Proportion of cancer cases and deaths attributable to potentially modifiable risk factors in Peru prior to the COVID-19 pandemic

Jhony A. De La Cruz-Vargas[1,*], Willy Ramos[1,*], Willer Chanduví[1], Lucy E. Correa-López[1], Nadia Guerrero[1], Joan Loayza-Castro[1], Irene M. Tami-Maury[2] and Diego Venegas[3]

1. Instituto de Investigaciones en Ciencias Biomédicas (INICIB). Universidad Ricardo Palma, Lima-Perú.
2. The University of Texas Health Science Center at Houston. Houston, USA
3. Facultad de Ciencias e Ingeniería. Universidad Peruana Cayetano Heredia, Lima-Perú

* Both authors contributed equally to this research

ABSTRACT

OBJECTIVE: To estimate the fraction of cancer cases and deaths attributable to potentially modifiable risk factors in Peru in 2018, prior to the COVID-19 pandemic.

MATERIAL AND METHODS: An ecological study was carried out using the prevalence of exposure of the Peruvian population to modifiable risk factors for cancer, relative risk of each risk factor, and number of cancer cases and deaths in 2018 as inputs. We used the Parkin formula with a Montecarlo statistical simulation model to calculate the population attributable fraction (PAF) and confidence intervals. The number of new cancer cases and deaths attributable to each risk factor was calculated by multiplying the number of cases and deaths in each sex by the PAF of each risk factor.

RESULTS: 38.4% of new cases (34.4% in men and 41.8% in women) and 43.2% of deaths by cancer in Peru (43.1% in men and 43.2% in women) were attributable to modifiable risk factors. The number of cancers attributable was 25,591 (10,616 in men and 14,975 in women) and the number of deaths attributable to cancer was 14,922 (6,996 in men and 7,926 in women). The modifiable risk factors that caused a greater number of cases and deaths were HPV infection (4563 cases, 2410 deaths), current tobacco use (3387 cases, 2198 deaths), and Helicobacter pylori infection (2686 cases, 1874 deaths). The oncogenic infections made up the group of risk factors that presented a greater PAF (16.6% for cases, 19.1% for deaths) followed by other unhealthy lifestyle factors (14.1% for cases, 16.5% for deaths), tobacco (7.2% for cases, 7.3% for deaths) and ultraviolet radiation (0.5% for cases, 0.3% for deaths).

CONCLUSION: Prior to the COVID-19 pandemic, a proportion of 38.4% of cancer cases and 43.2% of cancer deaths in Peru during 2018 were attributable to modifiable risk factors. Most preventable cancer cases and deaths are linked to oncogenic infections, primarily caused by HPV and Helicobacter pylori.

KEY WORDS: Cancer, population attributable fraction, modifiable risk factors, lifestyle, preventive medicine, Peru.

CORRESPONDENCE

Jhony A. De La Cruz-Vargas
Instituto de Investigaciones en Ciencias Biomédicas (INICIB), Universidad Ricardo Palma.
Av. Alfredo Benavides 5440, Santiago de Surco, Lima, 15039, Peru.
E-mail: jhony.delacruz@urp.edu.pe

FUNDING SOURCES

This Project was financed by the University Ricardo Palma, ACU N^{0} 2619-2019.

CONFLICTS OF INTEREST

The authors declare there were no conflicts of interests.

INTRODUCTION

Cancer constitutes a public health problem in Peru due to inequalities accessing oncological services, leading to late diagnosis and disparities in cancer treatment, which in turns leads to exacerbating the risk of premature deaths among Peruvians [(1-4)]. Peru's health profile has been influenced in the last decades by demographic transition, epidemiological transition, commercial diet and nutrition transition which has led to the predominance of non-communicable diseases such as cancer [(5)]. In addition, poverty, education, gender, urbanization/rurality, ethnicity, and race, environmental factors, as well as other health determinants affect the way Peruvians are exposed to risk factors and their access health services [(6)]. Despite this, the morbidity and mortality in the country is still impacted by transmissible diseases [(1,5-7)].

According to the estimates of the International Agency for Research on Cancer (IARC) published by the Global Cancer Observatory, in 2018 (prior to the COVID-19 pandemic), there were 66,669 new cancer cases and 34,570 cancer deaths in Peru [(2,3)].

Many cancers are causally related to potentially modifiable risk factors and current estimates of this proportion in a population, meaning, the population attributable fraction (PAF) constitutes a valuable tool for prioritizing cancer prevention and control programs and interventions [(8)]. PAF studies based on assessing modifiable cancer risk factors are available in North America (United States and Canada) , Europe (England) [(11)], Asia (China, Japan) [(12,13)] and the Middle East [(14)] with PAFs ranging from 23% to 45% for cancer cases and from 41% to 51% for cancer deaths. Most of these studies focused on PAF for cancer cases and only a few on PAF for cancer deaths [(9,12,13,15)].

By contrast, there is little evidence on PAF of cancer cases and deaths in Latin America, in Peru some studies on PAF of some risk factors and its related diseases have been published, as it occurs with tobacco use[(16)]. The only Latin American country that has a PAF study for cancer is Brazil [(15)], on the other hand, Chile has a PAF study that only considers lifestyle risk factors, not including oncogenic infections [(17)].

The objective of this study is to estimate the fraction of cancer cases and deaths in Peru attributable to potentially modifiable risk factors in 2018, prior to the COVID-19 pandemic.

MATERIAL AND METHODS

An ecological study was performed with data from the prevalence of the Peruvian population's exposure to modifiable risk factors for cancer, as well as cancer incidence and mortality prior to the COVID-19 pandemic.

PREVALENCE OF MODIFIABLE RISK FACTORS, CANCER CASES AND DEATHS

The prevalence of the Peruvian population's exposure to modifiable risk factors for cancer was obtained from the following sources of information:

- Population surveys: The Demographic and Family Health Survey (ENDES 2018) allowed to obtain data on cigarette, alcohol, fruit and vegetable salad use, overweight and obesity in people 15 years of age or above.
- Research articles: Allowed us to obtain information on the prevalence of oncogenic infections, sedentary behavior, among others.
- University thesis repositories: In some cases, we were able to obtain information specific to pre and postgraduate thesis, mainly on rare risk factors or those where few studies exist in the Peruvian population such as the prevalence of red meat and processed meat consumption.

RELATIVE RISK (RR)

To identify the relative risk for each potentially modifiable risk factor, we performed a systematic search of articles in PUBMED, SCOPUS, EMBASE, COCHRANE, and SCIELO. We considered in order of importance metanalysis, cohort and case-control studies, preferring the most recent, those that covered American countries and those that controlled for the confounder effect of other variables from a multivariate statistical analysis. For the factors in which the systematic search did not identify studies with RR for the potentially modifiable risk factors, we used research that obtained odds ratio (OR) as a statistical approximation to RR.

ESTIMATE OF THE PAF

We used the formula described by Parkin et al [18] for the calculation of the PAF:

$$\frac{(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2) + (p_3 \times \mathrm{ERR}_3) \dots + (p_n \times \mathrm{ERR}_n)}{1 + [(p_1 \times \mathrm{ERR}_1) + (p_2 \times \mathrm{ERR}_2) + (p_3 \times \mathrm{ERR}_3) \dots + (p_n \times \mathrm{ERR}_n)]}$$

Where p_1 is the proportion of the population in exposure level 1 (and so on), and ERR_1 is the excess relative risk (relative risk - 1) in exposure level 1 (and so on). We calculated PAF for the absence or decrease of risk factors. ERR were calculated as the natural logarithm of the reciprocal of relative risk, which is: $ERR = \ln\left(\frac{1}{RR}\right)$

The number of cancer cases and deaths attributable to each risk factor according to sex was calculated by multiplying the number of cancer cases and deaths per sex by the PAF.

The number of cancer cases and deaths in Peru were obtained from the Global Cancer Observatory (GLOBOCAN-Cancer today) which publishes the IARC estimates from the base population cancer registry data using the estimates from the year 2018 [3].

TABLE 1: Potentially modifiable risk factors considered for each type of cancer.

TOPOGRAPHY	MODIFIABLE RISK FACTORS

Mouth, pharynx (C00-C14)	HPV infection, tobacco use, alcohol use, low fruit and vegetable use
Esophagus (C15)	Current tobacco use, obesity, sedentary behavior, alcohol use
Stomach (C16)	*Helicobacter pylori* infection, current tobacco use, obesity, red meat consumption, processed meat consumption
Colorectal (C18-C21)	Current tobacco use, sedentary behavior, alcohol use, overweight, obesity, red meat consumption, processed meat consumption, low consumption of fruits and vegetables.
Liver (C22)	Hepatitis B virus, Hepatitis C virus, current tobacco use, obesity, overweight
Gallbladder (C23)	Obesity, overweight
Pancreas (C25)	Tobacco use, alcohol use, obesity
Larynx (C32)	HPV infection, current tobacco use, low fruit and vegetable consumption
Lung (C34)	Current tobacco use, passive tobacco smoke exposure, sedentary behavior, low fruit and vegetable consumption
Kaposi Sarcoma (C46)	HHV-8 infection, HIV
Breast (C50)	Tobacco use, passive exposure to tobacco smoke, obesity, overweight, sedentary behavior
Cervix (C53)	HPV infection, HIV infection, current tobacco use, sedentary behavior
Endometrium (C54.1)	Obesity, overweight, sedentary behavior
Ovaries (C56)	Obesity, overweight
Penis (C60)	HPV infection
Kidney (C64)	Tobacco use, overweight, obesity
Bladder (C67)	Current tobacco use, overweight, obesity
Hodgkin's Lymphoma (C81)	Epstein Barr virus, HIV, current tobacco use
Non-Hodgkin's Lymphoma (C82-C85, C96.3)	Epstein Barr virus, HIV, Hepatitis C virus
Leukemias (C91-C95)	Tobacco use, obesity, overweight

From an ethical point of view, the study did not imply risks since it was not carried out with data from people rather with aggregate prevalence data from population surveys, relative risks from metanalysis and scientific journal articles, as well as the IARC cancer incidence and mortality estimates for Peru which is why it did not require an informed consent. Additionally, the study was approved by the Research Ethics Committee from the Medical School of Ricardo Palma University.

RESULTS

In the year 2018, prior to the COVID-19 pandemic, it was estimated that 38.4% of new cancer cases in Peru were attributed to potentially modifiable risk factors. Cancers that showed greater PAF, in addition to cervix and Kaposi sarcoma, were cancers from the larynx (85.6%), stomach (82.6%), liver (82.3%), lung (80.7%) and penis (75.0%), while those with lower PAF were ovarian cancer (8.4%), leukemia (12.8%), pancreatic cancer (21.8%), skin melanoma (25.0%) and bladder cancer (27.9%) (Table 2).

TABLE 2: PAF of cancer according to topography and potentially modifiable risk factors.

TOPOGRAPHY	PAF (%)	C.I. 95%	% TOTAL PAF
Mouth, pharynx (C00-C14)			
HPV Infection	8.1	6.5 – 9.8	
Current tobacco use	20.5	11.8 – 30.8	65.7
Alcohol use	36.1	23.2 – 48.2	
Low fruit and vegetable consumption	1.1	0.1 – 2.2	
Esophagus (C15)			
Current tobacco use	11.0	6.9 – 15.9	
Obesity	12.3	3.9 – 36.3	60.8
Sedentary behavior	21.9	2.2 – 37.5	
Alcohol use	15.6	13.8 – 17.6	
Stomach (C16)			
Helicobacter pylori infection	46.4	18.6 – 65.9	
Current tobacco use	8.3	3.8 – 14.4	
Obesity	2.8	0.7 – 5.1	82.6
Red meat consumption	18.9	10.2 – 18.2	
Processed meat consumption	6.2	1.0 – 11.5	
Colorectal (C18-C21)			
Current tobacco use	2.1	1.1 – 3.1	
Sedentary behavior	18.5	8.3 – 27.1	
Alcohol use	4.1	2.1 – 6.3	
Obesity	4.1	2.4 – 6.1	53.6
Overweight	7.4	0.1 – 15.1	
Red meat consumption	5.9	1.5 – 9.8	
Processed meat consumption as	5.0	2.4 – 7.8	
Low fruit and vegetable consumption	6.6	0.9 – 12.4	
Liver (C22)			
Hepatitis B virus	32.4	30.2 – 34.6	
Hepatitis C virus	21.5	20.1 – 23.1	82.3
Current tobacco use	5.7	3.8 – 6.6	
Obesity	16.6	10.2 – 23.3	
Overweight	6.0	0.8 – 11.4	
Gallbladder (C23)			
Obesity	12.6	5.3 – 20.8	18.6
Overweight	6.0	2.6 – 9.6	
Pancreas (C25)			
Current tobacco use	7.3	6.1 – 8.4	

Alcohol use	7.2	4.7 – 9.6	21.8
Obesity	7.2	3.1 – 11.7	
Larynx (C32)			
HPV infection	22.1	10.9 – 37.0	85.6
Current tobacco use	38.8	18.5 – 60.6	
Low fruit and vegetable consumption	24.7	14.4 – 33.2	
Lung (C34)			
Current tobacco use	44.3	17.5 – 70.0	
Secondhand smoke	7.7	5.0 – 10.2	80.7
Sedentary behavior	17.0	4.4 – 28.3	
Low fruit and vegetable consumption	11.7	4.3 – 19.3	
Melanoma (C44)*			
Ultraviolet radiation	25.0	20.7 – 29.4	25.0
Kaposi sarcoma (C46)			
HHV-8 infection	100.0	96.4 – 100.0	100.0
Breast (C50)			
Current tobacco use	9.2	1.2 – 25.8	
Secondhand smoke	5.6	2.1 – 9.0	
Obesity	8.5	6.3 – 10.8	41.8
Overweight	6.0	3.6 – 8.5	
Sedentary behavior	12.5	2.5 – 21.7	
Cervix (C53)			
HPV infection	100.0	96.4 – 100.0	100.0
Endometrium (C54.1)			
Obesity	28.4	22.3 – 34.7	58.0
Overweight	10.6	5.6 – 15.6	
Sedentary behavior	19.0	6.3 – 30-8	
Ovary (C56)			
Obesity	5.9	3.5 – 8.4	8.4
Overweight	2.5	5.6 – 13.2	
Penis (C60)			
HPV infection	75,0	45,6 – 88,5	75,0
Kidney (C64)			
Current tobacco use	4.6	2.7 – 6.5	36.2
Obesity	16.9	13.3 – 20.4	
Overweight	14.8	11.4 – 18.0	
Bladder (C67)			
Current tobacco use	20.8	18.0 – 23.6	27.9
Obesity	16.9	13.3 – 20.4	
Overweight	14.8	11.4 – 18.0	
Hodgkin's Lymphoma (C81)			
Epstein Barr virus	59.7	34.1 – 79.1	63.8
HIV	0.7	0.2 – 1.9	
Current tobacco use	3.4	1.3 – 5.7	
Non-Hodgkin's Lymphoma (C82-C85, C96.3)			
Epstein Barr virus	68.0	39.1 – 84.5	69.6
HIV	1.0	0.7 – 1.39	

hepatitis C virus	0.6	0.4 – 0.9	
Leukemias (C91-C95)			
Current tobacco use	4.1	2.3 – 6.0	12.8
Obesity	5.5	3.7 – 7.6	
Overweight	3.3	1.5 – 5.0	

The fraction of cancer cases attributable to potentially modifiable risk factors were 34.4% in men and 41.8% in women, with potentially evitable cancers at 25,591 (10,616 in men and 14,975 in women). In addition to Kaposi Sarcoma, the cancers with greater PAF in men were larynx (98.5%), lung (97.8%), liver (95.7%), mouth/pharynx (87.8%) and stomach (75.8%). Meanwhile, in addition to cervical cancer and Kaposi Sarcoma, those with greater PAF in women were liver (73.7%), non-Hodgkin's lymphoma (69.2%), stomach (66.3%), larynx (65.5%) and Hodgkin's lymphoma (61.4%) (Table 3). The cancers with greater number of preventable cases in men were stomach (2,021 cases), lung (1,260 cases), liver (967 cases), colorectal (845 cases) and non-Hodgkin's lymphoma (578 cases) and in women were cervix (2,288 cases), stomach (1,534 cases), liver (798 cases), breast (762 cases) and colorectal (652 cases) (Table 3).

TABLE 3: PAF, cancer cases and deaths attributable to potentially modifiable risk factors in Peruvian men and women.

TOPOGRAPHY	MEN				WOMEN			
	PAF (%)	C.I. 95%	CASES	DEATHS	PAF (%)	C.I. 95%	CASES	DEATHS
Mouth, pharynx	87.8	64.7 – 100.0	464	178	29.2	15.7 – 45.1	156	58
Esophagus	69.1	33.6 – 100.0	186	174	40.2	9.3 – 83.6	32	29
Stomach	75.8	33.6 – 100.0	2526	2021	66.3	25.8 – 100.0	1968	1534
Colorectal	72.5	32.2 – 100.0	1632	845	54.3	23.0 – 81.8	1296	652
Liver	95.7	75.6 – 100.0	1016	967	73.7	57.0 – 91.4	819	798
Gallbladder	8.1	3.1 – 13.7	20	13	25.6	9.8 – 42.2	199	116
Pancreas	26.7	16.8 – 37.6	191	184	19.4	13.4 – 25.1	173	165
Larynx	98.5	53.0 – 100.0	165	95	65.5	32.9 – 100.0	43	24
Lung	97.8	46.7 – 100.0	1388	1260	41.6	13.2 – 100.0	611	544
Skin melanoma	46.9	43.8 – 50.0	301	97	1.2	0.9 – 2.7	8	2
Kaposi Sarcoma	100.0	96.4 – 100.0	297	56	100.0	96.4 – 100.0	55	19
Breast	NA	NA	NA	NA	41.8	15.6 – 75.8	2868	762
Cervix	NA	NA	NA	NA	100.0	96.4 – 100.0	4270	2288
Endometrium	NA	NA	NA	NA	58.0	34.1 – 81.1	725	180
Ovary	NA	NA	NA	NA	8.4	9.0 – 21.6	107	66
Penis	75.0	45.6 – 88.5	214	60	NA	NA	NA	NA
Kidney	33.4	23.3 – 44.0	403	168	34.3	27.3 – 41.5	283	105
Bladder	36.7	28.9 – 44.7	267	89	15.1	9.1 – 21.2	57	23
Hodgkin's Lymphoma	66.4	36.8 – 91.4	144	54	61.4	35.0 – 82.6	127	37
Non-Hodgkin's Lymphoma	70.2	40.5 – 87.7	1177	578	69.2	39.9 – 86.4	1066	444
Leukemias	15.8	6.4 – 26.9	225	157	10.2	1.9 – 14.8	112	80

NA: Not applicable

Oncogenic infections constitute the group of potentially preventable risk factors that presented greater PAF and were responsible for 11,021 cancer cases, with HPV infection associated to the greatest number of cancers (4,563 cases). The second most important group was unhealthy lifestyle factors which had a PAF of 14.1% and were responsible for 9,466 cancers, with obesity associated to the greatest number of cancers (2,151 cases). The third most important group was linked to tobacco exposure with a PAF of 7.2% and responsible for 4,793 cases, with current tobacco use associated to the greatest number of cancers (3,387 cases). Finally, ultraviolet radiation exposure was the least frequent with a PAF of 0.5% and responsible for 309 cancers (Tables 4 and 5).

It is estimated that by the year 2018, 43.2% of cancer deaths in Peru were attributable to potentially modifiable risk factors. The fraction of cancer deaths attributable to potentially modifiable risk factors were 43.1% in men and 43.2% in women, and the number of deaths potentially attributable to cancer were 14,992 (6,996 in men and 7,926 in women). The cancers with greatest potentially attributable number of deaths in men were stomach (2,526 deaths), colorectal (1,632 deaths), lung (1,388 deaths), non-Hodgkin's lymphoma (1,177 deaths), and liver (1,016 deaths) and in women they were cervix (4,270 deaths), breast (2,868 deaths), stomach (1,968 deaths), colorectal (1,296 deaths), and non-Hodgkin's lymphoma (1,066 deaths) (Table 3).

Oncogenic infections constituted the potentially modifiable risk factor group with greatest PAF (19.1%) that were responsible for 6,601 cancer deaths, with HPV infection associated to greatest number of deaths (2,410). The second most important group was other unhealthy lifestyle factors with PAF of 16.5% and responsible for 5,722 deaths, with obesity associated to the greatest number of deaths (1,413). The third most important group was linked to tobacco exposure with a PAF of 7.3% and responsible for 2,500 deaths, with current tobacco use associated to the greatest number of deaths (2,198). Finally, ultraviolet radiation exposure constituted the less frequent group with PAF of 0.3% and was responsible for 99 deaths (Tables 4 and 6).

TABLE 4: Number of cancer cases and deaths attributable to potentially modifiable risk factors in Peru distributed by sex.

FACTOR CLUSTERING	MODIFIABLE RISK FACTORS	MEN		WOMEN		BOTH SEXES	
		CASES	DEATHS	CASES	DEATHS	CASES	DEATHS
Tobacco (Lifestyle)	Current tobacco use	2191	1587	1196	611	3387	2198
	Secondhand smoke	106	96	1300	206	1406	302
Other unhealthy lifestyle factors (Lifestyle)	Sedentary behavior	779	492	1271	724	2050	1216
	Overweight	433	304	1244	416	1677	720
	Obesity	908	635	1243	778	2151	1413
	Red meat consumption	761	572	702	508	1463	1080
	Processed meat consumption	319	225	304	204	623	429
	Low fruit and vegetable consumption	486	318	145	125	631	443
	Alcohol use	593	323	278	98	871	421
UV Radiation (Environment-lifestyle).	UV Radiation	301	97	8	2	309	99
Infections (Lifestyle)	*Helicobacter pylori*	1213	970	1473	904	2686	1874
	HBV	396	377	239	306	635	683
	HCV	239	223	67	237	306	460
	HPV	293	98	4270	2312	4563	2410
	HHV8	297	56	55	19	352	75
	HIV	30	14	11	5	41	19
	EBV	1269	609	1169	471	2438	1080
	TOTAL	**10616**	**6996**	**14975**	**7926**	**25591**	**14922**

TABLA 5: Fraction of cancer cases attributable to potentially modifiable risk factors in Peru distributed by sex.

FACTOR CLUSTERING	MODIFIABLE RISK FACTORS	MEN		WOMEN		BOTH SEXES	
		PAF CASES	PAF CLUSTERED	PAF CASES	PAF CLUSTERED	PAF CASES	PAF CLUSTERED
Tobacco (Lifestyle)	Current tobacco use	7.1	7.5	3.3	7.0	5.1	7.2
	Secondhand smoke	0.3		3.6		2.1	
Other unhealthy lifestyle factors (Lifestyle)	Sedentary behavior	2.5	13.9	3.5	14.5	3.1	14.1
	Overweight	1.4		3.5		2.5	
	Obesity	2.9		3.5		3.2	
	Red meat consumption	2.5		2.0		2.2	
	Processed meat consumption	1.0		0.8		0.9	
	Low fruit and vegetable consumption	1.6		0.4		0.9	
	Alcohol use	1.9		0.8		1.3	
UV Radiation (Environment-lifestyle).	UV Radiation	1.0	1.0	0.0	0.0	0.5	0.5
Infections (Lifestyle)	*Helicobacter pylori*	3.9	12.1	4.1	20.3	4.0	16.6
	HBV	1.3		0.7		1.0	
	HCV	0.8		0.2		0.5	
	HPV	1.0		11.9		6.8	
	HHV8	1.0		0.2		0.5	
	HIV	0.1		0.0		0.1	
	EBV	4.1		3.3		3.7	
TOTAL	**All risk factors**	**34.4**	**34.4**	**41.8**	**41.8**	**38.4**	**38.4**

TABLE 6: Fraction of cancer deaths attributable to potentially modifiable risk factors in Peru distributed by sex.

FACTOR CLUSTERING	MODIFIABLE RISK FACTORS	MEN		WOMEN		BOTH SEXES	
		PAF DEATHS	PAF CLUSTERED	PAF DEATHS	PAF CLUSTERED	PAF DEATHS	PAF CLUSTERED
Tobacco (Lifestyle)	Current tobacco use	9.8	10.4	3.3	4.4	6.4	7.3
	Secondhand smoke	0.6		1.1		0.9	
Other unhealthy lifestyle factors (Lifestyle)	Sedentary behavior	3.0	17.6	3.9	15.5	3.5	16.5
	Overweight	1.9		2.3		2.1	
	Obesity	3.9		4.2		4.1	
	Red meat consumption	3.5		2.8		3.1	
	Processed meat consumption	1.4		1.1		1.2	
	Low fruit and vegetable consumption	2.0		0.7		1.3	
	Alcohol use	2.0		0.5		1.2	
UV Radiation (Environment-lifestyle).	UV Radiation	0.6	0.6	0.0	0.0	0.3	0.3
Infections (Lifestyle)	Helicobacter pylori	6.0	14.5	4.9	23.3	5.4	19.1
	HBV	2.3		1.7		2.0	
	HCV	1.4		1.3		1.3	
	HPV	0.6		12.6		7.0	
	HHV8	0.3		0.1		0.2	
	HIV	0.1		0.0		0.1	
	EBV	3.8		2.6		3.1	
TOTAL	All risk factors	43.1	43.1	43.2	43.2	43.2	43.2

DISCUSSION

This study shows an estimated 38.4% of new cases and 43.2% of cancer deaths in Peru were attributable to potentially modifiable risk factors in the year 2018, prior to the COVID-19 pandemic. Among the lifestyle related factors were oncogenic infections which constituted the group of factors that explained the greatest number of preventable cancer cases and deaths exceeding tobacco exposures, other unhealthy lifestyle factors and UV radiation exposure. The risk factors that cause greater number of cancer cases and deaths were HPV infection, current tobacco use and *Helicobacter pylori* infection.

The fraction of cancer cases in Peru attributable to potentially modifiable risk factors was intermediate, above Australia [(19)] (32.0%), Eastern Mediterranean countries [(14)] (33.4%), Japan [(13)] (35,9%) and Canada [(20)] (33-37%), below USA [(9)] (42.0%) and similar to that reported by the United Kingdom[(11)] (37.7%). Likewise, the fraction attributable to cancer deaths was intermediate, placed above Japan [(13)] (41%) but below USA [(9)] (45.1%) and China [(21)] (45.2%). Compared to Latin American countries, Brazil [(15)], is the only country that counts a PAF study for cancer cases and deaths that include oncogenic infections and unhealthy lifestyles among its risk factors, in fraction attributable to cases (38.4% versus 34.2%) as well as deaths (43.2% versus 42%).

Oncogenic infections constituted the group of factors with greatest PAF, with 16.6% of cancer cases and 19.1% of deaths. PAF obtained for cases greatly exceeded that described in other PAF studies such as those carried out in the USA [(9)], Canada [(20)], Australia [(19)] and UK [(11)] where infections explain 3.3%, 3.7%, 2.9% and 3.6% of cancer cases, respectively, and is slightly above that reported in Japan [(13)] (16.6%). The PAF of infections also greatly exceed that obtained in the USA [(9)] for cancer deaths where PAF was 2.7% and slightly above that obtained in Japan [(13)] which reached 17.7%. For Latin America, the study performed in Brazil [(15)] places oncogenic infections in second place, behind tobacco, however, the exact PAF value is not detailed. This speaks to the phenomenon known as "double burden", frequent in low- and middle-income countries, that on the one side must face the non-communicable disease load, but at the same time respond to an important component of communicable diseases, which also occurs with cancer [(22-24)]. In Peru, unlike other countries, the prevention and control of oncogenic infections has not been found, despite there being strategies for screening, early detection, or vaccination for many of them [(1,2)].

The second group with the greatest PAF in Peru was that of other factors related to unhealthy lifestyle (without including tobacco use) which was similar to that obtained by Islami in the USA [(9)] for cancer cases (14.1% versus 13.9%) and slightly above for cancer deaths (16.5% versus 14.9%). When tobacco is included in unhealthy lifestyle factors, PAF for Peru was 28%, which is slightly lower than that reported by countries in the region such as Chile (30%) but above that of Brazil (26.5%). An explanation would be the existence of diverse levels of progress in the epidemiologic transition in Latin America as opposed to countries with higher income in which its profiles are dominated by the unhealthy lifestyle factors [(1,5,6,25)].

The importance in Peru for risk factors such as tobacco and ultraviolet radiation, as well as cancer cases and deaths, is notably less than in the majority of countries that count on PAF studies in which the weight of these factors is described (9,11,13, 19,20) including much less than other neighboring Latin American countries such as Chile(26) and Brazil(15). This is possibly because of the policy developments oriented towards the control of tobacco use which is evidenced by the downward trend of consumption in the last two decades, in addition to the possible underdiagnosed and underreporting of mortality by lung cancer in Peru, linked to the gap of specialist and subspecialists in diverse regions of the country (2,27). On the other hand, UV radiation constitutes the factor with least relevance given that in Peru, the majority of skin melanomas are not related to UV radiation (acral melanomas) (28).

Our data supports the need to strengthen the national plan for integral attention of Peruvian cancer with cost effective interventions such as vaccination against oncogenic infections such as HPV and HBV (29,30) that, while they are being considered, it is necessary to increase its coverage in the population. It is also necessary to implement practical strategies for the promotion and implementation of a healthy lifestyle in the population, particularly in factors related to avoiding tobacco use, physical activity, and healthy eating (8,27). On the other hand, we need to consider the possibility of an aggressive policy of access to drinking water to reduce the burden of stomach cancer attributable to *Helicobacter pylori* (31-34).

From a public health approach, the results of this study are relevant and serve as input for researchers, scholars, and decision makers in the development of programs and strategies, mainly in regions with greatest vulnerability, for an answer to cancer prevention and control. All with the objective of decreasing cancer incidence and mortality, as well as reducing costs for the state and health services.

A limitation to the PAF research model was the bias from the use of secondary information sources that could result in some level of underreporting. For this reason, we used estimates of cases and deaths from the IARC, based on information from population-based cancer registry from Peru, which could have been affected in a smaller extent by the underreporting in comparison to deaths obtained from the vital records.

Another limitation was the few number of studies that reported the PAF for modifiable risk factors for cancer deaths, published in the last decade (the majority focused on the PAF for new cancer cases), which could have affected the comparability of our results. Despite this, it was possible to obtain some studies from high-income countries, as well as one of Latin America, which allowed to contextualize the results obtained for Peru.

There are some differences in the considered risk factors, such as the study by Islami(9) for USA or that of Poirier(20) for Canada, which do not take into account infection by the Epstein Barr virus as a risk factor for Hodgkin's and non-Hodgkin's lymphoma, as opposed to this study which did include EBV. It is important to mention that prostate cancer was not included in our study since it does not have studies with sufficient level of evidence of modifiable risk factors for this cancer. It was not possible to obtain attributable fraction to ionizing radiation for lack of data in the exposed population in Peru. Finally, in this study we did not include exposure to firewood as a source of cooking fuel as a risk factor for lung cancer, despite that it is used as fuel in a fifth of Peruvian homes, which is because the majority of PAF studies for cancer did not consider it, and the comparability between this and other studies was prioritized.

The results obtained in this study should be interpreted with caution, considering the methodological particularities that exist among the published studies consulted, which have not necessarily been carried out in the same period of time, in the same age groups and cancer locations.

CONCLUSION

Prior to the COVID-19 pandemic, a proportion of 38.4% cancer cases and 43.2% of cancer deaths in Peru during 2018 were attributable to modifiable risk factors. Most of the preventable cancer cases and deaths are linked to oncogenic infections, primarily caused by HPV and Helicobacter pylori.

BIBLIOGRAPHIC REFERENCES

1. Piñeros M, Ramos W, Antoni S, Abriata G, Medina LE, Miranda JJ, et al. Cancer patterns, trends, and transitions in Peru: a regional perspective. Lancet Oncol. 2017;18(10):e573-e586. doi: 10.1016/S1470-2045(17)30377-7.
2. Ramos W, Guerrero N, Medina J, Guerrero P. Análisis de la situación del Cáncer en el Perú, 2018. Lima: Ministerio de Salud del Perú; 2022. Available at: https://www.dge.gob.pe/epipublic/uploads/asis/asis_2020_27_120833.pdf.
3. International Agency for Reasearch on Cancer. Cancer Today. Lyon; IARC; 2018. Available at: https://gco.iarc.fr/today/home.
4. Centro Nacional de Epidemiología, Prevención y Control de Enfermedades, Ministerio de Salud del Perú. Carga de Enfermedad en el Perú. Estimación de los años de vida saludable perdidos 2016. Lima: Ministerio de Salud del Perú; 2019. Available at: https://www.dge.gob.pe/portal/docs/tools/Cargaenfermedad2016.pdf.
5. Valdez W, Miranda J, Ramos W. State of the epidemiologic transition in Peru during 1990 and 2006. Rev peru epidemiol. 2011;15(3):1-5.
6. Ramos W, Venegas D, Honorio H, Pesantes J, Arrasco J, Yagui M. Non-communicable diseases: effect of major transitions and social determinants. Rev peru epidemiol. 2014;18 (S1):e06.
7. Centro Nacional de Epidemiología, Prevención y Control de Enfermedades, Ministerio de Salud del Perú. Análisis de Situación de Salud del Perú, 2021. Lima: CDC-MINSA; 2023.
8. De La Cruz-Vargas JA, Ramos W, Chanduví W, Espinoza R, Guerrero N, Loayza-Castro J, et al. Feasibility study to evaluate the proportion of cancer attributable

to modificable risk factors in Peru and Latin America. Rev. Fac. Med. Hum. 2020;20(1):114-22. doi: 10.25176/RFMH.v20i1.2657.
9. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(1):31-54.
10. Brenner DR, Friedenreich CM, Ruan Y, Poirier AE, Walter SD, King WD, et al. The burden of cancer attributable to modifiable risk factors in Canada: Methods overview. Prev Med. 2019;122:3-8.
11. Brown KF, Rumgay H, Dunlop C, Ryan M, Quartly F, Cox A, et al. The fraction of cancer attributable to modifiable risk factors in England, Wales, Scotland, Northern Ireland, and the United Kingdom in 2015. Br J Cancer. 2018;118(8):1130-41. doi: 10.1038/s41416-018-0029-6.
12. Islami F, Chen W, Yu XQ, Lortet-Tieulent J, Zheng R, Flanders WD, et al. Cancer deaths and cases attributable to lifestyle factors and infections in China, 2013. Ann Oncol. 2017;28(10):2567-2574. doi: 10.1093/annonc/mdx342.
13. Inoue M, Hirabayashi M, Abe SK, Katanoda K, Sawada N, Lin Y, et al. Burden of cancer attributable to modifiable factors in Japan in 2015. Glob Health Med. 2022;4(1):26-36. doi: 10.35772/ghm.2021.01037.
14. Kulhánová I, Znaor A, Shield KD, Arnold M, Vignat J, Charafeddine M, et al. Proportion of cancers attributable to major lifestyle and environmental risk factors in the Eastern Mediterranean region. Int J Cancer. 2020;146(3):646-56. doi: 10.1002/ijc.32284.
15. Azevedo e Silva G, de Moura L, Curado MP, Gomes FdS, Otero U, Rezende LFMd, et al. The Fraction of Cancer Attributable to Ways of Life, Infections, Occupation, and Environmental Agents in Brazil in 2020. PLoS One 2016;11(2): e0148761. doi:10.1371/journal.pone.0148761.
16. Pichon-Riviere A, Bardach A, Rodríguez Cairoli F, Casarini A, Espinola N, Perelli L, et al. Health, economic and social burden of tobacco in Latin America and the expected gains of fully implementing taxes, plain packaging, advertising bans and smoke-free environments control measures: a modelling study. Tob Control. 2023:tc-2022-057618. doi: 10.1136/tc-2022-057618.
17. Rezende LFM, Murata E, Giannichi B, Tomita LY, Wagner GA, Sanchez ZM, et al. Cancer cases and deaths attributable to lifestyle risk factors in Chile. BMC Cancer. 2020;20(1):693. doi: 10.1186/s12885-020-07187-4.
18. Parkin DM. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. Br. J. Cancer 2011;105(S2):S2–S5. doi: 10.1038/bjc.2011.474.
19. Whiteman DC, Webb PM, Green AC, Neale RE, Fritschi L, Bain CJ, et al. Cancers in Australia in 2010 attributable to modifiable factors: summary and conclusions. Aust N Z J Public Health. 2015;39(5):477-84. doi: 10.1111/1753-6405.12471.
20. Poirier AE, Ruan Y, Volesky KD, King WD, O'Sullivan DE, Gogna P, et al. The current and future burden of cancer attributable to modifiable risk factors in Canada: Summary of results. Prev Med. 2019;122:140-147. doi: 10.1016/j.ypmed.2019.04.007.

21. Feng RM, Zong YN, Cao SM, Xu RH. Current cancer situation in China: good or bad news from the 2018 Global Cancer Statistics? Cancer Commun (Lond). 2019;39(1):22. doi: 10.1186/s40880-019-0368-6.
22. Bygbjerg IC. Double burden of noncommunicable and infectious diseases in developing countries. Science. 2012;337(6101):1499-501. doi: 10.1126/science.1223466.
23. Boutayeb A. The double burden of communicable and non-communicable diseases in developing countries. Trans R Soc Trop Med Hyg. 2006;100(3):191-9. doi: 10.1016/j.trstmh.2005.07.021.
24. Thun MJ, DeLancey JO, Center MM, Jemal A, Ward EM. The global burden of cancer: priorities for prevention. Carcinogenesis. 2010;31(1):100-10. doi: 10.1093/carcin/bgp263.
25. Szot Meza J. Demographic-epidemiologic transition in Chile, 1960-2001. Rev Esp Salud Publica. 2003;77(5):605-13.
26. Rezende LFM, Murata E, Giannichi B, Tomita LY, Wagner GA, Sanchez ZM, et al. Cancer cases and deaths attributable to lifestyle risk factors in Chile. BMC Cancer. 2020;20(1):693. doi: 10.1186/s12885-020-07187-4.
27. Torres-Roman JS, Valcarcel B, Martinez-Herrera JF, Bazalar-Palacios J, La Vecchia C, Raez LE. Mortality Trends for Lung Cancer and Smoking Prevalence In Peru. Asian Pac J Cancer Prev. 2022;23(2):435-443. doi: 10.31557/APJCP.2022.23.2.435.
28. Basurto-Lozada P, Molina-Aguilar C, Castaneda-Garcia C, Vázquez-Cruz ME, Garcia-Salinas OI, Álvarez-Cano A, et al. Acral lentiginous melanoma: Basic facts, biological characteristics and research perspectives of an understudied disease. Pigment Cell Melanoma Res. 2021;34(1):59-71. doi: 10.1111/pcmr.12885.
29. Palladini A, Landuzzi L, Lollini PL, Nanni P. Cancer immunoprevention: from mice to early clinical trials. BMC Immunol. 2018;19(1):16. doi: 10.1186/s12865-018-0253-0.
30. Lollini PL, Nicoletti G, Landuzzi L, Cavallo F, Forni G, De Giovanni C, et al. Vaccines and other immunological approaches for cancer immunoprevention. Curr Drug Targets. 2011;12(13):1957-73. doi: 10.2174/138945011798184146.
31. Castillo M, Bernabe L, Castaneda CA, Chavez I, Ruiz E, Barreda F, et al. Helicobacter Pylori Detected in Tap Water of Peruvian Patients with Gastric Cancer. Asian Pac J Cancer Prev. 2019;20(11):3193-6. doi: 10.31557/APJCP.2019.20.11.3193.
32. Eichelberger L, Murphy G, Etemadi A, Abnet CC, Islami F, Shakeri R, et al. Risk of gastric cancer by water source: evidence from the Golestan case-control study. PLoS One. 2015;10(5):e0128491. doi: 10.1371/journal.pone.0128491.
33. Klein PD, Graham DY, Gaillour A, Opekun AR, Smith EO. Water source as risk factor for Helicobacter pylori infection in Peruvian children. Gastrointestinal Physiology Working Group. Lancet. 1991;337(8756):1503–6.
34. Ranjbar R, Khamesipour F, Jonaidi-Jafari N, Rahimi E. Helicobacter pylori isolated from Iranian drinking water: vacA, cagA, iceA, oipA and babA2 genotype status

and antimicrobial resistance properties. FEBS Open Bio. 2016;6(5):433-41. doi: 10.1002/2211-5463.12054.