论著·公共卫生智库

后高接种率时代的挑战:中国慢性乙型肝炎疾病负担的存量特征、未来预测及基于危险因素控制的综合治理策略

郭芃芃[1],寇梦琳[1],黄静月[1],方静雅[1],黎 梅[2],薛爱国[1],梁靖蓉[1] [1]广州中医药大学东莞医院针灸科,广东东莞;[2]珠海市慢性病防治中心内科,广东珠海

[摘要] **目的** 基于全球疾病负担研究数据库(global burden of disease database,GBD)2021数据,描述1990—2021年全球及中国慢性乙型肝炎(含肝硬化)的流行趋势与疾病负担,评估社会发展不平等格局及人口学驱动因素,并预测中国未来疾病负担及危险因素贡献。**方法** 开展基于GBD 2021的二次分析,提取1990—2021年全球(204个国家/地区)及中国年龄标准化发病率(age-standardized incidence rate,ASIR)、年龄标准化患病率(age-standardized prevalence rate,ASPR)和年龄标准化伤残调整生命年率(age-standardized disability-adjusted life-year rate,ASDR)及95%不确定区间(uncertainty interval,UI)。采用Joinpoint分段回归估计年均变化百分比(average annual percentage change,AAPC)及95%置信区间(confidence interval,*CI*)。结合社会人口学指数(sociodemographic index,SDI)相关不平等指标、前沿分析与Das Gupta对称加法分解,量化负担差异及人口增长、人口老龄化和流行病学变化对总量变动的相对贡献。基于中国1990—2021年年度序列构建的自回归积分滑动平均模型(autoregressive integrated moving average,ARIMA)预测2022—2035年趋势,并在GBD比较风险评估框架下量化酒精使用与药物使用的归因负担。**结果** 1990—2021年全球ASIR、ASPR和ASDR总体下降AAPC值均具有统计学意义($P<0.05$),但在人口增长与老龄化叠加影响下,绝对病例数与伤残调整生命年(disability-adjusted life years,DALYs)未随标化率同步下降,负担主要集中于亚洲与撒哈拉以南非洲低-中SDI国家/地区。同期中国三项年龄标准化指标较1990年均下降>50%,儿童相关负担显著降低,但中老年男性仍为主要负担人群,总病例数与DALYs维持较高水平。分解分析显示,中国总量下降主要由流行病学变化降低驱动,而全球DALYs总量的变化更易受到人口增长与老龄化抵消/推动。ARIMA预测提示,在既往防控强度延续情景下,2035年前中国ASIR与ASDR将缓慢下降,而ASPR仍处相对高位。比较风险评估结果显示,酒精使用与药物使用为全球及中国慢性乙型肝炎(含肝硬化)相关DALYs的重要危险因素,其中中国酒精使用归因ASDR高于全球平均水平。**结论** 1990—2021年全球与中国慢性乙型肝炎(含肝硬化)年龄标准化负担总体下降,但全球仍存在由人口增长与老龄化驱动的总量压力且分布不均;中国虽在疫苗接种、预防母婴传播与抗病毒治疗方面取得显著进展,但存量管理与并发症预防仍是进一步减负的关键环节。**对策** 为实现世界卫生组织提出的"2030年消除病毒性肝炎公共卫生危害"目标,建议巩固新生儿乙肝疫苗及时首针与全程接种并强化预防母婴传播(prevention of mother-to-child transmission,PMTCT);聚焦中老年男性和高危地区,提升筛查-随访-治疗覆盖;将戒酒与物质使用障碍干预纳入乙肝管理;并向低-中SDI国家/地区及资源薄弱地区倾斜检测与治疗资源,缩小负担差距。

[关键词] 慢性乙型肝炎;肝硬化;全球疾病负担;伤残调整生命年;预测

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[通信作者] 梁靖蓉,E-mail:jingrongliang0606@126.com

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Challenges in the post-high vaccination coverage era: prevalence characteristics, future projections, and comprehensive management strategies based on risk factor control for chronic hepatitis B in China

GUO Pengpeng[1], KOU Menglin[1], HUANG Jingyue[1], FANG Jingya[1], LI Mei[2], XUE Aiguo[1], LIANG Jingrong[1]
[1]Department of Acupuncture and Moxibustion, Dongguan Hospital of Guangzhou University of Chinese Medicine, Dongguan, Guangdong; [2]Department of Internal Medicine, Zhuhai Center for Chronic Disease Control and Prevention, Zhuhai, Guangdong, China

[**Abstract**] Objective To analyze the epidemiological trends and disease burden in chronic hepatitis B (including cirrhosis) from 1990 to 2021 globally and in China based on Global Burden of Disease Database (GBD) 2021 study, assess development-related inequality patterns and demographic drivers, and project China's future burden and risk-factor contributions. Methods A secondary analysis was conducted on GBD 2021 data for 1990—2021 to extract the age-standardized incidence rate (ASIR), age-standardized prevalence rate (ASPR), and age-standardized disability-adjusted life-year rate (ASDR) globally (204 countries/territories) and in China, each with 95% uncertainty interval (*UI*). Joinpoint regression was used to estimate the average annual percent change (AAPC) with 95% confidence interval (*CI*). Combining sociodemographic index (SDI)-related inequality metrics, frontier analysis, and Das Gupta symmetric decomposition, differences in disease burden were quantified, and the relative contributions of population growth, population aging, and changes in age-specific rates to changes in absolute burden were also analyzed. Autoregressive integrated moving average (ARIMA) models were fitted to China's annual series for 1990—2021 to forecast trends for 2022—2035. Within the GBD comparative risk assessment framework, the attributable burden from alcohol consumption and drug use were quantified. Results Global ASIR, ASPR and ASDR in chronic hepatitis B were declined overall from 1990 to 2021 (all AAPCs, $P<0.05$). However, under the combined effects of population growth and aging, absolute numbers of cases and disability-adjusted life years (DALYs) did not decrease in parallel with age-standardized rates. The burden was concentrated primarily in low-middle SDI countries/territories in Asia and sub-Saharan Africa. In China, all 3 age-standardized indicators were decreased by more than 50% when compared with the values in 1990, and the burden was declined markedly in children; Nonetheless, middle-aged and old men remained the main high-burden group, with total cases and DALYs staying at relatively high levels. Decomposition analyses indicated that declines in age-specific rates (epidemiologic change) were the primary driver of reductions in China's absolute burden, whereas changes in global DALYs were more readily offset or driven by population growth and aging. ARIMA projections suggested that, under continuation of historical control intensity, China's ASIR and ASDR will decline slowly through 2035, while ASPR will remain comparatively high. Comparative risk assessment showed that alcohol consumption and drug use were important modifiable contributors to DALYs related to chronic hepatitis B (including cirrhosis) globally and in China; alcohol-attributable ASDR in China was higher than the global average. Conclusion From 1990 to 2021, the age-standardized burden of chronic hepatitis B (including cirrhosis) declined globally and in China, yet substantial absolute-burden pressure persists worldwide due to population growth and aging and is unevenly distributed. Despite major progress in China in vaccination, prevention of mother-to-child transmission, and antiviral therapy, strengthened management of prevalent infections and prevention of complications remain critical to further reduce residual burden. **Countermeasures** In line with the 2030 goal of eliminating viral hepatitis as a public health threat of World Health Organization, we recommend sustaining high coverage of timely birth-dose and full-course hepatitis B vaccination and strengthening prevention of mother-to-child transmission (PMTCT); prioritizing middle-aged and old men and high-risk areas to improve coverage of screening, follow-up, and treatment; integrating alcohol reduction and

services for substance use disorders into hepatitis B care; and directing testing and treatment resources toward low-middle SDI settings and other resource-limited areas to narrow burden disparities.

[**Key words**] hepatitis B, chronic; liver cirrhosis; global burden of disease; disability-adjusted life years; forecasting

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慢性乙型肝炎(hepatitis B virus,HBV)(含肝硬化)指所有慢性乙型肝炎病毒感染者,既包括已进展至肝硬化者,也包括未进展者,处于由慢性炎症-纤维化-肝硬化可进一步通向终末期肝病与肝细胞癌(hepatocellular carcinoma,HCC)的连续谱核心环节[1-2]。其负担在亚洲与撒哈拉以南非洲最为集中;诊断、抗病毒治疗与病毒学抑制的级联仍存在断点,导致可预防与可干预的存量长期累积[3]。循证研究表明,疫苗接种、预防母婴传播(prevention of mother-to-child transmission,PMTCT)、一线核苷(酸)类似物的持续治疗以及高危人群的规范随访,是降低并发症与死亡风险的关键措施[4-5]。

在全球疾病负担研究数据库(global burden of disease database,GBD)框架下,跨时期与跨地区的可比性建立在统一的原因清单、分层建模与标准化流程之上[6]。GBD 2021结果显示,自1990年以来,慢性乙型肝炎(含肝硬化)的年龄标准化指标总体下降,但人口增长与老龄化的叠加使部分地区的绝对数量未同步下降[7];按社会人口指数(sociodemographic index,SDI)分层,负担主要集中于低-中SDI国家/地区,并呈持续性不平等[8]。前瞻情景提示,若不加快有效的预防与诊疗策略,相关负担在未来仍可能上行[7]。

我国在乙肝防控方面取得持续进展:新生儿乙肝疫苗常规接种与及时首剂覆盖提升,PMTCT在真实世界得到验证与推广,儿童人群乙肝表面抗原(hepatitis B surface antigen,HBsAg)流行水平下降;但受历史高流行队列与人口老龄化叠加影响,慢性乙型肝炎(含肝硬化)的绝对规模与区域分布仍面临压力[9-10]。基于此,本研究利用GBD 2021数据,系统评估1990—2021年全球及中国在年龄标准化发病率(age-standardized incidence rate,ASIR)、年龄标准化患病率(age-standardized prevalence rate,ASPR)和年龄标准化伤残调整生命年率(age-standardized disability-adjusted life-year rate,ASDR)上的时空变化;在SDI维度量化不平等;采用分位前沿识别同等发展水平下的最低可达负担,并以对称加法分解区分人口增长、年龄结构与流行病学变化对总负担变动的相对贡献,为实现"2030年消除病毒性肝炎公共卫生危害"与我国综合防控提供证据支持。

1 资料与方法

1.1 数据来源

本研究为基于GBD 2021的二次分析,通过全球健康数据交换平台与配套结果库提取1990—2021年全球204个国家/地区及中国的逐年估计,其中"全球"估计包含中国在内的全部204个国家与地区,中国既单独报告亦计入全球汇总。指标包括发病率/数、患病率/数、伤残调整生命年率/数及其95%不确定性区间(uncertainty interval,UI),人口学与非致死负担估计均依GBD 2021统一框架与标准生命表执行,不对原始估计另行拟合或校正[11]。

通过全球健康数据交换平台(global health data exchange,GHDx)(https://ghdx.healthdata.org/gbd-results-tool)提取1990—2021年全球、5个SDI分层及中国慢性乙型肝炎(含肝硬化)的逐年估计,指标包括发病数、患病数、DALYs及相应的年龄标准化率和95%*UI*。数据于2025年9月21日下载,并严格遵循GBD协作网《数据使用协议》的引用与使用要求(https://www.healthdata.org/terms-use-data),报告方式参照GATHER指南。

1.2 疾病定义

主要结局为慢性乙型肝炎(含肝硬化),属于GBD 2021原因层级(level 4)条目,纳入所有慢性HBV感染者(含已进展至肝硬化与未进展者),与国际疾病分类(international classification of diseases,ICD)-10 B18.0、B18.1对应,并与急性乙型肝炎和乙型肝炎所致"肝硬化/肝癌"等条目区分以避免重复计量[6]。

本研究重点关注由HBV感染驱动的肝病负担。因此,文中所称"慢性乙型肝炎(含肝硬化)"排除了酒精性、非酒精性脂肪性等非病毒性病因所致肝硬化,限定于以HBV为主要病因的慢性肝病及肝硬化负担。

非致死端遵循GBD 2021非致死流程(如DisMod-MR 2.1)整合登记、调查与专病资料,得到发病率、患

病率与YLDs及其95%*UI*;死亡与YLLs由独立病因条目估计,再按病因分解口径与本条目对齐,保持致死与非致死端一致[2]。

1.3 指标与计算

核心率指标包括ASIR、ASPR与ASDR,均按GBD世界标准人口直接标化(/10万)。设第a个年龄组人口权重为w_a,对应年龄别率为r_a,则$ASR=\Sigma(w_a \cdot r_a)$。伤残调整生命年(disability-adjusted life years,DALYs)按标准分解:DALYs=YLLs+YLDs,其中$YLLs=\Sigma D_a \cdot L_a$($D_a$为该年龄死亡数,$L_a$为该年龄死亡对应的标准预期寿命),$YLDs=\Sigma P_i \cdot DW_i$($P_i$为相应健康状态患病人数,$DW_i$为相应伤残权重)GBD 2010以后不再采用时间贴现和年龄权重,GBD 2021亦延续这一设定,即不对未来生命年进行贴现,也不对不同年龄赋予额外权重。所有估计值及其95%*UI*均来源于GBD基于1 000次后验抽样形成的分布[6]。

1.4 趋势与不平等评估

长期趋势采用Joinpoint回归估计区间平均年变化百分比(average annual percent change,AAPC)置换检验,$\alpha=0.05$;$AAPC(\%)=\left\{\exp\left[\sum_j w_j \ln\left(1+\frac{APC_j}{100}\right)\right]-1\right\}\times 100\%$,其95%置信区间(*CI*)由Joinpoint软件基于模型方差估计获得。拐点数及模型优度通过Monte Carlo置换检验确定(双侧$P<0.05$)。对每一阶段计算年变化百分比[annual percent change,$APC=100\times(e^{\beta}-1)$],并按阶段长度对全期进行加权得到AAPC及其95%*CI*。AAPC及其95%*CI*下限>0判定为"上升",上限<0判定为"下降",其余视为"稳定"[12]。

健康不平等以SDI五分位为有序分层,采用斜率不平等指数(slope index of inequality, SII)与浓度指数(concentration index,CIX)评估。设人口加权SDI相对秩R_i(0-1)与结局率y_i回归:$y_i=\alpha+\beta R_i+\varepsilon_i$,则SII=β,反映从最低到最高SDI的绝对差值(/10万);CIX通过$CIX=2Cov(y_i, R_i)/\mu$估计(μ为y_i加权平均值),取值范围为-1~1,绝对值越大表示不平等程度越高[13-14]。

1.5 前沿分析

为识别在既定SDI下的最低可达负担,采用人口加权分位数回归拟合同年SDI与ASDR的下包络,形式为$Q_{\tau}(ASDR|SDI)=f(SDI)$,其中$\tau=0.05$表示5%分位数。选择5%分位而非极端分位(如1%)是为了在逼近相似SDI水平下负担最低的国家/地区的同时,避免少数异常值对前沿造成过度影响,这一做法已在近期GBD及国内GBD研究中得到应用。每年利用R的rq()函数(quantreg包)拟合5%分位数回归,得到给定SDI_i下的前沿预测值ASDR_frontier(SDI_i)。以观测值$ASDR_i$与前沿预测值之差量化"前沿缺口":$gap_i=ASDR_i-ASDR_frontier(SDI_i)$,gap>0表示负担高于前沿、存在改进空间,gap≈0视为接近前沿[15]。

1.6 分解分析(人口增长、年龄结构、流行病学变化)

以1990年为基期、2021年为末期,对总发病数、总患病数与总DALYs的变动进行Das Gupta对称加法分解。设总量$Y=N\times\sum_a(\pi_a r_a)$,其中N为总人口、$\pi_a$为年龄组占比、$r_a$为年龄别率;总变动$\Delta Y=Y_1-Y_0=\Delta Y_{pop}+\Delta Y_{age}+\Delta Y_{epi}$,通过对三因素全部排列路径的边际效应取平均,得到人口增长、年龄结构与流行病学变化3部分的绝对与相对贡献[16]。

由于3因素作用方向可能相反,其相对贡献百分比可出现>100%或为负值,反映某因素对总体变化的"抵消效应";采用Das Gupta对称加法框架,对所有可能排列路径的边际效应取平均,可减少分解结果对因素排序的依赖,已在近期基于GBD 2021的死亡与预期寿命分解研究中广泛应用,被认为具有较好的稳健性[17]。

1.7 疾病负担预测与危险因素分析

利用1990—2021年中国慢性乙型肝炎(含肝硬化)ASIR、ASPR和ASDR年度序列,采用Box-Jenkins方法构建非季节性ARIMA(p,d,q)模型;在对序列进行平稳性检验和必要差分后,以自相关/偏自相关图初选候选模型,并依据AIC、BIC和Ljung-Box残差检验确定最优模型,用于预测2022—2035年中国ASIR、ASPR和ASDR及其95%预测区间[18]。该方法可在GBD框架下外推既往趋势、评估中短期疾病负担变化,为检验防控目标和政策干预效果提供量化依据[19]。

危险因素分析采用GBD2021比较风险评估框架,提取饮酒和药物滥用等风险因素对慢性乙型肝炎(含肝硬化)年龄标化DALYs率和死亡率的可归因负担,比较2021年中国与全球的水平及构成,以识别贡献突出的可干预危险因素[20]。

1.8 统计学分析

数据处理与可视化在R(v4.4.2)环境完成;除非另有说明,双侧$P<0.05$具有统计学意义。

2 结果

2.1 中国与全球慢性乙型肝炎(含肝硬化)负担对比

1990—2021年,中国和全球慢性乙型肝炎(含肝硬化)的ASIR、ASPR与ASDR均呈显著下降趋势,但

中国3项指标降幅普遍快于全球(均>50%),尤其是ASDR降幅在各国中处于前列。至2021年,中国ASIR已接近全球平均,但ASPR和ASDR仍明显高于全球,提示在总患病规模和总体健康损失方面仍存在差距(表1,图1)。

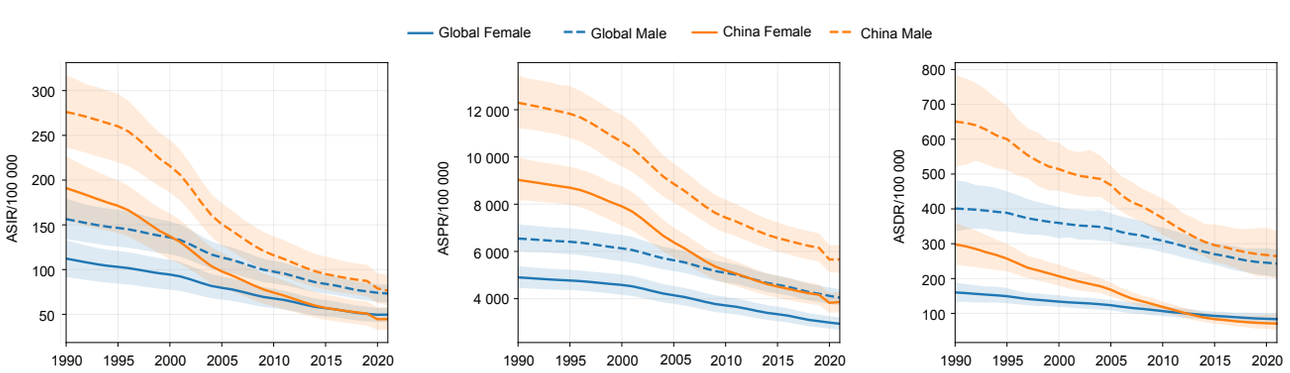
性别分层显示,男性长期承担更高的负担,且性别差距有扩大的趋势(表1,图1)。1990—2021年,中国男性ASIR、ASPR与ASDR虽整体下降,但男性/女性比均有所上升;尤其是ASDR的性别比由约2.2升至接近3.7,远高于全球平均水平。全球范围内,男性负担亦高于女性,但ASDR性别比的上升幅度小于中国。

表1 1990与2021年中国与全球慢性乙型肝炎(含肝硬化)负担概况

Table 1 Overview of chronic hepatitis B (including cirrhosis) burden in China and globally in 1990 and 2021

Sex	Location	Measure	1990	2021	1990—2021
			ASR/10^4(95%*UI*)	ASR/10^4(95%*UI*)	AAPC(95%*CI*)
Both	China	ASIR	235.00 (197.59~271.43)	60.98 (47.22~76.56)	−4.29(−4.56~−4.03)[a]
		ASPR	10 709.67 (9 767.87~11 756.70)	4 774.69 (4 282.97~5 260.42)	−2.58(−2.70~−2.45)[a]
		ASDR	479.32 (405.53~555.49)	167.03 (131.45~206.94)	−3.37(−3.51~−3.24)[a]
	Global	ASIR	134.58 (113.24~156.39)	61.51 (52.44~69.81)	−2.49(−2.59~−2.40)[a]
		ASPR	5 726.01 (5 234.40~6 271.39)	3 490.14 (3 197.57~3 789.02)	−1.59(−1.65~−1.54)[a]
		ASDR	279.53 (237.41~328.77)	161.92 (137.25~186.25)	−1.75(−1.82~−1.67)[a]
Male	China	ASIR	276.16 (236.12~317.12)	76.42 (60.17~94.21)	−3.98(−4.26~−3.70)[a]
		ASPR	12 295.26 (11 209.37~13 458.18)	5 662.48 (5 096.07~6 258.19)	−2.45(−2.63~−2.27)[a]
		ASDR	650.77 (521.51~783.60)	264.23 (200.03~336.31)	−2.88(−3.04~−2.73)[a]
	Global	ASIR	156.44 (134.10~179.27)	73.22 (63.22~83.05)	−2.41(−2.54~−2.29)[a]
		ASPR	6 545.96 (6 009.10~7 142.03)	4 043.81 (3 718.74~4 395.68)	−1.54(−1.59~−1.49)[a]
		ASDR	401.11 (335.01~482.14)	242.77 (204.41~283.18)	−1.61(−1.69~−1.53)[a]
Female	China	ASIR	191.03 (154.86~226.87)	44.71 (32.87~58.40)	−4.56(−4.86~−4.26)[a]
		ASPR	9 029.18 (8 157.60~10 004.34)	3 858.60 (3 419.51~4 295.76)	−2.71(−2.85~−2.56)[a]
		ASDR	298.22 (239.48~360.63)	70.56 (52.79~96.58)	−4.57(−4.70~−4.43)[a]
	Global	ASIR	112.29 (91.70~132.76)	49.67 (41.46~57.18)	−2.60(−2.68~−2.51)[a]
		ASPR	4 902.03 (4 455.07~5 373.17)	2 937.87 (2 681.26~3 211.27)	−1.65(−1.68~−1.63)[a]
		ASDR	160.26 (133.09~188.36)	83.49 (69.68~100.89)	−2.10(−2.17~−2.04)[a]

ASR: Age-standardized rate; ASIR: Age-standardized incidence rate; ASPR: Age-standardized prevalence rate; ASDR: Age-standardized disability-adjusted life-year rate; AAPC: Average annual percentage change; *UI*: Uncertainty interval; *CI*: Confidence interval; a: $P<0.05$



ASIR: Age-standardized incidence rate; ASPR: Age-standardized prevalence rate; ASDR: Age-standardized disability-adjusted life-year rate

图1 1990—2021年中国与全球慢性乙型肝炎(含肝硬化)年龄标准化发病率、年龄标准化患病率与年龄标准化伤残调整生命年率性别分层趋势

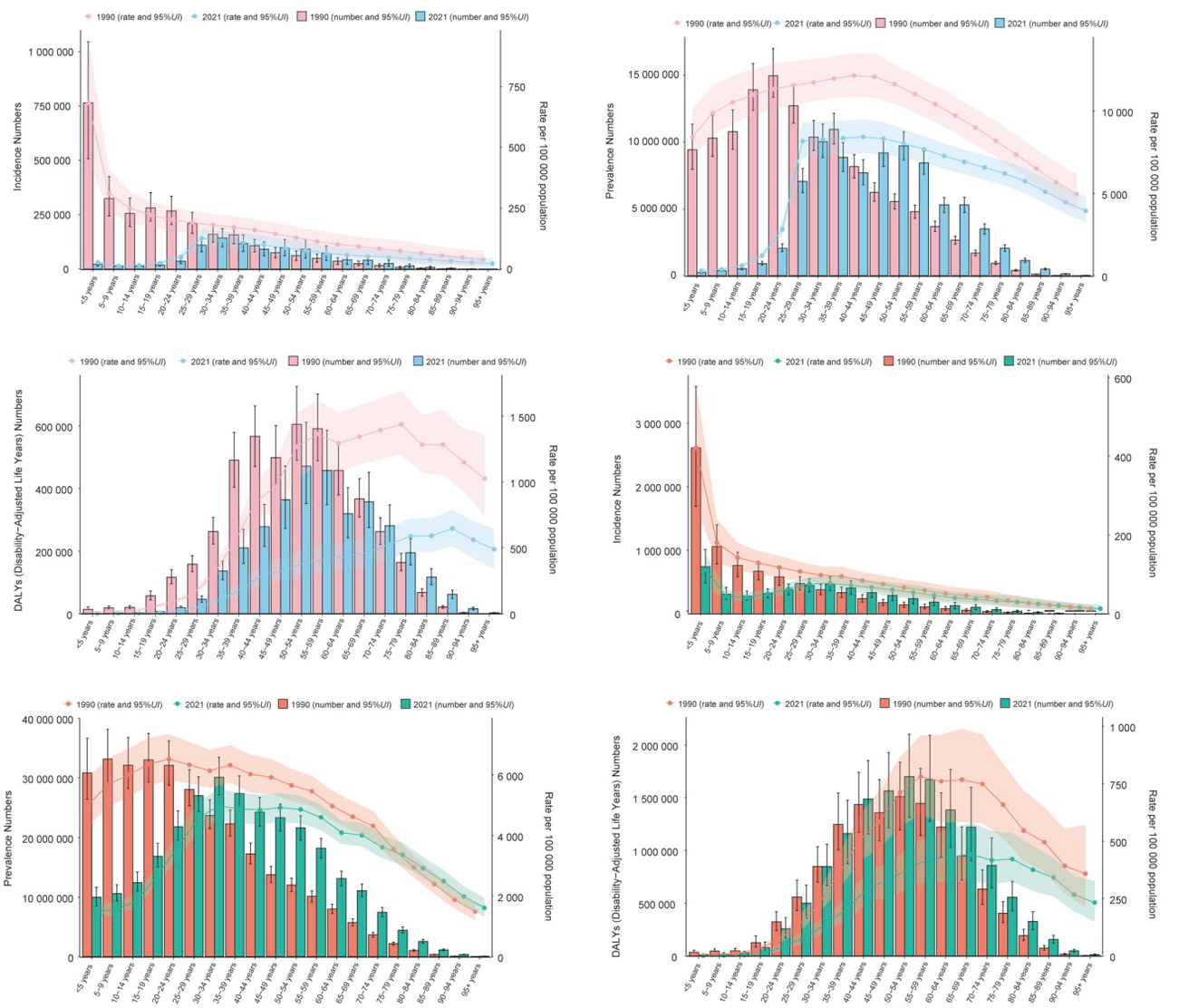
Figure 1 Sex-specific trends in ASIR, ASPR and ASDR of chronic hepatitis B (including cirrhosis) in China and globally, 1990—2021

2.2 中国与全球慢性乙型肝炎(含肝硬化)负担AAPC对比

1990—2021年国家层面AAPC显示,3项年龄标准化指标总体下降,但空间异质性显著。ASIR的国家中位数为-2.64%;中国为-4.29%(95%*CI*:-4.56~-4.03),在204个国家/地区中排名第7。ASPR的国家中位数为-1.72%(-2.10~-1.35);中国为-2.58%(-2.70~-2.45),排名第20。ASDR的国家中位数为-1.44%(-2.35~-0.92);中国为-3.37%(-3.51~-3.24),排名第17。全球范围内,发病、患病与总体负担均呈协同下降趋势,但降幅大小随国家而变;中国在3项指标上降幅均处于全球较快梯队,且在ASIR与ASDR上接近前列,见表1。

2.3 中国与全球慢性乙型肝炎(含肝硬化)负担年龄特征

2021年中国与全球的年龄分布呈现差异化峰型分布。粗发病率方面,中国峰值出现在25~29岁,为127.17(95%*UI*:92.20~164.27),而全球峰值位于<5岁,为112.57(95%*UI*:73.44~153.64);同期中国<5岁粗发病率为27.85(95%*UI*:17.86~38.52),显著低于全球,较1990年的中国<5岁峰值683.61(95%*UI*:453.12~935.03)大幅下降。发病例数方面,2021年中国峰值集中于30~34岁(142 686例),而全球峰值仍在<5岁(740 898例),反映两者新发负担的年龄集



DALYs: Disability-adjusted life-years

图2 中国与全球的年龄别发病、患病与伤残调整生命年:1990与2021年对比(5岁年龄组)

Figure 2 Age-specific incidence, prevalence and DALYs (5-year age bands) for China and globally: comparison between 1990 and 2021

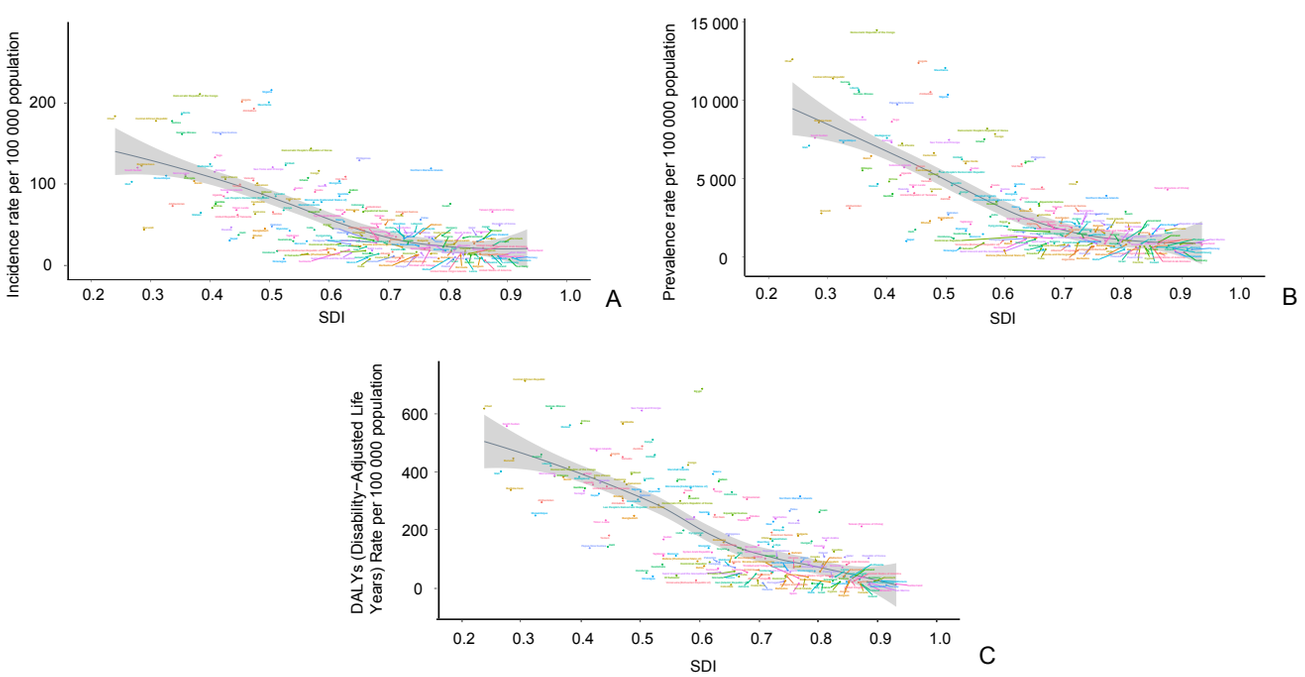
中区间不同。粗患病率方面,2021年中国在30~49岁形成高平台,峰值位于40~44岁,为8 424.10(95%*UI*:7 434.63~9 469.75),明显高于全球同年峰值30~34岁,为4 975.52(95%*UI*:4 489.42~5 529.34);对应患病例数峰值同位于30~34岁,中国为10 032 354例,全球为30 076 006例,显示随既往感染队列老化与存量病例累积,患病负担主要聚集于青壮年至中年阶段。粗DALY率方面,2021年中国随年龄持续上升并在85~89岁达到峰值647.44(95%*UI*:512.22~786.26),而全球峰值出现于65~69岁,为442.37(95%*UI*:327.87~578.83);DALY例数峰值则在两者均集中于50~54岁(中国471 206例;全球1 699 553例),提示总体健康损失在中老年阶段最为集中,但中国的率值峰位较全球明显后移,呈现更为"右移"的年龄分布,见图2。

2.4　ASIR、ASPR和ASDR与SDI的相关性

基于2021年204个国家/地区的横截面分析,3项年龄标准化指标与SDI均呈显著负相关:ASIR=−0.7120(95%*CI*:−0.7822~−0.6262)、ASPR=−0.7494(95%*CI*:−0.8098~−0.6684)、ASDR=−0.7828(95%*CI*:−0.8362~−0.7124),*P*均<0.001。随SDI升高,发病率、患病与总体健康损失同步下降,且在低SDI区间离散度较大,高负担"离群点"更为集中;高SDI区间点位收敛,提示负担与发展水平之间的单调递减关系在全球范围内较为稳健。中国定位于中高SDI国家簇中,ASIR接近同SDI拟合带中心,而ASPR与ASDR高于拟合值,见图3。

2.5　ASDR的不平等与前沿分析

基于2021年按SDI排序的浓度曲线与不平等指标,慢性乙型肝炎(含肝硬化)所致的ASDR呈显著"向低SDI端集中"的分布:浓度指数由1990年的−0.34(95%*CI*:−0.39~−0.29)下降至2021年的−0.40(95%*CI*:−0.44~−0.36),相对不平等加剧;同时,斜率不平等指数/10万绝对值由1990年的−544.63(95%*CI*:−607.93~−481.34)减小至2021年的−378.50(95%*CI*:−424.01~−333.00),提示在总体水平下降的背景下,绝对差距收窄而相对差距扩大,剩余负担更集中于低SDI国家(图4)。前沿分析显示,2021年在同等SDI水平下的"最优前沿"随SDI递增而单调下移,高SDI国家中日本、芬兰、韩国等点位接近前沿,低SDI国家如中非共和国、几内亚比绍、安哥拉、刚果、埃及等显著高于前沿;中国位于中-高SDI簇的拟合带上侧,仍存在与同等发展水平可达值之间的可压缩空间。1990—2021



SDI: Sociodemographic index; ASIR: Age-standardized incidence rate; ASPR: Age-standardized prevalence rate; ASDR: Age-standardized disability-adjusted life-year rate; *CI*: Confidence interval. The fitted curve (with 95%*CI*) depicts the overall trend, and the correlation coefficient (*r*) with 95%*CI* and *P* value are shown in each panel

图3　ASIR(A)、ASPR(B)、ASDR(C)和SDI的相关性

Figure 3　Associations of ASIR(A), ASPR(B) and ASDR(C) with the SDI

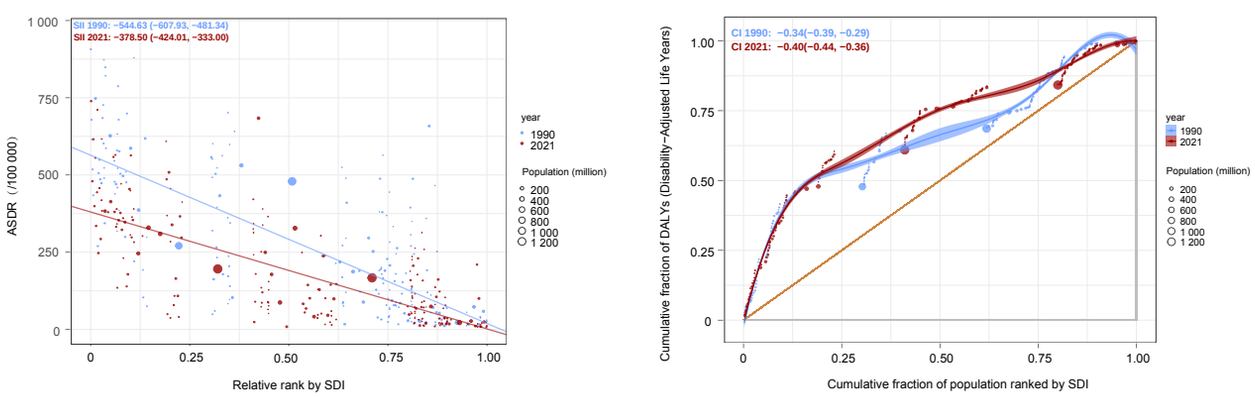
年多时点轨迹进一步表明,多数国家沿“SDI上升-ASDR下降”的路径收敛,少数低-中SDI国家出现停滞或反向变化,构成全球减负中的重点薄弱环节,见图5。

2.6 中国和全球发病、患病与DALYs的分解分析

依据1990—2021年分解结果(表2,图6),中国总发病数总体差异为-1 847 327.96,老龄化贡献-249 328.97、人口增长贡献355 529.02、流行病学变化贡献-1 953 528.01;相对贡献分别为13.50%、-19.25%、105.75%。中国总患病数总体差异为-44 566 116.60,老龄化贡献7 962 063.27、人口增长贡献20 040 752.30、流行病学变化贡献-72 568 932.20;相对贡献分别为-17.87%、-44.97%、162.83%。中国总DALYs总体差异为-1 394 733.58,老龄化贡献2 394 686.49、人口增长贡献860 206.11、流行病学变化贡献-4 649 626.18;相对贡献分别为-171.69%、-61.68%、333.37%。全球总发病数总体差异为-2 978 720.23,老龄化贡献-659 514.46、人口增长贡献2 561 741.22、流行病学变化贡献-4 880 946.98;相对贡献分别为22.14%、-86.00%、163.86%。全球总患病数总体差异为-25 751 579.30,老龄化贡献5 685 595.23、人口增长贡献118 826 012.00、流行病学变化贡献-150 263 187.00;相对贡献分别为-22.08%、-461.43%、583.51%。全球总DALYs总体差异为1 408 009.63,老龄化贡献3 601 782.03、人口增长贡献5 369 732.14、流行病学变化贡献-7 563 504.54;相对贡献分别为255.81%、381.37%、-537.18%。

2.7 慢性乙型肝炎(含肝硬化)疾病负担预测趋势及主要危险因素

基于1990—2021年中国慢性乙型肝炎(含肝硬化)ASIR、ASPR和ASDR序列建立ARIMA模型,对2022—2035年进行外推(图7)。模型预测显示,在既往防控水平延续的情景下,2022—2035年中国总人群ASIR将由60.98/10万进一步降至34.15/10万(95% *UI*:26.49~44.03),降幅约44.0%;ASPR由4 774.69/10万降至3 315.17/10万(95%*UI*:2 924.78~3 757.68),降幅



ASDR: Age-standardized disability-adjusted life-year rate; DALYs: Disability-adjusted life years; SDI: Sociodemographic index; SII: Slope index of inequality; CIX: Concentration index

图4 1990年与2021年按SDI的不平等分析(SII与CIX)

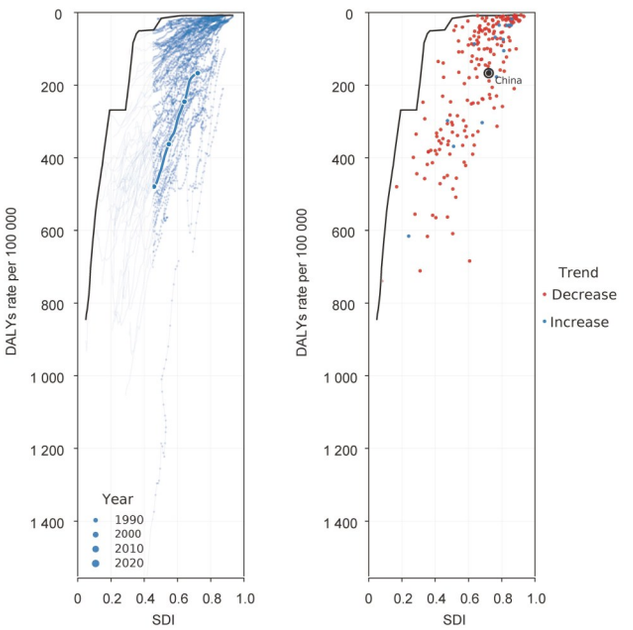
Figure 4 Inequality analysis of ASDR across SDI quintiles (SII and CIX)

表2 1990—2021年总发病数、总患病数与总DALYs变动的分解

Table 2 Decomposition of total changes in incidence, prevalence and DALYs, 1990-2021

Country/Region	Burden metric	Overall difference	Aging	Population growth	Epidemiological change	Aging/%	Population growth/%	Epidemiological change/%
China	Incident cases	−1 847 327.96	−249 328.97	355 529.02	−1 953 528.01	13.5	−19.25	105.75
	Prevalent cases	−44 566 116.60	7 962 063.27	20 040 752.30	−72 568 932.20	−17.87	−44.97	162.83
	DALYs	−1 394 733.58	2 394 686.49	860 206.11	−4 649 626.18	−171.69	−61.68	333.37
Global	Incident cases	−2 978 720.23	−659 514.46	2 561 741.22	−4 880 946.98	22.14	−86.00	163.86
	Prevalent cases	−25 751 579.30	5 685 595.23	118 826 012.00	−150 263 187.00	−22.08	−461.43	583.51
	DALYs	1 408 009.63	3 601 782.03	5 369 732.14	−7 563 504.54	255.81	381.37	−537.18

DALYs: Disability-adjusted life years



DALYs: Disability-adjusted life years; SDI: Sociodemographic index

图5 ASDR与SDI的前沿分析(1990—2021)

Figure5 Frontier analysis of the ASDR versus the SDI, 1990—2021

约30.6%;ASDR则由167.03/10万降至110.99/10万(95%*UI*:86.65~142.17),总体呈持续下降但下降速度略趋平缓的趋势。按性别分层看,男性与女性ASDR预测值虽同步下降(由2021年的264.23/10万*vs* 70.56/10万下降至2035年的183.61/10万*vs* 43.06/10万),但男性/女性比由1990年的约2.18上升至2021年的3.74,2035年仍可达4.26,提示未来男性仍将持续承担更高的疾病负担。基于GBD比较风险评估结果的2021年危险因素分析显示,饮酒和药物滥用是慢性乙型肝炎(含肝硬化)DALYs的主要可干预行为危险因素之一(图8)。在中国,饮酒归因的年龄标化DALYs率为73.64/10万(95%*UI*:51.75~101.13),约占当年总ASDR(167.03/10万)的44.1%,且明显高于全球平均水平的39.96/10万(95%*UI*:25.98~56.31);药物滥用归因率为1.20/10万(95%*UI*:0.58~2.08),约占中国总负担的0.7%,低于全球3.72/10万(95%*UI*:2.49~5.41)。

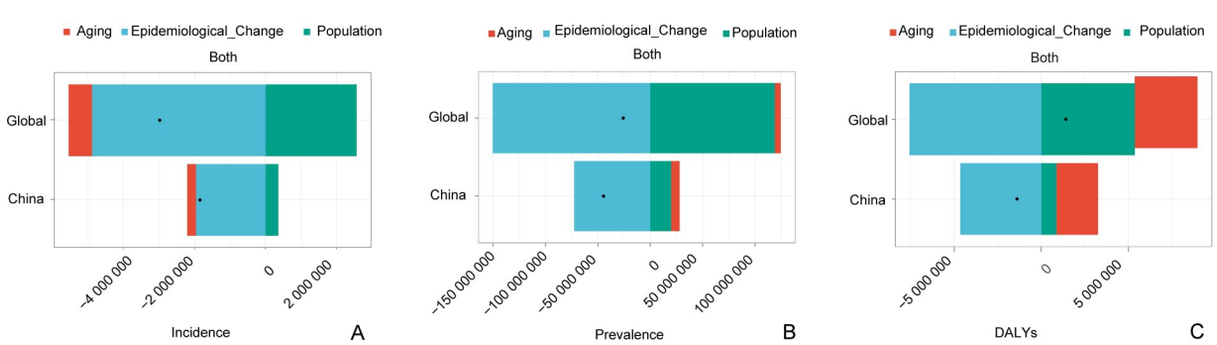
3 讨论

3.1 标准化率下降未必带来总量同步下降:全球负担仍向低-中SDI集中

本研究基于GBD 2021数据,系统评估1990-2021年全球及中国慢性乙型肝炎(含肝硬化)负担,并结合趋势、空间分布、不平等、分解、ARIMA预测及可归因危险因素进行综合分析。总体上,全球ASIR、ASPR与ASDR自1990年以来持续下降,但在人口增长与老龄化叠加作用下,相关发病数、患病数与DALYs绝对量仍处高位,部分地区仍呈上升趋势;负担高度集中于低-中SDI国家/地区,与最新基于GBD的乙肝及肝病负担研究一致[21]。中国3项年龄标化指标在观察期内持续下降且降速快于全球平均,符合我国扩大免疫规划、阻断母婴传播及推广核苷(酸)类似物抗病毒治疗后的流行病学变化[22];但至2021年中国ASPR与ASDR仍高于全球平均水平,提示存量病例管理与并发症预防仍有改进空间[9, 23]。

3.2 负担人群呈"新发右移、存量老化":中老年男性需作为重点

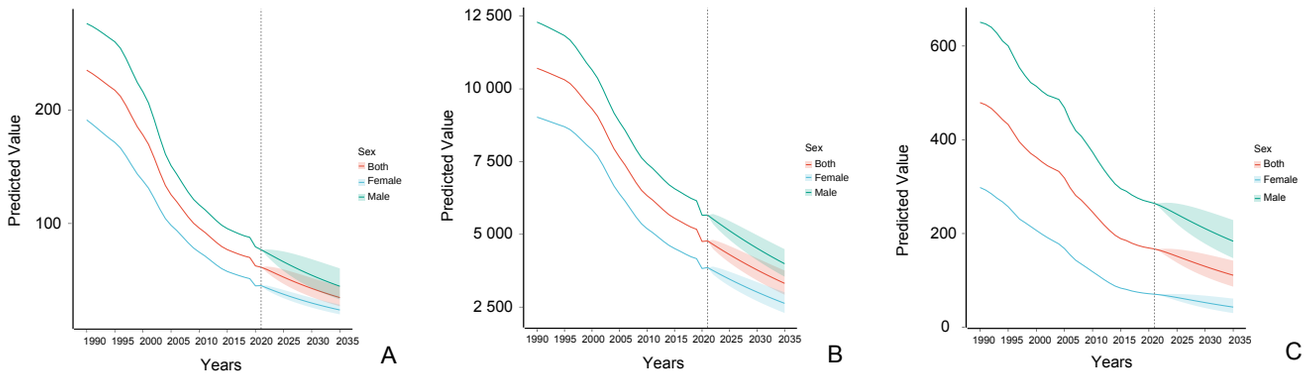
本研究揭示明显性别与年龄差异:男性ASIR、ASPR与ASDR长期高于女性,且差异持续存在,与既往关于乙肝自然史性别易感性及更高肝硬化/肝细胞癌风险的证据相吻合[8, 24]。年龄结构方面,2021年中



DALYs: Disability-adjusted life years. Bars indicate absolute contributions, and black dots denote the overall net change

图6 1990—2021年中国与全球发病率(A)、患病率(B)与伤残调整生命年(C)变动的分解

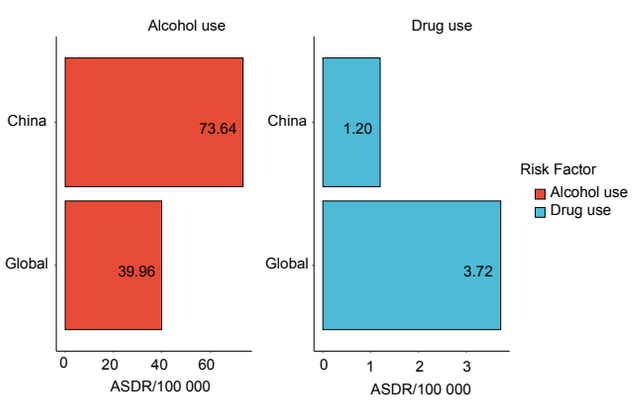
Figure 6 Decomposition of changes in incidence(A), prevalence(B) and DALYs(C) for China and globally, 1990—2021



ASIR: Age-standardized incidence rate; ASPR: Age-standardized prevalence rate; ASDR: Age-standardized disability-adjusted life-year rate

图7 1990—2035年中国慢性乙型肝炎(含肝硬化)年龄标准化发病率(A)、患病率(B)和伤残调整生命年率(C)的性别分层趋势及ARIMA预测

Figure 7 Sex-specific trends and ARIMA forecasts of ASIR (A), ASPR (B) and ASDR (C) for chronic hepatitis B including cirrhosis in China, 1990—2035



ASDR: Age-standardized disability-adjusted life-year rate

图8 2021年全球与中国慢性乙型肝炎(含肝硬化)因饮酒和药物滥用归因的ASDR比较

Figure 8 Comparison of ASDR attributable to alcohol use and drug use for chronic hepatitis B including cirrhosis, for China and globally, 2021

国发病率峰值较1990年由婴幼儿明显右移至25~29岁,而ASPR与DALY负担主要集中于30~59岁中青年及中老年;全球在较早年龄阶段仍形成较高负担平台。结合近年中国流行病学资料,儿童HBsAg流行率显著下降,但成年尤其是中老年男性仍承担主要并发症与死亡负担[25]。因此,应在中老年男性中加强主动筛查、非侵袭性分期、长期随访及规范抗病毒治疗,以降低后续肝硬化与肝细胞癌负担[26]。

3.3 不平等与前沿差距仍在:提高诊断与治疗覆盖仍有可压缩空间

不平等与前沿分析进一步刻画了发展水平与负担的关系。基于SDI分层的浓度曲线显示,慢性乙型肝炎(含肝硬化)ASDR长期呈"向低SDI端集中",随时间推移浓度指数持续为负且绝对值增大;同时斜率不平等指数绝对值下降,提示绝对差距有所收窄但并未消失[27-28]。前沿分析表明,多数国家沿"SDI上升-ASDR下降"轨迹向前沿线收敛,但仍有部分低-中SDI国家明显偏离前沿,是全球减负的薄弱环节[29-30]。中国位于中高SDI国家集群,ASIR接近同等SDI国家拟合带中心,但ASPR与ASDR仍偏离拟合带,提示在现有发展水平下,通过提高诊断率与抗病毒治疗覆盖、缩小地区与人群差距,仍可进一步压缩负担[31-33]。

3.4 分解提示人口学抵消效应明显:应以降低年龄别率为核心发力点

Das Gupta对称加法分解将1990—2021年总发病数、总患病数与总DALYs变动拆解为人口增长、年龄结构变化与年龄别率变化3部分。结果显示,中国3项总量指标整体下降主要由年龄别率下降驱动,人口增长与老龄化对降幅产生不同程度抵消;全球在年龄标化率下降的同时,人口增长与老龄化更为显著,其叠加效应在部分地区可部分或完全抵消率值改善,使总DALYs出现上升,该模式与近年肝病及多种慢性病的GBD分解研究一致[27]。在人口快速老龄化背景下,应在高负担人群中系统扩大高效干预,以持续降低年龄别率[34]。

3.5 预测与可归因风险提示:维持现状难以满足2030目标,应纳入控酒等综合干预

基于1990—2021年中国ASIR、ASPR与ASDR年度序列构建ARIMA模型并外推至2022—2035年,结果显示在维持既往防控强度的基线情景下3项年龄标

化指标仍将缓慢下降,但下降斜率低于1990—2021年的历史水平,其中ASPR下降最慢。近期全球与中国情景模拟研究亦显示,在目前诊断率与抗病毒治疗覆盖水平下,多数高负担国家在2030年前难以实现世界卫生组织提出的"新发感染减少90%、相关死亡减少65%"目标[31,35]。按GBD 2021比较风险评估框架,本研究量化了饮酒与药物滥用的可归因负担;并结合HBV感染者Meta分析证据,酒精摄入与肝硬化及肝细胞癌风险呈剂量-反应关系[20]。因此,在继续巩固疫苗接种与抗病毒治疗的同时,应将控酒、防药物滥用及心代谢综合管理纳入随访路径并协同推进[26]。

3.6 研究贡献、局限与后续方向

最后,面向"2030年消除病毒性肝炎公共卫生危害"的任务需求,我国慢性乙型肝炎(含肝硬化)防控应坚持"预防为主、防治并重",以扩大筛查诊断与规范治疗覆盖为抓手,推动免疫-筛查-治疗-随访一体化管理,并以风险因素干预与资源倾斜提升减负效率[36-39]。

本研究在统一的GBD 2021框架下,系统刻画了1990—2021年全球及中国慢性乙型肝炎(含肝硬化)负担的长期变化与空间分布,在统一口径下开展不平等指标与前沿分析以增强政策可读性,并通过Das Gupta分解区分人口增长、老龄化与年龄别率变化对总量变动的相对贡献;同时补充ARIMA预测并报告不确定性区间,结合比较风险评估量化饮酒与药物滥用的可归因负担,为评估"维持现状"情景下实现2030目标的差距提供量化参照[9,20,40-43]。

尽管如此,本研究仍有局限:①研究结果来源于GBD 2021整合建模,不同国家/地区基础数据质量与可得性存在差异,低SDI地区可能存在低估或结构性偏倚[44-45];②GBD"慢性乙型肝炎(含肝硬化)"条目难以进一步细分病程阶段与并发症类型,也难反映治疗方案与耐药等临床异质性[1,46];③危险因素分析受限于当前GBD可量化风险列表,且ARIMA预测为"维持既往防控强度"的时间序列外推,难以反映政策情景变化或新型疗法推广后的结构性改变,预测结果宜作为基线参照审慎解读[47-48]。

为提升证据的可操作性与外部效度,后续研究可从数据分层、方法提升与政策评估三方面推进:①在数据层面,补充省际、城乡及社会经济分层,细化不同性别与年龄段的重点人群与负担构成;②在方法层面,引入情景预测并纳入可观测外生变量,开展不同预测模型的比较验证,强化不确定性传播的多源量化;③在政策层面,开展与成本-效果及公平性相衔接的评估,比较不同筛查与治疗覆盖强度、随访管理强度以及行为风险干预强度的潜在影响,为分阶段、分人群的精准防控提供量化依据[31,35,37]。

综合本研究结果,建议:第一,继续巩固国家免疫规划与PMTCT策略,重点覆盖薄弱地区,维持出生及时首针与全程接种高覆盖并进一步降低母婴传播风险[36];第二,面向中老年高流行队列(尤其男性)推进主动筛查与分层管理,提高诊断率与长期抗病毒治疗覆盖,扩大筛查与治疗具有成本-效果性依据[37];第三,将控酒、药物滥用干预与心代谢综合管理系统嵌入随访路径,与抗病毒治疗形成协同,降低疾病进展风险[20,26,38];第四,依据不平等与前沿分析结果,对低SDI国家及国内资源薄弱地区优先配置疫苗、检测与治疗资源,在技术与资金上给予支持,缩小与前沿水平差距,推动全球及区域负担协同下降[39]。

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