Proportion and Number of Cancer Cases and Deaths Attributable to Potentially Modifiable Risk Factors in the United States

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Additional supporting information may be found in the online version of this article.

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Abstract: Contemporary information on the fraction of cancers that potentially could be prevented is useful for priority setting in cancer prevention and control. Herein, the authors estimate the proportion and number of invasive cancer cases and deaths, overall (excluding nonmelanoma skin cancers) and for 26 cancer types, in adults aged 30 years and older in the United States in 2014, that were attributable to major, potentially modifiable exposures (cigarette smoking; secondhand smoke; excess body weight; alcohol intake; consumption of red and processed meat; low consumption of fruits/vegetables, dietary fiber, and dietary calcium; physical inactivity; ultraviolet radiation; and 6 cancer-associated infections). The numbers of cancer cases were obtained from the Centers for Disease Control and Prevention (CDC) and the National Cancer Institute; the numbers of deaths were obtained from the CDC; risk factor prevalence estimates were obtained from nationally representative surveys; and associated relative risks of cancer were obtained from published, large-scale pooled analyses or meta-analyses. In the United States in 2014, an estimated 42.0% of all incident cancers (659,640 of 1570,975 cancers, excluding nonmelanoma skin cancers) and 45.1% of cancer deaths (265,150 of 587,521 deaths) were attributable to evaluated risk factors. Cigarette smoking accounted for the highest proportion of cancer cases (19.0%; 298,970 cases) and deaths (28.8%; 169,180 deaths), followed by excess body weight (7.8% and 6.5%, respectively) and alcohol intake (5.6% and 4.0%, respectively). Lung cancer had the highest number of cancers (184,970 cases) and deaths (132,960 deaths) attributable to evaluated risk factors, followed by colorectal cancer (76,910 cases and 28,290 deaths). These results, however, may underestimate the overall proportion of cancers attributable to modifiable factors, because the impact of all established risk factors could not be quantified, and many likely modifiable risk factors are not yet firmly established as causal. Nevertheless, these findings underscore the vast potential for reducing cancer morbidity and mortality through broad and equitable implementation of known preventive measures. **CA Cancer J Clin 2017;000:000-000. © 2017 American Cancer Society.**

Keywords: cancer, prevention, population-attributable fraction, risk factor

Introduction

Much progress against cancer has been made in the United States over the past several decades, as evidenced by the 25% decline in the cancer mortality rate since 1991.[1] However, the cancer burden remains substantial, with more than 1.6 million newly diagnosed cases and 600,000 deaths estimated to occur in 2017.[1] The costs associated with cancer morbidity and premature mortality are staggering, with approximately $88 to $124 billion per year for direct medical costs alone.[2,3]

Many cancers are causally related to potentially modifiable risk factors,[4,5] and contemporary estimates of this proportion in a population (ie, the population-attributable fraction [PAF]) are a valuable tool for setting priorities for cancer

prevention and control. Several previous studies provided estimates of PAFs in the United States, but they included a limited number of risk factors or cancer types, used data sources that may not be nationally representative, or are outdated.[4-11] Herein, we estimate the PAF of cases and deaths overall (excluding nonmelanoma skin cancers) and for 26 cancer types, in adults aged 30 years and older in 2014, attributable to potentially modifiable risk factors using nationally representative data on exposure prevalence and cancer occurrence. These risk factors include cigarette smoking; secondhand smoke (SHS); excess body weight; alcohol intake; consumption of red and processed meat; low consumption of fruits and vegetables, dietary fiber, and dietary calcium; physical inactivity; ultraviolet (UV) radiation exposure; and infection with *Helicobacter pylori*, hepatitis B virus (HBV), hepatitis C virus (HCV), human herpes virus type 8 (HHV8), human immunodeficiency virus (HIV), or human papillomavirus (HPV).

Materials and Methods

Data Sources

Risk factors and cancer types

We used reports published by the International Agency for Research on Cancer (IARC) and the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) to identify potentially modifiable risk factors with sufficient[12-17] or strong (either convincing or probable)[18-29] evidence for causing cancer in humans and for which risk factor exposure and cancer outcome data were available (Table 1). When a risk factor was evaluated more than once, we prioritized the more recent evaluation. A list of potentially modifiable risk factors that were not considered in this analysis is provided in Supporting Information Table 1.

Cancer occurrence

Numbers of new invasive cancer cases in 2014 in the United States by sex and age group (ages 30-79 years in 5-year increments and 80 years and older) were obtained from the Centers for Disease Control and Prevention's (CDC's) National Program of Cancer Registries (NPCR) and the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) program, which collectively provided complete coverage of the US population in 2014.[30] The corresponding numbers of cancer deaths were obtained from the CDC's National Center for Health Statistics.[31]

Cancer cases from the NPCR/SEER were adjusted for delays in reporting to central cancer registries, which have been shown to occur in the most recent data years, using composite, age-specific, delay adjustment factors derived from the North American Association of Central Cancer Registries (NAACCR) 2016 December submission (personal communication, Andy Lake [Information Management Services Inc. on behalf of NAACCR] and Eric Feuer [NCI]). The methodology for delay adjustment is described elsewhere.[32,33] Both cases and deaths were accessed via the NCI's SEER*Stat software program (version 8.3.4; NCI, Bethesda, MD) and were classified according to the *International Classification of Diseases for Oncology, third edition*[34] and the *International Classification of Diseases, 10th revision*, respectively. Because of high levels of misclassification and/or missing information on histologic and anatomic subtypes for mortality data, we used the corresponding proportions from incidence data to estimate the number of deaths from esophageal squamous cell carcinoma and adenocarcinoma, gastric cardia and noncardia cancers, and colon cancer (excluding rectal cancer).

Prevalence of exposures

Exposure data used in this analysis were based on sex-specific and age-specific (ages 30-79 years in 5-year increments and 80 years and older) prevalence estimates from nationally representative surveys and were weighted to account for the appropriate complex sample design using SAS (version 9.4; SAS Institute, Inc, Cary, North Carolina) and SAS-callable SUDAAN (release 11.0.1; RTI International, Research Triangle Park, North Carolina). Exposure definitions and data sources are summarized in Supporting Information Table 2.

Data on cigarette smoking status (current, former, and never) and alcohol intake (number of drinks per day) were obtained from averaging results from the 2013 and 2014 National Health Interview Surveys to ensure more stable subgroup estimates.[35] The number of alcoholic drinks per day was calculated for current drinkers only; former drinkers and lifetime abstainers were combined for this analysis and were considered to have consumed 0 drinks per day in the year before the survey. Because alcohol intake is generally highly underreported in surveys, we adjusted National Health Interview Survey alcohol intake using per-capita alcohol sales according to a method previously suggested by Rey et al (see Supporting Information).[36]

National Health and Nutrition Examination Survey (NHANES) data were used to calculate estimates for other exposures. NHANES does not collect data on the same items every survey cycle; therefore, we included data from the most recent years available. Survey years were also combined to provide stable subgroup estimates for SHS exposure (based on serum cotinine levels; survey years 2007-2010); body mass index (BMI), in kg/m^2 (as an indicator of excess body weight; survey years 2011-2014); red meat, processed meat, fruit, vegetable, and dietary fiber and calcium consumption (all in grams per day, except calcium, which was in milligrams per day; survey years 2007-2010); and physical activity (recreational activity in metabolic equivalent of task minutes per week; survey years 2011-2014).[37] We considered only

TABLE 1. Factors Associated With Increased Cancer Risk (by Cancer Type) Considered in This Analysis

RISK FACTOR (STUDY)	CANCER TYPE (ICD-10)[a]
Smoking (Secretan 2009[14])	Oral cavity, pharynx (C00-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-C31); larynx (C32); lung, bronchus, trachea (C33-C34); cervix (C53); kidney, renal pelvis, ureter (C64-C66); urinary bladder (C67); acute myeloid leukemia (C92.0, C92.4-C92.5, C94.0, C94.2)
Exposure to secondhand smoke (Secretan 2009[14])	Lung, bronchus, trachea (C33-C34; only among never-smokers and former-smokers)
Excess body weight (Lauby-Secretan 2016[17])	Esophagus (C15; adenocarcinoma only); stomach (C16.0; cardia only); 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); multiple myeloma (C90.0, C90.2)
Alcohol intake (Secretan 2009[14])	Lip, oral cavity, pharynx (C00-C14); esophagus (C15; squamous cell carcinoma only); colorectum (C18-C20, C26.0); liver (C22.0, C22.2-C22.4, C22.7, C22.9); larynx (C32); female breast (C50)
Poor diet	
Red meat consumption (WCRF/AICR 2017[28])	Colorectum (C18-C20, C26.0)
Processed meat consumption (WCRF/AICR 2016,[26] WCRF/AICR 2017[28])	Colorectum (C18-C20, C26.0); stomach (C16.1-C16.6; noncardia only)
Low fruit/vegetable consumption (WCRF/AICR 2007[19])	Oral cavity, pharynx, larynx (C00-C14, C32; associated with low consumption of both fruits and vegetables); lung, bronchus, trachea (C33-C34, associated with low fruit consumption only)
Low dietary fiber consumption (WCRF/AICR 2017[28])	Colorectum (C18-C20, C26.0)
Low dietary calcium consumption (WCRF/AICR 2017[28])	Colorectum (C18-C20, C26.0)
Physical inactivity (WCRF/AICR 2013,[21] WCRF/AICR 2017[28,29])	Colon, excluding rectum (C18, C26.0); female breast (C50; premenopausal cancers inversely associated with vigorous activity only, postmenopausal cancers inversely associated with all types of physical activity[b]); corpus uteri (C54-C55)
Ultraviolet radiation (El Ghissassi 2009[15])	Melanoma of the skin (C43)
Infections	
Helicobacter pylori (Bouvard 2009[13])	Stomach (C16.1-C16.6; noncardia only)
Hepatitis B virus (Bouvard 2009[13])	Liver (C22.0, C22.2-C22.4, C22.7, C22.9)
Hepatitis C virus (Bouvard 2009[13])	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 (Bouvard 2009[13])	Kaposi sarcoma (C46)
Human immunodeficiency virus (Bouvard 2009[13])	Anus (C21); Kaposi sarcoma (C46); cervix (C53); Hodgkin lymphoma (C81); non-Hodgkin lymphoma (C82-C85, C96.3)
Human papillomavirus (Bouvard 2009[13])	Oral cavity (C02-C06); oropharynx, tonsils and base of tongue (C01, C09-C10); anus (C21); cervix (C53); vulva (C51); vagina (C52); penis (C60)

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; ICD-O-3, International Classification of Diseases for Oncology, third edition; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research. [a]ICD-O-3 morphology codes for incidence data for acute myeloid leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and Kaposi sarcoma were defined per Surveillance, Epidemiology, and End Results (SEER) site recode ICD-O-3/World Health Organization 2008 definitions. Esophageal adenocarcinoma includes histologies 8050, 8140-8147, 8160-8162, 8180-8221, 8250-8507, 8514, 8520-8551, 8560, 8570-8574, 8576, and 8940-8941. Esophageal squamous cell carcinoma includes histologies 8070-8078 and 8083-8084. [b]In this analysis, women aged younger than 50 years were considered as premenopausal (and were not included in calculation of breast cancers attributable to excess body weight); and women aged 50 years or older were considered as postmenopausal.

recreational activity for the association between physical inactivity and cancer, because guidelines generally pertain to recreational activity, and most studies have investigated this type of activity.[38,39] SHS exposure was defined as having a serum cotinine level of 0.05 ng/mL or greater among never-smokers and former-smokers, according to definitions used for the 2014 US Surgeon General's report.[40,41] Anthropomorphic measurements for BMI estimates were collected in person by trained personnel. The NCI method[42,43] was implemented to estimate usual daily consumption of dietary factors using data from the two 24-hour recalls of NHANES (see Supporting Information).

Laboratory data from NHANES were used to calculate prevalence estimates for infections with HBV and HIV (survey years 2011-2014), HCV (survey years 2009-2012), *H. pylori* (survey years 1999-2000), oral HPV (survey years

2011-2014), and genital HPV (survey years 2013-2014). Because HIV tests were done and swab samples for HPV were only collected from younger age groups (younger than 60 years for HIV and vaginal and penile swabs; younger than 70 years for oral swabs), combined HIV or HPV prevalence from the 2 oldest 5-year age groups with available data were applied as the prevalence for older age groups without data. Equivocal tests for infections were considered as missing values, unless additional tests were performed (eg, HCV-RNA after an anti-HCV test).

Relative risks

We used relative risks (RRs) from large-scale pooled analyses or meta-analyses of studies in the United States when available. Otherwise, we used RRs from pooled or meta-analyses of studies conducted in North America and/or Europe or, tertiarily, from studies worldwide (see Supporting Information Table 3). For nonsex-specific cancers (except breast), we used the overall RRs for men and women. When multiple risk estimates were available, we selected the RR adjusted for the greatest number of confounders.

Statistical Analysis

We applied a simulation method[44] in which numbers from repeated draws were generated for all RRs, exposure levels, and numbers of cancer cases and deaths, allowing for uncertainty in the data. The simulation process was replicated 1000 times for each sex and age-group stratum. We used numbers from repeated draws to calculate the proportion and number of attributable cancer cases and deaths and their 95% confidence intervals. By using exposure prevalence (Pi) at the exposure category i and the corresponding RR (RRi), PAFs for categorical exposure variables for each stratum of sex and age group were calculated using the following approximate formula:

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

The number of cancer cases and deaths attributable to each risk factor by sex was calculated by multiplying the number of cancer cases or deaths in each sex and age group by the PAF in that sex and age group, and summing the results over age.[45]

The above approximate formula was used for all associations, with a few exceptions. Similar to previous studies, we attributed all cervical cancers to HPV infection and all Kaposi sarcomas to HHV8 infection.[10] Because of the lack of data on anal HPV infection, we attributed 88% of anal cancers to HPV[10] before applying the simulation method. We estimated PAFs for excess UV radiation-associated melanomas using the difference between observed melanoma incidence rates by sex and age group in the general population and the rates in blacks during 2010 through 2014, as applied in previous studies.[46] Melanoma occurrence in blacks can be considered a proxy for rates in people with minimal UV exposure, because UV radiation (through sun exposure and indoor tanning) is a much less important risk factor for melanoma among blacks compared with whites in the United States.[47]

To calculate the overall attributable proportion and number of cancer cases or deaths for a given cancer type when there were several risk factors, we assumed that the risk factors had no interactions. We also calculated proportions and numbers of cancer cases and deaths attributable to 4 risk factor groups: 1) tobacco smoking (cigarette and secondhand); 2) excess body weight, alcohol intake, poor diet (consumption of red and processed meat and low consumption of fruits/vegetables, dietary fiber, and dietary calcium), and physical inactivity; 3) UV radiation; and 4) 6 cancer-associated infections. It is believed that HIV only increases the risk of cancers associated with other carcinogenic viruses (several of which were considered in this analysis) indirectly and through immunosuppression.[10,13] Thus, for estimates of all infections and all evaluated risk factors combined, we excluded HIV-related cancers from the calculations, except for HIV-related Hodgkin and non-Hodgkin lymphomas, because the infection causally associated with these 2 cancer types (Epstein-Barr virus)[13] was not considered in our analysis.

Numbers of attributable cancer cases and deaths overall and by sex and individual cancer type were obtained from separate simulation models and rounded to the nearest 10. Thus, numbers of cancer cases or deaths by sex or for individual cancer types may not sum to the totals. All statistical analyses to calculate proportions and numbers of cancers attributable to evaluated risk factors were conducted using Stata statistical software (version 13; Stata Corporation LP, College Station, Texas). Detailed information on statistical analysis is provided in the Supporting Information.

Results

Incidence

In 2014, an estimated 42.0% of all incident cancers in adults aged 30 years and older (659,640 of 1570,975 incident cancers) were attributable to the potentially modifiable risk factors evaluated (Fig. 1). Cigarette smoking had by far the highest PAF (19.0% of all cases), accounting for 55.5% of all potentially preventable cancers in men (184,400 of 332,320 cancers) and 35.0% in women (114,520 of 327,240 cancers). Excess body weight had the second highest PAF (7.8%), followed by alcohol intake (5.6%), UV radiation (4.7%), and physical inactivity (2.9%). Excess body weight caused twice as many cancers in women as in men in terms of both the PAF (10.9% vs 4.8%) and case numbers (85,680 vs 37,670 cases).

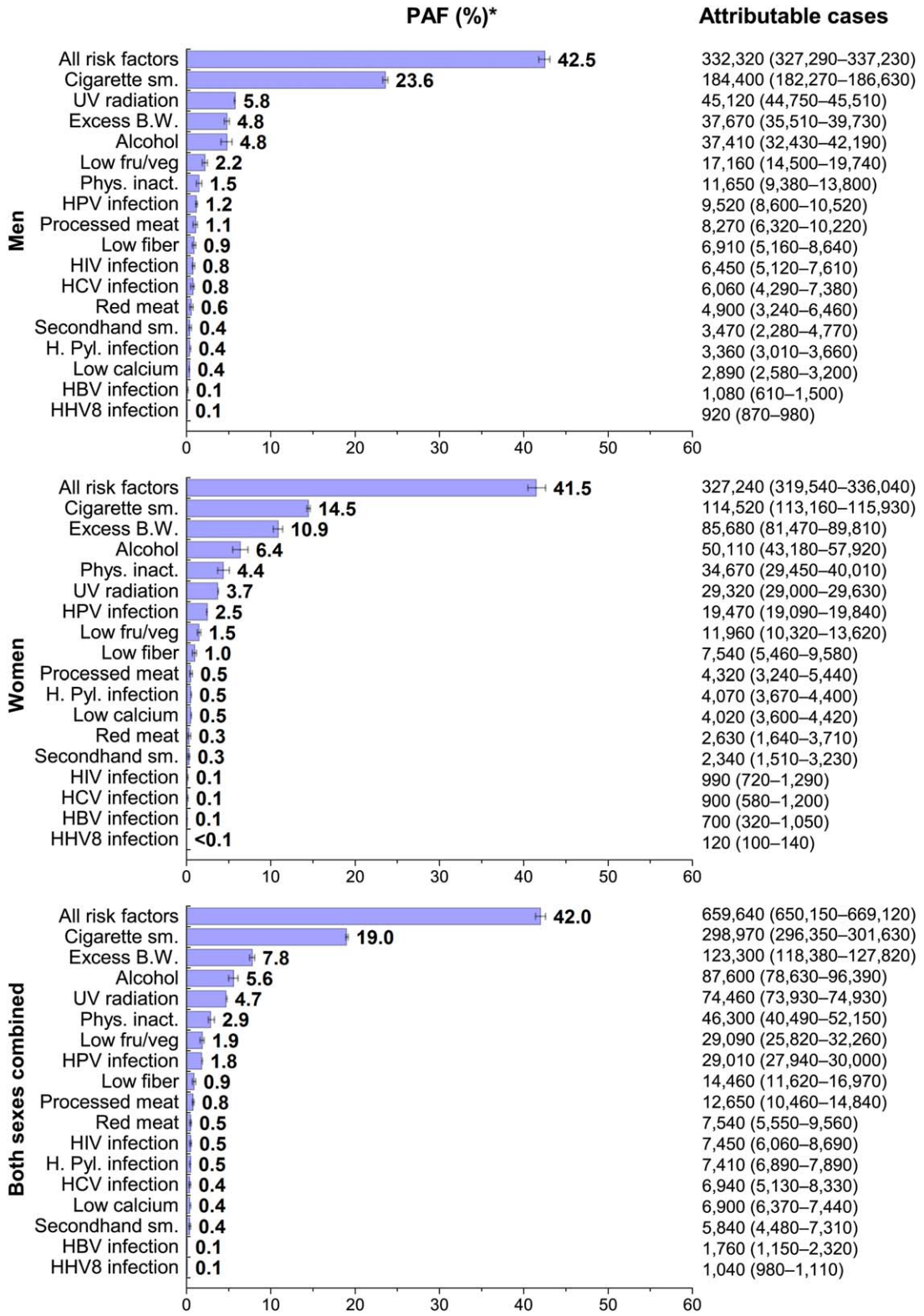

FIGURE 1. Estimated Proportion and Number of Incident Cancer Cases Attributable to Evaluated Risk Factors in Adults Aged 30 Years and Older in the United States in 2014, by Sex.

B.W. indicates body weight; CI, confidence interval; fru/veg, fruit and vegetable consumption; H. Pyl., *Helicobacter pylori*; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HPV, human papillomavirus; PAF, population-attributable fraction; Phys. inact., physical inactivity; sm., smoking; UV, ultraviolet radiation. PAFs are the percentages of all incident cancer cases in the United States in 2014. The total number of all incident cancer cases (excluding nonmelanoma skin cancer cases) in adults aged 30 years and older was 782,210 among men, 788,765 among women, and 1570,975 for both sexes combined. 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.

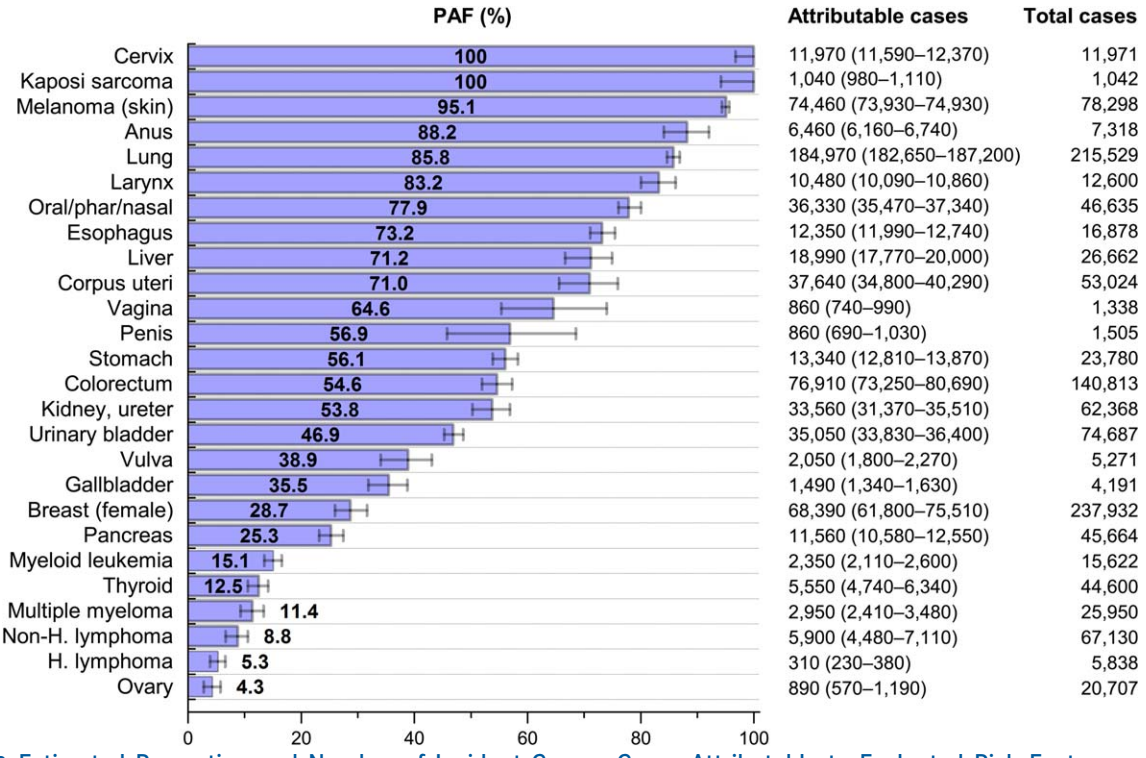

FIGURE 2. Estimated Proportion and Number of Incident Cancer Cases Attributable to Evaluated Risk Factors and Number of Total Cases in Adults Aged 30 Years and Older in the United States in 2014, by Cancer Type.

H. lymphoma indicates Hodgkin lymphoma; N-H. lymphoma, non-Hodgkin lymphoma. Here, kidney also includes renal pelvis and ureter, and lung includes bronchus and trachea. Population-attributable fractions (PAFs) are the percentages of total cases for each cancer type (both sexes combined). The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer cases are rounded to the nearest 10.

Similarly, physical inactivity accounted for 4.4% of cancers in women compared with 1.5% in men.

The proportion of cases caused by potentially modifiable risk factors ranged from 100% for cervical cancer and Kaposi sarcoma to 4.3% for ovarian cancer and was greater than 50% for 15 of the 26 cancer types (Fig. 2). In addition to cervical cancer and Kaposi sarcoma, more than three-quarters of all melanomas of the skin (95.1%) and cancers of the anus (88.2%), lung (85.8%), larynx (83.2%), and oral cavity/pharynx/nasal cavity/paranasal sinus (77.9%) were attributable to evaluated risk factors. Lung cancer had the highest number of cases attributable to evaluated risk factors in both men (99,860 cases) and women (85,050 cases), followed by skin melanoma (45,120 cases), colorectal cancer (43,080 cases), and urinary bladder cancer (28,050 cases) among men and cancers of the breast (68,390 cases), corpus uteri (37,640 cases), and colorectum (33,980 cases) among women (Table 2).

Cigarette and secondhand smoking

Cigarette smoking accounted for the highest proportion and number of cancer cases of all risk factors evaluated (23.6% of all cases in men and 14.5% in women), about three-fourths of which occurred in current smokers. Lung cancer had the highest proportion of smoking-attributable cases (81.7%), followed by cancers of the upper aerodigestive tract (larynx, 73.8%; esophagus, 50.0%; and oral and nasal cavity, pharynx, and paranasal sinuses, 49.2%), and the urinary bladder (46.9%) (Table 3). Lung cancer also had the highest burden of smoking-related cancer (176,190 cases), followed by urinary bladder cancer (35,050 cases), oral cavity/pharynx/nasal cavity/paranasal sinus cancers (22,960 cases), and colorectal cancer (16,510 cases). SHS exposure contributed an additional 5840 cases of lung cancer (2.7%).

Excess body weight

Excess body weight was associated with 4.8% of all cancers (37,670 cases) in men and 10.9% of all cancers (85,680 cases) in women (Fig. 1). However, it accounted for more than one-half of all cancers of the corpus uteri (60.3%) and one-third of gallbladder (35.5%), liver (33.9%), and kidney/renal pelvis (33.2%) cancers (Table 3). The case burden because of excess body weight was largest for cancers of the kidney/renal pelvis (12,250 cases), liver (6680 cases), and esophagus (4640 cases) among men and for cancers of the corpus uteri (31,950 cases), breast (26,780 cases), and kidney/renal pelvis (7740 cases) among women. Excess body weight accounted for a higher percentage of esophageal and gastric cancers in men than in women.

Alcohol intake

Alcohol intake was the third largest contributor to all cancer cases among women (6.4%; 50,110 cases) and the fourth largest contributor among men (4.8%; 37,410 cases). Almost one-half of oral cavity and pharyngeal cancers in

TABLE 2. Estimated Proportion and Number of Incident Cancer Cases Attributable to All Evaluated Risk Factors and Estimated Total Number of Cancer Cases in Adults Aged 30 Years and Older in the United States in 2014, by Sex and Cancer Type

CANCER	PAF (95% CI), %	ATTRIBUTABLE CASES, NO. (95% CI)	TOTAL NO. OF CASES
Men			
Kaposi sarcoma	100 (93.9-100)	920 (870-980)	921
Melanoma (skin)	96.0 (95.2-96.8)	45,120 (44,750-45,510)	47,021
Lung, bronchus, trachea	88.5 (87.0-90.0)	99,860 (98,150-101,570)	112,831
Anus	88.1 (81.5-94.8)	2310 (2130-2480)	2619
Larynx	84.4 (80.7-87.8)	8430 (8060-8780)	9997
Oral cavity, pharynx, nasal cavity, paranasal sinus	82.3 (80.0-84.9)	27,220 (26,460-28,060)	33,064
Esophagus	74.7 (72.3-77.1)	9940 (9620-10,270)	13,308
Liver	74.1 (68.1-78.7)	14,800 (13,620-15,730)	19,979
Colorectum	58.2 (54.0-61.9)	43,080 (39,980-45,810)	73,978
Penis	56.9 (45.8-68.6)	860 (690-1030)	1505
Stomach	53.6 (50.5-56.5)	7950 (7490-8380)	14,838
Kidney, renal pelvis, ureter	52.4 (47.2-56.5)	20,710 (18,670-22,350)	39,550
Urinary bladder	49.4 (47.2-51.6)	28,050 (26,800-29,290)	56,773
Gallbladder	32.9 (28.1-38.1)	430 (370-500)	1311
Pancreas	26.0 (23.2-29.0)	6160 (5480-6850)	23,633
Myeloid leukemia	17.1 (14.8-19.6)	1490 (1290-1710)	8718
Non-Hodgkin lymphoma	14.1 (10.6-17.3)	5190 (3880-6340)	36,732
Thyroid	11.5 (9.4-13.8)	1340 (1100-1600)	11,604
Multiple myeloma	10.9 (8.1-14.2)	1590 (1180-2060)	14,547
Hodgkin lymphoma	8.0 (5.7-10.3)	270 (190-350)	3364
Women			
Cervix	100 (96.8-100)	11,970 (11,590-12,370)	11,971
Kaposi sarcoma	100 (83.5-100)	120 (100-140)	121
Melanoma (skin)	93.7 (92.7-94.7)	29,320 (29,000-29,630)	31,277
Anus	88.3 (83.4-93.1)	4150 (3920-4370)	4699
Lung, bronchus, trachea	82.8 (81.4-84.3)	85,050 (83,580-86,550)	102,698
Larynx	78.5 (72.8-85.1)	2040 (1900-2220)	2603
Corpus uteri	71.0 (65.6-76.0)	37,640 (34,800-40,290)	53,024
Esophagus	67.5 (63.2-72.0)	2410 (2250-2570)	3570
Oral cavity, pharynx, nasal cavity, paranasal sinus	65.7 (62.7-68.7)	8920 (8510-9330)	13,571
Vagina	64.6 (55.4-74.0)	860 (740-990)	1338
Liver	62.6 (56.9-68.0)	4180 (3810-4540)	6683
Stomach	60.6 (56.8-64.0)	5420 (5080-5730)	8942
Kidney, renal pelvis, ureter	56.4 (51.7-61.1)	12,870 (11,790-13,930)	22,818
Colorectum	50.8 (47.4-54.1)	33,980 (31,650-36,130)	66,835
Urinary bladder	39.1 (37.1-41.2)	7010 (6640-7390)	17,914
Vulva	38.9 (34.1-43.1)	2050 (1800-2270)	5271
Gallbladder	36.5 (31.8-41.1)	1050 (920-1180)	2880
Breast	28.7 (26.0-31.7)	68,390 (61,800-75,510)	237,932
Pancreas	24.5 (21.6-27.8)	5390 (4750-6120)	22,031
Thyroid	12.8 (10.4-14.9)	4220 (3430-4930)	32,996
Myeloid leukemia	12.5 (10.7-14.3)	860 (740-990)	6904
Multiple myeloma	11.8 (8.9-15.0)	1350 (1010-1710)	11,403
Ovary	4.3 (2.8-5.8)	890 (570-1,190)	20,707
Non-Hodgkin lymphoma	2.4 (1.5-3.3)	720 (460-1,000)	30,398
Hodgkin lymphoma	1.5 (0.9-2.3)	40 (20-60)	2474

Abbreviations: CI, confidence interval; PAF, population attributable fraction. Cancer types are ordered by PAF, and numbers of attributable cancer cases are rounded to the nearest 10.

TABLE 3. Estimated Cancer Cases in Adults Aged 30 Years and Older in the United States in 2014 Attributable to Potentially Modifiable Risk Factors, by Sex, Risk Factor, and Cancer Type

	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	95,180 (94,380-95,950)	84.4 (83.6-85.0)	81,010 (79,980-81,950)	78.9 (77.9-79.8)	176,190 (174,910-177,390)	81.7 (81.2-82.3)
Larynx	7490 (7120-7810)	74.9 (71.2-78.1)	1810 (1700-1930)	69.5 (65.4-74.0)	9300 (8920-9650)	73.8 (70.8-76.6)
Esophagus	6940 (6680-7220)	52.1 (50.2-54.2)	1510 (1430-1590)	42.2 (40.0-44.6)	8450 (8180-8740)	50.0 (48.5-51.8)
Oral cavity, pharynx, nasal cavity, paranasal sinus	17,160 (16,260-18,000)	51.9 (49.2-54.4)	5810 (5480-6160)	42.8 (40.4-45.4)	22,960 (22,000-23,880)	49.2 (47.2-51.2)
Urinary bladder	28,050 (26,800-29,290)	49.4 (47.2-51.6)	7010 (6640-7390)	39.1 (37.1-41.2)	35,050 (33,830-36,400)	46.9 (45.4-48.6)
Liver	4950 (4460-5420)	24.8 (22.3-27.1)	1230 (1110-1350)	18.4 (16.6-20.1)	6180 (5700-6670)	23.2 (21.4-25.0)
Cervix	—	—	2380 (2040-2730)	19.9 (17.0-22.8)	2380 (2040-2730)	19.9 (17.0-22.8)
Kidney, renal pelvis, ureter	7580 (6860-8320)	19.2 (17.3-21.0)	3250 (2920-3590)	14.2 (12.8-15.8)	10,830 (10,040-11,660)	17.4 (16.1-18.7)
Stomach	2880 (2480-3260)	19.4 (16.7-22.0)	1280 (1110-1470)	14.3 (12.4-16.4)	4150 (3710-4570)	17.4 (15.6-19.2)
Myeloid leukemia	1490 (1290-1710)	17.1 (14.8-19.6)	860 (740-990)	12.5 (10.7-14.3)	2350 (2110-2600)	15.1 (13.5-16.6)
Colorectum	10,000 (9180-10,820)	13.5 (12.4-14.6)	6510 (5990-7040)	9.7 (9.0-10.5)	16,510 (15,550-17,540)	11.7 (11.0-12.5)
Pancreas	2770 (2430-3120)	11.7 (10.3-13.2)	1880 (1650-2090)	8.5 (7.5-9.5)	4640 (4230-5070)	10.2 (9.3-11.1)
Secondhand smoke						
Lung	3470 (2280-4770)	3.1 (2.0-4.2)	2340 (1510-3230)	2.3 (1.5-3.1)	5840 (4480-7310)	2.7 (2.1-3.4)
Excess body weight						
Corpus uteri	—	—	31,950 (29,190-34,840)	60.3 (55.1-65.7)	31,950 (29,190-34,840)	60.3 (55.1-65.7)
Gallbladder	430 (370-500)	32.9 (28.1-38.1)	1050 (920-1180)	36.5 (31.8-41.1)	1490 (1340-1630)	35.5 (31.9-38.8)
Liver	6680 (5460-7760)	33.4 (27.3-38.8)	2380 (2000-2770)	35.6 (30.0-41.4)	9050 (7800-10,230)	33.9 (29.2-38.4)
Kidney, renal pelvis	12,250 (10,830-13,450)	32.1 (28.3-35.2)	7740 (6980-8570)	35.2 (31.7-39.0)	19,980 (18,360-21,410)	33.2 (30.5-35.6)
Esophagus	4640 (4210-5050)	34.9 (31.7-38.0)	800 (710-880)	22.3 (20.0-24.6)	5440 (4990-5850)	32.2 (29.6-34.7)
Stomach	3210 (2760-3650)	21.7 (18.6-24.6)	960 (830-1090)	10.7 (9.3-12.2)	4170 (3700-4630)	17.5 (15.6-19.5)
Pancreas	3840 (3210-4560)	16.3 (13.6-19.3)	3860 (3210-4590)	17.5 (14.6-20.8)	7710 (6730-8750)	16.9 (14.7-19.2)
Thyroid	1340 (1100-1600)	11.5 (9.4-13.8)	4220 (3430-4930)	12.5 (10.7-14.3)	5550 (4740-6340)	12.5 (10.6-14.2)
Multiple myeloma	1590 (1180-2060)	10.9 (8.1-14.2)	1350 (1010-1710)	11.8 (8.9-15.0)	2950 (2410-3480)	11.4 (9.3-13.4)
Breast	—	—	26,780 (24,280-29,340)	11.3 (10.2-12.3)	26,780 (24,280-29,340)	11.3 (10.2-12.3)
Colorectum	3740 (3070-4400)	5.1 (4.1-6.0)	3600 (2970-4260)	5.4 (4.4-6.4)	7340 (6380-8290)	5.2 (4.5-5.9)
Ovary	—	—	890 (570-1190)	4.3 (2.8-5.8)	890 (570-1190)	4.3 (2.8-5.8)
Alcohol intake						
Oral cavity, pharynx	14,670 (13,880-15,450)	46.3 (43.8-48.8)	3450 (3210-3700)	27.4 (25.4-29.3)	18,130 (17,320-18,910)	40.9 (39.1-42.7)
Larynx	2560 (2290-2840)	25.6 (22.9-28.4)	370 (320-420)	14.0 (12.3-16.0)	2930 (2660-3200)	23.2 (21.1-25.4)

TABLE 3. *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), %
Alcohol intake [*Continued*]						
Liver	4960 (2920-7340)	24.8 (14.6-36.7)	800 (460-1180)	11.9 (6.9-17.7)	5750 (3740-8230)	21.6 (14.0-30.9)
Esophagus	2530 (2160-2840)	19.0 (16.2-21.4)	1010 (780-1250)	28.4 (21.9-35.1)	3540 (3120-3930)	21.0 (18.5-23.3)
Breast	—	—	39,060 (32,250-46,380)	16.4 (13.6-19.5)	39,060 (32,250-46,380)	16.4 (13.6-19.5)
Colorectum	12,670 (8250-17,150)	17.1 (11.1-23.2)	5380 (3630-7520)	8.1 (5.4-11.3)	18,090 (13,260-23,230)	12.8 (9.4-16.5)
Red meat consumption						
Colorectum	4900 (3240-6460)	6.6 (4.4-8.7)	2630 (1640-3710)	3.9 (2.5-5.5)	7540 (5550-9560)	5.4 (3.9-6.8)
Processed meat consumption						
Colorectum	7630 (5700-9560)	10.3 (7.7-12.9)	3850 (2780-4980)	5.8 (4.2-7.5)	11,530 (9340-13,770)	8.2 (6.6-9.8)
Stomach	660 (410-910)	4.4 (2.8-6.1)	470 (310-660)	5.3 (3.5-7.4)	1130 (840-1430)	4.8 (3.6-6.0)
Low fruit and vegetable consumption						
Oral cavity, pharynx	5400 (3710-7210)	17.1 (11.7-22.8)	2330 (1610-3030)	18.5 (12.8-24.0)	7770 (5810-9630)	17.6 (13.1-21.7)
Larynx	1700 (1130-2290)	17.0 (11.3-22.9)	480 (330-640)	18.3 (12.7-24.4)	2190 (1600-2780)	17.4 (12.7-22.1)
Lung	10,010 (8310-11,740)	8.9 (7.4-10.4)	9170 (7660-10,620)	8.9 (7.5-10.3)	19,150 (16,760-21,520)	8.9 (7.8-10.0)
Low dietary fiber consumption						
Colorectum	6910 (5160-8640)	9.3 (7.0-11.7)	7540 (5460-9580)	11.3 (8.2-14.3)	14,460 (11,620-16,970)	10.3 (8.3-12.1)
Low dietary calcium consumption						
Colorectum	2890 (2580-3200)	3.9 (3.5-4.3)	4020 (3600-4420)	6.0 (5.4-6.6)	6900 (6370-7440)	4.9 (4.5-5.3)
Physical inactivity						
Corpus uteri	—	—	14,140 (9940-17,890)	26.7 (18.8-33.7)	14,140 (9940-17,890)	26.7 (18.8-33.7)
Colon, excluding rectum[a]	11,650 (9380-13,800)	15.7 (12.7-18.6)	11,250 (9020-13,440)	16.8 (13.5-20.1)	22,930 (19,720-25,880)	16.3 (14.0-18.4)
Breast	—	—	9290 (6520-12,150)	3.9 (2.7-5.1)	9290 (6520-12,150)	3.9 (2.7-5.1)
Ultraviolet radiation						
Melanoma (skin)	45,120 (44,750-45,510)	96.0 (95.2-96.8)	29,320 (29,000-29,630)	93.7 (92.7-94.7)	74,460 (73,930-74,930)	95.1 (94.4-95.7)
H. pylori infection						
Stomach	3360 (3010-3660)	22.6 (20.3-24.7)	4070 (3670-4400)	45.5 (41.1-49.2)	7410 (6890-7890)	31.2 (29.0-33.2)
HBV infection						
Liver	1080 (610-1500)	5.4 (3.1-7.5)	700 (320-1050)	10.5 (4.8-15.7)	1760 (1150-2320)	6.6 (4.3-8.7)
HCV infection						
Liver	5670 (3920-7000)	28.4 (19.6-35.0)	780 (450-1070)	11.6 (6.8-15.9)	6450 (4660-7800)	24.2 (17.5-29.3)
Non-Hodgkin lymphoma	380 (250-570)	1.0 (0.7-1.5)	120 (60-200)	0.4 (0.2-0.6)	510 (370-700)	0.8 (0.5-1.0)

TABLE 3. *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), %
HHV8 infection						
Kaposi sarcoma	920 (870-980)	100 (93.9-100)	120 (100-140)	100 (83.5-100)	1040 (980-1110)	100 (94.2-100)
HIV infection						
Kaposi sarcoma	730 (590-790)	78.8 (64.5-86.0)	70 (40-100)	60.7 (30.6-80.6)	800 (660-870)	76.5 (63.6-83.3)
Anus	640 (450-770)	24.2 (17.1-29.5)	200 (120-290)	4.3 (2.5-6.3)	830 (650-1010)	11.4 (8.8-13.8)
Non-Hodgkin lymphoma	4850 (3520-5980)	13.2 (9.6-16.3)	590 (340-870)	1.9 (1.1-2.9)	5440 (4010-6640)	8.1 (6.0-9.9)
Hodgkin lymphoma	270 (190-350)	8.0 (5.7-10.3)	40 (20-60)	1.5 (0.9-2.3)	310 (230-380)	5.3 (3.9-6.6)
Cervix	—	—	80 (40-130)	0.7 (0.4-1.1)	80 (40-130)	0.7 (0.4-1.1)
HPV infection						
Cervix	—	—	11,970 (11,750-12,190)	100 (98.2-100)	11,970 (11,750-12,190)	100 (98.2-100)
Anus	2310 (2130-2480)	88.1 (81.5-94.8)	4150 (3920-4370)	88.3 (83.4-93.1)	6460 (6160-6740)	88.2 (84.1-92.1)
Vagina	—	—	860 (740-990)	64.6 (55.4-4.0)	860 (740-990)	64.6 (55.4-74.0)
Penis	860 (690-1030)	56.9 (45.8-68.6)	—	—	860 (690-1030)	56.9 (45.8-68.6)
Vulva	—		2050 (1800-2270)	38.9 (34.1-43.1)	2050 (1800-2270)	38.9 (34.1-43.1)
Oropharynx	5730 (4900-6690)	37.9 (32.4-44.2)	360 (260-480)	11.2 (8.0-14.9)	6100 (5240-7060)	33.2 (28.5-38.5)
Oral cavity	630 (380-940)	7.4 (4.5-11.1)	90 (50-160)	1.6 (0.9-2.7)	730 (480-1050)	5.1 (3.4-7.3)

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. Numbers of attributable cancer cases are rounded to the nearest 10, and cancer types associated with each risk factor are ordered by PAF for both sexes combined. [a]PAF values are the percentages of all colorectal cancers.

men (46.3%; 14,670 cases) and one-fourth of esophageal (28.4%; 1010 cases) and oral cavity and pharyngeal (27.4%, 3450 cases) cancers in women were associated with alcohol; however, the largest burden by far was for female breast cancer (39,060 cases). In general, the proportions of cases attributable to alcohol intake by cancer type were higher in men than in women, except for esophageal cancer.

Poor diet

The proportion of all cancers attributed to poor diet ranged from 0.4% for low dietary calcium consumption to 1.9% for low fruit and vegetable consumption. However, for colorectal cancer specifically, the PAFs ranged from 4.9% (6900 cases) for low dietary calcium to 10.3% (14,460 cases) for low dietary fiber. Red and processed meat consumption accounted for 5.4% and 8.2% of colorectal cancers, respectively, with higher PAFs in men than in women. Low fruit and vegetable consumption was associated with 17.6% of oral cavity/pharyngeal cancers, 17.4% of laryngeal cancers, and 8.9% of lung cancers, and the highest number of attributable cases was from lung cancer (19,150 cases). There were no substantial differences between men and women in the PAFs for low fruit and vegetable or dietary fiber, while the PAF for low dietary calcium consumption was slightly higher in women.

Physical inactivity

Physical inactivity accounted for 2.9% of all cancers, with the highest proportion for cancer of the corpus uteri (26.7%; 14,140 cases), but the largest number of cases were for colon cancer (22,930; 16.3% of all colorectal cancer cases); 3.9% of female breast cancers (9290 cases) were attributable to physical inactivity.

The combination of excess body weight, alcohol intake, poor diet, and physical inactivity accounted for 13.9% of cancer cases in men (second to tobacco smoking, 24.0%), but it accounted for the highest proportion of cancer cases

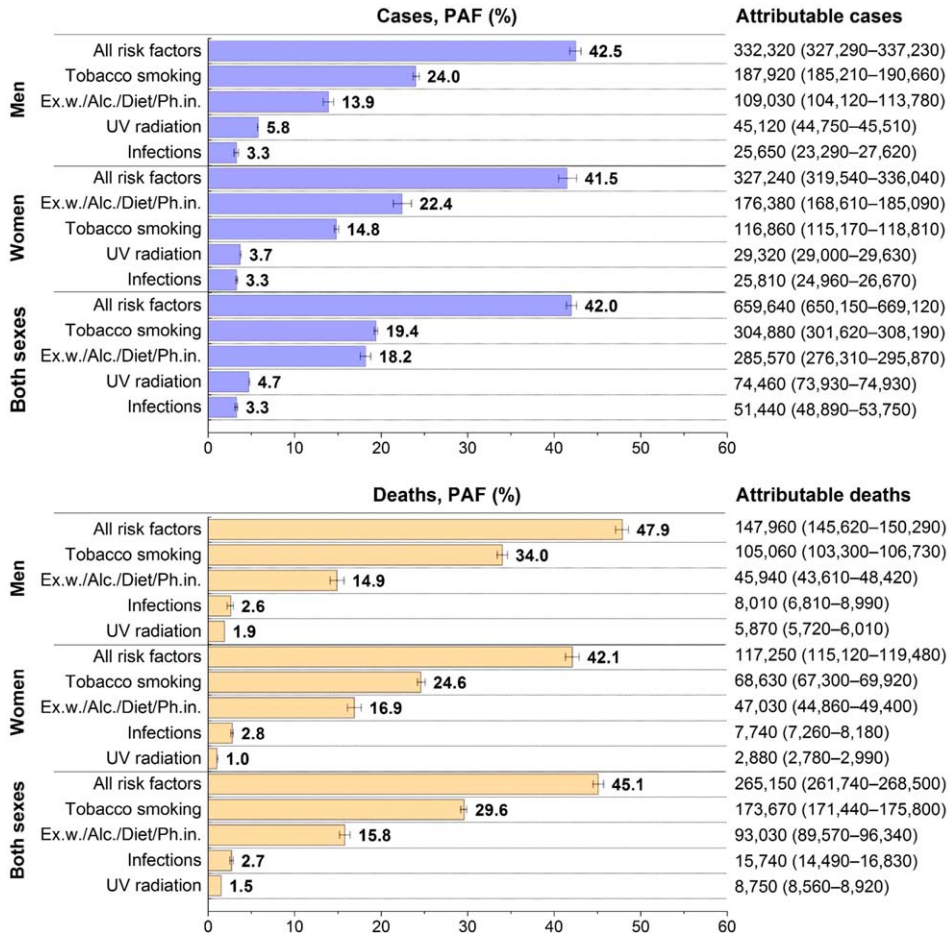

FIGURE 3. Estimated Proportion and Number of Incident Cancer Cases and Cancer Deaths Attributable to Risk Factor Groups in Adults Aged 30 Years and Older in the United States in 2014, by Sex.

Population-attributable fractions (PAFs) are the percentages of all incident cancer cases or cancer deaths (excluding nonmelanoma skin cancers). 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. Risk factor groups include tobacco smoking (cigarette and secondhand); excess body weight (Ex.w.), alcohol intake (Alc.), poor diet (Diet [consumption of red and processed meat; and low consumption of fruits/vegetables, dietary fiber, and dietary calcium]), and physical inactivity (Ph.in.); ultraviolet (UV) radiation (from any source); and infections (*Helicobacter pylori*; hepatitis B virus; hepatitis C virus; human herpes virus type 8; human immunodeficiency virus [only associated Hodgkin lymphoma and non-Hodgkin lymphoma], and human papillomavirus). The proportion of cancer cases attributable to poor diet only was 4.8% (37,810 cases) in men, 3.7% (28,880 cases) in women, and 4.2% (66,640 cases) in both sexes combined; the corresponding proportion for cancer deaths was 5.4% (16,630 deaths) in men, 4.7% (13,230 deaths) in women, and 5.1% (29,850 deaths) in both sexes combined.

in women (22.4%), followed by tobacco smoking (14.8%) (Fig. 3).

UV radiation

Despite an association with only one cancer, UV radiation was the second largest contributor to total cancer cases in men (5.8%; 45,120 cases) and the fifth largest contributor to total cancer cases in women (3.7%; 29,320 cases). Approximately 95% of skin melanoma cases were attributable to UV radiation exposure, with comparable PAFs in men and women.

Infections

Overall, 3.3% of all cancer cases were attributable to evaluated infections (Fig. 3). By infection type, the attributable fraction for all cases combined ranged from 0.1% to 1.2% in men and from less than 0.1% to 2.5% in women (Fig. 1). Although the number of gastric cancer cases attributable to *H. pylori* infection was similar in men (3360 cases) and women (4070 cases), the PAF in women (45.5%) was twice that in men (22.6%). While liver cancer in women was equally attributable to HBV infection (10.5%) and HCV infection (11.6%), in men, the PAF for HCV infection (28.4%) was 5 times that for HBV (5.4%). All cases of Kaposi sarcoma were attributed to HHV8. Non-Hodgkin lymphoma had the highest number of cancers (5440 cases) attributable to HIV infection.

All cervical cancers (11,970 cases) and 88.2% of anal cancers (6460 cases) were attributed to HPV infection. HPV infection also accounted for large fractions of cancers of the vagina (64.6%; 860 cases) and penis (56.9%; 860 cases). The proportion of HPV-attributable cases was higher in men than in women for cancers of the oropharynx (37.9% vs 11.2%) and oral cavity (7.4% vs 1.6%).

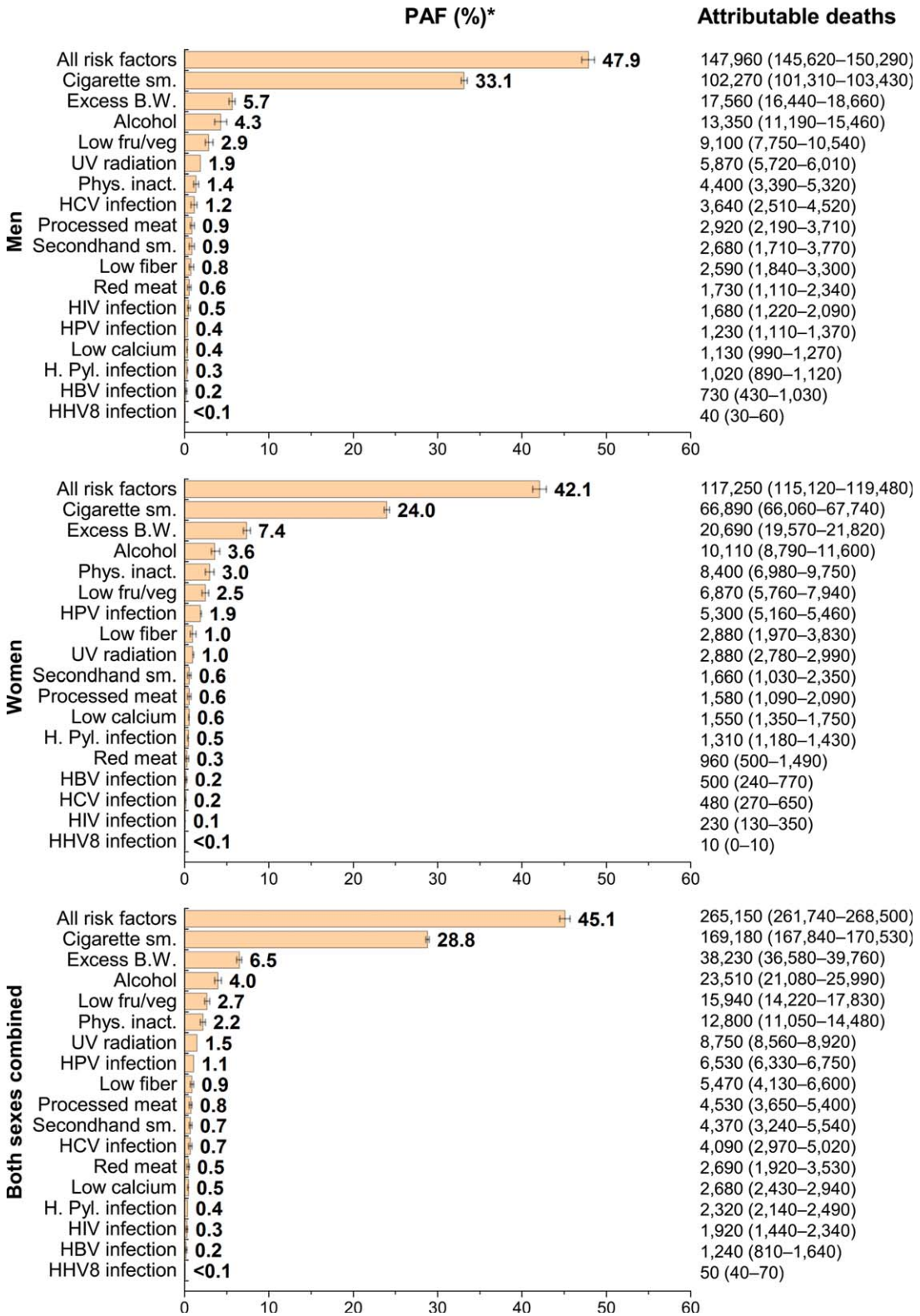

FIGURE 4. Estimated Proportion and Number of Cancer Deaths Attributable to Evaluated Risk Factors in Adults Aged 30 Years and Older in the United States in 2014, by Sex.

B.W. indicates body weight; CI, confidence interval; fru/veg, fruit and vegetable consumption; H. Pyl., *Helicobacter pylori*; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HPV, human papillomavirus; PAF, population-attributable fraction; Phys. inact., physical inactivity; sm., smoking; UV, ultraviolet. PAFs are the percentages of all cancer deaths in the United States in 2014. The total number of all cancer deaths (excluding nonmelanoma skin cancer deaths) in adults aged 30 years and older was 308,915 among men, 278,606 among women, and 587,521 in both sexes combined. The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer deaths are rounded to the nearest 10.

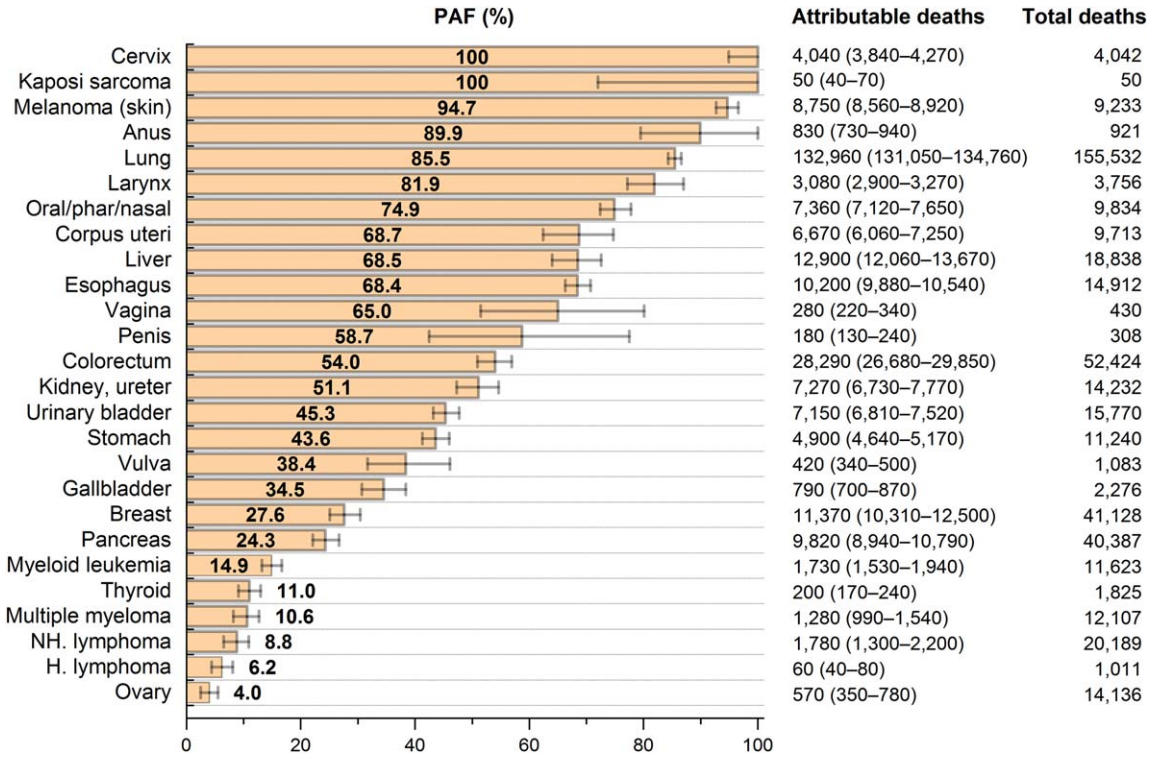

FIGURE 5. Estimated Proportion and Number of Cancer Deaths Attributable to Evaluated Risk Factors and Number of Total Cancer Deaths in Adults Aged 30 Years and Older in the United States in 2014, by Cancer Type.

H. lymphoma indicates Hodgkin lymphoma; NH. Lymphoma, non-Hodgkin lymphoma. Here, kidney also includes renal pelvis and ureter, and lung includes bronchus and trachea. Population-attributable fractions (PAFs) are the percentages of total deaths for each cancer type (both sexes combined). The bars in the figure and numbers in parentheses represent 95% confidence intervals. Numbers of attributable cancer deaths are rounded to the nearest 10.

Mortality

The PAF patterns for mortality were similar to those for incidence (Fig. 4). The proportion of all cancer deaths attributable to evaluated risk factors in 2014 was 47.9% (147,960 of 308,915 deaths) in men, 42.1% (117,250 of 278,606 deaths) in women, and 45.1% in both sexes combined (265,150 of 587,521 deaths). The risk factors considered in this analysis contributed to more than one-half of cancer deaths in 14 of the 26 cancer types (Fig. 5). By cancer type, lung cancer had the largest number of deaths attributable to evaluated risk factors in both men (74,990 deaths) and women (57,980 deaths), followed by colorectal cancer in both men (15,740 deaths) and women (12,570 deaths), liver cancer in men (9860 deaths), and breast cancer in women (11,370 deaths) (Table 4).

Cigarette smoking accounted for the greatest number (169,180 deaths) and proportion (28.8%) of overall cancer deaths, including 33.1% of deaths in men and 24.0% of deaths in women. In contrast to incidence, the fractions and numbers of cancer deaths because of excess body weight were similar in men (5.7%; 17,560 deaths) and women (7.4%; 20,690 deaths) (Fig. 4). Alcohol intake was the third largest contributor to overall cancer deaths in both men (13,350; 4.3% of all cancer deaths) and women (10,110; 3.6% of all cancer deaths). The combination of excess body weight, alcohol intake, poor diet, and physical inactivity accounted for 14.9% of cancer deaths in men and 16.9% in women (Fig. 3). The proportion of cancer deaths attributable to infections was 2.6% in men and 2.8% in women, which was slightly higher than that for UV radiation (1.9% and 1.0%, respectively). The proportions and numbers of cancer deaths attributable to evaluated risk factors by cancer type are shown in Table 5.

Discussion

We found that 42% of all incident cancer cases and almost one-half of all cancer deaths, representing 659,640 cancer cases and 265,150 deaths, were attributable to evaluated risk factors in the United States in 2014. Cigarette smoking was associated with far more cancer cases and deaths than any other single risk factor, accounting for nearly 20% of all cancer cases and 30% of all cancer deaths, followed by excess body weight. Lung cancer had the highest number of cancer cases or deaths attributable to potentially modifiable risk factors, followed by colorectal cancer.

The proportions of all cancer cases and deaths attributable to smoking, red and processed meat consumption, HCV infection, UV radiation, and HIV infection were higher in men compared with women, reflecting historically higher prevalence of these risk factors in men.[48-53] In contrast, the

TABLE 4. Estimated Proportion and Number of Cancer Deaths Attributable to All Evaluated Risk Factors and Estimated Total Number of Cancer Deaths in Adults Aged 30 Years and Older in the United States in 2014, by Sex and Cancer Type

CANCER	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	TOTAL NO. OF DEATHS
Men			
Kaposi sarcoma	100 (70.5-100)	40 (30-60)	44
Melanoma (skin)	96.0 (93.5-98.4)	5870 (5720-6010)	6113
Anus	90.1 (72.9-100)	320 (260-390)	351
Lung, bronchus, trachea	88.4 (86.7-90.0)	74,990 (73,570-76,350)	84,859
Larynx	83.1 (77.6-88.7)	2530 (2360-2700)	3045
Oral cavity, pharynx, nasal cavity, paranasal sinus	79.2 (76.3-82.7)	5570 (5360-5810)	7032
Liver	72.4 (66.3-77.7)	9860 (9020-10,570)	13,608
Esophagus	70.8 (68.3-73.3)	8450 (8150-8750)	11,936
Penis	58.7 (42.5-77.5)	180 (130-240)	308
Colorectum	57.5 (52.9-61.3)	15,740 (14,480-16,800)	27,393
Kidney, renal pelvis, ureter	50.5 (45.3-55.2)	4730 (4240-5170)	9369
Urinary bladder	48.7 (45.9-51.9)	5500 (5180-5860)	11,290
Stomach	44.0 (40.5-47.2)	2970 (2730-3180)	6742
Gallbladder	32.8 (27.1-39.5)	240 (190-280)	718
Pancreas	25.3 (22.3-28.6)	5240 (4620-5940)	20,737
Myeloid leukemia	17.1 (14.4-19.9)	1130 (950-1310)	6604
Non-Hodgkin lymphoma	14.2 (10.2-17.7)	1580 (1140-1980)	11,155
Thyroid	10.6 (8.0-13.7)	80 (60-110)	793
Multiple myeloma	10.3 (7.3-13.5)	680 (480-890)	6586
Hodgkin lymphoma	9.4 (6.5-12.5)	60 (40-70)	598
Women			
Cervix	100 (94.9-100)	4040 (3840-4270)	4042
Kaposi sarcoma	100 (33.3-100)	10 (0-10)	6
Melanoma (skin)	92.3 (89.2-95.8)	2880 (2780-2990)	3120
Anus	89.5 (75.9-100)	510 (430-590)	570
Lung, bronchus, trachea	82.0 (80.4-83.7)	57,980 (56,820-59,170)	70,673
Larynx	76.2 (66.6-86.8)	540 (470-620)	711
Corpus uteri	68.7 (62.4-74.7)	6670 (6060-7250)	9713
Vagina	65.0 (51.5-80.1)	280 (220-340)	430
Oral cavity, pharynx, nasal cavity, paranasal sinus	62.5 (57.9-68.0)	1750 (1620-1910)	2802
Esophagus	58.8 (54.6-63.3)	1750 (1620-1880)	2976
Liver	58.3 (52.6-64.4)	3050 (2750-3370)	5230
Kidney, renal pelvis, ureter	52.1 (46.0-58.0)	2540 (2240-2820)	4863
Colorectum	50.2 (45.8-54.5)	12,570 (11,470-13,650)	25,031
Stomach	43.1 (39.7-46.3)	1940 (1780-2080)	4498
Vulva	38.4 (31.7-46.1)	420 (340-500)	1083
Urinary bladder	36.9 (33.8-40.2)	1660 (1520-1800)	4480
Gallbladder	35.2 (30.5-40.2)	550 (480-630)	1558
Breast	27.6 (25.1-30.4)	11,370 (10,310-12,500)	41,128
Pancreas	23.2 (20.2-26.8)	4570 (3970-5270)	19,650
Myeloid leukemia	12.0 (10.1-14.1)	600 (510-710)	5019
Thyroid	11.2 (8.4-14.2)	120 (90-150)	1032
Multiple myeloma	10.7 (7.6-14.1)	590 (420-780)	5521
Ovary	4.0 (2.5-5.5)	570 (350-780)	14,136
Non-Hodgkin lymphoma	2.1 (1.0-3.4)	190 (90-310)	9034
Hodgkin lymphoma	1.4 (0.5-2.4)	10 (0-10)	413

Abbreviations: CI, confidence interval; PAF, population-attributable fraction. Cancer types are ordered by PAF, and numbers of attributable cancer deaths are rounded to the nearest 10.

TABLE 5. Estimated Cancer Deaths in Adults Aged ≥30 Years in the United States in 2014 Attributable to Potentially Modifiable Risk Factors, by Sex, Risk Factor, and Cancer Type

	MEN		WOMEN		BOTH SEXES COMBINED	
CANCER	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %
Cigarette smoking						
Lung	71,300 (70,630-71,940)	84.0 (83.2-84.8)	55,070 (54,330-55,820)	77.9 (76.9-79.0)	126,410 (125,360-127,370)	81.3 (80.6-81.9)
Larynx	2230 (2100-2370)	73.2 (68.8-77.8)	470 (430-510)	66.4 (60.5-72.4)	2700 (2570-2840)	72.0 (68.3-75.7)
Esophagus	6220 (5980-6460)	52.1 (50.1-54.1)	1230 (1150-1310)	41.2 (38.6-43.9)	7440 (7190-7690)	49.9 (48.2-51.6)
Oral cavity, pharynx, nasal cavity, paranasal sinus	3530 (3330-3740)	50.2 (47.3-53.2)	1100 (1010-1200)	39.4 (36.2-42.7)	4640 (4400-4870)	47.1 (44.7-49.5)
Urinary bladder	5500 (5180-5860)	48.7 (45.9-51.9)	1660 (1520-1800)	36.9 (33.8-40.2)	7150 (6810-7520)	45.3 (43.2-47.7)
Liver	3320 (3010-3630)	24.4 (22.1-26.7)	900 (800-990)	17.2 (15.4-18.9)	4220 (3890-4540)	22.4 (20.7-24.1)
Cervix	—	—	790 (680-920)	19.6 (16.7-22.8)	790 (680-920)	19.6 (16.7-22.8)
Kidney, renal pelvis, ureter	1820 (1620-2030)	19.4 (17.3-21.6)	650 (570-740)	13.4 (11.7-15.2)	2470 (2250-2700)	17.4 (15.8-18.9)
Stomach	1290 (1090-1470)	19.1 (16.2-21.8)	610 (510-710)	13.6 (11.3-15.7)	1900 (1680-2100)	16.9 (14.9-18.7)
Myeloid leukemia	1130 (950-1310)	17.1 (14.4-19.9)	600 (510-710)	12.0 (10.1-14.1)	1730 (1530-1940)	14.9 (13.2-16.7)
Colorectum	3630 (3290-3960)	13.3 (12.0-14.4)	2270 (2040-2510)	9.1 (8.2-10.0)	5890 (5480-6310)	11.2 (10.5-12.0)
Pancreas	2320 (2010-2660)	11.2 (9.7-12.8)	1540 (1310-1750)	7.8 (6.7-8.9)	3860 (3480-4270)	9.6 (8.6-10.6)
Secondhand smoke						
Lung	2680 (1710-3770)	3.2 (2.0-4.4)	1660 (1030-2350)	2.3 (1.5-3.3)	4370 (3240-5540)	2.8 (2.1-3.6)
Excess body weight						
Corpus uteri	—	—	5500 (4960-6070)	56.7 (51.1-62.4)	5500 (4960-6070)	56.7 (51.1-62.4)
Gallbladder	240 (190-280)	32.8 (27.1-39.5)	550 (480-630)	35.2 (30.5-40.2)	790 (700-870)	34.5 (30.7-38.4)
Liver	4450 (3670-5120)	32.7 (26.9-37.6)	1750 (1450-2050)	33.4 (27.8-39.2)	6210 (5390-6960)	32.9 (28.6-36.9)
Kidney, renal pelvis	2780 (2450-3080)	30.4 (26.8-33.7)	1490 (1300-1700)	31.9 (27.7-36.3)	4270 (3920-4620)	30.9 (28.3-33.4)
Esophagus	3540 (3190-3880)	29.7 (26.7-32.5)	480 (430-530)	16.1 (14.3-17.9)	4010 (3670-4380)	26.9 (24.6-29.4)
Pancreas	3300 (2740-3930)	15.9 (13.2-19.0)	3290 (2720-3990)	16.8 (13.8-20.3)	6610 (5810-7560)	16.4 (14.4-18.7)
Stomach	1180 (1010-1360)	17.5 (15.0-20.2)	340 (290-390)	7.5 (6.4-8.6)	1520 (1340-1700)	13.5 (11.9-15.1)
Breast	—	—	4710 (4260-5140)	11.4 (10.3-12.5)	4710 (4260-5140)	11.4 (10.3-12.5)
Thyroid	80 (60-110)	10.6 (8.0-13.7)	120 (90-150)	11.2 (8.4-14.2)	200 (170-240)	11.0 (9.1-13.0)
Multiple myeloma	680 (480-890)	10.3 (7.3-13.5)	590 (420-780)	10.7 (7.6-14.1)	1280 (990-1540)	10.6 (8.2-12.7)
Colorectum	1330 (1080-1570)	4.8 (3.9-5.7)	1250 (1000-1530)	5.0 (4.0-6.1)	2590 (2210-2940)	4.9 (4.2-5.6)
Ovary	—	—	570 (350-780)	4.0 (2.5-5.5)	570 (350-780)	4.0 (2.5-5.5)

TABLE 5. *Continued*

CANCER	MEN		WOMEN		BOTH SEXES COMBINED	
	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %
Alcohol intake						
Oral cavity, pharynx	3000 (2830-3180)	44.4 (41.9-47.2)	650 (590-710)	24.6 (22.5-27.1)	3640 (3460-3830)	38.9 (36.9-40.9)
Larynx	750 (660-830)	24.5 (21.7-27.3)	90 (80-110)	12.8 (11.1-14.9)	840 (750-920)	22.3 (20.1-24.6)
Liver	3270 (1970-4840)	24.0 (14.5-35.6)	570 (340-860)	10.9 (6.4-16.4)	3840 (2540-5420)	20.4 (13.5-28.8)
Esophagus	1900 (1620-2130)	15.9 (13.6-17.8)	610 (450-750)	20.6 (15.2-25.2)	2510 (2180-2780)	16.8 (14.6-18.6)
Breast	—		6350 (5250-7570)	15.4 (12.8-18.4)	6350 (5250-7570)	15.4 (12.8-18.4)
Colorectum	4460 (2870-6150)	16.3 (10.5-22.4)	1810 (1160-2660)	7.2 (4.6-10.6)	6290 (4590-8100)	12.0 (8.8-15.5)
Red meat consumption						
Colorectum	1730 (1110-2340)	6.3 (4.1-8.5)	960 (500-1490)	3.8 (2.0-5.9)	2690 (1920-3530)	5.1 (3.7-6.7)
Processed meat consumption						
Colorectum	2700 (1970-3490)	9.9 (7.2-12.7)	1430 (940-1940)	5.7 (3.7-7.7)	4160 (3310-5060)	7.9 (6.3-9.7)
Stomach	220 (140-310)	3.2 (2.0-4.6)	150 (100-210)	3.4 (2.2-4.6)	370 (270-480)	3.3 (2.4-4.2)
Low fruit and vegetable consumption						
Oral cavity, pharynx	1140 (790-1540)	17.0 (11.8-22.8)	480 (290-670)	18.5 (10.9-25.4)	1640 (1190-2060)	17.5 (12.7-22.0)
Larynx	520 (340-690)	17.0 (11.2-22.6)	130 (90-180)	18.4 (12.2-25.2)	650 (470-830)	17.3 (12.4-22.1)
Lung	7440 (6120-8740)	8.8 (7.2-10.3)	6250 (5150-7340)	8.8 (7.3-10.4)	13,660 (11,910-15,400)	8.8 (7.7-9.9)
Low dietary fiber consumption						
Colorectum	2590 (1840-3300)	9.5 (6.7-12.0)	2880 (1970-3830)	11.5 (7.9-15.3)	5470 (4130-6600)	10.4 (7.9-12.6)
Low dietary calcium consumption						
Colorectum	1130 (990-1270)	4.1 (3.6-4.6)	1550 (1350-1750)	6.2 (5.4-7.0)	2,680 (2430-2940)	5.1 (4.6-5.6)
Physical inactivity						
Corpus uteri	—	—	2670 (1840-3470)	27.5 (18.9-35.7)	2670 (1840-3470)	27.5 (18.9-35.7)
Colon, excluding rectum[a]	4400 (3390-5320)	16.0 (12.4-19.4)	4340 (3260-5350)	17.3 (13.0-21.4)	8740 (7220-10,130)	16.7 (13.8-19.3)
Breast	—	—	1410 (1080-1740)	3.4 (2.6-4.2)	1410 (1080-1740)	3.4 (2.6-4.2)
Ultraviolet radiation						
Melanoma (skin)	5870 (5720-6010)	96.0 (93.5-98.4)	2880 (2780-2990)	92.3 (89.2-95.8)	8750 (8560-8920)	94.7 (92.7-96.6)
***H. pylori* infection**						
Stomach	1020 (890-1120)	15.1 (13.2-16.6)	1310 (1180-1430)	29.1 (26.2-31.8)	2320 (2140-2490)	20.6 (19.1-22.1)
HBV infection						
Liver	730 (430-1030)	5.4 (3.1-7.6)	500 (240-770)	9.6 (4.5-14.6)	1240 (810-1640)	6.6 (4.3-8.7)

TABLE 5. *Continued*

CANCER	MEN		WOMEN		BOTH SEXES COMBINED	
	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %	ATTRIBUTABLE DEATHS, NO. (95% CI)	PAF (95% CI), %
HCV infection						
Liver	3550 (2420-4420)	26.1 (17.8-32.5)	450 (260-630)	8.7 (4.9-12.1)	3990 (2860-4900)	21.2 (15.2-26.0)
Non-Hodgkin lymphoma	90 (50-150)	0.8 (0.5-1.3)	20 (10-30)	0.2 (0.1-0.4)	110 (70-170)	0.6 (0.4-0.8)
HHV8 infection						
Kaposi sarcoma	40 (30-60)	100 (70.5-100)	10 (0-10)	100 (33.3-100)	50 (40-70)	100 (72.0-100)
HIV infection						
Kaposi sarcoma	40 (30-50)	88.6 (61.4-100)	0 (0-10)	50.0 (16.7-100)	40 (30-60)	86.0 (60.0-100)
Anus	90 (60-110)	25.1 (17.2-31.6)	20 (10-40)	4.0 (2.3-6.3)	110 (80-140)	12.1 (9.1-14.9)
Non-Hodgkin lymphoma	1500 (1040-1900)	13.5 (9.3-17.0)	170 (70-290)	1.9 (0.8-3.2)	1670 (1210-2090)	8.3 (6.0-10.4)
Hodgkin lymphoma	60 (40-70)	9.4 (6.5-12.5)	10 (0-10)	1.4 (0.5-2.4)	60 (40-80)	6.2 (4.4-8.1)
Cervix	—	—	30 (20-40)	0.6 (0.4-0.9)	30 (20-40)	0.6 (0.4-0.9)
HPV infection						
Cervix	—	—	4040 (3920-4170)	100 (97.1-100)	4040 (3920-4170)	100 (97.1-100)
Anus	320 (260-390)	90.1 (72.9-100)	510 (430-590)	89.5 (75.9-100)	830 (730-940)	89.9 (79.5-100)
Vagina	—	—	280 (220-340)	65.0 (51.5-80.1)	280 (220-340)	65.0 (51.5-80.1)
Penis	180 (130-240)	58.7 (42.5-77.5)	—	—	180 (130-240)	58.7 (42.5-77.5)
Vulva	—	—	420 (340-500)	38.4 (31.7-46.1)	420 (340-500)	38.4 (31.7-46.1)
Oropharynx	570 (480-660)	37.5 (31.8-43.9)	50 (30-70)	10.9 (7.7-15.0)	620 (530-710)	31.5 (27.0-36.5)
Oral cavity	180 (110-270)	7.3 (4.5-11.1)	20 (10-40)	1.5 (0.8-3.0)	200 (120-290)	5.4 (3.4-7.9)

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HHV8, human herpes virus type 8; HIV, human immunodeficiency virus; HPV, human papilloma virus; H. pylori, *Helicobacter pylori*; PAF, population-attributable fraction. Cancer types associated with each risk factor are ordered by PAF in both sexes combined, and the numbers of attributable cancer deaths are rounded to the nearest 10. [a]PAF values are the percentages of all colorectal cancers.

proportions were higher in women for excess body weight, alcohol intake, physical inactivity, and HPV infection, largely driven by the high burden of breast, endometrial, and cervical cancers attributable to these risk factors.

Our overall PAFs are generally comparable to those from recent studies that used similar methods.[5-11] However, there are some notable differences, mainly in the proportion of specific cancer types attributable to a given risk factor. For example, previous studies reported larger proportions of HCV-associated liver cancer in women (26%-28%) than in men (18%-19%),[8,54] whereas we found the reverse (28% in men vs 12% in women), consistent with higher HCV infection prevalence in men.[51] A previous estimate of the PAF for cancer mortality specifically because of excess weight reported a slightly lower PAF for men (4% vs 6% in our study) and a higher PAF for women (14% vs 7%).[55] However, these estimates were based on exposure data for a relatively narrow age group and used risk estimates for all cancers combined without taking into account the distribution of deaths and RRs by cancer type.

Several previous studies reported on the proportion of cancers attributable to various risk factors in the United States using cohort data,[56,57] and the findings from some of those studies differ slightly from ours. For example, compared with our study, the PAFs for cancer incidence within cohort studies of health professionals reported by Song and Giovannucci[56]

were lower than those in our study for both men (33% vs 43% in our study) and women (25% vs 42%), whereas the PAF for mortality was slightly lower in men (44% vs 48%) and higher in women (48% vs 42%). The lower PAFs in that study may be related in part to the lower numbers of risk factors considered and the inclusion of moderate alcohol drinkers and some former smokers in the low-risk group. In general, however, PAFs within cohort studies may not be directly generalizable to the entire US population, mainly because of potential differences in exposure prevalence between the general population and cohort study participants.[58,59]

Smoking

Despite substantial declines in overall smoking prevalence over the past 5 decades,[41,48,60] cigarette smoking remains the leading contributor to cancer cases and deaths in both men and women, accounting for 19% of all cancer cases and 29% of all cancer deaths. These estimates are comparable to findings from previous studies.[5,9] Our results reemphasize that expanding comprehensive tobacco-control programs could have the greatest impact on reducing the overall cancer burden in the United States. It is noteworthy that we did not include the use of tobacco products other than cigarettes[14,61] and only considered smoking for cancer types with an established causal association according to IARC reports, although there is accumulating evidence for causal associations between smoking and additional cancers (eg, breast cancer).[62] In an earlier study that also considered these cancer types, the proportion of cancer deaths attributable to cigarette smoking was about 32%.[63] Furthermore, a considerable proportion of cancer deaths categorized as unknown site actually may be caused by smoking-attributable cancers.[62] Thus, the burden of cancer attributable to smoking is likely higher than we have estimated.

Proven measures to reduce smoking include taxation, smoke-free laws, assistance with smoking cessation, warning labels and media campaigns, and marketing bans.[48] In the United States, taxation appears to have the strongest effect, followed by smoke-free laws, which can also substantially reduce exposure to SHS and related health issues.[48,64,65] Tobacco taxation has a higher impact on lower income people, who also have a higher smoking prevalence, and on youth, because taxation may prevent them from initiating smoking.[48,65,66] However, there is wide variation across states in the number and intensity of implemented measures.[9,64,66] For example, the state-level tax per cigarette pack as of April 2017 ranged from $0.17 in Missouri to $4.35 in New York (with an additional $1.50 in New York City).[67] In addition, as of July 2017, only 25 states and the District of Columbia had implemented comprehensive smoke-free laws in all 3 recommended locations (worksite, restaurants, and bars).[68] Currently, no state has fully implemented the CDC's recommended comprehensive tobacco-control measures.[69]

It is also important to integrate tobacco initiation prevention and support for cessation into the health care system,[70] but these services are generally underused, especially in low-income and uninsured individuals.[71] Moreover, only less than 4% of eligible current or former smokers received the recommended lung cancer screening in the United States in 2015.[72] Overall, broad implementation of effective cancer prevention and control interventions, including tobacco-control policies, has been challenging in the United States.[73] There is a need for increasing awareness about the health hazards of smoking to discourage initiation and promote cessation; for equitable access to cessation services; and, more important, for further political commitment to tobacco control (including securing financial resources) at the local, state, and federal levels to substantially reduce the burden of smoking-related diseases.[69,74]

Excess Body Weight, Alcohol Intake, Poor Diet, and Physical Inactivity

We estimated that nearly 7% to 8% of all cancer cases and deaths in the United States were attributable to excess body weight and 4% to 6% of cases and deaths were due to alcohol intake, respectively, similar to other recent estimates.[6,7,11,75] Previous PAFs for poor diet included variable dietary factors and criteria,[76] but more recent PAFs are comparable to our estimates (4% to 5% of all cancer cases and deaths).[77] Our estimated PAF for physical inactivity (2% to 3% of all cancer cases and deaths) is slightly higher than earlier PAFs.[4]

The combination of excess body weight, alcohol intake, poor diet, and physical inactivity accounted for the highest proportion of all cancer cases in women and was second only to tobacco smoking in men. These 4 combined risk factors also accounted for the second highest proportion of cancer deaths in both men and women. These findings underscore the importance of adherence to comprehensive guidelines on weight control, alcohol, diet, and physical activity. Indeed, large, prospective epidemiologic studies have demonstrated that adherence to a lifestyle consistent with the American Cancer Society's cancer prevention guidelines for maintaining a healthy body weight, limiting alcohol intake (for those who drink), consuming a healthy diet, and being physically active[38] is associated with a reduced risk of developing and dying from cancer.[78,79] Currently, nearly three-fourth of adults and one-third of children and adolescents aged 2 to 19 years are overweight or obese.[80,81] Furthermore, many Americans regularly drink alcohol and do not meet other dietary recommendations.[49,60,82] Despite a modest decrease in physical inactivity prevalence over the past few decades, it remains substantially high in the United States (see Supporting Information Table 2).[83]

For many children, excess body weight extends into adulthood and increases the risk of adverse health conditions and death,[84,85] so weight control in childhood should be a major focus of any strategy to control the obesity epidemic.[86,87] School-based interventions can provide an opportunity for promoting healthy diet, physical activity, and weight control, as well as family-based interventions.[88-90] Several studies have demonstrated that intensive lifestyle interventions to promote healthy eating and physical activity are effective among adults,[91,92] although long-term effects of such interventions at the population level have generally been modest at best.[83,88,89] Studies of behavioral interventions for reducing alcohol intake have focused primarily on alcohol use disorders and have produced mixed results,[93] whereas information on more commonly consumed levels is much more limited.

Effective implementation of preventive measures (consultation, screening, and treatment) in the health care system and increasing awareness through education campaigns may help to reduce excess body weight and alcohol intake and promote healthier diet and physical activity.[84,92,94-98] Some regulations may be highly beneficial, such as taxation and reducing marketing of nonessential high-calorie foods, sugary beverages, and alcohol; regulating alcohol outlet density and the days and hours of alcohol sale; and improving civil structure (eg, increasing public transportation and safe sidewalks).[99-103] For example, similar to the effect of taxation on tobacco smoking, higher excise taxes on alcohol have been associated with a substantial reduction in alcohol intake.[104] However, more research is still needed to identify tailored, more efficient interventions, particularly those that could be successfully applied at the community level.

UV Radiation

We estimated that nearly 95% of all skin melanoma cases and deaths in the United States are attributable to UV radiation, comparable to earlier studies.[46] Moreover, UV radiation from sun exposure and indoor tanning can increase the risk of nonmelanoma skin cancers (4.3 million individuals are treated annually in the United States), which are less fatal but associated with substantial financial burden.[105] Both melanoma and nonmelanoma skin cancers are increasing in the United States, making skin cancer prevention increasingly important.[105-107]

Sun-protection measures, including limiting excessive sun exposure; wearing protective clothing, hat, and sunglasses; and using broad-spectrum sunscreens, have been recommended to reduce skin cancer risk.[108] Although more research on the effectiveness of sunscreen use at the population level is needed,[109] several studies have either shown a direct decrease in melanoma risk after regular application of approved products[110,111] or have suggested a reduction in melanoma incidence rates in areas where sunscreens are freely available.[112] However, the uptake of sun-protection measures in the United States is far from optimal, but it may improve through multicomponent interventions at the community level.[108,113]

Reducing indoor tanning is particularly important among adolescents, because exposure at younger ages is associated with a higher risk of skin cancer up to at least age 50 years.[114,115] Federal- and state-level interventions to restrict access to indoor tanning or educate youth about the harms are likely to have contributed to a decrease in the overall indoor tanning prevalence among youth in the United States in recent years.[116-118] However, because of wide variations in regulation strictness (including the defined age limit) or compliance across states, high numbers of adolescents in the United States still engage in indoor tanning (eg, 1.2 million [7% of] high school students in 2015).[118]

Infections

Approximately 3% of all cancer cases in our study were attributable to infections, similar to 4% in an earlier study that also included less common infections (for which exposure prevalence could only be estimated).[10] *H. pylori* infection prevalence in the United States has decreased in the past century, probably because of improvements in sanitation and living conditions and more widespread antibiotic use.[119] This trend was followed by a decrease in gastric noncardia cancer incidence rates in the country.[120] Currently, screening for *H. pylori* and subsequent treatment is only recommended for people with certain conditions, and there is no evidence to support routine screening in other individuals.[121,122]

In contrast to *H. pylori* infection, chronic HCV infection prevalence in the United States increased in the last one-half of the 20th century (mainly among Baby Boomers),[51] which contributed in part to rising liver cancer rates.[123] Interventions to reduce HCV and HBV burden include increasing awareness; HBV vaccination; screening; treatment to cure HCV infection; and comprehensive programs to reduce transmission through high-risk behaviors (eg, using shared syringes); however, the uptake of many of these interventions is suboptimal in the United States.[123-127] For example, one-time HCV testing is recommended for Baby Boomers, but only 14% report HCV testing.[128] HBV vaccination coverage is only 65% among health care personnel and is even lower in other high-risk adults for whom HBV vaccination is recommended (eg, 27% among those with chronic liver conditions).[127]

Among people with HIV infection, highly active antiretroviral therapy reduces the risk of cancers that define the onset of acquired immunodeficiency syndrome (AIDS), ie, Kaposi sarcoma, non-Hodgkin lymphoma, and cervical cancer.[129,130] At the same time, however, increasing rates of

successful highly active antiretroviral therapy have also increased the number of HIV-infected individuals who are aging, leading to increased number of non–AIDS-defining cancers in this population.[129,130] As most carcinogenic infections (because of shared transmission routes with HIV) and smoking are more common in people with HIV infection,[131] receiving recommended vaccines (including HPV vaccine through age 26 years and HBV vaccine at any age),[132] screenings (eg, for HCV infection), and smoking-cessation services is even more important in this group.

Some cancer types that are highly associated with HPV infection have shown contradictory incidence rate trends in the United States in recent decades. Cervical cancer incidence and death rates have been decreasing since the mid-20th century, mainly because of the widespread use of cervical cancer screening.[133] Conversely, incidence rates for cancers of the tongue base and tonsil among younger men and anal cancer in both sexes have been increasing, in part because of changes in sexual behavior.[134-136] Although HPV vaccination can prevent anogenital cancer and is recommended at ages 11 and 12 years (but can be given up to age 26 years),[137] only 50% of females and 38% of males ages 13 to 17 years in the United States were up to date with HPV vaccination as of 2016.[138] Furthermore, the cervical cancer screening rate for uninsured women, among whom HPV infection is more common, is much lower than that for insured women (61% vs 84%, respectively).[60]

Strengths and Limitations

We have provided contemporary estimates of the PAFs of cancer cases and deaths for several potentially modifiable risk factors (including some risk factors that were not included in previous studies) in the United States using contemporary, nationally representative data on exposure, occurrence (accounting for delayed reporting), and RRs. Furthermore, we used a systematic approach, as well as exposure and outcome data largely from the same period, to compute PAFs; thus, our estimates are comparable across risk factors and cancer types.

However, there are several inherent limitations in studies that estimate the PAF of cancer caused by specific exposures. The selected RRs may not be homogenous across sexes and age groups. In addition, we used the same RRs in calculations for both cancer deaths and cases, because RRs were generally available only for cases, with some exceptions. However, some risk factors may affect the survival of patients with cancer and, thus, have an impact on cancer mortality beyond that for incidence. Similarly, survival for some cancer subtypes for which we estimated death counts using case-based proportions is known to be different from survival for other subtypes within the overall cancer type (eg, for colon cancer, 5-year relative survival is slightly lower than that for rectal cancer). Furthermore, in general, we used the most recent exposure data rather than historical data; because, for most risk factors, the latency from exposure to cancer occurrence is not well defined.[139,140] Therefore, our PAF estimates for exposures with declining or increasing prevalence in recent years could be underestimated or overestimated, respectively.

Finally, when calculating PAFs, we assumed that the risk factors were independent, and no robust, comprehensive information was available on the nature or magnitude of the amount of overlap among risk factors at the population level. Therefore, some PAFs may be slightly overestimated. Conversely, we did not include several other potentially modifiable risk factors, such as breastfeeding, because of a lack of representative exposure data (see Supporting Information Table 1), and we did not consider some other likely associations that had less than sufficient or strong evidence for a causal association with cancer according to the IARC or the WCRF/AICR, notably for smoking,[62] despite accumulating evidence for a causal association. Thus, we likely underestimated the actual proportions of cancers attributable to some individual risk factors and all potentially modifiable factors combined. Furthermore, some risk factors may be more important when exposure occurs in adolescence or earlier,[141] such as excess body weight and colorectal cancer,[142] which are likely unaccounted for by RRs from studies of mostly older adults. More research is needed on earlier life exposures that can increase the risk of cancer in adulthood.

Conclusions

An estimated 42% of all cancer cases and nearly one-half of all cancer deaths in the United States in 2014 were attributable to evaluated risk factors, many of which could have been mitigated by effective preventive strategies, such as excise taxes on cigarettes to reduce smoking and vaccinations against HPV and HBV infections. Our findings emphasize the continued need for widespread implementation of known preventive measures in the country to reduce the morbidity and premature mortality from cancers associated with potentially modifiable risk factors. Increasing access to preventive health care and awareness about preventive measures should be part of any comprehensive strategy for broad and equitable implementation of interventions to accelerate progress against cancer. However, for some of the risk factors considered in the current analysis, such as unhealthy diet, further implementation research is needed for widespread application of known interventions, particularly for populations at a higher risk. Further research is also needed on the etiology of cancer, particularly cancers for which avoidable risk factors with substantial PAFs are not well known (eg, prostate and pancreas cancers) or where the evidence is considered insufficient for causality in humans. ■

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