6	1,592	87.6
Vulva (C51)	9	18.3	38	18.3	92	18.3	109	18.3	157	18.3	93	18.3	498	18.3
Vagina (C52)	4	71.0	18	71.0	62	71.0	72	71.0	82	71.0	54	71.0	292	71.0
Cervix (C53)	427	100.0	826	100.0	1,074	100.0	840	100.0	501	100.0	245	100.0	3,913	100.0
Penis (C60)	4	32.2	17	32.2	44	32.2	75	32.2	82	32.2	35	32.2	257	32.2
All cancer types combined	492		1,560		3,585		4,523		4,919		4,922		17,676	

HCC, Hepatocellular carcinoma

eTable S10. Estimated number of site-specific incident cancer cases attributable to infections among men in Germany for the year 2018, stratified by age

	Total (N) and relative number (%) of attributable cancer site-specific cases by age at outcome													
	35–39 years		40–49 years		50–59 years		60–69 years		70–79 years		80–84 years		All ages combined	
Cancer site (ICD-10)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men														
Hepatitis B virus														
Liver (C22), HCC	0	3.7	11	13.4	20	3.7	179	13.4	237	16.2	23	3.7	470	11.6
Hepatitis C virus														
Liver (C22), HCC	-	0.0	-	0.0	65	11.8	134	10.0	63	4.3	-	0.0	262	6.5
Non-Hodgkin lymphoma (C82-C88)	-	0.0	-	0.0	13	0.9	16	0.7	8	0.3	-	0.0	37	0.4
Helicobacter pylori														
Stomach (C16), non-cardia	-	-	177	77.5	770	82.5	1,307	86.4	1,673	87.8	906	90.1	4,833	86.1
Gastric MALT lymphoma (C88.4)	-	-	11	53.3	32	60.9	54	67.8	74	70.5	37	75.0	208	66.4
Human immunodeficiency virus														
Non-Hodgkin lymphoma (C82-C88)	5	3.1	21	3.7	44	3.1	32	1.5	21	0.7	3	0.2	126	1.5
Human herpesvirus 8														
Kaposi’s sarcoma (C46)	11	100.0	16	100.0	17	100.0	15	100.0	28	100.0	11	100.0	98	100.0
Human papillomavirus														
Oral cavity (C02-C04)	1	3.7	7	3.7	30	3.7	31	3.7	17	3.7	5	3.7	91	3.7
Oropharynx (C01, C05, C09, C10)	4	19.9	47	19.9	262	19.9	281	19.9	131	19.9	24	19.9	749	19.9
Anus (C21)	14	87.6	69	87.6	166	87.6	145	87.6	149	87.6	51	87.6	594	87.6
Penis (C60)	4	32.2	17	32.2	44	32.2	75	32.2	82	32.2	35	32.2	257	32.2
All cancer types combined	37		377		1,464		2,269		2,483		1,094		7,725	

HCC, Hepatocellular carcinoma

eTable 11. Estimated number of site-specific incident cancer cases attributable to infections among women in Germany for the year 2018, stratified by age

	Total (N) and relative number (%) of attributable cancer site-specific cases by age at outcome													
	35–39 years		40–49 years		50–59 years		60–69 years		70–79 years		80–84 years		All ages combined	
Cancer site (ICD-10)	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Women														
Hepatitis B virus														
Liver (C22), HCC	1	5.5	3	7.2	-	0.0	15	3.7	21	3.7	-	0.0	40	2.6
Hepatitis C virus														
Liver (C22), HCC	-	0.0	-	0.0	8	4.4	9	2.2	47	8.4	67	21.5	131	8.7
Non-Hodgkin lymphoma (C82-C88)	-	0.0	-	0.0	3	0.3	3	0.1	14	0.6	23	1.8	43	0.6
Helicobacter pylori														
Stomach (C16), non-cardia	-	-	150	77.5	466	82.5	783	86.4	1,222	87.8	845	90.1	3,466	85.7
Gastric MALT lymphoma (C88.4)	-	-	10	53.3	38	60.9	64	67.8	92	70.5	53	75.0	257	67.3
Human immunodeficiency virus														
Non-Hodgkin lymphoma (C82-C88)	1	1.0	3	1.0	7	0.6	4	0.2	2	0.1	1	0.0	18	0.3
Human herpesvirus 8														
Kaposi’s sarcoma (C46)	-	100.0	-	100.0	3	100.0	3	100.0	10	100.0	2	100.0	18	100.0
Human papillomavirus														
Oral cavity (C02-C04)	0	3.7	2	3.7	11	3.7	15	3.7	11	3.7	4	3.7	43	3.7
Oropharynx (C01, C05, C09, C10)	1	19.9	17	19.9	73	19.9	84	19.9	44	19.9	15	19.9	234	19.9
Anus (C21)	13	87.6	114	87.6	284	87.6	255	87.6	232	87.6	100	87.6	998	87.6
Vulva (C51)	9	18.3	38	18.3	92	18.3	109	18.3	157	18.3	93	18.3	498	18.3
Vagina (C52)	4	71.0	18	71.0	62	71.0	72	71.0	82	71.0	54	71.0	292	71.0
Cervix (C53)	427	100.0	826	100.0	1,074	100.0	840	100.0	501	100.0	245	100.0	3,913	100.0
All cancer types combined	755		1,183		2,121		2,254		2,435		3,072		9,951	

HCC, Hepatocellular carcinoma

eTable 12. Sensitivity analyses of the estimated number of all incident cancer cases attributable to different infections in Germany for the year 2018, stratified by gender

Total and relative number of preventable cancer cases for all ages combined

	Main analysis		Sensitivity analysis: lower confidence limits of relative risks		Sensitivity analysis: upper confidence limits of relative risks	
Exposure	**N**	**%**	**N**	**%**	**N**	**%**
Men						
Hepatitis B virus	470	0.2	268	0.1	774	0.3
Hepatitis C virus	299	0.1	218	0.1	414	0.2
Helicobacter pylori	5,041	2.1	4,615	1.9	5,332	2.2
Human immunodeficiency virus	126	0.1	121	0.1	131	0.1
Human herpesvirus 8	98	<0.1	98	<0.1	98	<0.1
Human papillomavirus[1]	1,691	0.7	1,438	0.6	1,808	0.8
Women						
Hepatitis B virus	40	<0.1	21	<0.1	70	<0.1
Hepatitis C virus	174	0.1	128	0.1	233	0.1
Helicobacter pylori	3,723	1.8	3,359	1.7	3,957	2.0
Human immunodeficiency virus	18	<0.1	18	<0.1	19	<0.1
Human herpesvirus 8	18	<0.1	18	<0.1	18	<0.1
Human papillomavirus[1]	5,978	3.0	5,663	2.8	6,053	3.0
Men and women combined						
Hepatitis B virus	510	0.1	289	0.1	844	0.2
Hepatitis C virus	474	0.1	346	0.1	647	0.1
Helicobacter pylori	8,764	2.0	7,974	1.8	9,289	2.1
Human immunodeficiency virus	144	<0.1	139	<0.1	150	<0.1
Human herpesvirus 8	116	<0.1	116	<0.1	116	<0.1
Human papillomavirus[1]	7,669	1.7	7,101	1.6	7,861	1.8
All infections combined	17,633	4.0	15,952	3.6	18,821	4.3

[1] For human papillomavirus, the sensitivity analyses were based on the 95% confidence limits of prevalence of DNA in tumor cells (Supplementary Table S13).

eTable 13. Sensitivity analyses of the estimated number of site-specific cancer cases attributable to human papillomavirus in Germany for the year 2018

	Total and relative number of preventable cancer site-specific cases for all ages combined					
	Main analysis		Sensitivity analysis: lower confidence limits of prevalence		Sensitivity analysis: upper confidence limits of prevalence	
Cancer site	**N**	**%**	**N**	**%**	**N**	**%**
Oral cavity (C02–C04)[1]	134	3.7	81	2.2	153	4.2
Oropharynx (C01, C05, C09, C10)[1]	983	19.9	798	16.2	1,031	20.9
Anus (C21)	1,592	87.6	1,480	81.6	1,673	92.1
Vulva (C51)[2]	498	18.3	348	12.8	476	17.5
Vagina (C52)	292	71.0	259	63.0	320	78.0
Cervix (C53)	3,913	100.0	3,913	100.0	3,913	100.0
Penis (C60)	257	32.2	222	27.8	295	36.9
All cancer types combined	7,669		7,101		7,861	

[1]The sensitivity analyses of cancer of the oral cavity and oropharynx were conducted using the upper and lower confidence limits of prevalence estimates based on simultaneous positivity of all three markers (HPV-DNA+, HPV E6*I mRNA+ and p16INK4a+).

[2] The sensitivity analyses of vulva cancer were conducted using the upper and lower confidence limits of the adjusted prevalence estimate.

eTable 14. Estimated number of incident cases of lung cancer (ICD-10 C33-C34) cases attributable to second-hand smoke exposure among never smokers in Germany for the year 2018

	Total (N) and relative number (%) of attributable lung cancer cases by age at outcome									
	35–54 years		**55–64 years**		**65–74 years**		**75–84 years**		**All ages combined**	
Cancer site	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men and women combined	65	7.6	85	6.9	73	4.3	86	2.7	309	4.3
Men	41	9.4	60	7.8	47	5.1	64	3.5	212	5.4
Women	24	5.7	25	5.3	26	3.3	22	1.6	97	3.1

eTable 15. Estimated number of incident cases of lung cancer cases attributable to indoor radon exposure among men and women combined in Germany for the year 2018, stratified by smoking status

	Total (N) and relative number (%) of lung cancer cases attributable to radon by age and smoking status									
	35–54		**55–64**		**65–74**		**75–84**		**All ages combined**	
Age	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men and women combined										
Never smokers	51	1.1	76	0.5	103	0.6	195	1.2	425	0.8
Smokers (current and former)	259	4.9	797	5.5	950	5.4	754	4.8	2,760	5.2
All	310	6.0	873	6.0	1,053	6.0	949	6.0	3,185	6.0
Men										
Never smokers	26	0.9	47	0.5	56	0.5	110	1.0	239	0.7
Smokers (current and former)	148	5.1	503	5.5	636	5.5	545	5.0	1,832	5.3
All	174	6.0	550	6.0	692	6.0	655	6.0	2,071	6.0
Women										
Never smokers	25	1.1	29	0.5	47	0.8	85	1.7	186	1.0
Smokers (current and former)	111	4.9	294	5.5	314	5.2	209	4.3	928	5.0
All	136	6.0	323	6.0	361	6.0	294	6.0	1,114	6.0

eTable 16. Estimated number of incident cases of malignant melanoma (ICD-10 C43) attributable to ever-use of sunbeds among men and women combined in Germany for the year 2018, stratified by age and assuming a 10-year latency period between exposure and cancer incidence

	Total (N) and relative number (%) of attributable cases of malignant melanoma by age at outcome									
	35–39 years		**40–54 years**		**55–69 years**		**70–84 years**		**All ages combined**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men and women combined	58	7.5	362	8.1	276	4.1	196	2.8	892	4.7
Men	20	6.5	130	6.7	99	2.7	110	2.5	360	3.5
Women	38	8.1	232	9.3	177	5.8	86	3.1	532	6.1

eTable 17. Estimated number of incident cases of malignant melanoma (ICD-10 C43) attributable to highly frequent use of sunbeds (>10 times/year) among men and women combined in Germany for the year 2018, stratified by age and assuming a 10-year latency period between exposure and cancer incidence

	Total (N) and relative number (%) of attributable cases of malignant melanoma by age at outcome									
	35–39 years		**40–54 years**		**55–69 years**		**70–84 years**		**All ages combined**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Men and women combined	52	6.7%	265	6.0%	209	3.1%	192	2.7%	718	3.8%
Men	23	7.4%	108	5.6%	75	2.1%	124	2.9%	330	3.2%
Women	29	6.3%	158	6.3%	134	4.4%	68	2.5%	389	4.4%

eTable 18. Sensitivity analyses of the estimated number of incident cancer cases attributable to selected environmental factors in Germany for the year 2018, stratified by gender

	Total and relative number of preventable cancer cases for all ages combined					
	Main analysis		Sensitivity analysis: lower confidence limits of relative risks		Sensitivity analysis: upper confidence limits of relative risks	
Exposure	**N**	**%**	**N**	**%**	**N**	**%**
Men						
Second-hand smoke	212	0.1	129	0.1	127	0.1
Indoor radon	2,071	0.9	675	0.3	3,796	1.6
Particulate matter	682	0.3	0	0.0	1,396	0.0
Sunbed use	350	0.1	148	0.1	594	0.2
Women						
Second-hand smoke	97	<0.1	58	<0.1	143	<0.1
Indoor radon	1,114	0.3	363	0.1	2,041	0.5
Particulate matter	367	0.1	0	0.0	751	0.2
Sunbed use	532	0.1	222	0.1	862	0.2
Men and women combined						
Second-hand smoke	310	0.1	187	<0.1	452	0.1
Indoor radon	3,185	0.7	1,038	0.2	5,837	1.3
Particulate matter	1,049	0.2	0	0.0	2,147	0.5
Sunbed use	892	0.2	370	0.1	1,456	0.3
All selected environmental factors combined	5,338	1.2	1,534	0.3	9,589	2.2

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