Economic burden of liver disease in Colombia

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Abstract

Introduction: Liver diseases have a significant impact on global morbidity and mortality rates, primarily attributed to cirrhosis and hepatocellular carcinoma. However, the true extent of their impact on patients, healthcare systems, and countries is often underestimated. **Materials and methods:** This descriptive, cross-sectional study aimed to determine the economic burden associated with premature deaths caused by cirrhosis and primary liver cancer. The economic assessment was conducted by analyzing potentially productive years of life lost (PPYLL) due to liver diseases in Colombia between 2009 and 2016. **Results and conclusions:** The total burden of liver disease accounted for 687,861 disability-adjusted life years (DALYs). Men experienced a higher number of years of life lost from mortality (YLL), while women had a greater number of years lived with a disability (YLD). The economic burden of deaths caused by cirrhosis and primary liver cancer exceeded USD 8.6 million, highlighting the urgency to enhance intervention strategies ranging from promotion and prevention to timely diagnosis and treatment.

Keywords

Economic burden, disability-adjusted life years, years of life lost from mortality, years lived with a disability, liver cirrhosis, liver neoplasms, liver disease.

INTRODUCTION

Liver disease is one of the leading causes of worldwide morbidity and mortality[1-3]. It is a slow process that persists for long periods and results in the progressive destruction of the liver; its timely diagnosis and treatment manage to prolong life expectancy and improve patients' quality of life[4]. Disease burden studies allow the gap between the current health condition and an ideal health condition free of disease and disability to be measured based on the disability-adjusted life years (DALYs) lost, calculated from the sum of years of life lost due to premature death (YLLs) and years lived with disability (YLDs)[5]. In 2019, the number of DALYs due to all causes amounted to 2.54 billion (2.29 to 2.81) worldwide[6].

Chronic liver disease and its complications have been included in global disease burden estimates; however, they are undervalued. Liver disease causes around 844 million cases and more than 2 million deaths annually, so its morbidity and mortality can be compared with other chronic

diseases[7]. It is responsible for the progressive increase in recurrent hospital visits and years of life lost due to chronic diseases[2,8,9].

The epidemiology of liver disease varies by etiology, sex, territory, age, and disease-specific risk factors[8,10,11]. It imposes a substantial health burden in many countries and reports a progressive increase worldwide since 1990, partly due to the growth and aging of the population[12]. In the case of Latin America, deaths from liver cirrhosis doubled between 1980 (1,503) and 2010 (3,674)[1].

Cirrhosis is considered a public health threat due to its high mortality, mainly due to alcoholic liver disease (ALD), metabolic disease-associated fatty liver (MAFLD), and chronic hepatitis C virus infection[13].

In Colombia, from 2009 to 2016, there were 649,887 cases of liver disease, the highest proportion of patients corresponding to metabolic disorders, cirrhosis, and viral infections[10]. Liver cirrhosis has become one of the leading causes of disease burden worldwide. In 2019, it caused 46 million (43-49 million) DALYs (1.82%, confidence interval [CI]: 1.64%-2.02% of total DALYs) and was responsible for more than one million deaths, equivalent to 2.6% of deaths globally[6].

In the early stages, the disease is usually compensated and asymptomatic, and patients may have a life expectancy similar to that of healthy adults; however, as the disease progresses and decompensates, it can be lethal in up to 80% of cases and frequent and prolonged hospital stays are required with treatments that include mainly liver transplantation, meaning a burden for patients, the health system, and the government[12].

The close relationship between the per capita consumption of liters of alcohol and the increase in the mortality rate from liver disease has been studied throughout the world, and it is decisive given the variety of non-communicable diseases attributable to consumption (fatty liver, alcoholic hepatitis, and cirrhosis)[3,9,14].

Non-alcoholic steatohepatitis (NASH) is an essential cause of liver disease worldwide[15]. In 2019, it caused around 168,000 deaths and 4.4 million DALYs (3.3-5.6) (0.17% of total DALYs)[6]. Viral infections affect the world population and have gained significant importance due to their considerable increase despite the available vaccines against hepatitis A and B[14]. In 2015, they caused 1.34 million deaths (primarily due to chronic liver disease [720,000] and primary liver cancer [470,000]), a number comparable to deaths from tuberculosis (1.37 million) and more than deaths from human immunodeficiency virus (HIV; 1.06 million) or malaria (0.44 million)[16,17]. This scenario does not show much variation compared to 2019, when hepatitis B and C were responsible for 1.1 million deaths and 1.3% of the total DALYs worldwide[6].

In 2019, liver cancer was responsible for 484,000 deaths and 12,000 DALYs (0.49% of total DALYs worldwide) [6]. It is the leading cause of death in many countries with medium and low sociodemographic indices; however, countries with high sociodemographic indices have shown an increase due to risk factors such as alcohol abuse, hepatitis B and C, and NASH[18].

Patients with liver disease pose challenges for health professionals; their quality of life is inferior, representing a significant economic burden for the country[4]. This disease's treatment is expensive and inaccessible in most of the world[1]. In Colombia, approaches have been introduced to determine the impact of liver disease; nonetheless, few publications support intervention initiatives in public policy. Therefore, it is necessary to provide an overview of the main etiologies of liver disease.

MATERIALS AND METHODS

Estimation of the disease burden

This descriptive cross-sectional study determined Colombia's economic and liver disease burden between 2009 and 2016. From the definition of the diagnoses concerned and the creation of disease categories (cirrhosis, portal hypertension, congenital and birth, pregnancy, non-cirrhotic alcoholic liver disease [NAFLD], inflammatory, metabolic, toxic, primary liver tumors [hepatic tumors], vascular, and viral infections), the data were analyzed by sex, year of care/death, ICD-10 primary diagnosis grouped into categories, age in five-year periods, and geographic location. The study used the Data Warehouse-Cube population databases of Colombia's Integrated Social Protection Information System (SISPRO, for its acronym in Spanish) [19] as the primary source of prevalence data and the registry of vital statistics (deaths) of the National Administrative Department of Statistics (DANE, for its acronym in Spanish)[20].

To calculate the prevalence and mortality rate of liver disease per year, it was adjusted for underreporting using Bennett Horiuchi's method, based on the intercensal estimate of deaths between 2009 and 2016[21].

In the global disease burden study, disability weights were defined for the diseases included in the studies; however, since these data were not available for all disease categories, disability weights were determined with a group of four experts in liver disease using the Delphi method[22]. We explained to them that the disability weights reflect the severity of the disease on a scale from 0 (perfect health) to 1 (death), exemplified by disability weights from the study conducted worldwide by the Global Burden of Disease (GBD) 2016[23].

Each expert was sent a format with the list of diagnoses grouped into disease categories, in which, according to their medical criteria, they defined the weight of disability. Two rounds were completed for expert consensus; in the second, the results of the first round were sent, obtaining the final values defined by the experts for each disease category, with which YLDs were calculated.

Prevalence and mortality data were included in the Microsoft Excel template according to the World Health Organization's (WHO) Manual [21], with the disability weights assigned by the experts for each disease category. The outcome variables for the disease burden given by DALYs were YLL plus YLD. The data was consolidated into a matrix by category for analysis. The disease burden was calculated based on life expectancy at birth for a society with low mortality[24,25], with an average of 80 years for men and 82.5 years for women, like Japan[26].

Estimation of the economic burden

The economic burden associated with premature deaths from cirrhosis and liver tumors was estimated through the economic valuation of the potentially productive years of life lost (PPYLL). For this, the method applied by the authors in previous studies[27-30] was used. The PPYLL was valued based on the productive period of people in Colombia, which ranges from 18-57 years in women and up to 62 years in men. The economic valuation of the PPYLL was discounted using an annual discount rate of 3% to achieve international comparability[31,32]. All costs were reported in 2019 US dollars, using the average market representative rate published by Colombia's Central Bank (1 USD = 3,281 Colombian pesos)[33]. The PPYLL was calculated as follows:

$$\text{PPYLLi} = \left[\frac{\text{Ap} - 18, \text{ if Ad} \le 18}{\text{Ap} - (\text{sAdg} + k), \text{ if Ad} > 18} \right]$$

PPYLLi: potentially productive years of lost life of the individual; Ap: pension age (according to the sex of the individual); Ad: death age (adjusted by mid-term); sAdg: start age of the death age group; k: mid-cycle adjustment factor (for children under one year = 0.5; 1 to 4 years = 2; for the other age groups: 2.5).

The estimate of the economic burden associated with premature deaths caused by cirrhosis and liver tumors was modeled for two scenarios:

- Floor scenario (lower loss): PPYLLs are valued based on the annual minimum wage (AMW), calculated using the 2019 minimum monthly wage (COP 828,116). This value was multiplied by 13.5 months (12 calendar months + 1.5 months of social benefits).
- Ceiling scenario: It refers to the country's average productivity, evaluated as the gross domestic product per capita (GDPpc) of 2019 (COP 21,506,780)[34].

RESULTS

The burden of liver disease

Between 2009 and 2016, the total burden of liver disease represented 687,861 DALYs (1,835 x 1,000 people). By age group and sex, there is evidence of more DALYs in both sexes from age 30 (**Table 1**).

Table 1. Disability-adjusted life years (DALYs) and economic burden by sex and age group, liver disease, Colombia, 2009-2016

Age group	Men		Women		Total	
	DALY men	DALY/1,000	DALY women	DALY/1,000	Total DALY	DALY/1,000
0-4	5814	0.330	5584	0.332	11398	0.331
5-14	1966	0.056	2676	0.079	4642	0.067
15-29	6356	0.127	5914	0.122	12 270	0.124
30-44	24 900	0.686	15 547	0.402	40 448	0.540
45-59	84 219	3.021	52 584	1.714	136 802	2.336
60-69	139 309	13.477	151 583	13.038	290 892	13.245
70-79	63 549	11.729	77 288	11.568	140 837	11.640
80+	21 209	9.913	29 362	9.812	50 571	9.854
Total	**347 323**	**1.877**	**340 538**	**1.794**	**687 861**	**1.835**

Source: The authors.

Annual DALYs increased progressively between 2009 and 2014, from 1.59 to 2.13 DALYs per 1,000 people, with a subsequent decline in 2016 to 1.77 DALYs per 1,000 people (**Figure 1**). Of the total DALYs due to liver disease, 67% correspond to mortality and 33% to disability. When performing the analysis by sex, the proportion of DALYs due to mortality was higher in men than in women (37% vs. 30%); however, DALYs due to disability were higher in women than in men (19% vs. 14%) (**Figure 2**).

The main etiologies of liver disease burden were cirrhosis, liver tumors, and metabolic and viral diseases, with differences in burden due to disability and premature death (**Figure 3, Table 2**).

Liver cirrhosis had 307,412 DALYs (0.82 x 1,000 people), 58% in men. Of these, 245,651 DALYs were attributed to mortality (80%) and 60,793 to disability. Both men and women had the highest number of DALYs after 60. By year, it is evident that the highest DALY rates occurred between 2014 and 2015 (0.940 and 0.932 x 1,000 inhabitants, respectively) (**Table 2**).

Metabolic diseases had 109,280 DALYs (0.29 x 1,000 people), 43,535 DALYs (40%) in men, and 65,765 DALYs (60%) in women. Of the total DALYs, 3,800 (3%) correspond to mortality and 105,490 (97%) to disability. By age group, 82,366 DALYs (75.4%) belong to the 60-69 age group, followed by the 70-79 age group with 19,466
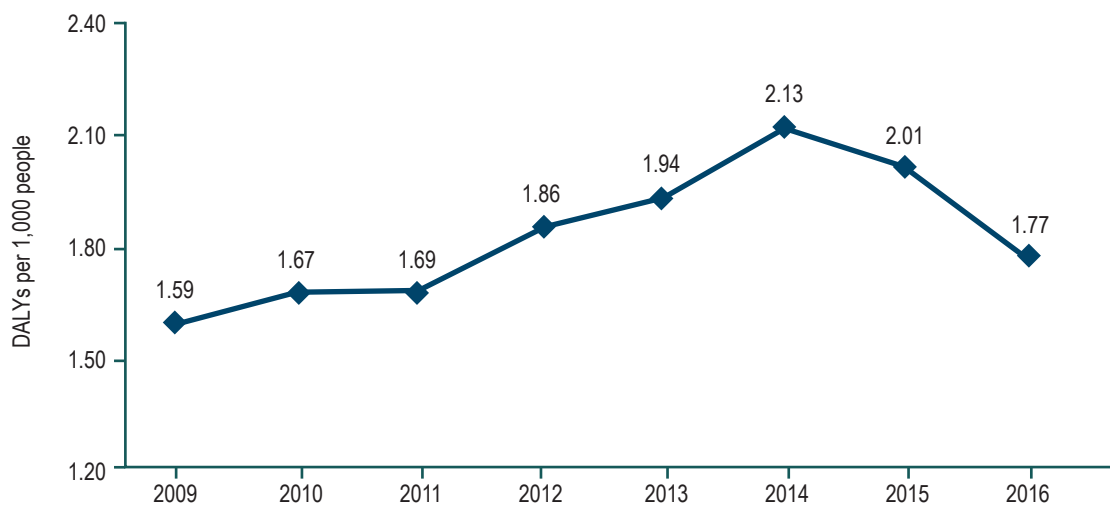

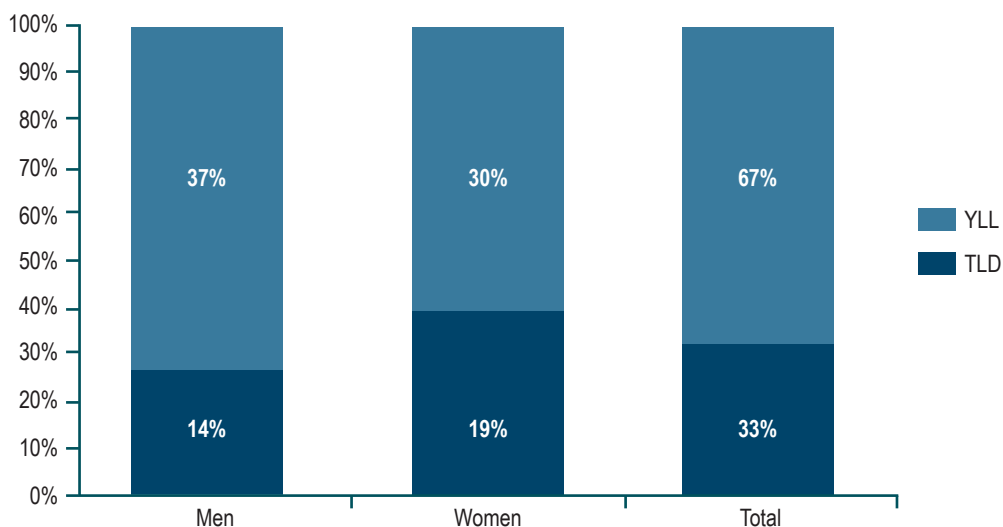**Figure 1.** DALY trend due to liver disease x 1,000 people, Colombia 2009-2016. Source: The authors.

Figure 2. The proportion of YLLs and YLDs over DALYs due to liver disease in Colombia, 2009-2016. Source: The authors.

Table 2. DALYs, YLLs, and YLD by sex, Colombia, 2009-2016

DALY						
Category	Men	Men *1,000	Women	Women *1,000	Total	Total *1,000
Cirrosis	177 255	7.656	130 157	5.473	307 412	6.55
Congénitas y del nacimiento	3591	0.155	6975	0.293	10 567	0.22
Del embarazo	0	0.000	538	0.023	538	0.01
EHANC	6009	0.260	2052	0.086	8061	0.17
Hipertensión portal	3017	0.131	3088	0.130	6105	0.13
Inflamatorias	2757	0.119	4127	0.173	6884	0.15
Metabólicas	43 525	1.868	65 765	2.754	109 290	2.32
Tóxicas	3992	0.173	5262	0.221	9254	0.20
Tumores hepáticos	93 254	4.031	109 047	4.601	202 300	4.32
Vasculares	623	0.027	725	0.030	1348	0.03
Virales	13 300	0.576	12 802	0.540	26 102	0.56
Enfermedad hepática	347 323	1.870	340 538	1.794	687 861	1.83

YLL						
Category	Men	Men *1,000	Women	Women *1,000	Total YLLs	%YLLs
Cirrosis	150 968	6.526	94 683	4.020	245 651	53%
Congénitas y del nacimiento	2683	0.116	3295	0.135	5978	1%
Del embarazo	0	0.000	536	0.017	536	0%
EHANC	3852	0.166	609	0.023	4461	1%
Hipertensión portal	1625	0.071	1273	0.059	2898	1%
Inflamatorias	1295	0.057	1330	0.055	2625	1%
Metabólicas	1715	0.073	2086	0.088	3800	1%
Tóxicas	1551	0.068	1461	0.061	3011	1%
Tumores hepáticos	80 278	3.466	94 969	4.022	175 246	38%
Vasculares	346	0.015	269	0.009	615	0%
Virales	9347	0.405	7316	0.310	16 663	4%
Enfermedad hepática	253 659	10.952	207 826	8.800	461 485	100%

YLD						
Category	Men	Men *1,000	Women	Women *1,000	Total de APMPs	% YLDs
Cirrosis	26 287	1.091	35 475	1.484	61 761	27%
Congénitas y del nacimiento	908	0.038	3680	0.154	4588	2%
Del embarazo	0	0.000	3	0.000	3	0%
EHANC	2157	0.090	1443	0.060	3600	2%
Hipertensión portal	1392	0.058	1815	0.076	3207	1%
Inflamatorias	1462	0.060	2798	0.117	4259	2%
Metabólicas	41 810	1.727	63 679	2.665	105 490	47%
Tóxicas	2442	0.101	3801	0.159	6242	3%
Tumores hepáticos	12 976	0.540	14 078	0.592	27 054	12%
Vasculares	277	0.011	455	0.019	732	0%
Virales	3952	0.165	5486	0.231	9438	4%
Enfermedad hepática	93 663	3.882	132 712	5.557	226 375	100%

Source: The authors.

DALYs (17.8%). Metabolic diseases showed 0.413 DALYs x 1m000 people in 2014, followed by 0.356 in 2016 and 0.337 in 2015; the other years had less than 0.332 DALYs x 1,000 people (**Table 2**).

Liver tumors had 202,300 DALYs (0.54 x 1,000 people), of which 93,254 DALYs (46%) were in men and 109,047 DALYs (54%) in women. 175,246 DALYs (87%) were reported for mortality, and 27,054 DALYs (13%) for disability. When analyzed by age groups, there are 65,709 DALYs (32.5%) between 60 and 69 years, followed by 51,248 DALYs (25.3%) between 70 and 79 years, and 46,270 DALYs (22.9%) between 45 and 59 years. In 2014, there was a rate of 0.595 DALYs x 1,000 people, followed by 2012, 2014, and 2015 with rates between 0.558 and 0.561 DALYs x 1,000 people (**Table 2**).

Viral infections featured 26,102 DALYs (0.07 x 1,000 people), of which 13,300 DALYs (51%) correspond to men and 12,802 DALYs (49%) to women. 16,663 DALYs (64%) were registered for mortality, and 9438 DALYs (36%) for disability. 10,983 DALYs (42%) were reported between 60 and 69 years, followed by 4,506 (17%) between 45 and 59 years and 3,795 (15%) between 70 and 79 years, and the year 2016 had the lowest DALY rate (0.058 x 1,000 people). In the other years, they ranged between 0.068 and 0.078 x 1,000 people (**Table 2**).

The DALY, YLD, and YLL data for alcoholic liver disease portal hypertension, congenital and birth, pregnancy, inflammatory, toxic, vascular diseases, and NAFLD are found in **Table 2** because they do not represent a significant disease burden.

Economic burden of deaths from cirrhosis and liver tumors

For 2016, deaths in productive ages due to cirrhosis caused 9,064 YPLL (69.5% in those over 40) and 4,103 (62.8%) from liver tumors. These YPLYL due to cirrhosis produced an economic burden that ranged between 19.6 and 37.8 million dollars, and for liver tumors, between 8.6 and 16.5 million dollars (**Table 3**).

Figure 4 shows the economic burden of premature mortality due to cirrhosis and liver tumors by sex and age group. Most of the economic burden of cirrhosis occurs in men, especially those aged 35 years or older (**Figure 4A**), and it ascends to 54 years. In turn, the economic burden of liver tumors is higher in women in the 15-19 and 35-39 age groups; the burden is more significant in men in the remaining groups. A variable economic burden is noted in the first age groups, rising from over 35 to 49 and then decreasing to 59 years (**Figure 4B**).

DISCUSSION AND CONCLUSIONS

The total burden of liver disease represented 687,861 DALYs (1,835 x 1,000 inhabitants), with an increase between 2009 and 2014 (1.59 to 2.13 DALYs x 1,000 people) and a subsequent decrease in 2016 (1.77 DALYs x 1,000 people).

The highest proportion of DALYs was due to mortality (67%). Men had more YLL, and women exhibited the highest YLDs due to liver disease. This trend was maintained throughout the study period, which may be related to a longer life expectancy in women, biological factors (genetic,
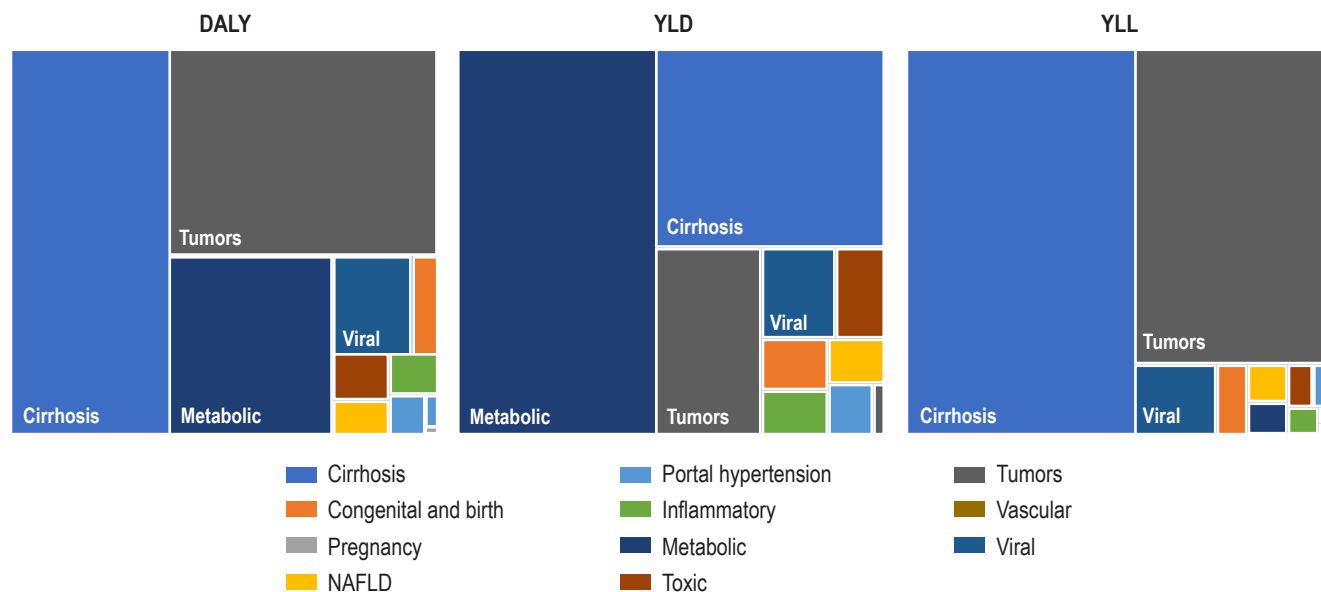

Figure 3. DALYs, YLDs, and YLL distribution due to liver disease in Colombia, 2009-2016. Source: The authors.

Table 3. Estimated PLYL and economic burden for cirrhosis and liver tumors, with and without discount. Colombia, 2016

Age group	Total PPYLL		PPYLL discount		Economic burden without discount*				Economic burden with discount *			
					Floor		Ceiling		Floor		Ceiling	
	F	M	F	M	F	M	F	M	F	M	F	M
Hepatic cirrhosis												
15-19	249	90	80	25	$ 847 305	$ 306 204	$ 1 630 010	$ 589 063	$ 271 523	$ 84 643	$ 522 345	$ 162 833
20-24	149	163	54	51	$ 506 182	$ 556 095	$ 973 772	$ 1 069 793	$ 182 567	$ 173 013	$ 351 215	$ 332 835
25-29	381	214	159	77	$ 1 298 467	$ 728 555	$ 2 497 937	$ 1 401 564	$ 542 916	$ 262 772	$ 1 044 440	$ 505 509
30-34	158	366	77	153	$ 539 194	$ 1 245 935	$ 1 037 279	$ 2 396 878	$ 261 356	$ 520 952	$ 502 786	$ 1 002 185
35-39	336	658	189	319	$ 1 144 412	$ 2 241 980	$ 2 201 572	$ 4 313 026	$ 643 067	$ 1 086 725	$ 1 237 106	$ 2 090 596
40-44	390	1007	254	566	$ 1 329 645	$ 3 431 601	$ 2 557 916	$ 6 601 571	$ 866 156	$ 1 928 284	$ 1 666 274	$ 3 709 551
45-49	450	1288	340	839	$ 1 533 219	$ 4 388 930	$ 2 949 542	$ 8 443 240	$ 1 157 845	$ 2 859 031	$ 2 227 414	$ 5 500 085
50-54	349	1501	305	1134	$ 1 188 428	$ 5 115 726	$ 2 286 248	$ 9 841 419	$ 1 040 412	$ 3 863 257	$ 2 001 501	$ 7 431 972
55-59	-	1315	-	1152	$ 0	$ 4 482 199	$ 0	$ 8 622 667	$ 0	$ 3 923 952	$ 0	$ 7 548 734
60-64	-	-	-	-	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0
Total	2461	6603	1457	4315	$ 8 386 853	$ 22 497 227	$ 16 134 275	$ 43 279 221	$ 4 965 843	$ 14 702 628	$ 9 553 081	$ 28 284 300
Liver tumors												
15-19	166	90	53	25	$ 564 870	$ 306 204	$ 1 086 673	$ 589 063	$ 181 015	$ 84 643	$ 348 230	$ 162 833
20-24	74	326	27	102	$ 253 091	$ 1 112 191	$ 486 886	$ 2 139 586	$ 91 284	$ 346 026	$ 175 608	$ 665 671
25-29	64	143	27	51	$ 216 411	$ 485 704	$ 416 323	$ 934 376	$ 90 486	$ 175 181	$ 174 073	$ 337 006
30-34	53	122	26	51	$ 179 731	$ 415 312	$ 345 760	$ 798 959	$ 87 119	$ 173 651	$ 167 595	$ 334 062
35-39	336	152	189	74	$ 1 144 412	$ 517 380	$ 2 201 572	$ 995 314	$ 643 067	$ 250 783	$ 1 237 106	$ 482 445
40-44	281	322	183	181	$ 957 345	$ 1 098 112	$ 1 841 699	$ 2 112 503	$ 623 632	$ 617 051	$ 1 199 718	$ 1 187 056
45-49	307	539	232	351	$ 1 045 376	$ 1 837 227	$ 2 011 051	$ 3 534 379	$ 789 440	$ 1 196 804	$ 1 518 691	$ 2 302 361
50-54	281	393	246	296	$ 957 345	$ 1 337 445	$ 1 841 699	$ 2 572 920	$ 838 110	$ 1 010 002	$ 1 612 320	$ 1 942 999
55-59	-	456	-	399	$ 0	$ 1 552 140	$ 0	$ 2 985 941	$ 0	$ 1 358 824	$ 0	$ 2 614 049
60-64	-	-	-	-	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0	$ 0
Total	1561	2542	981	1530	$ 5 318 581	$ 8 661 714	$ 10 231 664	$ 16 663 042	$ 3 344 153	$ 5 212 964	$ 6 433 341	$ 10 028 482

*Amounts in 2019 US dollars. Source: The authors.

hormonal, autoimmune), and social and behavioral factors (tobacco and alcohol use)[35,36].

Deaths from cirrhosis created an economic burden that ranged between US 19.6 and 37.8 million, and from liver tumors between US 8.6 and 16.5 million, which can be significantly impacted by immunization against hepatitis B in the pediatric population and strategies against alcohol[6], implemented since 1992 and 2007, respectively[37,38].

In 2017, liver disease caused more than 1.32 million deaths globally in Europe, North America, South America, and Central Asia, and alcohol is the most common cause of liver cirrhosis. In some countries of the European region, approximately 2 million years of life are lost due to liver disease in people under 50 years of age (60%-80% due to alcohol)[39].

In 2012, cirrhosis and liver cancer in the United States were among the top 5 causes of death from gastrointesti-
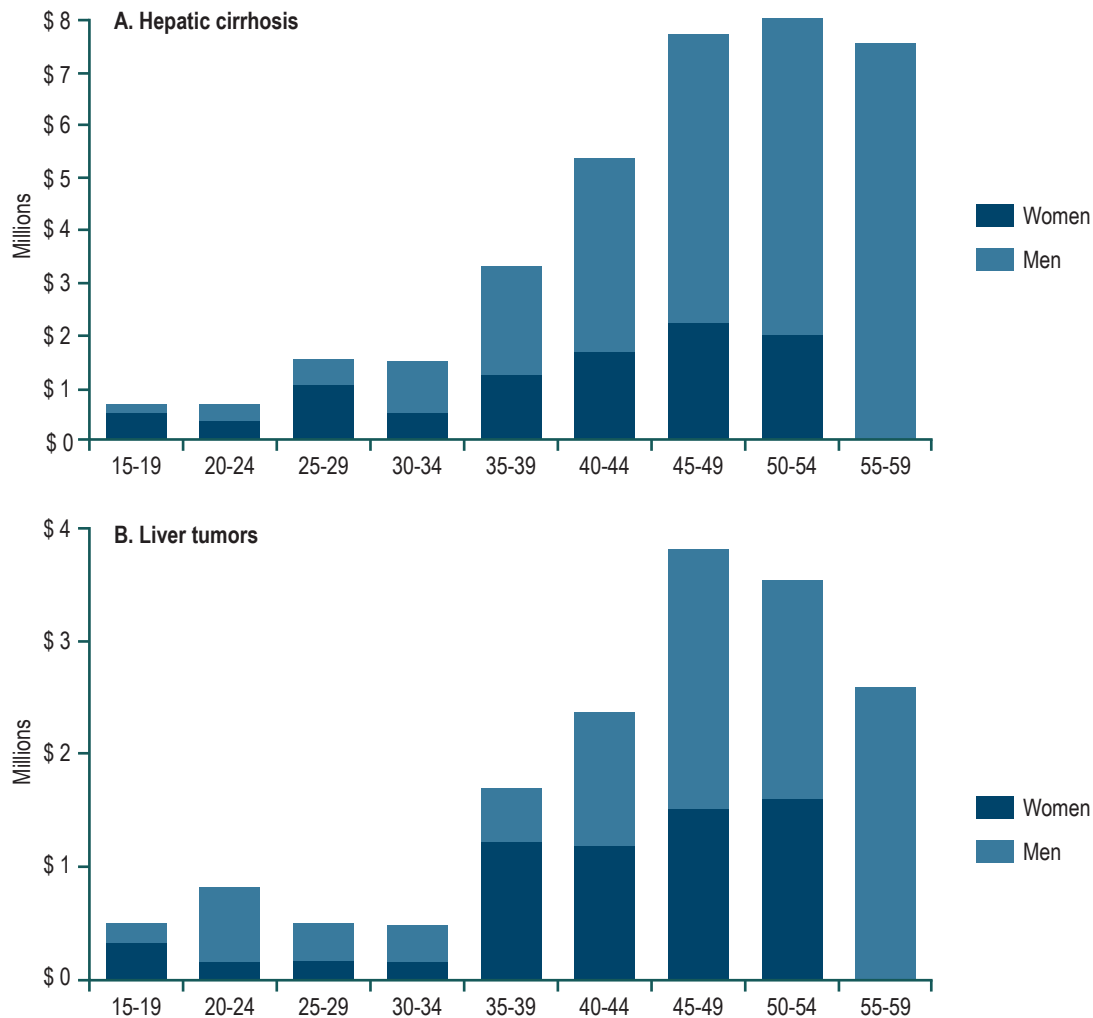
Figure 4. The economic burden associated with premature deaths from cirrhosis and liver tumors in Colombia, 2016. Source: The authors.

nal, liver, and pancreatic diseases[40]. In 2015, they were the 11th and 16th most frequent causes of death in the world, causing 1.16 million and 788,000 deaths, respectively, and when combined, they represent 3.5% of deaths worldwide[17]. These results are consistent with our findings, in which cirrhosis and primary liver tumors were Colombia's leading causes of death from liver disease.

By 2015, regionally, the highest proportion of deaths from cirrhosis and liver cancer was found in Latin America and the Caribbean, the Middle East, and North Africa[17]. Most liver cancers (83%) are diagnosed in less developed countries[41]; however, Fitzmaurice et al.[18] described that the chances of developing liver cancer are higher in countries with a medium sociodemographic index (SDI). In

2005, liver cancer in Santander, Colombia, represented 59.4 DALYs x 100,000 people, of which 89.7% correspond to mortality and 10.2% to disability[42].

The proportion in the distribution of mortality and disability does not show significant differences with our study since 202,300 DALYs (0.5 x 1,000 people) were estimated between 2009 and 2016, of which 87% correspond to mortality and 13% to disability. Considering the possibility of information systems underreporting mortality and prevalence in Colombia and studies worldwide, liver disease is related to geographic, socioeconomic, and sociocultural factors that lead to disparities with a significant impact on the health of the population and the country's development concerning disability and premature mortality outcomes[10,43,44].

Despite public health interventions related to immunization, healthy lifestyle habits (physical activity, diet), and measures to control alcohol use, the burden of liver disease in Colombia reflects the need to strengthen intervention strategies, from promotion and prevention to timely diagnosis and treatment, since economic and social expenses (drugs and technologies) can become unsustainable due to the increase in the disease burden[45].

LIMITATIONS

The study's main limitations in estimating cases and analyzing the population impact of public policy are the scarcity of epidemiological studies of liver disease in Colombia and underreporting in the information systems. This study does not include complications associated with the disease categories studied (such as variceal bleeding, ascites, hepatorenal syndrome, and portosystemic encephalopathy, among others, in the case of portal hypertension).

Care should be taken to interpret the data because the disease burden was assigned by disease category and does not include the severity scenario by disease category or other more complex situations in which multiple causes or risk factors contribute to disabilities or premature death individually.

The estimation of mortality costs was limited. Our analysis was performed from the perspective of the human capital method, which implied that friction costs were not considered. Some authors suggest that the friction cost method is an alternative to the human capital method. The latter would overestimate the costs associated with premature mortality because the production not obtained due to the death of a worker can be replaced by unemployed individuals[46-48]. This article justified the assessment of premature mortality due to liver diseases by selecting a floor scenario that illustrates these losses according to the annual minimum wage, which is close to 86.2% of the country's median salaries[49]. The second scenario, or ceiling scenario, is the country's average productivity evaluated as GDP per capita[50,51].

BIASES

Information bias regarding disability weights for all liver disease categories included in the study was controlled by expert consensus to assign values between 0 (perfect health) and 1 (death) because they were not fully defined in previous disease burden studies. Subjectivity bias in data analysis was contained by involving all researchers.

RECOMMENDATIONS

Despite national efforts to prevent and control chronic diseases, there is a substantial burden of liver disease in the Colombian population, requiring a more significant approach through strategies that contain, eliminate, or minimize the risk of developing the disease and its negative impact on the country, including the costs attributable to disability and premature mortality.

Our study shows that liver disease in Colombia and globally is a public health problem. It must be addressed with comprehensive strategies for prevention, control, treatment, and rehabilitation (particularly for patients with liver transplantation), with a multisectoral focus. Decisive public policy actions are required, such as vaccination (viral hepatitis, liver cancer), education on and restriction of alcohol use (cirrhosis), prevention and control of chronic non-communicable diseases such as diabetes and obesity (non-alcoholic cirrhosis), and of course, improved information systems to have the most reliable data to assess the impact of these public health measures.

Conflicts of interest

There were no conflicts of interest in the conduct of the research.

REFERENCES

1. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Medicine. 2014;12:145.
https://doi.org/10.1186/s12916-014-0145-y
2. Khan F, Samad M, Arif F. The Burden of Chronic Liver Disease Patients: Their Clinical and Laboratory Profiles at Jinnah Postgraduate Medical Centre, Karachi. J Med Res Health Educ. 2018;2(1):1-7.
3. Wang F, Fan J, Zhang Z, Gao B, Wang H. The Global Burden of Liver Disease: The Major Impact of China. Hepatology. 2014;60(6):2099-108.
https://doi.org/10.1002/hep.27406
4. Rohra DK, Jaipal, Khowaja AA, Mahmood K, Ahuja KL. Modes of presentation and reasons of hospitalization for patients with decompensated chronic liver disease at civil hospital Karachi. Journal of the Dow University of Health Sciences. 2008;2(2):50-4.

5. Murray CJL, Lopez AD. The global burden of disease: a comprehensive assessment of mortality and disability from deceases, injuries and risk factors in 1990 and projected to 2020. Harvard University Press; 1996.

6. Abbafati C, Machado DB, Cislaghi B, Salman OM, Karanikolos M, McKee M, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet. 2020;396(10258):1204-22. https://doi.org/10.1016/S0140-6736(20)30925-9

7. Marcellin P, Kutala BK. Liver diseases: A major, neglected global public health problem requiring urgent actions and large-scale screening. Liver International. 2018;38(Suppl 1):2-6. https://doi.org/10.1111/liv.13682

8. Rowe IA. Lessons from Epidemiology: The Burden of Liver Disease. Digestive Diseases. 2017;35(4):304-9. https://doi.org/10.1159/000456580

9. Moon AM, Singal AG, Tapper EB. Contemporary Epidemiology of Chronic Liver Disease and Cirrhosis. Clinical Gastroenterology and Hepatology. 2020;18(12):2650-66. https://doi.org/10.1016/j.cgh.2019.07.060

10. Bejarano Ramírez DF, Carrasquilla Gutiérrez G, Porras Ramírez A, Vera Torres A. Prevalence of liver disease in Colombia between 2009 and 2016. JGH Open. 2020;4(4):603-10. https://doi.org/10.1002/jgh3.12300

11. Orman ES, Roberts A, Ghabril M, Nephew L, Desai A, Patidar K, et al. Trends in Characteristics, Mortality, and Other Outcomes of Patients with Newly Diagnosed Cirrhosis. JAMA Network Open. 2019;2(6):1-13. https://doi.org/10.1001/jamanetworkopen.2019.6412

12. Sepanlou SG, Safiri S, Bisignano C, Ikuta KS, Merat S, Saberifiroozi M, et al. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Gastroenterol Hepatol. 2020;5(3):245-66. https://doi.org/10.1016/S2468-1253(19)30349-8

13. Gonzalez-Chagolla A, Olivas-Martinez A, Ruiz-Manriquez J, Servín-Rojas M, Kauffman-Ortega E, Carlos Chavez-García L, et al. Cirrhosis etiology trends in developing countries: Transition from infectious to metabolic conditions. Report from a multicentric cohort in central Mexico. Lancet Reg Health Am. 2021;7:100151. https://doi.org/10.1016/j.lana.2021.100151

14. Tyrfingsson T, Olafsson S, Bjornsson ES, Rafnsson V. Alcohol consumption and liver cirrhosis mortality after lifting ban on beer sales in country with state alcohol monopoly. Eur J Public Health. 2015;25(4):729-31. https://doi.org/10.1093/eurpub/cku127

15. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, et al. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1789-858. https://doi.org/10.1016/S0140-6736(18)32279-7

16. World Health Organization. Global hepatitis report, 2017 [Internet]. Geneva: WHO; 2017. p. 1-83. [consultado el 18 de marzo de 2021]. Disponible en: https://www.who.int/publications/i/item/9789241565455

17. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol. 2019;70(1):151-71. https://doi.org/10.1016/j.jhep.2018.09.014

18. Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, Allen C, et al. Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life-Years for 29 Cancer Groups, 1990 to 2016: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncology. 2018;4(11):1553-68. https://doi.org/10.1001/jamaoncol.2018.2706

19. Sistema Integral de Información de la Protección Social [Internet]. Ministerio de Salud y Protección Social. [consultado el 7 de junio 06 de 2018]. Disponible en: http://www.sispro.gov.co/

20. Departamento Administrativo Nacional de Estadística - DANE [Internet]. Gobierno de Colombia [consultado el 7 de junio 06 de 2018]. Disponible en: https://www.dane.gov.co/index.php/en/

21. Mathers C, Vos T, Lopez A, Salomon J, Ezzati M. National Burden of Disease Studies: A practical Guide. Global Program on Evidence for Health Policy. Geneva: World Health Organization; 2001.

22. Hsu C chien, Ohio T. The Delphi Technique: Making Sense of Consensus. Practical Assessment, Research & Evaluation. 2007;12(10).

23. GBD 2016 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet. 2017;390(10100):1345-1422. https://doi.org/10.1016/S0140-6736(17)32366-8

24. Coale A, Guo G. Revised regional model life tables at very low levels of mortality. Population Index. 1989;55(4):613-43. https://doi.org/10.2307/3644567

25. Coale AJ, Demeny P, Vaughan B. Regional Model Life Tables and Stable Populations. 2.ª edición. Nueva York; Academic Press; 1983. https://doi.org/10.1016/B978-0-12-177080-8.50011-1

26. Dantés HG, Castro MV, Franco-Marina F, Bedregal P, Rodríguez García J, Espinoza A, et al. La carga de la enfermedad en países de América Latina. Salud Publica Mex. 2011;53 supl 2:S72-S77.

27. Chaparro Narváez PE, Cotes Cantillo KP, Díaz Jiménez DP, Vargas Sandoval GA, Salas Quijano SP, Rodríguez Salazar MN, et al. Tercer Informe: Mortalidad evitable en Colombia para 1998-2011 [Internet]. Bogotá: Observatorio Nacional de Colombia; 2014 [consultado el 18 de marzo de 2018]. Disponible en: https://www.ins.gov.

co/Direcciones/ONS/Informes/3.%20Mortalidad%20
evitable.pdf

28. Acosta Gómez JC, Castañeda Orjuela CA, Cotes Cantillo KP. Consecuencias del conflicto armado en la salud en Colombia. Informe Técnico 9/2017 [Internet]. Bogotá, D.C.: Observatorio Nacional de Salud; 2017 [consultado el 18 de marzo de 2018]. Disponible en: https://www.ins.gov.co/Direcciones/ONS/Resumenes%20Ejecutivos/Resumen%20ejecutivo%20informe%209%20Consecuencias%20del%20Conflicto%20Armado%20en%20Salud%20en%20Colombia.pdf

29. Cotes Cantillo KP, Díaz Jiménez DP, Valencia Aguirre S, Vargas Sandoval GA, Chaparro Narváez PE, Escobar Díaz FA, et al. Carga de Enfermedad Ambiental; Informe Técnico Especial 10 [Internet]. Bogotá, D.C.: Observatorio Nacional de Salud; 2018 [consultado el 18 de marzo de 2018]. Disponible en: https://www.ins.gov.co/Direcciones/ONS/Informes/10%20Carga%20de%20enfermedad%20ambiental%20en%20Colombia.pdf

30. Alvis N, Correa Reyes J, Carcamo A. AIDS mortality and its economic impact in Cartagena de Indias, Colombia, 1995-2000. Biomedica. 2002;22(3):303-18.

31. Bonneux L, Birnie E. The discount rate in the economic evaluation of prevention: A thought experiment. Journal of Epidemiology and Community Health. 2001;55(2):123-5. https://doi.org/10.1136/jech.55.2.123

32. Haacker M, Hallett TB, Atun R. On discount rates for economic evaluations in global health. Health Policy and Planning. 2020;35(1):107-14. https://doi.org/10.1093/heapol/czaa073

33. Banco de la República. Tasa Representativa del Mercado (TRM - Peso por dólar) [Internet]. Banco de la República; 2019 [consultado el 20 de septiembre de 2018]. Disponible en: https://www.banrep.gov.co/es/estadisticas/trm

34. DANE. Producto Interno Bruto [Internet]. DANE; 2020 [consultado el 20 de septiembre de 2020]. Disponible en: https://www.dane.gov.co/files/investigaciones/boletines/pib/presen_rueda_de_prensa_PIB_IVtrim19.pdf

35. Sundby J. Are women disfavoured in the estimation of Disability Adjusted Life Years and the Global Burden of Disease? Scandinavian Journal of Public Health. 1999;27(4):279-85. https://doi.org/10.1177/14034948990270041301

36. Nusselder WJ, Wapperom D, Looman CWN, Yokota RTC, Van Oyen H, Jagger C, et al. Contribution of chronic conditions to disability in men and women in France. Eur J Public Health. 2019;29(1):99-104. https://doi.org/10.1093/eurpub/cky138

37. Porras R. A, De la Hoz F. Impacto de la vacunación contra hepatitis B en el Amazonas colombiano 18 años después de su introducción. Rev. Fac. Nac. Salud Pública. 2012;30(Supl 1):32-5.

38. Grupo Gestión Integrada para la Salud Mental; Grupo de Investigación "Estilo de Vida y Desarrollo Humano". Estrategia nacional de respuesta integral frente al consumo de alcohol en Colombia. Ministerio de Salud y Protección Social, Universidad Nacional de Colombia; 2013.

39. Buchanan R, Sinclair JMA. Alcohol use disorder and the liver. Addiction. 2020;116(5):1270-8. https://doi.org/10.1111/add.15204

40. Peery AF, Crockett SD, Barritt AS, Dellon ES, Eluri S, Gangarosa LM, et al. Burden of Gastrointestinal, Liver, and Pancreatic. Gastroenterology. 2015;149(7):1731-1741.e3. https://doi.org/10.1053/j.gastro.2015.08.045

41. Wong MCS, Jiang JY, Goggins WB, Liang M, Fang Y, Fung FDH, et al. International incidence and mortality trends of liver cancer: A global profile. Sci Rep. 2017;7:45846. https://doi.org/10.1038/srep45846

42. Esquiaqui-Felipe R, Posso-Valencia H, Peñaloza RE, Rodriguez-García J. Carga de enfermedad por cáncer en Santander, Colombia, 2005. Revista de Salud Pública. 2012;14(2):213-25. https://doi.org/10.1590/S0124-00642012000200003

43. Scaglione S, Kliethermes S, Cao G, Shoham D, Durazo R, Luke A, et al. The epidemiology of cirrhosis in the United States a population-based study. J Clin Gastroenterol. 2015;49(8):690-6. https://doi.org/10.1097/MCG.0000000000000208

44. Corbould E, Cortez-Pinto H, Webber L, Sheron N, Pimpin L, Lazarus JV, et al. Burden of liver disease in Europe: Epidemiology and analysis of risk factors to identify prevention policies. J Hepatol. 2018;69(3):718-35. https://doi.org/10.1016/j.jhep.2018.05.011

45. Valencia O, Lopes G, Sánchez P, Acuña L, Uribe D, González J. Incidence and Prevalence of Cancer in Colombia: The Methodology Used Matters. J Glob Oncol. 2018;4:1-7. https://doi.org/10.1200/JGO.17.00008

46. Koopmanschap MA, Rutten FFH, van Ineveld BM, Van Roijen L. The friction cost method for measuring indirect costs of disease. Journal of health economics. 1995;14(2):171-89. https://doi.org/10.1016/0167-6296(94)00044-5

47. Liljas B. How to Calculate Indirect Costs in Economic Evaluations. Pharmacoeconomics. 1998;13(1 Pt 1):1-7. https://doi.org/10.2165/00019053-199813010-00001

48. Johannesson M, Karlsson G. The friction cost method: a comment. J Health Econ. 1997;16(2):249-55. https://doi.org/10.1016/S0167-6296(97)00006-4

49. Corrales JS, Alvarado V, Gómez S, Navarrete N, Otero M, Pinchao A. Informe mensual del mercado laboral: Productividad y Salario Mínimo [Internet]. Bogotá: Fedesarrollo; 2018 [consultado el 10 de septiembre de 2019]. Disponible en: https://www.fedesarrollo.org.co/sites/default/files/imlenero.pdf

50. Baltussen RMP, Adam T, Tan-Torres Edejer T, Hutubessy RCW, Acharya A, Evans DB, et al. Making choices in health: WHO guide to cost-effectiveness analysis [Internet]. Génova: WHO; 2003 [consultado el 10 de septiembre de 2019]. Disponible en: https://apps.who.int/iris/bitstream/handle/10665/42699/9241546018.pdf?sequence=1&isAllowed=y

51. Sachs JD. Macroeconomics and Health: Investing in Health for Economic Development. 1.ª edición. Geneva: World Health Organization; 2001.