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ARTICLE

Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States, 2019

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Abstract

In 2018, the authors reported estimates of the number and proportion of cancers attributable to potentially modifiable risk factors in 2014 in the United States. These data are useful for advocating for and informing cancer prevention and control. Herein, based on up-to-date relative risk and cancer occurrence data, the authors estimated the proportion and number of invasive cancer cases (excluding nonmelanoma skin cancers) and deaths, overall and for 30 cancer types among adults who were aged 30 years and older in 2019 in the United States, that were attributable to potentially modifiable risk factors. These included cigarette smoking; second-hand smoke; excess body weight; alcohol consumption; consumption of red and processed meat; low consumption of fruits and vegetables, dietary fiber, and dietary calcium; physical inactivity; ultraviolet radiation; and seven carcinogenic infections. Numbers of cancer cases and deaths were obtained from data sources with complete national coverage, risk factor prevalence estimates from nationally representative surveys, and associated relative risks of cancer from published large-scale pooled or meta-analyses. In 2019, an estimated 40.0% (713,340 of 1,781,649) of all incident cancers (excluding nonmelanoma skin cancers) and 44.0% (262,120 of 595,737) of all cancer deaths in adults aged 30 years and older in the United States were attributable to the evaluated risk factors. Cigarette smoking was the leading risk factor contributing to cancer cases and deaths overall (19.3% and 28.5%, respectively), followed by excess body weight (7.6% and 7.3%, respectively), and alcohol consumption (5.4% and 4.1%, respectively). For 19 of 30 evaluated cancer types, more than one half of the cancer cases and deaths were attributable to the potentially modifiable risk factors considered in this study. Lung cancer had the highest number of cancer cases (201,660) and deaths (122,740) attributable to evaluated risk factors, followed by female breast cancer (83,840 cases), skin melanoma (82,710), and colorectal cancer

(78,440) for attributable cases and by colorectal (25,800 deaths), liver (14,720), and esophageal (13,600) cancer for attributable deaths. Large numbers of cancer cases and deaths in the United States are attributable to potentially modifiable risk factors, underscoring the potential to substantially reduce the cancer burden through broad and equitable implementation of preventive initiatives.

KEYWORDS
cancer, population attributable fraction, prevention, risk factor

INTRODUCTION

We previously estimated that about 660,000 (42% of all) incident cancer cases and 265,000 (45% of all) cancer deaths in the United States in 2014 were attributable to potentially modifiable risk factors.[1] However, information on risk factors associated with specific cancer types and the magnitude of associations may evolve over time and since the publication of our previous report, more precise information has become available for some of the associations, notably for physical inactivity and carcinogenic infections.[2–4] This new information, alongside changes in the number of cancer cases and deaths over time—because of changes in population size, aging, and cancer trends—and variations in the risk factor prevalence, can collectively affect estimates of the burden of cancer attributable to known risk factors. Contemporary estimates of this burden are useful for setting more pertinent priorities for cancer control initiatives.

In this study, we used nationally representative data on cancer incidence and mortality and risk factor prevalence to estimate the proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors, both overall (excluding nonmelanoma skin cancers) and for 30 cancer types in adults aged 30 years and older in 2019. These risk factors included cigarette smoking (current and former smoking); second-hand smoke; excess body weight; alcohol consumption; consumption of red and processed meat; low consumption of fruits and vegetables, dietary fiber, and dietary calcium; physical inactivity; ultraviolet (UV) radiation; and infection with Epstein–Barr virus (EBV), *Helicobacter pylori*, hepatitis B virus (HBV), hepatitis C virus (HCV), human herpesvirus-8 (HHV-8; also called Kaposi sarcoma herpesvirus), human immunodeficiency virus (HIV), and human papillomavirus (HPV).

MATERIALS AND METHODS

A list of potentially modifiable risk factors with sufficient[5–9] or strong (either convincing or probable)[2,10] evidence for causing cancer in humans and associated cancer types considered for this analysis are shown in Table 1. Some other, generally less common risk factors or cancer types were not considered because of inadequate data or for other limitations (see Table S1). Relative risks (RRs) for associations between risk factors and cancers were abstracted from published, large-scale pooled or meta-analyses of studies in the United States when available. Otherwise, RRs were obtained from pooled or meta-analyses of studies conducted in North America and/or Europe or tertiarily from studies worldwide (see Table S2).

Although cancer occurrence data were available for 2020, we chose to use the 2019 data to avoid any distortion of results because of considerable declines in the number of new cancer cases diagnosed in 2020, largely because of suspension of cancer screening programs and reduced capacity for cancer diagnosis during the coronavirus disease 2019 pandemic, disruptions in employment and health insurance, and fear of coronavirus disease 2019.[11,12] Numbers of new invasive cancer cases in 2019 in the United States by sex and age group (aged 30–84 years in 5-year increments and 85 years and older) were obtained from the Centers for Disease Control and Prevention's (CDC's) National Program of Cancer Registries and the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) Program, which collectively provided complete coverage of the US population.[13] Numbers of cancer deaths with the same stratifications were obtained from the CDC's National Center for Health Statistics.[14] Both cases and deaths were retrieved using the NCI's SEER*Stat software (version 8.4.2). We limited our analysis to those aged 30 years and older because cancer cases and deaths in younger ages accounted for only 2.0% (37,090 of 1,818,739) of all cancer cases and 0.6% (3852 of 599,589) of all cancer deaths in 2019, for many of which genetic predisposition to cancer might have been a strong contributing factor.

In this analysis, we estimated prevalence of risk factors by averaging data from three cycles of nationally representative surveys for more stable estimates for each sex and age group and allowed for an approximately 10-year lag period between exposure and cancer occurrence when data were available. Sex-specific and age-specific prevalence estimates for cigarette smoking (current, former, and never) and alcohol consumption (average number of drinks per day in the past month) were obtained from averaging the 2008, 2009, and 2010 National Health Interview Surveys (NHIS; see Table S2).[15] We adjusted NHIS alcohol consumption by using per capita alcohol sales according to a method previously suggested to account for underreporting of alcohol consumption in surveys.[16]

National Health and Nutrition Examination Survey (NHANES)[17] data were used to estimate prevalence for second-hand smoke exposure (defined as a serum cotinine level of ≥0.05 nanograms per milliliter among never-smokers and former-smokers[18,19]); body mass index (in kg/m^2); red meat, processed meat, fruits and vegetables, and

TABLE 1 Potentially modifiable risk factors and associated cancer types considered in this analysis.

Risk factor	Cancer type (International Classification of Diseases, 10th revision codes)[a]
Cigarette smoking (IARC Working Group 2012[7])	Oral cavity (C00–C08); pharynx (C09–C14); esophagus (C15); stomach (C16); colorectum (C18–C20, C26.0); liver (C22.0, C22.2-C22.4, C22.7, C22.9); pancreas (C25); nasal cavity, paranasal sinus (C30.0–C31); larynx (C32); trachea (C33); lung, bronchus (C34); cervix uteri (C53); ovary (C56) [mucinous type only]; kidney, renal pelvis (C64–C65), ureter (C66); urinary bladder (C67); acute myeloid leukemia (C92.0, C92.4–C92.6, C92.8, C94.0, C94.2)
Second-hand smoke exposure (IARC Working Group 2012[7])	Lung, bronchus (C34) [only among never-smokers and former-smokers]
Excess body weight (Lauby-Secretan 2016[9])	Esophagus (C15) [adenocarcinoma only]; stomach, cardia only (C16.0); colorectum (C18–C20, C26.0); liver (C22.0, C22.2-C22.4, C22.7, C22.9); gallbladder (C23); pancreas (C25); female breast (C50) [postmenopausal cancers only[b]]; corpus uteri (C54–C55); ovary (C56); kidney, renal pelvis (C64–C65); thyroid (C73); myeloma (C90.0, C90.2, 90.3)
Alcohol consumption (IARC Working Group 2012[7])	Oral cavity (C00–C08); pharynx (C09–C14); esophagus (C15) [squamous cell carcinoma only]; colorectum (C18–C20, C26.0); liver (C22.0) [hepatocellular carcinoma only]; larynx (C32); female breast (C50)
Dietary factors	
Red meat consumption (WCRF/AICR 2018[10])	Colorectum (C18–C20, C26.0)
Processed meat consumption (Bouvard 2015,[8] WCRF/AICR 2018[10])	Colorectum (C18–C20, C26.0)
Low fruit and nonstarchy vegetable consumption (WCRF/AICR 2018[10])	Aerodigestive organs, aggregated, including oral cavity, pharynx, esophagus, larynx (C00–C15, C32)
Low dietary fiber consumption (WCRF/AICR 2018[10])	Colorectum (C18–C20, C26.0)
Low dietary calcium consumption (WCRF/AICR 2018[10])	Colorectum (C18–C20, C26.0)
Physical inactivity (U.S. Department of Health and Human Services 2018[2])	Esophagus (C15) [adenocarcinoma only]; stomach (C16); colon excluding rectum (C18, C26.0); female breast (C50); corpus uteri (C54–C55); kidney, renal pelvis (C64–C65); urinary bladder (C67)
Ultraviolet radiation (IARC Working Group 2012[6])	Melanoma of the skin (C43)
Infections	
Epstein-Barr virus (IARC Working Group 2012[5])	Nasopharynx (C11); Hodgkin lymphoma (C81)
Helicobacter pylori (IARC Working Group 2012[5])	Stomach, noncardia only (C16.1–C16.6)
Hepatitis B virus (IARC Working Group 2012[5])	Liver (C22.0, C22.2-C22.4, C22.7, C22.9)
Hepatitis C virus (IARC Working Group 2012[5])	Liver (C22.0, C22.2-C22.4, C22.7, C22.9); non-Hodgkin lymphoma (C82–C85, C96.3)
Human herpes virus type 8 (Kaposi sarcoma herpes virus; IARC Working Group 2012[5])	Kaposi sarcoma (C46)
Human immunodeficiency virus (IARC Working Group 2012[5])	Anus (C21); Kaposi sarcoma (C46); cervix uteri (C53); Hodgkin lymphoma (C81); non-Hodgkin lymphoma (C82–C85, C96.3)
Human papillomavirus (IARC Working Group 2012[5])	Oral cavity excluding lip and base of tongue (C02–C06); oropharynx, tonsils, base of tongue (C01, C09–C10); anus (C21); vulva (C51); vagina (C52); cervix uteri (C53); penis (C60)

Abbreviations: AICR, American Institute for Cancer Research; IARC, International Agency for Research on Cancer; WCRF, World Cancer Research Fund.

[a]International Classification of Diseases for Oncology, third edition histology codes for incidence data were as follows: esophageal adenocarcinoma (8140–8147, 8200–8201, 8250–8507, 8560, 8570–8574, 8576); esophageal squamous cell carcinoma (8050–8078, 8083–8084); hepatocellular carcinoma (8170–8175); ovarian mucinous type (8470–8474, 8480–8482, 8490, 9015); acute myeloid leukemia (9840, 9860–9867, 9871–9876, 9895–9898, 9910–9911, 9920, 9945–9946); Hodgkin lymphoma (9650–9667); non–Hodgkin lymphoma (9590–9597, 9670–9671, 9673, 9675, 9678–9680, 9684, 9687–9691, 9695, 9698–9702, 9705, 9708–9709, 9712, 9714–9719, 9724–9729, 9735, 9737–9738, 9811–9818, 9823, 9827, 9837); myeloma (9731–9732, 9734); melanoma of the skin (8720–8790, site codes C440–C449); and Kaposi sarcoma (9140).

[b]In this analysis, women 50 years and older were considered as postmenopausal and were included in the calculation of female breast cancers attributable to excess body weight.

dietary fiber and calcium consumption (all in grams per day except calcium, which was in milligrams per day); physical activity (metabolic equivalent of task-minutes per week); and carcinogenic infections (based on biologic samples), as shown in Table S2. Data were averaged over the 2007–2008, 2009–2010, and 2011–2012 NHANES surveys, except for oral (2009–2012 surveys) and penile (2013–2016 surveys) HPV infections, for which data collection started more recently, and for *H. pylori* (1999–2000 survey; latest available data). The NCI method was implemented to estimate the usual daily consumption of dietary factors using data from the two 24-hour recalls of NHANES (see Supporting Methods).[20,21] All risk factor prevalence estimates were weighted to account for the appropriate complex sample design using SAS (version 9.4; SAS Institute, Inc.) and SAS-callable SUDAAN (release 11.0.4; RTI International).

Statistical analysis

To allow for uncertainty in the data, we applied a simulation method in which numbers from 1000 repeated draws were generated for RRs (log-transformed) and risk factor prevalence for each sex and age group stratum.[22] Standard errors for risk factors were available from the survey data; and, for log-transformed RRs, they were calculated based on the reported 95% confidence intervals (CIs). By using numbers from repeated draws, we first calculated the population-attributable fraction (PAF; i.e., the proportion of cancer attributable to risk factors in the population) for each risk factor and associated cancer in each stratum of sex and age group based on the following approximate formula, in which *Pi* represents risk factor prevalence at the exposure category *i*, and *RRi* represent the corresponding RR:

$$PAF = \frac{\sum P_i(RR_i - 1)}{1 + \sum P_i(RR_i - 1)}$$

The sex and age group-specific PAF values were then multiplied by the number of cancer cases or deaths in that stratum and summed the results over age to calculate the number of cases and deaths for each cancer type attributable to each risk factor by sex.[23,24] For a few risk factors, however, we did not use the above approximate formula mostly because of the lack of adequate exposure data. Similar to previous studies, we attributed all cervical cancers to HPV infection and all Kaposi sarcomas to HHV8 infection; attributed 90.2% of anal cancers in men and 96.3% of anal cancers in women to HPV infection; and attributed 61.2% of nasopharyngeal cancers, 20.5% of Hodgkin lymphomas in ages 30–44 years, and 42.5% of Hodgkin lymphomas in ages 45 years and older to EBV infection (see Table S3).[4] We estimated melanoma cases attributable to UV radiation based on the difference between observed melanoma cases by sex and age group and expected numbers based on historical melanoma incidence rates during 1942–1954 in Connecticut, as applied in our previous study.[25] Sex and age group-specific PAFs for incidence were applied to melanoma mortality data to calculate melanoma deaths attributable to UV radiation.

To calculate the overall attributable proportion and number of cancer cases or deaths for a given cancer type associated with multiple risk factors, we used the following equation to calculate the joint PAF based on PAFs for individual risk factors (*PAFi*), assuming that the risk factors had no interactions.

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

In addition to individual risk factors, we calculated proportions and numbers of cancer cases and deaths attributable to tobacco use (cigarette and second-hand smoke combined); infections (all carcinogenic infections combined); dietary factors associated with cancer risk (consumption of red and processed meat and low consumption of fruits and vegetables, dietary fiber, and dietary calcium combined); and a combination of excess body weight, alcohol consumption, dietary factors, and physical inactivity. HIV is believed to act indirectly by increasing the risk of cancers associated to other carcinogenic viruses,[26,27] several of which are considered in this analysis. As such, we excluded HIV-related cancers from the calculations of estimates for all infections and all evaluated risk factors combined, except for non-Hodgkin lymphoma, because only a negligible proportion of this cancer was attributable to another virus considered in the current study (HCV).

In a sensitivity analysis, we repeated the analysis using contemporary risk factor data, i.e., with little lag period, similar to our previous analysis.[1] The data were obtained from 2018 and 2019 NHIS surveys for smoking and alcohol consumption and from 2017 to March 2020 NHANES surveys for other risk factors, except for dietary items (2015 to March 2020 for more stable estimates), *H. pylori* infection (1999–2000, latest available data), and HBV, HIV, and HPV infection (2013–2016).

Numbers of cancer cases or deaths by sex or for individual cancer types may not sum to the totals because numbers for all cancers combined were obtained from separate simulation models, and all numbers were rounded to the nearest 10. We used Stata, version 15.1 (StataCorp) for the simulation and calculation of proportions and numbers of cancers attributable to evaluated risk factors. More detailed information on data sources and statistical analysis is provided in the Supporting Methods.

RESULTS

Incident cancer cases attributable to evaluated risk factors

An estimated 40.0% of all incident cancers in adults aged 30 years and older in the United States in 2019 (713,340 of 1,781,649 incident cancer cases excluding nonmelanoma skin cancer) were attributable to the potentially modifiable risk factors evaluated in this analysis (Figure 1). The corresponding proportion was 40.5% in men (368,600 of 909,295) and 39.5% in women (344,740 of 872,354).

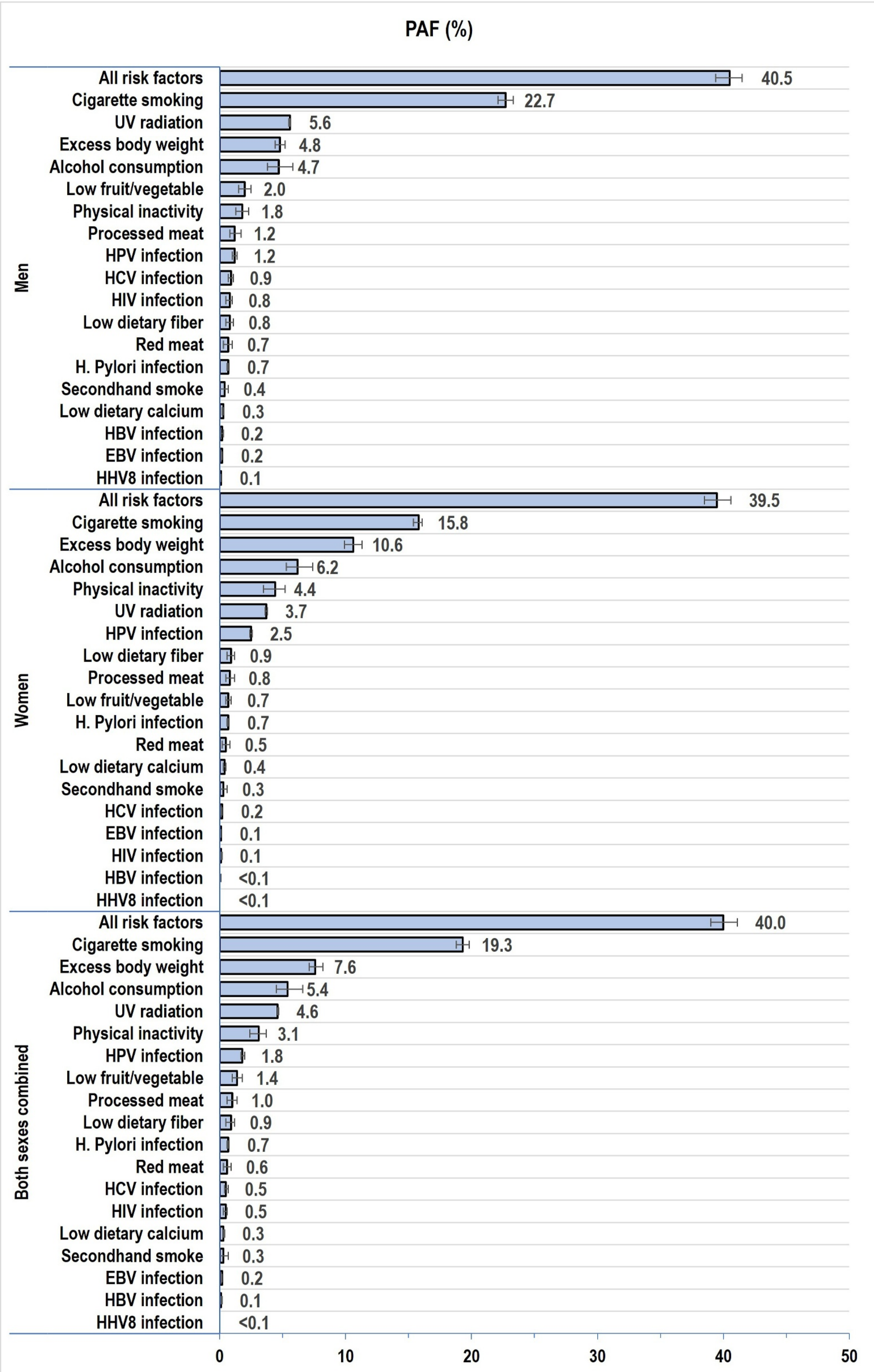

FIGURE 1 Estimated proportion and number of incident cancer cases (excluding nonmelanoma skin cancers) attributable to evaluated risk factors in adults 30 years and older by sex, United States, 2019. The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer cases are rounded to the nearest 10. EBV indicates Epstein–Barr virus; *H. pylori*, *Helicobacter pylori*; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HIV, human immunodeficiency virus; HPV, human papillomavirus; PAF, population-attributable fraction; UV, ultraviolet.

Cigarette smoking had the largest PAF and attributable cancer cases (344,070 cases; 19.3% of all cases), contributing to 56.0% of all potentially preventable cancers in men (206,550 of 368,600) and 39.9% in women (137,520 of 344,740). Excess body weight had the second largest PAF (7.6%), followed by alcohol consumption (5.4%), UV radiation exposure (4.6%), and physical inactivity (3.1%).

The proportions of cancer cases attributable to smoking, UV radiation, HCV infection, and HIV infection usually were larger in men than in women (Table 2), reflecting historically higher prevalence of these risk factors in men (see Table S2). In contrast, the PAFs were higher in women for excess body weight, alcohol consumption, physical inactivity, and HPV infection, largely driven by the high burden of female-specific (female breast, endometrial, and cervical) cancers attributable to these risk factors (Table 2).

By cancer type, the proportion of cases caused by potentially modifiable risk factors ranged from 100% for cervical cancer and Kaposi sarcoma to 4.9% for ovarian cancer, and exceeded 50% for 19 of 30 evaluated cancer types (Figure 2). In addition to cervical cancer and Kaposi sarcoma, more than 80% of all melanomas of the skin (92.2%) and cancers of the anus (94.2%), larynx (89.9%), lung and bronchus (lung; 88.2%), pharynx (87.4%), trachea (85.6%), esophagus (85.4%), and oral cavity (83.7%) were attributable to evaluated risk factors. Lung cancer had the largest number of cases attributable to evaluated risk factors in both men (104,410 cases) and women (97,250), followed by skin melanoma (50,570), colorectal cancer (44,310), and urinary bladder cancer (32,000) in men and breast (83,840), corpus uteri (35,790), and colorectal (34,130) cancer in women (Table 3).

Cigarette and second-hand smoking

Cigarette smoking contributed to 22.7% and 15.8% of all cancer cases in men and women, respectively (Figure 1). By cancer type, the largest proportion of smoking-attributable cases were for cancers of the lung (85.6%) and trachea (85.6%), followed by laryngeal (80.1%), pharyngeal (56.8%), oral cavity (54.8%), nasal cavity and paranasal sinus (54.2%), esophageal (53.9%), and urinary bladder (50.7%) cancer (Table 2). Lung cancer also had the largest number of smoking-attributable cancer cases (195,590), followed by urinary bladder (39,280), colorectal (19,830), and oral cavity (17,030) cancer. Second-hand smoke contributed an additional 6070 cases of lung cancer (2.7% of lung cancer cases). The proportions of cases attributable to cigarette smoking and second-hand smoke by cancer type in men and women were comparable or were slightly higher in men.

Excess body weight

Excess body weight was the third largest contributor to total cancer cases in men (4.8%; 43,720 cases) and second in women (10.6%; 92,200; Figure 1). By cancer type, however, excess body weight contributed to more than half of all cancers of the corpus uteri (53.1%) and one-third of gallbladder (37.1%), esophageal (35.4%), liver (34.9%), and kidney and renal pelvis (33.8%) cancer (Table 2). The number of cancer cases attributable to excess body weight was largest for cancers of the kidney and renal pelvis (14,680 cases), liver (7,590), and esophagus (5,800) in men and for cancers of the corpus uteri (32,090), breast (30,720), and kidney and renal pelvis (8,950) in women. In contrast to other cancer types that showed comparable PAFs for excess body weight in men and women or larger PAFs in women, PAFs for esophageal and gastric cancers were larger in men than in women, likely because the subtypes associated with excess body weight (esophageal adenocarcinoma and gastric cardia cancer) constituted a greater proportion of these two cancer types in men.[28]

Alcohol consumption

Alcohol consumption was the fourth largest contributor to all cancer cases in men (4.7%; 42,400 cases) and the third largest contributor in women (6.2%; 54,330; Figure 1). Approximately one half of oral cavity (49.9%; 10,350) and pharyngeal (44.6%; 6460) cancers in men and one-fourth of oral cavity (25.1%; 2600), esophageal (24.2%; 1000), and pharyngeal (22.5%, 760) cancers in women were attributable to alcohol consumption (Table 2). However, female breast cancer had the largest number of attributable cases (44,180 cases), followed by colorectal cancer in both men (13,850) and women (4630). The proportions of cases attributable to alcohol consumption by cancer type were higher in men than in women, except for esophageal cancer.

Dietary factors associated with cancer risk

The proportion of all cancers attributable to dietary factors ranged from 0.3% for low dietary calcium consumption to 1.4% for low fruit and vegetable consumption (Figure 1). By cancer type, the proportion of colorectal cancer cases attributable to dietary factors ranged from 4.2% (6090 cases) for low dietary calcium, to 7.3% (10,610) for red meat, to 10.5% (15,150) for low dietary fiber, and to 12.8% (18,540) for processed meat consumption (Table 2). Low fruit and vegetable consumption was associated with 30.7% of oral cavity, pharyngeal, esophageal, and laryngeal cancers, with oral cavity cancer having the largest number of attributable cases (9520). There were no substantial differences between men and women in PAFs for dietary factors, except for a slightly larger PAF for low dietary calcium consumption in women, reflecting higher prevalence among women (see Table S2).

The estimated proportion of cancer cases attributable to dietary factors associated with cancer risk (all dietary factors combined) was 4.9% in men (44,850 cases) and 3.4% in women (29,380; Figure 3). The PAF for a combination of excess body weight, alcohol consumption, dietary factors, and physical inactivity was 15.3% in men (second to a combination of cigarette and second-hand smoke, 23.1%) and 22.5% in women (followed by a combination of cigarette and second-hand smoke, 16.1%).

TABLE 2 Estimated cancer cases in adults 30 years and older attributable to potentially modifiable risk factors by sex, risk factor, and cancer type: United States, 2019.

	Men		Women		Both sexes combined	
Cancer	**Attributable cases, No. (95% CI)**	**PAF (95% CI), %**	**Attributable cases, No. (95% CI)**	**PAF (95% CI),%**	**Attributable cases, No. (95% CI)**	**PAF (95% CI), %**
Cigarette smoking						
Lung, bronchus	101,010 (100,260–101,770)	87.2 (86.6–87.9)	94,580 (93,750–95,440)	83.9 (83.1–84.6)	195,590 (194,010–197,210)	85.6 (84.9–86.3)
Trachea	100 (100–100)	88.6 (86.8–89.5)	60 (60–60)	84.9 (83.6–86.3)	160 (160–170)	85.6 (85.6–90.9)
Larynx	8000 (7240–8580)	80.7 (73.1–86.5)	1960 (1740–2120)	77.8 (69.2–84.4)	9960 (8980–10,700)	80.1 (72.3–86.1)
Pharynx	8390 (7380–9340)	58.0 (50.9–64.5)	1770 (1520–2000)	52.0 (44.8–58.8)	10,160 (8900–11,340)	56.8 (49.8–63.4)
Oral cavity	11,840 (10,410–13,180)	57.1 (50.3–63.6)	5200 (4480–5900)	50.3 (43.3–57.1)	17,030 (14,890–19,090)	54.8 (47.9–61.5)
Nasal cavity, paranasal sinus	860 (750–960)	56.8 (50.0–63.4)	500 (430–570)	50.2 (43.3–57.1)	1360 (1190–1530)	54.2 (47.5–61.0)
Esophagus	8510 (7800–9170)	55.5 (50.8–59.8)	1990 (1800–2170)	48.2 (43.7–52.7)	10,500 (9600–11,350)	53.9 (49.3–58.3)
Urinary bladder	30,990 (28,370–33,330)	52.6 (48.1–56.6)	8300 (7490–9030)	44.8 (40.4–48.8)	39,280 (35,850–42,360)	50.7 (46.3–54.7)
Ureter	730 (670–780)	52.4 (48.3–56.4)	380 (340–410)	44.1 (40.1–48.2)	1100 (1010–1190)	49.2 (45.2–53.2)
Liver	6100 (4800–7480)	27.4 (21.6–33.7)	1690 (1320–2110)	22.1 (17.3–27.5)	7790 (6120–9590)	26.1 (20.5–32.1)
Cervix uteri	—	—	2740 (1650–3750)	21.6 (13.0–29.6)	2740 (1650–3750)	21.6 (13.0–29.6)
Stomach	3360 (2230–4490)	22.1 (14.7–29.4)	1720 (1120–2340)	17.7 (11.6–24.0)	5090 (3360–6830)	20.4 (13.5–27.4)
Kidney, renal pelvis	8920 (6420–11,390)	20.0 (14.4–25.5)	4080 (2890–5330)	16.2 (11.5–21.1)	13,000 (9310–16,710)	18.6 (13.3–23.9)
Acute myeloid leukemia	1620 (1040–2200)	18.5 (12.0–25.2)	990 (630–1380)	14.5 (9.2–20.3)	2600 (1670–3580)	16.7 (10.7–23.0)
Pancreas	4480 (3460–5490)	15.5 (11.9–19.0)	3240 (2470–4010)	12.1 (9.2–15.0)	7720 (5930–9500)	13.9 (10.6–17.0)
Colorectum	11,710 (9280–14,090)	15.2 (12.1–18.3)	8120 (6390–9870)	12.0 (9.4–14.6)	19,830 (15,670–23,970)	13.7 (10.8–16.6)
Ovary	—	—	170 (110–230)	0.8 (0.6–1.2)	170 (110–230)	0.8 (0.6–1.2)
Second-hand smoke						
Lung, bronchus	3440 (440–6620)	3.0 (0.4–5.7)	2630 (320–5180)	2.3 (0.3–4.6)	6070 (760–11,800)	2.7 (0.3–5.2)
Excess body weight						
Corpus uteri	—	—	32,090 (28,530–35,640)	53.1 (47.2–58.9)	32,090 (28,530–35,640)	53.1 (47.2–58.9)
Gallbladder	520 (470–580)	35.1 (31.2–39.2)	1120 (990–1260)	38.2 (33.7–43.1)	1640 (1450–1850)	37.1 (32.8–41.8)
Esophagus	5800 (5090–6460)	37.8 (33.2–42.1)	1100 (960–1230)	26.6 (23.3–29.9)	6900 (6050–7690)	35.4 (31.1–39.5)
Liver	7590 (5850–9140)	34.1 (26.3–41.1)	2830 (2170–3520)	37.0 (28.4–46.0)	10,420 (8020–12,660)	34.9 (26.8–42.4)

(Continues)

TABLE 2 (Continued)

	Men		Women		Both sexes combined	
Cancer	**Attributable cases, No. (95% CI)**	**PAF (95% CI), %**	**Attributable cases, No. (95% CI)**	**PAF (95% CI),%**	**Attributable cases, No. (95% CI)**	**PAF (95% CI), %**
Kidney, renal pelvis	14,680 (12,710–16,790)	32.9 (28.5–37.6)	8950 (7610–10,380)	35.5 (30.2–41.2)	23,630 (20,320–27,170)	33.8 (29.1–38.9)
Pancreas	5040 (3640–6220)	17.4 (12.6–21.5)	4960 (3690–6100)	18.5 (13.8–22.8)	10,000 (7330–12,310)	17.9 (13.2–22.1)
Stomach	2560 (2120–3020)	16.8 (13.9–19.8)	880 (720–1,060)	9.1 (7.4–10.9)	3450 (2840–4070)	13.8 (11.4–16.3)
Myeloma	1870 (1220–2510)	11.5 (7.5–15.4)	1600 (1060–2170)	12.3 (8.2–16.7)	3470 (2280–4680)	11.9 (7.8–16.0)
Thyroid	1350 (970–1680)	11.4 (8.2–14.1)	3570 (2590–4490)	11.8 (8.6–14.9)	4920 (3570–6170)	11.7 (8.5–14.7)
Breast, female	—	—	30,720 (27,550–34,240)	11.4 (10.2–12.7)	30,720 (27,550–34,240)	11.4 (10.2–12.7)
Colorectum	4020 (3030–5070)	5.2 (3.9–6.6)	3720 (2840–4640)	5.5 (4.2–6.8)	7740 (5860–9710)	5.3 (4.0–6.7)
Ovary	—	—	810 (430–1260)	4.1 (2.2–6.4)	810 (430–1260)	4.1 (2.2–6.4)
Alcohol consumption						
Oral cavity	10,350 (7900–13,450)	49.9 (38.1–64.9)	2600 (2010–3490)	25.1 (19.5–33.8)	12,950 (9910–16,940)	41.7 (31.9–54.5)
Pharynx	6460 (4160–9410)	44.6 (28.7–65.0)	760 (530–1160)	22.5 (15.6–34.2)	7220 (4690–10,570)	40.4 (26.2–59.1)
Larynx	2920 (2250–3810)	29.5 (22.7–38.4)	360 (290–450)	14.3 (11.5–17.9)	3280 (2540–4260)	26.4 (20.4–34.3)
Liver	5030 (2120–9470)	22.6 (9.6–42.6)	590 (270–1150)	7.7 (3.6–15.0)	5620 (2400–10,620)	18.8 (8.0–35.5)
Esophagus	2650 (2030–3130)	17.2 (13.2–20.4)	1000 (700–1410)	24.2 (17.0–34.2)	3650 (2730–4540)	18.7 (14.0–23.3)
Breast, female	—	—	44,180 (36,860–53,930)	16.4 (13.7–20.1)	44,180 (36,860–53,930)	16.4 (13.7–20.1)
Colorectum	13,850 (7390–22,610)	18.0 (9.6–29.4)	4630 (2710–7340)	6.8 (4.0–10.8)	18,480 (10,090–29,950)	12.8 (7.0–20.7)
Red meat consumption						
Colorectum	6250 (3150–9540)	8.1 (4.1–12.4)	4360 (2160–6620)	6.4 (3.2–9.8)	10,610 (5320–16,160)	7.3 (3.7–11.2)
Processed meat consumption						
Colorectum	11,220 (7020–15,410)	14.6 (9.1–20.0)	7320 (4470–10,260)	10.8 (6.6–15.1)	18,540 (11,500–25,660)	12.8 (7.9–17.7)
Low fruit and vegetable consumption						
Oral cavity	6320 (3060–9510)	30.5 (14.8–45.9)	3190 (1540–4780)	30.9 (14.9–46.2)	9520 (4600–14,280)	30.7 (14.8–46.0)
Esophagus	4690 (2170–7070)	30.6 (14.2–46.1)	1280 (590–1900)	31.0 (14.3–46.0)	5970 (2760–8970)	30.7 (14.2–46.1)
Pharynx	4440 (2070–6510)	30.6 (14.3–45.0)	1050 (490–1560)	31.0 (14.4–45.8)	5490 (2570–8070)	30.7 (14.4–45.1)
Larynx	3040 (1470–4480)	30.7 (14.8–45.2)	780 (370–1160)	31.0 (14.7–46.2)	3820 (1840–5640)	30.7 (14.8–45.4)

TABLE 2 (Continued)

Cancer	Men		Women		Both sexes combined	
	Attributable cases, No. (95% CI)	PAF (95% CI), %	Attributable cases, No. (95% CI)	PAF (95% CI),%	Attributable cases, No. (95% CI)	PAF (95% CI), %
Low dietary fiber consumption						
Colorectum	7180 (4510–9850)	9.3 (5.9–12.8)	7970 (5060–10,790)	11.8 (7.5–15.9)	15,150 (9570–20,630)	10.5 (6.6–14.3)
Low dietary calcium consumption						
Colorectum	2370 (1880–2870)	3.1 (2.4–3.7)	3720 (2980–4450)	5.5 (4.4–6.6)	6090 (4860–7320)	4.2 (3.4–5.1)
Physical inactivity						
Stomach	2680 (630–4580)	17.6 (4.1–30.0)	1840 (430–3100)	18.9 (4.4–31.9)	4520 (1060–7670)	18.1 (4.2–30.7)
Corpus uteri	—	—	7870 (4800–10,970)	13.0 (7.9–18.1)	7870 (4800–10,970)	13.0 (7.9–18.1)
Esophagus	1880 (90–3770)	12.3 (0.6–24.5)	550 (30–1090)	13.4 (0.7–26.5)	2430 (120–4860)	12.5 (0.6–25.0)
Kidney	4750 (2550–7250)	11.2 (6.0–17.1)	2870 (1570–4350)	12.1 (6.6–18.3)	7620 (4120–11,600)	11.5 (6.2–17.5)
Colon excluding rectum	4780 (3360–6230)	9.3 (6.5–12.1)	5150 (3620–6690)	10.2 (7.2–13.3)	9930 (6980–12,920)	9.8 (6.9–12.7)
Breast, female	—	—	18,810 (12,420–24,870)	7.0 (4.6–9.2)	18,810 (12,420–24,870)	7.0 (4.6–9.2)
Urinary bladder	2290 (0–4800)	3.9 (0.0–8.1)	790 (0–1630)	4.3 (0.0–8.8)	3080 (0–6430)	4.0 (0.0–8.3)
Ultraviolet radiation						
Melanoma of the skin	50,570 (50,080–51,010)	94.5 (93.6–95.3)	32,140 (31,560–32,740)	88.8 (87.2–90.4)	82,710 (81,630–83,740)	92.2 (91.0–93.3)
EBV infection						
Nasopharynx	790 (710–850)	61.5 (55.8–66.7)	340 (310–370)	61.1 (56.0–66.2)	1130 (1020–1220)	61.6 (55.6–66.5)
Hodgkin lymphoma	1190 (1110–1260)	35.5 (33.2–37.8)	870 (820–930)	34.5 (32.5–36.6)	2060 (1930–2190)	35.1 (32.9–37.3)
H. pylori infection						
Stomach	6220 (5530–6700)	40.8 (36.3–44.0)	5720 (5060–6210)	58.9 (52.1–63.9)	11,940 (10,590–12,920)	47.8 (42.4–51.8)
HBV infection						
Liver	2100 (1170–3170)	9.5 (5.3–14.3)	400 (220–620)	5.2 (2.9–8.2)	2500 (1400–3800)	8.4 (4.7–12.7)
HCV infection						
Liver	7640 (5630–9560)	34.4 (25.3–43.0)	1280 (820–1740)	16.7 (10.7–22.7)	8920 (6460–11,300)	29.9 (21.6–37.8)
Non-Hodgkin lymphoma	540 (270–910)	1.4 (0.7–2.3)	200 (90–350)	0.6 (0.3–1.1)	730 (360–1260)	1.0 (0.5–1.8)
HHV8 infection						
Kaposi sarcoma	820 (820–820)	100 (100–100)	80 (80–80)	100 (100–100)	890 (890–890)	100 (100–100)
HIV infection						
Kaposi sarcoma	670 (560–730)	82.1 (68.7–89.2)	40 (20–50)	50.0 (28.8–64.1)	710 (580–780)	79.5 (64.9–87.3)

(Continues)

TABLE 2 (Continued)

	Men		Women		Both sexes combined	
Cancer	Attributable cases, No. (95% CI)	PAF (95% CI), %	Attributable cases, No. (95% CI)	PAF (95% CI),%	Attributable cases, No. (95% CI)	PAF (95% CI), %
Anus	600 (400–770)	21.5 (14.3–27.4)	300 (160–450)	5.5 (3.0–8.2)	910 (560–1220)	11.0 (6.8–14.7)
Non-Hodgkin lymphoma	5690 (3460–7590)	14.3 (8.7–19.1)	700 (390–1030)	2.2 (1.2–3.2)	6380 (3850–8620)	8.9 (5.3–12.0)
Hodgkin lymphoma	250 (170–330)	7.5 (5.1–10.0)	30 (20–50)	1.3 (0.7–1.9)	280 (190–380)	4.8 (3.2–6.5)
Cervix uteri	—	—	80 (40–130)	0.6 (0.3–1.0)	80 (40–130)	0.6 (0.3–1.0)
HPV infection						
Cervix uteri	—	—	12,690 (12,690–12,690)	100 (100–100)	12,690 (12,690–12,690)	100 (100–100)
Anus	2530 (2450–2610)	90.2 (87.4–92.9)	5270 (5180–5350)	96.3 (94.6–97.7)	7800 (7630–7950)	94.2 (92.2–96.0)
Vagina	—	—	900 (630–1120)	64.1 (44.7–79.6)	900 (630–1120)	64.1 (44.7–79.6)
Penis	940 (480–1260)	60.5 (30.7–81.1)	—	—	940 (480–1260)	60.5 (30.7–81.1)
Vulva	—	—	2250 (1660–2810)	39.3 (29.0–49.0)	2250 (1660–2810)	39.3 (29.0–49.0)
Oropharynx, tonsils, base of tongue	6880 (5040–8710)	38.4 (28.1–48.6)	430 (260–630)	12.0 (7.2–17.6)	7310 (5300–9340)	34.0 (24.6–43.4)
Oral cavity	700 (10–1770)	3.4 (0.1–8.5)	100 (0–300)	1.0 (0.0-2.9)	800 (10–2070)	2.6 (0.0–6.7)

Note: Numbers of attributable cancer cases are rounded to the nearest 10. Cancer types associated with each risk factor are ordered by PAF in both sexes combined. PAFs are the proportions of the cancer types, as listed in the first column, attributable to the evaluated risk factor; for example, the PAFs for alcohol consumption and esophageal cancer shown in this table are the proportion of all esophageal cancers (any subtype, not the proportion of esophageal squamous cell carcinomas only) attributable to alcohol consumption.

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HIV, human immunodeficiency virus; HPV, human papillomavirus; *H. pylori*, *Helicobacter pylori*; PAF, population attributable fraction.

Physical inactivity

Physical inactivity was the sixth largest contributor to total cancer cases in men (1.8%; 16,540 cases) and the fourth largest contributor in women (4.4%; 38,030; Figure 1). Cancer of the stomach had the largest PAF for physical inactivity (18.1%; 4520 cases), but female breast (18,810) and colon (9930) cancer had the largest number of attributable cases (Table 2). The PAFs were comparable in men and women.

Ultraviolet radiation

Despite an association with only one cancer, UV radiation was the second largest contributor to total cancer cases in men (5.6%; 50,570 cases) and the fifth largest contributor in women (3.7%; 32,140; Figure 1). An estimated 92.2% of skin melanoma cases were attributable to UV radiation exposure, with slightly larger PAFs in men (94.5%) than in women (88.8%; Table 2).

Infections

Overall, 3.4% of all cancer cases were attributable to evaluated infections (Figure 3). By infection type, the PAF for all cases combined ranged from 0.1% to 1.2% in men and from <0.1% to 2.5% in women, with HPV infection having the largest PAF in both sexes, followed by HCV infection (0.9%) among men and *H. pylori* infection among women (0.7%; Figure 1). The cancer types with the largest number of cases attributable to a specific infection were cervical cancers attributable to HPV (12,690 cases), gastric cancers attributable to *H. pylori* (11,940), and liver cancers attributable to HCV (8920) infection (Table 2).

The PAFs were larger in men than in women for all cancer types attributable to HIV infection, HCV-attributable liver cancer, and HPV-attributable oropharyngeal, tonsils, and base of tongue cancer, whereas the proportion of anal cancers attributable to HPV infection and gastric cancer cases attributable to *H. pylori* was greater in women. The latter finding largely reflects a higher proportion of noncardia gastric cancers (the subtype associated with *H. pylori*

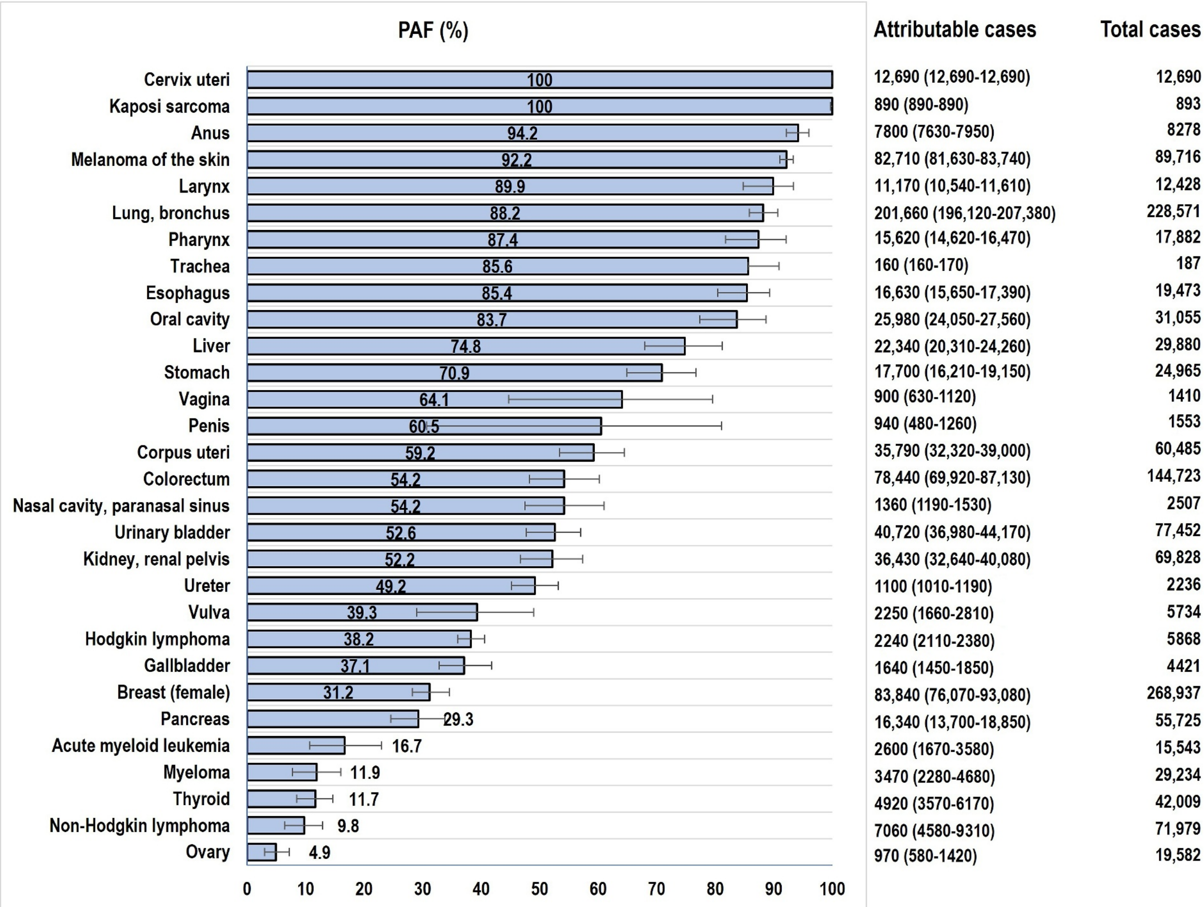

FIGURE 2 Estimated proportion and number of incident cancer cases attributable to evaluated risk factors and number of total cases in adults 30 years and older by cancer type, United States, 2019. The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer cases are rounded to the nearest 10. PAF indicates population-attributable fraction.

infection) among women; the prevalence of *H. pylori* infection in men and women was comparable (see Table S2). The PAFs for other cancer types attributable to carcinogenic infections were comparable by sex. The number of anal cancer cases attributable to HPV infection was larger in women (5270) than in men (2530); but, for other infections and associated cancer types, the number of attributable cancer cases was larger in men.

Cancer deaths attributable to evaluated risk factors

The PAF patterns for mortality were generally similar to those for incidence (Figure 4). The estimated proportion of all cancer deaths attributable to evaluated risk factors in adults aged 30 years and older in the United States in 2019 was 47.1% (147,810 of 313,711 deaths) in men, 40.5% (114,300 of 282,026) in women, and 44.0% in both sexes combined (262,120 of 595,737). Cigarette smoking contributed to 68.3% of all cancer deaths attributable to evaluated risk factors in men (100,950 of 147,810) and 60.2% in women (68,860 of 114,300). By cancer type, the risk factors considered in this analysis contributed to more than one half of the cancer deaths in 19 of 30 evaluated cancer types (Figure 5). Lung cancer had the largest number of attributable cancer deaths in both men (67,370 deaths) and women (55,370), followed by colorectal (14,580) and liver (11,300) cancer in men and breast (13,180) and colorectal (11,220) cancer in women (Table 4).

In both men and women, cigarette smoking contributed to the largest proportion and number of overall cancer deaths (32.2% [100,950] in men, 24.4% [68,860] in women), followed by excess body weight (6.5% [20,370] in men, 8.2% [23,150] in women), and alcohol consumption (4.6% [14,390 in men], 3.6% [10,020 in women]; Figure 4). The combination of excess body weight, alcohol consumption, dietary factors, and physical inactivity contributed to 17.0% of cancer deaths in men and 17.2% in women; the PAF for dietary factors (all dietary factors evaluated in this study combined) was 5.0% in men and 3.4% in women (Figure 3). The proportion of cancer deaths attributable to infections was 3.5% in men and 3.4% in women and was larger than the PAFs for UV radiation (1.6% in men, 0.9% in women). The proportions and numbers of cancer deaths attributable to evaluated risk factors by cancer type are shown in Table 5. Of note, 118,790 lung cancer deaths were attributable to cigarette smoking, contributing to 45.3% of all cancer deaths attributable to all evaluated risk factors in this study.

TABLE 3 Estimated proportion and number of incident cancer cases attributable to all evaluated risk factors and total number of cancer cases in adults 30 years and older by sex and cancer type: United States, 2019.

Cancer	PAF (95% CI), %	No. of attributable cases (95% CI)	Total no. of cases
Men			
Kaposi sarcoma	100 (100–100)	820 (820–820)	815
Melanoma of the skin	94.5 (93.6–95.3)	50,570 (50,080–51,010)	53,515
Larynx	90.6 (86.0–93.9)	8980 (8520–9310)	9911
Lung, bronchus	90.2 (87.5–92.9)	104,410 (101,340–107,570)	115,798
Anus	90.2 (87.4–92.9)	2530 (2450–2610)	2805
Pharynx	89.3 (84.0–93.8)	12,940 (12,170–13,590)	14,483
Trachea	88.6 (86.8–89.5)	100 (100–100)	114
Oral cavity	87.8 (82.3–92.1)	18,190 (17,060–19,070)	20,716
Esophagus	86.1 (81.3–89.7)	13,220 (12,480–13,770)	15,347
Liver	78.3 (71.3–84.7)	17,410 (15,860–18,840)	22,231
Stomach	68.2 (62.4–74.4)	10,400 (9510–11,340)	15,243
Penis	60.5 (30.7–81.1)	940 (480–1260)	1553
Colorectum	57.6 (51.1–64.4)	44,310 (39,350–49,560)	76,943
Nasal cavity, paranasal sinus	56.8 (50.0–63.4)	860 (750–960)	1508
Urinary bladder	54.3 (49.6–58.7)	32,000 (29,220–34,580)	58,928
Ureter	52.4 (48.3–56.4)	730 (670–780)	1384
Kidney, renal pelvis	52.1 (46.9–57.2)	23,270 (20,910–25,550)	44,633
Hodgkin lymphoma	40.4 (37.8–42.9)	1350 (1260–1430)	3341
Gallbladder	35.1 (31.2–39.2)	520 (470–580)	1489
Pancreas	30.1 (25.4–34.7)	8730 (7350–10,050)	28,964
Acute myeloid leukemia	18.5 (12.0–25.2)	1620 (1040–2200)	8732
Non–Hodgkin lymphoma	15.5 (10.1–20.2)	6170 (4010–8040)	39,776
Myeloma	11.5 (7.5–15.4)	1870 (1220–2510)	16,256
Thyroid	11.4 (8.2–14.1)	1350 (970–1680)	11,863
Women			
Cervix uteri	100 (100–100)	12,690 (12,690–12,690)	12,690
Kaposi sarcoma	100 (100–100)	80 (80–80)	78
Anus	96.3 (94.6–97.7)	5270 (5180–5350)	5473
Melanoma of the skin	88.8 (87.2–90.4)	32,140 (31,560–32,740)	36,201
Larynx	87.0 (80.2–91.5)	2190 (2020–2300)	2517
Lung, bronchus	86.2 (84.0–88.5)	97,250 (94,780–99,810)	112,773
Trachea	84.9 (83.6–86.3)	60 (60–60)	73
Esophagus	82.9 (77.0–87.7)	3420 (3180–3620)	4126
Pharynx	79.0 (72.1–84.7)	2690 (2450–2880)	3399
Oral cavity	75.3 (67.6–82.1)	7790 (6990–8480)	10,339
Stomach	75.1 (69.0–80.4)	7300 (6700–7820)	9722
Liver	64.4 (58.1–70.9)	4930 (4450–5420)	7649
Vagina	64.1 (44.7–79.6)	900 (630–1120)	1410
Corpus uteri	59.2 (53.4–64.5)	35,790 (32,320–39,000)	60,485

TABLE 3 (Continued)

Cancer	PAF (95% CI), %	No. of attributable cases (95% CI)	Total no. of cases
Kidney, renal pelvis	52.2 (46.6–57.7)	13,160 (11,730–14,530)	25,195
Colorectum	50.4 (45.1–55.4)	34,130 (30,560–37,570)	67,780
Nasal cavity, paranasal sinus	50.2 (43.3–57.1)	500 (430–570)	999
Urinary bladder	47.0 (41.9–51.8)	8710 (7760–9590)	18,524
Ureter	44.1 (40.1–48.2)	380 (340–410)	852
Vulva	39.3 (29.0–49.0)	2250 (1660–2810)	5734
Gallbladder	38.2 (33.7–43.1)	1120 (990–1260)	2932
Hodgkin lymphoma	35.3 (33.3–37.4)	890 (840–950)	2527
Breast, female	31.2 (28.3–34.6)	83,840 (76,070–93,080)	268,937
Pancreas	28.4 (23.7–32.9)	7610 (6350–8800)	26,761
Acute myeloid leukemia	14.5 (9.2–20.3)	990 (630–1380)	6811
Myeloma	12.3 (8.2–16.7)	1600 (1060–2170)	12,978
Thyroid	11.8 (8.6–14.9)	3570 (2590–4490)	30,146
Ovary	4.9 (3.0–7.2)	970 (580–1420)	19,582
Non-Hodgkin lymphoma	2.8 (1.8–3.9)	890 (570–1270)	32,203

Note: Numbers by sex may not sum to the totals because numbers were rounded to the nearest 10. Cancer types are ordered by PAF.
Abbreviations: CI, confidence interval; PAF, population-attributable fraction.

Sensitivity analysis using contemporary risk factor data

Among men, the overall PAF for cancer cases (39.3%; see Figure S1) and cancer deaths (45.3%; see Figure S2) using contemporary risk factor data were slightly smaller than the PAFs described above (40.5% and 47.1%, respectively), largely because of the smaller PAFs for cigarette smoking in the sensitivity analysis (21.3% vs. 22.7% for cancer cases; 30.3% vs. 32.2% for cancer deaths). Among women, the PAF was smaller for cigarette smoking (14.4% vs. 15.8% for cancer cases; 22.4% vs. 24.4% for cancer deaths) but was slightly larger for excess body weight (11.5% vs. 10.6% for cancer cases; 8.7% vs. 8.2% for cancer deaths). Consequently, the overall PAFs for cancer cases among women in the main and sensitivity analyses were comparable. In both sexes, PAFs for other risk factors in the main and sensitivity analyses were similar.

DISCUSSION

Based on up-to-date data on RRs and cancer occurrence, we estimated that 40% of all incident cancer cases and almost one half of all cancer deaths in the United States in 2019 were attributable to evaluated risk factors, representing 713,340 cancer cases and 262,120 deaths. Cigarette smoking was associated with far more cancer cases and deaths than any other single risk factor, contributing to nearly 20% of all cancer cases and 30% of all cancer deaths (344,070 cases and 169,810 deaths), followed by excess body weight (135,910 cases and 43,520 deaths), and alcohol consumption (96,730 cases and 24,410 deaths). Lung cancer had the largest number of cancer cases or deaths attributable to potentially modifiable risk factors.

Our overall PAFs are generally comparable to those from recent studies using similar methods.[4,25,29,30] For example, a previous study estimated that 4.3% of cancer cases among individuals aged 20 years and older in the United States in 2017 were attributable to infections[4]; our estimated proportion for those aged 30 years and older was 3.4%. However, there are some notable differences. For example, previous studies reported larger proportions of liver cancers attributable to HCV infection in women (26%–28%) than in men (18%–19%),[31,32] whereas we observed the reverse (34% in men vs. 17% in women), consistent with higher HCV infection prevalence in men.[33] Higher proportions of cancer ceases (7.4%) and deaths (7.7%) among US adults in 2017 attributable to dietary factors over a lifetime in another study, compared with our study (4.2% and 4.3%, respectively), may be caused in part by the inclusion of sugar-sweetened beverage consumption in that study because it may increase the risk of obesity-associated cancers by contributing to obesity.[34] We considered obesity separately and did not include these beverages in our analysis. Moreover, that study[34] linked processed meat consumption to noncardia gastric cancer and included low consumption of whole grains and dairy products, whereas we included dietary fiber and calcium.

In addition to differences in sources of RRs, evaluated risk factors and cancer types, targeted populations, and other methodological variations, some of the differences between our estimates and

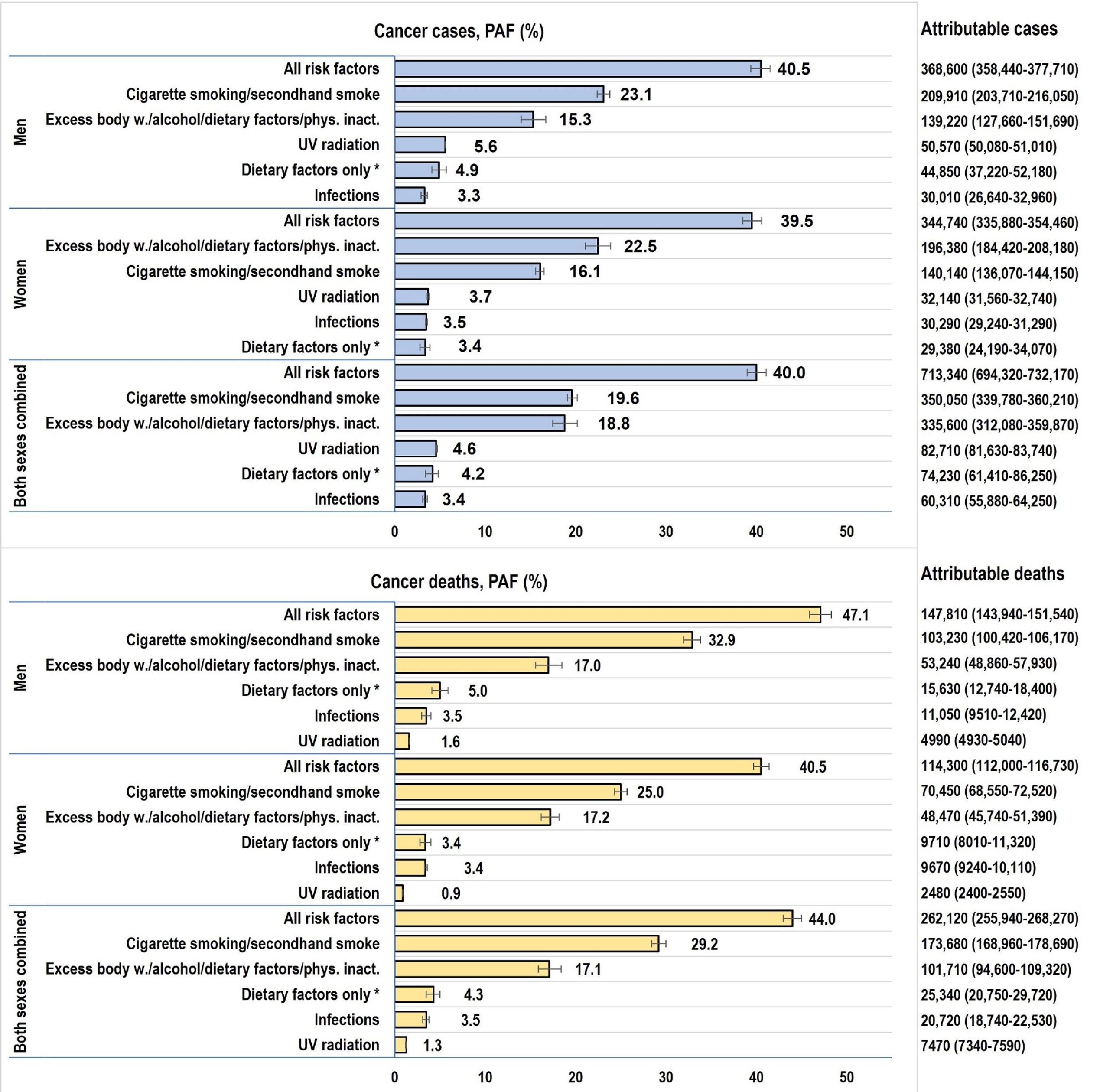

FIGURE 3 Estimated proportion and number of incident cancer cases (excluding nonmelanoma skin cancers) and cancer deaths attributable to risk factor groups in adults 30 years and older by sex, United States, 2019. The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer cases and deaths are rounded to the nearest 10. Infections include *Helicobacter pylori*; hepatitis B virus; hepatitis C virus; human herpes virus type 8; human immunodeficiency virus (only associated non-Hodgkin lymphoma); and human papillomavirus infections. Excess body w. indicates excess body weight; PAF, population-attributable fraction; phys. inact., physical inactivity; UV, ultraviolet. *Dietary factors associated with cancer risk (consumption of red and processed meat and low consumption of fruits and vegetables, dietary fiber, and dietary calcium) are also included in the larger group of excess body weight, alcohol consumption, dietary factors, and physical inactivity combined.

results from other studies may be attributed to variations in the year of risk factor measurement because the prevalence of risk factors in the population may change over time. For example, larger PAFs for cigarette smoking and cancer deaths in previous studies,[35,36] e.g., 33% based on smoking prevalence in 2003–2006,[36] likely in part reflect higher prevalence of cigarette smoking in the United States in earlier periods.[37,38]

The overall PAF for cancer cases in this study (40.0%) was slightly smaller than our previous estimate (42.0% for 2014),[1] but the number of cancer cases attributable to evaluated risk factors was greater in the current study (713,340 vs. 659,640), largely reflecting an increase in the number of cancers from 2014 to 2019 in the United States caused by aging and population growth. An increase in the number of attributable cases for some cancer types, such as

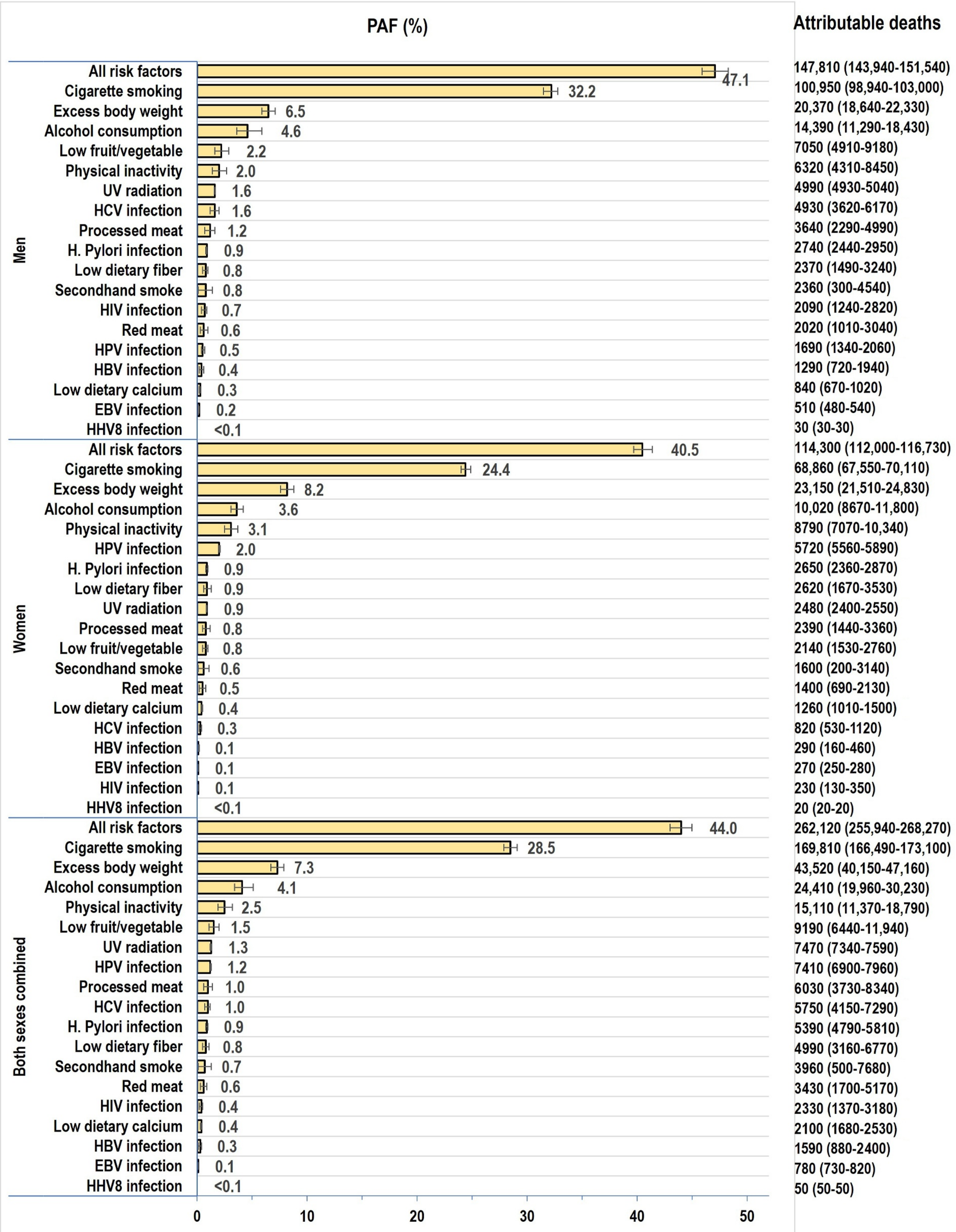

FIGURE 4 Estimated proportion and number of cancer deaths attributable to evaluated risk factors in adults 30 years and older by sex, United States, 2019. The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer deaths are rounded to the nearest 10. EBV indicates Epstein–Barr virus; *H. pylori*, *Helicobacter pylori*; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HPV, human papillomavirus; PAF, population-attributable fraction; UV, ultraviolet.

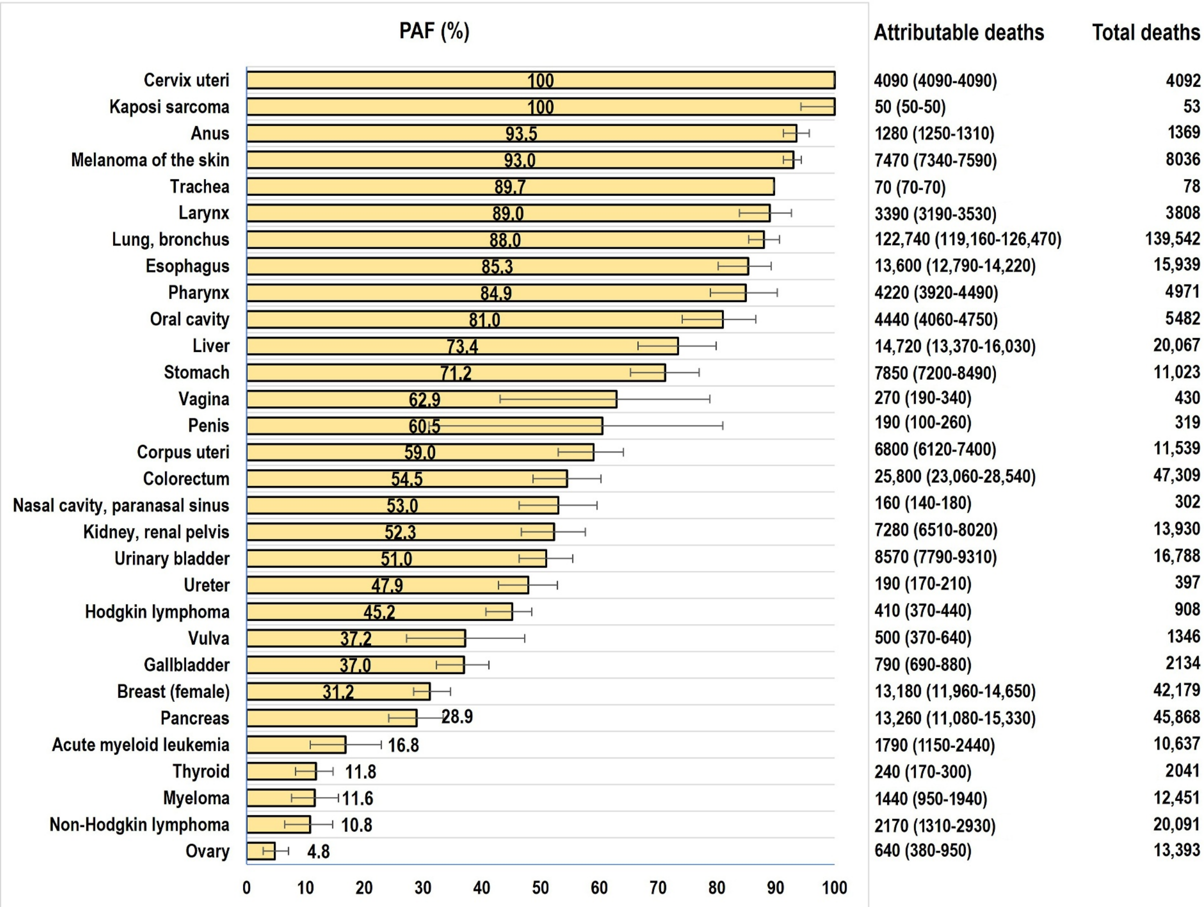

FIGURE 5 Estimated proportion and number of cancer deaths attributable to evaluated risk factors and number of total cancer deaths in adults 30 years and older by cancer type, United States, 2019. The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer deaths are rounded to the nearest 10.

breast and pancreatic cancer, may additionally reflect a continuous rise in incidence rates.[39] In contrast, the estimated proportion and number of attributable cancer deaths were both slightly smaller in this study (44.1%; 262,120 deaths) than in the previous study (45.1%; 265,150 deaths).[1] Of note, for our previous estimates, we used contemporary risk factor data, mostly from 2011–2014. In addition to differences in the years of exposure and cancer occurrence data, there were some other differences between our two studies and estimates. The most notable difference was an increase in the number of cancer types associated with physical inactivity, from three in the previous study to seven based on a more recent evaluation of evidence.[2] Conversely, the updated RRs for physical inactivity and cancer risk from a large-scale pooled analysis of cohort studies[3] were generally smaller than the RRs used for our previous estimates, largely offsetting the effect of increases in the number of cancer types associated with physical inactivity. The other notable differences include updated RRs for carcinogenic infections[4] and updated cancer types associated with low fruit and vegetable consumption; in the previous report, low fruit consumption was considered to be associated with lung cancer risk.[10] It should be noted that, because of these methodological differences, our current and previous estimates are not directly comparable.

Cigarette smoking

Among potentially modifiable risk factors evaluated in this study, cigarette smoking remains the leading contributor to cancer cases and deaths in both men (22.7% and 32.2%, respectively) and women (15.8% and 24.4%, respectively). As such, expanding comprehensive tobacco control programs can have the greatest impact on reducing cancer cases and deaths. Among tobacco control policies, increasing the price of cigarettes through excise taxes has shown the strongest effect in the United States.[40,41] The US Surgeon General has suggested raising the average retail price of cigarettes to at least $10 a pack.[19] In 2019, the average price of a pack of cigarettes in the United States ranged from $5.21 in Missouri to $10.53 in New York; and, because of a low cigarette excise tax in many states, the price was $10 or higher in only two states and the District of Columbia.[42] As of December 2023, the state cigarette excise tax ranged from $0.17 in Missouri to $5.35 in New York (with an additional $1.50 in New York City) per cigarette pack, with the highest combined state and local excise tax in Chicago ($7.16 per cigarette pack); in the majority of states with the lowest cigarette excise tax, the tax had not increased in more than 10 years.[43] There is also wide variation across states in the implementation of other effective measures to

TABLE 4 Estimated proportion and number of cancer deaths attributable to all evaluated risk factors and total number of cancer deaths in adults 30 years and older by sex and cancer type: United States, 2019.

Cancer	PAF (95% CI), %	Attributable deaths (95% CI)	Total deaths
Men			
Kaposi sarcoma	100 (100–100)	30 (30–30)	34
Melanoma of the skin	94.8 (93.8–95.8)	4990 (4930–5040)	5259
Anus	90.2 (87.4–3.1)	510 (490–520)	563
Lung, bronchus	90.0 (87.2–93.0)	67,370 (65,270–69,570)	74,827
Larynx	90.0 (84.9–93.3)	2730 (2580–2840)	3037
Pharynx	87.5 (81.6–92.5)	3340 (3110–3530)	3812
Trachea	87.5 (87.5–87.5)	40 (40–40)	48
Esophagus	86.0 (81.2–89.6)	11,010 (10,390-11,480)	12,803
Oral cavity	85.9 (79.7–90.6)	3040 (2820–3210)	3540
Liver	77.4 (70.5–84.0)	11,300 (10,290–12,260)	14,595
Stomach	68.4 (62.6–74.5)	4500 (4120–4910)	6582
Penis	60.5 (31.0–81.0)	190 (100–260)	319
Colorectum	58.0 (51.9–64.4)	14,580 (13,030–16,170)	25,115
Nasal cavity, paranasal sinus	56.2 (49.4–62.4)	100 (90-110)	178
Urinary bladder	53.6 (49.0–57.9)	6450 (5910–6970)	12,051
Kidney, renal pelvis	52.5 (47.1–57.7)	4810 (4320–5290)	9171
Ureter	51.6 (47.0–56.3)	110 (100–120)	215
Hodgkin lymphoma	46.6 (43.1–50.2)	250 (230–270)	536
Gallbladder	34.8 (31.0–38.8)	240 (220–270)	701
Pancreas	29.8 (25.0–34.4)	7060 (5920–8160)	23,718
Acute myeloid leukemia	18.6 (12.1–25.2)	1150 (750–1570)	6216
Non-Hodgkin lymphoma	17.5 (10.5–23.3)	1990 (1190–2650)	11,367
Thyroid	11.5 (8.4–14.3)	110 (80–140)	955
Myeloma	11.3 (7.4–15.1)	780 (510–1050)	6957
Women			
Cervix uteri	100 (100–100)	4090 (4090–4090)	4092
Kaposi sarcoma	100 (100–100)	20 (20–20)	19
Anus	96.3 (94.5–97.9)	780 (760–790)	806
Melanoma of the skin	89.2 (86.6–91.7)	2480 (2400–2550)	2777
Trachea	86.7 (86.7–90.0)	30 (30–30)	30
Larynx	85.9 (79.1–90.6)	660 (610–700)	771
Lung, bronchus	85.6 (83.3–87.9)	55,370 (53,890–56,900)	64,715
Esophagus	82.5 (76.5–87.4)	2590 (2400–2740)	3136
Pharynx	76.6 (69.4–82.7)	890 (800–960)	1159
Stomach	75.3 (69.3–80.8)	3340 (3080–3590)	4441
Oral cavity	72.3 (64.0–79.4)	1400 (1240–1540)	1942
Vagina	62.9 (43.1–78.8)	270 (190–340)	430
Liver	62.4 (56.3–69.0)	3420 (3080–3780)	5472

(Continues)

TABLE 4 (Continued)

Cancer	PAF (95% CI), %	Attributable deaths (95% CI)	Total deaths
Corpus uteri	59.0 (53.0–64.1)	6800 (6120–7400)	11,539
Kidney, renal pelvis	51.9 (46.1–57.3)	2470 (2200–2730)	4759
Colorectum	50.6 (45.2–55.7)	11,220 (10,030–12,370)	22,194
Nasal cavity, paranasal sinus	46.8 (40.3–53.2)	60 (50–70)	124
Urinary bladder	44.6 (39.8–49.4)	2120 (1880–2340)	4737
Hodgkin lymphoma	41.8 (38.4–45.1)	160 (140–170)	372
Ureter	41.2 (37.4–46.2)	80 (70–80)	182
Gallbladder	37.8 (33.3–42.6)	540 (480–610)	1433
Vulva	37.2 (27.2–47.3)	500 (370–640)	1346
Breast, female	31.2 (28.4–34.7)	13,180 (11,960–14,650)	42,179
Pancreas	28.0 (23.3–32.4)	6200 (5160–7170)	22,150
Acute myeloid leukemia	14.3 (9.0–19.8)	630 (400–880)	4421
Thyroid	12.1 (8.7–15.1)	130 (90–160)	1086
Myeloma	12.0 (7.9–16.3)	660 (440–890)	5494
Ovary	4.8 (2.8–7.1)	640 (380–950)	13,393
Non-Hodgkin lymphoma	2.1 (1.3–3.1)	190 (110–280)	8724

Note: Numbers by sex may not sum to the totals because numbers were rounded to the nearest 10. Cancer types are ordered by PAF.
Abbreviations: CI, confidence interval; PAF, population-attributable fraction.

reduce smoking, including smoke-free laws, assistance with smoking cessation, warning labels and media campaigns, and marketing bans.[40,41,44] These variations have collectively contributed to substantial differences in smoking prevalence and the burden of cancer attributable to cigarette smoking across states.[45] Although cigarette smoking prevalence has declined dramatically during the past few decades,[46] there is a need for further political commitment to tobacco control at the local, state, and federal levels to substantially reduce the burden of diseases caused by smoking.[44,47,48]

It is important to enhance support for smoking cessation because quitting smoking in all ages, especially in younger ages, is associated with a substantial reduction in the excess cancer mortality risk associated with smoking.[49,50] However, smoking cessation services, such as counseling and medication, are generally underused,[51] particularly in individuals with lower incomes and those who are uninsured[52] and in several states with the highest cigarette smoking prevalence,[53] underscoring the need for enhancing equitable access to cessation services. Moreover, receipt of the recommended lung cancer screening among high-risk current and former smoking individuals remains low, e.g., less than 7% nationally in 2019 and 2021, with substantial variations across states.[54]

Excess body weight, alcohol consumption, dietary factors, and physical inactivity

We estimated that of all cancer cases and deaths in the United States, nearly 7%–8% were attributable to excess body weight, 4%–5% were attributable to alcohol consumption, 4% were attributable to dietary factors (all evaluated dietary factors combined), and 3% were attributable to physical inactivity. Among dietary factors, low fruit and vegetable consumption contributed to most cancer cases and deaths. The combination of excess body weight, alcohol consumption, dietary factors, and physical inactivity contributed to the largest proportion of all cancer cases in women (nearly one fourth of all cases) and was second only to tobacco smoking in men (one sixth of all cases). These four combined risk factors also contributed to the second highest proportion of cancer deaths in both sexes, i.e., nearly one fifth of all cancer deaths in men and one fourth of all cancer deaths in women.

These findings suggest that maintaining a healthy body weight, cessation or limiting alcohol consumption (for those who drink), consuming a healthy diet, and being physically active can substantially reduce the number of cancer cases and deaths in the United States. This conclusion is consistent with results of several previous studies that have shown a reduced risk of developing and dying from cancer in individuals who adhere to comprehensive guidelines on weight, nutrition, and physical activity,[55–58] including those of the American Cancer Society.[59] Of note, the prevalence of obesity and severe obesity among US adults and children has substantially increased during the past few decades.[60,61] Currently, 42% of adults aged 20 years and older and 20% of children and adolescents aged 2–19 years are affected by obesity.[62] Furthermore, more than one half (54%) of adults aged 21 years and older reported alcohol consumption in the past month in 2021–2022,[63] and only 12% of individuals aged 18 years and older met recommended vegetable and fruit consumption in 2021.[64]

TABLE 5 Estimated cancer deaths in adults 30 years and older attributable to potentially modifiable risk factors by sex, risk factor, and cancer type: United States, 2019.

Cancer	Men		Women		Both sexes combined	
	Attributable cases, No. (95% CI)	PAF, % (95% CI)	Attributable cases, No. (95% CI)	PAF, % (95% CI)	Attributable cases, No. (95% CI)	PAF, % (95% CI)
Cigarette smoking						
Trachea	40 (40–40)	87.5 (87.5–87.5)	30 (30–30)	86.7 (86.7–90.0)	70 (70–70)	89.7 (89.7–89.7)
Lung, bronchus	65,040 (64,550–65,530)	86.9 (86.3–87.6)	53,750 (53,250–54,270)	83.1 (82.3–83.9)	118,790 (117,800–119,800)	85.1 (84.4–85.9)
Larynx	2420 (2180–2600)	79.6 (71.9–85.6)	590 (520–640)	76.4 (67.4–83.1)	3010 (2700–3240)	79.0 (70.9–85.1)
Pharynx	2170 (1900–2410)	56.9 (49.9–63.3)	570 (490–650)	49.5 (42.6–56.3)	2740 (2390–3060)	55.1 (48.1–61.6)
Esophagus	7080 (6500–7620)	55.3 (50.7–59.5)	1490 (1360–1630)	47.6 (43.2–51.9)	8570 (7850–9250)	53.8 (49.3–58.0)
Nasal cavity, paranasal sinus	100 (90–110)	56.2 (49.4–62.4)	60 (50–70)	46.8 (40.3–53.2)	160 (140–180)	53.0 (46.4–59.6)
Oral cavity	1970 (1740–2200)	55.8 (49.2–62.2)	910 (780–1040)	46.8 (40.3–53.4)	2880 (2530–3240)	52.5 (46.2–59.1)
Urinary bladder	6230 (5690–6730)	51.7 (47.2–55.9)	2000 (1800–2190)	42.3 (38.1–46.2)	8230 (7500–8920)	49.0 (44.7–53.1)
Ureter	110 (100–120)	51.6 (47.0–56.3)	80 (70–80)	41.2 (37.4–46.2)	190 (170–210)	47.9 (42.8–52.9)
Liver	3980 (3130–4870)	27.3 (21.4–33.3)	1160 (900–1440)	21.2 (16.5–26.3)	5140 (4030–6310)	25.6 (20.1–31.4)
Cervix uteri	—	—	900 (530–1240)	22.0 (13.0–30.3)	900 (530–1240)	22.0 (13.0–30.3)
Stomach	1430 (940–1900)	21.7 (14.2–28.9)	750 (490–1020)	17.0 (11.0–22.9)	2180 (1420–2920)	19.8 (12.9–26.5)
Kidney, renal pelvis	1880 (1370–2360)	20.5 (14.9–25.7)	740 (530–940)	15.6 (11.2–19.8)	2620 (1900–3300)	18.8 (13.6–23.7)
Acute myeloid leukemia	1150 (750–1570)	18.6 (12.1–25.2)	630 (400–880)	14.3 (9.0–19.8)	1790 (1150–2440)	16.8 (10.8–22.9)
Pancreas	3580 (2750–4420)	15.1 (11.6–18.6)	2590 (1970–3220)	11.7 (8.9–14.5)	6170 (4710–7640)	13.5 (10.3–16.7)
Colorectum	3780 (3010–4530)	15.1 (12.0–18.1)	2500 (1980–3050)	11.3 (8.9–13.7)	6280 (4990–7580)	13.3 (10.5–16.0)
Ovary	—	—	90 (60–120)	0.6 (0.4–0.9)	90 (60–120)	0.6 (0.4–0.9)
Second-hand smoke						
Lung, bronchus	2360 (300–4540)	3.1 (0.4–6.1)	1600 (200–3140)	2.5 (0.3–4.8)	3960 (500–7680)	2.8 (0.4–5.5)
Excess body weight						
Corpus uteri	—	—	6060 (5410–6720)	52.5 (46.9–58.2)	6060 (5410–6720)	52.5 (46.9–58.2)
Gallbladder	240 (220–270)	34.8 (31.0–38.8)	540 (480–610)	37.8 (33.3–42.6)	790 (690–880)	37.0 (32.3–41.2)
Esophagus	4820 (4230–5350)	37.6 (33.0–41.8)	840 (730–940)	26.6 (23.3–29.9)	5650 (4960–6290)	35.4 (31.1–39.5)
Liver	4960 (3820–5950)	34.0 (26.2–40.8)	1990 (1520–2470)	36.4 (27.9–45.2)	6950 (5340–8430)	34.6 (26.6–42.0)

(Continues)

TABLE 5 (Continued)

Cancer	Men: Attributable cases, No. (95% CI)	Men: PAF, % (95% CI)	Women: Attributable cases, No. (95% CI)	Women: PAF, % (95% CI)	Both sexes combined: Attributable cases, No. (95% CI)	Both sexes combined: PAF, % (95% CI)
Kidney, renal pelvis	2970 (2560–3390)	32.4 (27.9–37.0)	1650 (1410–1900)	34.7 (29.6–39.9)	4620 (3970–5290)	33.2 (28.5–38.0)
Pancreas	4100 (2970–5070)	17.3 (12.5–21.4)	4080 (3040–5020)	18.4 (13.7–22.7)	8180 (6010–10,100)	17.8 (13.1–22.0)
Stomach	1080 (890–1270)	16.4 (13.5–19.3)	390 (320–470)	8.9 (7.3–10.7)	1470 (1210–1740)	13.3 (11.0–15.8)
Breast, female	—	—	5080 (4530–5640)	12.0 (10.7–13.4)	5080 (4530–5640)	12.0 (10.7–13.4)
Thyroid	110 (80–140)	11.5 (8.4–14.3)	130 (90–160)	12.1 (8.7–15.1)	240 (170–300)	11.8 (8.3–14.7)
Myeloma	780 (510–1050)	11.3 (7.4–15.1)	660 (440–890)	12.0 (7.9–16.3)	1440 (950–1940)	11.6 (7.6–15.6)
Colorectum	1290 (980–1630)	5.2 (3.9–6.5)	1190 (910–1480)	5.3 (4.1–6.7)	2480 (1880–3110)	5.2 (4.0–6.6)
Ovary	—	—	560 (300–870)	4.1 (2.2–6.5)	560 (300–870)	4.1 (2.2–6.5)
Alcohol consumption						
Oral cavity	1730 (1320–2260)	48.8 (37.2–63.7)	450 (340–600)	22.9 (17.7–30.7)	2170 (1660–2850)	39.6 (30.3–52.0)
Pharynx	1670 (1060–2450)	43.7 (27.8–64.3)	240 (170–370)	21.1 (14.6–32.3)	1910 (1230–2830)	38.4 (24.7–56.9)
Larynx	870 (670–1150)	28.8 (22.1–37.7)	110 (90–130)	13.6 (11.0–17.0)	980 (760–1280)	25.7 (20.0–33.6)
Esophagus	2190 (1670–2600)	17.1 (13.1–20.3)	740 (520–1050)	23.6 (16.5–33.4)	2930 (2190–3650)	18.4 (13.7–22.9)
Liver	3260 (1380–6140)	22.3 (9.5–42.0)	400 (190–770)	7.3 (3.4–14.0)	3660 (1570–6900)	18.2 (7.8–34.4)
Breast, female	—	—	6620 (5530–8080)	15.7 (13.1–19.2)	6620 (5530–8080)	15.7 (13.1–19.2)
Colorectum	4360 (2310–7160)	17.4 (9.2–28.5)	1390 (810–2250)	6.3 (3.6–10.1)	5760 (3120–9410)	12.2 (6.6–19.9)
Red meat consumption						
Colorectum	2020 (1010–3040)	8.1 (4.0–12.1)	1400 (690–2130)	6.3 (3.1–9.6)	3430 (1700–5170)	7.3 (3.6–10.9)
Processed meat consumption						
Colorectum	3640 (2290–4990)	14.5 (9.1–19.9)	2390 (1440–3360)	10.8 (6.5–15.1)	6030 (3730–8340)	12.7 (7.9–17.6)
Low fruit and vegetable consumption						
Larynx	930 (450–1360)	30.6 (14.8–44.9)	240 (110–350)	30.6 (14.7–45.6)	1170 (560–1720)	30.7 (14.7–45.2)
Esophagus	3910 (1810–5,880)	30.5 (14.1–45.9)	970 (450–1440)	30.9 (14.4–45.9)	4880 (2260–7320)	30.6 (14.2–45.9)
Pharynx	1150 (540–1690)	30.2 (14.1–44.4)	350 (170–520)	30.5 (14.4–45.1)	1510 (710–2220)	30.4 (14.3–44.7)
Oral cavity	1070 (530–1610)	30.2 (14.8–45.6)	590 (290–890)	30.6 (15.0–45.7)	1660 (820–2500)	30.3 (15.0–45.6)

TABLE 5 (Continued)

Cancer	Men		Women		Both sexes combined	
	Attributable cases, No. (95% CI)	PAF, % (95% CI)	Attributable cases, No. (95% CI)	PAF, % (95% CI)	Attributable cases, No. (95% CI)	PAF, % (95% CI)
Low dietary fiber consumption						
Colorectum	2370 (1490–3240)	9.4 (5.9–12.9)	2620 (1670–3530)	11.8 (7.5–15.9)	4990 (3160–6770)	10.5 (6.7–14.3)
Low dietary calcium consumption						
Colorectum	840 (670–1020)	3.4 (2.7–4.1)	1260 (1010–1500)	5.7 (4.5–6.8)	2100 (1680–2530)	4.4 (3.6–5.3)
Physical inactivity						
Stomach	1170 (270–1990)	17.7 (4.1–30.3)	860 (190–1440)	19.3 (4.2–32.5)	2020 (460–3440)	18.3 (4.2–31.2)
Corpus uteri	—	—	1550 (940–2170)	13.5 (8.2–18.8)	1550 (940–2170)	13.5 (8.2–18.8)
Esophagus	1580 (70–3160)	12.3 (0.5–24.7)	420 (20–850)	13.5 (0.6–27.0)	2000 (90–4010)	12.5 (0.6–25.2)
Kidney	1050 (560–1610)	11.6 (6.2–17.7)	600 (310–910)	12.8 (6.6–19.4)	1650 (870–2520)	12.0 (6.3–18.3)
Colon, excluding rectum	2000 (1410–2610)	9.5 (6.6–12.4)	2070 (1440–2700)	10.5 (7.3–13.7)	4080 (2850–5320)	10.0 (7.0–13.0)
Breast, female	—	—	3060 (1990–4090)	7.3 (4.7–9.7)	3060 (1990–4090)	7.3 (4.7–9.7)
Urinary bladder	480 (0–1020)	4.0 (0.0–8.4)	210 (0–440)	4.4 (0.0–9.3)	690 (0–1460)	4.1 (0.0–8.7)
Ultraviolet radiation						
Melanoma of the skin	4990 (4930–5040)	94.8 (93.8–95.8)	2480 (2400–2550)	89.2 (86.6–91.7)	7470 (7340–7590)	93.0 (91.3–94.4)
EBV infection						
Nasopharynx	290 (270–320)	61.3 (55.9–66.7)	120 (110–130)	61.7 (56.4–67.0)	410 (370–450)	61.4 (55.4–67.4)
Hodgkin lymphoma	220 (200–230)	40.3 (37.4–43.3)	150 (140–170)	41.1 (37.6–44.4)	370 (340–400)	40.7 (37.4–44.1)
H. pylori infection						
Stomach	2740 (2440–2950)	41.6 (37.0–44.8)	2650 (2360–2870)	59.7 (53.0–64.5)	5390 (4790–5810)	48.9 (43.5–52.7)
HBV infection						
Liver	1290 (720–1940)	8.9 (4.9–13.3)	290 (160–460)	5.3 (3.0–8.4)	1590 (880–2400)	7.9 (4.4–12.0)
HCV infection						
Liver	4800 (3510–5990)	32.9 (24.1–41.1)	780 (500–1090)	14.3 (9.1–19.8)	5580 (4010–7080)	27.8 (20.0–35.3)
Non-Hodgkin lymphoma	130 (60–210)	1.1 (0.6–1.9)	40 (20–60)	0.4 (0.2–0.7)	160 (80–280)	0.8 (0.4–1.4)
HHV8 infection						
Kaposi sarcoma	30 (30–30)	100 (100–100)	20 (20–20)	100 (100–100)	50 (50–50)	100 (100–100)
HIV infection						
Kaposi sarcoma	30 (30–30)	94.1 (73.5–100)	10 (10–20)	57.9 (26.3–78.9)	40 (30–50)	75.5 (56.6–94.3)

(Continues)

TABLE 5 (Continued)

	Men		Women		Both sexes combined	
Cancer	**Attributable cases, No. (95% CI)**	**PAF, % (95% CI)**	**Attributable cases, No. (95% CI)**	**PAF, % (95% CI)**	**Attributable cases, No. (95% CI)**	**PAF, % (95% CI)**
Anus	130 (90–170)	23.8 (15.3–30.7)	40 (20–60)	4.7 (2.6–6.9)	170 (110–230)	12.4 (8.0–16.8)
Non-Hodgkin lymphoma	1870 (1090–2550)	16.5 (9.5–22.4)	150 (80–240)	1.7 (0.9–2.7)	2020 (1170–2790)	10.1 (5.8–13.9)
Hodgkin lymphoma	60 (30–80)	10.6 (6.4–14.6)	10 (0–10)	1.3 (0.5–2.2)	60 (40–90)	6.6 (4.4–9.9)
Cervix uteri	—	—	30 (20–50)	0.7 (0.4–1.2)	30 (20–50)	0.7 (0.4–1.2)
HPV infection						
Cervix uteri	—	—	4090 (4090–4090)	100 (100–100)	4090 (4090–4090)	100 (100–100)
Anus	510 (490–520)	90.2 (87.4–93.1)	780 (760–790)	96.3 (94.5–97.9)	1280 (1250–1310)	93.5 (91.3–95.7)
Vagina	—	—	270 (190–340)	62.9 (43.1–78.8)	270 (190–340)	62.9 (43.1–78.8)
Penis	190 (100–260)	60.5 (31.0–81.0)	—	—	190 (100–260)	60.5 (31.0–81.0)
Vulva	—	—	500 (370–640)	37.2 (27.2–47.3)	500 (370–640)	37.2 (27.2–47.3)
Oropharynx, tonsils, base of tongue	780 (530–1050)	38.0 (25.8–50.9)	60 (30–100)	10.5 (5.7–17.5)	840 (570–1150)	31.8 (21.6–43.6)
Oral cavity	190 (0–480)	5.4 (0.1–13.7)	20 (0–60)	1.0 (0.0–3.1)	210 (0–550)	3.8 (0.0–10.0)

Note: Numbers of attributable cancer deaths are rounded to the nearest 10. Cancer types associated with each risk factor are ordered by PAF in both sexes combined. PAFs are the proportions of the cancer types, as listed in the first column, attributable to the evaluated risk factor; for example, the PAFs for alcohol consumption and esophageal cancer shown in this table are the proportion of all esophageal cancer deaths (any subtype, not the proportion of esophageal squamous cell carcinoma deaths only) attributable to alcohol consumption.

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HIV, human immunodeficiency virus; HPV, human papillomavirus; H. pylori, *Helicobacter pylori*; PAF, population-attributable fraction.

Because individual behavioral choices often occur within the context of the community, promoting healthy weight, diet, and physical activity will require individual-level and community-level interventions, with the engagement of public, private, and community organizations at local, state, and national levels.[59] The CDC recommends a combination of evidence-based interventions targeting different settings, such as schools, workplaces, media, and communities.[65,66] Examples for promoting healthy diet include increasing the availability of affordable, healthier food and beverage options at food service venues and vending machines in schools, worksites, and public places; education programs; facilitation of the establishment of farmers markets and grocery stores, especially in historically marginalized neighborhoods and food deserts; and limitation of advertisements of less healthy foods and beverages.[65] Taxes on sugar-sweetened beverages have shown promising results in terms of reduced purchasing and consumption,[67] which may help reduce obesity in the population. Maintaining healthy weight in childhood should be a major focus of any strategy to control the obesity epidemic, because for many children, excess body weight extends into adulthood.[68,69] The US Preventive Services Task Force (USPSTF) recommends that health care providers screen children and adolescents aged 6 years and older for obesity and offer or refer them to comprehensive, intensive behavioral interventions to promote healthier body weight.[70]

Examples for promoting physical activity include improving the built environment (e.g., enhancing activity-friendly routes to everyday destinations, public transit, and access to places for physical activity, such as parks and safe sidewalks), school and youth programs (e.g., well designed physical education and before and after-school activities), individual and social support, and community-wide campaigns.[66]

An expert panel convened by the International Agency for Research on Cancer recently reported that there is sufficient evidence that reduction or cessation of alcoholic beverage consumption reduced the risk of oral cavity and esophageal cancer; evidence for other alcohol-related cancer sites was either limited or inadequate.[71] At the community level, the US Community Preventive Services Task Force recommend strategies to reduce alcohol consumption, including strengthening restrictions on alcohol availability, robust enforcement of laws concerning the minimum drinking age, and increasing alcoholic beverage prices through taxation.[72–74] The USPSTF recommends that primary care providers screen individuals aged 18 years and older for unhealthy alcohol use and provide persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce unhealthy alcohol use.[75]

Ultraviolet radiation

We estimated that nearly 93% of all skin melanoma cases and deaths in the United States are attributable to UV radiation. We did not evaluate the burden of nonmelanoma skin cancers attributable to UV radiation. Although nonmelanoma skin cancers are generally less fatal than melanoma, they are much more common (with an estimated 4.3 million new cases in 2019)[76] and are associated with substantial financial burden in the United States.[77]

Several sun-protection measures have been recommended to reduce skin cancer risk.[78] These measures include limiting excessive sun exposure (e.g., avoiding direct sun exposure between 10 a.m. and 4 p.m., seeking shade); wearing protective clothing, hat, and sunglasses; and regular application of broad-spectrum UVA and UVB blocking sunscreens with a sun-protection factor of 30 or greater.[79] It should be noted that sunscreens have been shown to prevent sunburns and actinic keratoses, but more research is needed on the effectiveness of sunscreens in preventing skin cancer.[80] The uptake of several sun-protection measures, including seeking shade and the use of sunscreens, wide-brimmed hats, and long-sleeved shirts, among US adults has increased during the past decade, but the prevalence for these four measures remains far from optimal, ranging from 16% to 40% in 2020.[81] Moreover, the increase in the uptake of these measures—with the possible perception of being protected—might have contributed to a decrease in sun-avoidance behavior, from 7% in 2010 to 4% in 2020.[81] Increasing the use of interventions to protect against excessive sun exposure—e.g., providing sufficient shading in parks, children playgrounds, and other places—will require multicomponent interventions at the community level.[78,80,82,83] Interventions early in life are quite important because excessive UV exposure early in life can have a great impact on the eventual risk of skin cancer.[84]

Reducing indoor tanning, particularly among adolescents, through federal and state-level interventions is also important to reduce the burden of skin cancer.[85,86] During the last decade, indoor tanning significantly decreased in states with legislation to limit or ban access to indoor tanning for youth, whereas it remained stable in other states.[87]

Infections

Approximately 3%–4% of all cancer cases and deaths in our study were attributable to infections. HPV infection contributed to the largest proportion of cancer cases (1.8%) and deaths (1.2%) attributable to any carcinogenic infection evaluated in this study. Cervical cancer incidence and death rates have been decreasing since the mid-20th century, mainly because of the widespread use of cervical cancer screening.[88,89] In more recent years, the decline continued overall and in all age groups except in women aged 30–44 years, among whom rates increased.[90] Among women aged 24 years and younger, however, the decline in cervical cancer incidence rates has substantially accelerated in more recent years,[90] e.g., from an average annual decline of 3.1% in 2001–2012 to 12.4% in 2012–2019,[91] largely reflecting the effect of HPV vaccination. In the United States, HPV vaccination was recommended in mid-2006, primarily for females aged 11–12 years, and through ages 26 years if not previously vaccinated.[92] However, the uptake of cervical cancer screening and HPV vaccination remains suboptimal; only 73% of women aged 21–65 years and 64% of girls aged 13–17 years were up-to-date with cervical cancer screening and HPV vaccination nationally in 2021, respectively.[64] Concerted efforts are needed to increase HPV vaccination coverage to fully realize its promise in reducing the burden of cervical cancer and other HPV-related cancers.[93] Anal cancer incidence rates have increased among women in more recent years,[94] and men have seen an increase in incidence rates for subtypes of oropharyngeal cancers that are generally attributable to HPV infection (e.g., base of the tongue and tonsillar cancers), except in younger men, among whom rates have declined since 2008.[95,96]

Following HPV infection, HCV infection had the second largest PAF among carcinogenic infections in men (about 1%). The prevalence of chronic HCV infection in the United States increased in the second one half of the 20th century, mainly in individuals born during 1945–1965,[97] among whom HCV prevalence in 2013–2016 was several times higher than in individuals from other birth cohorts (1.6% vs. 0.2%–0.5%).[98] This trend was followed by increases in liver cancer incidence and death rates in both sexes until around the mid-2010s, after which the incidence rates became stable in men and continued to increase in women at a slower pace.[90] However, substantial increases in acute HCV infection rates associated with the opioid epidemic in younger adults in the past 2 decades (e.g., a 300%–400% increase in rates among those aged 20–39 years during 2009–2018) can result in an increase in chronic HCV infections and liver cancer incidence rates in the future unless appropriate preventive measures are implemented.[99,100] In 2020, the USPSTF expanded an earlier recommendation to screen for HCV infection in adults born during 1945–1965 to adults aged 18–79 years.[101] Early detection of chronic HCV infections is important because oral direct-acting antivirals are highly effective in treating HCV infections and may reduce HCV-related liver cancer.[102,103] However, screening for HCV and access to high-cost anti-HCV medications are suboptimal.[104–106] For example, only less than one third of adults with HCV infection who had health insurance received direct-acting antivirals in 2019–2020[106]; this proportion is likely to be even smaller among individuals without health insurance, who bear a disproportionately high burden of HCV infection.[107]

H. pylori infection contributed to about 1% of all cancer cases and deaths. The prevalence of *H. pylori* infection in the United States has decreased in the past century, likely because of improvements in sanitation and living conditions and more widespread antibiotic use,[108] followed by a decline in gastric noncardia cancer rates.[28,109] Currently, screening for *H. pylori* is only recommended for people with certain conditions, such as active or past peptic ulcer disease, low-grade gastric mucosa-associated lymphoid tissue lymphoma, or a history of endoscopic resection of early gastric cancer, and individuals who test positive should be offered treatment.[110] There is no evidence to support routine screening in other individuals.[110]

Some risk factors of cancer, notably smoking and other carcinogenic infections (because of shared transmission routes with HIV), are more common among people with HIV infection than in others.[111,112] As such, receiving recommended smoking cessation services, vaccines (including HPV and HBV vaccines),[113] and screenings (e.g., for HCV infection)[114] can be even more important in reducing the burden of cancer among people with HIV infection.

Limitations

This study is subject to several limitations, some of which are inherent in studies that estimate the burden of cancer attributable to specific exposures. First, the 10-year lag period between exposure and cancer incidence or mortality at the population level may not be an accurate exposure window for all cancer types and risk factors. It should be noted, however, that the choice of lag period could considerably affect the estimates only with substantial changes in exposure to risk factors over time; the results of our sensitivity analysis using contemporary exposure data were generally similar to the main results, with only relatively small differences for cigarettes smoking and excess body weight. Second, we used the same RRs across sexes and age groups, although the RRs may not be homogenous across these groups. Third, the use of adjusted RRs may have introduced bias because our weighted-sum approach did not calculate a PAF for each combination of adjustment factors, and we could not determine the direction or magnitude of the bias.[24,115] Fourth, we were not able to examine the effects of exposure to risk factors in adolescence or earlier.[116,117] Finally, no robust, comprehensive information was available to account for the nature and magnitude in the amount of overlap among risk factors at the population level. As such, we assumed that the risk factors were independent, which might have resulted in slight overestimation of some PAFs for several risk factors combined. Conversely, we likely underestimated the actual PAFs for some individual risk factors and all risk factors combined because we did not include several other potentially modifiable risk factors as a result of inadequate data or for other reasons (see Table S1) as well as cancer sites without sufficient or strong evidence of a causal association with evaluated risk factors. There is accumulating evidence for a causal association between some risk factors and additional cancer types, notably for smoking.[118]

CONCLUSIONS

An estimated 40% of all cancer cases and nearly one half of all cancer deaths in the United States in 2019 were attributable to the evaluated potentially modifiable risk factors. These findings reinforce that the morbidity and premature mortality from cancer in the United States can be substantially reduced through broad and equitable implementation of known preventive initiatives, such as excise taxes on cigarettes to reduce smoking, screening for and treating HCV infection, and vaccination against HPV infection. However, further implementation research is needed for broad application of known interventions, particularly for excess body weight, unhealthy diet, alcohol consumption, and physical inactivity. Tailored and mutually reinforcing interventions are more likely to mitigate these risk factors, especially in historically marginalized populations, which are usually disproportionally affected by these factors. Further research is also needed on the association between potentially modifiable risk factors and cancers for which the current evidence for causality in humans is limited; on common cancers with few established modifiable risk factors (e.g., prostate cancer and non-Hodgkin lymphoma); on other potentially modifiable exposures, such as occupational carcinogens, air pollution, and other environmental risk factors; on associations of exposures throughout the lifetime; and on interactions between risk factors.

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CONFLICT OF INTEREST STATEMENT

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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