Burden of viral hepatitis caused by specific aetiologies in China, 1990-2016: findings from the GBD 2016

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Abstract

Purpose

The aim of this study is to quantify the burden caused by viral hepatitis in China from 1990 to 2016. Methods: Data from the GBD 2016 study were extracted to calculate incidence, prevalence and disability-adjusted life years (DALYs). Trends in DALYs were assessed in 33 provinces/regions. Results: From 1990 to 2016, the total incidence of hepatitis decreased by 88.5%. However, the prevalence of hepatitis (counts in thousands), increased by 37.6% from 153,856 (95% UI: 136,047-172,319) in 1990 to 211,721 (95% UI: 179,776-240,981) in 2016, with age-standardized prevalence rates changing slightly. The number and age-standardized prevalence rates increased by 35.9% and 1.6% for hepatitis B and by 81.8% and 30.4% for hepatitis C, respectively. Guangxi, Guangdong and Hainan had the highest age-standardized prevalence rates (≥16,500 per 100,000). Tibet, Qinghai and Gansu had the highest age-standardized DALYs rates (≥40 per 100,000). The largest absolute number of DALYs was observed in the 15-49 year age group in 2016. The highest rate of DALYs occurred in males aged 50-69 years and in females aged ≥70 years. Conclusion: The incidence and DALYs of viral hepatitis decreased dramatically from 1990 to 2016. However, the prevalence still remains at a high level, which may result in heavy burdens in the future.

Background

Viral hepatitis, which results from inflammation of the liver, is a major public health concern [1–4]. Viral hepatitis can be caused by a series of viruses, namely, hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus
(HDV), and hepatitis E virus (HEV). HBV and HCV frequently cause chronic hepatitis, which can lead to progressive cirrhosis and to primary liver cancer. WHO estimated that 1 in 3 people throughout the world had been infected by either HBV or HCV [5] in 2015 and 640 million people had been infected globally in 2016. Among these, 304.6 million were new cases. Approximately 159 million people are infected with acute HAV and 119 million people are infected with HBV [6]. Viral hepatitis causes approximately 1.5 million deaths and significantly affects the quality of life of hundreds of millions of people at the global level [7].

China is a high epidemic area of hepatitis: in the past few decades, China has made great efforts to prevent and control infectious diseases, including hepatitis, and has achieved good results, with the incidence of hepatitis dropping dramatically. However, due to the large population base in China, there are still many cases of hepatitis. China’s legal infectious disease reporting system has found that more than 1.3 million cases of viral hepatitis are diagnosed annually, accounting for one third of the total reported cases. Viral hepatitis ranks first among infectious diseases, of which hepatitis B accounts for 80% of all hepatitis cases. In addition to seriously threatening human health, viral hepatitis also brings heavy economic burdens to patients. The direct economic loss caused by hepatitis B in China is at least 500 billion RMB every year. The medical costs associated with the management of chronic hepatitis B in a few areas in China have been reported [8, 9]. Despite the large burden of disease, investments in hepatitis remain limited at the national and international levels when compared with some other major infectious diseases.

In this study, we first presented a systematic analysis of four kinds of viral hepatitis at the age-sex-provincial level by using updated data from the Global Burden of
Diseases, Injuries, and Risk Factors Study (GBD2016), to estimate the incidence and prevalence of hepatitis, and to calculate years of lost (YLLs), years of disability (YLDs) and disability-adjusted life years (DALYs). Therefore, it can provide basic information on the current status of hepatitis for policy decision-makers to identify high-risk populations and regions and to make reasonable allocations of the limited funds for prevention and treatment.

Methods

All data used in this study were obtained from the data from China in the GBD study 2016, which covered 195 countries and territories between 1990 and 2016. The incidence, prevalence, YLLs, YLDs and DALYs for hepatitis from 33 provinces/regions were analyzed, including the Hong Kong and Macao Special Administrative Regions (SAR). The Socio-Demographic Index (SDI) levels of the 33 provinces/regions were classified into high-middle SDI, middle SDI and low-middle SDI according to the SDI value estimated from GBD 2016 locations.

The definitions for acute hepatitis A, hepatitis B, hepatitis C, and acute hepatitis E were infection with the corresponding virus resulting in anti-HAV IgG, HBsAg, anti-HCV IgG, and anti-HEV IgG seroconversion, respectively, regardless of symptoms. All ICD-10 codes under the headings B15, B16, B17.0, B19.1, B35.3, B17.1, B19.2 and B17.2 were included.

Details of the methodology used in the GBD studies in general and the main changes incorporated into the GBD 2016 methods, have been described previously [6, 10]. In brief, DisMod-MR 2.1, a Bayesian meta-regression tool, was used as the main method of estimation, ensuring consistency between incidence, prevalence, remission, and cause of death rates for each condition. DALYs were calculated as
the sum of YLLs and YLDs for each cause, location, age group, sex, and year. YLDs were the number of years living with a disability multiplied by a disability weighting, which was derived from general population-based surveys [11] and reflected the severity of the disability. YLLs were calculated by multiplying the number of deaths from each cause in each age-group by the reference life expectancy at the average age of death for those who die in that age group. Age-standardized rates were computed using the world standard population developed for the GBD study [12]. Spearman correlation was used to relate the SDI index with DALYs. Spearman correlation was used to relate the SDI index with DALYs.

The 95% uncertainty interval (UI) for each quantity used in the analyses was estimated by taking 1000 samples from the posterior distribution of each quantity, and using the 25th- and 975th-ordered draws of the uncertainty distribution.

Results

1. Incidence and prevalence

We used over 110,000 outcomes of incidence, prevalence, YLD, YLL and DALYs for hepatitis and the following three levels: 29 age groups; 33 provinces/regions; and 7 individual years from 1990 to 2016.

From 1990 to 2016, the incidence of hepatitis in China (counts in thousands) decreased by 88.5%, from 117,492 (95% UI: 66,517–151,302) to 13502 (95% UI: 10,918–15,967), and age-standardized incidence rates per 100,000 decreased by 87.1% from 10,114 (95% UI: 5,734–12,988) to 1,305 (95% UI: 950–1,549). However, the prevalence of hepatitis in China (counts in thousands) increased by 37.6%, from 153,856 (95% UI: 136,047–172,319) in 1990 to 211,721 (95% UI: 179,776–240,981) in 2016, and age-standardized prevalence rates per 100,000 changed slightly by –
3.3%, from 13,537 (95% UI: 12,075–15,156) to 13,089 (95% UI: 11,882–15,760) (Table 1).

Among the four kinds of hepatitis, the incidence and prevalence of acute hepatitis A and acute hepatitis E, along with the age-standardized rates, all decreased dramatically. The case numbers and age-standardized rates increased by 35.9% and 1.6% for hepatitis B and by 81.8% and 30.4% for hepatitis C, respectively.

In 2016, Guangdong province ranked first among the 33 provinces_regions of China in the number of newly infected hepatitis patients with 1,170,000 counts. Tibet, Qinghai and Gansu had the highest age-standardized incidence rates at >2,000/100,000 people; Tibet had the highest of all at 12,563/100,000. Guangxi, Guangdong and Hainan had the highest age-standardized prevalence rates at >16,500/100,000, whereas Beijing, Hong Kong and Macao had the lowest age-standardized incidence rate and prevalence rate (Table 2).

Among the four kinds of viral hepatitis, the incidence rates for acute hepatitis A, hepatitis B, and acute hepatitis E decreased dramatically over the last few decades, especially acute hepatitis A and hepatitis B (Fig. 1). However, the age-standardized prevalence rate for hepatitis B decreased slightly from 1990 to 2000 then increased from 2005 and has sustained a high level for the past ten years.

The incidence rates and prevalence rates of the four kinds of hepatitis by sex and age group in 2016 are presented in Fig. 2. The low age group (<5 year) had the highest incidence rate. For example, the incidence rate of acute hepatitis A was 5,733/100,000 for males and 6,381/100,000 for females and the incidence rate of acute hepatitis C was 815/100,000 for males and 884/100,000 for females. In most of the age groups, the incidence rates in males were higher than those in females. The prevalence rates slightly increased starting from the <5 year age group and
then sharply increased at 15–49 year age group. The prevalence rates for males and females stabilized starting from the 50–69 year age group.

2. DALYs

The DALYs for hepatitis decreased by 78.5%, from 1403,788 (95% UI: 1,319,601–1507,691) in 1990 to 302,026 (95% UI: 287,096–319,734) in 2016. In 2016, the DALYs for acute hepatitis A, hepatitis B, hepatitis C and acute hepatitis E were 14.1, 263.6, 4.1 and 20.2 (in thousands), respectively. The overall age-standardized DALY rate decreased by 85.5% from 135.2 (95% UI: 127.2–1145.0) to 19.6 (95% UI: 18.6–20.8) per 100,000 (Table 1).

Provincial-level DALYs and age-standardized rates of DALYs per 100,000 in 1990 and 2016 are also shown in Table 2. In 2016, the top three provinces with the heaviest disease burden caused by viral hepatitis were Hunan, Guangdong and Sichuan, with the number of DALYs >21,000. Tibet, Qinghai and Gansu had the highest age-standardized DALY rates at >40/100,000 people. However, Hong Kong, Beijing, and Tianjin had the lowest age-standardized DALY rates.

DALYs number and DALY rates in 2016 by sex and age group are shown in Table 3 and Fig.3. In the <5 year age group, the burden of disease was mainly caused by acute hepatitis A, with the number of DALYs and an age-standardized rate of 8673 (95% UI: 7320–10839) and 14.3 (95% UI: 12.1–17.9)/100,000, respectively. The overall number of DALYs for viral hepatitis gradually increased starting from the 5–14 year age group and peaked at the 50–69 year age group for male and ≥70 year age group for female. The DALY rates in males were higher than those in females except that in <5 year age group.

According to the socio-demographic index value in 2016, the 33 provinces were classified into three groups. The mean number of DALYs of hepatitis B in 2016 was
5,970 for the high-middle SDI region, 8,533 for the middle SDI region, and 7,828 for the low-middle SDI region. The age-standardized DALY rates for hepatitis of the four aetiologies all decreased dramatically after 2000. In 2016, the age-standardized DALY rates for hepatitis B were approximately 9.1/100,000 for high-middle SDI level regions, 17.4/100,000 for middle SDI level regions and 56.4/100,000 for low-middle SDI level regions (Table. 4). There was a moderate negative correlation between SDI index and DALYs ($r_s = -0.808, P<0.001$).

Discussion

According to the report from the World Health Organization, the Western Pacific (6.2% or 115 million individuals) and African regions (6.1% or 60 million individuals) have the highest prevalence levels of viral hepatitis [13]. The incidence of viral hepatitis in China has gone a gentle decline to a steady but was still high level [14]. At the same time, our results showed that the prevalence in China is 211,721 (in thousands) in 2016, which accounts for one third of the world population of hepatitis sufferers [6].

The results of national serum epidemiology survey of viral hepatitis in China in 1992 showed that the prevalence rate of hepatitis B virus HBsAg in the 1–59 age groups was 9.75% [15]. In 2006, a national epidemiological survey of hepatitis B found that the rate of HBsAg prevalence in the 1–59 age groups dropped to 7.18% [16]. However, in our study, the age-standardized prevalence rates for hepatitis from 1990 to 2016 decreased slightly by 3.3% from 13,537 to 13,089 per 100,000 individuals, while the age-standardized prevalence rates for hepatitis B increased slightly by 1.6% from 10,605 to 10,777 per 100,000 individuals. We accounted for differences in factors such as diagnostic criteria, test levels, reporting system, and
different standard populations. However, these differences do not prevent us from comparing the 33 provinces’ data, which can help us to judge the burden of viral hepatitis for each province and make the right medical decisions for them.

HAV, HBV, HCV and HEV are biologically unrelated, having different modes of transmission and different natural histories of infection. Hepatitis B and hepatitis C are mainly transmitted through blood, mother-to-child transmission, and sexual transmission, while hepatitis A and E are mainly transmitted through the digestive tract. The prevalence of hepatitis A is mainly related to poor socio-economic conditions including high housing density, poor sanitation system and low water quality [17–19]. The incidence of hepatitis A has dropped significantly in China since the introduction of the vaccine in the 1990s. In China, hepatitis B is one of the major diseases that threaten our health. Although the age-standard incidence rate of hepatitis B virus has decreased significantly after the widespread use of the HBV prophylactic vaccine, the prevalence rate remains high. For hepatitis B patients who have established chronic infections, there is lack of effective treatment strategies due to the complicated course, poor prognosis and difficulty in curing the infections.

The global prevalence of HCV has been estimated at 1%, which equates to approximately 71 million people [20]. Chronic hepatitis C virus infection varies between 0.6% and 10% depending on geographical location [21]. In Western Europe, the estimated prevalence of hepatitis C is 1.5%–3.5% [22]. In China, HCV infection is a commonly reported disease. Indeed, China has the largest HCV-infected population in terms of absolute number [23]. In our study, the prevalence of hepatitis C in 2016 was approximately 45 million, an increase of 81.8% from the prevalence in 1990. Other investigations report similarly rising trends [24]. There are two possible reasons for this trend. First, it may be due to a dearth of effective
vaccines. There are vaccines to prevent HAV and HBV that are safe and effective, and one vaccine for HEV is commercialized for use only in China, but there are no Federal Drug Administration-approved vaccines for HCV [25]. Second, it may be due to increasing access to HCV diagnostics over time [26, 27]. Although the age-standardized prevalence rate in China remains at a high level, the DALY rate had sharply declined by 85.5% from 1990 to 2016. The clinical course of hepatitis viruses can be acute and chronic for HBV and HCV. The clinical manifestations of hepatitis can be absent or appear when the disease is advanced [28]. No disability weightings were used for asymptomatic acute hepatitis A, B, C or E cases or chronic hepatitis B or C cases [10]. Similar trends for prevalence and DALYs could be observed in most provinces. The top five provinces suffering a heavy burden of hepatitis were Tibet, Qinghai, Gansu, Jiangxi and Yunnan. To realize the “2030 Agenda for Sustainable Development Goals” of the WHO [29] and support national hepatitis elimination plans, priority access to limited funding should be given to those provinces.

Hepatitis A/E cause only acute hepatitis and are transmitted mostly through exposure to contaminated food or water. In our analysis, although the disease burden caused by hepatitis A decreased dramatically from 1990 to 2016, the percentage of disease burden caused by hepatitis A was still high in the low age group population. It is necessary to recommend vaccination to all children aged 1 year and older [19]. In China, thanks to the universal HBV immunization programme for newborn babies initiated in 1992, the prevalence of anti-HBs was higher in fully immunized children (63.2%-74.3%) than in non-immunized children (21.1%-34.8%) [30]. The burden of hepatitis B in 2016 decreased dramatically with the total DALYs peaking in the 50-69 year age group. The age-standardized prevalence rate in males
was higher than that in females, which was also represented in other reports [31–33].

Our study provided the most up-to-date systematic analysis on the disease burden of hepatitis in China. We can not only compare the prevalence rate, incidence rate, and DALY rate to other countries, but also compare them at the provincial level. The data we used in the study were mainly from the GBD2016 study. To improve model validity and decrease uncertainty from various sources, GBD allows annual improvement to the methods and available data sources. However, limitations still remained [6, 10, 34], which were also applied in our study. First, severity distribution data across sequelae for most diseases were from high-income countries, which might lead to underestimation of YLDs. Second, data sources from national surveys, cancer registries, and surveillance systems of the Disease Control and Prevention could not represent the overall trend of prevalence and DALYs.

Conclusion

The burden of hepatitis decreased rapidly in China from 1990 to 2016. However, the prevalence rates of hepatitis B and C remained high, with large gaps among provinces and populations. Communicable disease-control challenges persist. Especially for hepatitis B, effective treatment should be carried out to prevent chronic patients from developing cirrhosis and liver cancer, which may exert a large burden on society in the future.

Abbreviations

DALYs: Disability-adjusted Life Years; GBD2016: the Global Burden of Diseases, Injuries, and Risk Factors Study 2016; HAV: Hepatitis A Virus; HBV: Hepatitis B
Virus; HCV: Hepatitis C Virus; HDV: Hepatitis D Virus; HEV: Hepatitis E Virus; SDI: Socio-Demographic Index; UI: Uncertainty Interval; YLLs: Years of Lost; YLDs: Years of Disability

Declarations

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Authors’ contributions

ML, ZQW, LZ and HZ analyzed the data and wrote the manuscript. ML and DWL planned the study. DWL and MGZ reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Ethical Approval

All analyses were based on available data, thus no ethical approval and patient consent are required.

Conflict of interest statement

All authors disclose no conflicts of interest.

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Tables

Table1. Incidence, prevalence and DALYs for hepatitis by aetiology
| Region         | Incidence | Prevalence | DALYs |
|----------------|-----------|------------|-------|
|                | Count in thousands | Age-standard rate per 100,000 | Count in thousands | Age-standard rate per 100,000 | Count in thousands | Age-standard rate per 100,000 |
| Hepatitis      | 1990      | 117492 (66517-151302) | 10114 (5734-12988) | 153856 (136047-172319) | 13537 (12075-15156) | 1403.8 (1319.6-1507.7) | 135.2 (127.2-145.0) |
|                | 2016      | 13502 (10918-15967) | 1305 (950-1549) | 211721 (179776-240981) | 13089 (11882,15 760) | 13537 (12075-15156) | 1403.8 (1319.6-1507.7) | 135.2 (127.2-145.0) |
| Change (%)     | -88.5     | -87.1      | 37.6  | -3.3  | -78.5  | -85.5 |
| Acute hepatitis A | 1990 | 84988 (32621-117655) | 7216 (2767-9983) | 6538 (2509-9050) | 555 (213-768) | 220.4 (188.0-257.8) | 18.9 (16.1-22.0) |
|                | 2016      | 4522 (2350-5778) | 648 (298-848) | 348 (181-444) | 50 (23-65) | 14.1 (12.1-16.5) | 1.8 (1.5-2.1) |
| Change (%)     | -94.7     | -91.0      | -94.7 | -91.0 | -93.6  | -90.5 |
| Hepatitis B    | 1990      | 28886 (23305-35481) | 2577 (2121,311 7) | 122212 (105637-140054) | 10605 (9216-12150) | 970.8 (898.0-1059.6) | 97.8 (90.8-106.3) |
|                | 2016      | 8025 (6304-10036) | 547 (441-672) | 166042 (134231-194796) | 10777 (8786-12645) | 263.6 (248.2-279.9) | 15.7 (14.9-16.7) |
| Change (%)     | -72.2     | -78.8      | 35.9  | 1.6   | -72.8  | -83.9 |
| Hepatitis C    | 1990      | 1180 (1062-1304) | 110 (100-122) | 24919 (21906-28054) | 2361 (2088,264 0) | 14.6 (11.6-18.5) | 1.6 (1.2-2.00) |
|                | 2016      | 655 (581-739) | 86 (75-99) | 45308 (40742-49995) | 3079 (2760,340 6) | 4.1 (3.1-5.5) | 0.3 (0.2-0.4) |
| Change (%)     | -44.5     | -21.8      | 81.8  | 30.4  | -71.9  | -81.3 |
| Acute hepatitis E | 1990 | 2438 (2208-2701) | 209 (192-228) | 188 (170-208) | 16 (15-18) | 198.0 (173.4-225.9) | 16.8 (14.8-19.1) |
|                | 2016      | 300 (266-333) | 24 (22-27) | 23 (20-26) | 2.0 (1.7-2.1) | 20.2 (17.1-24.0) | 1.8 (1.6-2.1) |
| Change (%)     | -87.7     | -88.5      | -87.8 | -87.5 | -89.8  | -89.3 |

Table 2. Incidence, prevalence and DALYs for hepatitis by province
|        | 1990     | 1996     | 2000     | 1990     | 1996     | 2000     | 1990     | 1996     | 2000     | 1990     | 1996     | 2000     |
|--------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| China  | 117491   | 13504    | 10115    | 130656   | 153856   | 211720   | 13537 8  | 13908  (12075 1515 6) | 140378  (1319601 - 1507691) | 3020798  (2870963197 34) | 1352127  (1270145.0 20.8) |
| Hong Kong SAR | 35 (29,43) | 22 (20,26) | 645 (543-679) | 395 (356-447) | 673 (578-800) | 971 (867-1096) | 1146 (984-1535 9) | 1173 (4-104 72-1324 0) | 573 (496-665) | 259 (211-321) | 9.7 (8.4-11.3) | 2.8 (2.3-3.4) |
| Macao SAR | 10 (7,12) | 3.4 (3.0, 3.9) | 2698 (199-3224) | 677 (606-753) | 42 (36,5 0) | 90 (81,1 00) | 1185 (2-102 09-1392 1) | 1382 (4-125 08-1534 0) | 178 (147-213) | 76 (59- 96) | 53.9 (44.8- 64.8) | 10.3 (8.2-12.9) |
| Anhui | 5808 (313,73 45) | 492 (400, 587) | 9161 (512, 1149 7) | 1087 (809- 1283 1) | 7370 (649, 83 53) | 8368 (694, 497 9) | 1314 (116, 1478 1) | 1316 (4-109 80- 1535 5) | 5741 (8-487 50- 6792 4) | 1093 (3-924 3- 1291 6) | 1119 (96.1- 130.9 | 16.4 (14.0- 19.1) |
| Beijing | 163 (124, 198) | 102 (84.1 25) | 1822 (125, 722 81) | 478 (363, 579) | 898 (801, 1022) | 2277 (199, 9265 4) | 8281 (741, 9380 5) | 8053 (710, 9222) | 4234 (345, 5094 5) | 1812 (147, 2180 7) | 39.4 (32.8- 46.9) | 6.5 (5.4- 7.7) |
| Chongqing | 1834 (72, 646) | 211 (163, 256) | 1146 (9, 1654 6) | 1218 (715- 1581 1) | 1978 (173, 62 47) | 3886 (335, 1444 5) | 1254 (5-110 54- 1419 6) | 1298 (5-112 58- 1492 6) | 1917 (2-156 93- 2346 7) | 4846 (405, 5711 4) | 1259 (104, 0- 153.5) | 15.8 (13.3- 18.5) |
| Fujian | 1131 (597, 1532) | 203 (162, 250) | 3384 (191, 4495 6) | 638 (475, 774) | 3817 (333, 243 10) | 5619 (460, 5646 4) | 1271 (0-111 98- 1430 0) | 1335 (0-110 64- 1526 1) | 1545 (0-131 37- 1827 9) | 3121 (262, 9- 3720) | 59.2 (50.4- 69.6) | 7.5 (6.4- 9.0) |
| Gansu | 6983 (354, 0.89 98) | 458 (345, 546) | 2566 (5, 136 62- 3278 9) | 2746 (171, 8- 3317 ) | 3195 (279, 0.36 01) | 3608 (314, 2418 3) | 1395 (5-123 08- 1571 3) | 1324 (8-116 49- 1534 1) | 5974 (2-499 70- 1730 1) | 1136 (6-966 7- 1327 4) | 283.9 (240, 5- 334.3) | 41.8 (35.9- 48.2) |
| Guangdong | 3507 (254, 143 78) | 1170 (944, 1411) | 5859 (435, 7197 9) | 1131 (879, 1383 3) | 8919 (769, 79 22) | 2132 (783, 175 31,24 775) | 1538 (5-136 21- 1707 9) | 1672 (8-139 72- 1882 6) | 6562 (2-559 07- 7756 3) | 2222 (3-189 40- 2633 6) | 130.9 (110, 7- 154.3) | 18.8 (16.1- 22.1) |
| Guangxi | 4132 (253, 8.52 07) | 618 (476, 739) | 9544 (592, 1193 8) | 1586 (113, 1- 1890) | 7717 (679, 8543 ) | 9387 (790, 5105 63) | 1830 (1-162 35- 2020 0) | 1867 (0-157 75- 2102 1) | 5771 (6-482 90- 6887 2) | 1287 (8-108 1536 3) | 161.8 (135, 8- 194.1) | 25.5 (21.5- 30.1) |
| Guizhou | 5251 (209, 325,) | 447 (325, 1340 6) | 1835 (105, 4136 361) | 4616 (398) | 1279 (5) | 1284 (4) | 5569 (7) | 1177 (4) | 186.9 (158, 33.0) | 186.9 (158, 33.0) | 186.9 (158, 33.0) | 186.9 (158, 33.0) |
| Province   | Code (Year)      | 2019 Population | 2018 Population | 2017 Population |
|------------|------------------|-----------------|-----------------|-----------------|
| Anhui      | 2357 (358, 1135) | 8,778,000       | 8,778,000       | 8,778,000       |
| Hebei      | 1764 (491, 2384) | 6,080,000       | 6,080,000       | 6,080,000       |
| Henan      | 7423 (419, 594, 24) | 12,976,000     | 12,976,000     | 12,976,000     |
| Hubei      | 5216 (277, 76, 83) | 7,978,000       | 7,978,000       | 7,978,000       |
| Hunan      | 7947 (459, 2, 1077) | 10,000,000     | 10,000,000     | 10,000,000     |
| Inner Mongolia | 1300 (574, 1825) | 5,978,000       | 5,978,000       | 5,978,000       |
| Jiangsu    | 2688 (147, 7, 36) | 3,536,000       | 3,536,000       | 3,536,000       |
| Jiangxi    | 9004 (339, 0, 13, 050) | 7,700,000    | 7,700,000       | 7,700,000       |
| Jilin      | 1880 (129, 5, 22, 86) | 3,958,000     | 3,958,000       | 3,958,000       |
| Liaoning   | 1365 (984, 1635) | 8,778,000       | 8,778,000       | 8,778,000       |
| Province  | Code | Capital       | 18-9-1507 | 14-1-747 | 79-3-075 | 8017 | 84.4 | 13.9 |
|-----------|------|---------------|-----------|-----------|---------|------|------|------|
| Ningxia   | 1 | Taiyuan       | 692       | 70        | 1107    | 1127  | 1379  | 1295  |
|           |     |               |           |           |         |       |       |       |
| Qinghai   | 2 | Xining        | 1720      | 143       | 2609    | 1236  | 3671  | 1394  |
|           |     |               |           |           |         |       |       |       |
| Shaanxi   | 3 | Xi'an         | 4749      | 511       | 1458    | 1921  | 4120  | 1287  |
|           |     |               |           |           |         |       |       |       |
| Shandong  | 4 | Jinan         | 3730      | 641       | 4984    | 823   | 1053  | 1280  |
|           |     |               |           |           |         |       |       |       |
| Shanxi    | 5 | Xi'an         | 326       | 184       | 3414    | 793   | 1631  | 1220  |
|           |     |               |           |           |         |       |       |       |
| Sichuan   | 6 | Chengdu       | 2932      | 388       | 9649    | 1450  | 2869  | 1017  |
|           |     |               |           |           |         |       |       |       |
| Tianjin   | 7 | Tianjin       | 117       | 71        | 1640    | 552   | 805   | 1045  |
|           |     |               |           |           |         |       |       |       |
| Tibet     | 8 | Lhasa         | 1094      | 267       | 4411    | 1265  | 337   | 1529  |
|           |     |               |           |           |         |       |       |       |
| Xinjiang  | 9 | Urumqi        | 1930      | 309       | 9624    | 1854  | 1924  | 1250  |
|           |     |               |           |           |         |       |       |       |
| Yunnan    | 10| Kunming       | 7507      | 664       | 1591    | 1893  | 4921  | 1300  |

21
Table 3. DALYs and age-standardized DALYs rates in 2016 by aetiology and age-group

| Characteristic | DALY in count | DALYs rates (per 100,000) |
|----------------|---------------|--------------------------|
|                | Acute hepatitis A | Hepatitis B | Hepatitis C | Acute hepatitis E | Acute hepatitis A | Hepatitis B | Hepatitis C | Acute hepatitis E |
| Sex            |               |               |             |                 |               |               |             |                 |
| male           | 7918 (6667-9434) | 188799 (176058-202826) | 2638 (1912-3704) | 12035 (9874-14674) | 1.8 (1.5-2.2) | 22.1 (20.7-23.8) | 0.4 (0.3-0.5) | 2.0 (1.7-2.3) |
| female         | 6191 (5199-7367) | 74800 (69795-80525) | 1440 (1064-1910) | 8203 (6914-9826) | 1.8 (1.5-2.1) | 9.2 (8.6-9.9) | 0.2 (0.2-0.3) | 1.6 (1.4-1.9) |
| Age-group      |               |               |             |                 |               |               |             |                 |
| <5             | 8673 (7320-10839) | 980 (510-1665) | 472 (228-920) | 2654 (2254-3292) | 14.3 (12.1-17.9) | 1.6 (0.8-2.7) | 0.8 (0.4-1.5) | 4.4 (3.7-5.4) |
| 5 to 14        | 321 (223-454) | 509 (328-742) | 151 (108-203) | 4089 (3609-4672) | 0.2 (0.1-0.3) | 0.3 (0.2-0.5) | 0.1 (0.1-0.1) | 2.6 (2.3-3.0) |
| 15 to 49       | 2713 (1989-3592) | 115597 (107488-124995) | 1085 (746-1529) | 8039 (6003-10422) | 0.4 (0.3-0.5) | 15.5 (14.4-16.8) | 0.1 (0.1-0.4) | 1.1 (0.8-1.4) |
| 50 to 69       | 1767 (1246-2446) | 116715 (109037-124962) | 1931 (1171-3045) | 3254 (1887-5270) | 0.6 (0.4-0.8) | 36.4 (34.0-38.9) | 0.6 (0.4-1.0) | 1.0 (0.6-1.6) |
| ≥70            | 634 (439-874) | 29798 (27195-32331) | 440 (267-684) | 2202 (1366-3398) | 0.8 (0.5-1.0) | 35.5 (32.4-38.5) | 0.5 (0.3-0.8) | 2.6 (1.6-4.1) |

Table 4. The DALYs number and age-standardized DALYs rates per 100,000 of viral hepatitis by SDI in China
|                   | Acute Hepatitis A | Acute Hepatitis B | Acute Hepatitis C | Acute Hepatitis E |
|-------------------|--------------------|--------------------|--------------------|--------------------|
| High-middle level | 2892, 1639, 455, 319 | 2106, 2023, 7471, 5970 | 319, 301, 105, 96 | 3252, 2376, 666, 468 |
|                   | -88.9, 4.5, 1.2, 0.9 | -71.7, 62.9, 41.5, 12.7 | -69.9, 1, 0.7, 0.2 | -85.6, 8.8, 5.3, 1.5 |
|                   |                    |                    |                    |                    |
| Middle level      | 7608, 3072, 661, 440 | 3266, 2490, 9493, 8533 | 490, 398, 135, 133 | 6555, 3552, 854, 630 |
|                   | -94.2, 19.4, 11.7, 2.9 | -73.9, 101, 66.4, 21.4 | -72.9, 1.6, 1.1, 0.3 | -90.4, 17.8, 10.2, 2.7 |
|                   |                    |                    |                    |                    |
| Low-middle level  | 8752, 4447, 940, 531 | 2624, 2280, 8847, 7828 | 401, 363, 121, 111 | 7061, 4362, 1027, 705 |
|                   | -93.9, 53.7, 40.1, 14.5 | -70.2, 253.4, 195.2, 68.1 | -72.3, 4, 3.1, 1 | -90.0, 49.4, 32.7, 10.1 |

Ge from 1990 to 2016 %
Figures

Figure 1

Trends in China from 1990-2016 for: (A) all age and age-standardized incidence rates.
Figure 2

Trends in China in 2016 for: (A) incidence rates of hepatitis by sex and age-group
Sex difference in DALY rates per 100,000 for four etiologies of viral hepatitis by age group in 2016.