# The establishment of Public Health Policies and Burden of Non-alcoholic fatty liver disease (NAFLD) in the Americas

Running title: Public health policies on NAFLD in the Americas

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#### ABSTRACT

**Background:** Non-alcoholic fatty liver disease (NAFLD) is a global health challenge. Yet, there is no information regarding the impact of national public health policies (PHP) addressing NAFLD-related conditions on its prevalence. We described the development of PHP addressing NAFLD-related conditions and the burden of NAFLD in the Americas.

**Methods:** We performed a cross-sectional study in 17 American countries. A group of NAFLD experts in each country completed a survey on national policies, guidelines, awareness, monitoring of NAFLD, and its related health conditions (e.g., obesity or diabetes). We also registered data on NAFLD-related outcomes (prevalence and mortality) and hepatocellular carcinoma (HCC) attributable to NAFLD in each country from the Global Burden of Disease database.

**Findings:** None of the included countries had a specific national policy for NAFLD. The median number of PHP on NAFLD-related conditions were 4 [4-6]. Only Brazil (6%) had a national strategy for cirrhosis and three (18%) had for HCC (Brazil, Chile, and Panama). In addition, 15 (88%) countries had policies to prevent diabetes, 14 (82%) to prevent hypertension, 14 (82%) to prevent cardiovascular diseases, 11 (65%) to decrease alcohol use disorders, and 9 (53%) countries had PHP on obesity. Six countries (35%) had national clinical NAFLD guidelines. Only five (29%) countries had national campaigns to raise awareness and inform about NAFLD, and seven (41%) countries had a registry of disease burden due to NAFLD.

**Interpretation:** There is a significant lack of PHP addressing NAFLD and its health consequences in the Americas. We also identify a low registry of disease burden due to NAFLD among countries. Our findings support the need for national policies to address NAFLD.

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#### **RESEARCH IN CONTEXT**

#### **Evidence before this study**

- Non-alcoholic fatty liver disease (NAFLD) affects 20-25% of the general population and is associated with morbidity, increased mortality, and elevated healthcare costs.
- A recent cross-sectional study of 29 European countries demonstrated that none of the countries had official national strategies for NAFLD prevention and control.
- There is no information about the development and implementation of PHP in the Americas.

#### Added value of this study

- None of the included countries have established national public health policies to specifically address NAFLD in the Americas.
- We found a low awareness about NAFLD, its related conditions, and an unsatisfactory registry of the burden of NAFLD in the 17 countries studied.

#### Implications of all the available evidence

- Additional public health policies on NAFLD-related conditions (including policies to decrease obesity, diabetes, hypertension, dyslipidemia, and cardiovascular diseases) could contribute to decreasing the burden of NAFLD.
- Implementation of public health policies is urgently needed in the Americas to decrease the NAFLD burden.

#### Search strategy and selection criteria

We did an electronic search up to July 1, 2021, in the MEDLINE (via PubMed) database. We used keywords and free-text words related to NAFLD, diabetes, obesity, hypertension, dyslipidemia,

cirrhosis, hepatocellular carcinoma, cardiovascular diseases, and its public health policies. We hand searched (up to July 1, 2021) governmental websites. We did not limit our search by language.

#### SUMMARY

Non-alcoholic fatty liver disease (NAFLD) affects 20-25% of the general population and is associated with morbidity, increased mortality, and elevated healthcare costs. Most of the NAFLD risk factors are modifiable and, therefore, potentially susceptible to being reduced by public health policies (PHP). To date, there is no information about NAFLD-related PHP in the Americas. In this study, we analyzed the data from 17 American countries and found that none of them have established national PHP to decrease NAFLD-related burden. There is important heterogeneity in the existence of PHP to prevent NAFLD-related conditions. The most developed PHP were related to diabetes (88%), hypertension (82%), cardiovascular diseases (82%), obesity (53%), and dyslipidemia (35%). Further, only seven countries had a registry of the burden of NAFLD, accompanied by scarce efforts to raise awareness in the Americas. Additional policies and the implementation of public health policies are urgently needed in the Americas to decrease the NAFLD burden.

#### INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD), also named metabolic dysfunction-associated fatty liver disease (MAFLD), currently represents the most frequent liver disease globally<sup>1,2</sup>. NAFLD encompasses a broad spectrum of clinical phenotypes ranging from isolated steatosis, different degrees of inflammation and fibrosis, to cirrhosis and its complications such as hepatocellular carcinoma (HCC). To date, it affects 20–25% of the general global population, and its prevalence could increase up to 18% by 2030, due to sedentary lifestyles, obesity, and the increasing prevalence of type 2 diabetes mellitus (T2DM)<sup>3–7</sup>. NAFLD constitutes the second leading cause of liver transplant in several high-income countries, including the United States (US)<sup>8–11</sup>.

To date, liver fibrosis has been correlated with worse long-term prognosis and higher mortality, as opposed to steatosis, which has been generally considered "benign"<sup>12,13</sup>. However, a recent nationwide cohort study in Sweden suggested that even isolated steatosis is associated with higher mortality <sup>14</sup>. Therefore, it is difficult to measure the health care and economic burden of NAFLD due to its underdiagnosis and complex relationship with other diseases<sup>6,15</sup>. In the US, the annual direct medical costs of NAFLD are estimated at \$103 billion dollars, and four European countries (Germany, France, Italy, and the United Kingdom) spend together about €35 billion annually<sup>16</sup>. These costs are highest in patients aged 45-65, and the burden is significantly higher when societal costs are included.

Most risk factors for NAFLD are modifiable. For example, the International Diabetes Federation states that 80% of T2DM cases are preventable with a healthy diet and physical activity<sup>7,17</sup>. Thus, early identification and treatment of individual components of metabolic syndrome are critical in

preventing both cardiovascular and liver-related mortality. Nationwide interventions to reduce obesity and diabetes, such as unhealthy food taxes, and increased access to healthy foods and physical activity could potentially reduce the NAFLD prevalence. However, there is a gap in the evidence regarding the availability and effect of these public health policies (PHP) worldwide. To our knowledge, there is only one cross-sectional study of 29 European countries demonstrating that none of the countries had official national strategies for NAFLD prevention and control<sup>18</sup>.

The Americas are characterized by important social, cultural, ethnic, and economic differences<sup>19,20</sup>. These differences are reflected in its different health problems. Similarly, there are large differences in governance across the region. To date, there is no comprehensive information about the PHP on NAFLD-related conditions in the Americas and the burden of disease related to NAFLD. We aimed to assess the presence of different PHP on NAFLD-related conditions and scientific guidelines including NAFLD-related conditions across 17 American countries. We also evaluated the burden of disease related to NAFLD in terms of prevalence and mortality of chronic liver disease (CLD) due to NAFLD, the incidence of NAFLD-related HCC, and the NAFLD's total burden in disability-adjusted life years (DALYs) in each country included.

#### MATERIALS AND METHODS

#### Data on public health policies

We conducted a cross-sectional multi-national study with data from 17 American countries: Argentina, Bolivia, Brazil, Canada, Chile, Colombia, Cuba, Ecuador, Guatemala, Haiti, Honduras, Mexico, Panama, Paraguay, Peru, the United States, and Uruguay. We constructed a questionnaire to assess the presence of NAFLD PHP and related conditions (e.g., diabetes, obesity, hypertension, among others) in each country, including the questions previously published by Lazarus et al.<sup>18</sup>. We also assessed the main healthcare providers involved in the management of patients with NAFLD, scientific guidelines, awareness, and monitoring mechanisms available in each country. The information was gathered using an electronic form, and the questionnaire is detailed in Appendix (see page 3). The participants were recruited through the American Association for the Study of Liver Diseases (AASLD) and the Latin-American Association for the Study of the Liver (ALEH). We selected hepatologists who actively participated in special interest groups or have a position in governmental institutions related to NAFLD and public health policies. The data of the professionals who answer the questionnaire is summarized in Appendix (see page 4). We requested participation from up to three participants in each country. We only included countries where we obtained a complete response from at least one participant. Two independent reviewers (FV and LL) corroborated the information in government agencies and official media, and the differences were settled by a third reviewer (LAD). We clarified the unclear responses with participants, and supporting documentation was required in cases of inconsistency. Data collection for all countries closed in July 2021. This study was considered IRB exempt since all the information was aggregated at a country level and relied on publicly available data.

#### Data on risk factors and health consequences from NAFLD

We collected the basic socio-demographic information from the World Bank Open Data source (http://databank.worldbank.org) (updated to 2019). We included the prevalence of obesity, diabetes, and hypertension. Data on metabolic dysfunction measures in each country was obtained from the World Health Organization (WHO) Global Information System of Alcohol and Health (GISAH)(up to 2016)<sup>21</sup>. We defined overweight and obesity as a body mass index (BMI) over 25 or 30 kg/m<sup>2</sup>, respectively. Diabetes was defined as fasting glucose  $\geq$ 126 mg/dl (7·0 mmol/l) or history of diagnosis with diabetes or use of insulin or oral hypoglycemic drugs. Finally, we considered hypertension as systolic blood pressure  $\geq$ 140 mmHg or diastolic blood pressure  $\geq$ 90 mmHg. Since NAFLD can coexist with alcohol-associated liver disease (ALD), we also registered alcohol per capita consumption (APC) (in liters of pure alcohol per year)<sup>22</sup>.

The main health consequences related to NAFLD included prevalence and mortality of CLD and cirrhosis due to NAFLD, the incidence of NAFLD-related HCC, and the DALYs related to NAFLD. Data on NAFLD health consequences was collected from the Global Burden of Disease database (updated to 2019)<sup>23</sup>. We also recorded the deceased donor liver transplantation rate from the International Registry in Organ Donation and Transplantation (IRODaT) (https://www.irodat.org) (updated to 2019).

#### Statistical analysis

We described the number of PHP on NAFLD, PHP on NAFLD-related conditions, and the presence of guidelines on NAFLD-related conditions in 2021. We also registered the prevalence and mortality of CLD due to NAFLD, the incidence of NAFLD-related HCC, the NAFLD's total burden in DALYs, and the deceased donor liver transplantation rate in the 17 included countries. We described nominal

data using percentages. The normally distributed data were reported using mean and standard deviation, and not normally distributed data using median and interquartile range. All analyses were performed with STATA software version 16 (StataCorp, College Station, Texas).

#### RESULTS

#### Baseline characteristics of the participant countries

A total of 17 countries were included, accounting for an overall population of 943,784,880 inhabitants in 2019 (93·3% of the continent's population). There was one low-income country, three lower-middle countries, nine upper-middle countries, and four high-income countries (**Table 1**). The median life expectancy at birth was 76 [75-78] years. Haiti and Bolivia had the lowest life expectancy at birth (63 and 71 years, respectively), while the highest life expectancy was observed in Canada, Chile, the US, and Cuba (82, 80, 79, and 79 years, respectively) (**Table 1**). Overall, the median prevalence of overweight and obesity was 34·7% [34·4%-36·0%] and 22·7% [21·2%-28·0%], respectively. The median prevalence of diabetes in adults was 8·5% [8·0%-9·5%], and 19·9% [17·9%-21·4%] of the overall adult population had hypertension. The median APC of included countries was 6·4 [4·4-8·0] liters of pure alcohol per year. **Appendix (see page 5)** summarizes the main incidence and prevalence of risk factors and conditions related to NAFLD.

#### The burden of disease related to NAFLD

A total of 133,748,892 had CLD due to NAFLD, with a median prevalence of 13.6% [11.2%-16.8%]. Cuba, Ecuador, and Mexico had the highest-burden related to NAFLD (22.7%; 19.9%; and 18.1%, respectively), while the lowest burden of disease was observed in Argentina, Canada, and Peru (8.8%; 9.3%; and 10.5%, respectively) (**Figure 1A**).

A total of 28,741 individuals died due to NAFLD CLD in 2019. The median mortality due to NAFLD CLD was 2.5 [1.9-5.0] per 100,000 inhabitants. Mexico, Honduras, and Guatemala exhibited a higher mortality rate due to NAFLD CLD (7.7, 6.5, and 6.0 per 100,000 inhabitants, respectively)

compared to other countries (**Figure 1B**). Inversely, Paraguay, Canada, and Uruguay had a lower mortality rate (1·0, 1·2, and 1·5 per 100,000 inhabitants, respectively). There were 4,602 cases of NAFLD-related HCC in 2019, with a median incidence rate of 0·3 [0·2-0·4] cases per 100,000 inhabitants. The highest incidence rate of NAFLD-related HCC was observed in Canada, the US, and Honduras (1·1, 0·9, and 0·7 per 100,000 inhabitants, respectively) (**Figure 1C**). Also, the median DALYs due to NAFLD were 79·8 [49·2-124·2] DALYs per 100,000 inhabitants, which were higher in Mexico, Guatemala, and Honduras (218·6, 195·4, 187·1, respectively) (**Figure 1D**).

#### Public health policies on NAFLD and related conditions

None of the included countries had a national policy or action plan addressing NAFLD (**Figure 2**). The median number of PHP on NAFLD-related conditions were 4 [4-6]. Only Brazil (6%) had a national strategy for cirrhosis and three (18%) countries had a national strategy on HCC (Brazil, Chile, and Panama). Regarding policies on NAFLD-related conditions, 15 (88%) countries had policies to prevent diabetes, 14 (82%) to prevent hypertension, 14 (82%) to prevent cardiovascular diseases (CVD), and 11 (65%) to decrease alcohol use disorders. The national policies on obesity were one of the less developed categories. In fact, only 9 (53%) countries had PHP on obesity, 12 (71%) had established policies on food labeling, and 15 (88%) had policies to promote physical activity.

#### National guidelines on NAFLD and related conditions

Six countries (35%) had published national clinical NAFLD guidelines. Four out of six countries with national guidelines were those with the highest number of public policies (Brazil, Colombia, Mexico, and Argentina). After the NAFLD diagnosis, all recommended the assessment of cirrhosis and diabetes. Five (83%) included recommendations for dyslipidemia and screening of HCC. Also, four

(67%) clinical guidelines recommended the assessment of CVD and hypertension (Appendix, see page 6).

#### Management of patients with NAFLD, awareness, and monitoring

The hepatologists reported important differences among healthcare providers to manage NAFLD. The foremost specialists in charge of the diagnosis and treatment of NAFLD were gastroenterologists & hepatologists (94%), internal medicine specialists (71%), diabetologists (47%), and primary care providers (41%) (**Figure 3**). There were important differences in the availability of healthcare providers among countries. For example, Brazil, Chile, and Mexico have a wide range of healthcare providers to manage NAFLD, including primary care providers, internal medicine specialists, gastroenterologists, and diabetologists. In contrast, Haiti and Honduras had a limited offer to attend patients with NAFLD. Moreover, only five countries (29%) had referral algorithms for diagnosing and managing patients with NAFLD.

Thirteen countries performed deceased donor liver transplantation in 2019, with a median deceased donor liver transplant rate of 1.7 [0.3-8.1] per million inhabitants (**Table 1**). Countries with the highest transplantation rate were the US, Canada, Argentina, and Chile. Notably, three countries without liver transplantation available were also the countries with the lower number of PHP on NAFLD-related conditions (Honduras, Haiti, and Guatemala).

Just five (29%) countries had national campaigns to raise awareness and inform about NAFLD. Interestingly, only 7 out of 17 countries had a registry of disease burden due to NAFLD. Three (18%) countries had a registry of the incidence and prevalence of NAFLD, and only four (24%) countries included NAFLD among their national disease registries; however, none had a detailed registry of mortality in governmental institutions (**Table 2**).

#### DISCUSSION

NAFLD, defined as hepatic steatosis in the presence of metabolic dysregulation (overweight, obesity, T2DM),<sup>22,24</sup> represents a huge healthcare burden in the Americas. A recent meta-analysis estimated NAFLD prevalence to be 24% and 30% in North and South America, respectively<sup>3</sup>. Therefore, PHP are urgently needed to face this public health problem. In this study, we show that: 1. None of the 17 included countries had established national PHP to decrease NAFLD specifically, and only one country (6%) had PHP to prevent cirrhosis; 2. There is important heterogeneity in the existence of PHP to prevent NAFLD-related conditions, such as diabetes (88%), hypertension (82%), CVD (82%), obesity (53%), and dyslipidemia (35%); 3. There is a low registry of disease burden due to NAFLD, accompanied by scarce efforts to raise awareness in the Americas.

The countries with higher numbers of PHP were Brazil, Colombia, and Mexico. However, there is a critical lack of planning and implementation of PHP in the Americas. We evidenced that even high-income countries (such as the US and Canada) have no established national PHP addressing NAFLD. This lack of NAFLD PHP has also been described in a recent European study where none of the 29 included countries had written strategies or action plans for NAFLD<sup>18</sup>. This finding is of concern due to the high burden of NAFLD and the wide distribution of high-risk genetic polymorphisms in our region. In fact, one of the most important is the Patatin-like phospholipase domain protein 3 (PNPLA3) I148M G/G polymorphism, which is significantly more frequent in individuals with Native American ancestry and is a risk factor for the severity of the disease in NAFLD<sup>25,26</sup>. The access barriers to healthcare systems and the lack of liver transplantation in several countries from the Americas also contribute to increasing the burden of NAFLD. Thus, several access barriers could also be explained by substantial socioeconomic inequalities in different Latin-American countries<sup>27</sup>.

In our study, national clinical guidelines addressing NAFLD were reported in only 35% of countries (Argentina, Bolivia, Brazil, Colombia, Mexico, and the US), which is low and concerning, and comparable to a European study (34%)<sup>18</sup>. The development of NAFLD national clinical guidelines is not trivial and must be encouraged, since adequate surveillance and management of NAFLD could stop progression of the disease's course. The impact of national guidelines in improving the patient outcomes has also been observed in other diseases, such as pneumonia, where the implementation of clinical guidelines led to a decrease of hospital costs, length of stay, and mortality<sup>31–34</sup>. Similarly, several hepatology associations have contributed with guidelines to improve care on NAFLD<sup>4,24,35</sup>. Undoubtedly, the impact of these guidelines is invaluable and the recommendations should be disseminated to physicians in clinical practice.

Increasing trends in obesity and T2DM prevalence may lead to a higher NAFLD prevalence in the next decades<sup>36,37</sup>. We observed an important establishment of PHP aimed to decrease diabetes, obesity, hypertension, and dyslipidemia. The development of those policies is relevant since prior evidence has demonstrated a strong effect in decreasing disease burden due to NAFLD<sup>38–40</sup>. In fact, a study from the US using a microsimulation model estimated that a 20% reduction in added sugar consumption is projected to avert 0.767 million DALYs and a total of US\$ 10.3 billion, annually<sup>39</sup>. Additionally, the odds of NAFLD increased by 13% to 38% for every 1 unit increase in BMI, and by 3% to 10% for every 1 cm increase in waist circumference<sup>38</sup>. Therefore, it is important to involve key stakeholders, including scientific societies, governments, non-governmental organizations, the pharmaceutical industry, and others to promote the PHP on NAFLD development with a whole society approach<sup>40,41</sup>.

There is growing evidence that patients with NAFLD have increased cardiovascular morbidity and mortality. Many studies have shown an association of NAFLD with several markers of subclinical atherosclerosis (i.e., increased carotid artery intimal-medial thickness, impaired flow-mediated vasodilation, increased arterial stiffness, or increased coronary artery calcification) independent of traditional risk factors and metabolic syndrome<sup>42–44</sup>. Thus, the patients with NAFLD have demonstrated a significantly increased prevalence of clinically manifest CVD<sup>45–47</sup>. In a recent meta-analysis, NAFLD was significantly associated with an increased risk of CVD events, which was directly proportional to the NAFLD severity<sup>48</sup>. Several mechanisms could explain this relationship, including elevated insulin resistance and oxidative stress<sup>48</sup>. Notably, 14 out of 17 countries had policies on CVD, which could potentially impact the development of NAFLD, progression, and mortality due to CVD among patients with NAFLD.

The excessive accumulation of free fatty acids increases the production of hepatotoxic free oxygen radical species, contributing to the development of cirrhosis and HCC<sup>49–51</sup>. NAFLD is the third most common risk factor for HCC and it is increasing worldwide<sup>52,53</sup>. Moreover, HCC has also been reported in NAFLD patients without advanced liver fibrosis or cirrhosis<sup>54</sup>. There has been a tenfold increase in liver transplantation for NAFLD-related HCC in the US between 2003-2015, and it is expected that there will be up to 45,000 cases by 2025<sup>7</sup>. Furthermore, HCC incidence is disproportionately increasing in certain ethnic groups, including African Americans, Hispanics, and whites<sup>55</sup>. Patients with NAFLD-related HCC are older, have a shorter survival time, more often have CVD, and are more likely to die from their primary liver cancer than other HCC patients<sup>52,53,56</sup>. In spite of this, a recent study showed that NAFLD patients were less likely to receive HCC screening than their hepatitis C virus counterparts (HR 0.44, 95%CI 0.19–0.99, p<0.05)<sup>57</sup>. Unfortunately, only

active screening for HCC in patients with NAFLD. Consequently, the establishment of PHP is needed to tackle NAFLD-related HCC in the Americas.

Multiple aspects could be developed to improve the prevention, screening, and treatment of NAFLD. The development of a written national plan to decrease NAFLD could have a strong impact, in the same line as other important public health problems such as alcohol<sup>21,28</sup>. Indeed, it reflects the commitment of countries to reduce health consequences due to NAFLD. These policies could be established as separate documents or included in a broader PHP, including clear responsibilities, objectives, strategies, and targets. Preparedness is also a relevant aspect and contributes to preventing and managing the burden of NAFLD<sup>29</sup>. A recent study including 102 assessed a preparedness index that considers policies, guidelines, civil awareness, epidemiology and data, NAFLD detection, and NAFLD care management, demonstrating that a third of countries scored zero<sup>29</sup>. It is crucial to increase awareness about NAFLD and advocate for PHP development on NAFLD, which could be facilitated by frameworks especially designed for this purpose<sup>30</sup>.

Finally, this study has some limitations to address. The most important limitation was that we did not measure the implementation along the time for each PHP. Therefore, the PHP could be established several years ago or near the end of data collection. Thus, it is not adequate to establish associations with health outcomes. Also, we did not have information about the implementation, since policies may exist but they may not be currently enforced or fully implemented. Another important aspect to mention is the potential heterogeneity of registry between countries. In fact, we could have differences in the registry of PHP and also in disease burden due to NAFLD and related health conditions, especially in countries with a lower income. In conclusion, the current study demonstrates a lack of PHP addressing NAFLD and low awareness of NAFLD and its consequences in the Americas. There was a significant establishment of PHP on NAFLD-related conditions, especially to decrease diabetes, hypertension, and cardiovascular diseases. Our findings constitute a call for action and encourage the development of national policies against NAFLD and national guidelines to decrease the burden of NAFLD.

# **ABBREVIATIONS:**

- AASLD: American Association for the Study of Liver Diseases
- ALD: alcohol-associated liver disease
- ALEH: Latin-American Association for the Study of the Liver
- APC: alcohol per capita consumption
- CLD: chronic liver disease
- CVD: cardiovascular disease
- DALYs: disability-adjusted life years
- GDP: Gross domestic product
- GISAH: Global Information System of Alcohol and Health
- HCC: hepatocellular carcinoma
- MAFLD: metabolic dysfunction-associated fatty liver disease
- NAFLD: non-alcoholic fatty liver disease
- PHP: public health policies
- PNPLA3: Patatin-like phospholipase domain protein 3
- T2DM: type 2 Diabetes Mellitus
- UK: United Kingdom
- **US: United States**
- WHO: World Health Organization

#### REFERENCES

- 1 Younossi Z, Tacke F, Arrese M, *et al.* Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. *Hepatology* 2019; **69**: 2672–82.
- 2 Cheemerla S, Balakrishnan M. Global Epidemiology of Chronic Liver Disease. *Clin Liver Dis* 2021; **17**: 365–70.
- 3 Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016; **64**: 73–84.
- 4 Chalasani N, Younossi Z, Lavine JE, *et al.* The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology* 2018; **67**: 328–57.
- 5 Mahady SE, George J. Predicting the future burden of NAFLD and NASH. J. Hepatol. 2018; **69**: 774–5.
- 6 Pimpin L, Cortez-Pinto H, Negro F, *et al.* Burden of liver disease in Europe: Epidemiology and analysis of risk factors to identify prevention policies. *J Hepatol* 2018; **69**: 718–35.
- 7 Shetty A, Syn W-K. Health and Economic Burden of Nonalcoholic Fatty Liver Disease in the United States and Its Impact on Veterans. *Fed Pract* 2019; **36**: 14–9.
- 8 Wong RJ, Aguilar M, Cheung R, *et al.* Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. Gastroenterology. 2015; **148**: 547–55.
- 9 Singal AK, Hasanin M, Kaif M, Wiesner R, Kuo Y-F. Nonalcoholic Steatohepatitis is the Most Rapidly Growing Indication for Simultaneous Liver Kidney Transplantation in the United States. *Transplantation* 2016; **100**: 607–12.
- 10 Díaz LA, Norero B, Lara B, *et al.* Prioritization for liver transplantation using the MELD score in Chile: Inequities generated by MELD exceptions.: A collaboration between the Chilean Liver Transplant Programs, the Public Health Institute and the National Transplant Coordinator. *Ann Hepatol* 2019; **18**: 325–30.
- 11 Haldar D, Kern B, Hodson J, *et al.* Outcomes of liver transplantation for non-alcoholic steatohepatitis: A European Liver Transplant Registry study. *J Hepatol* 2019; **71**: 313–22.
- 12 Angulo P, Kleiner DE, Dam-Larsen S, *et al.* Liver Fibrosis, but No Other Histologic Features, Is Associated With Long-term Outcomes of Patients With Nonalcoholic Fatty Liver Disease. *Gastroenterology* 2015; **149**: 389–97.e10.
- 13 Ekstedt M, Hagström H, Nasr P, *et al.* Fibrosis stage is the strongest predictor for diseasespecific mortality in NAFLD after up to 33 years of follow-up. *Hepatology* 2015; **61**: 1547–54.
- 14 Simon TG, Roelstraete B, Khalili H, Hagström H, Ludvigsson JF. Mortality in biopsy-confirmed

nonalcoholic fatty liver disease: results from a nationwide cohort. *Gut* 2021; **70**: 1375–82.

- 15 Targher G, Tilg H, Byrne CD. Non-alcoholic fatty liver disease: a multisystem disease requiring a multidisciplinary and holistic approach. *Lancet Gastroenterol Hepatol* 2021; **6**: 578–88.
- 16 Younossi ZM, Blissett D, Blissett R, *et al.* The economic and clinical burden of nonalcoholic fatty liver disease in the United States and Europe. *Hepatology* 2016; **64**: 1577–86.
- 17 Tuomilehto J, Lindström J, Eriksson JG, *et al.* Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *N Engl J Med* 2001; **344**: 1343–50.
- 18 Lazarus JV, Ekstedt M, Marchesini G, *et al.* A cross-sectional study of the public health response to non-alcoholic fatty liver disease in Europe. *J Hepatol* 2020; **72**: 14–24.
- 19 Díaz LA, Roblero JP, Bataller R, Arab JP. Alcohol-Related Liver Disease in Latin America: Local Solutions for a Global Problem. *Clin Liver Dis* 2020; **16**: 187–90.
- 20 Arab JP, Bataller R, Roblero JP. Are We Really Taking Care of Alcohol-Related Liver Disease in Latin America? *Clin Liver Dis* 2020; **16**: 91–5.
- 21 World Health Organization. Global Status Report on Alcohol and Health 2018. World Health Organization, 2019.
- 22 Eslam M, Newsome PN, Sarin SK, *et al.* A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. *J Hepatol* 2020; **73**: 202–9.
- 23 Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2019 (GBD 2019) reference life table. 2021. DOI:10.6069/1D4Y-YQ37.
- 24 Arab JP, Dirchwolf M, Álvares-da-Silva MR, *et al.* Latin American Association for the study of the liver (ALEH) practice guidance for the diagnosis and treatment of non-alcoholic fatty liver disease. *Ann Hepatol* 2020; **19**: 674–90.
- 25 Salameh H, Raff E, Erwin A, et al. PNPLA3 Gene Polymorphism Is Associated With Predisposition to and Severity of Alcoholic Liver Disease. Am J Gastroenterol 2015; 110: 846– 56.
- 26 Martínez LA, Larrieta E, Kershenobich D, Torre A. The Expression of PNPLA3 Polymorphism could be the Key for Severe Liver Disease in NAFLD in Hispanic Population. *Ann Hepatol* 2017; 16: 909–15.
- 27 Houghton N, Bascolo E, Del Riego A. Socioeconomic inequalities in access barriers to seeking health services in four Latin American countries. *Rev Panam Salud Publica* 2020; **44**: e11.
- 28 Díaz LA, Idalsoaga F, Fuentes-López E, et al. Impact of public health policies on alcoholassociated liver disease in Latin America: An ecological multi-national study. *Hepatology* 2021; published online June 16. DOI:10.1002/hep.32016.
- 29 Lazarus JV, Mark HE, Villota-Rivas M, *et al.* The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge? *J Hepatol* 2021;

published online Dec 8. DOI:10.1016/j.jhep.2021.10.025.

- 30 Lazarus JV, Mark HE, Colombo M, *et al.* A sustainable development goal framework to guide multisectoral action on NAFLD through a societal approach. *Aliment Pharmacol Ther* 2021; published online Dec 5. DOI:10.1111/apt.16720.
- 31 Cabana MD, Rand CS, Powe NR, *et al.* Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999; **282**: 1458–65.
- 32 Rello J, Lorente C, Bodí M, Diaz E, Ricart M, Kollef MH. Why do physicians not follow evidence-based guidelines for preventing ventilator-associated pneumonia?: a survey based on the opinions of an international panel of intensivists. *Chest* 2002; **122**: 656–61.
- 33 Dean NC, Bateman KA, Donnelly SM, Silver MP, Snow GL, Hale D. Improved clinical outcomes with utilization of a community-acquired pneumonia guideline. *Chest* 2006; **130**: 794–9.
- 34 Martínez R, Reyes S, Lorenzo MJ, Menéndez R. Impact of guidelines on outcome: the evidence. *Semin Respir Crit Care Med* 2009; **30**: 172–8.
- 35 European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the Management of Non-Alcoholic Fatty Liver Disease. *Obes Facts* 2016; **9**: 65–90.
- 36 Gallardo-Rincón H, Cantoral A, Arrieta A, *et al.* Review: Type 2 diabetes in Latin America and the Caribbean: Regional and country comparison on prevalence, trends, costs and expanded prevention. *Prim Care Diabetes* 2021; **15**: 352–9.
- 37 Targher G, Corey KE, Byrne CD, Roden M. The complex link between NAFLD and type 2 diabetes mellitus mechanisms and treatments. *Nat Rev Gastroenterol Hepatol* 2021; published online May 10. DOI:10.1038/s41575-021-00448-y.
- 38 Pang Q, Zhang J-Y, Song S-D, *et al.* Central obesity and nonalcoholic fatty liver disease risk after adjusting for body mass index. *World J Gastroenterol* 2015; **21**: 1650–62.
- 39 Vreman RA, Goodell AJ, Rodriguez LA, Porco TC, Lustig RH, Kahn JG. Health and economic benefits of reducing sugar intake in the USA, including effects via non-alcoholic fatty liver disease: a microsimulation model. *BMJ Open* 2017; **7**: e013543.
- 40 Arab JP, Díaz LA, Dirchwolf M, *et al.* NAFLD: Challenges and opportunities to address the public health challenge in Latin America. *Ann Hepatol* 2021; **24**: 100359.
- 41 Lazarus JV, Mark HE, Anstee QM, *et al.* Advancing the global public health agenda for NAFLD: a consensus statement. *Nat Rev Gastroenterol Hepatol* 2021; published online Oct 27. DOI:10.1038/s41575-021-00523-4.
- 42 Oni ET, Agatston AS, Blaha MJ, *et al.* A systematic review: burden and severity of subclinical cardiovascular disease among those with nonalcoholic fatty liver; should we care? *Atherosclerosis* 2013; **230**: 258–67.

- 43 Puchner SB, Lu MT, Mayrhofer T, *et al.* High-risk coronary plaque at coronary CT angiography is associated with nonalcoholic fatty liver disease, independent of coronary plaque and stenosis burden: results from the ROMICAT II trial. *Radiology* 2015; **274**: 693–701.
- 44 Johnston MP, Patel J, Byrne CD. Update on cardiovascular risk in nonalcoholic fatty liver disease. *Curr Opin Cardiol* 2021; **36**: 478–86.
- 45 Ballestri S, Lonardo A, Bonapace S, Byrne CD, Loria P, Targher G. Risk of cardiovascular, cardiac and arrhythmic complications in patients with non-alcoholic fatty liver disease. *World J Gastroenterol* 2014; **20**: 1724–45.
- 46 Byrne CD, Targher G. NAFLD: a multisystem disease. J Hepatol 2015; 62: S47–64.
- 47 Lonardo A, Sookoian S, Pirola CJ, Targher G. Non-alcoholic fatty liver disease and risk of cardiovascular disease. *Metabolism* 2016; **65**: 1136–50.
- 48 Targher G, Byrne CD, Lonardo A, Zoppini G, Barbui C. Non-alcoholic fatty liver disease and risk of incident cardiovascular disease: A meta-analysis. *J Hepatol* 2016; **65**: 589–600.
- 49 Sanyal AJ, Campbell-Sargent C, Mirshahi F, *et al.* Nonalcoholic steatohepatitis: association of insulin resistance and mitochondrial abnormalities. *Gastroenterology* 2001; **120**: 1183–92.
- 50 Angulo P. Nonalcoholic fatty liver disease. N Engl J Med 2002; 346: 1221–31.
- 51 Marra F, Svegliati-Baroni G. Lipotoxicity and the gut-liver axis in NASH pathogenesis. *J Hepatol* 2018; **68**: 280–95.
- 52 Ascha MS, Hanouneh IA, Lopez R, Tamimi TA-R, Feldstein AF, Zein NN. The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis. Hepatology. 2010; **51**: 1972–8.
- 53 Younossi ZM, Otgonsuren M, Henry L, *et al.* Association of nonalcoholic fatty liver disease (NAFLD) with hepatocellular carcinoma (HCC) in the United States from 2004 to 2009. Hepatology. 2015; **62**: 1723–30.
- 54 Loomba R, Lim JK, Patton H, El-Serag HB. AGA Clinical Practice Update on Screening and Surveillance for Hepatocellular Carcinoma in Patients With Nonalcoholic Fatty Liver Disease: Expert Review. Gastroenterology. 2020; **158**: 1822–30.
- 55 Kulik L, El-Serag HB. Epidemiology and Management of Hepatocellular Carcinoma. *Gastroenterology* 2019; **156**: 477–91.e1.
- 56 Mohamad B, Shah V, Onyshchenko M, *et al.* Characterization of hepatocellular carcinoma (HCC) in non-alcoholic fatty liver disease (NAFLD) patients without cirrhosis. Hepatology International. 2016; **10**: 632–9.
- 57 Tavakoli H, Robinson A, Liu B, *et al.* Cirrhosis Patients with Nonalcoholic Steatohepatitis Are Significantly Less Likely to Receive Surveillance for Hepatocellular Carcinoma. *Dig Dis Sci* 2017; **62**: 2174–81.

# TABLES

Table 1. Main socio-demographic characteristics of the included countries. Data was updated to

# 2019.

Country	Population	Gross domestic product per capita*	Gini index	Classification by incoming level	Life expectancy at birth (years)	Deceased liver transplantation rate <sup>+</sup>
Argentina	44,938,710	9912	42.9	Upper-middle	76	10.7
Bolivia	11,513,100	3552.1	41.6	Lower-middle	71	0
Brazil	211,049,530	8717·2	53.4	Upper-middle	75	10
Canada	37,593,380	46189.7	33.3	High-income	82	14.1
Chile	18,952,040	14896.5	44.4	High-income	80	8.1
Colombia	50,339,440	6428.7	51.3	Upper-middle	77	5.3
Cuba	11,333,480	8821.8	40.7	Upper-middle	79	0.9
Ecuador	17,373,660	6183.8	45.7	Upper-middle	77	1.6
Guatemala	16,604,030	4620	48.3	Lower-middle	74	0
Haiti	11,263,080	1272.5	41.1	Low-income	63	0
Honduras	9,746,120	2574.9	48.2	Lower-middle	75	0
Mexico	127,575,530	9946	45.4	Upper-middle	75	1.7
Panama	4,246,440	15731	49.8	Upper-middle	78	2.1
Paraguay	7,044,640	5414.8	45.7	Upper-middle	74	0.3
Peru	32,510,450	6977.7	41·5	Upper-middle	76	1.4
United States	328,239,520	65297.5	41.4	High-income	79	25.4
Uruguay	3,461,730	16190.1	39.7	High-income	78	7

\* In US dollars (actual prizes) \* Per million population

Country	Management and referral algorithms in primary care	National awareness campaigns about NAFLD	National registry of NAFLD incidence and prevalence	National registry of NAFLD mortality	National registry of diseases includes NAFLD
Argentina	Yes	-	-	-	-
Bolivia	-	-	-	-	Yes
Brazil	Yes	Yes	-	-	Yes
Canada	-	Yes	-	-	-
Chile	-	-	Yes	-	-
Colombia	-	-	Yes	-	-
Cuba	Yes	-	Yes	-	-
Ecuador	-	-	-	-	-
Guatemala	-	-	-	-	-
Haiti	-	-	-	-	-
Honduras	-	-	-	-	-
Mexico	Yes	Yes	-	-	-
Panama	-	-	-	-	-
Paraguay	-	-	-	-	-
Peru	Yes	-	-	-	-
United States	-	Yes	-	-	Yes
Uruguay	-	Yes	-	-	Yes

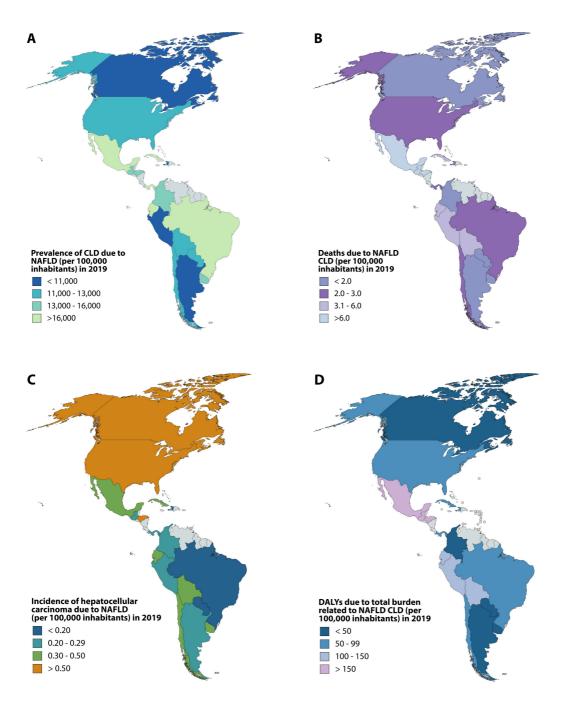
# Table 2. National surveillance and control of NAFLD among American countries.

# **FIGURE LEGENDS**

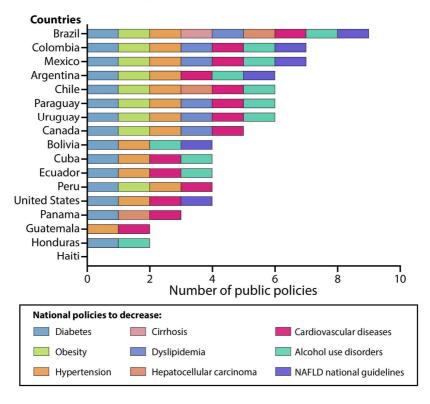
**Figure 1. Main NAFLD related outcomes among the Americas in 2019.** (A) Prevalence of cirrhosis due to NAFLD; (B) NAFLD-attributable deaths; (C) Incidence of hepatocellular carcinoma in patients with NAFLD; (D) Disability Adjusted Life Years (DALYs) due to NAFLD.

**Figure 2.** Public health policies on NAFLD related conditions in **17** countries from the Americas. Each bar represents the national public policies to decrease the NAFLD related conditions.

Figure 3. The healthcare providers that are usually responsible for the care for NAFLD patients in **17 American countries.** Each bar represents the type of physician responsible for NAFLD patients.



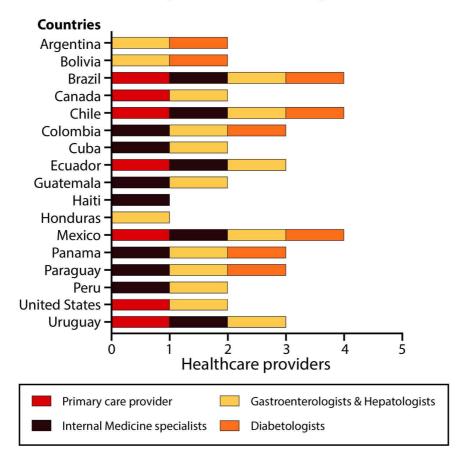
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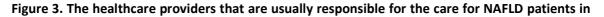
# Publich health policies on NAFLD related conditions

# Figure 2. Public health policies on NAFLD related conditions in 17 countries from the Americas.

Each bar represents the national public policies to decrease the NAFLD related conditions.



# Healthcare providers to manage NAFLD



17 American countries. Each bar represents the type of physician responsible for NAFLD patients.