The global, regional, and national burden and trends of NAFLD in 204 countries and territories: an analysis from Global Burden of Disease 2019

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Research Article

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Abstract

Background

Nonalcoholic fatty liver disease (NAFLD) poses a substantial socioeconomic burden and is becoming the fastest-growing driver of chronic liver disease, potentially accompanied by a poor prognosis. We aim to elucidate the global and regional epidemiologic changes in NAFLD during the past thirty years and explore the relevant causes.

Methods

Data on NAFLD incidence, prevalence, death, and disability-adjusted life-years (DALYs) were extracted from the Global Burden of Disease Study 2019. In addition, we also investigated the correlation between the NAFLD burden and the social development degree. Finally, the associations of the three common comorbidities with NAFLD were determined.

Results

Globally, the incidence and prevalence of NAFLD both increased drastically from 1990 to 2019, mainly affecting young adults. Meanwhile, the deaths and DALYs increased significantly as well, dominating the aged group. However, the overall age-standardized death rate (ASDR) and DALY rate presented decreasing trends. Moreover, the sociodemographic index (SDI) appeared to have obvious negative associations with the age-standardized prevalence rate (ASPR), ASDR and age-standardized DALYs, indicating a more serious NAFLD burden in less developed regions. Finally, we found that the incidence and prevalence of NAFLD were positively related to those of diabetes mellitus type 2 (DM2), stroke and ischaemic heart disease (IHD).

Conclusions

NAFLD is leading to increasingly serious health challenges worldwide. Comprehensive acquisition of the epidemiologic pattern for NAFLD and the identification of high-risk comorbidities may help policy-makers and clinical physicians develop cost-effective prevention and control strategies, especially in countries with a high NAFLD burden.

1. Introduction

Nonalcoholic fatty liver disease (NAFLD), characterized by the accumulation of fat (hepatic steatosis) in more than 5% of hepatocytes, is currently recognized as an important driver leading to an increasing burden of chronic liver disease (CLD) worldwide and thus far lacks effective pharmacological therapies[1-4]. Among individuals with NAFLD, some will develop nonalcoholic steatohepatitis (NASH) and potentially progress to end-stage liver cirrhosis and carcinoma, with possible requirements for liver transplants and a poor prognosis[5-8]. In this context, many articles have investigated the epidemic pattern and attributable risk factors for NAFLD[2, 3, 9] to provide beneficial references for the prevention and control of this disease and thereby to alleviate the global and regional socioeconomic burden of NAFLD.

In fact, tremendous heterogeneity of the NAFLD burden is observed around the world, and NAFLD has become the most rapidly growing contributor to liver mortality and morbidity[10]. Substantial NAFLD burdens have been reported successively in Asia, the Middle East, North Africa, Canada and the United Kingdom[2, 11-13], which all indicate an urgent need for the systematic management and control of this disease. In addition to the liver insult itself, concomitant complications and comorbidities in other organs and systems related to NAFLD have likewise been investigated intensely[14]. The development of NAFLD necessitates the retention of intrahepatic triacylglycerol (IHTAG), whereas IHTAG has been reported to be strongly associated with obesity, insulin resistance and diabetes mellitus type 2 (DM2)[15]. Self-evident associations between NAFLD and these disorders have been demonstrated in the clinic, and NAFLD patients tend to have DM2, dyslipidaemia, and hypertension, which increase the susceptibility to cardiovascular complications[14, 16, 17]. The common factors contributing to the death of NAFLD patients are often manifested in various complications, such as stroke and cardiovascular emergencies[18]. Accordingly, a greater understanding of the risk factors or possible comorbidities of NAFLD may help to decrease morbidity and mortality and thereby alleviate the disease burden.

To systematically and comprehensively grasp the global and regional socioeconomic burden of NAFLD during the past thirty years and to explore the interconnected diseases, we summarized the incidence, prevalence, mortality and disability-adjusted life years (DALYs) from the GBD Study 2019 in the current article. This updated epidemiologic pattern and potential risk factors for NAFLD are expected to benefit the development of efficient prevention and control policies, especially for those dedicated to the clinical treatment of NAFLD and public health care.

2. Methods

2.1 Data acquisition

Global Burden of Disease 2019 (GBD 2019) provides the information about the burdens of 369 diseases and injuries along with 87 risk factors in the globe, different geographic areas, and 204 countries and territories[19]. Data on the NAFLD burden from 1990 to 2019, including its incidence, prevalence, death, DALY, and their corresponding age-standardized rates (ASRs), were acquired from the Global Health Data Exchange GBD Results Tool (http://ghdx.healthdata.org/gbd-results-tool). Meanwhile, information about the distributions of sex and age and related comorbidities, including DM2, stroke,

and ischaemic heart disease (IHD), was also obtained. The rates were standardized according to the GBD world population and were reported per 100 000 person-years. For the current report, we used the GBD Results Tool to extract the estimates and their 95% certainty intervals (CIs) for the prevalence of cases, deaths, and DALYs as measures of the NAFLD burden from 1990 to 2019 by region and country. To better exhibit the age distribution of the NAFLD burden, the patients were classified into 3 groups, namely, those aged 15 to 49 years, 50 to 69 years, and above 70 years (no data for those under 15 years). The social developmental index (SDI) is a composite indicator of total fertility, per capita income, and the years of schooling and was formulated to reflect the social developmental degree, which has been reported to be correlated with the incidence and mortality of diseases. Base on that, the 204 countries and territories were classified into 5 groups according to the SDI quintile (low-SDI, low-middle-SDI, middle-SDI, high-middle-SDI, and high-SDI) to explore the association between NAFLD burden and social development degrees in different regions.

2.2 Statistical analysis

The incidence, prevalence, death and DALYs and their corresponding ASRs were the main metrics characterizing the NAFLD burden and were compared at the global, regional, and country levels. CIs were calculated from 1000 estimates for each parameter, and 95% CIs were defined by the 25th and 975th values of the ordered 1000 estimates; 95% CI excluding 0 was considered statistically significant. To investigate the dynamic changes in NAFLD burden, we further calculated the estimated annual percentage change (EAPC) to delineate the temporal trend in different ASRs for the NAFLD burden. Moreover, we constructed a regression model fitting the natural logarithm of the ASR with the calendar year, namely, ln (ASR) = $\alpha + \beta^*$ calendar year + ε, to estimate the EAPC with its 95% confidence interval (CI) based on the formula of $100 \times (\exp(\beta) - 1)$. If the EAPC value and its 95% CI were both above zero, the change trend of ASR was considered upwards, and vice versa. Otherwise, the ASR was considered stable over time[20]. Finally, we examined the shapes of the association between the ASRs of NAFLD and the SDI using fit spline models[21], as well as associations between the incidence/prevalence and DM2/stroke/IHD. All statistical analyses were performed using GraphPad Prism 8 software.

3. Results

3.1 NAFLD's incidence

Globally, the incidence of NAFLD increased sharply in the past thirty years from 88,180 (95% CI: 62,300~128,320) in 1990 to 172,330 in 2019 (95% CI: 125,780~243,640), while there were no obvious changes after standardization by age (EAPC: 0.1 (95% CI: -0.04~0.23)) (Table 1). As shown in Figure 1A and Table 1, there were elevations in the incidence in both sexes, with a slightly higher incidence in women. Meanwhile, various SDI regions presented with gradually increasing NAFLD incidences, which mainly affected the low-middle (from 10,950 in 1990 to 26,640 in 2019) and middle SDI regions (from 32,460 in 1990 to 69,670 in 2019). However, there were no clear changes in ASIR among different SDI regions or by sex (Figure S1A).

Although the overall incidences displayed upward conditions, ASIR of NAFLD and its change trend presented immense heterogeneity among different countries and territories (Figure 3A and 3E, Table 1). Specifically, the top 3 ASIRs of NAFLD were Central Latin America (6.88 per 100,000 populations), Andean Latin America (5.62 per 100,000 populations), and Central Asia (4.19 per 100,000 populations). Central Asia, Eastern Europe and the Middle East presented with great increases in ASIR changes during the past thirty years, with relatively higher EAPCs of ASIRs. East Asia had a negative change trend in ASIR (Figure 3E). Furthermore, from the country perspective, Mongolia had the highest ASIR in 2019, and Papua New Guinea had the lowest. Finally, we analysed the associations between SDI and ASIR among 21 regions and 204 countries from 1990 to 2019, which presented no obvious correlations (Figure 4A and 4E).

3.2 NAFLD's prevalence

In the past three decades, the prevalence of NAFLD increased by more than two-fold at the global level from 561,370,000 (95% CI: 498,430,000~633,300,000) in 1990 to 1,235,700,000 (95% CI: 1,109,540,000~1,378,530,000) in 2019 (Table 2). EAPC, indicating the temporal trend of NAFLD ASPR, also presented significant upregulation (0.77 (95% CI: 0.69~0.85)). There were few marked differences between sexes or among various SDI regions regarding the prevalence and its change trend, all showing obvious upward changes (Figure 1B, Figure S1B, Table 2).

In Table 2, East Asia, South Asia, North Africa and the Middle East maintained the highest prevalence globally in 1990 and 2019. However, the top three prevalences after age standardization were in North Africa and the Middle East, Southeast Asia, and Southern Sub-Saharan Africa (Figure 3B, Table 2). Meanwhile, the regions with a higher EAPC of ASPR were around the Mediterranean (Figure 3F). Egypt had the highest ASPR in 2019 among all countries. Moreover, there were slightly negative correlations between ASPR and SDI among 21 regions (R=-0.44, P<0.0001) and 204 countries (R=-0.28, P<0.0001) (Figure 4B and 4F), which demonstrated that the more developed the region was, the lower the ASPR.

3.3 NAFLD's death

Although the global deaths due to NAFLD increased by almost 2-fold (from 93,760 in 1990 to 168,970 in 2019), the age-standardized death rate appeared to descend from 2.39 per 100,000 population (95% CI: 1.84~3.05) in 1990 to 2.09 per 100,000 population (95% CI: 1.61~2.60) in 2019, as demonstrated by the EAPC of ASDR with a negative value (-0.67 (95% CI: -0.76~-0.57)) (Table 3). After classification by sex and SDI value, the cases of death sharply increased and the ASDR visibly decreased among all groups, which is similar to that observed at the global level (Figure 1C, Figure S1C, Table 3).

Throughout various regions, NAFLD mortality and ASDR revealed extreme variations. East and south Asia had the highest mortality in both 1990 and 2019, while the top three ASDRs were Central Latin America, Andean Latin America, and Eastern Sub-Saharan Africa (Figure 3C, Table 3). However, due to the relatively high ASDR in 1990, the temporal changes displayed negative trends in most regions. The most significant reductions in ASDR were observed in East Asia (EAPC: -3.04 (95% CI: -3.4~-2.69)), high-income Asia Pacific (EAPC: -1.66 (95% CI: -1.97~-1.34)), and Western Europe (EAPC: -1.32 (95% CI: -1.41~-1.24)) (Figure 3G, Table 3). Similar to ASPR, Egypt had the highest ASDR in 2019. In addition, correlation analyses demonstrated that SDI had a negative association

with ASDR among 21 regions (R=-0.48, P<0.0001) and 204 countries (R=-0.58, P<0.001) (Figure 4C and 4G), which might indicate higher ASDR in developing territories.

3.4 NAFLD's DALY

DALY is a critical parameter assessing disease burden, including years of life lost (YLL) due to premature death and years lived with disability (YLD). As shown in Table 4, global DALYs regarding NAFLD were elevated from 2,711,270 (95% CI: 2,078,580~3,478,940) to 4,417,280 (95% CI: 3,348,220~5,671,200). However, age-standardized DALYs presented decreased changes, with an EAPC of -0.82 (95% CI: -0.93~-0.70). In Figure 1D, the DALYs in both sexes and among different SDI regions exhibited obvious increases. However, the age-standardized DALYs all presented decreasing trends, with a more significant decline in women relative to men and in the middle SDI region relative to other SDI regions (Figure S1D, Table 4).

Similar to the epidemiologic pattern of NAFLD death, the highest DALYs affected East and South Asia. Central Latin America, Andean Latin America, and Central Asia occupied the top three age-standardized DALYs (Figure 3D). The decline in age-standardized DALY was most pronounced in East Asia (EAPC: -3.42 (95% CI: -3.82~-3.03)), the high-income Asia Pacific (EAPC: -2.15 (95% CI: -2.48~-1.81)), and Western Europe (EAPC: -1.62 (95% CI: -1.71~-1.53)), whereas Eastern Europe and Central Asia presented significant elevations (Figure 3H, Table 4). Finally, we discovered that age-standardized DALYs had a marked negative correlation with SDI among 21 territories (R=-0.45, P<0.0001) (Figure 4D) or among 204 countries (R=-0.56, P<0.0001) (Figure 4H).

3.5 Age distribution

As depicted in Figure 2, all age groups presented gradually increasing trends in incidence, prevalence, death and DALYS, especially in low-middle SDI regions, regardless of sex and SDI values. Nevertheless, there was a certain heterogeneity in the specific age distribution. Young adults (age from 15 to 49 years) dominated the NAFLD incidence and prevalence. In terms of NAFLD deaths, those aged 50 to 69 years were mostly men, and the elderly (age above 70 years) held the dominant place among women, whereas young adults had relatively low mortality, which might correlate with the chronic and slow progression of NAFLD. The NAFLD DALYs mainly influenced the quinquagenarians, but in relatively underdeveloped regions, the DALYs of young adults remained close to the quinquagenarians. Consequently, age may be a vital factor affecting the NAFLD burden in various regions.

3.6 Associations between NAFLD and other comorbidities

To further explore this hazardous disease, we analysed the associations between NAFLD and three common interconnected disorders[22]. Interestingly, we uncovered that the incidence and prevalence of NAFLD both presented strongly positive correlations with that of DM2, stroke, and IHD (Figure 5), in 21 territories and 204 countries.

4. Discussion

In this study, we comprehensively assessed the global burden of NAFLD and compared its associations with common correlative diseases. In general, the increasing disease burden caused by NAFLD has placed heavy pressure on contemporary society at a gradual pace over recent decades, with corresponding epidemiological parameters showing upward changes, including increases in incidence, prevalence, deaths, and DALYs. A previous study[23] suggested a significant shift in NAFLD burden toward a younger population, which was echoed by our findings. However, after age standardization, there were no obvious upregulations in NAFLD incidence, even though declining alterations in ASDR and age-standardized DALYs were observed. Meanwhile, we uncovered distinctly negative correlations between the SDI and ASPR, ASDR, and age-standardized DALYs. Finally, we confirmed three strongly relevant diseases accompanied by NAFLD incidence and prevalence, namely, DM2, stroke, and IHD. Therefore, the systematic understanding of global epidemiologic patterns for NAFLD and its interrelated disorders may be valuable for the development of corresponding prevention and control strategies, especially for public health policy-makers and clinical physicians.

Compared to 1990, the overall incidence and prevalence of NAFLD in 2019 increased by approximately two-fold, mainly impacting low and middle SDI regions, such as some countries in the Middle East and North Africa[2, 24]. Furthermore, the same rising socioeconomic burden of NAFLD has influenced relatively developed regions. Williams reported in their study that the prevalence of NAFLD was up to 46%, with the highest rate in Hispanics (58.3%), followed by Caucasians (44.4%) and African Americans (35.1%)[25]. Other European countries, including Italy, Greece and Britain, presented with a markedly increased incidence and prevalence, resulting in an increasing socioeconomic burden[26-28]. In addition, relatively young patients dominated NAFLD morbidity and their prevalence rapidly increased, especially in low-middle SDI regions. Given the pathogenesis of NAFLD associated with fat accumulation in hepatocytes and the growing obesity of youngsters[1, 29], this seems reasonable to explain the increasing number of young patients.

NAFLD is a complex and multifactor disorder that is affected by metabolic and environmental factors, along with genetic and epigenetic predispositions involving multiple organs and diverse mechanisms[30]. The exact contribution of each factor to the development of NAFLD is unknown, requiring further investigation and it may vary by geographic location, which is associated with the great heterogeneity of the NAFLD prevalence in different districts. Recently, metabolic imbalances have been gradually considered the predominant risk factor, and an international expert group has agreed to change the name of NAFLD to metabolic (dysfunction)-associated fatty liver disease (MAFLD)[31, 32]. DM2, as the most prevalent metabolic disease worldwide, was discovered in our study to correlate significantly with the NAFLD incidence and prevalence, which agreed with previous studies[33, 34] and further demonstrated the vital role of metabolic dysfunction in NAFLD. Meanwhile, due to alterations in the diet structure in modern life, obese populations are increasing at a rapid pace, which is regarded as the main risk factor for diabetes and fuels NAFLD morbidity. In fact, NAFLD may in turn be a pathogenic component of the development of DM2, and the bidirectional relationship between NAFLD and type 2 diabetes remains controversial and needs more exploration[35]. However, active prevention and control of obesity and diabetes can help to alleviate the morbidity of NAFLD to some extent.

NAFLD poses a substantial threat to individual health, with the number of deaths and DALYs increasing dramatically from 1990 to 2019, which was primarily driven by population growth and ageing across the globe, specifically in low-middle-income countries[36]. In the meantime, the patients aged above 50 years had the most deaths and DALYs, regardless of sex or the different SDI regions, which could be expected because of the ageing population and the worse response to therapy among the elderly population. However, the age-standardized death and DALY rates were decreased and lower in higher SDI regions. Therefore, we observed relatively high ASDR and age-standardized DALYs in Latin America, North Africa and the Middle East. High-income Asia Pacific, Central Europe and high-income North America had lower ASDRs and age-standardized DALYs. It could be speculated that most NAFLD-related deaths could be reduced in high-income countries through better access to health care and a stronger health infrastructure, such as early-stage identification of NAFLD and education of patients. In the general population, more than 10% of all NAFLD patients may develop NASH[37], which is characterized by steatosis, hepatocellular ballooning, lobular inflammation, and often fibrosis[38]. During the response to tissue damage, hepatocytes are replaced by type I collagen produced by stellate cells, leading to the progression of NASH toward fibrosis and cirrhosis with overt clinical consequences[39-41]. Furthermore, NASH patients have been reported to be highly susceptible to liver cancer[42]. Failure to recognize high-risk individuals and provide prompt treatment for NAFLD might lead to progression to NASH and even cirrhosis or carcinoma with a poor prognosis and high mortality, especially in low-income countries. Accordingly, to decrease the mortality and lessen the DALYs of NAFLD, preventing its development into NASH and then cirrhosis or liver cancer is essential.

In addition to hepatic causes, cardiovascular disease is the leading cause of death in patients with NAFLD, with mortality up to approximately 20%[43]. In the current study, we showed that common cardiovascular diseases, including stroke and ischaemic heart disease, had strong positive associations with the incidence and prevalence of NAFLD, which can be attributable to shared risk factors between these two diseases, such as dyslipidaemia, insulin resistance, hypertension, and obesity[44, 45]. Consequently, co-occurring stroke and IHD in NAFLD patients merits considerable attention for better prevention of cardiovascular events and lower mortality.

There remain some obvious limitations of this study. First, we relied heavily on GBD estimates for this study. The accuracy of the GBD estimates was limited by the quality and availability of each country's vital registration system and a mass of undefined NAFLD cases in their registry data. Moreover, other potential interconnected diseases with NAFLD await further investigation. Finally, subgroup analyses in NAFLD patients grouped by whether they were accompanied by metabolic syndrome or medication therapy or other factors were not performed.

In summary, the global burden of NAFLD is increasingly severe and is predicted to continue to increase in the future. The morbidity presented a clear shift toward young populations. Meanwhile, higher age-standardized death and DALY rates can be observed in the aged and low-SDI regions. Furthermore, NAFLD presented strong correlations with three high-risk comorbidities, namely, diabetes mellitus type 2, stroke and ischaemic heart disease. Therefore, the development of cost-effective global and regional strategies to mitigate NAFLD morbidity and mortality, alleviate the socioeconomic burden and prevent risky interconnected diseases are urgently required by policy-makers and clinical physicians.

Declarations

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Author Contributions

ZLZ had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved the final manuscript. Concept and design: ZLZ and LYC. Acquisition, analysis and interpretation of data: HLC, YZ, JXZ, SC and YHZ. Drafting of the manuscript: HLC and YZ. Revision of the manuscript: ZLZ and LYC. Statistical analysis: HLC and YZ; Supervision: ZLZ and LYC.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The datasets used in the present study are available in GBD 2019.

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Tables

Table 1. The incidence of NAFLD in 1990/2019 and temporal trends

Characteristics	1990		2019		1990-2019
	Incident cases No×10^3 (95% CI)	ASIR/10^5 No. (95% CI)	Incident cases No×10^3 (95% CI)	ASIR/10^5 No. (95% CI)	EAPC No. (95% CI)
Overall	88.18(62.3~128.32)	1.94(1.38~2.77)	172.33(125.78~243.64)	2.08(1.52~2.93)	0.1(-0.04~0.23)
Sex					
Male	40.98(28.48~61.17)	1.79(1.27~2.56)	77.87(55.78~111.24)	1.93(1.4~2.74)	0.06(-0.07~0.2)
Female	47.19(33.5~66.22)	2.08(1.48~2.93)	94.46(67.94~132.2)	2.23(1.6~3.12)	0.12(-0.02~0.26)
Socio-demographic factor					
High SDI	17.35(12.13~25.24)	1.87(1.3~2.75)	28.92(21.91~39.2)	2.16(1.58~3.06)	0.31(0.22~0.41)
High-middle SDI	23.49(16.69~34.07)	2.08(1.48~2.94)	36.64(26.06~53.1)	1.99(1.41~2.92)	-0.28(-0.44~-0.12)
Middle SDI	32.46(22.8~46.32)	2.49(1.8~3.44)	69.67(50.16~98.09)	2.58(1.9~3.57)	0.04(-0.14~0.21)
Low-middle SDI	10.95(7.51~15.99)	1.4(0.99~2)	26.64(18.85~38.65)	1.66(1.19~2.39)	0.40(0.15~0.64)
Low SDI	3.87(2.53~5.74)	1.28(0.85~1.89)	10.51(7.25~15.58)	1.5(1.04~2.19)	0.41(0.28~0.54)
Region					
East Asia	28.17(20.36~39.05)	2.67(1.96~3.65)	42.27(29.93~59.58)	2.1(1.51~2.93)	-1.26(-1.64~-0.88)
Southeast Asia	7.32(4.89~10.8)	2.15(1.44~3.14)	17.48(12.61~24.54)	2.54(1.86~3.52)	0.55(0.49~0.62)
Oceania	0.04(0.02~0.05)	0.81(0.58~1.13)	0.08(0.06~0.12)	0.82(0.6~1.13)	-0.01(-0.09~0.06)
Central Asia	0.99(0.65~1.49)	1.81(1.18~2.74)	3.96(2.66~5.83)	4.19(2.87~6.08)	3.17(3.06~3.28)
Central Europe	1.97(1.43~2.79)	1.45(1.04~2.06)	1.97(1.39~2.82)	1.3(0.89~1.93)	-0.2(-0.31~-0.1)
Eastern Europe	2.86(1.81~4.58)	1.18(0.74~1.88)	4.93(3.04~7.94)	2.04(1.22~3.32)	2.34(2.19~2.49)
High-income Asia Pacific	2.84(2.18~3.78)	1.39(1.07~1.84)	4.59(3.64~5.81)	1.27(0.99~1.65)	-0.59(-0.88~-0.29)
Australasia	0.31(0.21~0.44)	1.4(0.95~2)	0.65(0.48~0.87)	1.74(1.27~2.4)	1.02(0.86~1.18)
Western Europe	11.66(7.93~17.37)	2.71(1.82~4.05)	13.55(9.72~19.42)	2.46(1.7~3.62)	-0.43(-0.56~-0.3)
Southern Latin America	0.91(0.58~1.39)	1.96(1.24~2.99)	1.98(1.29~3.01)	2.65(1.72~4.06)	0.98(0.91~1.05)
High-income North America	5.97(3.94~9.34)	1.9(1.24~2.95)	11.22(8.1~15.71)	2.58(1.81~3.79)	0.81(0.61~1.02)
Caribbean	0.79(0.56~1.13)	2.74(1.95~3.87)	1.47(1.01~2.13)	2.9(2~4.22)	0.08(-0.06~0.22)
Andean Latin America	0.89(0.62~1.31)	3.44(2.39~4.97)	3.42(2.34~4.87)	5.62(3.86~7.97)	1.7(1.56~1.83)
Central Latin America	7.34(4.79~11.11)	6.11(4.03~9.06)	17.86(12.13~25.98)	6.88(4.7~9.98)	0.64(0.53~0.76)
Tropical Latin America	2.24(1.38~3.5)	1.77(1.08~2.72)	4.4(2.79~6.58)	1.72(1.1~2.56)	-0.24(-0.41~-0.07)
North Africa and Middle East	3.86(2.74~5.47)	1.95(1.37~2.76)	15.29(10.77~21.69)	3.01(2.14~4.22)	1.65(1.54~1.76)
South Asia	5.63(3.5~8.73)	0.76(0.5~1.12)	14.86(9.9~22.53)	0.91(0.62~1.33)	0.34(0.02~0.67)
Central Sub-Saharan Africa	0.36(0.23~0.56)	1.09(0.7~1.69)	1.2(0.77~1.82)	1.37(0.89~2.1)	0.56(0.37~0.75)
Eastern Sub-Saharan Africa	1.9(1.18~2.89)	1.91(1.18~2.93)	5.35(3.49~8.07)	2.31(1.48~3.5)	0.56(0.47~0.66)
Southern Sub-Saharan Africa	0.51(0.35~0.74)	1.48(1~2.16)	1.06(0.78~1.47)	1.61(1.2~2.17)	0.01(-0.2~0.22)
Western Sub-Saharan Africa	1.61(1.04~2.42)	1.52(1~2.24)	4.73(3.13~6.97)	1.83(1.22~2.66)	0.53(0.43~0.62)

Note: ASIR, age-standardized incident rate; SDI, social-demographic index; EAPC, estimated annual percentage change.

Table 2. The prevalence of NAFLD in 1990/2019 and temporal trends

Characteristics	1990		2019		1990-2019
	prevalence No×10^6(95% CI)	ASPR×10^3/10^5 No. (95% CI)	prevalence No×10^6 (95% CI)	ASPR×10^3/10^5 No. (95% CI)	EAPC No. (95% CI)
Overall	561.37(498.43~633.3)	12.07(10.78~13.54)	1235.7(1109.54~1378.53)	15.02(13.49~16.76)	0.77(0.69~0.85)
Sex					
Male	309.5(274.83~348.28)	13.42(12~15.04)	679.29(610.68~753.74)	16.79(15.14~18.61)	0.76(0.66~0.86)
Female	251.87(223.79~285.52)	10.75(9.58~12.15)	556.41(499.07~625.01)	13.28(11.9~14.93)	0.77(0.7~0.85)
Socio-demographic factor					
High SDI	72.14(64.38~81.12)	7.64(6.8~8.61)	138.64(125.51~153.33)	10.53(9.43~11.73)	1.21(1.17~1.26)
High-middle SDI	141.26(126.2~158.55)	12.27(10.96~13.75)	278.09(251.21~308.48)	15.34(13.8~17.1)	0.78(0.66~0.89)
Middle SDI	201.44(178.61~226.66)	14.63(13.11~16.37)	464.28(417.31~516.04)	17.6(15.84~19.53)	0.65(0.54~0.75)
Low-middle SDI	103.56(91.62~117.47)	12.94(11.52~14.69)	245.75(219.06~276.67)	15.23(13.66~17.08)	0.55(0.46~0.64)
Low SDI	42.62(37.51~48.45)	12.87(11.42~14.52)	108.18(95.42~122.65)	14.28(12.74~16.05)	0.34(0.31~0.37)
Region					
East Asia	138.89(122.56~157.83)	12.54(11.11~14.23)	303.13(272.38~339.5)	15.68(14.02~17.55)	0.81(0.52~1.1)
Southeast Asia	56.61(50.13~63.62)	16.11(14.46~18.02)	128.07(114.73~142.46)	18.3(16.51~20.31)	0.45(0.44~0.47)
Oceania	0.7(0.62~0.8)	15.75(14.08~17.65)	1.74(1.54~1.97)	16.87(15.13~18.73)	0.18(0.13~0.24)
Central Asia	6.86(6.11~7.7)	12.3(11.06~13.71)	12.82(11.45~14.33)	14.15(12.74~15.75)	0.5(0.46~0.54)
Central Europe	14.76(13.29~16.37)	10.68(9.63~11.86)	18.63(16.91~20.48)	11.9(10.76~13.11)	0.34(0.33~0.35)
Eastern Europe	28.74(25.93~31.99)	11.03(9.93~12.23)	34.11(30.98~37.56)	12.3(11.1~13.6)	0.38(0.37~0.4)
High-income Asia Pacific	13.54(12.04~15.25)	6.84(6.08~7.69)	20.94(18.78~23.28)	7.67(6.83~8.63)	0.56(0.45~0.67)
Australasia	1.62(1.45~1.83)	7.27(6.46~8.17)	3.46(3.12~3.82)	9.44(8.46~10.48)	0.92(0.85~1)
Western Europe	37.03(33.05~41.68)	7.88(7.04~8.88)	59.01(53.31~65.21)	9.93(8.93~11.04)	0.81(0.73~0.89)
Southern Latin America	3.14(2.79~3.56)	6.62(5.89~7.49)	6.48(5.83~7.19)	8.6(7.72~9.56)	0.92(0.82~1.01)
High-income North America	23.25(20.6~26.33)	7.26(6.42~8.25)	44.32(39.7~49.55)	9.4(8.4~10.54)	0.98(0.95~1.02)
Caribbean	4.34(3.86~4.86)	14.54(13.03~16.2)	8.18(7.38~9.02)	16.17(14.59~17.87)	0.4(0.38~0.42)
Andean Latin America	3.23(2.87~3.63)	11.76(10.56~13.13)	8.44(7.6~9.33)	13.69(12.38~15.09)	0.5(0.48~0.53)
Central Latin America	17.06(15.12~19.2)	14.59(13.11~16.25)	42.17(37.82~46.84)	16.62(14.96~18.39)	0.43(0.41~0.44)
Tropical Latin America	15.65(13.87~17.62)	13.16(11.83~14.66)	37.99(34.23~41.95)	15.24(13.72~16.82)	0.49(0.48~0.51)
North Africa and Middle East	60.11(54.01~67.06)	24.42(22.22~26.87)	161.46(146.41~177.66)	27.75(25.41~30.28)	0.47(0.46~0.49)
South Asia	95.44(83.69~108.91)	12.25(10.87~13.94)	241.84(214.85~273.69)	14.51(12.97~16.4)	0.54(0.42~0.65)
Central Sub-Saharan Africa	4.25(3.71~4.87)	12.57(11.11~14.25)	11.34(9.89~13)	13.33(11.8~15.1)	0.16(0.15~0.18)
Eastern Sub-Saharan Africa	13.97(12.17~15.98)	12.56(11.14~14.17)	36.09(31.61~41.13)	13.71(12.22~15.37)	0.29(0.28~0.3)

Southern Sub-Saharan Africa	6.09(5.4~6.87)	16(14.36~17.87)	13.16(11.81~14.68)	18.08(16.35~20)	0.41(0.4~0.42)
Western Sub-Saharan Africa	16.08(14.19~18.25)	13.16(11.72~14.78)	42.32(37.19~48.14)	14.28(12.76~15.95)	0.22(0.17~0.26)

Note: ASPR, age-standardized prevalent rate; SDI, social-demographic index; EAPC, estimated annual percentage change.

Table 3. The death of NAFLD in 1990/2019 and temporal trends

Characteristics	1990		2019		1990-2019
	Death No×10^3 (95% CI)	ASDR/10^5 No. (95% CI)	Death No×10^3 (95% CI)	ASDR/10^5 No. (95% CI)	EAPC No. (95% CI)
Overall	93.76(71.66~119.1)	2.39(1.84~3.05)	168.97(130.58~211.29)	2.09(1.61~2.6)	-0.67(-0.76~-0.57)
Sex					
Male	48.69(36.64~62.98)	2.66(2.02~3.42)	89.76(68.19~114.46)	2.38(1.82~3.02)	-0.61(-0.71~-0.52)
Female	45.07(34.98~57.25)	2.15(1.66~2.72)	79.21(61.14~98.75)	1.82(1.41~2.27)	-0.73(-0.82~-0.64)
Socio-demographic factor					
High SDI	14.37(10.96~18.26)	1.41(1.07~1.82)	25.22(19.77~31.16)	1.37(1.07~1.72)	-0.23(-0.31~-0.14)
High-middle SDI	21.02(16.16~26.38)	2.02(1.56~2.53)	31.22(24.09~39.33)	1.57(1.22~1.97)	-1.08(-1.17~-0.98)
Middle SDI	33.93(26.37~42.47)	3.51(2.73~4.42)	65.53(50.28~82.54)	2.8(2.17~3.52)	-0.92(-1.04~-0.81)
Low-middle SDI	16.5(12.28~21.39)	2.79(2.09~3.63)	32.89(24.84~42.44)	2.47(1.88~3.16)	-0.67(-0.83~-0.52)
Low SDI	7.86(5.64~10.7)	3.47(2.49~4.67)	13.98(10.23~18.73)	2.79(2.05~3.74)	-0.92(-0.99~-0.85)
Region					
East Asia	21.51(17.07~26.73)	2.53(2~3.09)	25.41(19.63~31.41)	1.29(1.01~1.58)	-3.04(-3.4~-2.69)
Southeast Asia	10.73(7.85~14.11)	4.25(3.12~5.65)	23.7(17.8~30.7)	4.18(3.14~5.37)	0.004 (-0.08~0.09)
Oceania	0.05(0.03~0.07)	1.51(1.11~2.05)	0.11(0.07~0.15)	1.46(1.04~1.96)	-0.07(-0.11~-0.04)
Central Asia	0.97(0.69~1.31)	2.08(1.48~2.81)	3.07(2.22~4.15)	4.22(3.11~5.58)	2.39(2.05~2.72)
Central Europe	2.21(1.65~2.85)	1.53(1.17~1.97)	2.66(1.92~3.58)	1.32(0.96~1.78)	-0.57(-0.71~-0.42)
Eastern Europe	2.98(2.16~4.01)	1.09(0.8~1.44)	8.17(5.89~10.98)	2.65(1.91~3.56)	3.36(2.75~3.98)
High-income Asia Pacific	2.31(1.85~2.79)	1.18(0.95~1.42)	3.98(3.09~4.86)	0.82(0.66~0.99)	-1.66(-1.97~-1.34)
Australasia	0.26(0.19~0.33)	1.15(0.84~1.48)	0.64(0.5~0.79)	1.32(1.04~1.63)	0.82(0.6~1.04)
Western Europe	10.61(7.72~13.83)	1.9(1.39~2.46)	12.36(9.39~15.78)	1.38(1.05~1.74)	-1.32(-1.41~-1.24)
Southern Latin America	0.94(0.65~1.29)	2.05(1.45~2.78)	1.63(1.17~2.18)	1.96(1.42~2.64)	0.09(-0.08~0.26)
High-income North America	4.49(3.4~5.81)	1.32(0.98~1.71)	9.9(7.65~12.62)	1.65(1.27~2.1)	0.9(0.71~1.09)
Caribbean	1.06(0.79~1.36)	4.08(3.08~5.23)	1.77(1.25~2.43)	3.43(2.44~4.69)	-0.8(-1.09~-0.51)
Andean Latin America	1.25(0.92~1.68)	6.1(4.45~8.19)	3.13(2.18~4.27)	5.68(3.93~7.71)	-0.28(-0.38~-0.18)
Central Latin America	6.04(4.58~7.69)	6.96(5.28~8.81)	14.76(11~18.94)	6.24(4.65~8.02)	-0.53(-0.63~-0.44)
Tropical Latin America	2.07(1.55~2.72)	2.25(1.69~2.96)	4.83(3.62~6.21)	2(1.5~2.56)	-0.29(-0.51~-0.08)
North Africa and Middle East	6.02(4.27~8.13)	4.24(2.92~5.86)	14.48(10.13~20.2)	3.84(2.71~5.3)	-0.12(-0.26~0.01)
South Asia	11.57(8.58~15.3)	2.01(1.51~2.62)	21.9(16.59~28.26)	1.6(1.21~2.05)	-1.2(-1.4~-1)
Central Sub-Saharan Africa	0.74(0.5~1.05)	3.32(2.3~4.7)	1.55(0.99~2.32)	2.89(1.9~4.24)	-0.75(-0.87~-0.64)
Eastern Sub-Saharan Africa	3.54(2.45~4.93)	5.02(3.53~6.94)	6.73(4.78~9.13)	4.4(3.14~5.94)	-0.56(-0.62~-0.51)
Southern Sub-Saharan Africa	0.7(0.5~0.94)	2.51(1.72~3.41)	1.32(1.04~1.67)	2.41(1.91~3.01)	-0.33(-0.75~0.09)
Western Sub-Saharan Africa	3.73(2.55~5.47)	4.49(3.06~6.53)	6.87(4.81~9.46)	3.8(2.68~5.19)	-0.58(-0.63~-0.52)

Note: ASDR, age-standardized death rate; SDI, social-demographic index; EAPC, estimated annual percentage change.

Table 4. The DALYs of NAFLD in 1990/2019 and temporal trends

Characteristics	1990		2019		199
	DALYs No×10^3 (95% CI)	Age standardized DALYs/10^5 No. (95% CI)	DALYs No×10^3 (95% CI)	Age standardized DALYs/10^5 No. (95% CI)	EAF No.
Overall	2711.27(2078.58~3478.94)	63.28(48.58~80.86)	4417.28(3348.22~5671.2)	53.33(40.73~68.29)	-0.8
Sex					
Male	1505.98(1104.46~1972.29)	72.2(54.06~93.52)	2528.55(1894.89~3311.25)	54.51(42.12~69.54)	-0.7
Female	1205.29(932.77~1536.54)	62.98(47.7~81.89)	1888.73(1463.88~2375.66)	43.92(34.03~55.32)	-0.9
Socio-demographic factor					
High SDI	365.87(275.87~477.98)	37.26(27.74~48.87)	554.91(423.15~707.93)	34.16(26.14~44.21)	-0.4
High-middle SDI	575.74(442.31~725.9)	52.09(40.11~65.58)	813.58(613.15~1052.67)	41.67(31.71~53.6)	-0.9
Middle SDI	1002.51(773.83~1265.3)	86.1(67.01~107.57)	1679.78(1270.33~2139.73)	65.4(50.66~82.14)	-1.1
Low-middle SDI	526.68(389.4~703.67)	73.8(55.05~95.91)	948.33(698.97~1251.28)	63.25(47.35~82.85)	-0.8
Low SDI	238.59(171.42~331.23)	86.65(62.74~117.91)	417.42(300.27~562.04)	68.06(49.42~91.9)	-1.0
Region					
East Asia	637.9(500.55~806.51)	65.25(51.77~81.38)	630.14(481.51~782.01)	30.28(23.4~37.39)	-3.4
Southeast Asia	334.44(244.6~444.27)	109.76(81.15~144.49)	635.25(464.29~836.79)	98.16(73.28~126.92)	-0.3
Oceania	1.68(1.17~2.41)	42.59(30.36~59.09)	3.73(2.44~5.49)	40.15(27.11~56.22)	-0.1
Central Asia	28.16(20.33~38.08)	55.32(39.54~74.56)	95.21(67.8~131.25)	112.39(81.58~151.17)	2.3(
Central Europe	58.5(43.04~77.61)	40.28(30.09~52.96)	66.35(47.15~91.42)	36.13(25.46~49.93)	-0.5
Eastern Europe	83.52(60.1~113.55)	30.49(22.13~40.6)	263.01(183.27~361.83)	91.22(63.75~127.09)	4.06
High-income Asia Pacific	57.39(46.39~70.46)	27.97(22.63~34.2)	68.82(55.49~82.92)	17.25(13.94~20.86)	-2.1
Australasia	6.73(4.95~8.9)	29.9(21.92~40.29)	13.91(10.82~17.36)	32.08(24.94~40.72)	0.65
Western Europe	254.63(184.16~340.56)	49.07(35.48~65.56)	250(188.02~320.23)	32.8(24.61~42.87)	-1.6
Southern Latin America	25.79(17.74~36.26)	55.24(38.08~77.69)	38.19(26.91~52.64)	47.56(33.39~65.99)	-0.2
High-income North America	115.89(86.66~152.26)	35.83(26.33~47.46)	236.66(178.74~311.2)	43.04(32.54~56.6)	0.82
Caribbean	28.56(21~38.28)	104.15(76.67~138.37)	45.1(30.71~63.86)	87.48(59.86~123.71)	-0.8
Andean Latin America	35.41(25.41~48.45)	154(110.25~209.78)	73.96(50.8~102.84)	128.67(88.56~178.85)	-0.7
Central Latin America	187.58(142.3~243.49)	188.76(141.59~244.26)	396.84(291~522.91)	161.39(118.97~212.38)	-0.7
Tropical Latin America	65.39(47.81~87.46)	60.38(44.4~79.55)	128.79(93.98~169.79)	51.56(37.88~67.46)	-0.4
North Africa and Middle East	142.84(104.85~189.17)	82.7(59.85~110.82)	336.02(235.32~461.22)	76.39(53.56~104.61)	-0.0
South Asia	392.53(285.99~525.73)	54.98(40.85~72.78)	651.07(487.49~865.51)	41.62(31.43~54.69)	-1.4
Central Sub-Saharan Africa	23.68(15.95~34.69)	85.74(58.63~122.02)	50.35(32.15~77.03)	74.24(47.51~110.75)	-0.7
Eastern Sub-Saharan	102.55(69.63~144.1)	120.23(83.43~167.08)	192.73(134.39~268.18)	101.32(71.94~139.19)	-0.7

Africa					
Southern Sub-Saharan Africa	21.65(15.54~29.57)	66.17(46.96~90.54)	38.06(29.49~48.86)	59.97(47.1~75.87)	-0.5
Western Sub-Saharan Africa	106.43(71.42~156.12)	107.51(72.73~159.03)	203.09(137.26~292.86)	89.75(62.2~124.88)	-0.6

Note: DALYs, disability-adjusted life-years; SDI, social-demographic index; EAPC, estimated annual percentage change.

Figures

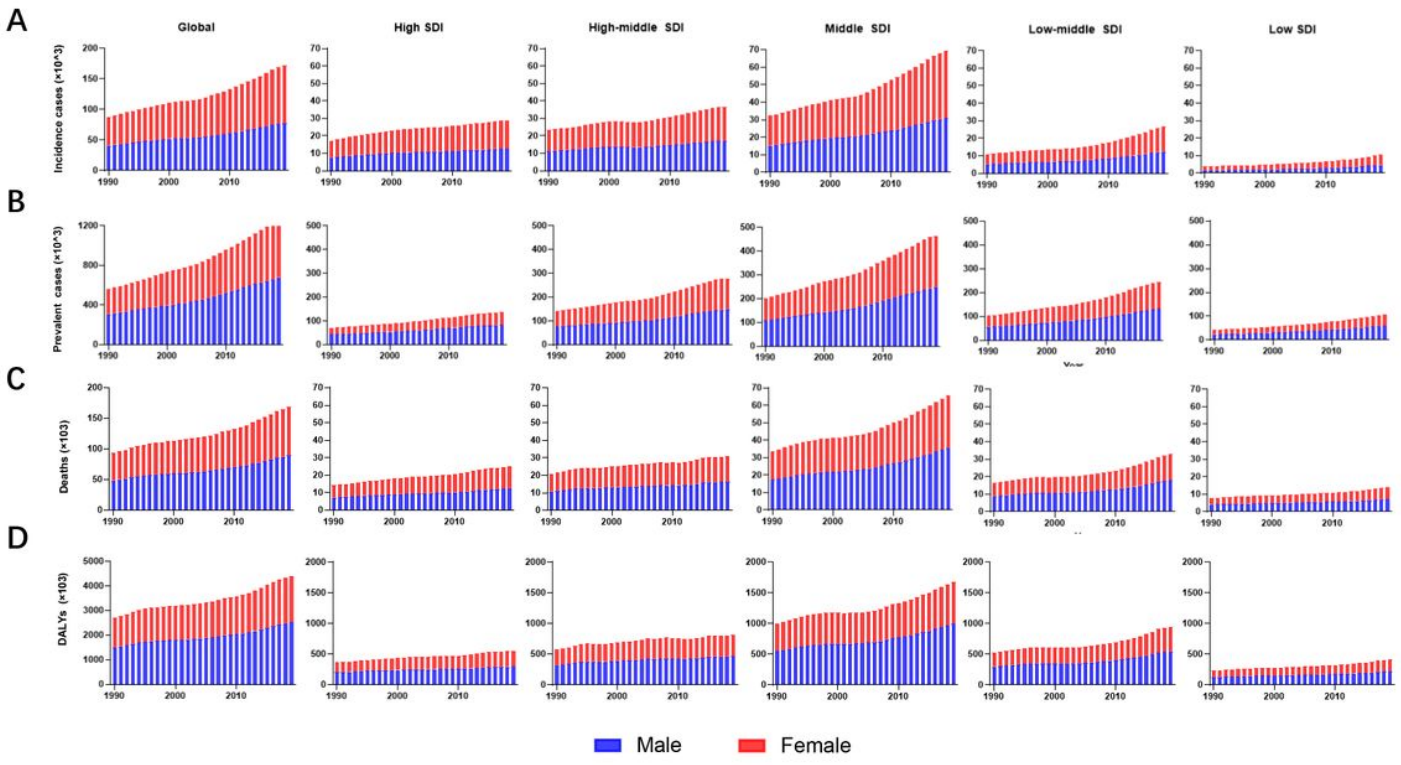

Figure 1

Figure 1. The change trends of NAFLD incidence, prevalence, deaths and DALYs from 1990 to 2019. The change trends of incidences (A), the change trends of prevalence (B), the change trends of deaths (C), and the change trends of DALYs (D) are shown. Blue bars represent males, and red bars represent females. Note: NAFLD, non-alcoholic fatty liver disease; DALYs, disability-adjusted life years; SDI, social-demographic index.

Figure 2

Figure 2. The change trends of NAFLD incidence, prevalence, deaths and DALYs from 1990 to 2019 in different age groups. The change trends of incidence (A); the change trends of prevalence (B); the change trends of deaths (C); and the change trends of DALYs (D). Note: NAFLD, non-alcoholic fatty liver disease; DALYs, disability-adjusted life years; SDI, social-demographic index.

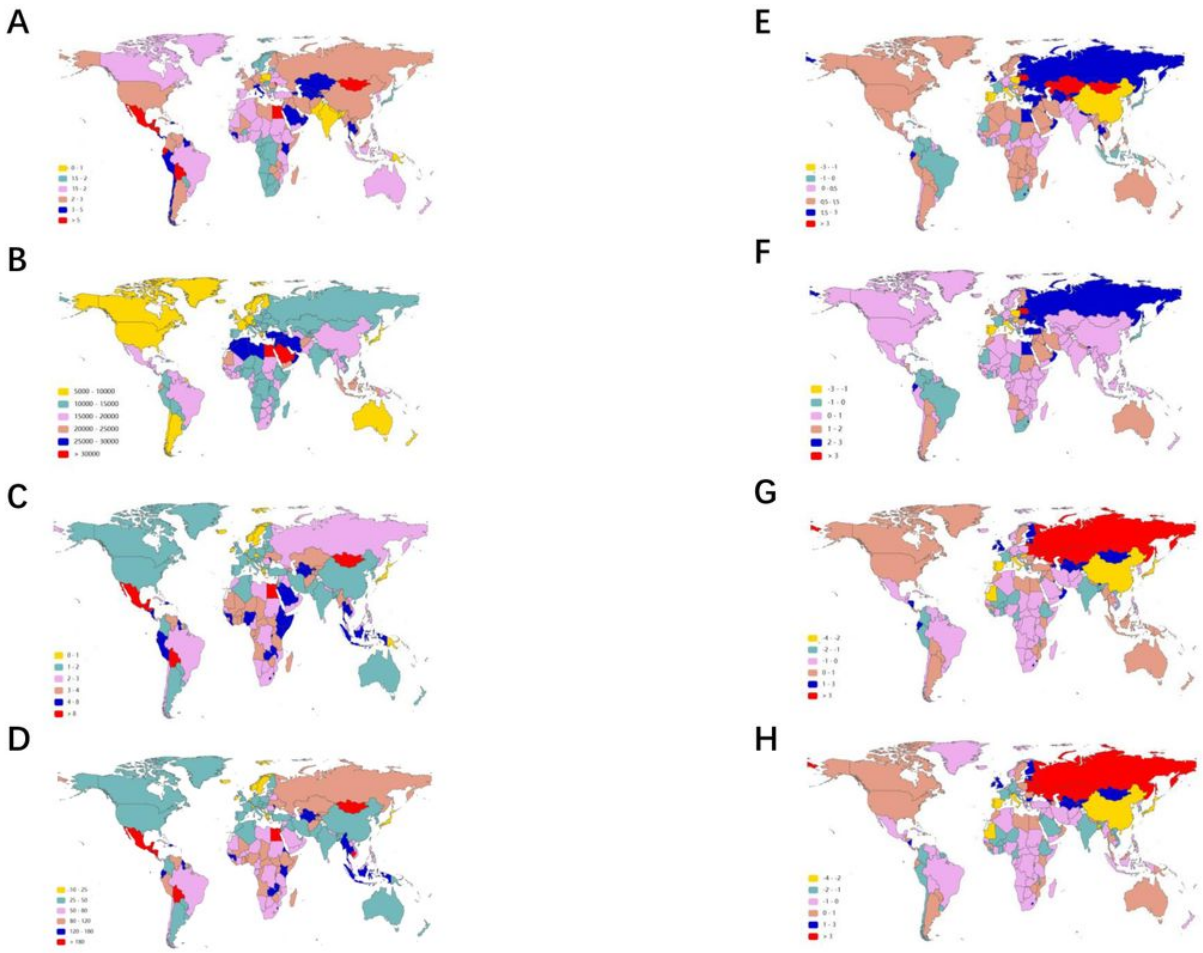

Figure 3

Figure 3. The age-standardized rates of NAFLD in 2019 and EAPC of NAFLD ASRs from 1990 to 2019 in 204 countries and territories. The ASIR (A), ASPR (B), ASDR (C) and age-standardized DALYs (D) of NAFLD around the world in 2019 are shown. The EAPC of ASIR (E), ASPR (F), ASDR (G), and age-standardized DALYs (H) in the past 30 years are shown. Note: NAFLD, non-alcoholic fatty liver disease; ASIR, age-standardized incident rate; ASPR, age-standardized prevalent rate; ASDR, age-standardized death rate; DALYs, disability-adjusted life years; EAPC, estimated annual percentage change; ASRs, age-standardized rates.

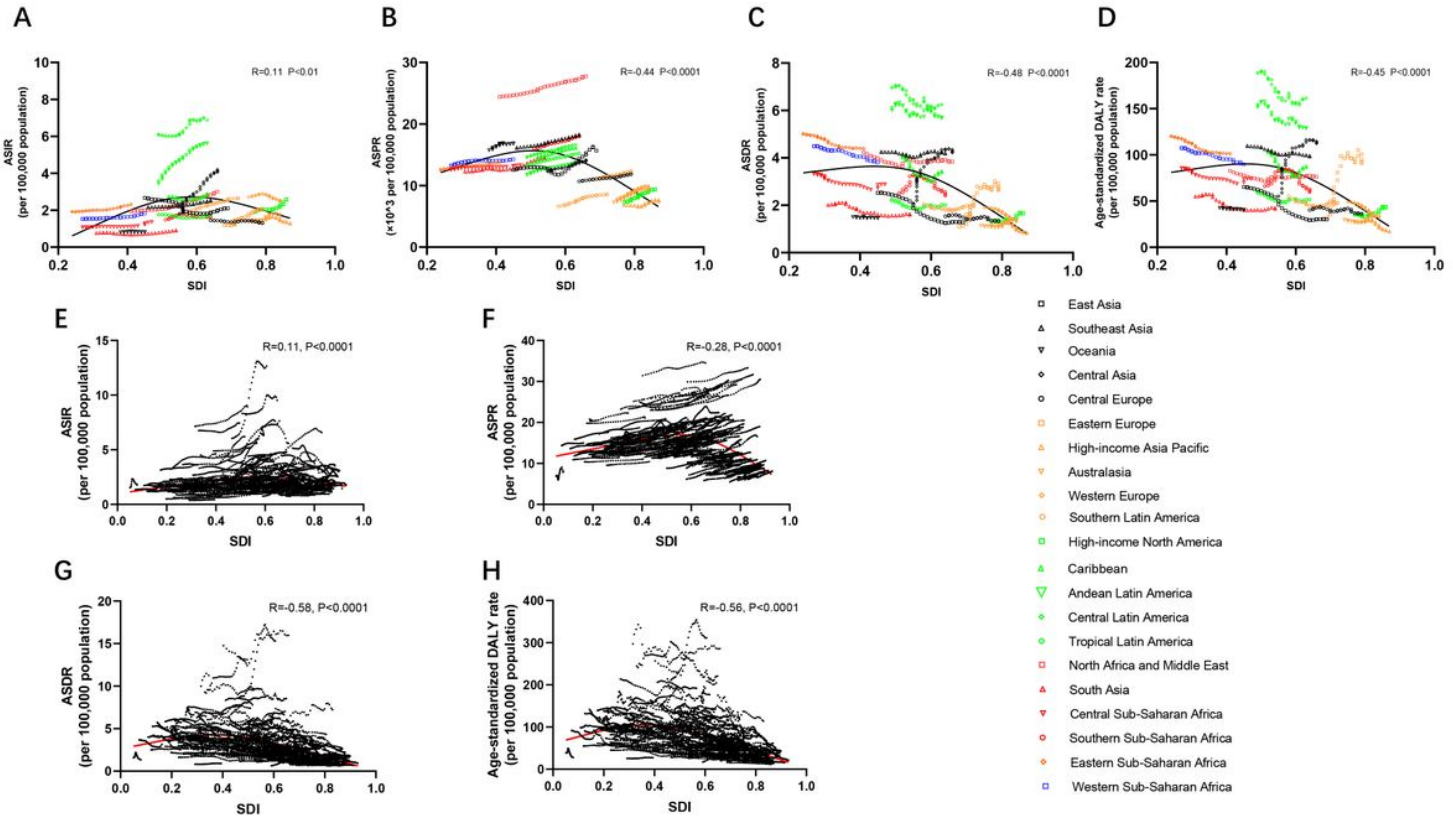

Figure 4

Figure 4. Correlation analyses between ASRs of NAFLD and SDI in 21 regions and 204 territories from 1990 to 2019. The SDI presented no obvious correlation with the ASIR (A, E) and negative correlations with ASPR (B, F), ASDR (C, G) and age-standardized DALYs (D, H) in 21 regions and 204 territories from 1990 to 2019. Note: NAFLD, non-alcoholic fatty liver disease; ASRs, age-standardized rates; ASIR, age-standardized incident rate; ASPR, age-standardized prevalent rate; ASDR, age-standardized death rate; DALYs, disability-adjusted life years; SDI, social-demographic index.

Figure 5

Figure 5. The associations of incidence/prevalence between NAFLD and other comorbidities in 21 regions and 204 territories from 1990 to 2019. NAFLD presented strongly positive correlations of incidence/prevalence with DM2 (A, D, G, J), stroke (B, E, H, K), and IHD (C, F, I, L) in 21 regions and 204 territories from 1990 to 2019. Note: NAFLD, non-alcoholic fatty liver disease; DM2, diabetes mellitus type 2; IHD, ischemic heart disease.

Supplementary Files

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- FigureS1.jpg
- SupplementaryfilefigureS1legend.docx