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Proportion and number of cancer cases and deaths attributable to behavioral risk factors in Vietnam

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Abstract

Identifying modifiable risk factors that contribute to cancer is essential in setting up preventive strategies. Therefore, this study aimed to estimate the number and proportion of cancer cases and deaths attributable to five behavior-related risk factors—tobacco smoking, second-hand smoking, alcohol consumption, high body mass index and insufficient physical activity in Vietnam in 2020. Population attributable fractions were calculated for relationships of risk factors and cancer types based on sufficient evidence according to IARC or strong evidence according to WCRF/AICR. Relative risks were retrieved from meta-analyses where possible. Prevalence of risk factors was obtained from the most current available nationally representative population surveys in Vietnam. Cancer cases and deaths were obtained from GLOBOCAN 2020. An estimated 40.5% of all cancer cases in men (39 924 cases) and 7.8% in women (6542 cases) were attributable to these risk factors. The proportions of cancer deaths attributable to these risk factors were 44.0% in men (32 807 cases) and 8.9% in women (4235 cases). Tobacco smoking was the leading cause of cancer cases and deaths in men, followed by alcohol consumption and high BMI. In women, high BMI accounted for the highest proportion of cancer cases and second-hand smoking accounted for the highest proportion of cancer deaths. Lung and upper aerodigestive tract cancer cases and deaths could have been reduced at least by half if these risk factors had been eliminated. To reduce cancer incidence and mortality, preventive actions focusing on tobacco control are likely to have the most significant impact, especially in men.

KEYWORDS

behavior, cancer, population-attributable fraction, prevention

What's new?

Behavioral risk factors contribute substantially to cancer cases and deaths; however, in Vietnam, reliable data and methods to estimate the attributable causes of cancer incidence and mortality have been lacking. Using nationally representative data on exposures and cancer occurrence in

Abbreviations: ASR, age-standardized incidence rates; BMI, body mass index; DALY, disability-adjusted life years; GDP, gross domestic product; IARC, International Agency for Research on Cancer; MET, metabolic equivalent; PAF, population attributable fractions; RR, relative risk; WCRF/AICR, World Cancer Research Fund/ American Institute for Cancer Research; WHO, World Health Organization; YLL, years of life lost.

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Vietnam in 2020, this study comprehensively estimates the proportion and number of cancer cases and deaths attributable to five major behavior-related factors (tobacco smoking, second-hand smoking, alcohol consumption, high body mass index and insufficient physical activity). Around 25% of all cancer cases and 30% of all cancer deaths in Vietnam could have been prevented if these risk factors had been eliminated.

1 | INTRODUCTION

Worldwide, nearly 19.3 million new cancer cases and almost 10.0 million cancer deaths occurred in 2020.[1] The cancer burden in Vietnam has increased rapidly in recent decades; the estimated number of new cases in 2020 was 182 563 (188 per 100 000 persons) and that of deaths was 122 690 (126 per 100 000 persons),[2] which have tripled in the last 30 years (52 700 cases and 37 700 deaths in 1990).[3,4] The number of new cancer cases in males was higher than females in 2020 (98 916 vs 83 647), and men also had higher age-standardized incidence rates (ASR) per 100 000 than women in all of the top cancers except for thyroid cancer.[2] Specifically, lung and liver cancer cases and ASR per 100 000 in males are more than triple the numbers in females, which may be influenced largely by higher smoking and drinking rates in men.[2] In terms of new cases from 2000 to 2020, lung and liver cancer also showed the greatest uptick in men while breast cancer showed the greatest increase in women.[2,4] Compared with the worldwide average estimate of ASR per 100 000 from IARC in 2020, Vietnamese men had higher ASR for lung, liver and stomach cancer but lower ASR for colorectal and other cancer while women had an overall lower or equivalent ASR for most cancers.[5]

Apart from the extensive morbidity and mortality, the economic impact of cancer is enormous for both the patients and the society, especially in low-middle-income countries, including Vietnam.[6] Of 2012 Vietnam's Gross Domestic Product (GDP), 0.22% (around 619 million U.S. dollars) was expended for treating six common cancers (breast, ovary, liver, colon, stomach and pharynx); and 37% of the households with cancer patients were pushed into poverty due to the high treatment costs.[6] In addition, cancer accounted for the second highest burden of diseases in Vietnam in 2008, responsible for 22% of the total years of life lost (YLL; nearly 1.5 million years) and 14% of total disability-adjusted life years (DALYs; nearly 1.7 million years).[7]

Cancer is caused by an interplay of environmental, behavioral, genetic, mutation and familial factors.[8] The World Health Organization (WHO) estimated that 30% to 50% of cancer cases can be prevented by modifying behavioral risk factors, including avoiding tobacco products, reducing alcohol consumption, maintaining a healthy body weight and exercising regularly.[9] These behavioral risk factors together have been reported to be associated with higher risk of at least 22 types of cancer.[10,11]

The burden of cancer due to risk factors can be estimated by the Population Attributable Fraction (PAF), which was first introduced by Levin in 1953.[12] PAF assesses the proportion of cases or deaths that could be avoided if the exposure distribution in the entire population was reduced to the ideal reference level, in which none of the individuals were exposed to the risk factor.[13] PAF approach is a valuable tool for setting priorities for cancer prevention and control strategies, and has been used mostly in high-income countries.[14-17] However, in Vietnam, systematic study on such issues using this approach is nascent. The two previous studies only focused on cancer incidence or mortality, a single risk factor at a time or only one sex.[18,19] Moreover, in the study estimating PAFs for cancer cases attributable to some risk factors in Vietnam in 2018, the prevalence data sources for many risk factors, such as infectious agents, pollutants and nulliparity, was not nationally representative and were outdated.[19] This previous study did not provide detailed methods on how relative risks were reviewed and pooled to calculate PAFs, how factors like secondary smoking and BMI were handled in the analysis, and why physical activity was excluded even though reliable and updated prevalence data was available. Therefore, our study aims to comprehensively estimate the proportion and number of cancer cases and deaths attributable to five behavior-related risk factors (tobacco smoking, second-hand smoke, alcohol consumption, high body mass index and insufficient physical activity) using nationally representative data on exposures and cancer occurrence in Vietnam in 2020 as well as provide detailed methods for future replication. The results can inform strategic policy responses and initiatives for cancer control in the future.

2 | MATERIALS AND METHODS

2.1 | Data sources

2.1.1 | Selection of risk factors and cancer types

Our study focused on five behavior-related risk factors in Vietnam: tobacco smoking, second-hand smoke, alcohol consumption, high body mass index and insufficient physical activity. We used reports published by the International Agency for Research on Cancer (IARC)[10] and the World Cancer Research Fund/ American Institute for Cancer Research (WCRF/AICR)[11] to identify potentially modifiable risk factors, and selected the risk factors for which prevalence data were available in Vietnam National Survey. Diet, infections, air pollution and other potentially modifiable factors were not included in our study due to the lack of detailed national representative data for Vietnamese population. While data on air pollution and infection would greatly enrich the results, they typically are less modifiable on the behavioral aspect at the individual level. Nonetheless, a substantial proportion of the dietary effect on cancer is mediated through body weight gain, so by considering BMI, we indirectly capture important aspects of diet.[11] Cancer types associated with risk factors were selected based on *sufficient evidence* classification of IARC or *strong evidence* (*both convincing and probable*) classification of WCRF/AICR. If both the IARC and the WCRF/AICR identified the combinations of risk factors and cancer types, the classification in the most recently year was noted and presented in the Data S1A.

2.1.2 | Risk factors prevalence

Data on prevalence of these five risk factors were pooled from the Vietnam National Survey on the Risk Factor of Non-Communicable Diseases (STEPS), a cross-sectional design with a nationally representative sample of the population aged 18-69 residing in all 63 provinces/cities of Vietnam in 2015.[20] In our study, the prevalence of tobacco smoking was assessed based on both current and former smoking. For estimating the burden of second-hand smoke, prevalence of exposure to tobacco smoke at home or at workplace among never smokers was calculated following the questions "During the past 30 days, did someone smoke in your home?" and "During the past 30 days, did someone smoke in closed areas in your workplace (in the building, in a work area or a specific office)?". Alcohol consumption was assessed through average grams per day drinking in the past month and was categorized into non-drinking (0.0 g), light (<12.5 g), moderate (12.5-49.9 g) and heavy (≥50 g) daily consumption.[14,21] Regarding physical inactivity, we used the percentage of respondents not meeting WHO recommendations on physical activity for health (including all types of work-, transport- or recreational-related physical activity)—achieving at least 600 metabolic equivalent (MET) minutes of total activity per week (ie, respondents doing <150 min of moderate-intensity physical activity per week, or equivalent).[22] All risk factor prevalence estimates were stratified by sex in order to align with sex differences in relative risks and estimated cancer occurrence data (Data S1B).

2.1.3 | Relative risks

A total of 22 types of cancer were included in our analysis, based on its established causal relationship to the risk factors selected (Data S1A). We obtained relative risks (RRs) of each exposure-cancer pair through a systematic PubMed/MEDLINE search (search terms are shown in Data S1C, selected RRs, and references were shown in Data S1D). When selecting RRs, we preferably used meta-analysis, then pooled analysis (of cohort studies), and finally individual cohort studies. Case-control studies were only used when there was no data from these preferred study designs. Due to a lack of prospective studies on cancer etiology in Vietnam, we obtained RRs from research conducted in Asian countries or worldwide if specific RRs were not available for Asian population. Sex-specific RRs would be used when there was a report of gender difference; otherwise, we used the same values of RR for both sexes. We used the same RRs for both outcome of incidence and mortality, which is the method recommended in many previous PAF studies,[15,16,23,24] because the RRs for cancer specific mortality were not widely available from large-scale studies or even when available, they did not show a substantial difference. Moreover, cancer incidence data are far more complete and of higher quality.[16]

2.1.4 | Cancer incidence and mortality

The number of cancer cases and deaths in Vietnam were retrieved from the Global Cancer Observatory (GLOBOCAN) 2020 analysis.[5] More detailed information on cancer incidence and mortality data was noted in Data S1E. Throughout the results of this paper, cancer case refers to the number of incidents cancers in Vietnam in 2020, and cancer death or mortality refers to the number of new cancer deaths in Vietnam in 2020.

2.2 | Data analysis

PAF was estimated based on the relative risk of cancer associated with a particular risk factor and the prevalence of the risk factor in a general population (P). 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 by the corresponding PAF. The main results of attributable cases and deaths was calculated with cancer data for all ages. As our prevalence data was obtained from STEPS 2015 sampled in the population aged 18-69, we added a supplementary analysis (Data S1F for cancer cases and Data S1G for cancer deaths) to apply the PAFs to cancer data for the 25 to 74 age group after taking into account the 5- to 7-year latency between the 2015 survey and 2020 cancer cases or deaths.

2.2.1 | PAF for each risk factor and cancer type

PAF for categorical exposures including tobacco smoking, second-hand smoke, alcohol consumption, insufficient physical activity was calculated using Levin's formula for multiple categories, as proposed by Hanley[12,25]:

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

where P_i is exposure distribution at the exposure category *i*, and RR_i is the relative risk for the association between exposure category *i* and site-specific cancer.

When the PAF was to be calculated for the absence of/decrease in that risk factor (ie, physical activity) but the RR was provided as reduced risk from an increase in the risk factor (eg, increased physical activity), excess relative risk $(RR_i - 1)$ was calculated as the natural logarithm of the reciprocal of the RR, which is ln(1/RR).[14]

PAF for continuous exposure (ie, BMI) was calculated based on another re-written form of PAF formula[25,26]:

$$\text{PAF} = \frac{\int RR(x)P(x)dx - \int RR(x)P^*(x)dx}{\int RR(x)P(x)dx}$$

where $P(x)$ is the current population distribution of BMI (in kg/m^2), $P^*(x)$ is the distribution of theoretical minimum BMI, $RR(x)$ is the relative risk of cancer per 1 kg/m^2 increase in BMI, and dx indicates the integration according to BMI units. Since we used 1 kg/m^2 increment in BMI (i represent each one unit increase in BMI), the aforementioned formula is equivalent to:

$$\text{PAF} = \frac{\sum RR_i P_i - \sum RR_i P^*{}_i}{\sum RR_i P_i}$$

The theoretical minimum distribution of BMI was defined as mean 22 kg/m^2 and SD 1 kg/m^2 in some previous Western countries studies.[27,28] However, average BMI of Asian populations is lower compared with Caucasians.[29] Therefore, we decided to use a mean of 21 kg/m^2 and a SD of 1 kg/m^2 as the theoretical minimum distribution of BMI, where we assumed the cancer burden would be lowest at the population level.

When RRs reported were provided for multiple units (eg, 5 kg/m^2) and did not match our predefined category levels, we recalculated the RRs assuming a linear dose-response of BMI and cancer risk/mortality.[15] For instance, for a study that reported a RR associated with A units of exposure (ie, RR_A), the RR of new units of exposure (B units) that matches our predefined exposure category (ie, RR_B) was calculated by this formula[15]:

$$RR_B = e^{\frac{\ln(RR_A)}{A} * B}$$

2.2.2 | PAF combined for all risk factors in each cancer type

To estimate the proportion of each cancer site attributable to combined risk factors, we used the combined PAF equation assuming that risk factors are independent (no statistical interaction):

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

where PAF_i is the PAF for each individual risk factor.

2.2.3 | PAF combined for all cancer types in each risk factor

We summed the number of cases or deaths attributable to each risk factor across associated cancer sites assuming the effects of risk factors on each cancer were independent from each other. To obtain the overall proportion of all cancer attributable to each risk factor, we divided these results by the total number of all cancer cases or deaths, respectively.

3 | RESULTS

3.1 | Cancer incidence due to the five behavior-related risk factors

An estimated 25.6% of all new cancer cases (46 799 of 182 563 cases) in Vietnam in 2020 were attributable to behavior-related risk factors. The proportion of total cases was five times higher in men, at 40.4% (39 924 of 98 916 cases) compared with 7.8% in women (6542 of 83 647 cases). Among five risk factors, tobacco smoking accounted for the highest PAF of all incident cancers in men (33.9%), followed by alcohol consumption (5.4%), and high BMI (3.2%). In women, the greatest attributable proportion of cancer cases was for high BMI (3.1%), followed by secondhand smoke (2.1%) (Figure 1).

The proportion of type-specific cancer cases attributable to all five risk factors ranged from 2.4% for prostate to 84.1% for lung cancer in men, and from 0.7% for leukemia to 32.8% for lung in women. Lung cancer had the highest overall number of cases attributable to all studied risk factors in both men (15 709 cases) and women (2482 cases), followed by liver cancer (8149 cases), stomach cancer (3256 cases) and colorectal cancer (2137 cases) among men and cancers of endometrium (1153 cases), liver (732 cases) and colorectum (666 cases) among women. Colorectal cancer was the only cancer type attributed to all modifiable risk factors included in our study, with a total PAF of 17.2% for new cases (2825 cases) (Figure 2).

3.1.1 | Tobacco and secondhand smoke

Tobacco smoking represented the largest risk factor for all cancer cases in men (33.9%) and accounted for around 83% of cancer cases that were associated with the five behavior-related risk factors in our study (33 494 cases out of 40 159 cases). The PAF pattern attributable to smoking was much higher in men than in women (33.9% vs 1.3%, respectively) (Figure 1). Cancer types with the highest PAFs for smoking were lung, larynx and pharynx cancer in both sexes (78.1%, 76.6% and 75.8%, respectively, in men and 9.5%, 9.1% and 8.7%, respectively, in women). Lung cancer also had the highest number of smoking-related cancer cases (15 318 cases), followed by liver cancer (5777 cases) and stomach cancer (3033 cases) (Table 1).

Meanwhile, second-hand smoking accounted the second highest proportion of cancer cases in women (2.1%). The number of lung cancer cases attributable to second-hand smoking among never-smokers was greater in women (1724 cases) than in men (357 cases). Additionally, in women, second-hand smoking caused more lung cancer than primary smoking did (719 cases) (Table 1).

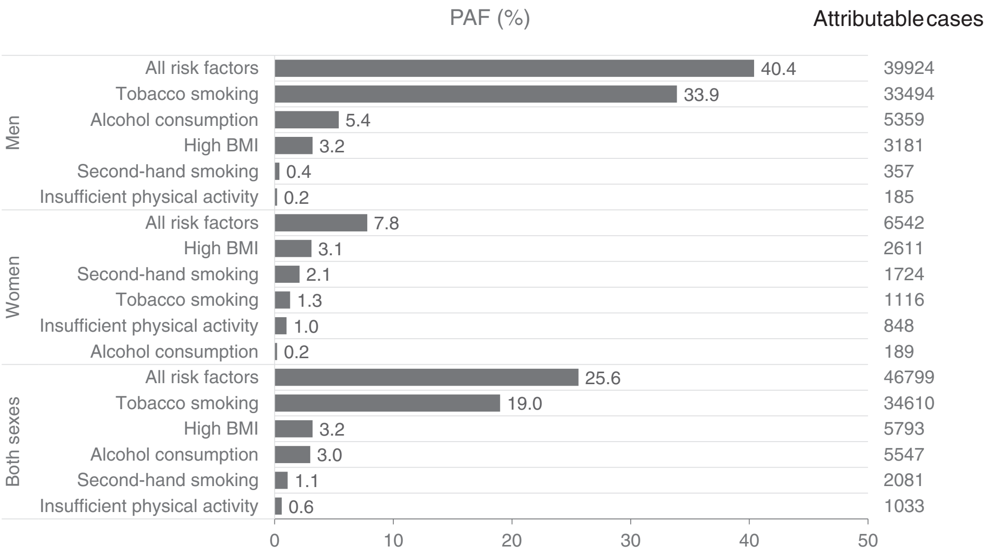

FIGURE 1 Proportion and number of all cancer cases attributable to lifestyle risk factors in Vietnam in 2020, by sex and exposure. All risk factors, all studied risk factors; BMI, body mass index; PAF, population attributable fraction. The total number of all cancer cases was 98 916 among men, 83 647 among women and 182 563 for both sexes.

3.1.2 | High BMI

High BMI was the largest contributor for all cancer cases among women, at 3.1% (2611 of 83 647 cases) and the third largest contributor among men, at 3.2% (3181 of 98 916 cases) (Figure 1). Cancer types with the highest PAFs for high BMI were 15.3% of endometrial cancers in women, and 9.9% of liver cancers in men. Among men, the absolute number of cancer cases attributable to high BMI was largest for liver, colorectal and stomach cancers (2013, 434 and 210 cases, respectively); while among women, these numbers belong to endometrial, liver and colorectal cancers (819, 631 and 377 cases, respectively) (Table 1).

3.1.3 | Alcohol consumption

Alcohol consumption was responsible for 5.4% of all cancer cases (5359 of 98 916 cases) in men, which was much greater compared with that in women, at 0.2% of all cancer cases (189 of 83 647 cases) (Figure 1). Contributing the highest cancer burden, more than one-third of esophageal (39.3%; 1157 cases), oral cavity (33.6%; 553 cases) and pharyngeal (33.6%; 809 cases) cancer were associated with alcohol in men. In women, the highest rank order was similar, at 3.6% for esophageal cancer and 2.3% for oral cavity and pharyngeal cancer, each. Regarding the absolute cancer cases due to alcohol consumption, liver cancer (1576 cases) and breast cancer (127 cases) caused the largest in men and women, respectively (Table 1).

3.1.4 | Insufficient physical activity

Insufficient physical activity accounted for 1.0% of all cancer cases in women (848 of 83 647 cases), five times higher compared with 0.2% in men (189 of 98 916 cases) (Figure 1). The highest proportion was for cancer of the endometrium (7.4%; 395 cases) in women. 2.8% of colorectal cancers (458 cases) were attributable to insufficient physical activity, with the proportion higher in women (3.6%; 273 cases) than in men (2.1%; 185 cases). Finally, 1.2% of breast cancers (180 cases) were attributed to this risk factor (Table 1).

3.2 | Cancer mortality

The selected behavior-related risk factors were responsible for 30.4% of all cancer deaths (37 273 of 122 690 deaths) in Vietnam in 2020. The proportion of all cancer deaths attributable to these factors was 44.0% in men and 8.8% in women (Figure 3). The ranking of cancer mortality due to these risk factors was quite similar to those for cancer incidence; however, there was a disparity in women, that second-hand smoking was the greatest contributor for all cancer deaths, and high BMI was the second. By cancer type, lung cancer had the largest number of deaths attributable to all five risk factors in both men (14 350 deaths) and women (2204 deaths), followed by liver cancer in both men (7813 deaths) and women (695 deaths) (Figure 4).

Tobacco smoking accounted for the highest figure (37.2%, 27 699 of 74 481 deaths) of overall cancer deaths in men. While in women, second-hand smoking was the greatest contributor, associated with 3.2% of all cancer deaths, and caused more cancer deaths than primary smoking, at 1531 deaths compared with 638 deaths. High BMI ranked in second place of cancer mortality burden in women, at 2.8%, and in third place in men, at 3.5%. The proportion of all cancer deaths attributed to alcohol consumption in men was 5.4%, higher than that for insufficient physical activity, at 0.1%. In contrast, PAFs were 0.7% for insufficient physical activity and 0.2% for alcohol consumption in women. The detailed proportion and number of cancer deaths attributable to evaluated risk factors by sex, exposure and cancer type are displayed in Table 2.

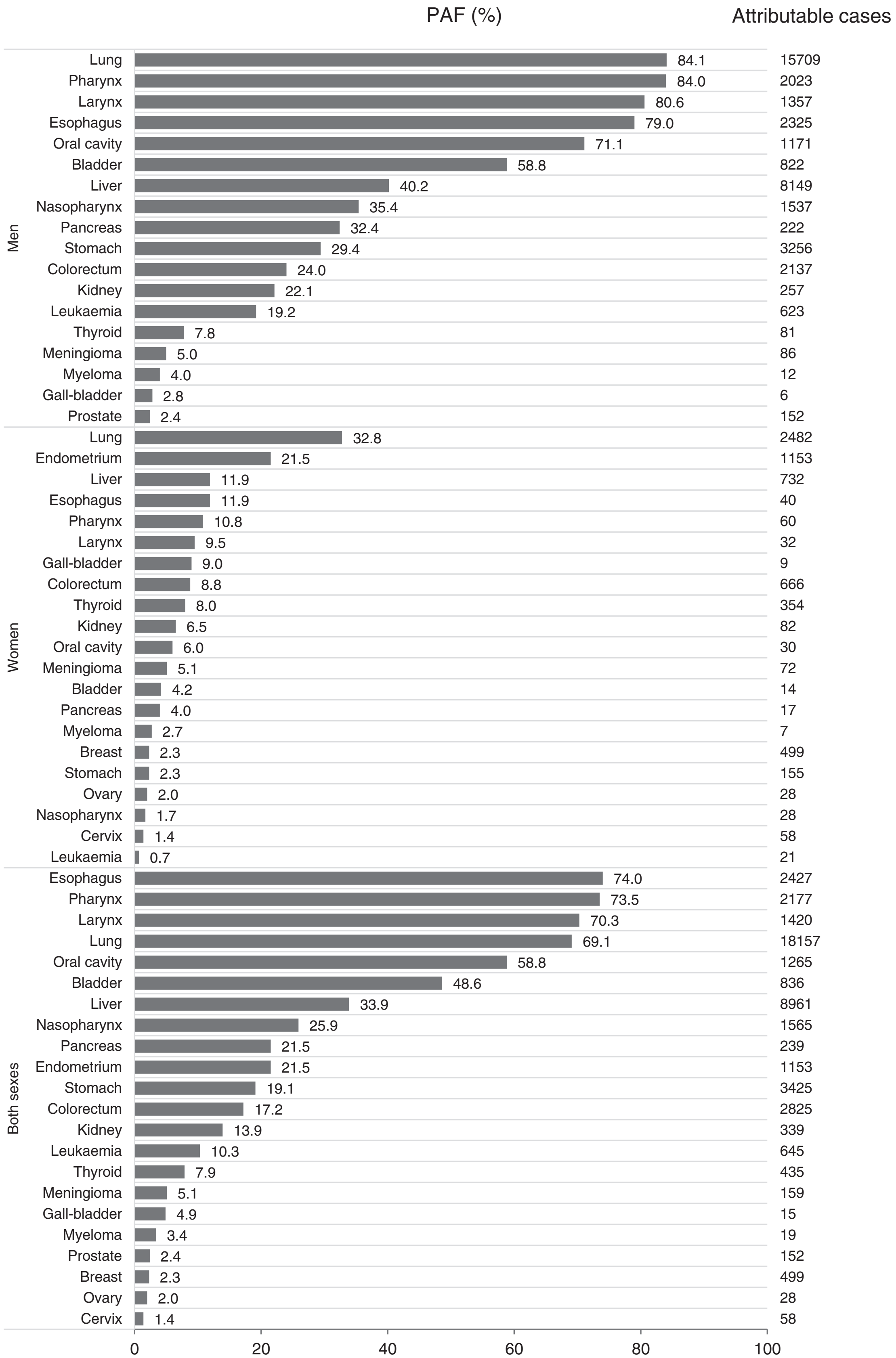

FIGURE 2 Proportion and number of cancer cases attributable to all selected lifestyle risk factors in Vietnam in 2020, by sex and cancer type.

TABLE 1 Proportion and number of cancer cases attributable to individual behavior-related risk factors in Vietnam in 2020, by sex, risk factor and cancer type

	Men			Women			Both sexes		
Risk factors associated cancer types	Number of cases	PAF (%)	Attrib. cases	Number of cases	PAF (%)	Attrib. cases	Number of cases	PAF (%)	Attrib. cases
Tobacco smoking									
Oral cavity	1646	56.5	930	506	3.8	19	2152	44.1	950
Pharynx	2409	75.8	1827	552	8.7	48	2961	63.3	1875
Nasopharynx	4340	35.4	1537	1700	1.7	28	6040	25.9	1565
Esophagus	2942	64.2	1888	339	5.2	18	3281	58.1	1906
Stomach	11 059	27.1	3001	6847	0.3	20	17 906	16.9	3022
Colorectum	8887	9.9	882	7539	0.4	27	16 426	5.5	910
Liver	20 256	28.0	5680	6162	1.6	97	26 418	21.9	5777
Pancreas	685	30.5	209	428	1.3	6	1113	19.3	215
Larynx	1685	76.6	1291	336	9.1	30	2021	65.4	1322
Lung	18 685	78.1	14 600	7577	9.5	719	26 262	58.3	15 318
Cervix	–	–	–	4132	1.4	58	4132	1.4	58
Ovary	–	–	–	1404	0.1	1	1404	0.1	1
Bladder	1397	58.8	822	324	4.2	14	1721	48.6	836
Kidney	1165	17.3	202	1270	0.6	8	2435	8.6	210
Leukemia	3240	19.2	623	3049	0.7	21	6289	10.3	645
Second-hand smoking (among never smokers)									
Lung	1316	27.1	357	6707	25.7	1724	8023	25.9	2081
Alcohol consumption									
Oral cavity	1646	33.6	553	506	2.3	12	2152	26.2	565
Pharynx	2409	33.6	809	552	2.3	13	2961	27.8	822
Esophagus	2942	39.3	1157	339	3.6	12	3281	35.6	1169
Stomach	11 059	1.3	142	6847	0.0	3	17 906	0.8	145
Colorectum	8887	9.4	840	7539	0.1	5	16 426	5.1	845
Liver	20 256	7.8	1576	6162	0.2	15	26 418	6.0	1590
Larynx	1685	16.8	282	336	0.5	2	2021	14.0	284
Breast	–	–	–	21 555	0.6	127	21 555	0.6	127
High BMI									
Esophagus	2942	3.5	103	339	3.6	12	3281	3.5	115
Stomach	11 059	1.9	210	6847	1.9	132	17 906	1.9	343
Colorectum	8887	4.9	434	7539	5.0	377	16 426	4.9	811
Liver	20 256	9.9	2013	6162	10.2	631	26 418	10.0	2644
Gall-bladder	199	2.8	6	102	9.0	9	301	4.9	15
Pancreas	685	2.7	18	428	2.7	12	1113	2.7	30
Breast	–	–	–	15 182	0.6	85	15 182	0.6	85
Endometrium	–	–	–	5354	15.3	819	5354	15.3	819
Ovary	–	–	–	1404	1.9	27	1404	1.9	27
Prostate	6248	2.4	152	–	–	–	6248	2.4	152
Kidney	1165	5.7	67	1270	5.8	74	2435	5.8	141
Thyroid	1038	7.8	81	4433	8.0	354	5471	7.9	435
Myeloma	291	4.0	12	259	2.7	7	550	3.4	19
Meningioma	1717	5.0	86	1403	5.1	72	3120	5.1	159
Insufficient physical activity									
Colorectum	8887	2.1	185	7539	3.6	273	16 426	2.8	458

TABLE 1 (Continued)

Risk factors associated cancer types	Men Number of cases	Men PAF (%)	Men Attrib. cases	Women Number of cases	Women PAF (%)	Women Attrib. cases	Both sexes Number of cases	Both sexes PAF (%)	Both sexes Attrib. cases
Breast	–	–	–	15 182	1.2	180	15 182	1.2	180
Endometrium	–	–	–	5354	7.4	395	5354	7.4	395

Note: Cancer types associated with each risk factor are ordered by International Classification of Diseases version 10 (ICD-10).
Abbreviation: PAF, population attributable fraction.

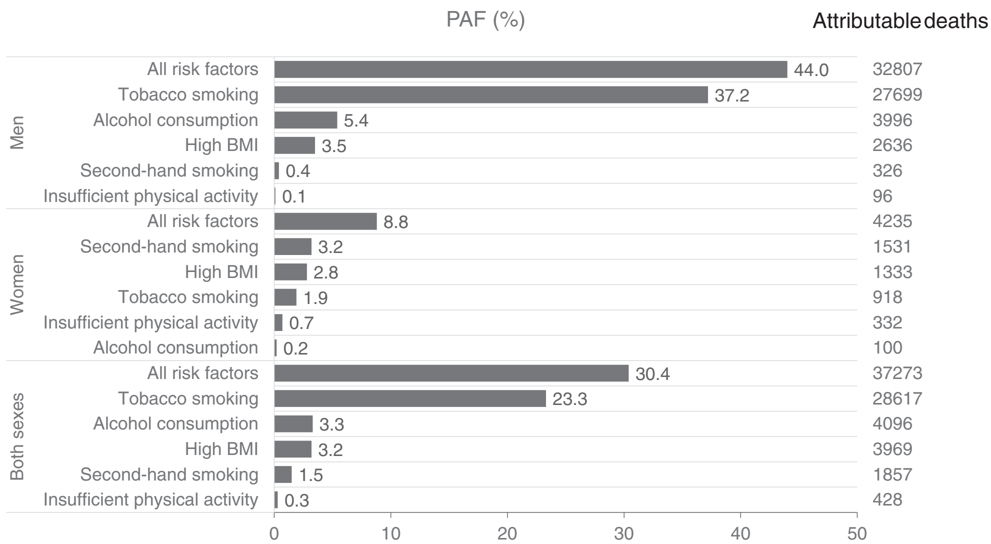

FIGURE 3 Proportion and number of all cancer deaths attributable to lifestyle risk factors in Vietnam in 2020, by sex and exposure. All risk factors, all studied risk factors; BMI, body mass index; PAF, population attributable fraction. The total number of all cancer deaths was 74 481 among men, 48 209 among women and 122 690 for both sexes.

4 | DISCUSSION

We found that 25.6% of all cancer cases and 30.4% of all cancer deaths, representing 46 799 cancer cases and 37 273 deaths in Vietnam in 2020, were attributable to behavior-related risk factors and were potentially preventable. Smoking contributed most to cancer cases and deaths among the five studied behavior-related risk factors, especially among men. Lung and upper aerodigestive tract (oral cavity, pharynx, esophagus and larynx) cancer cases and deaths could be reduced the most, at least by half if all these risk factors were eliminated. Colorectal cancer was the only cancer type attributed to all modifiable risk factors included in our study, with a total PAF of 17.2% for both cancer cases and deaths. In addition to the human toll, the cost of treating cancer in Vietnam is very high, putting patients into poverty and leaving a significant financial burden for their families.[6] Therefore, preventing these risk factors is critical in reducing the social burden and out-of-pocket expenses associated with cancer in Vietnam.

Our study had some differences in methods and results compared with the previous PAF study for Vietnam by Nguyen et al.[19] While they considered more attributable factors: infections, air pollution and reproductive factors (although they excluded physical activity), we did not include them in our analysis due to our greater focus on readily modifiable-behaviors factors and the unreliable, outdated and not nationally representative data sources. As for risk factors included in both studies (smoking, second-hand smoke, alcohol consumption, high BMI), we used a more appropriate way to compute PAFs as reference from literature. Comparisons in results for each risk factor are discussed in separate section below. Furthermore, compared with the Global Burden of Disease (GBD) results tool[30] estimating the percentages of all cancer deaths caused by different risk factors for Vietnam, our PAF results for cancer deaths were comparatively similar, with minor disparity (Table 3). Across other countries, our overall PAF results were quite comparable to several recent studies, using similar methods, conducted in Western and Asian countries (Data S1H). In terms of sex-specific estimates, in Vietnam and other Asian countries, there are 5- to 30-fold differences between male and female PAF except for BMI; meanwhile, the sex-specific estimates were fairly similar in Western and Latin America population. Details of each exposure are presented below.

4.1 | Smoking

In our study, the PAFs of all incident cancers attributable to smoking was 19.0% for both sexes and was much higher in men (33.9%) than in women (1.3%), reflecting a low smoking prevalence in women (1.5% for current and 0.7% for former smokers) compared with men (50.7% for current and 17.1% for former smokers). Tobacco smoking

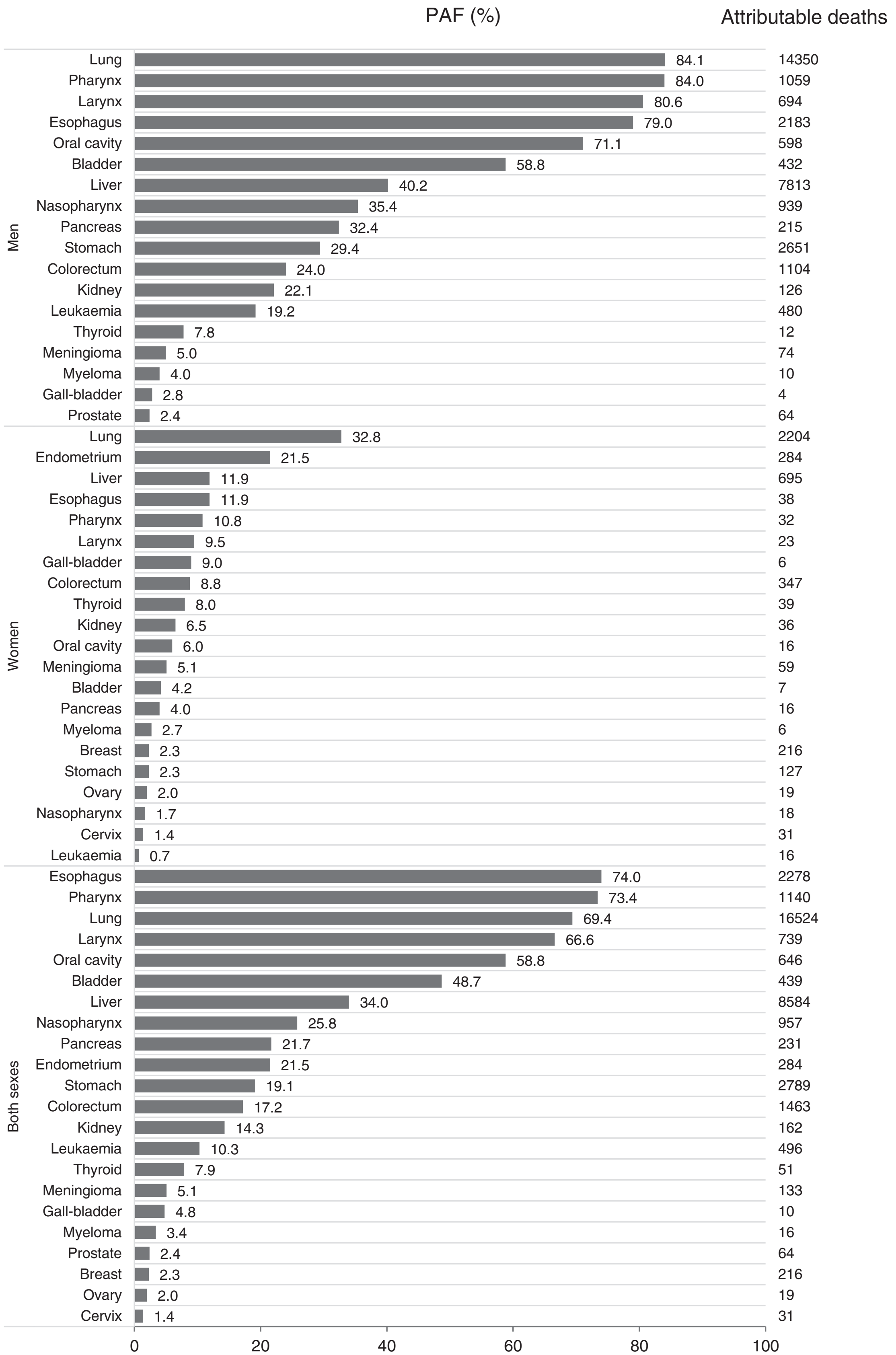

FIGURE 4 Proportion and number of cancer deaths attributable to all selected lifestyle risk factors in Vietnam in 2020, by sex and cancer type.

TABLE 2 Proportion and number of cancer deaths attributable to individual behavior-related risk factors in Vietnam in 2020, by sex, risk factor and cancer type.

	Men			Women			Both sexes		
Risk factors Associated cancer types	Number of deaths	PAF (%)	Attrib. deaths	Number of deaths	PAF (%)	Attrib. deaths	Number of deaths	PAF (%)	Attrib. deaths
Tobacco smoking									
Oral cavity	841	56.5	475	258	3.8	10	1099	44.1	485
Pharynx	1261	75.8	956	291	8.7	25	1552	63.3	982
Nasopharynx	2652	35.4	939	1054	1.7	18	3706	25.8	957
Esophagus	2762	64.2	1773	318	5.2	17	3080	58.1	1789
Stomach	9003	27.1	2443	5612	0.3	17	14 615	16.8	2460
Colorectum	4592	9.9	456	3932	0.4	14	8524	5.5	470
Liver	19 420	28.0	5445	5852	1.6	92	25 272	21.9	5538
Pancreas	663	30.5	203	402	1.3	5	1065	19.5	208
Larynx	862	76.6	661	247	9.1	22	1109	61.6	683
Lung	17 069	78.1	13 337	6728	9.5	638	23 797	58.7	13 975
Cervix	—	—	—	2223	1.4	31	2223	1.4	31
Ovary	—	—	—	923	0.1	1	923	0.1	1
Bladder	734	58.8	432	168	4.2	7	902	48.7	439
Kidney	571	17.3	99	559	0.6	4	1130	9.1	103
Leukemia	2493	19.2	480	2298	0.7	16	4791	10.3	496
Second-hand smoking (among never smokers)									
Lung	1202	27.1	326	5956	25.7	1531	7157	25.9	1857
Alcohol consumption									
Oral cavity	841	33.6	283	258	2.3	6	1099	26.3	289
Pharynx	1261	33.6	424	291	2.3	7	1552	27.7	430
Esophagus	2762	39.3	1086	318	3.6	12	3080	35.6	1097
Stomach	9003	1.3	116	5612	0.0	2	14 615	0.8	118
Colorectum	4592	9.4	434	3932	0.1	3	8524	5.1	437
Liver	19 420	7.8	1510	5852	0.2	14	25 272	6.0	1524
Larynx	862	16.8	144	247	0.5	1	1109	13.1	146
Breast	—	—	—	9345	0.6	55	9345	0.6	55
High BMI									
Esophagus	2762	3.5	96	318	3.6	11	3080	3.5	108
Stomach	9003	1.9	171	5612	1.9	109	14 615	1.9	280
Colorectum	4592	4.9	224	3932	5.0	196	8524	4.9	421
Liver	19 420	9.9	1930	5852	10.2	600	25 272	10.0	2529
Gall-bladder	144	2.8	4	70	9.0	6	214	4.8	10
Pancreas	663	2.7	18	402	2.7	11	1065	2.7	29
Breast	—	—	—	7772	0.6	43	7772	0.6	43
Endometrium	—	—	—	1319	15.3	202	1319	15.3	202
Ovary	—	—	—	923	1.9	18	923	1.9	18
Prostate	2628	2.4	64	—	—	—	2628	2.4	64
Kidney	571	5.7	33	559	5.8	33	1130	5.8	65
Thyroid	157	7.8	12	485	8.0	39	642	7.9	51
Myeloma	257	4.0	10	214	2.7	6	471	3.4	16
Meningioma	1463	5.0	74	1151	5.1	59	2614	5.1	133

(Continues)

TABLE 2 (Continued)

Risk factors Associated cancer types	Men			Women			Both sexes		
	Number of deaths	PAF (%)	Attrib. deaths	Number of deaths	PAF (%)	Attrib. deaths	Number of deaths	PAF (%)	Attrib. deaths
Insufficient physical activity									
Colorectum	4592	2.1	96	3932	3.6	143	8524	2.8	238
Breast				7772	1.2	92	7772	1.2	92
Endometrium				1319	7.4	97	1319	7.4	97

Note: Cancer types associated with each risk factor are ordered by International Classification of Diseases version 10 (ICD-10).
Abbreviation: PAF, population attributable fraction.

TABLE 3 Comparison of PAFs for cancer attributable to studied risk factors in Vietnam with the previous study (Nguyen et al.) and the Global Burden of Disease (GBD) results tool.

		Tobacco smoking		Second-hand smoking		Alcohol consumption		High BMI		Insufficient physical activity	
		PAF cases	PAF deaths	PAF cases	PAF deaths	PAF cases	PAF deaths	PAF cases	PAF deaths	PAF cases	PAF deaths
Vietnam, 2020 (our study)	Both sexes	19.0%	23.3%	1.1%	1.5%	3.0%	3.3%	3.2%	3.2%	0.6%	0.3%
	Men	33.9%	37.2%	0.4%	0.4%	5.4%	5.4%	3.2%	3.5%	0.2%	0.1%
	Women	1.3%	1.9%	2.1%	3.2%	0.2%	0.2%	3.1%	2.8%	1.0%	0.7%
Vietnam, 2018 (Nguyen et al.)	Both sexes	13.5%	—	6.0%	—	6.0%	—	0.8%	—	—	—
	Men	23.9%	—	3.6%	—	10.3%	—	0.7%	—	—	—
	Women	0.8%	—	8.8%	—	0.6%	—	0.8%	—	—	—
Vietnam, 2019 (GBD study)	Both sexes	—	24.1%	—	1.8%	—	7.5%	—	2.2%	—	0.3%
	Men	—	39.9%	—	1.2%	—	12.2%	—	1.5%	—	0.3%
	Women	—	3.4%	—	2.5%	—	1.3%	—	3.2%	—	0.4%

was the leading cause of preventable cancer cases in all other countries. The proportion of all cancer cases attributable to smoking in Vietnam was higher compared with Western countries[14,15,23,24,31] and this difference could be explained by a remarkable higher prevalence of smoking among men. Moreover, in these countries, the prevalence of tobacco smoking and corresponding PAF in women was substantially higher compared with Asian studies. Meanwhile, in Asian countries, similar to Vietnam, PAF of tobacco smoking was higher among men because of the significantly higher prevalence among men compared with women. Despite the low prevalence of active smoking, second-hand smoking is an important cancer risk factor for women in Vietnam, causing more lung cancer (1724 cases, 1531 deaths) than primary smoking did (719 cases, 638 deaths). Second-hand smoking was responsible for 2.1% of all cancer cases in women, which was much greater than in men (0.3%). Our results for second-hand smoking in women were slightly higher compared with several Western countries, Latin America countries and Japan,[14,15,17,23,24,31] but were lower compared with China.[32]

Compared with our study, Nguyen et al.'s study in Vietnam reported a lower proportion of cancer cases due to smoking in both men (23.9% vs 33.9% in our study) and women (0.8% vs 1.3% in our study). The reason for this discrepancy could be that the authors omitted a few cancers for which a causal association with tobacco smoking has been demonstrated, including colorectal and kidney cancers.[19] The PAF for second-hand smoking in their analysis was much higher than ours (women: 8.8% vs 1.3% in our study, men: 3.6% vs 0.3% in our study); however, it is not clear which cancer types were included for each exposure association, as well as data of prevalence and relative risks in this previous study.[19]

Our results reemphasize that expanding comprehensive tobacco control programs could have the greatest impact on reducing the overall cancer burden in Vietnam. Over the last two decade, the Government of Vietnam implemented the National Tobacco Control Policy 2000 to 2010[33] aiming to reduce tobacco-related diseases morbidity and mortality, specifically to reduce the proportion of male smokers from 50% to 20%, through a number of public interventions including excise tax and advertising bans. However, in 2010, current smoking prevalence remained high among adult males at 47.4% according to Global Adult Tobacco Survey (GATS). In 2012, the National Assembly enacted the first comprehensive law on Prevention and Control of Tobacco Harms, which established smoke-free places, increased the pictorial health warning printed on every cigarette packages, as well as health education and promotion campaigns.[34] After three years implementation, despite showing a progress in applying all six MPOWER measures introduced by WHO (including Monitor tobacco use and prevention policies; Protect people from tobacco smoke; Offer help to quit tobacco use; Warn about the dangers of tobacco; Enforce bans on tobacco advertising, promotion and sponsorship; and Raise taxes on tobacco), it is not ultimately effective and the prevalence of current smoking was still high, at 45.3%.[35] It is also suggested that an action plan should be developed to effectively implement WHO MPOWER, with special consideration on raising tobacco tax and enforcing smoke-free policies.[35] In 2018, the Vietnam Health Program approved by the Prime Minister have set several specific objectives to reduce the proportion of male smokers to 37% in 2025 and 32.5% in 2030[36]; and these targets might not be achieved if Vietnam does not strengthen the law and enforce stronger tobacco control policies. Apart from reinforcing the interventions, some new challenges in tobacco control should also be addressed; for instance, regulation of flavored and candy-like tobacco product and other youth-specific marketing strategies could be used to prevent tobacco smoking in the future generations.[37]

4.2 | High BMI, insufficient physical activity and alcohol consumption

More than 3% of all cancer cases and deaths in Vietnam were attributable to high BMI. In order to estimate the burden of excess body weight attributable to cancer, we calculated the PAFs using the formula for continuous exposure (each 1 kg/m^2 increment in BMI), instead of using that for categorical exposure of overweight (BMI between 25 to <30 kg/m^2) or obesity (BMI ≥ 30 kg/m^2) based on WHO classification. There is evidence supporting the use of lower cut-points in Asian populations[38] to avoid underestimating the real burden of high BMI for cancer in Vietnam. The previous study in Vietnam using the cut-point for BMI as WHO classification found that only 0.8% of all cancer cases attributed to overweight and obesity.[19] Otherwise, using full distribution of BMI would capture information more comprehensively compared with dividing into categories, and several PAF studies in Western countries estimated the burden of high BMI attributable to cancer by using this approach.[15,23,27,28] These countries used mean 22 kg/m^2 and SD 1 kg/m^2 as the theoretical minimum distribution of BMI. However, to be applicable for Asian population, our study used different distribution (ie, mean 21 kg/m^2 and SD 1 kg/m^2). Furthermore, the prevalence of obesity in Vietnam is increasing, particularly among the younger population. When conducting an analysis on the STEPS 2009 and 2015 survey, we observed that among the 25-29 age group, the prevalence of obesity using WHO BMI cut-off for Asian population was 1.7% in 2009 and doubled to 3.6% in 2015. Therefore, weight control in young generation may have a substantial impact on controlling obesity, which would result in reducing cancer incidence in the future.

Insufficient physical activity played a small role in total cancer burden in Vietnam, accounting for 0.6% of all cancer cases and 0.4% of all cancer deaths. We included in our study colorectal, breast and endometrial cancer, which are strong evidence graded by WCRF/AICR.[11] The PAF pattern attributable to insufficient physical activity was higher in women (1.1%) than in men (0.2%), largely because two of three cancer types included were female cancer. Our findings were relatively similar to studies conducted in Asian countries, such as Japan[17] and China,[32] but estimates were slightly lower compared with that in some Western countries, except UK[14] (included only colorectal cancer). Moreover, our results showed that endometrial cancer contributed the highest PAFs for both the risk factors of high BMI and insufficient physical activity. The PAF model assumed that insufficient physical activity and high BMI are independent factors, while in fact, increasing physical activity could help maintain a healthy body weight, reduce BMI and consequently, reduce cancer burden. Therefore, further promotion of physical activity is necessary for obesity control and cancer prevention.[39,40]

Alcohol drinking was the second most important risk factor for cancer in Vietnam. Similar to tobacco smoking, a majority of cancer cases and deaths caused by alcohol consumption occurred among Vietnamese men, at 5359 cases and 3996 deaths compared with 189 cases and 100 deaths among women. The proportion of all cancer cases attributable to alcohol consumption was 5.4% in men and 0.2% in women, which was relatively similar to China (4.8% in men, 0.5% in women),[32] but was lower compared with Japan (9.0% in men, 2.5% in women)[17] and Brazil (5.9% in men, 1.7% in women).[24] Otherwise, in contrast to some Western countries, their PAF of alcohol consumption among women were slightly higher compared with men, such as in USA (6.4% in women vs 4.8% in men)[15] and in UK (3.5% in women vs 3.1% in men).[14] To reduce alcohol consumption, WHO's recommended strategies are generally similar to that of tobacco control interventions, including increasing awareness, labeling, taxation, marketing restrictions and addressing illicit and informal production.[41] Higher prices and excise taxes on alcohol may be highly beneficial for reduction in alcohol consumption.[42]

4.3 | Strengths and Limitations

Our study has several strengths. First, we provided contemporary estimates of PAFs for cancer cases and deaths attributable to potentially modifiable behavioral risk factors in Vietnam. Second, we used nationally representative data on prevalence of exposure, occurrence and RRs from large-scale meta-analysis or cohort studies. Furthermore, we used a systematic methodological approach to compute PAFs to ensure the consistency of our estimates and only selected risk factors and cancer types with sufficient evidence according to IARC or strong evidence according to WCRF/AICR.

However, there were several limitations in our study. First, we used the traditional approach to calculate PAF, which assumes no interaction among risk factors and no correlation between cancer types in each risk factors. However, these assumptions may not take into account that multiple risk factors can interact and increase the risk of developing cancer.[43] There are some recent developments in this field to better account for the exposure interaction and subgroup analysis[43,44]; however, we did not have data to use these methods.

Second, we obtained RRs mostly from meta-analysis and pooled data of observational studies conducted worldwide or in Asian population to a lesser extend due to the lack of high quality and long-term prospective cohort studies on cancer etiology in Vietnam. Whether these RRs are applicable to Vietnamese population is still debatable and needs further investigation; therefore, our PAF estimates could be biased.

Third, the results might be different among different regions within Vietnam or different age groups; however, we could not conduct analyses for specific groups due to the lack of prevalence estimates for these groups, RRs and cancer data. Besides, our scope is to estimate the proportion and number of cancer cases and deaths for the whole population. It would be more feasible for policy makers to implement new strategies for cancer control and prevention in the future. More studies are needed to compare the prevalence and cancer cases/deaths in specific-region and specific-age group in Vietnam.

Fourth, certain risk factors are associated with cancer subtypes based on histology (eg, BMI with esophageal adenocarcinoma and stomach cardia, alcohol consumption with esophageal SCC, smoking with mucinous ovary); however, as we did not have the data on cancer sub-types, we use the total number of that cancer cases/deaths. Although we conducted the literature review focusing on RRs for cancer types rather than sub-types to take into account these differences, our results on number of attributable cancer/deaths could be biased.

Fifth, we limited our estimates to only risk factors and cancer associations classified as sufficient evidence by the IARC or convincing/ probable evidence according to the WCRF/AICR; thus, our PAF results did not cover all cancer types associated with each risk factor. For instance, physical activity was reported as associated with lower risks of 13 cancers by a recent pooled analysis[45]; or smoking was associated with higher mortality of additional cancers that were not established by IARC, such as breast and prostate cancer.[46] Moreover, the decision for selecting risk factors was largely based on the availability of prevalence data in Vietnam, so we could not include in our analysis dietary factors due to the lack of detailed data. Therefore, we likely underestimated the actual proportions of cancers attributable to some individual risk factors and all behavior-related factors combined. Nonetheless, a large proportion of the dietary effect as determined by WCRF/AICR is mediated through body adiposity.

Moreover, to calculate the PAF for high BMI by using the formula for continuous exposure, we used the theoretical minimum distribution of BMI defined as mean 21 kg/m^2 and SD 1 kg/m^2, where we assumed no increased cancer risk below this value. This reference distribution did not follow previous studies conducted in Western. Therefore, it may not be the best theoretical minimum distribution of BMI to use for Asian population and could bias our results. Moreover, there is growing evidence showing that visceral fat (estimated indirectly by waist circumference and waist-to-hip ratio, or other direct methods) at low BMIs could be more important than BMI in Asian populations in predicting cancer outcome.[47]

Finally, this study focused on behavior-related risk factors, and omitted other potentially modifiable risk factors, such as infections and air pollution. Despite the large burden of cancers caused by infections (*Helicobacter pylori*, hepatitis B virus, hepatitis C virus and human papillomavirus), we could not include these factors due to the lack of representative nation-scaled data. Thus, further studies are needed to investigate the attribution of other modifiable risk factors to contribute for future cancer prevention and control strategies in Vietnam.

5 | CONCLUSION

In Vietnam, around one in every four new cancer cases and nearly one in every three new cancer deaths could have been prevented if risk factors such as tobacco smoking, second-hand smoking, alcohol consumption, high BMI and insufficient physical activity had been eliminated. Among those behavior-related factors, smoking emerges as the major driver, especially in Vietnamese men, due to the high prevalence of smoking. For efficient reduction of cancer incidence and mortality, preventive actions focusing on tobacco control are likely to have the most significant impact, especially in men. More research is needed to identify modifiable risk factors among women in Vietnam.

AUTHOR CONTRIBUTIONS

Linh Ha: Conceptualization, Methodology, Software, Formal analysis, Visualization, Writing—Original Draft, Writing—Review & Editing. An Tran: Conceptualization, Methodology, Software, Formal analysis, Writing—Original Draft. Linh Bui: Conceptualization, Writing—Original Draft, Writing—Review & Editing. Edward Giovannucci: Conceptualization, Writing—Original Draft, Writing—Review & Editing. Lorelei Mucci: Conceptualization, Writing—Original Draft, Writing—Review & Editing. Mingyang Song: Conceptualization, Writing—Original Draft, Writing—Review & Editing. PhuongThao D. Le: Writing—Review & Editing. Minh Hoang: Conceptualization, Writing—Original Draft, Writing—Review & Editing. Huong Tran: Conceptualization, Writing—Original Draft, Writing—Review & Editing. Giang Kim: Conceptualization, Writing—Original Draft, Writing—Review & Editing. Tung Pham: Conceptualization, Methodology, Software, Formal analysis, Data Curation, Visualization Writing—Original Draft, Writing—Review & Editing, Supervision, Project administration. The work reported in the paper has been performed by the authors, unless clearly specified in the text.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are available in the database of the Vietnam National Survey on the Risk Factor of Non-Communicable Diseases (STEPS) 2015. Further information is available from the corresponding author upon request.

ETHICS STATEMENT

The datasets used in this study is a publicly available datasets, and the original study was approved by the Research Ethics Committee of the Hanoi School of Public Health and the Vietnam Ministry of Health.

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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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