STATE-OF-THE-ART REVIEW

Tobacco, Alcohol, and Cancer in Low and High Income Countries

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ABSTRACT

Background: Tobacco use is a well-established risk factor for cancers of the lung, head and neck, nasopharynx, esophagus, stomach, pancreas, liver, kidney, bladder, leukemia, and cervix. Alcohol consumption is a well-established risk factor for cancers of the head and neck, esophagus, liver, colorectum, and breast for women only. The majority of studies on tobacco and alcohol were conducted in high-income countries (HICs).

Objective: The aim of this review was to assess the extent of tobacco and alcohol usage and to compare the cancer burden between low- and high-income regions.

Findings: Overall, tobacco smoking is estimated to account for 21% of cancer deaths worldwide (29% in HICs and 18% in low- and middle-income countries [LMICs]). Alcohol consumption is estimated to account for 5% of all cancer deaths worldwide, with similar proportions in LMICs. Cancers of the breast, lung, stomach, liver, head and neck, esophagus, cervix, and nasopharynx, and leukemia are already diagnosed in greater numbers each year in less-developed countries compared with more developed countries. The future burden of tobacco- and alcohol-related cancers on less-developed regions is expected to increase greatly based on demographic effects, with a 69.9% increase in tobacco-related cancer cases and a 68% increase in cancers related to alcohol. Although HICs have experienced a decrease in tobacco prevalence in recent decades, LMICs are still in the early stages of the tobacco epidemic.

Conclusion: Tobacco use and alcohol consumption will clearly remain important risk factors that must be targeted with public health efforts particularly in LMICs.

Key Words: alcohol, cancer, low- and middle-income countries, tobacco

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INTRODUCTION

The majority of studies on tobacco and alcohol were conducted in high-income countries (HICs). The aim of this review was to assess the extent of tobacco and alcohol usage and to compare the cancer burden between low- and high-income regions.

TOBACCO

Tobacco use is a well-established risk factor for cancers of the lung, head and neck (oral cavity, pharynx, larynx), nasopharynx, esophagus, stomach, pancreas, liver, kidney, bladder, and cervix, and leukemia.[1] Each year worldwide, approximately 6.7 million smoking-related cancer cases are diagnosed (Table 1).[2] Approximately 2.3 million smoking-related cancer cases are diagnosed in developed countries and approximately 4.3 million are diagnosed in less-developed countries. The number of lung, stomach, liver, head and neck, esophagus, cervical, and nasopharyngeal cancer and leukemia cases that are diagnosed each year in less-developed countries is greater than in more developed countries (Fig. 1). Cigarette smoking confers a 15- to 30-fold increase of lung cancer, a 10-fold increase of laryngeal cancer, a 4- to 5-fold increase of both oral cavity and oropharyngeal cancers, a 1.5- to 5-fold increase of esophageal cancer, a 2- to 4-fold increase of pancreatic cancer, and a 1.5 to 2.5-fold increase of nasopharyngeal, stomach, liver, kidney, cervix cancers, and leukemia.[3]

In HICs, tobacco-use prevalence has been decreasing over the past several decades due to anti-smoking campaigns (Fig. 2A). The tobacco epidemic has been described in 4 stages: Stage 1 reflects the beginning of the epidemic with cigarette smoking prevalence less than 20%. Stage 2 shows an increase in the prevalence to around 40% to 80%. Stage 3 is characterized by a plateau and the beginnings of a decline in prevalence. Stage 4

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shows a final decline in prevalence.[4] Thus, HICs are in stage 4 or the last stage for both men and women, with an overall tobacco prevalence of 30% among men and 19% among women.[4] In the United States, the tobacco prevalence among men decreased from 52% in 1960 to 22% in 2010. Among American women, the tobacco prevalence decreased from 34% in 1960 to 17% in 2010.[4] The major concern is that low- and middle-income countries (LMICs) are in stages 1 and 2 of the tobacco epidemic, respectively, with prevalence expected to continue to increase. In middle-income countries, the overall male prevalence of tobacco smoking is 34% and the overall female prevalence is 5%.[4] In low-income countries, the prevalence of tobacco smoking is approximately 21% and 3% for men and women, respectively.[4]

Overall, tobacco smoking is estimated to account for 21% of cancer deaths worldwide (29% in HICs and 18% in LMICs).[5] In terms of cancer deaths worldwide, tobacco smoking accounts for 42% (37% in LMICs/71% in HICs) of oral and oropharyngeal cancer, 42% (37%/71%) of esophageal cancer, 13% (11%/25%) of stomach cancer, 14% (11%/29%) of liver cancer, 22% (15%/30%) of pancreatic cancer, 70% (60%/86%) of trachea, bronchus, and lung cancers, 2% (2%/11%) of cervical cancer, 28% (21%/41%) of bladder cancer, 9% (6%/17%) of leukemia, 21% (18%/29%) of all cancers.[5] Thus, as a large portion of these cancers can be attributed to tobacco use, it is the most preventable risk factor for smoking-related cancer deaths. Based on a study from the United Kingdom, the attributable fractions for tobacco on cancer incidence was 19% overall, accounting for 23% among men and 16% among women.[6]

Associations with smokeless tobacco are suggested for cancers of the oral cavity, esophagus, and the pancreas.[1] The attributable fraction of tobacco-related cancer incidence for smokeless tobacco varies considerably by region and sex. Oral cavity cancer cases that are attributed to smokeless tobacco in men are estimated to be 1.6% in Canada, 6.6% in the United States, 52.5% in India, and 68.2% in Sudan.[7] Among women, approximately 13.6% of oral cavity cancer cases in Sudan and 51.6% of cases in India are attributed to smokeless tobacco.[7] Esophageal cancer cases that are attributed to smokeless tobacco are estimated to be 2.1% in Denmark, 3.5% in Norway, and 10.7% in Sweden among men.[7] Among women, approximately 0.6% of esophageal cancer cases in Sweden are attributed to smokeless tobacco.[7] Pancreatic cancer cases that are attributed to smokeless tobacco are estimated to be 2.7% in Denmark, 4.6% in Norway, and 13.8% in Sweden among men.[7] Among women, approximately 0.8% of pancreatic cancer cases in Sweden are attributed to smokeless tobacco.[7]

ALCOHOL

Cancers of the head and neck, esophagus, liver, colorectum, and breast for women only are considered to be alcohol-related cancers.[1] Each year worldwide, approximately 4.6 million alcohol-related cancer cases are diagnosed (Table 2).[2] In developed countries, approximately 1.9 million alcohol-related cancer cases are estimated, whereas in less-developed countries, 2.8 million alcohol-related cancer cases are estimated. All of the alcohol-related cancers other than colorectal cancers are diagnosed in greater numbers in less-developed countries than in more developed countries (Fig. 1).

The prevalence of alcohol consumption varies greatly by geographic location and sex.[8] In some Eastern European countries, the amount of alcohol consumption is around 2.5 times more than the global average of 6.2 L of pure alcohol per year. In general, the lowest consumption of alcohol is in Africa and the Eastern Mediterranean (Fig. 2B). The proportions consuming alcohol are 44% worldwide (average 14 g/d), 55% among men (average 21 g/d), and 34% in women (average 6 g/d). By region, the

Table 1. Incidence and Mortality Numbers and Age-Standardized Rates (ASR/100,000) for Tobacco-related Cancers*[,2]

	Incidence		Mortality	
	Men	Women	Men	Women
Worldwide				
Number	4,186,000	2,499,000	3,193,000	1,811,000
ASR	115.7	60.7	87.2	41.9
More developed countries				
Number	1,490,000	848,000	980,000	568,000
ASR	139.8	66.1	86.7	37.4
Less-developed countries				
Number	2,697,000	1,651,000	2,212,000	1,242,000
ASR	105.6	58.5	87.0	43.7

*Tobacco-related cancers included cancers of the lung, head and neck, nasopharynx, esophagus, stomach, pancreas, liver, kidney, bladder, and cervix, and leukemia. These are the total number of tobacco-related cancers, not the estimate of cancer cases attributed to tobacco.

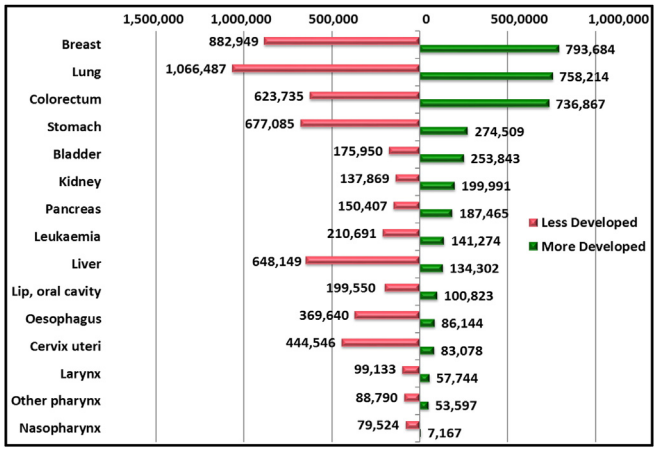

Figure 1. Tobacco- and alcohol-related cancer cases in less-developed versus more developed countries.[2]

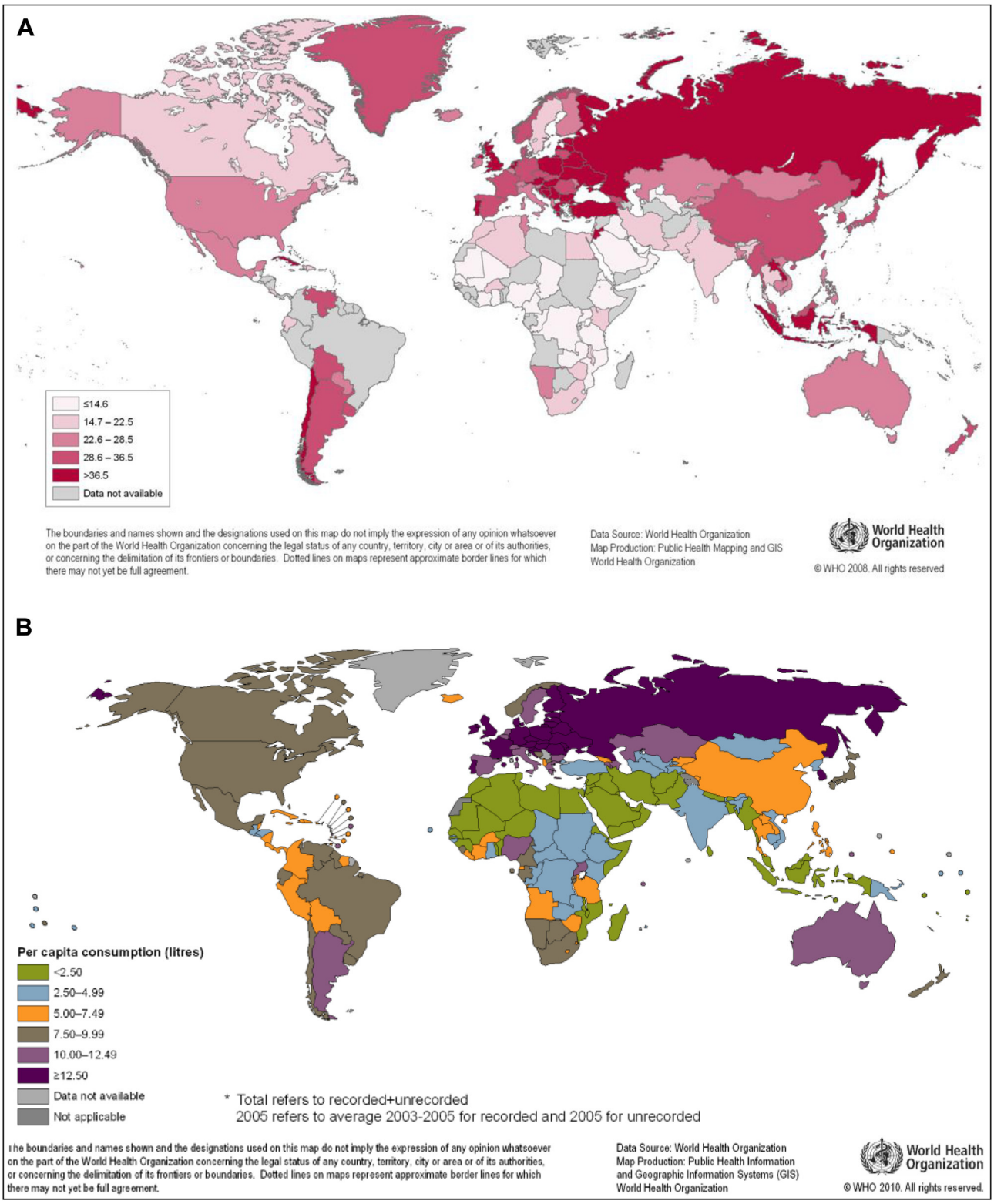

Figure 2. **(A)** Proportion of tobacco use among adults in 2005 **(B)** Total adult per capita consumption of pure alcohol (in liters) in 2005 (Reproduced, with the permission of the publisher, from the Global Health Observatory Map Gallery, World Health Organization, 2008(A)/2010(B); http://gamapserver.who.int/mapLibrary/, accessed January 23, 2014).

proportions of the population consuming alcohol are 36% in LMICs of Africa (average 16 g/d), 12% in LMICs of Southeast Asia (average 4 g/d), 58% in HICs of the Americas (average 21 g/d), 69% in LMICs in the Americas (average 18 g/d), 10% in HICs of Eastern Mediterranean (average 2 g/d), 6% in LMICs of Eastern Mediterranean (average 1 g/d), 83% in HICs of Europe (average 27 g/d), 66% in LMICs of Europe (average 25 g/d), 73% in HICs

of Western Pacific (average 19 g/d), and 56% in LMICs of Western Pacific (average 15 g/d).[8]

Overall, alcohol consumption is estimated to account for 5% of all cancer deaths worldwide, with similar proportions in LMICs.[5] Worldwide in terms of cancer deaths, alcohol consumption accounts for 16% (14% in LMICs/33% in HICs) of oral and oropharyngeal cancer, 26% (24%/41%) of esophageal cancer, 25% (23%/32%) of liver cancer, 5% (4%/9%) of breast cancer, 3% (5%/4%) of all cancers.[5]

The alcohol-attributable fractions of incident cancer cases are 30.4% (38.8% in men/10.9% in women) for oral cavity and pharynx, 18.5% (25%/4.5%) for esophagus, 3.2% (4.6%/1.7%) for colon and rectum, 9.4% (12.2%/2.9%) for liver, 23% (25.3%/7.3%) for larynx, 4.5% for female breast cancer.[9] Alcohol consumption accounts for a large proportion of cancer in Europe, particularly in Central and Eastern Europe, America, East Asia, Oceania, and sub-Saharan Africa, whereas it accounts for a smaller proportion of cancer in Northern Africa, and Western and Southern Asia.[9]

TOBACCO AND ALCOHOL

Cancers of the oral cavity, pharynx, larynx, esophagus, and liver are both tobacco- and alcohol-related,[1] with 1.9 million estimated cases (439,000 in more developed regions; 1.5 million in less-developed regions) and 1.5 million deaths (282,000 in more developed regions; 1.2 million in less-developed regions).[2]

An interaction between tobacco and alcohol is well established for head and neck cancers.[10] An analysis of 11,211 head and neck cancer cases and 16,152 controls by the International Head and Neck Cancer Epidemiology (INHANCE) Consortium demonstrated an interaction between tobacco and alcohol on a multiplicative scale.[10] The multiplicative interaction parameter for oral cavity cancer was 3.08 (95% confidence interval [CI], 1.82-5.23), suggesting that the interaction observed was almost 3-fold greater than the product of the individual effects of tobacco and alcohol. Similarly, for pharyngeal cancer, an analysis of 4038 cases (including both oro- and hypopharyngeal cancer cases) and 16,152 controls showed that there was an interaction on the multiplicative scale between tobacco and alcohol, with a multiplicative interaction parameter of 1.90 (95% CI, 1.41-2.56).[10] Finally, for laryngeal cancer, an analysis of 2959 cases and 13,130 controls suggested a multiplicative interaction parameter of 1.62 (95% CI, 0.85-3.09).[10] The assessment of attributable fraction for tobacco and alcohol combined showed that most cases would be attributed to tobacco alone or a combination of tobacco and alcohol,[10] whereas very few cases would be attributed to alcohol alone. Based on the INHANCE data, including mainly the United States and most developed countries, the attributable fraction

Table 2. Incidence and Mortality Numbers and Age-Standardized Rates (ASR/100,000) for Alcohol-related Cancers*[2]

	Incidence		Mortality	
	Men	Women	Men	Women
Worldwide				
Number	2,137,000	2,825,000	1,460,000	1,277,000
ASR	59.2	70.4	39.9	29.9
More developed countries				
Number	727,000	1,243,000	382,000	431,000
ASR	68.8	105.9	33.9	28.9
Less-developed countries				
Number	1,410,000	1,582,000	1,079,000	846,000
ASR	54.8	56.2	42.1	29.8

*Alcohol-related cancers included cancers of the head and neck, esophagus, liver, colorectum, and breast for female only. These are the total number of alcohol-related cancers, not the estimate of cancers attributed to alcohol.

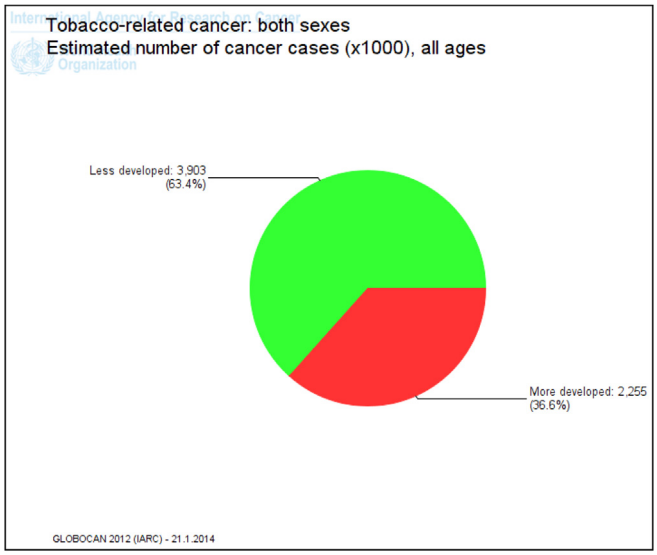

Figure 3. Estimated number of tobacco-related cancer cases (in 1000s).[2]

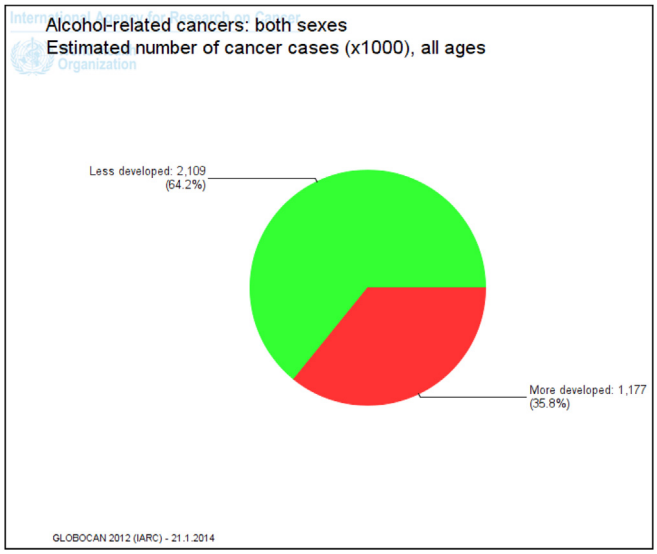

Figure 4. Estimated number of alcohol-related cancer cases (in 1000s).[2]

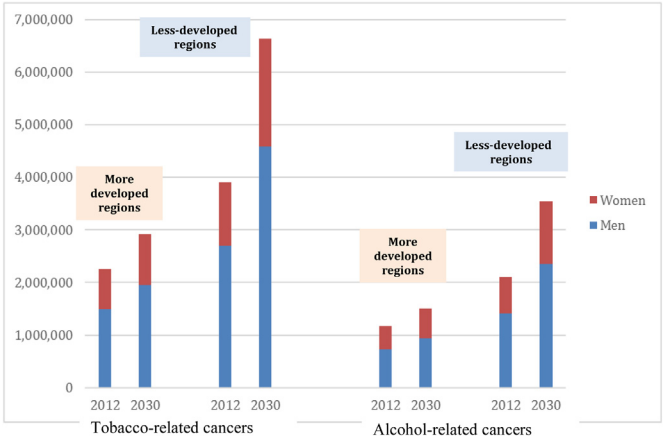

Figure 5. Projections of tobacco- and alcohol-related cancer cases for 2030 for more developed versus less-developed regions.[2]

for head and neck cancers by alcohol or tobacco combined was estimated to be 72%.[10]

Esophageal and liver cancers are also tobacco- and alcohol-related. A positive joint effect of tobacco and alcohol has been suggested with departure from multiplicatively of the individual effects of tobacco and alcohol on esophageal cancer.[1] Such an interaction was found to be stronger for squamous cell carcinoma of the esophagus. However, interactions between tobacco and alcohol for liver cancer have not been extensively investigated. Alcohol has been considered a confounding factor in examining the association between tobacco smoking and liver cancer.[1]

SUMMARY

Cancer is already a major burden in LMICs (Figs. 3 and 4) and the burden is expected to increase in the next decades due to the growing population, adoption of health behaviors of HICs, and decreasing competing risk for infectious diseases.[11] The future burden of tobacco- and alcohol-related cancers on less-developed regions is expected to increase greatly based on demographic effects alone, with a 69.9% increase (from 3,903,275 in 2012 to 6,632,135 new cases in 2030) in tobacco-related cancer cases and a 68% increase (from 2,108,521 in 2012 to 3,542,299 in 2030) in alcohol-related cases (Fig. 5). On the other hand, the future burden increases to a lesser extent for the more developed regions, with a 29.3% increase (from 2,255,073 in 2012 to 2,916,117 in 2030) in tobacco-related cancer cases and a 28.3% increase (from 1,176,644 in 2012 to 1,510,144 in 2030) in alcohol-related cases.[2] The projected number of tobacco-related cancer cases in less-developed countries for the year 2030 (6,632,135 cases) is expected to be much greater than the projected number of alcohol-related cases (3,542,299 cases). If the tobacco epidemic in the less-developed countries is further accounted for in addition to the demographic changes in the projections, the case numbers would be a heavy burden.[12] The countries with the highest tobacco-smoking prevalence among men (Table 3) also represent chiefly LMICs. The projected number of cancer cases in these countries, based on demographic effects, again shows large increases, although they do not yet have the highest incidence rates worldwide. Alarming increases in tobacco-related cancer cases are expected for Papua New Guinea (78.2%), Tunisia (78.3%), China (70.2%), and Indonesia (69.9%).[2]

The highest tobacco-related cancer incidence rates are observed in Mongolia (160/100,000), Hungary (130.9/100,000), Republic of Korea (127.4/100,000), and China (113.1/100,000).[2] Thus, the countries with the highest

Table 3. Tobacco-related Cancer Incidence Rates and Case Numbers for Countries with the Top 10 Highest Male Tobacco-smoking Prevalence Worldwide

	Currently Smoking Any Tobacco Product*		Tobacco-related† Cancer Incidence Rates (per 100,000)	Tobacco-related Cancer Incident Cases		% Change from
Country	Male	Female	in 2012‡	2012	2030 Projection	2012 to 2030
Greece	63	41.4	70.0	18,387	22,678	23.3
Albania	60.1	19.4	85.4	3,536	5,461	54.4
Russian Federation	59.4	23.9	82.3	188,969	205,554	8.8
Papua New Guinea	57.7	30.8	65.6	2,739	4,881	78.2
Indonesia	61.3	3.7	50.1	109,996	186,908	69.9
Georgia	56.6	5.7	55.2	4,002	4,465	11.6
Tunisia	52.7	3.6	46.3	5,053	9,007	78.3
Armenia	50.9	2.1	103.4	4,584	5,854	27.7
China	50.4	2.1	113.1	2,010,520	3,421,773	70.2
Latvia	50.1	22.3	93.2	3,976	3,719	−6.5

*WHO Tobacco Atlas 2012.[13]
†Smoking-related cancers include lung, oral cavity, nasopharynx, oropharynx, hypopharynx, larynx, esophagus, stomach, pancreas, liver, kidney, bladder, leukemia (but NOT cervix).
‡Age-standardized to the world population.[2]

prevalence of smoking observed in Table 3 are not consistently those with the highest tobacco-related cancer incidence rates; however, there is likely a time lag for the effect of the tobacco epidemic to be observed in cancer incidence rates. This observation also highlights that the tobacco-related cancer etiology is complex and multifactorial with other important risk factors such as alcohol consumption, HPV, and chewing other products such as betel quid and areca nut (with or without tobacco). The high incidence rates observed in Eastern Asia are thought to be due to the combined high smoking prevalence and alcohol consumption among men.

CONCLUSIONS

Although HICs have experienced a decrease in tobacco prevalence in recent decades, LMICs are still in the early stages of the tobacco epidemic. The future burden of expected smoking- and alcohol-related cancer cases was already expected to be large due to demographic effects, but with the tobacco epidemic the burden will be very heavy in LMICs. Tobacco use and alcohol consumption will clearly remain important risk factors that must be targeted with public health efforts.

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