Attributable Causes of Cancer in Vietnam

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PURPOSE Vietnam is undergoing rapid socio-economic transition with an increasing cancer burden. The contribution of modifiable risk factors to cancers in Vietnam has not been studied. Therefore, we sought to evaluate the attributable causes of cancer in Vietnam.

METHODS We reviewed the data on burden of cancer in Vietnam from 2 cancer registries in Hanoi and Ho Chi Minh City between 1995 and 2012. Next, we calculated the fractions of cancers occurring in 2018 attributable to established modifiable risk factors whose impact could be quantified. Data on exposure prevalence were obtained for the period from 2000 to 2010 from national sources wherever possible.

RESULTS Cancer incidence in Vietnam has decreased slightly in both sexes. Cancer related to infectious agents decreased sharply, whereas cancer related to nutrition and metabolism has increased. In 2018, established carcinogens included in the analysis explained 47.0% of cancer burden in Vietnam. Chronic infections accounted for 29.1% of cancers (34.7% in men and 22.1% in women), tobacco smoking for 13.5% (23.9% in men and 0.8% in women), and alcohol drinking for 10.3%. Passive smoking was responsible for 8.8% of cancers in women. Other risk factors, including overweight or obesity, nulliparity, and low vegetable and fruit intake, accounted for < 1% of all cancers each.

CONCLUSION Cancer incidence is slowly decreasing in Vietnam, and the causes of more than half of cancers remain unexplained. This result underlines the need for further epidemiologic and fundamental research. Our findings confirm the notion that controlling oncogenic infections and decreasing tobacco smoking are the most effective approaches to reduce the burden of cancer in Vietnam, but other risk factors, including alcohol drinking and diet, should not be neglected.

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INTRODUCTION

Vietnam has undergone rapid and far-reaching economic development during the past decades. Over the past 30 years, average growth of the gross national product has been 6.7% per year, one of the highest in the world. In parallel, the country has experienced impressive progress toward improving the health status of the population; estimated life expectancy in Vietnam in 2018 was 76.3 years (71.7 years for men and 80.9 years for women),² a level that is higher than that in many countries with similar levels of gross domestic product per capita. As in other less developed countries that underwent a rapid socioeconomic and health transition, the increase in life expectancy was primarily a result of a decline in mortality from communicable and maternal and childhood diseases. Consequently, noncommunicable diseases, and cancer in particular, have increased their con-

tribution to the burden of disease.3

Although there have been several efforts to evaluate the role of modifiable risks factors for cancer in Vietnam, 4-7 systematic study on such issues is unavailable. Under this evolving scenario, we aim to provide a comprehensive assessment of the burden of cancer and the role of its main causes in Vietnam today by calculating population attributable fractions (AFs).

METHODS

We reviewed the data on the burden of cancer in Vietnam. Next, we calculated the fractions of cancers in Vietnam in 2018 attributable to known modifiable causes of cancer for which sufficient data were available.

Burden of Cancer: Sources of Data

The Cancer Incidence in Five Continents program compiles data from cancer registries around the world that satisfy a set of quality criteria, including the proportion of microscopically verified cancers, the proportion of cancers identified from death certificates, and

ASSOCIATED CONTENT Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

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CONTEXT

Key Objective

What are the attributable causes of cancer in Vietnam?

Knowledge Generated

Almost half of all cancer cases in Vietnam in 2018 are attributable to known modifiable risk factors and therefore can be prevented, at least in theory. Infectious agents, tobacco (including passive smoke) and alcohol consumption are leading causes for cancer in Vietnam.

Relevance

This result underlines the need for further epidemiological and fundamental research. Controlling oncogenic infections and tobacco smoking are the most effective approach to reduce the burden of cancer in Vietnam, but other risk factors, including alcohol drinking and diet, should not be neglected.

the proportion of patients of unknown age, allowing for valid comparisons across areas and time periods. Updates of data are published every 5 years; the most recent collection (Volume XI) comprises data for 2008-2012.8 The only registry from Vietnam, which was included in Volume XI of the series, is that of Ho Chi Minh City (HCMC), which was also included in Volume VIII (data from 1993-1997).9 Volume VIII also included data from the Cancer Registry of Hanoi.

In addition, the GLOBOCAN program provides estimates of cancer incidence, mortality, and prevalence from the whole country. The most recent version of GLOBOCAN provides data for 2018. Priefly, the 2018 estimates for cancer incidence in Vietnam are based on weighted average from the most recent data from the HCMC Cancer Registry with 2018 population. Mortality data were estimated from incidence estimates, using mortality/incidence ratios derived from cancer registries in neighboring countries. Prevalence data were estimated using national incidence data and prevalence ratios from Nordic countries for the period of 2000-2009 and scaled using Human Development Index (HDI) ratios. 11,12

Risk Factors Included in the Current Analysis

Risk factors for each cancer type were included in the estimate of AFs if they were classified either as established human carcinogens (Group 1) by the International Agency for Research on Cancer (IARC)13 or as agents with convincing or probable evidence by the World Cancer Research Fund (WCRF).¹⁴ The main risk factors included in the analysis were infectious agents, tobacco smoking, alcohol drinking, passive smoking, pollutants (particulate matter $< 2.5 \mu m$ [PM_{2.5}]), overweight and obesity, nulliparity, and low vegetable and fruit intake. Although it has never been evaluated by either IARC or WCRF, nulliparity, as a reproductive factor, was included in the review because a large body of evidence supports its role in breast cancer. 15,16 Other reproductive factors linked to cancer in humans were not included as a result of insufficient exposure data in Vietnam. Some established carcinogens were not included in the analysis because exposure is rare (eg, radioiodine, radium and its decay products) or because data on the prevalence of such exposures were unavailable (eg, exposure to occupational carcinogens, exogenous hormones, x-ray radiation, γ -radiation, or UV light). Genetic factors for cancer were also excluded because they are unavoidable. The risk factors retained in the analysis are listed in Table 1.

Risk Factors: Exposure Prevalence

We obtained the sex-specific prevalence of exposure to the risk factors from census data or representative nation-scaled surveys. Where nationally representative data were unavailable, we obtained data on prevalence of exposure from the most robust epidemiologic studies conducted in Vietnam. Data sources are listed in Table 1. The cancer burden observed at any given time reflects past exposures' cumulative effect. The time between the relevant exposure and the development of cancer (commonly defined as latency) varies by cancer and risk factor and is not always well defined. For most associations between cancers and risk factors, we chose a latency of 10-15 years between exposure and cancer onset (ie, we considered exposures occurring around 2000-2010), if relevant exposure data were available.

Relative Risks

Because of the unavailability of robust studies to determine the association between carcinogens and cancers in Vietnam by the time we conducted this analysis, we obtained relative risks (RRs) from recent published metanalyses, with preference given to studies in Asia. If metanalyses were unavailable, results from pooled analyses, cohort studies, and case-control were considered in the respective order. If $> 1~\rm RR$ for the same risk factor was available, preference was given to the study with largest sample size and with results most comprehensively adjusted for confounders. Where there was a statistically significant difference between RRs among males and females, sex-specific RRs were extracted. Otherwise, total RRs were applied for both sexes.

AF Calculation

AF estimates the proportion of cancer that could be avoided if exposure to a given agent were eliminated. We used the AF formula proposed by Levin, ¹⁷ which is widely used by

TABLE 1. Risk Factors Included in the Current Analysis	n the Current Analysis		
Risk Factor	Specific Exposures	Data Source	Comments
Tobacco smoking	Current smoking; former smoking	The Global Adult Tobacco Survey Vietnam 2010 ²⁷	Estimated excess risk in former smokers was 50% of current smoker ³⁹
Passive tobacco smoking	Involuntary smoking at home; involuntary smoking at workplace	The Global Adult Tobacco Survey Vietnam 2010 ²⁷	
Alcohol drinking	Level of drinking on daily average	Van Bui et al, 40 and National Survey on the Risk Factors of Non-Communicable Diseases (STEPS) Viet Nam 2015 ³³	Risk levels different for men and women
Infectious agents	Epstein-Barr virus; human papillomavirus; hepatitis B virus; hepatitis C virus; Helicobacter pylori	Most robust epidemiologic studies ⁴¹⁻⁴³	
	ΛIH	Vietnam Authority of HIV/AIDS Control, data from 2005 ⁴⁴	
Overweight and obesity	Overweight defined as BMI $>$ 25 kg/m²; obesity defined as BMI $>$ 30 kg/m²	National Survey on the Risk Factors of Non-Communicable Diseases (STEPS) Viet Nam 2015 ³³	
Vegetable and fruit intake	Consumption of < 5 portions (400 g) of vegetables and fruit daily	National Survey on the Risk Factors of Non-Communicable Diseases (STEPS) Viet Nam 2015 ³³	
Air pollution	PM _{2.5} level	Ambient Air Pollution Exposure Estimation for the Global Burden of Disease 2013, Vietnam data from 2010 ⁴⁵	
Reproductive factors	Nulliparity	Vietnam Demographic and Health Survey 2002⁴6	Risk was estimated for all nulliparous women regardless of age

Abbreviations: BMI, body mass index; $PM_{2.5}$, particulate matter of $< 2.5~\mu m$.

epidemiologists worldwide, to calculate the AF of an association between a dichotomous exposure and a cancer:

$$\mathsf{AF}_{p} = \frac{\left\{\mathsf{RR} - 1\right\} \times \mathsf{PF}_{1}}{1 + \left\{\mathsf{RR} - 1\right\} \mathsf{PF}_{1}},$$

where PF_1 is the underlying prevalence of the risk factor in the population and RR is the RR of developing a type of cancer when exposed to the risk factor.

For polytomous exposures, we used the formula described by Hanley¹⁸ to calculate the total AF for that exposure:

$$\mathsf{AF}_{p} = \frac{\mathsf{PF}_{1}\big\{\mathsf{RR}_{1} - 1\big\} + \mathsf{PF}_{2}\big\{\mathsf{RR}_{2} - 1\big\}}{1 + \mathsf{PF}_{1}\big\{\mathsf{RR}_{1} - 1\big\} + \mathsf{PF}_{2}\big\{\mathsf{RR}_{2} - 1\big\}},$$

which can be extended to more than 2 exposure categories.

For some infections, AFs were obtained from generally accepted results from published studies because no data for RR were available. ^{19,20} This applied to AFs for Epstein-Barr virus (EBV) for nasopharyngeal cancer and Hodgkin lymphoma, *Helicobacter pylori* for stomach cancer, and HIV for Kaposi sarcoma and non-Hodgkin lymphoma.

Combining AFs

For each type of cancer, the individual AFs for different risk factors cannot be numerically added together because a patient may have been exposed to more than one of them. With insufficient information on the nature of risk factors' interactions and their combined distributions, to estimate the total AFs, we assumed that there was independence of both exposure prevalence and carcinogenic action between risk factors and applied the following formula:

Total AF =
$$1 - \prod_{i=1}^{n} (1 - AF_i)$$
.

RESULTS

Burden of Cancer

The overall incidence of cancer (age-standardized rates, excluding nonmelanoma skin cancer) in HCMC during 2008-2012 was 130.1 per 100,000 in men and 105.8 per 100,000 in women. The incidence for 1995-1998 was 143.1 per 100,000 in men and 108.6 per 100,000 in women, equivalent to an average decline in cancer incidence of 0.7% in men and 0.2% in women.

Figures 1A and 1B report incidence rates of specific cancers in 2008-2012 and 1995-1998 in HCMC by sex. Among men, the 3 most common cancers are lung, liver, and stomach cancer; the incidence of the 2 latter cancers decreased remarkably during the 2 time periods, whereas that of lung cancer remained stable. Among women, a remarkable shift took place in the period under study. Cervical cancer was the most common cancer in 1995-1998, but it was reduced by half in 2008-2012. The incidence of breast

cancer increased by 76%, and this was the most common cancer in women in 2008-2012. The incidence of stomach and liver cancer decreased in both sexes.

The overall incidence of cancer in Hanoi during 1993-1997 was 151.7 per 100,000 in men and 99.1 per 100,000 in women (6% higher than in HCMC in the same period in men and 9% lower in women). The incidence of lung cancer in men was 28% higher in Hanoi than in HCMC, whereas the incidence of liver cancer was 26% lower. Among women, the incidence of breast cancer was 54% higher in Hanoi than in HCMC, that of cervical cancer was 42% lower, and that of lung cancer was 4% lower (data not shown).

The estimated number of cancers in 2018 in Vietnam was 164,671 (55% in men). The estimated number of cancer deaths was 114,871 (62% in men), and the number of 5-year prevalent cases of cancer was 300,033 (Table 2). The top 5 causes of cancer death in 2018 were liver cancer (25,404 estimated deaths, 22.1% of the total), lung cancer (20,710 deaths, 18.0%), stomach cancer (15,065 deaths, 13.1%), breast cancer (6,103 deaths, 5.3%), and leukemia (4,923 deaths, 4.3%; data not shown).

Estimation of AFs

Estimation of AFs by risk factors in Vietnam is provided in Table 3. Infectious agents (29.1%) and tobacco smoking (13.5%) were accountable for the largest proportion of cancers in Vietnam. Among men, chronic infections accounted for one third of cancers, whereas tobacco smoking accounted for one fourth of all cancers. One of every 10 cancers could be attributed to drinking alcohol. In women, the 2 leading risk factors were infectious agents (22.1%) and passive smoking (8.8%). The remaining factors included in the analysis accounted for a relatively small fraction of cancers. Overall, the risk factors selected for the analysis were responsible for 59.2% of cancers in men and 32.0% in women (47% in both sexes).

Table 4 lists the summary results of AFs for individual cancers. EBV, human papillomavirus, and HIV accounted for 100% of nasopharyngeal cancers, cervical cancers, and Kaposi sarcomas, respectively. Large AFs (\geq 70%) were observed for cancers strongly associated with tobacco smoking, alcohol drinking, and chronic infections (eg, head and neck, cervical cancers, liver, stomach). For lung cancer, the AF was 65%, with a large difference between men and women. AFs in the range of 20% to 60% were observed for cancer with \geq 1 important, but not predominant, risk factor (eg, esophagus, lymphoma, reproductive system, bladder, and pancreas). AFs < 10% were observed for several common cancers (eg, colorectum, gallbladder, prostate, kidney, and ovary), for which the etiology is largely unknown.

DISCUSSION

To our knowledge, this analysis was the first systematic assessment of cancers attributable to modifiable risk

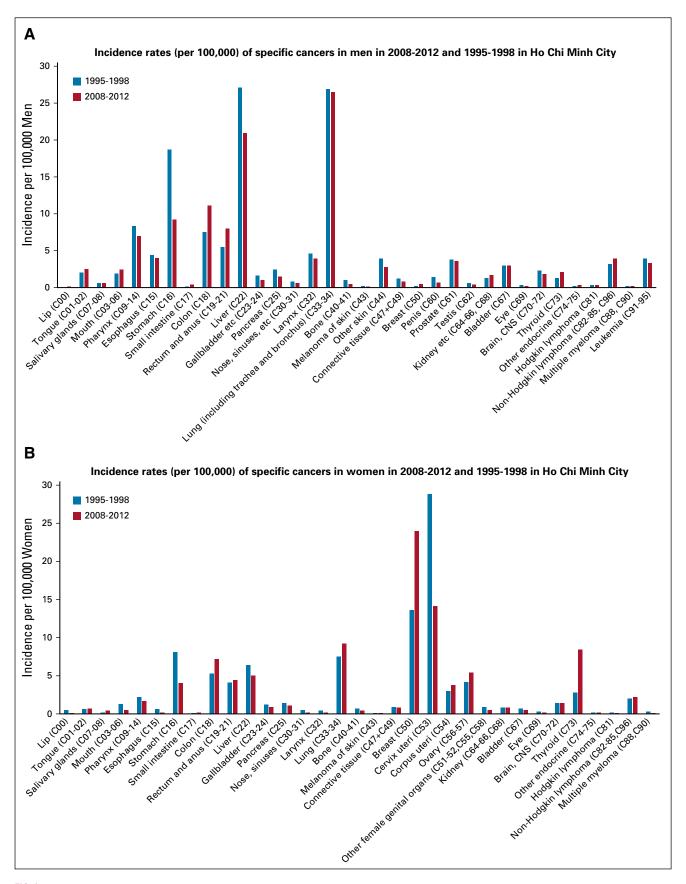


FIG 1. (A) Incidence rates (per 100,000) of specific cancers in men in 2008-2012 and 1995-1998 in Ho Chi Minh City. (B) Incidence rates (per 100,000) of specific cancers in women in 2008-2012 and 1995-1998 in Ho Chi Minh City.

TABLE 2. Estimated Number of Incident Cancers, Cancer Deaths, and 5-Year Prevalent Cancers in Vietnam, 2018, by Sex (Globocan 2018)

Measure	Men	Women	Total
Incident cancers	90,822	73,849	164,671
Cancer deaths	70,888	43,983	114,871
5-year prevalent cases of cancer	138,602	161,431	300,033

factors in Vietnam. Cancer incidence in Vietnam observed a minor decline over a 20-year period. Overall, cancer morbidity and mortality were higher among men than women. Lung cancer remained the most common cancer among men over the years, whereas breast cancer replaced cervical cancer to become the most common cancer among women. Cancers related to infectious agents (ie, stomach, liver, and cervical cancer) decreased, whereas cancers related to nutrition and metabolism (ie, breast, ovarian, and colorectal cancer) were on the rise. This changing pattern reflects the changes in risk factor prevalence for Vietnam, a country undergoing socioeconomical development, rapid urbanization, and lifestyle changes. This pattern is similar to China's²¹ and that of most other Asian countries.²²

Infectious agents are the most common cancer risk factors in Vietnam. In our analysis, we could not include several relatively minor oncogenic infections, such as *Opisthorchis riverine, Clonorchis sinensis*, human herpesvirus 8, and liver flukes because of lack of exposure data. Chronic infections had a larger contribution to the total number of cancers in Vietnam than in global analyses (23.4% of total cancers in less developed region²³), regional analyses (19.6% in Asian countries²⁰), and results from other Asian countries such as China (25.3%),²¹ Japan (17.5%),²⁴ and Korea (17.8%).²⁰ This disparity could be explained by the fact that Vietnam is one of the countries with the highest prevalence of hepatitis B virus (10%)²⁵ and *H pylori* (> 70%)²⁶ in Asia. There is no national surveillance to monitor the trend of carcinogenic infections over time, but

ad hoc epidemiologic studies showed a decreasing trend for most infectious agents included in our analysis (Appendix Table A1). These trends parallel those observed for infection-related cancers such as liver, stomach, and cervical cancer (Figs 1A and 1B).

Tobacco smoking is the second leading cause for cancer in Vietnam. Notably, > 97% of cancers caused by tobacco smoking occurred among men, reflecting a low tobacco smoking prevalence in women (1.9%) compared with men (60.1%).²⁷ Despite the low prevalence of active smoking, passive smoking is a significant cancer risk factor for women in Vietnam, causing 8.8% of all cancers among women. Overall, smoking-related cancers accounted for one fifth of all cancers in Vietnam (27.5% in men and 9.6% in women). Our findings might underestimate the true burden of tobacco-related cancer in Vietnam because cancers with established but weak association with tobacco smoking (eg. colorectal and kidney cancer) were not included in the analysis. Ever-smoking as cancer risk factor accounted for a significantly smaller proportion of cancers among women in Vietnam (0.8%) than among women of other Asian populations (5% in China²¹ and 5.2% in Korea²⁸ and Japan²⁹). This could be explained by the low rate of active smoking among Vietnamese women (1.9%)²⁷ compared with that of women in other studies (10.5% in Japan²⁹ and 4.1% in Korea²⁸). Smoking prevalence in Vietnam is decreasing slowly, by only 5% over a 10-year period²⁷; hence, tobaccorelated cancer will remain a major burden in the future.

Alcohol drinking was the third most important risk factor for cancer in Vietnam included in our analysis and accounted for 6% of cancers. Similar to tobacco smoking, a majority of alcohol drinking–related cancers (95.2%) occurred among men. Our estimation is higher than results from studies in China (3.63%³0 to 4.4%²¹ of cancers caused by drinking alcohol) and previous global studies (3%-5% of cancer deaths caused by drinking alcohol across the globe).³1,32 The risk of developing cancer increases with higher levels of drinking.³2 Studies in China did not disaggregate by alcohol

TABLE 3. Cancers Attributable to Selected Risk Factors in Vietnam in 2018

	M	en	Wo	men	Both	Sexes
Risk Factor	AF (%)	No.	AF (%)	No.	AF (%)	No.
Tobacco smoking	23.9	21,695	0.8	617	13.5	22,312
Passive smoking	3.6	3,290	8.8	6,522	6.0	9,812
Alcohol drinking	10.3	9,342	0.6	469	6.0	9,811
Infectious agents	34.7	31,506	22.1	16,345	29.1	47,851
Overweight and obesity	0.7	654	0.8	598	0.8	1,252
Low vegetable and fruit intake	0.7	679	0.1	49	0.4	728
Air pollution (PM _{2.5})	2.0	1,791	1.0	744	1.5	2,535
Nulliparity	_	_	1.7	1,280	0.8	1,280
All of the above	59.2	53,773	32.0	23,637	47.0	77,410

Abbreviations: AF, attributable fraction; PM_{2.5}, particulate matter of < 2.5 μm .

TABLE 4. Cancers Attributable to Known Risk Factors by Type of Cancer, Vietnam 2018

Troulain 2010	M	en	Wor	nen	Both	Sexes
Cancer	No.	AF (%)	No.	AF (%)	No.	AF (%)
Oral cavity	1,163	89.0	337	59.4	1,500	79.9
Pharynx	2,132	89.2	308	60.4	2,440	84.1
Nasopharynx	4,559	100.0	1,653	100.0	6,212	100.0
Esophagus	1,222	59.0	64	19.2	1,286	53.3
Stomach	9,393	84.2	5,042	79.2	14,435	82.4
Colorectum	936	12.3	342	4.8	1,278	8.7
Liver	17,674	90.3	4,789	83.0	22,463	88.7
Gallbladder	8	3.4	7	3.2	15	3.0
Pancreas	169	32.3	24	5.6	193	20.0
Larynx	1,210	83.9	139	57.7	1,349	80.1
Lung	13,244	79.2	2,114	30.4	15,358	64.9
Breast	_	_	3,968	26.1	3,968	26.1
Kaposi sarcoma	597	100.0	67	100.0	664	100.0
Cervix uteri	_	_	4,177	100.0	4,177	100.0
Ovary	_	_	11	0.7	11	0.7
Vulva	_	_	80	43.0	80	43.0
Vagina	_	_	33	70.0	33	70.0
Prostate	51	1.3	_	_	51	1.3
Penis	165	50.0	_	_	165	50.0
Urinary bladder	384	32.8	3	1.1	387	25.8
Kidney	20	1.6	2	0.2	22	0.9
Non-Hodgkin lymphoma	632	32.1	326	21.3	958	27.3
Hodgkin lymphoma	214	50.0	151	50.0	365	50.0
Other, unspecified	0	0.0	0	0.0	0	0.0
All cancers	53,773	59.2	23,637	32.0	77,410	47.0

Abbreviation: AF, attributable fraction.

consumption level, which may lead to underestimation of AFs. However, differences in AFs for alcohol drinking could mainly be explained by a remarkable higher prevalence of alcohol consumption among men in Vietnam (82% in Vietnam compared with 39% in China³⁰ and 55% globally³²). Strikingly, alcohol consumption in Vietnam observed a remarkable increase of 21% between 2010 and 2015,³³ suggesting that alcohol consumption may result in a more significant burden of cancer in the future.

Because of lack of exposure data, we excluded most of the occupational and environmental agents in our analysis; however, we could estimate the impact of outdoor air pollutants (ie, level of PM_{2.5}) on cancer in Vietnam. Few studies in the past have evaluated such attribution. A similar study in France estimated that only 0.2% of all cancer deaths were caused by air pollutants.³⁴ Further studies in this area in Vietnam are warranted.

Other lifestyle and reproductive factors included in this analysis contributed little to the cancer burden in Vietnam.

Because of lack of data on hormonal, reproductive, and nutritional factors, we likely underestimated the impact of such risk factors in Vietnam. Our estimation for AFs of overweight and obesity (0.8%) was much lower than that of developed countries (ie, 1.6% in France, 34 5.3% in very high HDI countries, and 4.8% in high HDI countries³⁵). We used the prevalence of overweight and obesity in 2010 for the analysis, and a prompt growth in the prevalence was observed in recent years, with an increase from 12% in 2010 to 23.9% in 2015,33 indicating the possibility of a larger contribution of overweight and obesity to the burden of cancer in Vietnam in the future. Low fruit and vegetable intake played a small role in total cancer burden in Vietnam, accounting for just 0.4% of all cancers. Globally, consuming an insufficient amount of fruit and vegetables daily could cause 14% of GI cancer deaths worldwide.³⁶ Other dietary factors potentially associated with cancer¹⁴ (eg, red meat intake, salting-preserved food consumption, high-dose β-carotene supplements) were not included in our study, which might hamper our current analysis on diet and nutrition component. Nulliparity is the only reproductive factor included in this analysis and accounted for < 2% of all cancers in women; again, underestimation of the role of reproductive and hormonal factors on the cancer burden in Vietnam is likely to have occurred.

Although we understand well the role of infections and tobacco smoking in cancer, leading to opportunities for cancer prevention in the future, we understand less well the causes of hormonal and metabolic-related cancers. Because these factors are emerging in societies under transition, such as Vietnam, it is important to conduct further studies to investigate their contribution to cancer in the country.

Our study has several strengths, including being the first effort, to our knowledge, to systematically assess the role of established cancer risk factors in Vietnam. In addition, most of the exposure data included in our analysis were derived from large-scale representative studies of the Vietnamese population. However, there were several drawbacks to our study. First, cancer diagnosis in Vietnam has many challenges. Access to quality pathology services has been limited in the past. Modern technologies for cancer diagnosis have become available in a few comprehensive cancer centers in recent years.³⁷ In addition, the accuracy of pathology testing is also limited.³⁸ These limitations may hinder the accuracy of data for the cancer registries. Second, we lack data for several important established risk factors. Third, some prevalence of exposure either might not be representative of the country (ie, infectious agents) or was based on the estimation outside of Vietnam (ie, exposure to outdoor pollution). Fourth, risk factors were referring to a time period that may not be fully relevant to cancer development. Finally, RRs were obtained from non-Vietnamese population studies,

which may lead to potential under- or overestimation of certain risk factors specifically for the Vietnamese population.

Overall, approximately half of cancers in Vietnam can be attributed to known risk factors and therefore can be prevented, at least in theory. The effect of risk factors excluded from the analysis on the burden of cancer in Vietnam remains unknown. Therefore, it is important to monitor the exposures to such risk factors and to study the

effect of these factors on cancer because there are no robust studies on the association between different risk factors and cancer in Vietnam currently available. Our findings once again confirmed the notion that controlling oncogenic infections and decreasing tobacco smoking are the most effective approaches to reduce the burden of environmental cancer in Vietnam, but other risk factors, including alcohol use, diet, and indoor and outdoor air pollution should not be neglected.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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REFERENCES

- 1. The World Bank: Vietnam at a glance. http://www.worldbank.org/en/country/vietnam/overview
- 2. WHO: Vietnam country profile. https://www.who.int/countries/vnm/en/
- 3. Institute for Health Metrics and Evaluation: Findings from the Global Burden of Disease Study 2017. Seattle, WA, Institute for Health Metrics and Evaluation, 2018
- 4. Van Hoang D, Lee AH, Pham NM, et al: Prostate cancer risk reduced by physical activity even among men with prolonged sitting time: A study from Vietnam. Asia Pac J Public Health 30:227-234, 2018
- 5. Binh TT, Tuan VP, Dung HDQ, et al: Advanced non-cardia gastric cancer and Helicobacter pylori infection in Vietnam. Gut Pathog 9:46, 2017
- 6. Lai HT, Koriyama C, Tokudome S, et al: Waterpipe tobacco smoking and gastric cancer risk among Vietnamese men. PLoS One 11:e0165587, 2016
- 7. Trieu PD, Mello-Thoms C, Peat JK, et al: Inconsistencies of breast cancer risk factors between the northern and southern regions of Vietnam. Asian Pac J Cancer Prev 18:2747-2754. 2017
- 8. Bray F, Colombet M, Mery L, et al: Cancer Incidence in Five Continents Volume XI. International Agency for Research on Cancer. http://ci5.iarc.fr
- 9. Parkin DM, Whelan SL, Ferlay J, et al: Cancer Incidence in Five Continents, Volume VIII. Lyon, France, International Agency for Research on Cancer, 2002
- 10. Ferlay J, Ervik M, Lam F, et al: Global Cancer Observatory (GCO): Cancer today. International Agency for Research on Cancer. https://gco.iarc.fr/foday
- 11. Bray F, Ferlay J, Soerjomataram I, et al: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394-424, 2018
- 12. Ferlay J, Colombet M, Soerjomataram I, et al: Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. Int J Cancer 144:1941-1953, 2019
- 13. International Agency for Research on Cancer: Agents classified by the IARC monographs, volumes 1–123. IARC Monographs on the Identification of Carcinogenic Hazards to Humans. https://monographs.iarc.fr/agents-classified-by-the-iarc/
- 14. World Cancer Research Fund, American Institute for Cancer Research: Continue Update Project: Diet, nutrition, physical activity and the prevention of cancer—Summary of strong evidence. https://www.wcrf.org/sites/default/files/Matrix-for-all-cancers-A3.pdf
- 15. Opdahl S, Alsaker MDK, Janszky I, et al: Joint effects of nulliparity and other breast cancer risk factors. Br J Cancer 105:731-736, 2011
- 16. Fioretti F, Tavani A, Bosetti C, et al: Risk factors for breast cancer in nulliparous women. Br J Cancer 79:1923-1928, 1999
- 17. Levin ML: The occurrence of lung cancer in man. Acta Unio Int Contra Cancrum 9:531-541, 1953

- 18. Hanley JA: A heuristic approach to the formulas for population attributable fraction. J Epidemiol Community Health 55:508-514, 2001
- de Martel C, Ferlay J, Franceschi S, et al: Global burden of cancers attributable to infections in 2008: A review and synthetic analysis. Lancet Oncol 13:607-615, 2012
- 20. Huang H, Hu X-F, Zhao F-H, et al: Estimation of cancer burden attributable to infection in Asia. J Epidemiol 25:626-638, 2015
- 21. Wang JB, Jiang Y, Liang H, et al: Attributable causes of cancer in China. Ann Oncol 23:2983-2989, 2012
- 22. Sankaranarayanan R, Ramadas K, Qiao YL: Managing the changing burden of cancer in Asia. BMC Med 12:3, 2014
- 23. Plummer M, de Martel C, Vignat J, et al: Global burden of cancers attributable to infections in 2012: A synthetic analysis. Lancet Glob Health 4:e609-e616, 2016
- 24. Inoue M, Sawada N, Matsuda T, et al: Attributable causes of cancer in Japan in 2005: Systematic assessment to estimate current burden of cancer attributable to known preventable risk factors in Japan. Ann Oncol 23:1362-1369, 2012
- Razavi-Shearer D, Gamkrelidze I, Nguyen MH, et al: Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: A modelling study. Lancet Gastroenterol Hepatol 3:383-403, 2018
- 26. Hooi JKY, Lai WY, Ng WK, et al: Global prevalence of Helicobacter pylori infection: Systematic review and meta-analysis. Gastroenterology 153:420-429, 2017
- 27. Ministry of Health of Vietnam, Hanoi Medical University, General Statistics Office, et al: Global Adult Tobacco Survey (GATS) Vietnam 2010. https://www.who.int/tobacco/surveillance/en_tfi_gats_vietnam_report.pdf
- 28. Park S, Jee SH, Shin H-R, et al: Attributable fraction of tobacco smoking on cancer using population-based nationwide cancer incidence and mortality data in Korea. BMC Cancer 14:406, 2014
- 29. Katanoda K, Marugame T, Saika K, et al: Population attributable fraction of mortality associated with tobacco smoking in Japan: A pooled analysis of three large-scale cohort studies. J Epidemiol 18:251-264, 2008
- 30. Liang H, Wang J, Xiao H, et al: Estimation of cancer incidence and mortality attributable to alcohol drinking in China. BMC Public Health 10:730, 2010
- 31. Danaei G, Vander Hoorn S, Lopez AD, et al: Causes of cancer in the world: Comparative risk assessment of nine behavioural and environmental risk factors. Lancet 366:1784-1793. 2005
- 32. Boffetta P, Hashibe M, La Vecchia C, et al: The burden of cancer attributable to alcohol drinking. Int J Cancer 119:884-887, 2006
- 33. Ministry of Health of Vietnam: National Survey on the Risk Factors of Non-Communicable Diseases (STEPS) Viet Nam 2015. https://www.who.int/ncds/surveillance/steps/VietNam_2015_STEPS_Report.pdf
- 34. Boffetta P, Tubiana M, Hill C, et al: The causes of cancer in France. Ann Oncol 20:550-555, 2009
- 35. Arnold M, Pandeya N, Byrnes G, et al: Global burden of cancer attributable to high body-mass index in 2012: A population-based study. Lancet Oncol 16:36-46, 2015
- 36. WHO: Promoting fruit and vegetable consumption around the world. https://www.who.int/dietphysicalactivity/fruit/en/index2.html
- 37. Nguyen BD: Results of the national cancer program 2011-2014. Vietnam Oncol J 2:8, 2014
- 38. Pham T, Bui L, Kim G, et al: Cancers in Vietnam: Burden and control efforts—A narrative scoping review. Cancer Control 26:1073274819863802, 2019 CHECK PAGE REF
- 39. WHO: Fact sheet about health benefits of smoking cessation. Tobacco Free Initiative (TFI). https://www.who.int/tobacco/quitting/benefits/en/
- 40. Van Bui T, Blizzard CL, Luong KN, et al: Alcohol consumption in Vietnam, and the use of "standard drinks" to measure alcohol intake. Alcohol Alcohol 51:186-195, 2016
- 41. Hipgrave DB, Nguyen TV, Vu MH, et al: Hepatitis B infection in rural Vietnam and the implications for a national program of infant immunization. Am J Trop Med Hyg 69:288-294, 2003
- 42. Tran HT-T, Ushijima H, Quang VX, et al: Prevalence of hepatitis virus types B through E and genotypic distribution of HBV and HCV in Ho Chi Minh City, Vietnam. Hepatol Res 26:275-280, 2003
- 43. Hoang TTH, Bengtsson C, Phung DC, et al: Seroprevalence of Helicobacter pylori infection in urban and rural Vietnam. Clin Diagn Lab Immunol 12:81-85, 2005
- 44. Vietnam Administration of HIV/AIDS Control: Vietnam HIV/AIDS estimates and projections 2007-2012. http://www.ilo.org/wcmsp5/groups/public/—ed_protect/—protrav/—ilo_aids/documents/legaldocument/wcms_174609.pdf
- 45. Brauer M, Freedman G, Frostad J, et al: Ambient air pollution exposure estimation for the global burden of disease 2013. Environ Sci Technol 50:79-88, 2016
- 46. Committee for Population Family and Children: Vietnam Demographic and Health Survey 2002. https://dhsprogram.com/pubs/pdf/fr139/00frontmatter00.pdf

APPENDIX

TABLE A1. Prevalence of Infectious Carcinogens in Vietnam

Infectious

Year of Data Collection

imecuous Carcinogens	1997	1998	1998-2001	2002	2003	2004-2006	2006	2007	2008	2009	2010	2012	2013	2015
ЛВИ		18.8% ⁴¹ (single province, general population)	10% ⁴² (single province, low-risk and high-risk population)	19%* (single province, general population)	10% ^b (single province, pregnant women population)	8.3%° (single province, general emale population)	8.8% ^d (single province, general population)	(single province, voluntary blood donors)		9.4%¹ (multiple provinces, general population)		15.3% ⁸ (single province, general population)		
ЛОН			2%*2 (single province, low-risk and high-risk	1% ^a (single province, general population)			2.9% ⁴ single province, general population)	0.17%¹ (single province, voluntary blood donors)		0.9%" (multiple provinces, military recruits)		3.3% ⁸ (single province, general population)		
АРУ	1%-5% to 9.6% ¹ (multiple provinces, married women)							5.13% (single province, general female population)	7.6%k (single province, general female population)	10.84%' (single province, general female population)	6.1%-10.2%" (multiple provinces, married women)		(single province, general female population)	9.5%° (single province, general female population)
Helicobacter pylori					74.6% ⁴³ (multiple provinces, general population)					65.6% P (multiple provinces, general population)		29.3%-51% ^q (multiple provinces, minor ethnic groups)		
EBV	DUV	DUV	And	DUV	DUV	DUV	DUV	DUV	DUV	DUV	DUV	DUV	DUV	DUV
HIV (national data, age 15-49 years)'	0.05%	0.1%	0.14%	0.17%	0.2%	0.22%-0.25%	0.24%	0.26%	0.27%	0.28%	0.28%	0.29%	0.29%	0.29%
Abbreviations: DUV, data unavailable for Viehnam; EBV, Epstein-Barr virus; HBV, hepatitis C virus; HPV, human papilomavirus. "Nguyen VT, Malaws MI, Doe GI. Highly endemic hepatitis B infection in rural Viehnam. J Gastnenterot Hepatil 22:2093-2100, 2007. "Nguyen VT, Malaws MI, Doe GI. Highly endemic hepatitis B infection in rural Viehnam. J Gastnenterot Hepatil 22:2093-2100, 2007. "You Li. Sexually viehteror and other reproductive fract infections associated the tract infections associated the tract infection in rural Viehnam. Asia may be made in microstoms for control. https://openarchhe.ki.se/milurbistream/hander/10516/99145/thesss.pdf;sequence=1, 9boxing TH, Nguyen PH, Henley K, et al: Risk factors for hepatitis B infection in rural Viehnam. Asian Pac. J Cancer Pev 10:97-102, 2009. "Vet I, Lan NTM, Jy PK, et al: Prevalence of hepatitis B and hepatitis of more in rural Viehnam. India J Med Res 136:7481, 2012. "Vet I, Lan NTM, Jy PK, et al: Prevalence of hepatitis B and bepatitis of more and prevalence of hepatitis B and over increased patients involving diverse and novel virus variants. PLoS One 7:e41266, 2012. "Vet I, Lan NTM, Jy PK, et al: Hepatitis C virus in Viehnam. High prevalence of infection among women in South and Number 104:132-220, 2003. "Vet I, Than VH; Study on the bypas of HPV (Imman papillomavirus in Viehnam, Half Landson Milh City J Med 14:5, 2010. "Phan TT, Naguen CA, Cao AMI, Human papillomavirus infection among women in South and packed to the Citi Milhn City J Med 14:5, 2010. "Tan TL, Bu D, Le HT; Prevalence of cervical infection may women of child-bearing age. Ho Citi Milhn City J Med 14:5, 2010. "Tan TL, Bu D, Le HT; Prevalence of cervical infection of sexually active women in Ho Citi Milhn City J Med 14:10, 2010. "No year TT, Naguen R, Ord Strump papillomavirus infection and genotype distribution of human papillomavirus more demonded by a through an packed cancer among termales in Da Nagu, Viehnam, Anticanner Res 37:1243-1247, 2017. "Naguen TT, Uchida T, Tsukamoto Y, et al.	ita unavailable MIL, Dore GJ.: H ham NIM, et al. transmitted infe transmitted infe H, Henley K, et al. Prevalk ean J, et al. A I glimoto M, et al. 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Int J Cancer 104:213-220, 200 in detected by PCR among women in Hanci city. Ho Chi Minh City J Med I vietnam: Implications for vaccine campaign. BMC Cancer 13:53, infection and investigation on knowledge, attitude and practice on cervical notype distribution of human papilloma virus among females in Da Nang, gastroduodenal diseases in Vietnam: A cross-sectional, hospital-based st ar pylori infection in a minor ethnic group of Vietnam: A multiethnic, populyetical part international, 2013.	; HPV, human r. S3-2100, 2007. gnant women ir anagement and 10:97-102, 20C I Vitenam. India Wet Nam. PLoS Thuan provinct sed patients in vi. J. Cancer 104:; city. Ho Chi Mir city. Ho Chi mpaign. BMC Cs. among females s-sectional, hossy Vietnam: A muttl Health Internati	apillomavirus. ten communes implications fo 99. n J Med Res 1: One 7.e39027, One 7.e39027, y, Vetnam. Her olving diverse 213-220, 2003, hh City J Med 1 J, 2010. Minh City J Med 1 S, 2010. Minh City J Med 1 S, 2010. Alian City J Med 1 S, 2010.	in Nighe An Pre control. https:// 2012. 2012. aatol Res 45,256 and novel virus v 3.5, 2009. 3.5, 2009. 3.13. cancer among reference. Tiefnam. Antican y. BMC Gastroe	vince, Vietnam. openarchive.ki.s268, 2015. ariants. PLoS Or ariants. PLoS Or ariants. PLoS III-14, 23 Int J Mol Sci II.	IBV, hepatitis B virus; HCV, hepatitis C virus; HPV, human papillomavirus. ural Vietnam. J Gastroenterol Hepatol 22:2093-2100, 2007. ural Vietnam. J Gastroenterol Hepatol 22:2093-2100, 2007. with reproductive tract infections among pregnant women in ten communes in Nghe An Province, Vietnam. J Epidemiol 15:163-172, 2006. scrions in rural Vietnam. Current situation, management and implications for control. https://openarchive.ki.se/xmlui/bitstream/handle/10616/n in rural Vietnam. Asian Pac J Cancer Prev 10:97-102, 2009. s infections in potential blood donors in rural Vietnam. Indian J Med Res 136:74-81, 2012. s virus infections among adults living in Binh Thuan province, Vietnam. Hepatol Res 45:259-268, 2015. ence of infection in dialysis and multi-transfused patients involving diverse and novel virus variants. PLoS One 7:e41266, 2012. ong women in South and North Vietnam. Int J Cancer 104:213-220, 2003. In detected by PCR among women in Hanoi city. Ho Chi Minh City J Med 13:5, 2009. In women of child-bearing age. Ho Chi Minh City J Med 14:5, 2010. Setton of sexually active women in Ho Chi Minh city. Ho Chi Minh City J Med 14:10, 2010. It is in Vietnam: Implications for vaccine campaign. BMC Cancer 13:53, 2013. Indiction and investigation on knowledge, attitude and practice on cervical cancer among reproductive aged women in DakLak in 2013. We notype distribution of human papilloma virus among females in Da Nang, Vietnam. Anticancer Res 37:1247, 2017. gastroducdenal diseases in Vietnam: A cross-sectional, hospital-based study. BMC Gastroenterol 10:114, 2010. Set Pylori infection in a minor ethnic group of Vietnam: A multiethnic, population-based study. Int J Mol Sci 19:E708, 2018.	63-172, 2005. handle/10616/3	9145/thesis.pdf	;sequence=1.