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Preventable liver cancer cases through reduced exposure to overweight/obesity, alcohol consumption, tobacco use, and hepatitis B infection.

Casos de cáncer de hígado prevenibles mediante la reducción de la exposición a sobrepeso/obesidad, consumo de alcohol, uso de tabaco e infección de hepatitis B

Gustavo Díaz [1*], Miguel Torres [2], Esther de Vries [3], Sandra Perdomo [4], Martha Rojas [5], Oscar Herrán [6], Maria-Paula Rugeles[7], Felipe Ballesteros[8], Maria-Paula Belalcazar [9].

1. Universidad El Bosque, Faculty of Medicine. Bogotá, Colombia. ORCID 0000-0002-9216-7873
2. National Institute of Cancer, Clinical Research Group. Bogotá, Colombia
3. Pontificia Universidad Javeriana, Faculty of Medicine, Department of Clinical Epidemiology and Biostatistics. Bogotá, Colombia. ORCID 0000-0002-5560-2258
4. International Agency for Research on Cancer (IARC/WHO), Genomic Epidemiology Branch. Lyon, France
5. National Institute of Cancer, Research Support and Follow-up Group. Bogotá, Colombia
6. Universidad Industrial de Santander. Bucaramanga, Colombia
7. Universidad El Bosque, Faculty of Medicine. Bogotá, Colombia

*Corresponding author: diazgustavo@unbosque.edu.co

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ABSTRACT

Introduction: Liver cancer is among the most prevalent cancers globally and in Colombia. Key modifiable risk factors include overweight/obesity, excessive alcohol consumption, tobacco use, and hepatitis B virus (HBV) infection. This study aimed to estimate the potential impact of reducing exposure to these modifiable risk factors on liver cancer incidence in Colombia from 2016 to 2050. **Methods**: A population-based microsimulation model was implemented using the Prevent V3.1 software. The model integrates age- and sex-specific liver cancer incidence rates, latency and lag times, risk factor prevalence (with and without interventions), relative risks, and national demographic projections. **Results**: A 10% reduction in the prevalence of risk factors could prevent up to 728 liver cancer cases. Complete elimination of exposure could avert up to 8,648 new cases during the study period. The population attributable fractions (PAF) were 1.09% for HBV infection, 1.90% for alcohol consumption, 6.14% for tobacco use, and 14.52% for overweight/obesity. **Conclusions**: Reducing population-level exposure to overweight/obesity, alcohol consumption, tobacco, and HBV infection could substantially decrease the future burden of liver cancer incidence in Colombia. These projections support prioritizing risk factor reduction in national cancer prevention and public health strategies.

Key words: liver cancer; tobacco; overweight; obesity; hepatitis B infection; alcohol intake.

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RESUMEN

Introducción: El cáncer de hígado es uno de los cánceres más prevalentes a nivel mundial y en Colombia. Entre los principales factores de riesgo modificables se encuentran el sobrepeso/obesidad, el consumo excesivo de alcohol, el tabaquismo y la infección por el virus de la hepatitis B (VHB). Este estudio tuvo como objetivo estimar el impacto potencial de la reducción de la exposición a estos factores de riesgo modificables en la incidencia de cáncer de hígado en Colombia entre 2016 y 2050. **Métodos**: Se implementó un modelo de microsimulación poblacional utilizando el software Prevent V3.1. El modelo integra las tasas de incidencia específicas por edad y sexo, los tiempos de latencia y retardo, la prevalencia de factores de riesgo (con y sin intervenciones), los riesgos relativos y las proyecciones demográficas. **Resultados**: Una reducción del 10 % en la prevalencia de factores de riesgo podría prevenir hasta 728 casos de cáncer de hígado. La eliminación completa de la exposición podría evitar hasta 8648 nuevos casos durante el período de estudio. Las fracciones atribuibles poblacionales fueron del 1,09 % para la hepatitis B, del 1,90 % para el alcohol, del 6,14 % para el tabaco y del 14,52 % para el sobrepeso/obesidad. **Discusión**: Reducir la exposición poblacional al tabaco, el sobrepeso/obesidad, la hepatitis B y el alcohol podría reducir sustancialmente la incidencia futura de cáncer de hígado en Colombia. Estos hallazgos constituyen una valiosa fuente de información para priorizar las estrategias de prevención en las políticas nacionales de salud pública.

Palabras clave: cáncer de hígado; tabaco; sobrepeso; obesidad; infección por hepatitis B; consumo de alcohol.

KEY MESSAGES

- Microsimulation modeling projects over 59,000 new liver cancer cases in Colombia by 2050 if current exposure to key risk factors remains unchanged.
- The four main modifiable risk factors for liver cancer in Colombia are high BMI (PAF: 14.52%), tobacco use (PAF: 6.14%), alcohol consumption (PAF: 1.9%), and hepatitis B infection (PAF: 1.09%).
- A 10% reduction in the prevalence of these risk factors could prevent up to 728 cases, while their complete elimination could avoid up to 8,648 new cases by 2050.
- This study supports prioritizing evidence-based public health interventions targeting these four risk factors as part of Colombia's national liver cancer prevention strategy.

INTRODUCTION

In 2022, an estimated 865.269 new cases of liver cancer were reported globally. Liver cancer ranks as the sixth most frequently diagnosed and the third leading cause of cancer-related mortality worldwide [1]. Between 2010 and 2021, incident cases increased by 26%, with the highest prevalence observed in the America continent (51%). The crude global mortality rate reached 6.13 per 100.000 population, disproportionately affecting men and underscoring a high case- fatality rate [2]. Temporal trends indicate a continuous rise in both incidence and mortality rates worldwide [2,3]. In Colombia, the age-standardized rate was 3.5 cases per 100.000 person-years, with projections suggesting a potential increase of up 55% annually between 2020 and 2040 [3].

Liver cancer development is influenced by both non-modifiable and modifiable risk factors. Non-modifiable factors include hepatitis C virus infection, age, sex, and rare genetic conditions such as hemochromatosis, primary cirrhosis of the bile ducts, Nonalcoholic fatty liver disease, and alpha 1 antitrypsin deficiency [4,5]. Modifiable factors encompass hepatitis B virus infection, obesity, physical inactivity, tobacco use, diabetes mellitus, drug use, metabolic syndrome, hypercaloric diets, alcoholism, and exposure to foodborne mycotoxins such as aflatoxin B1 [4–6].

The evidence suggest that healthy lifestyle practices can reduce the incidence of liver cancer [7]. As a result, public health recommendations have emphasized mitigating modifiable risk factors, particularly alcohol intake, overweight, obesity, and high cholesterol, have been formulated [8] . Furthermore, modeling studies have demonstrated a beneficial impact of reducing these risk factors on the occurrence of various chronic diseases [7,9].

Simulation modelling is a valuable tool for informing public health decision-making, enabling policymakers and territorial health entities to evaluated alternative scenarios based on scientific evidence. These simulations can support efforts to enhance patient safety and improve population health outcomes. This study aimed to estimate the potential impact of reducing four key modifiable risk factors -tobacco use, overweight/obesity, hepatitis B infection, and alcohol consumption- on the incidence of liver cancer in Colombia from 2016 to 2050.

MATERIAL & METHODS

This was a static microsimulation modeling study conducted using Prevent software V3.1, a tool previously applied in Europe and Colombia [7,9,10]. The specific data inputs used in the microsimulation are detailed below.

Baseline prevalence and risk functions

The four modifiable risk factors analyzed were tobacco use, overweight/obesity, hepatitis B virus infection, and alcohol intake. These factors were selected based on the availability of national data. Prevent software requires population-based, age- and sex-specific prevalence data for each risk factor, along with incidence rates, as essential model inputs. Table 1 shows international recommendations for the four risk factors studied, their operational definitions, and the relative risks for exposure to these risk factors in terms of liver cancer risk.

Table 1. Summary of the reference values and relative risks (RRs) used in the microsimulation models

Exposure	International recommendation	Operationalization	Risks for liver cancer analyzed in Prevent
Hepatitis B	No infection	Dichotomous (infected/not infected)	RR 1,36 IC95% 1,17–1,58 [11]
Alcohol	No alcohol consumption	Consumptions during the past month. Dichotomous (Yes/no)	Males: RR 1,03 CI95% 1,01–1,05 Female: RR 1,19 CI95%1,04–1,35 [12]
Tobacco consumption	No tobacco consumption	The current smoker. Dichotomous (Yes/no)	Males: RR 1,61 CI95% 1,38–1,89 Females: RR 1,86 CI95%1,33–2,6 [13]
BMI	Healthy weight	Continuous variable (kg/m^2)	Overweight (point estimate 25 kg/m^2): RR 1,02 CI95% 1,02–1,03 Obesity (point estimate 30 kg/m$^{2)}$: RR 1,35 CI95% 1,24–1,47 [14]

BMI: Body mass index; CI: confidence interval; Kg: kilograms; RR: Relative risk.

Prevalence and mean values for each risk factors were derived from national population survey (Table 2 and 3). In the absence of data, the last prevalence/mean value was repeated in the remaining categories.

As no national studies have evaluated the association between these risk factors and liver cancer in Colombia, the relative risks used in the model were extracted from a literature review. Eligible studies included those with exposure categories comparable to those reported in Colombian population surveys. Two researchers independently assessed study quality using an adapted AMSTAR tool for meta-analyses. Final inclusion was based on quality scores, with additional weighting given to studies with larger sample sizes and those including Colombian or Latin American populations. Ultimately, relative risk estimates from four meta-analyses were selected (Table 1).

Age- and sex-specific incidence rates and population projections

National liver cancer incidence rates, stratified by age and sex, were estimated using data extrapolated from four high-quality, population-based cancer registries in Colombia (Cali, Bucaramanga Metropolitan Area, Manizales, and Pasto), as published in Volumes X and XI of Cancer Incidence in Five Continents, along with departmental-level mortality data. Age-standardized incidence rates, adjusted using the SEGI world standard population, were 12.1 per 100,000 for males and 12.4 per 100,000 for females [18].

The latency and lag times

Latency (LAT) refers to the period following a change in exposure prevalence during which no measurable change in relative risk (RR) is observed. Lag time (LAG) is defined as the interval from the end of the LAT period until the full effect of the exposure change is reflected in the RR. These parameters were incorporated into the model as follows: for alcohol consumption, a LAT of 2 years and a LAG of 10 years were assumed; for BMI, 3 and 20 years, respectively; and for tobacco use, 5 and 10 years.

Table 2. Summary of the prevalence and averages used in the microsimulation models

	Prevalence of alcohol consumption				Prevalence of hepatitis B [15]				Prevalence of Tobacco consumption			Mean BMI (kg/m^2) (provide SD)			
	UNDOC 2013 [16]		ENSIN2015 [17]		1990		2005		UNDOC 2013 [16]			ENSIN 2005 [17]		ENSIN 2010 [17]	
Age	Men	women	Men	Women	Men	Women	Men	WOMEN	Men	Women	Age	Men	Women	Men	Women
0–4	0,00	0,00	0	0	0,05	0,04	0,05	0,05	0,00	0,00	0–4	15,97	15,76	16,44	16,09
5–9	0,00	0,00	0	0	0,05	0,04	0,05	0,05	0,00	0,00	5–17	17,58	18,37	17,74	18,26
10–14	0,00	0,00	0	0	0,04	0,04	0,05	0,04	0,02	0,01	18–22	21,90	22,77	22,46	22,96
15–19	0,44	0,28	0,37	0,26	0,04	0,40	0,04	0,04	0,16	0,04	23–27	23,85	23,82	24,29	24,41
20–24	0,62	0,37	0,62	0,35	0,00	0,04	0,04	0,04	0,27	0,07	28–32	24,61	25,04	25,50	25,82
25–29	0,62	0,38	0,67	0,32	0,04	0,04	0,04	0,04	0,26	0,10	33–37	25,45	25,97	25,83	26,41
30–34	0,54	0,29	0,64	0,36	0,04	0,04	0,04	0,04	0,22	0,07	38–42	25,81	26,81	26,22	26,83
35–39	0,49	0,31	0,58	0,26	0,04	0,03	0,04	0,03	0,17	0,07	43–49	26,01	27,56	25,98	27,70
40–44	0,48	0,25	0,61	0,31	0,04	0,03	0,04	0,03	0,16	0,08	50–64	25,67	28,03	25,62	27,82
45–49	0,46	0,24	0,51	0,24	0,03	0,03	0,04	0,03	0,17	0,10					
50–54	0,40	0,18	0,51	0,18	0,03	0,03	0,04	0,03	0,20	0,12					
55–59	0,39	0,15	0,42	0,09	0,03	0,03	0,03	0,03	0,20	0,10					
60–64	0,29	0,11	0,34	0,12	0,03	0,03	0,03	0,03	0,18	0,07					
65 –69	0,56	0,49	0,34	0,12	0,03	0,02	0,03	0,03	0,18	0,07					
70–74	0,56	0,49	0,34	0,12	0,03	0,02	0,03	0,03	0,18	0,07					
75–79	0,56	0,49	0,34	0,12	0,02	0,02	0,03	0,03	0,18	0,07					
80–más	0,56	0,49	0,34	0,12	0,02	0,02	0,03	0,03	0,18	0,07					

Table 3. Summary of liver cancer incidence used in the microsimulation [18]

Age	Incidence[1]	
	male	**female**
0–14	0,3	0.0
15–44	0,3	0.4
45–54	2,1	2.4
55–64	7,7	5.8
65 +	24,4	24.5

[1] Rates — 100000 inhabitants

The baseline population structure for 2016 was obtained from the Colombian National Statistics Department. Demographic projections, including population growth and aging through 2050, were based on estimates from the Economic Commission for Latin America and the Caribbean [19].

Modeled scenarios

Following approaches used in previous modeling studies [7,9], three scenarios were simulated:

- Model 1 (reference scenario): The prevalence of each risk factor followed the observed trends without intervention.
- Model 2 (intervention scenario): A gradual 10% reduction in the prevalence of all four risk factors was modeled over a 10-year period starting in 2017. This reduction was considered a realistic public health target, reflecting the likely impact of feasible interventions [7,9]. Age- and sex-specific adjustments were applied annually. Prevent then estimated the change in disease occurrence, assuming demographic trends remained constant.
- Model 3 (counterfactual scenario): A theoretical scenario in which exposure to all four risk factors was entirely eliminated (i.e., no HBV infection, no tobacco or alcohol use, and normal BMI across the population). This scenario was used to estimate the population attributable fraction (PAF) of each risk factor for liver cancer in Colombia.

RESULTS

If the prevalence of the four modifiable risk factors -tobacco use, overweight/obesity, hepatitis B infection, and alcohol consumption- remain unchanged (Model 1), approximately 59000 new cases of liver cancer are projected to occur in Colombia between 2016 and 2050, with a disproportionately higher burden observed among women (Table 4).

Table 4. Modeling of baseline tendency and reduction in liver cancer 2016–2050.

Risk factor	Sex	Model 1: number of cases without intervention	Model 2: avoidable cases by reduction of 10% on risk factors		Model 3: avoidable cases by reduction of 100% on risk factors	
			n	%	n	%
Hepatitis B	Male	28,598	33	0.12	323	1.13
	Female	30,977	33	0.11	328	1.06
	Total	59,575	66	0.11	651	1.09
Alcohol	Male	28,569	32	0.11	329	1.15
	Female	30,196	72	0.24	789	2.61
	Total	58,765	104	0.18	1118	1.90
Tobacco	Male	27,999	172	0.61	2056	7.34
	Female	30,534	123	0.40	1538	5.04
	Total	58533	295	0.50	3594	6.14
Body mass index	Male	28,598	288	1.01	3488	12.20
	Female	30,977	440	1.42	5160	16.66
	Total	59,575	728	1.22	8648	14.52

In a scenario assuming a 10% reduction in the prevalence of each risk factor over a 10-year period (Model 2), between 66 and 728 incident cases of liver cancer could be prevented, depending on the specific risk factor (Table 4). As expected, gradual reductions in exposure prevalence led to corresponding gradual decreases in incidence rates. Under this model, the projected incidence rate among men decreases modestly from 2.54 to 2.39 per 100,000 inhabitants, while a slight reduction is observed among women, from 2.45 to 2.38 per 100,000 inhabitants (Figure 1).

In the hypothetical scenario of complete elimination of exposure to all four risk factors (Model 3), up to 8,648 new cases of liver cancer could be prevented. The PAF for liver cancer in Colombia is estimated at 1.09% for hepatitis B infection, 1.9% for alcohol consumption, 6.14% for tobacco use, and 14.52% for overweight/obesity (Table 4). Eliminating exposure to tobacco and elevated BMI notably reduces projected incidence rates: from 2.54 to 2.05 per 100,000 inhabitants in men, and from 2.45 to 1.83 per 100,000 inhabitants in women (Figure 1).

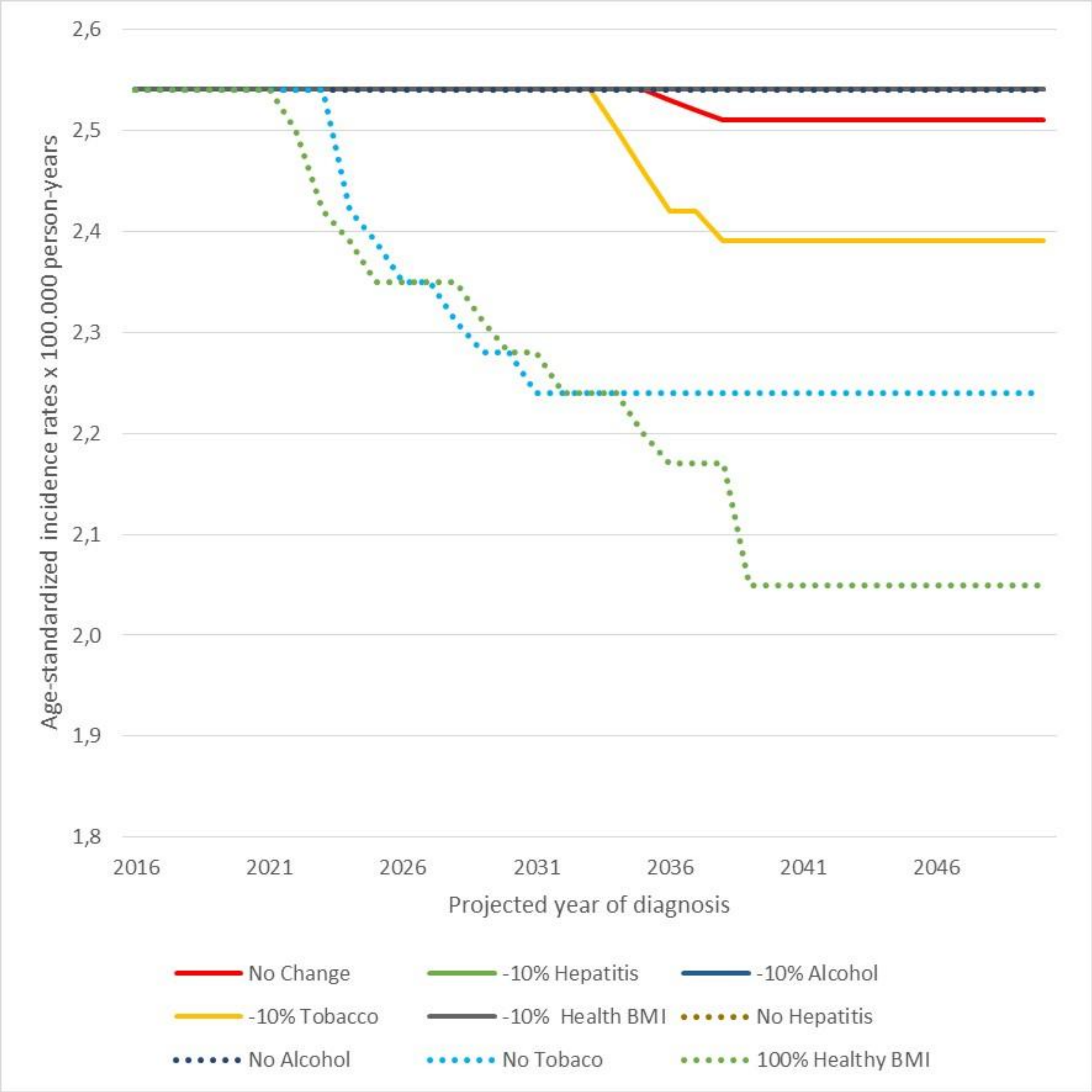

Figure 1A. Males. The potential effect of lowering the exposures to the risk factors in the expected rates of liver cancer incidence, period 2016–2050 under the reference (model 1), and intervention situations (model 2: reduction of −10% in solid line; model 3: −100% in dashed line).

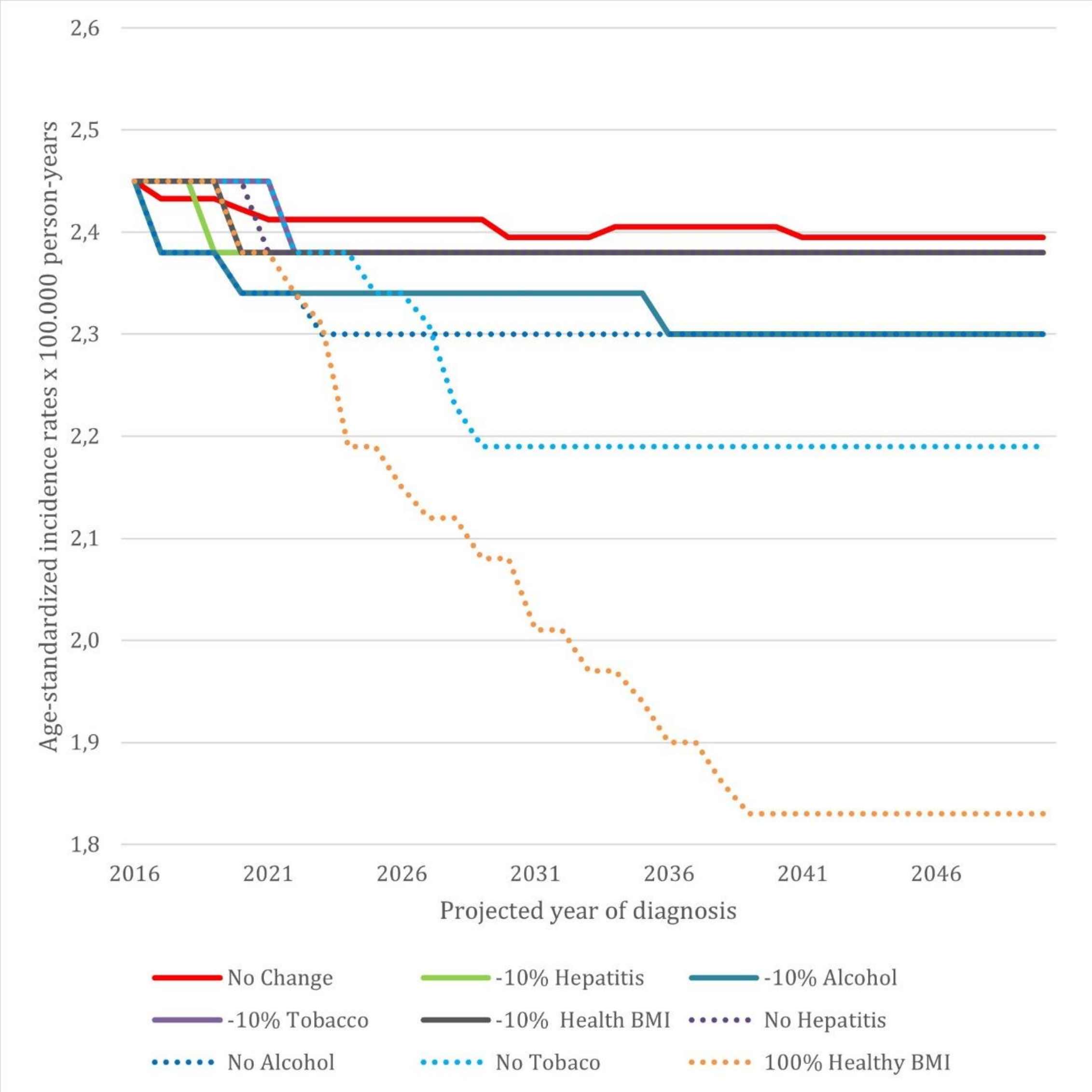

Figure 1B. Female. The potential effect of lowering the exposures to the risk factors in the expected rates of liver cancer occurrence, time 2016–2050 under the reference (model 1), and intervention situations (model 2: reduction of −10% in solid line; model 3: −100% in dashed line).

DISCUSSION

Our microsimulation modeling highlights a potentially alarming increase in new cases of liver cancer in Colombia if current trends in modifiable risk factors (hepatitis B infection, alcohol and tobacco consumption, and high body mass index) persist (Model 1). Conversely, even modest reductions (Model 2) or complete elimination (Model 3) of these exposures can significantly reduce liver cancer incidence, with marked differences by sex.

Our results reveal a higher burden of liver cancer among women, and a more pronounced impact of reducing smoking and BMI in females compared to males. These sex-specific differences are consistent with international findings and may be attributed to hormonal influences, body composition, genetic predisposition, cellular metabolism, gut microbiota, underlying comorbidities, sociodemographic variables, and unmeasured risk factors [20].

The PAF estimates in Model 3 suggest that hepatitis B (1.09%), alcohol (1.9%), and tobacco (6.14%) contribute to fewer liver cancer cases in Colombia than global averages. For instance, the global PAF for hepatitis B exceeds Colombian values, likely due to effective national prevention and control strategies [21]. While the worldwide PAF for alcohol is 17.3%, Colombia's lower estimate reflects different patterns of alcohol use—less frequent but more harmful binge drinking during weekends and holidays [17,22,23]. Similarly, the relatively low smoking prevalence explains the modest PAF for tobacco (6.14% vs. 23.24% globally) [24]. In contrast, the PAF for overweight/obesity (14.52%) aligns with global trends and reinforces BMI as a key target for cancer prevention [25].

This modeling underscores the urgent need to curb the rise of these risk factors. For example, by 2030, 64% of adults in Colombia are projected to have a high BMI, representing over 27.9 million people [17]. Alarming increases in alcohol and tobacco use have also been reported [17,22].

Although a 10% reduction in exposure appears modest, it presents considerable challenges for public health, requiring coordinated, multisectoral efforts [7]. Effective, evidence-based interventions include: smoking bans, tax policies, anti-smoking campaigns, health warnings, and nicotine replacement [26]; for alcohol, taxation, limited availability, and marketing restrictions [27]; and for obesity, sugar taxes, food labeling, healthy eating campaigns, physical activity promotion, and restrictions on ultra-processed food advertising [28]. Each intervention has variable cost-effectiveness depending on the context [29,30].

These results provide valuable insights for policymakers, showing the relative contribution of each risk factor to liver cancer and supporting evidence-informed prioritization. Importantly, interventions targeting these four factors may also reduce the burden of other cancers and chronic diseases. For instance, a 10% reduction in alcohol consumption, tobacco use, and physical inactivity could prevent approximately 26 to 149 cases of colorectal cancer annually [7]. Achieving healthy BMI levels could further reduce the incidence of breast cancer by 4,009 cases, colorectal cancer by 2,086 cases, and liver cancer by 728 cases [7,9], as well as other related chronic diseases such as cardiovascular disease, diabetes, etc.

Strengths and limitations

This study has several strengths. First, it focuses on four key modifiable risk factors—tobacco use, alcohol consumption, hepatitis B infection, and overweight/obesity—with clear implications for cancer prevention strategies. Second, the use of the validated Prevent V3.1 microsimulation model allows for robust projections using age- and sex-specific data, with proven applicability in Latin America and Europe. Third, the simulation of three scenarios—status quo, 10% reduction, and complete elimination—offers policymakers evidence to support planning and resource allocation for liver cancer control.

There are limitations that should be acknowledged. First, not all relevant risk factors for liver cancer could be included due to the limited availability of population-based data in Colombia, such as dietary composition, diabetes, or aflatoxin B1 exposure [4–6]. Including these factors in future microsimulation studies could enhance the accuracy and comprehensiveness of the model.

Second, the absence of data on co-exposures in national health surveys limited our ability to model the potential interactions between risk factors, such as the combined effects of tobacco use and alcohol consumption. Given that co-exposures may exert synergistic effects on liver cancer risk, future research could address this gap by incorporating joint exposure prevalence data and using interaction terms within the simulation model to estimate the combined attributable risk. This approach would allow for the quantification of the potential increase in preventable liver cancer cases under scenarios that consider the synergistic effects of multiple exposures. Despite these limitations, the modeling of each risk factor individually aligns with the operational design of most public health interventions, which typically target specific lifestyle behaviors [7].

Additionally, part of the prevalence data used in the model was derived from national surveys. Although these sources were the most robust data available, they may not fully reflect recent population trends, potentially affecting the validity of long-term projections. Future modeling studies should consider adjusting prevalence estimates using updated survey data or incorporating correction factors that align with recent demographic and epidemiological patterns to enhance the accuracy of projections. Additionally, in an ideal scenario one would incorporate models representing sub-regions with different exposure patterns within the country.

CONCLUSION

This modeling study shows that interventions aimed at reducing exposure to high BMI, alcohol and tobacco consumption, and hepatitis B infection could significantly reduce the future incidence and rate of liver cancer in Colombia. Notably, high BMI and tobacco use are projected to have the greatest impact on liver cancer burden, with additional benefits for the prevention of other chronic diseases. Even a modest 10% reduction in the occurrence of each risk factor could lead to a meaningful decline in liver cancer cases, emphasizing the value of gradual, sustained public health efforts.

These findings support the development of comprehensive national strategies that target multiple risk factors simultaneously. Implementing population-level interventions—such as prevention and vaccination programs, regulatory and fiscal policies, and health promotion campaigns—can guide Colombia toward a measurable reduction in liver cancer incidence and contribute to improved population health.

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AUTHORSHIPS

Conceptualization: MT, EdV; data curation: MT, EdV, MR, OH; formal analysis: MT, EdV; funding acquisition: MT, EdV; investigation: GD, MT, EdV, SP, MR, OH; methodology: GD, MT, EdV, SP, MR, OH; project administration: MT, EdV; resources: GD, MT, EdV, SP, MR, OH; supervision: MT, EdV; validation: GD, MT, EdV, SP, MR, OH; analysis: MT, EdV; visualization: GD, MPR, FB, MPB; writing – original draft: GD, MPR, FB, MPB; writing – review & editing: GD, MT, EdV, SP, MR, OH, MPR, FB, MPB.

Where authors are identified as personnel of the International Agency for Research on Cancer/World Health Organization, the authors alone are responsible for the views expressed in this article and they do not necessarily represent the decisions, policy, or views of the International Agency for Research on Cancer /World Health Organization.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare for this study.

DATA AVAILABILITY STATEMENT

Data availability is subject to request by email to the corresponding author.

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