

Figure 3 Male and female comparison of the age-standardized YLD rate / YLL rate of alcohol use disorders between China and the regions with different income levels over the world from 1990 to 2019. Panel A. Comparison of the age-standardized YLD rate / YLL rate caused by male's alcohol use disorders in China and the regions with different income levels over the world from 1990 to 2019. Panel B. Comparison of the age-standardized YLD rate / YLL rate caused by female's alcohol use disorders in China and the regions with different income levels over the world from 1990 to 2019.

DISCUSSION

The rates of YLD, YLL and DALY caused by AUD in China increased in different level, which was harmful to public health and hindered the development of economy and society. In 1990-2019, there were significant difference in the rates of YLL and YLD of different genders in China, and the rates of men were higher than those of women. Two reasons were speculated to be the causes of this phenomenon. The first reason is that men have more unhealthy lifestyle habits and greater life and work stress than women, and the second, Chinese traditional culture believes that women's drinking will reflect their own image and hold negative attitude towards for women drinking behavior [34]. Therefore, preventive interventions targeting men with alcohol use disorders to reduce the burden of alcohol use disorders are more effective than for women [35].

We conducted a comprehensive and systematic analysis of the disease burden of AUD in China and the regions with the different income levels over the world from 1990 to 2019, Our findings underscore the importance of preventing and reducing the burden of AUD in HICs. The age-standardized YLD rate for AUD were higher in HICs than in other regions, which was associated with better access to quality health care and lower mortality rates in HICs. From 1990 to 2019, the AUD age-standardized YLD rates in China and the regions with different income levels over the world were significantly different. The age-standardized YLD rate in globe, China and other income regions showed a decreasing trend with different extents, while LICs has an upward trend (1.57%), which relates to the evidence that rising income inequality accelerates health disparities between countries. In the LICs, the resources available to meet the needs of the people are limited, and smokers with AUD do not receive prompt diagnosis and treatment. On the other hand, persistent drinkers are perceived by the public as lacking self-management skills and at risk for social harm [36]. When patients were diagnosed with AUD, they felt discriminated and the inferiority reduced their likelihood of seeking treatment [37]. The age-standardized YLD rate in China and other income regions decreased to different extents, presumably due to WHO's effective policies, such as restricting alcohol sales, controlling the drinking environment, early intervention and treatment services [41]. Age-standardized YLD rate (2.90%) declined with the slowest rate in China. This may be related to the fact that in 2005, the China government implemented a relatively loose new tax policy, which canceled the difference on taxes of potato liquor and grain liquor, thus the alcohol consumption of Chinese population increased significantly [43], which strongly explains the increasing burden of disease of AUD in China after 2005.

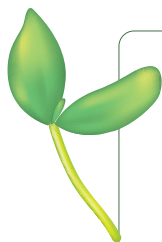
This study shows that compared with different income regions, China's age-standardized YLD/YLL rate (3.02) was higher, implying that YLD is the main contribution to the AUD's disease burden in China. The government issued two documents of "The Health of China 2030" and "China's medium and long-term plan for the prevention and treatment of chronic diseases (2017-2025)" and pointed out the suggestions to improve health education on alcohol restriction, to prevent alcohol abuse, to strengthen the monitoring of harmful alcohol use, and to study and improve alcohol taxation policies [44,45]. At present, the control of alcohol use in China is weak and has not formed a comprehensive system of work. The existing alcohol control policy lacks specific goals and measures, so the improvement of the alcohol control policy in China is a long and difficult task [46]. Therefore, China should limit the length of alcohol product advertisement [47], strengthen the propaganda

of AUD's disease, focus on the prevention and treatment of AUD, include the disease in the medical insurance [48-50], and provide free psychological treatment, to prevent its sequelae and complications and improve the quality of life of patients. The results of this study suggest that the disease burden of alcohol use disorders in China is increasing from 2005 to 2019. The government and primary health service organizations should strengthen the study on the risk factors and pathogenesis of AUD, identify the key groups of disease incidence and take intervention measures, especially strengthen the health education for the male high-risk group aged 15-49 and improve their knowledge of three-level prevention of AUD to reduce the risk of diseases.

It is worth noting that there is need to emphasize better guidance in the implementation of public health interventions according to different economic levels to ensure that medical and health care services are used properly for the treatment and management of AUD. In this way, reducing the burden of preventable AUD should be marked as a priority agenda for international and national health care policy makers. Based on the data of GBD 2019, this study analyzed the trend of the burden of disease of AUD between China and the regions with different income levels over the world from 1990 to 2019, the results provide a basis for future policies on AUD. There are some limitations in our study. For example, in GBD 2019's estimates of YLD, the disability weight is derived from data from several countries around the world, so there is uncertainty in the estimates of diseases in China and the regions with different income over the world [7]. In addition, the comprehensive evaluation of disease burden should include economic, family, social and other factors, and increase the multi-dimensional analysis to improve the accuracy of the results [51].

CONCLUSION

AUD's attributable disability burden remains high in the regions with different income levels over the world, which is the main source of the burden of disease. Given the large variations in AUD burden of disease by income level, future strategies to prevent and reduce the burden should be developed and implemented based on country-specific development status. Our findings can serve as a useful reference to inform targeted strategies that account for economic development at both regional and country levels.



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REFERENCES

- 1 Winslow BT, Onysko M, Hebert M. Medications for Alcohol Use Disorder. *Am Fam Physician*. 2016;93:457-65. Medline:26977830
- 2 Rehm J, Shield KD. Global Burden of Disease and the Impact of Mental and Addictive Disorders. *Curr Psychiatry Rep*. 2019;21:10. Medline:30729322 doi:10.1007/s11920-019-0997-0
- 3 Huang Y, Wang Y, Wang H, Liu Z, Yu X, Yan J, et al. Prevalence of mental disorders in China: a cross-sectional epidemiological study. *Lancet Psychiatry*. 2019;6:211-24. Medline:30792114 doi:10.1016/S2215-0366(18)30511-X
- 4 Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA Psychiatry*. 2015;72:757-66. Medline:26039070 doi:10.1001/jamapsychiatry.2015.0584
- 5 Oliveira LM, Bermudez MB, Macedo MJA, Passos IC. Comorbid social anxiety disorder in patients with alcohol use disorder: A systematic review. *J Psychiatr Res*. 2018;106:8-14. Medline:30236640 doi:10.1016/j.jpsychires.2018.09.008
- 6 Schuckit MA. Alcohol-use disorders. *Lancet*. 2009;373:492-501. Medline:19168210 doi:10.1016/S0140-6736(09)60009-X
- 7 GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1204-22. Medline:33069326 doi:10.1016/S0140-6736(20)30925-9
- 8 Gowing LR, Ali RL, Allsop S, Marsden J, Turf EE, West R, et al. Global statistics on addictive behaviours: 2014 status report. *Addiction*. 2015;110:904-19. Medline:25963869 doi:10.1111/add.12899

- 9 Huang H, Chen H, Dong H, Ning K, Zhang R, Sun W, et al. Prevalence, correlates and treatment status of alcohol use disorders in psychiatric patients in China. *Gen Hosp Psychiatry*. 2017;45:70-5. Medline:28274343 doi:10.1016/j.genhosppsych.2017.01.002
- 10 Rehm J, Dawson D, Frick U, Gmel G, Roerecke M, Shield KD, et al. Burden of disease associated with alcohol use disorders in the United States. *Alcohol Clin Exp Res*. 2014;38:1068-77. Medline:24428196 doi:10.1111/acer.12331
- 11 Huang J, Li K, Liu D, Cui L, Gao Y, Li G. Epidemiological investigation of Alcohol abuse and dependence Disorder in Hebei Province. *Chinese Journal of Drug Abuse Prevention and Treatment*. 2008;33-34+58.
- 12 Lohoff FW. Pharmacotherapies and personalized medicine for alcohol use disorder: a review. *Pharmacogenomics*. 2020;21:1117-38. Medline:32807012 doi:10.2217/pgs-2020-0079
- 13 Carvalho AF, Heilig M, Perez A, Probst C, Rehm J. Alcohol use disorders. *Lancet*. 2019;394:781-92. Medline:31478502 doi:10.1016/S0140-6736(19)31775-1
- 14 GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1223-49. Medline:33069327 doi:10.1016/S0140-6736(20)30752-2
- 15 GBD 2019 Demographics Collaborators. Global age-sex-specific fertility, mortality, healthy life expectancy (HALE), and population estimates in 204 countries and territories, 1950-2019: a comprehensive demographic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1160-203. Medline:33069325 doi:10.1016/S0140-6736(20)30977-6
- 16 Wang CR, Meng X, Wang C, Liu S. Trends of burden on ischemic heart disease and epidemiological transition of related risk factors in China, 1990-2017. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2020;41:1703-9. Medline:33297630
- 17 Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T. Global estimates of the need for rehabilitation based on the Global Burden of Disease study 2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2021;396:2006-17. Medline:33275908 doi:10.1016/S0140-6736(20)32340-0
- 18 Yu C, Cui F. The study of Global Disease burden and its Enlightenment to China. *Journal of Public Health and Preventive Medicine*. 2014;25:1-5.
- 19 Zou Z, Cini K, Dong B, Ma Y, Ma J, Burgner D, et al. Time Trends in Cardiovascular Disease Mortality Across the BRICS: An Age-Period-Cohort Analysis of Key Nations With Emerging Economies Using the Global Burden of Disease Study 2017. *Circulation*. 2020;141:790-9. Medline:31941371 doi:10.1161/CIRCULATIONAHA.119.042864
- 20 Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. *JAMA*. 2018;320:815-24. Medline:30167705 doi:10.1001/jama.2018.11406
- 21 Edelman EJ, Fiellin DA. In the Clinic. Alcohol Use. *Ann Intern Med*. 2016;164:ITC1-16. Medline:26747315 doi:10.7326/AITC201601050
- 22 Mathers CD, Lopez AD, Murray CJL. The Burden of Disease and Mortality by Condition: Data, Methods, and Results for 2001. *Global Burden of Disease and Risk Factors*. Washington (DC): The International Bank for Reconstruction and Development / The World Bank; 2006.
- 23 Iorio R. The Future Is Here: Bundled Payments and International Statistical Classification of Diseases, 10th Revision. *J Arthroplasty*. 2016;31:931. Medline:27040392 doi:10.1016/j.arth.2016.02.040
- 24 Zeng X, Qi J, Yin P, Wang L, Liu Y, Liu J, et al. Report on Disease burden of China and Provincial Administrative regions from 1990 to 2016. *Chinese Circulation Journal*. 2018;33:1147-58.
- 25 GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392:1789-858. Medline:30496104 doi:10.1016/S0140-6736(18)32279-7
- 26 Devleeschauwer B, Havelaar AH, Maertens de Noordhout C, Haagsma JA, Praet N, Pierre D, et al. Calculating disability-adjusted life years to quantify burden of disease. *Int J Public Health*. 2014;59:565-9. Medline:24752429 doi:10.1007/s00038-014-0552-z
- 27 Wang C, Sun Y, Jiang D, Wang C, Liu S. Risk-Attributable Burden of Ischemic Heart Disease in 137 Low- and Middle-Income Countries From 2000 to 2019. *J Am Heart Assoc*. 2021;10:e021024. Medline:34585592 doi:10.1161/JAHA.121.021024
- 28 Li HZ, Du L. Application of Joinpoint regression model in temporal trend analysis of tumor epidemiology. *Zhonghua Yu Fang Yi Xue Za Zhi*. 2020;54:908-12. Medline:32842323
- 29 Zeng S, Li Y, Liu J, Xie S, Fu X, Long Q, et al. joinpoint regression model and its application in epidemic trend analysis of infectious diseases. *China health statistics*. 2021;38:307-11.
- 30 Ji N, Liu M, Xu J, Xu Z, Bai Y. Health hazards of harmful use of alcohol. *Zhongguo Manxingbing Yufang Yu Kongzhi*. 2017;25:714-7.
- 31 Li J. Study on gender difference in the causes of death and disease burden of the residents in Chengyang district, Qingdao city, China. 2014, Shandong University.
- 32 Wang J, Ma H, Wang Z, Zhang Y. Prevalence of tobacco and alcohol use in ethnic Hui and Han residents in Ningxia. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2015;36:1231-5. Medline:26850242
- 33 Rehm J, Anderson P, Barry J, Dimitrov P, Elekes Z, Feijao F, et al. Prevalence of and potential influencing factors for alcohol dependence in Europe. *Eur Addict Res*. 2015;21:6-18. Medline:25342593 doi:10.1159/000365284
- 34 Shen Q. Comparative study of Liquor Culture between China and Japan. *Consume Guide*. 2019;52(4):82.
- 35 McCrady BS, Epstein EE, Fokas KF. Treatment Interventions for Women With Alcohol Use Disorder. *Alcohol Res*. 2020;40(2):08. Medline:32742894 doi:10.35946/arc.v40.2.08

- 36 Humphries KH, van Doorslaer E. Income-related health inequality in Canada. *Soc Sci Med.* 2000;50:663-71. Medline:10658847 doi:10.1016/S0277-9536(99)00319-6
- 37 Fortney J, Mukherjee S, Curran G, Fortney S, Han X, Booth BM. Factors associated with perceived stigma for alcohol use and treatment among at-risk drinkers. *J Behav Health Serv Res.* 2004;31:418-29. Medline:15602142 doi:10.1007/BF02287693
- 38 Schomerus G, Lucht M, Holzinger A, Matschinger H, Carta MG, Angermeyer MC. The stigma of alcohol dependence compared with other mental disorders: a review of population studies. *Alcohol Alcohol.* 2011;46:105-12. Medline:21169612 doi:10.1093/alcalc/agg089
- 39 Keyes KM, Hatzenbuehler ML, McLaughlin KA, Link B, Olfson M, Grant BF, et al. Stigma and treatment for alcohol disorders in the United States. *Am J Epidemiol.* 2010;172:1364-72. Medline:21044992 doi:10.1093/aje/kwq304
- 40 Wallhed Finn S, Bakshi AS, Andréasson S. Bakshi, and S. Andréasson, Alcohol consumption, dependence, and treatment barriers: perceptions among nontreatment seekers with alcohol dependence. *Subst Use Misuse.* 2014;49:762-9. Medline:24601784 doi:10.3109/10826084.2014.891616
- 41 Jernigan DH, Trangenstein PJ. What's next for WHO's global strategy to reduce the harmful use of alcohol? *Bull World Health Organ.* 2020;98:222-3. Medline:32132758 doi:10.2471/BLT.19.241737
- 42 White A, Hingson R. The burden of alcohol use: excessive alcohol consumption and related consequences among college students. *Alcohol Res.* 2013;35:201-18. Medline:24881329
- 43 Axley PD, Richardson CT, Singal AK. Epidemiology of Alcohol Consumption and Societal Burden of Alcoholism and Alcoholic Liver Disease. *Clin Liver Dis.* 2019;23:39-50. Medline:30454831 doi:10.1016/j.cld.2018.09.011
- 44 Issued by the CPC Central Committee and the State Council "Healthy China 2030 Planning outline". *Gazette of the State Council of the People's Republic of China.* 2016:5-20.
- 45 Circular of the General Office of the State Council on the issuance of China's medium-and long-term Plan for the Prevention and treatment of chronic Diseases (2017-2025). *Gazette of the State Council of the People's Republic of China.* 2017:17-24.
- 46 Huang F, Zhou S, Si X, Zhang X, Guo Y, Dong W, et al. Drinking behavior of Chinese residents and public health measures to control harmful drinking. *Zhongguo Manxingbing Yufang Yu Kongzhi.* 2020;28:861-5.
- 47 Anderson P, Chisholm D, Fuhr DC. Effectiveness and cost-effectiveness of policies and programmes to reduce the harm caused by alcohol. *Lancet.* 2009;373:2234-46. Medline:19560605 doi:10.1016/S0140-6736(09)60744-3
- 48 Summers LH. 267 signatories. Economists' declaration on universal health coverage. *Lancet.* 2015;386:2112-3. Medline:26388531 doi:10.1016/S0140-6736(15)00242-1
- 49 Patel V, Saxena S, Lund C, Thornicroft G, Baingana F, Bolton P, et al. The Lancet Commission on global mental health and sustainable development. *Lancet.* 2018;392:1553-98. Medline:30314863 doi:10.1016/S0140-6736(18)31612-X
- 50 Vigo DV, Patel V, Becker A, Bloom D, Yip W, Raviola G, et al. A partnership for transforming mental health globally. *Lancet Psychiatry.* 2019;6:350-6. Medline:30704963 doi:10.1016/S2215-0366(18)30434-6
- 51 Wang F, Qi Y, Li H. The methodological development of disease burden's research-comprehensive evaluation of disease burden. *Chinese Journal of Disease Control and Prevention.* 2003:537-9.