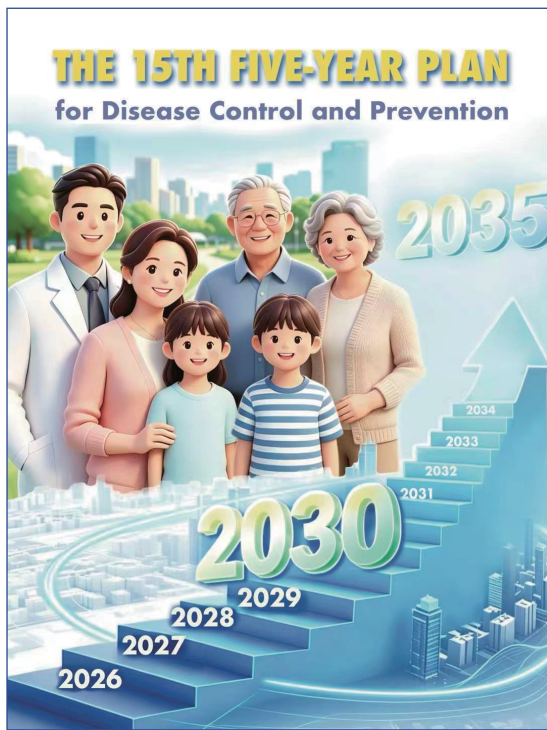


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The 15th Five-Year Plan for Disease Control and Prevention — A Crucial Five-Year Progression Toward a Modernized Disease Control and Prevention System

Jianwei Wang^{1,†}

ABSTRACT

On July 21, 2026, China released the 15th Five-Year Plan for Disease Control and Prevention (15th FYPDCP), the country's first national-level five-year special plan for disease prevention and control, aiming to establish a Chinese-style modernized disease control and prevention system by 2030 and accelerate progress toward the goal of "Building a Healthy China by 2035." This article provides a systematic interpretation of the Plan's core content and innovations. The 15th FYPDCP designates 2026–2030 as a critical window for transitioning from "system restructuring" to "substantive development" and from "passive response" to "active prevention." With capacity enhancement as the foundation, system strengthening as the safeguard, and risk prevention as the primary goal, the 15th FYPDCP focuses on key areas as follows: reshaping disease control concepts and strategies through multi-disease prevention and control; breaking institutional barriers through medical-prevention coordination and integration; promoting social co-governance through joint prevention and control mechanisms; injecting core momentum through scientific research and innovation; and driving digital and intelligent empowerment to shift disease prevention and control from experience-driven to data-driven approaches and from post-event handling to pre-event early warning. The implementation of the 15th FYPDCP will provide an action framework for building a Chinese-style modernized disease control and prevention system and contribute China's wisdom and solutions to global public health governance.

On July 21, 2026, China released the 15th Five-Year Plan for Disease Control and Prevention (15th FYPDCP) (1), the country's first national-level five-year special plan for disease prevention and control,

aiming to establish a Chinese-style modernized disease control and prevention system by 2030. The promulgation of the 15th FYPDCP is of profound and far-reaching historical significance. In addition to setting out a five-year action plan for disease prevention and control, it serves the critical mission of accelerating progress toward the goal of "Building a Healthy China by 2035" (2). Whether the modernization of the disease control and prevention system is completed by 2030 is not merely a matter of the health and well-being of China's population of more than 1.4 billion; it also bears on the strategic baseline for national public health security.

The Next Five Years: A Critical Five-year Period for Establishing A Modernized Disease Control and Prevention System

In the 15th FYPDCP, the period 2026–2030 constitutes a crucial window for the current disease control and prevention system to transition from "system restructuring" to "substantive development" and from "passive response" to "active prevention". First, the public health environment is undergoing accelerated changes, and the situation for infectious disease prevention and control is becoming increasingly complex. The risk of outbreaks of emerging and re-emerging infectious diseases persists, alongside a continually increasing risk of imported diseases. Traditional infectious disease prevention and control faces unprecedented challenges, while the burden of noncommunicable diseases remains high because of the interrelated and compounding effects of population aging and diverse health-related factors, such as climate change, environmental pollution, occupational hazards, and food safety risks. Second, during the 14th FYP period, China achieved internationally recognized accomplishments in disease prevention and control. These include a major and decisive victory in the COVID-19 response, the granting of malaria-free certification by the World

Health Organization (WHO), sustained control of AIDS at a low prevalence level, interruption of schistosomiasis transmission, and general control of the endemic echinococcosis. In terms of system development, these accomplishments include the promulgation and implementation of the new Law on the Control and Prevention of Infectious Diseases and the Law on Response to Public Health Emergencies; the establishment of national- and provincial-level disease prevention and control administrations; the incorporation of the relevant disease prevention and control administration designations into city- and county-level health commissions; the integration and restructuring of disease prevention and control agencies and health supervision agencies; the comprehensive upgrading of infrastructure in disease prevention and control institutions; and the strengthening and expansion of the disease prevention and control workforce.

Improving the public health system requires a transformation from "structural shaping" to "core forging" and from "framework building" to "function strengthening". This transformation represents a major leap that must be achieved under the 15th FYPDCP. Therefore, the launch of the 15th FYPDCP at this juncture between past and future indicates that the plan is intended not merely to continue past work but also to require systematic resource deployment for modernizing the disease control and prevention system. Under the 15th FYPDCP, capacity enhancement, system strengthening, and risk prevention will serve as the foundation, safeguard, and primary goal, respectively, forming the core framework for disease prevention and control efforts during this period. Centered on the two major phases of "foundation consolidation and core enhancement" and "quality and efficiency improvement and comprehensive upgrading", this framework focuses on addressing gaps and weaknesses, optimizing mechanisms and enhancing quality and efficiency, and preventing risks and safeguarding health to comprehensively accelerate the modernization of the disease control and prevention system and related capabilities.

Reshaping Disease Control and Prevention Concepts and Strategies Through Multi-disease Prevention and Control

One of the most emblematic conceptual innovations

of the 15th FYPDCP is the systematic establishment of a "multi-disease prevention and control" strategy. In the context of the increasingly severe and complex situation of infectious disease prevention and control and the growing demands on disease prevention and control, the multi-disease prevention and control strategy represents a crucial measure for coordinating resources and improving the quality and efficiency of disease prevention and control. Accordingly, the rationale for disease prevention and control is reconstructed through systems thinking. By adhering to the principles of "commonalities as the link, integration as the means, coordination as the pathway, and effectiveness as the goal", this strategy aims to achieve a shift from "passively waiting for disease emergence" to "actively identifying diseases". The core value of multi-disease prevention and control lies in the attaining maximum disease prevention and control effectiveness at minimal cost.

Regarding specific deployment efforts, the 15th FYPDCP adopts a systematic resource deployment approach to strengthen the prevention and control of six major disease categories (respiratory infectious diseases, vector-borne diseases, bloodborne and sexually transmitted infectious diseases, zoonotic diseases, vaccine-preventable diseases, and other diseases) based on the concept of multi-disease prevention and control. It promotes multi-disease testing, prevention, and management. In addition, it calls for coordinated surveillance, judgment, and handling across the various stages of the disease prevention and control process, from surveillance and early warning, prevention and intervention, and emergency response and handling to disease management, supervision and enforcement, and health education. This approach will effectively accelerate the development of a comprehensive work and strategy framework for multi-disease prevention and control.

Breaking Institutional Barriers Through Medical-prevention Coordination and Medical Prevention Integration for Disease Prevention and Control

Historical experiences clearly demonstrate that disease prevention and control efforts cannot succeed without the deep involvement of the healthcare system; otherwise, they amount to a one-legged endeavor. Likewise, unless the concept of prevention is deeply embedded, medical services will find it difficult to shift from a disease treatment-centered approach to a

health-centered approach.

Therefore, the 15th FYPDCP introduces a series of groundbreaking institutional arrangements. At the organization level, it explicitly promotes deep collaboration between healthcare institutions and professional public health institutions, the attainment of full coverage of public health departments in secondary and higher-level hospitals, and the incorporation of healthcare institutions' fulfillment of disease prevention and control responsibilities as a criterion for hospital grading assessment.

At the institution level, the 15th FYPDCP proposes the establishment and improvement of disease prevention and control supervision systems and the advancement of pilot programs to grant prescribing authority to public health physicians. These initiatives will enable public health physicians to serve as genuine health gatekeepers, delivering integrated disease prevention and treatment at the community level and providing the public with a full spectrum of health services spanning prevention, treatment, rehabilitation, and health management.

At the grassroots level, the 15th FYPDCP requires primary healthcare institutions to designate specific departments or personnel to assume responsibility for infectious disease prevention and control. This will help reinforce the grassroots public health safety net in China, thereby extending the reach of disease prevention to every village and community across the country.

The coordination and integration of medical care and prevention constitute a major requirement for establishing a modernized disease control and prevention system in the new era. This requires top-down design of the service content, integration processes, and resource coordination, and targeted measures should be adopted at various stages of the prevention and control process to enhance the quality and efficiency of coordination between medical care and prevention. In future disease control and prevention system, prevention and treatment will no longer be separated. Instead, an integrated full-spectrum service model of "prevention-screening-diagnosis-treatment-rehabilitation" will be developed, which is precisely the hallmark of modernized disease control and prevention system.

Developing A Social Co-governance Framework Through Joint Control and Prevention Mechanisms

Disease prevention and control is not the sole

responsibility of the dedicated disease prevention and control authorities. Rather, governments at all levels must strengthen their accountability and give greater prominence to the "prevention first" principle (3). One of the most striking features of the 15th FYPDCP is its emphasis on the concept of "comprehensive disease prevention and control" and its promotion of social co-governance.

At the mechanism level, the 15th FYPDCP proposes to maintain the regular operation of joint prevention and control mechanisms at all levels for major infectious disease outbreaks, ensure the capacity for efficient transitions between routine and emergency response states, and improve the quality and efficiency of situation assessment, coordination and scheduling, and information sharing.

Regarding interdepartmental coordination, the 15th FYPDCP emphasizes strengthened joint prevention and control mechanisms across multiple departments and regions, as well as between military and local authorities. It specifically promotes the optimization of external defense measures to prevent the importation of infectious diseases. To this end, it adopts a framework centered on three major components — remote prevention and control, border control measures, and domestic prevention and control — to achieve closed-loop management across the entire process chain for imported infectious disease prevention and control.

For social participation, the 15th FYPDCP requires village (resident) committees and public health committees to play a role in promoting whole-society support for and participation in disease prevention and control efforts. Activating of such grassroots self-governance capacity, strengthening the area responsibility system for disease prevention and control in communities, and improving the grid-based grassroots disease prevention and control network will transform disease prevention and control from "the government's responsibility" to "everyone's responsibility". This shift will be a precise manifestation of the spirit of social co-governance.

The essence of joint prevention and control mechanisms is to build an epidemic prevention and control network with comprehensive horizontal and vertical coverage, where "horizontal" refers to coordinated action across multiple departments and regions, and "vertical" refers to seamless implementation from the national level down to the provincial, municipal, county, and grassroot levels. The smooth operation of every node and link in this

network will be crucial for maintaining composure in responding to disease outbreaks.

Injection of Core Momentum Through The Enhancement of Scientific Research and Innovation

The 15th FYPDCP places scientific research and innovation in a prominent position and explicitly calls for enhancing of scientific research breakthrough systems and public health capacity building, as well as improving science and technology innovation systems in the field of disease prevention and control. These measures will inject considerable momentum into the high-quality development of disease prevention and control efforts.

Specifically, the 15th FYPDCP proposes to maximize the role of national laboratory platforms in strengthening the development of scientific and technological innovation platforms and bases and in creating core bases for research on infectious disease prevention and control. China's national laboratories play an indispensable role in coordinating scientific research resources related to disease prevention and control nationwide and in facilitating interdisciplinary collaborative research and joint efforts to achieve breakthroughs. Consequently, scientific research on disease prevention and control will shift from "isolated efforts" to "unified leadership and coordinated action".

The 15th FYPDCP calls for advancing the development of national and provincial preventive medicine academies, enhancing capacity for scientific research support and technical assurance, and implementing incentive policies for scientific research. Currently, preventive medicine academies have been established at all national and provincial centers for disease control and prevention in China. For preventive medicine academies to truly fulfill their role as scientific research institutions, comprehensive supporting systems must be established for scientific research organization, project management, technology transfer, and talent incentives, thereby enabling scientific research to become an integral part of disease prevention and control efforts.

The 15th FYPDCP places particular emphasis on driving research to achieve breakthroughs in key core technologies and on strengthening the generation and translation of research findings. It is imperative that research findings be rapidly translated from the laboratory to the frontline of disease prevention and control, so that they can be truly transformed into

tangible capacity to safeguard public health.

The deep integration of scientific research and innovation with disease prevention and control efforts is a key distinguishing feature of modernized disease control and prevention system. In the 15th FYPDCP, "strengthening scientific research and innovation" constitutes the core driving force for accelerating disease prevention and control through science and technology empowerment.

Driving The Modernization of The Disease Control and Prevention System Through Digital and Intelligent Empowerment

With digital and intelligent empowerment, data will become a core factor of production in the disease control and prevention system. The 15th FYPDCP calls for the establishment of a comprehensive surveillance and early-warning system for infectious diseases, with expansion and refinement of monitoring risk factors and related events, including disease cases, public health emergencies, clinical syndromes, laboratory pathogens, vectors, and the environment factors, and of surveillance channels for global epidemic information, interdepartmental coordination, and community-based sensing. Surveillance will no longer rely on a single channel; instead, it will be triggered at multiple points by signals from hospitals, laboratories, pharmacies, schools, elderly care institutions, online public sentiment, and other sources, and these signals will be consolidated into a unified surveillance and early-warning platform.

The deployment and application of national intelligent infectious disease surveillance and early-warning software in healthcare institutions will be a key enabler of digital and intelligent empowerment. Building on the current progress whereby the software has already been deployed and implemented in secondary and higher-level medical institutions nationwide, the 15th FYPDCP proposes extending its deployment and application to medical institutions below the secondary level. The software will enable the automatic collection and intelligent analysis of infectious disease-related data and support the automatic identification and early warning of abnormal signals.

The ultimate goal of digital and intelligent empowerment is to shift disease prevention and control from "experience-driven" to "data-driven", from "manual judgment" to "intelligence-supported

judgment", and from "post-event handling" to "pre-event early warning". This represents a profound paradigm shift in disease prevention and control efforts.

Contributions of The Modernization of China's Disease Control and Prevention System to Global Public Health Governance

Global public health governance is currently at a critical juncture of profound transformation. In May 2025, the 78th World Health Assembly adopted the WHO Pandemic Agreement, a landmark, legally binding international instrument aimed at strengthening pandemic prevention, preparedness, and response (4). Concurrently, the disease control and prevention systems in major countries and regions are undergoing accelerated transformation. The United States Centers for Disease Control and Prevention (US CDC) is advancing science and health equity through its 2022–2027 Strategic Plan, with a focus on strengthening data, laboratory, and epidemiological capacities (5). The European Centre for Disease Prevention and Control (ECDC), based on its revised founding regulation, has made substantial efforts to advance the digitalization and interoperability of infectious disease surveillance systems (6). It is therefore evident that modernizing disease control and prevention systems has become a common theme in public health governance worldwide.

By 2030, China will work closely with other countries to promote the joint development of a global surveillance and early-warning network for emerging infectious diseases, facilitate appropriate technological exchanges, and contribute China's unique wisdom,

solutions, and strengths to building a global community of health for all humankind.

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Preplanned Studies

Long-Term Trends and Regional Heterogeneity in Overweight and Obesity Among Adults — 11 Intermittent Surveys in China, 1991–2024

Jiale Li¹; Xiaofan Zhang^{1,2}; Ziyu Zhang^{3,4}; Li Li^{1,2,#}; Chengdong Xu^{3,5,#}

Summary

What is already known about this topic?

Overweight and obesity have increased in China. Evidence integrating long-term trends, regional heterogeneity, and multilevel factors remains limited.

What is added by this report?

From 1991 to 2024, age-standardized combined prevalence of overweight and obesity rose from 20.20% (1,567/8,445) to 53.10% (7,286/13,112) and obesity from 3.70% (259/8,445) to 18.10% (2,303/13,112). Men, adults aged 40–79 years, and those with lower education showed outcome-specific higher odds.

What are the implications for public health practice?

Regionally tailored population-wide prevention, weight management for higher-burden adults, healthier diets and community food environments, and attention to air quality as a contextual factor are suggested.

$P < 0.001$). The prevalence was the highest for combined overweight and obesity and for overweight in North China and for obesity in Northeast China. Men and adults age 40–79 years had higher odds of combined overweight and obesity and of overweight; high education was inversely associated with all outcomes. Drinking and meat intake were positively associated with combined overweight and obesity and with obesity. Community Western fast-food restaurant availability was associated with combined overweight and obesity, and provincial PM_{2.5} with all outcomes.

Conclusion: Overweight and obesity increased over three decades but varied regionally. Population-wide prevention should be complemented by targeted measures for higher-burden groups and for North and Northeast China.

ABSTRACT

Introduction: Overweight and obesity have increased substantially in China. Limited studies integrate long-term trends, regional heterogeneity, and multilevel factors.

Methods: Eleven China Health and Nutrition Survey waves (1991 to 2024) provided 115,541 person-wave observations (ages 18–79). Prevalence was age-standardized to the 2020 Chinese census population. Inverse-variance weighted regression assessed trends; Cochran's *Q* test assessed regional heterogeneity. Three-level logistic regression examined individual-, community-, and provincial-level factors.

Results: From 1991 to 2024, age-standardized prevalence increased from 20.20% (1,567/8,445) to 53.10% (7,286/13,112) for combined overweight and obesity, from 16.51% (1,308/8,445) to 35.00% (4,983/13,112) for overweight, and from 3.70% (259/8,445) to 18.10% (2,303/13,112) for obesity (all

Overweight and obesity pose challenges to noncommunicable disease prevention and control. Over recent decades in China, their prevalence has risen substantially (1), with national surveillance efforts having identified considerable provincial variation in adult obesity (2). Temporal and geographic patterns have been examined separately; separating overweight from obesity can show whether regional differences reflect either/both outcomes. Because excess weight is associated with multilevel factors (3), whether provincial heterogeneity persists after considering individual and community characteristics and how it relates to provincial socioeconomic and environmental indicators remain unclear. This repeated cross-sectional study used 11 China Health and Nutrition Survey (CHNS) waves to estimate age-standardized trends among adults and compare seven regions.

The 11 CHNS waves used in this study were 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, 2015, 2018, and the combined 2022–2024 follow-up round (4). Participating provincial-level administrative

divisions (PLADs) increased from nine in 1991–2009 to 12 in 2011, 15 in 2015, and 16 in 2018. In 2022–2024, Hainan was added and Beijing was not included, leaving 16 PLADs; all others were unchanged. Analyses included adults aged 18–79 years with non-missing body mass index (BMI) and excluded identified pregnant women. Standing height and weight were measured with participants in light clothing and no shoes. BMI was calculated as weight in kilograms divided by height in meters squared. Overweight, obesity, and combined overweight and obesity were defined as $24.0 \leq \text{BMI} < 28.0 \text{ kg/m}^2$, $\text{BMI} \geq 28.0 \text{ kg/m}^2$, and $\text{BMI} \geq 24.0 \text{ kg/m}^2$, respectively (5). Prevalence and 95% confidence intervals (CIs) were directly age-standardized to the 2020 Chinese population using 12 groups: 18–24 and five-year groups from 25–29 through 75–79 years (6). Standard errors were derived from age-specific binomial variances and CIs used the normal approximation.

Temporal trends were assessed by the inverse-variance weighted least-squares regression of age-standardized prevalence on survey year. Coefficients were average annual percentage-point changes with 95% CIs. The 16 participating PLADs were grouped into North, Northeast, East, Central, South, Southwest, and Northwest China. For each outcome, regional observations were pooled before direct age standardization. Cochran's *Q* tests with inverse-variance weighting assessed regional heterogeneity.

Three-level random-intercept logistic models were fitted using only 2022–2024 data to reassess provincial heterogeneity, with individuals (level 1) nested within communities (level 2) and communities within PLADs (level 3). Each binary outcome was modeled separately; participants not meeting its definition formed the comparison group. Covariates were sex, age (18–39, 40–59, or 60–79 years), education, household income, smoking, alcohol consumption, total energy intake, percentage energy from fat, and daily staple food, vegetable, fruit, and meat intakes. Community variables were residence, agricultural labor force proportion, and availability of Western fast-food restaurants and a park or stadium. PLAD variables were mean GDP per capita from the 2023–2025 editions of the China Statistical Yearbook (7) and mean $\text{PM}_{2.5}$ concentration from the 1-km ChinaHigh $\text{PM}_{2.5}$ V4 product (8). Household income and continuous dietary variables were winsorized at the 0.5th and 99.5th percentiles; income was log₂-transformed. Continuous covariates were scaled and grand-mean-centered at their respective analytical

levels. Multilevel analyses used complete cases. Model 0 (M0) included community- and PLAD-level random intercepts; Models 1–3 (M1–M3) sequentially added individual-, community-, and PLAD-level covariates. PLAD intraclass correlation coefficients (ICCs) and community variance partition coefficients used the latent logistic scale with $\pi^2/3$ individual-level variance. Parametric-bootstrap likelihood-ratio tests evaluated the M0 PLAD variance component. The proportional change in PLAD variance from M2 to M3 quantified reduction after adding GDP per capita and $\text{PM}_{2.5}$. Fixed effects were reported as odds ratios (ORs) with 95% CIs. PLAD random effects were assumed independent and did not incorporate geographic adjacency; models quantified between-PLAD heterogeneity and associated factors, not spatial clustering.

Analyses used R (version 4.4.3, R Foundation for Statistical Computing, Vienna, Austria) and two-sided tests (significance: $P < 0.05$). All participants provided written informed consent.

After exclusions (adults aged ≥ 80 years, 2,967 observations; pregnant women, 577; missing BMI, 5,562), 115,541 adult person-wave observations remained across 11 waves. The 2022–2024 round comprised 13,112 observations from 16 PLADs; multilevel analyses included 12,748 participants with complete covariates from 380 communities.

The age-standardized combined overweight and obesity prevalence increased from 20.20% (1,567/8,445) (95% CI: 19.27%–21.13%) in 1991 to 53.10% (7,286/13,112) (52.02%–54.18%) in 2024; overweight from 16.51% (1,308/8,445) (15.65%–17.36%) to 35.00% (4,983/13,112) (34.01%–36.00%); obesity from 3.70% (259/8,445) (3.24%–4.15%) to 18.10% (2,303/13,112) (17.25%–18.94%) (Table 1). Average annual percentage-point increases were 0.991 (0.911–1.071), 0.552 (0.464–0.640), and 0.422 (0.362–0.482), respectively (all $P < 0.001$; Figure 1).

In 2022–2024, the age-standardized prevalence differed across regions for all outcomes (all Cochran's *Q* $P < 0.001$; Table 2). Combined prevalence was the highest in North China at 67.56% (456/668) (95% CI: 62.82%–72.29%) and the lowest in South China at 42.74% (763/1,710) (40.12%–45.36%); results for overweight were similar (North China: highest, 42.34%, 274/668, 95% CI: 37.37%–47.31%; South China: lowest, 30.86%, 566/1,710, 95% CI: 28.51%–33.21%). Obesity was the highest in Northeast China at 27.12% (346/1,575)

TABLE 1. Age-standardized prevalence of combined overweight and obesity, overweight, and obesity by survey wave, China, 1991–2024.

Survey wave	N	Combined overweight and obesity n, % (95% CI)	Overweight n, % (95% CI)	Obesity n, % (95% CI)
1991	8,445	1,567, 20.20 (19.27–21.13)	1,308, 16.51 (15.65–17.36)	259, 3.70 (3.24–4.15)
1993	8,033	1,659, 21.89 (20.94–22.85)	1,406, 18.28 (17.38–19.18)	253, 3.61 (3.16–4.07)
1997	8,379	2,200, 26.99 (26.02–27.96)	1,771, 21.49 (20.59–22.39)	429, 5.50 (4.99–6.02)
2000	9,327	3,029, 31.99 (31.05–32.93)	2,386, 25.11 (24.23–25.99)	643, 6.88 (6.36–7.40)
2004	8,932	3,211, 33.87 (32.90–34.83)	2,486, 26.22 (25.33–27.12)	725, 7.64 (7.10–8.18)
2006	8,852	3,308, 35.11 (34.10–36.11)	2,563, 27.26 (26.32–28.20)	745, 7.84 (7.28–8.40)
2009	9,194	3,694, 37.57 (36.56–38.59)	2,801, 28.47 (27.52–29.42)	893, 9.10 (8.50–9.70)
2011	12,208	5,510, 42.13 (41.21–43.05)	4,023, 30.50 (29.65–31.35)	1,487, 11.63 (11.03–12.23)
2015	14,857	7,152, 45.42 (44.57–46.27)	5,091, 31.86 (31.08–32.63)	2,061, 13.56 (12.97–14.16)
2018	14,202	7,166, 46.60 (45.73–47.48)	4,977, 31.81 (31.01–32.61)	2,189, 14.79 (14.15–15.43)
2022–2024	13,112	7,286, 53.10 (52.02–54.18)	4,983, 35.00 (34.01–36.00)	2,303, 18.10 (17.25–18.94)

Note: The data stem from the China Health and Nutrition Survey, specifically from the 1991 to the 2024 survey rounds. Participating PLADs were not identical across survey waves because the China Health and Nutrition Survey coverage changed over time; each wave-specific estimate reflects the PLADs participating in that round.

Abbreviation: CI=confidence interval.

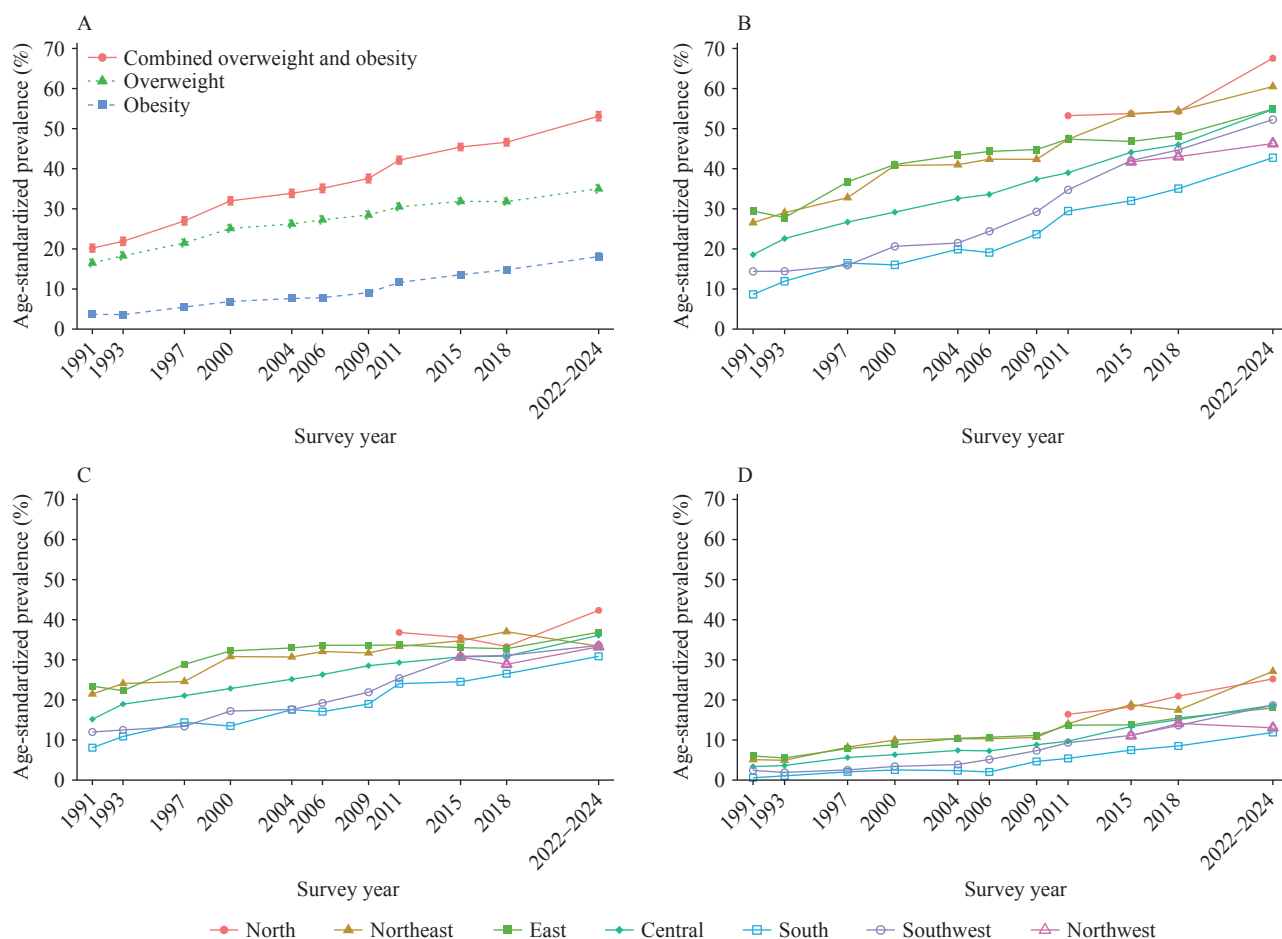


FIGURE 1. Age-standardized prevalence trends for combined overweight and obesity, overweight, and obesity at the national level and by geographic region, China, 1991–2024. (A) National; (B) Combined overweight and obesity by geographic region; (C) Overweight by geographic region; (D) Obesity by geographic region.

Note: The data stem from the China Health and Nutrition Survey's rounds from 1991 to 2024. The regional estimates are shown for survey rounds for which there are available data.

TABLE 2. Age-standardized prevalence of overweight and obesity by geographic region, China, 2022–2024.

Region	No. of PLADs*	N	Combined overweight and obesity n, % (95% CI)	Overweight n, % (95% CI)	Obesity n, % (95% CI)
North	1	668	456, 67.56 (62.82–72.29)	274, 42.34 (37.37–47.31)	182, 25.22 (21.23–29.20)
Northeast	2	1,575	947, 60.50 (55.96–65.05)	601, 33.38 (30.64–36.12)	346, 27.12 (22.65–31.60)
East	4	3,400	1,992, 54.88 (52.62–57.15)	1,392, 36.88 (34.75–39.00)	600, 18.00 (16.27–19.74)
Central	3	2,424	1,347, 54.77 (51.96–57.59)	949, 36.09 (33.55–38.64)	398, 18.68 (16.34–21.02)
South	2	1,710	763, 42.74 (40.12–45.36)	566, 30.86 (28.51–33.21)	197, 11.88 (10.10–13.66)
Southwest	3	2,481	1,371, 52.26 (49.92–54.59)	894, 33.59 (31.44–35.73)	477, 18.67 (16.88–20.46)
Northwest	1	854	410, 46.28 (42.26–50.31)	307, 33.25 (29.68–36.82)	103, 13.04 (10.12–15.95)
Cochran's Q (df=6)	–	–	120.15, $P<0.001$	26.88, $P<0.001$	81.44, $P<0.001$

Note: The data stem from the China Health and Nutrition Survey's 2022–2024 survey round.

Abbreviation: CI=confidence interval; PLAD=provincial-level administrative division.

* The number of participating PLADs included in each geographic region.

(22.65%–31.60%) and the lowest in South China at 11.88% (197/1,710) (10.10%–13.66%).

In intercept-only models, PLAD-level ICCs were 2.77%, 0.56%, and 3.18% for combined overweight and obesity, overweight, and obesity, respectively. Bootstrap tests supported a PLAD variance component for each outcome (Supplementary Table S1, available at <https://weekly.chinacdc.cn/>). In M3 (adding GDP per capita and PM_{2.5}), the estimated PLAD-level variance was 46.02% lower for combined overweight and obesity and 25.75% lower for obesity (*vs.* M2; Supplementary Table S2, available at <https://weekly.chinacdc.cn/>).

Fully adjusted models showed higher odds of combined overweight and obesity and of overweight among men ($ORs=1.349$ and 1.299), adults aged 40–59 years (1.378 and 1.400), and those aged 60–79 years (1.179 and 1.425). High education was inversely associated with all outcomes ($ORs=0.727$, 0.853 , and 0.780). Each income doubling was positively associated with combined overweight and obesity and with overweight (1.026 and 1.016). Current smoking was inversely associated with all outcomes ($ORs=0.799$, 0.874 , and 0.862 ; all $P<0.05$). Current drinking ($ORs=1.158$ and 1.215) and meat intake per 100 g/day (1.058 and 1.071) were positively associated with combined overweight and obesity and with obesity. Vegetable intake per 100 g/day was inversely associated with obesity ($OR=0.941$). At the community-level, Western fast-food restaurant availability was associated with combined overweight and obesity ($OR=1.167$, 95% CI: 1.024 – 1.331). At the PLAD-level, per 10 $\mu g/m^3$ PM_{2.5} increase, the ORs were 1.366 (95% CI: 1.136 – 1.642) for combined overweight and obesity, 1.156 (1.082 – 1.234) for overweight, and 1.304 (1.029 – 1.653) for obesity (Table 3).

DISCUSSION

From 1991 to 2024, combined overweight and obesity, overweight, and obesity prevalence increased substantially among adult CHNS participants. Combined prevalence more than doubled, while obesity increased nearly fivefold, indicating a broad expansion of excess weight and increase in its more severe form. This sustained age-standardized rise is consistent with previous evidence from China and occurred alongside major changes in food consumption, transportation, work patterns, and living environments during the country's rapid socioeconomic development (1,3).

Increases were widespread but geographically unequal. North China had the highest combined and overweight prevalence, whereas obesity was the highest in Northeast China, consistent with reported disparities among Chinese adults (2). This regional distribution suggests that conditions associated with moderate and more severe excess weight may differ. The substantial burden across regions, nonetheless, shows that excess weight is not confined to a few high-prevalence areas. Regional differences should guide intervention delivery within population-wide prevention.

Individual-level findings situated this transition within demographic, socioeconomic, and behavioral changes. Men and adults aged 40–79 years had higher odds of combined overweight and obesity and of overweight, making them potential targets for prevention and weight-management services. Higher education was consistently associated with lower odds of all outcomes, whereas income was positively associated with combined overweight and obesity and with overweight. Accordingly, increased economic

TABLE 3. Associations of individual-, community-, and PLAD-level characteristics with overweight and obesity in the fully adjusted three-level logistic regression models, China, 2022–2024.

Characteristics	Combined overweight and obesity		Overweight		Obesity	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Individual-level variables						
Sex		–				
Female	1.000	–	1.000	–	1.000	–
Male	1.349 (1.221–1.490)	<0.001	1.299 (1.178–1.433)	<0.001	1.067 (0.941–1.210)	0.312
Age group (years)						
18–39	1.000	–	1.000	–	1.000	–
40–59	1.378 (1.234–1.539)	<0.001	1.400 (1.250–1.569)	<0.001	0.993 (0.864–1.143)	0.927
60–79	1.179 (1.041–1.335)	0.009	1.425 (1.257–1.615)	<0.001	0.749 (0.638–0.879)	<0.001
Education						
Low	1.000	–	1.000	–	1.000	–
Middle	0.899 (0.821–0.983)	0.020	0.968 (0.886–1.057)	0.463	0.897 (0.800–1.005)	0.061
High	0.727 (0.630–0.839)	<0.001	0.853 (0.741–0.983)	0.027	0.780 (0.649–0.937)	0.008
Household income, per doubling	1.026 (1.010–1.042)	0.001	1.016 (1.001–1.031)	0.040	1.016 (0.996–1.036)	0.124
Current smoking						
No	1.000	–	1.000	–	1.000	–
Yes	0.799 (0.717–0.891)	<0.001	0.874 (0.785–0.972)	0.013	0.862 (0.752–0.989)	0.034
Current drinking						
No	1.000	–	1.000	–	1.000	–
Yes	1.158 (1.053–1.273)	0.003	1.025 (0.933–1.125)	0.610	1.215 (1.078–1.370)	0.001
Energy intake, per 500 kcal/day	1.040 (1.006–1.075)	0.019	1.018 (0.986–1.050)	0.274	1.040 (0.999–1.084)	0.057
Fat-derived energy, per 10 percentage points	1.000 (0.966–1.035)	0.980	1.011 (0.977–1.045)	0.536	0.983 (0.940–1.027)	0.439
Staple food intake, per 100 g/day	0.991 (0.961–1.022)	0.548	0.980 (0.952–1.010)	0.192	1.006 (0.968–1.047)	0.753
Vegetable intake, per 100 g/day	0.973 (0.945–1.002)	0.070	1.005 (0.977–1.033)	0.747	0.941 (0.905–0.978)	0.002
Fruit intake, per 100 g/day	0.964 (0.917–1.013)	0.148	1.002 (0.955–1.051)	0.933	0.945 (0.886–1.007)	0.083
Meat intake, per 100 g/day	1.058 (1.006–1.113)	0.028	1.013 (0.966–1.062)	0.597	1.071 (1.005–1.141)	0.035
Community-level variables						
Residence						
Rural	1.000	–	1.000	–	1.000	–
Urban	1.059 (0.934–1.201)	0.371	0.997 (0.898–1.106)	0.951	1.119 (0.961–1.303)	0.149
Agricultural labor, per 10 percentage points	0.991 (0.972–1.010)	0.359	0.991 (0.976–1.007)	0.270	0.999 (0.976–1.022)	0.921
Western fast-food restaurant: not available	1.000	–	1.000	–	1.000	–
Western fast-food restaurant: available	1.167 (1.024–1.331)	0.021	1.101 (0.989–1.226)	0.078	1.117 (0.955–1.306)	0.165
Park or stadium: not available	1.000	–	1.000	–	1.000	–
Park or stadium: available	0.977 (0.881–1.084)	0.667	0.987 (0.907–1.074)	0.756	0.987 (0.870–1.121)	0.843
PLAD-level variables						
GDP per capita, per 10,000 CNY	1.008 (0.975–1.041)	0.651	1.013 (1.001–1.024)	0.026	0.995 (0.955–1.038)	0.831
PM _{2.5} , per 10 µg/m ³	1.366 (1.136–1.642)	<0.001	1.156 (1.082–1.234)	<0.001	1.304 (1.029–1.653)	0.028

Note: The data stem from the China Health and Nutrition Survey's 2022–2024 survey round. Estimates are ORs (95% CIs) from the fully adjusted three-level logistic regression models (M3; $n=12,748$). Reference categories are indicated by OR=1.000. Continuous covariates were scaled as shown and grand-mean-centered. All tests are two-sided.

Abbreviation: BMI=body mass index; CI=confidence interval; CNY=Chinese yuan; GDP=gross domestic product; OR=odds ratio; PLAD=provincial-level administrative division; PM_{2.5}=particulate matter with an aerodynamic diameter ≤ 2.5 µm.

resources do not necessarily translate into healthier weight. This is despite education being associated with healthier choices during socioeconomic transitions (3). Positive associations of current drinking and meat intake with combined overweight and obesity and with obesity, and the inverse vegetable–obesity association connect excess weight with changing consumption patterns. Inverse associations with current smoking may reflect post-cessation weight gain, illness-related weight loss, or residual confounding by other health behaviors — not smoking's protective effect. These findings support health education and practical support for healthier diets.

These individual characteristics operated within community and provincial contexts. Community fast-food availability was positively associated with combined overweight and obesity, while higher PLAD-level PM_{2.5} concentrations were associated with all outcomes, consistent with evidence connecting food environments and air pollution to excess-weight risk (9–10). The lower estimated between-PLAD variance in M3 (*vs.* M2) suggests that GDP per capita and PM_{2.5} accounted (without establishing causality) for part of the observed between-PLAD variation. Most of the variation occurred among individuals and communities within PLADs; provincial conditions remain relevant, but prevention should also address local conditions.

The findings in this report are subject to at least five limitations. First, CHNS participants were recruited from selected communities, reducing generalizability to included PLADs' complete populations (4). Second, PLAD participation varied across waves, so part of the temporal and regional variation may reflect coverage changes. Third, only 16 PLADs were included, limiting macro-level characteristics assessments. Fourth, the latest-round multilevel analysis was cross-sectional; *ORs* indicate associations, and the available community and PLAD indicators could not capture all relevant contextual conditions. Finally, complete-case analysis, measurement error, residual confounding, and BMI's inability to characterize body-fat distribution may also have affected the findings.

The continuing shift toward obesity calls for coordinated actions toward the general adult population that are responsive to regional- and community-level circumstances. Prevention should combine health education, weight-management services, and healthy food environment promotion. The role of broader environmental conditions warrants evaluation. Population groups and areas experiencing a

greater burden require attention without limiting prevention to selected regions or PLADs.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

SUPPLEMENTARY TABLE S1. Parametric bootstrap tests of the PLAD-level random-intercept variance in intercept-only models, China, 2022–2024.

Outcome	PLAD variance	LRT statistic	Asymptotic <i>P</i>	Bootstrap <i>P</i>	Requested simulations	Used simulations
Combined overweight and obesity	0.097	92.938	<0.001	0.001	1,000	793
Overweight	0.019	20.677	<0.001	0.001	1,000	910
Obesity	0.112	67.236	<0.001	0.003	1,000	340

Note: The data stem from the China Health and Nutrition Survey's 2022–2024 survey round. The intercept-only model containing PLAD- and community-level random intercepts was compared with a reduced model containing only a community-level random intercept. Each parametric bootstrap test requested 1,000 simulations; 793, 910, and 340 simulations produced usable model fits for combined overweight and obesity, overweight, and obesity, respectively. Bootstrap *P* values were calculated from these valid simulations and should be interpreted together with the variance estimates.

Abbreviation: LRT=likelihood ratio test.

SUPPLEMENTARY TABLE S2. Variance components and intraclass correlation coefficients across the sequential three-level logistic regression models, China, 2022–2024.

Outcome	Model	PLAD variance	Community variance	PLAD ICC (%)	Community VPC (%)	Same-community ICC (%)	PLAD PCV, M3 vs. M2 (%)	Fit status
Combined overweight and obesity	M0	0.097	0.102	2.77	2.93	5.70	—	Non-singular
Combined overweight and obesity	M1	0.102	0.104	2.91	2.98	5.89	—	Non-singular
Combined overweight and obesity	M2	0.098	0.101	2.80	2.89	5.69	—	Non-singular
Combined overweight and obesity	M3	0.053	0.101	1.53	2.92	4.46	46.02	Non-singular
Overweight	M0	0.019	0.034	0.56	1.02	1.57	—	Non-singular
Overweight	M1	0.011	0.034	0.34	1.01	1.35	—	Non-singular
Overweight	M2	0.009	0.033	0.27	0.99	1.26	—	Non-singular
Overweight	M3	0.000	0.031	0.00	0.94	0.94	100.00	Singular
Obesity	M0	0.112	0.125	3.18	3.53	6.71	—	Non-singular
Obesity	M1	0.122	0.124	3.44	3.52	6.95	—	Non-singular
Obesity	M2	0.121	0.122	3.42	3.46	6.88	—	Non-singular
Obesity	M3	0.089	0.122	2.56	3.49	6.05	25.75	Non-singular

Note: The data stem from the China Health and Nutrition Survey's 2022–2024 survey round. All models used the same complete-case sample ($N=12,748$; 380 communities; 16 PLADs). M0 included only PLAD- and community-level random intercepts; M1 added individual-level covariates; M2 added community-level covariates; M3 added PLAD-level GDP per capita and $PM_{2.5}$. ICCs were calculated on the latent logistic scale using $\pi^2/3$ as the individual-level variance. The same-community ICC represents the correlation between two individuals from the same community, and includes both PLAD- and community-level variance components. PLAD-level PCV was calculated as (variance in M2 – variance in M3)/variance in M2 $\times$ 100%. The PLAD-level variance for overweight reached the boundary at zero in M3; accordingly, its nominal 100% proportional change in variance should be interpreted cautiously.

Abbreviation: GDP=gross domestic product; ICC=intraclass correlation coefficient; PCV=proportional change in variance; PLAD=provincial-level administrative division; $PM_{2.5}$ =particulate matter with an aerodynamic diameter ≤ 2.5 μm ; VPC=variance partition coefficient.

Preplanned Studies

Prevalence and Associated Factors of Hypertension–Diabetes–Dyslipidemia Clustering Among Adults — Hainan Province, China, 2023

Juan Jiang¹; Tingting Ou¹; Ying Liu¹; Yang Cheng¹; Xingren Wang¹; Lu Zhong¹; Xiaohuan Wang¹; Saiku Chen¹; Bin He^{1,†}

Summary

What is already known about this topic?

Hypertension, diabetes, and dyslipidemia are metabolically interconnected. Although each may arise independently, shared pathophysiology commonly drives synergistic co-occurrence.

What is added by this report?

In Hainan, China's tropical island province, the weighted prevalence of hypertension–dyslipidemia comorbidity exceeded that of diabetes–dyslipidemia and hypertension–diabetes, as well as their triple comorbidity. Hypertensive–dyslipidemic clustering represented the predominant comorbidity phenotype, with implications for targeted screening and integrated prevention.

What are the implications for public health practice?

This study provides a descriptive baseline assessment highlighting high-risk subpopulations, establishing a critical evidence base for planning/design of intervention strategies.

Results: Among 32,857 surveyed residents, the weighted rate of triple comorbidity of hypertension, diabetes, and dyslipidemia was 4.07% (1,865/32,812). The weighted pairwise comorbidity rates ranked in descending order were as follows: hypertension–dyslipidemia (10.55%, 4,174/32,812), diabetes–dyslipidemia (3.65%, 1,446/32,812), and hypertension–diabetes (2.73%, 1,341/32,857). For individual conditions, the weighted prevalence rates were 27.52% (11,612/32,857) for hypertension, 13.74% (5,951/32,857) for diabetes, and 40.23% (14,225/32,812) for dyslipidemia. Multilevel multinomial logistic regression analysis identified male sex, older age, central obesity, and frequent alcohol consumption (≥ 5 days/week) as consistently associated with higher odds of having one/two/three, compared with none (all $P < 0.05$). Sensitivity analyses excluding self-reported cases yielded consistent findings.

Conclusion: As a descriptive baseline investigation, this study identifies key high-risk subgroups and offers foundational data to help guide the development of future targeted interventions.

ABSTRACT

Introduction: Hypertension, diabetes, and dyslipidemia — the three most prevalent cardiometabolic conditions — are metabolically interrelated. Although each may arise independently, shared pathophysiological mechanisms often promote synergistic co-occurrence. This study examined the prevalence/determinants of comorbidity among adults in Hainan province, China.

Methods: From January to June 2023, a two-stage unequal-probability cluster sampling design was employed to recruit permanent residents aged ≥ 18 years across Hainan province. Participants completed structured questionnaire interviews, standardized physical measurements, and laboratory testing.

Chronic non-communicable diseases represent a major global health challenge, with hypertension, diabetes, and dyslipidemia constituting the most prevalent cardiometabolic conditions (1). Although each can arise independently, shared pathological mechanisms commonly drive synergistic co-occurrence (2). In China, this burden is immense and growing: in 2018, an estimated 310, 130, and 310 million adults had hypertension, diabetes, and dyslipidemia, respectively (3). Despite the breadth of single-disease research, authoritative comorbidity data remain scarce. A recent national survey reported a triple comorbidity rate of 7.6% among individuals aged ≥ 45 years (4); however, the burden across all adults aged ≥ 18 years

remains uncharacterized.

As China's only tropical island province, Hainan features a distinctive residential environment characterized by high heat, high humidity, and elevated airborne salinity — all of which may synergistically promote cardiometabolic disorders. Consequently, this community merits attention in chronic disease and environmental health research. Nevertheless, the prevalence, determinants, and comorbidity patterns of hypertension, diabetes, and dyslipidemia among Hainan adults have not been systematically examined. Thus, the present study examined the prevalence, associated factors, and co-occurrence of these conditions, to establish an evidence base for future intervention planning/design.

This cross-sectional survey was conducted among permanent residents aged ≥ 18 years in Hainan Province, China, from January to June 2023. The required sample size was calculated as: $N = deff \frac{Z^2 p(1-p)}{d^2}$, with the following parameters: a 95% confidence level (two-sided, $Z=1.96$); a prevalence (p) of 7.6%, derived from the national hypertension-diabetes-dyslipidemia (HP-DB-DL) triple comorbidity rate among adults aged ≥ 45 years in China (4); a design effect ($deff$) of 3; a relative error (r) of 20%; and a precision $d=r \times p$. Four strata were defined by sex (male, female) and region (Urban, Rural), with approximately 3,503 participants required per stratum, yielding a base total of 14,012 participants. To account for an anticipated 15% non-response rate, this figure was divided by 0.85, yielding a minimum final sample size of 16,486.

This study employed a two-stage cluster sampling design with unequal selection probabilities. First, all 24 cities, counties, and districts of Hainan island were included as implicit strata to ensure comprehensive geographic coverage; within each administrative unit, one township or subdistrict was randomly selected as the primary sampling unit. Second, a single village or urban residential committee was randomly selected from each sampled township/subdistrict. All permanent residents aged ≥ 18 years within the selected villages/communities were invited to participate. Eligibility criteria were: 1) age ≥ 18 years; 2) resided in the selected village or community for ≥ 6 months during the preceding year; and 3) voluntarily participated, providing written informed consent. Individuals were excluded if they were pregnant, had cognitive impairment, a severe illness, or any disabling condition that could compromise study integrity. The study was approved by the Medical Ethics Committee

of the Hainan Provincial Center for Disease Control and Prevention, China (Approval No. 202360), and was conducted following the Declaration of Helsinki.

Data were collected through questionnaires, physical measurements, and laboratory tests. All participants were instructed to fast for ≥ 8 h before their scheduled appointment, and all procedures were conducted by trained personnel following standardized protocols. To ensure reliability, validity, and cross-study comparability, the questionnaire was adapted from the 2018 China Chronic Disease Risk Factor Surveillance instrument, developed by the National Center for Chronic and Non-communicable Disease Control and Prevention. Survey measures, methods and definitions of key variables are provided in the Supplementary Materials (available at <https://weekly.chinacdc.cn/>).

All statistical analyses were conducted using R software (version 4.6.0; R Foundation for Statistical Computing, Vienna, Austria). Between-group comparisons were assessed using the chi-square test; the Mantel–Haenszel trend chi-square test was applied for ordinal variables (age groups, education levels, and alcohol consumption frequency). Multilevel multinomial logistic regression was applied to identify factors independently associated with comorbidity, with results expressed as odds ratios (*OR*) and 95% confidence intervals (*CI*). A sensitivity analysis excluding participants whose diagnoses were based solely on selfreport was performed. All prevalence estimates represent screeningbased point prevalence, and were weighted for the complex survey design. All were poststratified and standardized by age and sex to the 2020 Seventh National Census of China, aligning the sample with the national reference standard. A two-sided *P* value < 0.05 was considered statistically significant.

Overall, 32,857 residents aged ≥ 18 years (mean age: 51.94 years [SD 14.97]) were enrolled (Supplementary Table S1, available at <https://weekly.chinacdc.cn/>). The weighted prevalences of hypertension, diabetes, and dyslipidemia were 27.52% (11,612/32,857), 13.74% (5,951/32,857), and 40.23% (14,225/32,812), respectively. The weighted pairwise comorbidity rates were 2.73% (1,341/32,857) for hypertension-diabetes (HP-DB), 10.55% (4,174/32,812) for hypertension-dyslipidemia (HP-DL), and 3.65% (1,446/32,812) for diabetes-dyslipidemia (DB-DL), with a weighted rate of triple comorbidity of 4.07% (1,865/32,812). All four comorbidity indicators increased monotonically with age, body mass index (BMI), and alcohol consumption frequency, and were

TABLE 1. Weighted prevalence and comorbidity of HP, DB, and DL among survey respondents by different characteristics in Hainan Province, 2023.

Characteristics	HP		DB		DL		HP-DB		HP-DL		DB-DL		HP-DB-DL	
	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)
Total	11,612	27.52	5,951	13.74	14,225	40.23	1,341	2.73	4,174	10.55	1,446	3.65	1,865	4.07
Gender														
Male	6,155	32.15	3,091	15.16	7,354	47.64	696	3.00	2,286	13.21	751	4.15	1,031	4.76
Female	5,457	22.40	2,860	12.17	6,871	32.04	645	2.43	1,888	7.57	695	3.09	834	3.30
χ^2	91,879.984		14,511.298		195,753.840		2,313.275		65,147.684		6,215.004		10,657.262	
P	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Age (years)														
18–44	1,838	14.55	838	6.36	3,894	35.11	88	0.57	818	6.98	284	2.27	193	1.40
45–64	5,869	37.17	2,970	19.15	7,024	46.21	619	3.82	2,178	13.71	760	5.11	976	6.03
≥65	3,905	54.58	2,143	29.30	3,307	45.63	634	8.50	1,178	16.65	402	5.43	696	9.70
χ^2	847,014.487		464,728.212		75,412.826		212,774.361		118,752.073		40,916.947		185,255.099	
P	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Ethnicity														
Han	8,514	27.05	4,498	13.87	11,080	40.75	966	2.71	3,150	10.37	1,173	3.83	1,392	4.02
Li	2,887	30.00	1,346	13.07	2,890	37.72	352	2.86	955	11.45	250	2.79	427	4.10
Others	211	25.90	107	13.81	255	39.93	23	2.07	69	9.42	23	3.04	46	6.26
χ^2	4,789.224		568.182		4,202.226		269.376		1,423.050		3,370.587		1,409.587	
P	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Education														
Primary or below	5,077	37.58	2,475	18.20	5,092	41.40	674	4.61	1,676	12.79	514	4.03	774	5.59
Middle school/technical	5,987	24.99	3,158	12.78	8,119	40.55	612	2.14	2,287	10.3	841	3.73	996	3.68
secondary school														
College degree or above	548	15.44	318	7.58	1,014	35.90	55	1.03	211	6.23	91	2.31	95	2.24
χ^2	198,934.755		71,992.303		6,651.855		43,534.782		30,249.113		4,392.397		23,122.566	
P	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Marital status														
Not married	634	15.13	322	6.52	1,045	35.67	67	0.87	255	6.85	71	1.59	109	1.99
Married/cohabiting	10,377	29.52	5,320	14.97	12,661	41.04	1,179	2.98	3,731	11.13	1,311	4.06	1,657	4.39

Continued

Characteristics	HP		DB		DL		HP-DB		HP-DL		DB-DL		HP-DB-DL	
	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)
Divorced/widowed	601	53.24	309	26.51	519	47.17	95	8.25	188	18.06	64	5.17	99	8.71
χ^2	178,009.068		93,157.595		17,210.766		40,245.614		31,980.038		20,621.512		26,786.677	
<i>P</i>	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Region														
Urban	2,945	28.04	1,650	14.21	3,503	38.68	395	3.11	945	9.68	415	3.72	498	4.23
Rural	8,667	27.33	4,301	13.56	10,722	40.81	946	2.59	3,229	10.85	1,031	3.62	1,367	4.01
χ^2	387.771		556.612		2,917.845		1,585.976		2,236.098		41.592		190.020	
<i>P</i>	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
BMI group														
Underweight	430	13.02	289	8.63	482	18.75	85	1.92	106	3.62	41	0.98	38	1.06
Normal weight	4,899	22.52	2,484	11.41	6,186	33.57	571	2.40	1,647	7.68	610	2.97	664	2.77
Overweight	4,542	34.80	2,300	16.55	5,498	49.85	506	3.27	1,722	14.45	578	4.49	822	5.90
Obesity	1,739	39.52	878	19.78	2,057	57.94	179	3.26	698	17.11	208	6.11	341	6.81
χ^2	228,979.883		72,113.648		382,540.978		5,664.647		136,576.415		36,825.573		63,801.257	
<i>P</i>	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Central obesity														
No	6,933	22.29	3,492	10.97	9,089	34.99	779	2.19	2,429	8.13	870	2.84	930	2.74
Yes	4,678	42.58	2,459	21.72	5,135	55.34	562	4.28	1,744	17.47	576	5.97	935	7.90
χ^2	304,959.365		144,132.210		253,044.882		24,156.272		136,157.679		40,929.428		100,585.629	
<i>P</i>	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Smoking status														
Never smoking	7,528	25.49	3,875	13.17	8,966	34.91	908	2.82	2,578	8.82	901	3.24	1,182	3.76
Current smoking	3,299	29.29	1,682	13.86	4,565	49.69	324	2.18	1,337	13.12	473	4.32	545	4.30
Former smoking cessation	785	46.34	394	22.31	694	45.87	109	6.15	259	16.53	72	4.43	138	7.17
χ^2	64,391.561		18,893.784		157,661.351		15,578.373		44,224.314		6,148.428		8,504.376	
<i>P</i>	<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001	
Secondhand smoke exposure														
No	8,034	29.17	4,172	14.59	9,795	42.74	945	2.87	2,914	11.40	1,024	3.92	1,327	4.40
Yes	3,578	23.89	1,779	11.87	4,430	34.75	396	2.42	1,260	8.64	422	3.05	538	3.33

Continued

Characteristics	HP		DB		DL		HP-DB		HP-DL		DB-DL		HP-DB-DL	
	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)	Number	Prevalence (%)
χ^2		23,205.010		10,359.222		44,577.366		1,292.972		13,541.122		3,583.353		4,922.673
<i>P</i>		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
Frequency of alcohol consumption														
No alcohol use	6,428	25.60	3,585	14.20	8,128	36.69	790	2.91	2,241	8.89	884	3.54	1,062	3.91
<3 days per month	1,818	23.69	830	10.35	2,495	41.32	180	1.81	674	9.92	207	3.15	267	3.26
1–4 days per week	1,588	28.46	731	12.34	1,915	46.08	176	2.27	630	13.38	185	3.91	238	3.69
5–7 days per week	1,778	43.57	805	19.06	1,687	49.95	195	3.99	629	16.85	170	4.75	298	6.87
χ^2		75,395.903		2,581.685		69,976.820		252.625		53,451.129		2,203.116		7,092.270
<i>P</i>		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001
Insufficient physical activity														
No	8,056	27.30	3,955	13.06	9,787	39.88	879	2.54	2,896	10.62	947	3.47	1,217	3.79
Yes	3,515	28.02	1,979	15.35	4,397	41.12	457	3.15	1,266	10.36	494	4.04	643	4.71
χ^2		417.831		7,207.004		1,069.695		2,245.132		105.381		1,515.508		3,502.942
<i>P</i>		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001		<0.001

Note: The sample size for analyses of hypertension and diabetes was 32,857. For analyses involving dyslipidemia, the sample size was 32,812, as 45 participants in the total sample were missing blood lipid measurement data.

Abbreviation: HP=hypertension; DB=diabetes; DL=dyslipidemia; HP-DB=hypertension and diabetes without dyslipidemia; HP-DL=hypertension and dyslipidemia without diabetes; DB-DL=diabetes and dyslipidemia without hypertension; HP-DB-DL=hypertension, diabetes, and dyslipidemia; BMI=body mass index.

consistently higher in males than in females and in individuals with central obesity (all $P < 0.05$; Table 1).

Subtype analysis of the blood lipid profiles revealed that the prevalences of hypercholesterolemia, hypertriglyceridemia, hypoalphalipoproteinemia, and hyper-low-density lipoproteinemia were 21.58% (8,416/32,812), 18.81% (5,958/32,812), 11.70% (3,423/32,812), and 13.46% (5,324/32,812), respectively. Regarding the clustering of lipid abnormalities, the weighted prevalences of participants with one, two, three, and four concurrent abnormal subtypes were 20.71% (7,200/32,812; males 23.95%, 3,730/15,099; females 17.12%, 3,470/17,713), 14.58% (5,342/32,812; males 16.75%, 2,619/15,099; females 12.19%, 2,723/17,713), 4.36% (1,495/32,812; males 5.99%, 872/15,099; females 2.55%, 623/17,713), and 0.65% (188/32,812; males 1.03%, 133/15,099; females 0.23%, 55/17,713), respectively. Males consistently exhibited a higher prevalence of clustering across all levels (Figure 1).

Multilevel multinomial logistic regression analysis identified male sex, older age, central obesity, and frequent alcohol consumption (≥ 5 days/week) as consistently associated with higher odds of having one/two/three diseases (hypertension, diabetes, dyslipidemia) compared with having none (all $P < 0.05$). The strength of these associations between older age and central obesity generally increased with the number of comorbidities (Table 2). The associations remained directionally consistent with the main

analysis after excluding participants whose diagnoses were based solely on self-reporting, although effect sizes were slightly attenuated. Detailed results are presented in Supplementary Table S2 (available at <https://weekly.chinacdc.cn/>).

DISCUSSION

This study, which is the first to characterize HP-DB-DL comorbidity in Hainan, identified a triple comorbidity prevalence of 4.07%, with HP-DL representing the predominant pairwise pattern (10.55%). The prevalence of dyslipidemia (40.23%) substantially exceeded both prior provincial estimates (36.6%) (5) and national figures (35.6%) (6), indicating an escalating public health burden likely attributable to nutritional transition and accelerating urbanization. The co-occurrence of these conditions compounds cardiovascular risk, underscoring a critical need to move beyond single-disease management towards integrated cardiometabolic multimorbidity control in Hainan.

Internationally, directly comparable multimorbidity studies remain scarce. Within China, Hainan's triple comorbidity rate (4.07%) exceeded those reported in Fujian (2.9%) (7), Xinjiang (3.0%) (8), and Xizang (2.2%) (9). Consistent with findings from other Chinese provinces, HP-DL was the most prevalent of the three pairwise combinations. This combination is of particular clinical concern, as hypertension and

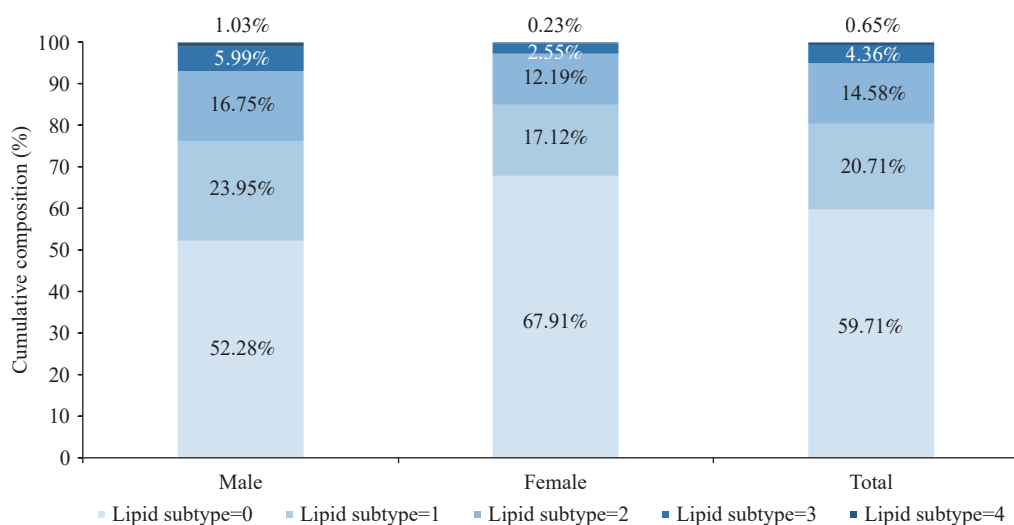


FIGURE 1. Cumulative composition of blood lipid subtypes by gender in Hainan Province, 2023.

Note: Lipid subtypes were defined by the number of abnormal findings among the four assessed lipid parameters (hypercholesterolemia, hypertriglyceridemia, hypoalphalipoproteinemia, and hyper-low-density lipoproteinemia). Subtype = 0 indicates that all four parameters were within the normal range; subtype = 1, 2, 3, and 4 correspond to 1, 2, 3, and 4 abnormal parameters, respectively.

TABLE 2. Multilevel multinomial logistic regression analysis of the factors associated with comorbidity of HP, DB, and DL among residents of Hainan Province, 2023.

Characteristics	One condition vs. Disease-free				Two conditions vs. Disease-free				Three conditions vs. Disease-free			
	β	S	P	OR (95% CI)	β	S	P	OR (95% CI)	β	S	P	OR (95% CI)
Intercept	-0.858	0.081	<0.001	0.424 (0.362, 0.497)	-2.144	0.110	<0.001	0.117 (0.094, 0.146)	-3.813	0.174	<0.001	0.022 (0.016, 0.031)
Gender												
Female	-	-	-	-	-	-	-	-	-	-	-	-
Male	0.508	0.042	<0.001	1.661 (1.529, 1.805)	0.658	0.052	<0.001	1.931 (1.744, 2.138)	0.641	0.083	<0.001	1.899 (1.616, 2.233)
Age (years)												
18–44	-	-	-	-	-	-	-	-	-	-	-	-
45–64	0.700	0.033	<0.001	2.013 (1.886, 2.148)	1.300	0.046	<0.001	3.671 (3.357, 4.015)	1.793	0.094	<0.001	6.010 (4.998, 7.227)
≥65	1.088	0.047	<0.001	2.969 (2.711, 3.253)	1.994	0.059	<0.001	7.342 (6.546, 8.235)	2.564	0.107	<0.001	12.989 (10.524, 16.033)
Ethnicity												
Han	-	-	-	-	-	-	-	-	-	-	-	-
Li	0.030	0.056	0.587	1.031 (0.924, 1.150)	0.030	0.074	0.691	1.030 (0.890, 1.191)	0.214	0.123	0.082	1.239 (0.973, 1.576)
Others	0.025	0.112	0.822	1.026 (0.823, 1.277)	-0.035	0.143	0.807	0.966 (0.730, 1.277)	0.512	0.209	0.015	1.669 (1.107, 2.515)
Education												
Primary or below	-	-	-	-	-	-	-	-	-	-	-	-
Middle school/technical	-0.089	0.033	0.007	0.915 (0.858, 0.976)	-0.078	0.041	0.055	0.925 (0.854, 1.002)	-0.006	0.065	0.924	0.994 (0.875, 1.129)
secondary school												
College degree or above	-0.182	0.057	0.001	0.834 (0.745, 0.933)	-0.358	0.080	<0.001	0.699 (0.598, 0.817)	-0.133	0.137	0.331	0.876 (0.670, 1.144)
Marital status												
Not married	-	-	-	-	-	-	-	-	-	-	-	-
Married/cohabiting	0.093	0.053	0.076	1.098 (0.990, 1.217)	-0.041	0.072	0.573	0.960 (0.834, 1.106)	-0.469	0.127	<0.001	0.626 (0.487, 0.803)
Divorced/widowed	0.289	0.099	0.004	1.335 (1.099, 1.621)	0.248	0.118	0.036	1.281 (1.017, 1.615)	-0.259	0.188	0.167	0.772 (0.534, 1.114)
Region												
Rural	-	-	-	-	-	-	-	-	-	-	-	-
Urban	-0.174	0.106	0.103	0.841 (0.682, 1.036)	-0.202	0.149	0.175	0.817 (0.610, 1.094)	-0.148	0.200	0.459	0.863 (0.583, 1.276)
Central obesity												
No	-	-	-	-	-	-	-	-	-	-	-	-
Yes	0.716	0.033	<0.001	2.046 (1.917, 2.185)	1.207	0.039	<0.001	3.342 (3.097, 3.606)	1.511	0.060	<0.001	4.530 (4.028, 5.094)
Smoking status												
Never smoking	-	-	-	-	-	-	-	-	-	-	-	-
Current smoking	0.093	0.048	0.054	1.098 (0.999, 1.207)	0.031	0.059	0.601	1.031 (0.919, 1.157)	-0.035	0.092	0.707	0.966 (0.807, 1.157)
Former smoking	-0.103	0.079	0.193	0.902 (0.773, 1.053)	-0.055	0.090	0.544	0.947 (0.794, 1.129)	-0.003	0.131	0.983	0.997 (0.771, 1.290)
Secondhand smoke exposure												
No	-	-	-	-	-	-	-	-	-	-	-	-
Yes	-0.017	0.034	0.623	0.984 (0.921, 1.051)	-0.093	0.043	0.031	0.911 (0.837, 0.992)	-0.137	0.072	0.057	0.872 (0.758, 1.004)
Frequency of alcohol consumption												
No alcohol use	-	-	-	-	-	-	-	-	-	-	-	-
<3 days per month	-0.048	0.040	0.236	0.954 (0.881, 1.032)	-0.108	0.053	0.041	0.898 (0.809, 0.996)	-0.204	0.089	0.022	0.815 (0.685, 0.970)

Continued

Characteristics	One condition vs. Disease-free				Two conditions vs. Disease-free				Three conditions vs. Disease-free			
	β	S	P	OR (95% CI)	β	S	P	OR (95% CI)	β	S	P	OR (95% CI)
1–4 days per week	0.003	0.050	0.946	1.003 (0.910, 1.106)	0.284	0.061	<0.001	1.329 (1.178, 1.498)	0.136	0.101	0.177	1.146 (0.940, 1.397)
5–7 days per week	0.249	0.056	<0.001	1.283 (1.150, 1.432)	0.538	0.066	<0.001	1.713 (1.504, 1.950)	0.538	0.100	<0.001	1.712 (1.408, 2.082)
Insufficient physical activity												
No	–	–	–	–	–	–	–	–	–	–	–	–
Yes	0.048	0.035	0.167	1.049 (0.980, 1.122)	0.145	0.043	<0.001	1.156 (1.062, 1.259)	0.283	0.070	<0.001	1.328 (1.157, 1.523)

Note: “–” means this level is the reference level and there are no corresponding parameter values.

Abbreviation: HP=hypertension; DB=diabetes; DL=dyslipidemia; β =regression coefficient; S= standard error; OR=odds ratio; CI=confidence interval.

dyslipidemia share common pathophysiological pathways and synergistically elevate the risk of cardiovascular events beyond the level of either condition alone. As these two conditions are among the most prevalent and modifiable cardiovascular risk factors worldwide (10), the dominance of HP-DL in Hainan underscores an urgent need to conduct integrated screening and management strategies targeting this highrisk concurrent phenotype.

The persistently higher comorbidity odds in men may reflect clustered behavioral risks (smoking, alcohol use, and occupational psychosocial stress), compounded by a greater propensity for visceral adiposity, a key driver of insulin resistance/dyslipidemia. These factors may synergistically promote hypertension, diabetes, and dyslipidemia co-occurrence. Frequent alcohol consumption (≥ 5 days/week) was a potentially modifiable risk factor across all comorbidity patterns. Central obesity showed a graded association, with effect sizes rising as coexisting conditions increased, indicating that even modest waist reduction may yield disproportionate benefits in those already burdened by one/two conditions. These findings have several public health implications. For men, workplace screening and brief interventions in male-dominated industries should be integrated with occupational health programs. For adults ≥ 45 years, primary care should establish an integrated screening–comorbidity assessment–intervention pathway. Central obesity and frequent alcohol use warrant alcohol sales restrictions and community behavioral programs leveraging Hainan's outdoor setting. The large migrant population also requires chronic disease management via temporary-residence registration, seasonal screening, and cross-provincial health record linkage. All actions should align with the Healthy Hainan framework.

Several limitations should be acknowledged. First, the crosssectional design precludes assessing causal inference. Second, selfreported lifestyle and behavioral data are subject to recall and social desirability biases. Third, singlevisit assessments provided screeningbased point prevalence, rather than clinically confirmed diagnoses. Fourth, although the initial sample size calculation was based on a 7.6% prevalence from a population aged ≥ 45 years, posthoc power calculations using our observed prevalence of 4.07% confirmed that the final sample ($n=32,857$) exceeds the required minimum ($n=31,713$), ensuring adequate precision. Finally, despite standardizing Hainan estimates to the 2020 China census, the lack of standardized data from comparator regions limits robust crossregional comparisons. These findings should therefore be interpreted cautiously.

In conclusion, this study provides a preliminary characterization of the prevalence and comorbidity profiles of hypertension, diabetes, and dyslipidemia in Hainan Province. By establishing a descriptive baseline and identifying high-risk subpopulations, this study furnishes a vital evidence base for the subsequent design and implementation of targeted interventions.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIALS

Survey Measures and Methods

Demographic characteristics (age, sex, ethnicity, education, marital status) and behavioral risk factors (smoking, alcohol use, physical activity) were captured from face-to-face interviews. Physical measurements included waist circumference (WC) and blood pressure (BP). WC was measured twice using a flexible tape measure, while BP was measured thrice using an Omron HBP1300 electronic sphygmomanometer (Dalian Omron Co., Ltd.), with a minimum one-minute interval between consecutive readings. Laboratory tests comprised fasting plasma glucose (FPG), an oral glucose tolerance test (OGTT), total cholesterol (TCHO), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Blood samples were collected by trained nurses, after which they were processed (centrifuged and aliquoted), stored, and transported under cold-chain conditions. All analyses were conducted at local secondary-level or higher medical institutions where available; otherwise, qualified third-party laboratories were used. Blood glucose was measured by the hexokinase method within 24 h of collection; TCHO and TG were quantified enzymatically, while HDL-C and LDL-C were quantified by direct methods.

Definitions of Key Variables

1) Hypertension

Following the 2018 Chinese guidelines for the management of hypertension (1), hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg (18.6 kPa) and/or diastolic blood pressure (DBP) ≥ 90 mmHg (12 kPa), in the absence of antihypertensive medication. Blood pressure was measured thrice, with intervals of at least one minute; the average of the second and third readings served as the final value. In the present survey, participants were classified as hypertensive if their final blood pressure met the above criteria, or if they had any prior diagnosis of hypertension from a medical institution at or above the township/community level and had taken antihypertensive medication within the preceding two weeks.

2) Diabetes

Diabetes was defined according to the diagnostic criteria of the *Report on Chronic Disease Risk Factor Surveillance in China: 2018* (2). Participants meeting any of the following criteria were considered diabetic: fasting plasma glucose (FPG) ≥ 7.0 mmol/L; 2 hour plasma glucose during an oral glucose tolerance test (OGTT2h) ≥ 11.1 mmol/L; or a previous diagnosis of diabetes made by a medical institution at or above the township/community level.

3) Dyslipidemia

Dyslipidemia was defined in accordance with the *Chinese Guidelines for the Prevention and Treatment of Adult Dyslipidemia (2016 Edition)* (3) as individuals exhibiting any of the following: total cholesterol (TCHO) ≥ 6.22 mmol/L (240 mg/dL) [hypercholesterolemia]; high-density lipoprotein cholesterol (HDL-C) < 1.04 mmol/L (40 mg/dL) [hypoalphalipoproteinemia]; low-density lipoprotein cholesterol (LDL-C) ≥ 4.14 mmol/L (160 mg/dL) [hyperlow-density lipoproteinemia]; or triglycerides (TG) ≥ 2.26 mmol/L (200 mg/dL) [hypertriglyceridemia]. The dyslipidemia prevalence was calculated as the proportion of individuals with at least one abnormal lipid parameter among all participants who had undergone blood lipid testing.

4) Biological risk factors

The biological risk factors assessed included weight, height, WC, smoking status, smoking cessation, secondhand smoke exposure, and physical activity level. Body mass index (BMI) was calculated as: weight (kg)/height (m)². Following the Chinese national standard Assessment of Adult Body Weight (WS/T 428-2013) (4), the BMI categories were: underweight (< 18.5 kg/m²), normal weight (18.5–23.9 kg/m²), overweight (24.0–27.9 kg/m²), and obesity (≥ 28.0 kg/m²). Central obesity was defined as a waist circumference ≥ 90 cm in men and ≥ 85 cm in women (2).

Current smokers were defined as individuals who had smoked for ≥ 6 months (continuously or cumulatively) during their lifetime and had smoked within 30 days prior to the survey (5); this included both daily and occasional smokers. Smoking cessation was defined as having previously smoked, but having successfully quit by the time of the survey (2). Secondhand smoke exposure was defined as exposure of nonsmokers to sidestream smoke from

SUPPLEMENTARY TABLE S1. Demographic characteristics of the survey respondents in Hainan Province, 2023.

Characteristics	Total		Male		Female	
	Number (n=32,857)	Proportion (%)	Number (n=15,124)	Proportion (%)	Number (n=17,733)	Proportion (%)
Age (years)						
18–44	10,879	33.11	5,104	33.75	5,775	32.57
45–64	14,776	44.97	6,731	44.51	8,045	45.37
≥65	7,202	21.92	3,289	21.75	3,913	22.07
Ethnicity						
Han	24,805	75.49	11,322	74.86	13,483	76.03
Li	7,470	22.73	3,514	23.23	3,956	22.31
Others	582	1.77	288	1.90	294	1.66
Education						
Primary or below	11,988	36.49	3,873	25.61	8,115	45.76
Middle school/technical secondary school	18,289	55.66	9,925	65.62	8,364	47.17
College degree or above	2,580	7.85	1,326	8.77	1,254	7.07
Marital status						
Not married	2,606	7.93	1,922	12.71	684	3.86
Married/cohabiting	29,117	88.62	12,904	85.32	16,213	91.43
Divorced/widowed	1,134	3.45	298	1.97	836	4.71
Region						
Urban	8,474	25.79	3,820	25.26	4,654	26.24
Rural	24,383	74.21	11,304	74.74	13,079	73.76
BMI group						
Underweight	1,998	6.08	944	6.24	1,054	5.94
Normal weight	16,233	49.40	7,348	48.59	8,885	50.10
Overweight	10,958	33.35	5,172	34.20	5,786	32.63
Obesity	3,665	11.15	1,657	10.96	2,008	11.32
Central obesity						
No	23,349	71.06	10,871	71.88	12,478	70.37
Yes	9,507	28.93	4,252	28.11	5,255	29.63
Smoking status						
Never smoking	22,340	67.99	4,840	32.00	17,500	98.69
Current smoking	8,997	27.38	8,801	58.19	196	1.11
Former smoking	1,520	4.63	1,483	9.81	37	0.21
Secondhand smoke exposure						
No	21,639	65.86	12,802	84.65	8,837	49.83
Yes	11,218	34.14	2,322	15.35	8,896	50.17
Frequency of alcohol consumption						
No alcohol use	19,270	58.65	5,531	36.57	13,739	77.48
<3 days per month	5,894	17.94	3,281	21.69	2,613	14.74
1–4 days per week	4,183	12.73	3,300	21.82	883	4.98
5–7 days per week	3,510	10.68	3,012	19.92	498	2.81
Insufficient physical activity						
No	23,241	70.73	10,596	70.06	12,645	71.31
Yes	9,494	28.89	4,472	29.57	5,022	28.32

Note: Data were missing for BMI (n=3), central obesity (n=1), and insufficient physical activity (n=122).

Abbreviation: BMI=body mass index.

SUPPLEMENTARY TABLE S2. Changes in effect estimates in the sensitivity analysis.

Outcome	Variable	Main analysis OR (95% CI)	Sensitivity analysis OR (95% CI)	Percent change (%)	Direction consistency	Change in significance
One condition vs. Disease-free	(Intercept)	0.424 (0.362, 0.497)	0.425 (0.362, 0.500)	0.20%	Consistent	No change
	Gender					
	Female	—	—	—	—	—
	Male	1.661 (1.529, 1.805)	1.609 (1.482, 1.748)	-3.10%	Consistent	No change
	Age group (years)					
	18–44	—	—	—	—	—
	45–64	2.013 (1.886, 2.148)	2.008 (1.880, 2.143)	-0.20%	Consistent	No change
	≥65	2.969 (2.711, 3.253)	2.737 (2.500, 2.996)	-7.80%	Consistent	No change
	Ethnicity					
	Han	—	—	—	—	—
	Li	1.031 (0.924, 1.150)	1.022 (0.915, 1.141)	-0.90%	Consistent	No change
	Others	1.026 (0.823, 1.277)	1.054 (0.845, 1.315)	2.70%	Consistent	No change
	Education					
	Primary or below	—	—	—	—	—
	Middle school/technical secondary school	0.915 (0.858, 0.976)	0.916 (0.859, 0.976)	0.10%	Consistent	No change
	College degree or above	0.834 (0.745, 0.933)	0.827 (0.739, 0.926)	-0.80%	Consistent	No change
	Marital status					
	Not married	—	—	—	—	—
	Married/cohabiting	1.098 (0.990, 1.217)	1.082 (0.975, 1.200)	-1.50%	Consistent	No change
	Divorce/widowhood	1.335 (1.099, 1.621)	1.285 (1.061, 1.558)	-3.70%	Consistent	No change
	Region					
	Rural	—	—	—	—	—
	Urban	0.841 (0.682, 1.036)	0.827 (0.667, 1.027)	-1.70%	Consistent	No change
	Central obesity					
	No	—	—	—	—	—
	Yes	2.046 (1.917, 2.185)	1.985 (1.860, 2.118)	-3.00%	Consistent	No change
	Smoking status					
	No smoking	—	—	—	—	—
	Current smoking	1.098 (0.999, 1.207)	1.136 (1.033, 1.249)	3.50%	Consistent	Changed from marginal to significant*
	Smoking cessation	0.902 (0.773, 1.053)	0.899 (0.771, 1.048)	-0.30%	Consistent	No change
	Second-hand smoke exposure					
	No	—	—	—	—	—
	Yes	0.984 (0.921, 1.051)	0.972 (0.910, 1.038)	-1.20%	Consistent	No change
	Frequency of alcohol consumption					
	No alcohol use	—	—	—	—	—
	<3 days per month	0.954 (0.881, 1.032)	0.974 (0.901, 1.054)	2.10%	Consistent	No change
	1–4 days per week	1.003 (0.910, 1.106)	1.051 (0.953, 1.159)	4.80%	Consistent	No change
	5–7 days per week	1.283 (1.150, 1.432)	1.218 (1.092, 1.359)	-5.10%	Consistent	No change

Continued

Outcome	Variable	Main analysis OR (95% CI)	Sensitivity analysis OR (95% CI)	Percent change (%)	Direction consistency	Change in significance
Two conditions vs. Disease-free	Insufficient physical activity					
	No	—	—	—	—	—
	Yes	1.049 (0.980, 1.122)	1.045 (0.976, 1.118)	−0.40%	Consistent	No change
	(Intercept)	0.117 (0.094, 0.146)	0.115 (0.093, 0.143)	−1.70%	Consistent	No change
	Gender					
	Female	—	—	—	—	—
	Male	1.931 (1.744, 2.138)	1.904 (1.717, 2.111)	−1.40%	Consistent	No change
	Age group (years)					
	18–44	—	—	—	—	—
	45–64	3.671 (3.357, 4.015)	3.395 (3.101, 3.716)	−7.50%	Consistent	No change
	≥65	7.342 (6.546, 8.235)	5.962 (5.309, 6.695)	−18.80%	Consistent	No change
	Ethnicity					
	Han	—	—	—	—	—
	Li	1.030 (0.890, 1.191)	1.045 (0.903, 1.209)	1.50%	Consistent	No change
	Others	0.966 (0.730, 1.277)	0.988 (0.742, 1.315)	2.30%	Consistent	No change
	Education					
	Primary or below	—	—	—	—	—
	Middle school/technical secondary school	0.925 (0.854, 1.002)	0.927 (0.855, 1.005)	0.20%	Consistent	No change
	College degree or above	0.699 (0.598, 0.817)	0.674 (0.574, 0.792)	−3.60%	Consistent	No change
	Marital status					
	Not married	—	—	—	—	—
	Married/cohabiting	0.960 (0.834, 1.106)	0.945 (0.820, 1.089)	−1.60%	Consistent	No change
	Divorce/widowhood	1.281 (1.017, 1.615)	1.205 (0.954, 1.523)	−5.90%	Consistent	Change*
	Region					
	Rural	—	—	—	—	—
	Urban	0.817 (0.610, 1.094)	0.765 (0.578, 1.013)	−6.40%	Consistent	No change
	Central obesity					
	No	—	—	—	—	—
	Yes	3.342 (3.097, 3.606)	3.261 (3.021, 3.521)	−2.40%	Consistent	No change
	Smoking status					
	No	—	—	—	—	—
	Current smoking	1.031 (0.919, 1.157)	1.084 (0.965, 1.217)	5.10%	Consistent	No change
	Smoking cessation	0.947 (0.794, 1.129)	0.976 (0.818, 1.164)	3.10%	Consistent	No change
	Second-hand smoke exposure					
	No	—	—	—	—	—
	Yes	0.911 (0.837, 0.992)	0.927 (0.851, 1.011)	1.80%	Consistent	Change*
	Frequency of alcohol consumption					
	No alcohol use	—	—	—	—	—
	<3 days per month	0.898 (0.809, 0.996)	0.943 (0.849, 1.047)	5.00%	Consistent	Change*

Continued

Outcome	Variable	Main analysis OR (95% CI)	Sensitivity analysis OR (95% CI)	Percent change (%)	Direction consistency	Change in significance
Three conditions vs. Disease-free	1–4 days per week	1.329 (1.178, 1.498)	1.443 (1.278, 1.628)	8.60%	Consistent	No change
	5–7 days per week	1.713 (1.504, 1.950)	1.729 (1.519, 1.967)	0.90%	Consistent	No change
	Insufficient physical activity					
	No	–	–	–	–	–
	inactivity_Yes	1.156 (1.062, 1.259)	1.142 (1.047, 1.244)	–1.20%	Consistent	No change
	(Intercept)	0.022 (0.016, 0.031)	0.020 (0.014, 0.028)	–9.10%	Consistent	No change
	Gender					
	Female	–	–	–	–	–
	Male	1.899 (1.616, 2.233)	1.982 (1.668, 2.355)	4.40%	Consistent	No change
	Age group (years)					
	18–44	–	–	–	–	–
	45–64	6.010 (4.998, 7.227)	5.380 (4.443, 6.515)	–10.50%	Consistent	No change
	≥65	12.989 (10.524, 16.033)	9.276 (7.431, 11.579)	–28.60%	Consistent	No change
	Ethnicity					
	Han	–	–	–	–	–
	Li	1.239 (0.973, 1.576)	1.397 (1.095, 1.783)	12.80%	Consistent	Changed from marginal to significant*
	Others	1.669 (1.107, 2.515)	1.810 (1.176, 2.785)	8.40%	Consistent	No change
	Education					
	Primary or below	–	–	–	–	–
	Middle school/technical secondary school	0.994 (0.875, 1.129)	0.982 (0.857, 1.124)	–1.20%	Consistent	No change
	College degree or above	0.876 (0.670, 1.144)	0.850 (0.636, 1.136)	–3.00%	Consistent	No change
	Marital status					
	Not married	–	–	–	–	–
	Married/cohabiting	0.626 (0.487, 0.803)	0.618 (0.478, 0.799)	–1.30%	Consistent	No change
	Divorce/widowhood	0.772 (0.534, 1.114)	0.821 (0.561, 1.201)	6.30%	Consistent	No change
	Region					
	Rural	–	–	–	–	–
	Urban	0.863 (0.583, 1.276)	0.815 (0.572, 1.160)	–5.60%	Consistent	No change
	Central obesity					
	No	–	–	–	–	–
	Yes	4.530 (4.028, 5.094)	4.325 (3.816, 4.901)	–4.50%	Consistent	No change
	Smoking status					
	No smoking	–	–	–	–	–
	Current smoking	0.966 (0.807, 1.157)	1.021 (0.845, 1.233)	5.70%	Consistent	No change
	Smoking cessation	0.997 (0.771, 1.290)	0.943 (0.716, 1.242)	–5.40%	Consistent	No change
	Second-hand smoke exposure					
	No	–	–	–	–	–
	Yes	0.872 (0.758, 1.004)	0.867 (0.745, 1.009)	–0.60%	Consistent	No change

Continued

Outcome	Variable	Main analysis OR (95% CI)	Sensitivity analysis OR (95% CI)	Percent change (%)	Direction consistency	Change in significance
Frequency of alcohol consumption						
	No alcohol use	—	—	—	—	—
	<3 days per month	0.815 (0.685, 0.970)	0.861 (0.715, 1.038)	5.60%	Consistent	Change*
	1–4 days per week	1.146 (0.940, 1.397)	1.299 (1.058, 1.594)	13.40%	Consistent	Change*
	5–7 days per week	1.712 (1.408, 2.082)	1.819 (1.488, 2.224)	6.30%	Consistent	No change
Insufficient physical activity						
	No	—	—	—	—	—
	Yes	1.328 (1.157, 1.523)	1.217 (1.050, 1.411)	–8.40%	Consistent	No change

Note: In the main analysis, disease status was ascertained based on both physical measurements and self-reported diagnoses. However, in the sensitivity analysis, participants whose diagnoses relied solely on self-reporting were excluded.

“—” means this level is the reference level and there are no corresponding parameter values.

* indicates that the sensitivity analysis results differed from the original study results.

Abbreviation: CI=confidence interval.

others' burning cigarettes or exhaled mainstream smoke for an average of at least 1 day per week (2).

Following the WHO Comprehensive Monitoring Framework for Noncommunicable Diseases (2,6), insufficient physical activity was defined as <150 minutes per week of combined moderate and highintensity activity. Total activity was calculated as: minutes of moderateintensity activity + 2 × minutes of highintensity activity. Highintensity activities were defined as those requiring substantial effort (e.g., heavy lifting, digging) that substantially increased breathing and heart rates; conversely, moderateintensity activities required moderate effort (e.g., sawing wood, laundry, cleaning) and led to only slight elevations in respiratory and heart rates.

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Preplanned Studies

Global Burden of Disease Study on the Changing Landscape of Hematologic Malignancies and the Growing Impact of Elevated Body Mass Index — Asia, 1990–2023

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Summary

What is already known about this topic?

Hematologic malignancies constitute a growing health burden in Asia. Their long-term subregional patterns, future trajectories, and the contribution of high body mass index (BMI) have not been comprehensively evaluated within a unified framework.

What is added by this report?

From 1990 to 2023, leukemia mortality declined across Asia, whereas non-Hodgkin lymphoma and multiple myeloma incidence and mortality increased in most subregions with multiple myeloma showing the fastest growth through 2040. Mendelian randomization suggested a potential association between BMI and malignant lymphoma in East Asian populations.

What are the implications for public health practice?

Priorities include improving multiple myeloma detection and treatment access, strengthening care for aging populations, and integrating obesity prevention into cancer prevention programs.

ABSTRACT

Introduction: Hematologic malignancies are an increasing public health concern in Asia. However, regional trends, future trajectories, and the contribution of high body mass index (BMI) remain incompletely characterized.

Methods: Data from the Global Burden of Disease Study 2023 were used to evaluate leukemia, non-Hodgkin lymphoma (NHL), and multiple myeloma (MM) across 34 Asian countries and territories from 1990 to 2023. Average annual percentage changes and Bayesian age-period-cohort projections through 2040 were estimated. Mortality attributable to high BMI was assessed, and Mendelian randomization was used to examine the association between BMI and a broadly defined malignant lymphoma phenotype in an East

Asian population.

Results: Leukemia mortality declined in all five Asian subregions, whereas NHL incidence, alongside MM incidence and mortality, increased in most subregions. MM incidence increased fastest in East Asia (average annual percentage change: 3.69%). In 2023, Central Asia had the highest proportion of deaths attributable to high BMI. Genetically predicted higher BMI was associated with malignant lymphoma (odds ratio: 2.86; 95% confidence interval: 1.39, 5.87).

Conclusion: Asia faces a shifting hematologic cancer burden, particularly with increasing MM and NHL incidence. Region-specific surveillance, equitable diagnosis and treatment, services for older adults, and obesity prevention could help reduce future burden.

Hematologic malignancies (HMs) comprise a heterogeneous group of cancers originating from the blood, bone marrow, or lymphatic system. Leukemia, non-Hodgkin lymphoma (NHL), and multiple myeloma (MM) are among the most prevalent and clinically important subtypes worldwide (1–2). In Asia, their absolute burden continues to increase despite relatively low age-standardized rates in many countries. Substantial disparities persist in diagnostic capacity, cancer registration, access to advanced therapies, and treatment outcomes. Given Asia's large and rapidly aging population and socioeconomic diversity, understanding the changing HM burden is essential for guiding cancer control and resource allocation. High body mass index (BMI) is a potentially modifiable risk factor for leukemia, NHL, and MM. This study assessed the incidence, mortality, temporal trends, regional heterogeneity, and future burden of these malignancies in five Asian subregions and further evaluated the relationship between BMI and malignant lymphoma using Mendelian randomization (MR).

Epidemiological data were obtained from the Global Burden of Disease Study 2023 (GBD 2023) (3). Thirty-four Asian countries and territories were classified into high-income Asia Pacific, Central Asia, South Asia, Southeast Asia, and East Asia. Disease burden was quantified using incident cases, deaths, age-standardized incidence rates (ASIRs), and age-standardized mortality rates (ASMRs), with 95% uncertainty intervals (UIs). Temporal trends from 1990 to 2023 were assessed using average annual percentage changes (AAPCs) derived from segmented regression (4). Bayesian age-period-cohort models were used to project ASIRs and ASMRs from 2024 to 2040 (5). High BMI was defined according to GBD criteria as BMI ≥ 25 kg/m² among adults aged ≥ 20 years, and BMI-attributable mortality estimates were obtained from the GBD Results Tool (6).

Two-sample MR utilized summary-level genome-wide association study (GWAS) data from East Asian populations. The BMI dataset (bbj-a-1) included 158,284 participants, while the malignant lymphoma dataset (ebi-a-GCST90018658) included 335 cases and 177,342 controls from BioBank Japan (7). As the outcome was reported as malignant lymphoma, the specific exclusion of Hodgkin lymphoma could not be confirmed. Fifty-eight independent BMI-associated single-nucleotide polymorphisms were selected as instrumental variables. Random-effects inverse-variance weighting served as the primary analysis, while weighted median, MR-Egger, weighted mode, simple mode, and leave-one-out analyses were used for sensitivity assessments. Analyses were conducted using R software (version 4.2.3; R Foundation for Statistical Computing, Vienna, Austria), with two-sided $P < 0.05$ considered statistically significant.

Between 1990 and 2023, the number of new HM cases increased in all five Asian subregions, whereas the trends in age-standardized rates differed substantially by disease type. Leukemia incidence declined in most subregions, and leukemia mortality declined in all five subregions. East Asia experienced the most pronounced reduction, with the ASMR decreasing from 7.04 per 100,000 population in 1990 to 3.23 in 2023 [AAPC: -2.31% ; 95% confidence interval (CI): -2.42% , -2.20%]. In contrast, NHL incidence increased in most subregions. By 2023, the high-income Asia Pacific had the highest NHL ASIR at 10.52 per 100,000 population (95% UI: 7.05, 14.97), with an AAPC of 2.10% (95% CI: 1.90% , 2.31%). NHL mortality increased in high-income Asia Pacific, South Asia, and Southeast Asia, but declined in East

Asia and Central Asia. MM exhibited the most consistent and rapid increase among the three malignancies. In East Asia, the ASIR reached 0.96 per 100,000 population in 2023 — more than three times the 1990 level — with an AAPC of 3.69% (95% CI: 3.21% , 4.18%). MM mortality also increased markedly in East Asia, Southeast Asia, and South Asia, with AAPCs of 2.38% , 1.83% , and 1.51% , respectively (Table 1).

At the country level, Japan had the highest ASIRs for leukemia and NHL, whereas Brunei Darussalam had the highest ASIR for MM (Table 2). Age-specific incidence and mortality increased sharply after the age of 50 years and rates were generally higher among males. NHL and MM were concentrated in older populations, whereas leukemia also showed an additional incidence peak in childhood (Supplementary Figure S1, available at <https://weekly.chinacdc.cn/>).

Leukemia ASIRs and ASMRs were projected to decline or stabilize by 2040 in most subregions. NHL incidence was projected to increase moderately, whereas mortality trends varied by region. MM incidence and mortality were projected to continue increasing in all subregions except for the high-income Asia Pacific (Figure 1). The proportion of HM deaths attributable to high BMI increased from 1990 to 2023. In 2023, Central Asia had the highest attributable proportions, including 9.53% of MM deaths, 8.72% of leukemia deaths, and 5.96% of NHL deaths. These proportions were generally higher among females than males (Supplementary Figure S2, available at <https://weekly.chinacdc.cn/>).

In the MR analysis, genetically predicted higher BMI was associated with the broadly defined malignant lymphoma phenotype (random-effects inverse-variance weighted odds ratio: 2.86 ; 95% CI: 1.39 , 5.87 ; $P = 0.004$) (Figure 2). Results were directionally consistent across sensitivity methods, and no evidence of directional horizontal pleiotropy was observed (Supplementary Figure S3, available at <https://weekly.chinacdc.cn/>). These findings support a potential association between higher BMI and broadly defined malignant lymphoma in the East Asian population.

DISCUSSION

Using the latest GBD 2023 estimates along with MR analysis, this study identified substantial shifts and regional heterogeneity in the burden of major HMs

TABLE 1. Incidence of the three major HMs in five Asian subregions between 1990 and 2023.

Subregion	1990		2023		1990–2023	
	Count (95% UI)	ASIR/100,000 population (95% UI)	Count (95% UI)	ASIR/100,000 population (95% UI)	PC (%; 95% UI)	AAPC (%; 95% CI)
Leukemia						
High-income Asia Pacific	13,602 (10,467, 20,311)	7.64 (5.78, 11.64)	27,167 (17,497, 42,134)	8.18 (4.94, 12.95)	99.72 (18.24, 237.28)	0.37 (0.14, 0.60)
Central Asia	3,819 (3,472, 4,365)	5.83 (5.32, 6.55)	4,059 (3,508, 4,849)	4.16 (3.60, 4.94)	6.30 (-11.90, 33.22)	-0.98 (-1.23, -0.72)
South Asia	33,813 (24,708, 45,406)	3.70 (2.69, 4.95)	52,275 (40,159, 67,297)	3.10 (2.37, 4.01)	54.60 (4.08, 116.30)	-0.44 (-0.59, -0.29)
Southeast Asia	23,249 (18,137, 29,146)	5.92 (4.68, 7.38)	37,933 (30,622, 47,169)	5.43 (4.36, 6.74)	63.16 (20.72, 117.38)	-0.22 (-0.29, -0.14)
East Asia	106,577 (84,753, 126,772)	9.29 (7.43, 11.00)	119,788 (87,505, 170,426)	7.68 (5.24, 11.71)	12.40 (-19.79, 81.21)	-0.53 (-0.61, -0.44)
Non-Hodgkin lymphoma						
High-income Asia Pacific	11,516 (9,223, 14,472)	5.86 (4.69, 7.36)	49,446 (33,124, 69,926)	10.52 (7.05, 14.97)	329.38 (177.23, 557.09)	2.10 (1.90, 2.31)
Central Asia	1,699 (1,337, 2,261)	2.75 (2.20, 3.56)	2,782 (2,039, 3,779)	2.85 (2.11, 3.85)	63.75 (9.41, 143.97)	-0.01 (-0.35, 0.32)
South Asia	19,717 (14,665, 25,752)	2.65 (1.99, 3.47)	58,520 (42,215, 81,516)	3.52 (2.56, 4.87)	196.80 (89.81, 347.97)	0.99 (0.75, 1.23)
Southeast Asia	8,762 (6,771, 11,025)	2.69 (2.09, 3.39)	27,807 (20,482, 37,418)	3.78 (2.79, 5.10)	217.35 (115.35, 361.37)	1.07 (0.99, 1.16)
East Asia	39,722 (32,381, 50,011)	3.90 (3.18, 4.92)	112,864 (75,930, 163,221)	5.21 (3.50, 7.54)	184.13 (87.68, 351.67)	1.00 (0.80, 1.19)
Multiple myeloma						
High-income Asia Pacific	3,932 (3,351, 4,638)	1.98 (1.69, 2.35)	11,277 (8,665, 13,736)	2.13 (1.64, 2.65)	187.18 (109.11, 285.90)	0.30 (0.10, 0.49)
Central Asia	149 (127, 177)	0.30 (0.26, 0.35)	478 (390, 607)	0.50 (0.41, 0.63)	221.79 (147.29, 326.38)	1.54 (0.84, 2.24)
South Asia	4,325 (2,984, 6,007)	0.77 (0.53, 1.07)	20,519 (14,538, 27,394)	1.32 (0.94, 1.77)	352.86 (161.93, 593.52)	1.77 (1.61, 1.94)
Southeast Asia	736 (531, 1,032)	0.28 (0.20, 0.39)	4,257 (3,063, 6,035)	0.57 (0.42, 0.81)	468.27 (296.97, 705.11)	2.17 (2.08, 2.25)
East Asia	2,978 (1,882, 5,017)	0.31 (0.20, 0.53)	22,833 (15,283, 31,884)	0.96 (0.64, 1.36)	664.86 (313.86, 1,382.52)	3.69 (3.21, 4.18)

Abbreviation: HMs=hematologic malignancies; ASIR=age-standardized incidence rate; UI=uncertainty interval; PC=percentage change; AAPC=average annual percentage change; CI=confidence interval.

across Asia. Leukemia mortality declined in all five subregions, whereas NHL incidence increased in most subregions. Notably, MM exhibited the most consistent and rapid increase in both incidence and mortality. The decline in leukemia mortality may reflect improvements in diagnosis, standardized treatment, supportive care, and expanded access to effective therapies. In contrast, the rising burden of MM is likely driven by population aging, improved case detection, and unequal access to resource-intensive treatments. As MM predominantly affects older adults and typically requires prolonged treatment, its continued growth may increasingly strain health systems, particularly in resource-constrained settings.

High BMI has emerged as an increasingly important modifiable contributor to HM-related mortality (2). Excess adiposity may promote hematologic carcinogenesis through chronic inflammation, insulin

resistance, adipokine dysregulation, altered immune function, and changes in the bone marrow microenvironment (8–10). The MR findings provide complementary genetic evidence indicating that higher BMI may increase susceptibility to malignant lymphoma in East Asian populations. As the outcome was broadly defined, this association should be interpreted at the overall lymphoma level rather than as an NHL subtype-specific effect.

The findings in this report are subject to at least four limitations. First, GBD estimates depend on the underlying quality of national surveillance systems and cancer registries, which varies across countries and may affect regional comparisons. Second, this analysis was restricted to three broad HM categories and did not assess subtype-specific patterns. Third, the projections assumed that historical trends would continue linearly and did not account for future changes in diagnosis,

TABLE 2. ASIR and ASMR of three major HMs across 34 Asian countries and territories in 2023.

Country	ASIR/100,000 population (95% UI)			ASMR/100,000 population (95% UI)		
	Leukemia	Non-Hodgkin lymphoma	Multiple myeloma	Leukemia	Non-Hodgkin lymphoma	Multiple myeloma
Armenia	3.91 (3.21, 5.10)	2.67 (1.87, 3.99)	0.73 (0.58, 1.00)	2.54 (2.29, 2.83)	1.04 (0.91, 1.18)	0.56 (0.48, 0.64)
Azerbaijan	5.98 (4.78, 7.79)	2.23 (1.51, 3.46)	0.27 (0.18, 0.41)	4.07 (3.42, 5.23)	1.06 (0.76, 1.46)	0.23 (0.16, 0.34)
Bangladesh	3.62 (2.59, 4.85)	3.44 (2.32, 5.03)	1.50 (0.95, 2.33)	3.05 (2.20, 4.18)	2.43 (1.63, 3.46)	1.37 (0.88, 2.01)
Bhutan	3.42 (2.55, 4.75)	3.01 (2.14, 4.36)	1.26 (0.73, 2.08)	2.84 (2.04, 3.96)	2.18 (1.54, 2.97)	1.15 (0.70, 1.80)
Brunei Darussalam	5.67 (4.40, 7.17)	8.17 (6.18, 10.66)	2.29 (1.67, 3.04)	4.42 (3.54, 5.46)	6.30 (4.84, 7.94)	2.07 (1.63, 2.61)
Cambodia	4.99 (3.77, 6.41)	2.65 (1.84, 3.51)	0.38 (0.21, 0.62)	4.38 (3.27, 5.65)	2.19 (1.57, 2.85)	0.34 (0.19, 0.58)
China	7.70 (5.25, 11.79)	5.17 (3.44, 7.55)	0.94 (0.62, 1.34)	3.20 (2.82, 3.99)	1.85 (1.59, 2.17)	0.53 (0.40, 0.64)
Democratic People's Republic of Korea	5.77 (4.04, 7.89)	2.97 (2.06, 4.02)	0.60 (0.33, 1.02)	3.76 (2.80, 4.84)	2.20 (1.57, 2.93)	0.48 (0.27, 0.82)
Georgia	6.07 (5.16, 7.25)	6.19 (4.55, 8.78)	1.42 (1.16, 1.89)	4.51 (3.99, 5.07)	3.08 (2.69, 3.45)	1.15 (0.99, 1.32)
India	3.00 (2.30, 3.90)	3.32 (2.44, 4.56)	1.26 (0.91, 1.66)	2.60 (2.00, 3.40)	2.48 (1.85, 3.26)	1.17 (0.86, 1.53)
Indonesia	5.48 (4.09, 7.10)	2.95 (2.09, 4.00)	0.42 (0.24, 0.67)	4.68 (3.59, 6.11)	2.33 (1.64, 3.11)	0.37 (0.20, 0.60)
Japan	8.46 (5.20, 13.05)	11.39 (7.53, 16.68)	2.13 (1.68, 2.69)	3.59 (3.19, 3.89)	4.35 (3.59, 5.01)	1.33 (1.12, 1.49)
Kazakhstan	3.45 (2.86, 4.19)	2.55 (1.89, 3.69)	0.69 (0.55, 0.91)	2.30 (2.08, 2.54)	1.15 (1.03, 1.26)	0.54 (0.47, 0.61)
Kyrgyzstan	2.40 (2.06, 3.01)	1.43 (1.03, 2.05)	0.29 (0.24, 0.38)	1.73 (1.54, 1.94)	0.69 (0.61, 0.78)	0.24 (0.21, 0.27)
Lao People's Democratic Republic	5.05 (3.76, 6.57)	2.50 (1.75, 3.38)	0.61 (0.37, 1.01)	4.43 (3.30, 5.74)	2.09 (1.49, 2.78)	0.56 (0.34, 0.92)
Malaysia	4.55 (3.57, 5.65)	4.84 (3.58, 6.58)	1.20 (0.86, 1.66)	3.79 (3.05, 4.58)	3.44 (2.71, 4.22)	1.01 (0.76, 1.32)
Maldives	4.35 (3.21, 6.01)	3.23 (2.30, 4.47)	1.07 (0.72, 1.45)	3.52 (2.74, 4.45)	2.11 (1.68, 2.60)	0.89 (0.64, 1.17)
Mauritius	4.27 (3.59, 5.09)	2.82 (2.22, 3.52)	1.55 (1.25, 2.04)	3.43 (2.98, 3.87)	1.84 (1.63, 2.09)	1.25 (1.09, 1.42)
Mongolia	2.72 (2.13, 3.41)	1.86 (1.30, 2.66)	0.40 (0.28, 0.53)	2.15 (1.69, 2.75)	1.04 (0.78, 1.36)	0.34 (0.24, 0.44)
Myanmar	5.02 (3.79, 6.51)	2.48 (1.77, 3.33)	0.56 (0.33, 0.92)	4.28 (3.17, 5.69)	1.99 (1.46, 2.68)	0.52 (0.31, 0.84)
Nepal	2.69 (2.01, 3.64)	2.31 (1.61, 3.21)	0.85 (0.52, 1.30)	2.37 (1.78, 3.28)	1.84 (1.27, 2.55)	0.81 (0.49, 1.24)
Pakistan	3.10 (2.37, 4.01)	4.63 (3.25, 6.51)	1.79 (1.22, 2.48)	2.61 (2.02, 3.37)	3.38 (2.42, 4.63)	1.69 (1.13, 2.38)
Philippines	4.88 (4.02, 5.96)	3.12 (2.48, 3.98)	0.49 (0.37, 0.63)	4.07 (3.32, 5.10)	2.43 (1.94, 2.98)	0.44 (0.35, 0.55)
Republic of Korea	7.39 (3.99, 12.93)	7.77 (5.33, 11.45)	2.11 (1.35, 3.19)	2.84 (2.31, 3.21)	3.02 (2.59, 3.44)	1.33 (1.09, 1.65)
Seychelles	6.81 (5.30, 8.59)	7.99 (6.15, 10.69)	1.94 (1.37, 2.70)	5.31 (4.25, 6.47)	5.40 (4.40, 6.70)	1.62 (1.22, 2.07)
Singapore	7.30 (4.10, 12.54)	8.44 (5.58, 11.93)	1.18 (0.81, 1.66)	2.98 (2.60, 3.35)	3.42 (2.90, 3.89)	0.77 (0.66, 0.88)
Sri Lanka	4.79 (3.65, 6.41)	4.32 (3.16, 5.83)	1.65 (1.20, 2.27)	3.60 (2.94, 4.35)	2.56 (1.96, 3.24)	1.26 (0.99, 1.55)
Tajikistan	3.58 (2.78, 5.05)	3.96 (2.75, 5.72)	0.30 (0.21, 0.43)	2.80 (2.26, 3.77)	2.34 (1.66, 3.24)	0.27 (0.19, 0.38)
Thailand	8.10 (6.33, 10.93)	5.24 (3.80, 7.25)	0.69 (0.48, 1.04)	5.87 (4.97, 7.09)	2.84 (2.33, 3.44)	0.52 (0.41, 0.71)
Timor-Leste	5.44 (4.18, 7.04)	2.55 (1.88, 3.40)	0.37 (0.22, 0.57)	4.69 (3.63, 6.10)	2.08 (1.46, 2.81)	0.34 (0.20, 0.55)
Turkmenistan	3.53 (3.04, 4.17)	1.28 (0.97, 1.69)	1.16 (0.95, 1.45)	2.68 (2.34, 3.07)	0.72 (0.62, 0.82)	0.98 (0.83, 1.15)
Uzbekistan	4.37 (3.75, 5.27)	3.02 (2.18, 4.30)	0.23 (0.19, 0.29)	3.04 (2.74, 3.35)	1.43 (1.26, 1.60)	0.19 (0.17, 0.22)
Viet Nam	4.11 (2.81, 5.70)	5.76 (3.84, 8.74)	0.40 (0.26, 0.61)	3.01 (2.19, 4.17)	3.40 (2.36, 4.72)	0.31 (0.22, 0.43)

Abbreviation: HMs=hematologic malignancies; ASIR=age-standardized incidence rate; ASMR=age-standardized mortality rate; UI=uncertainty interval.

treatment, or prevention. Finally, MR analysis was restricted to malignant lymphoma because large-scale, Asian-specific GWAS data for leukemia and MM were unavailable, thereby limiting assessment of obesity-related causal effects across other HM subtypes.

Given the projected increase in MM burden and the growing contribution of high BMI to HM-related

mortality, region-specific cancer prevention and control strategies are needed across Asia. Priorities should include strengthening early detection, expanding equitable access to effective treatments, promoting healthy weight management alongside other lifestyle interventions, and improving genomic research capacity in Asian populations. Furthermore,

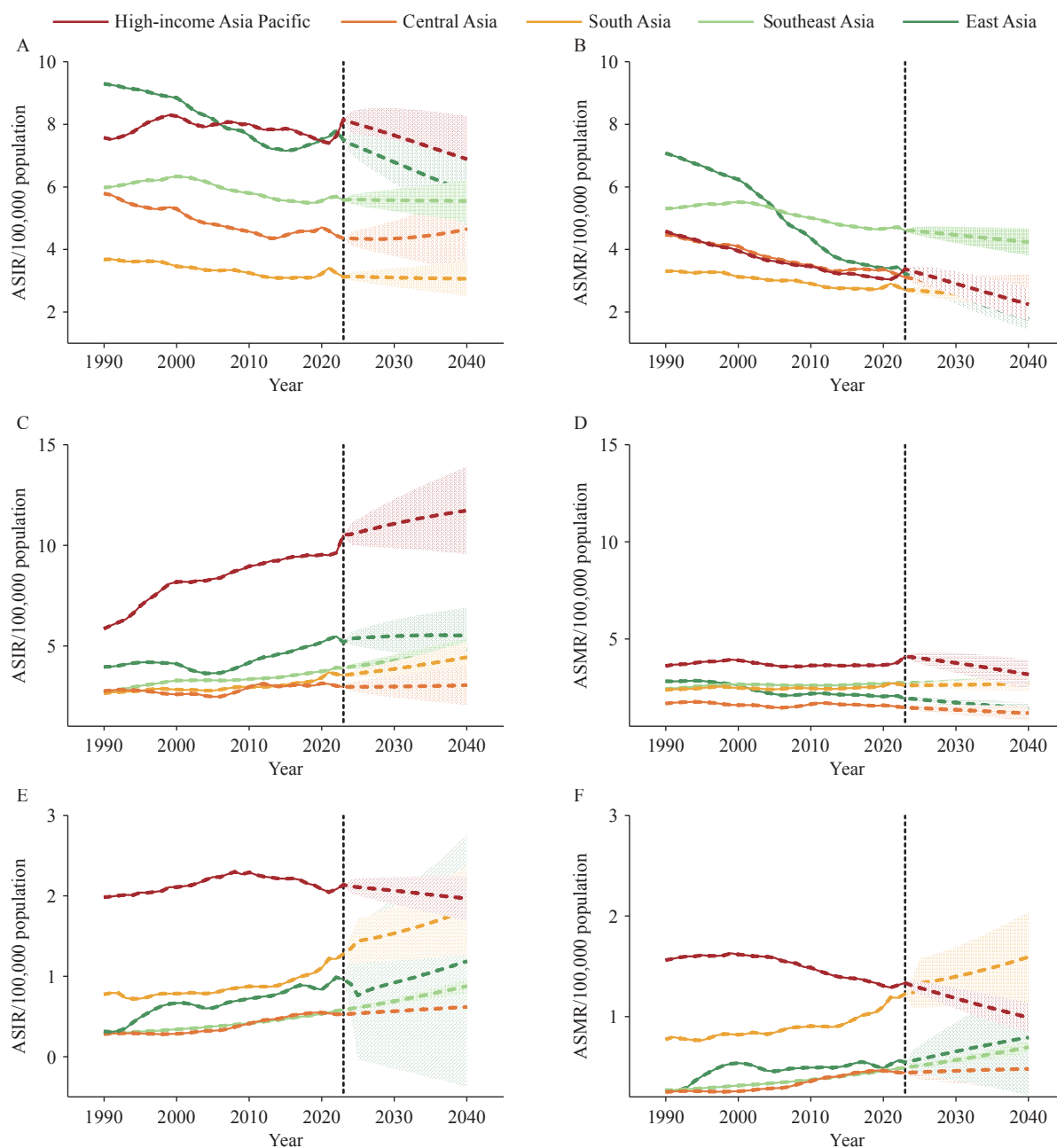


FIGURE 1. Projected trends of HM burden in five Asian subregions from 2024 to 2040. (A) Age-standardized incidence rate (ASIR) of leukemia; (B) Age-standardized mortality rate (ASMR) of leukemia; (C) ASIR of non-Hodgkin lymphoma; (D) ASMR of non-Hodgkin lymphoma; (E) ASIR of multiple myeloma; (F) ASMR of multiple myeloma. The shaded regions represent the 95% uncertainty intervals.

Note: Projected trends in the ASIR (left) and ASMR (right) of HMs (leukemia, NHL, and MM) in five Asian subregions from 2024 to 2040. The outermost shaded area indicates the 95% uncertainty intervals.

Abbreviation: HMs=hematologic malignancies; NHL=non-Hodgkin lymphoma; MM=multiple myeloma; ASIR=age-standardized incidence rate; ASMR=age-standardized mortality rate.

establishing tailored services for older adults is essential for addressing population aging, treatment inequality, and increased metabolic risk.

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Conflicts of interest: No conflicts of interest.

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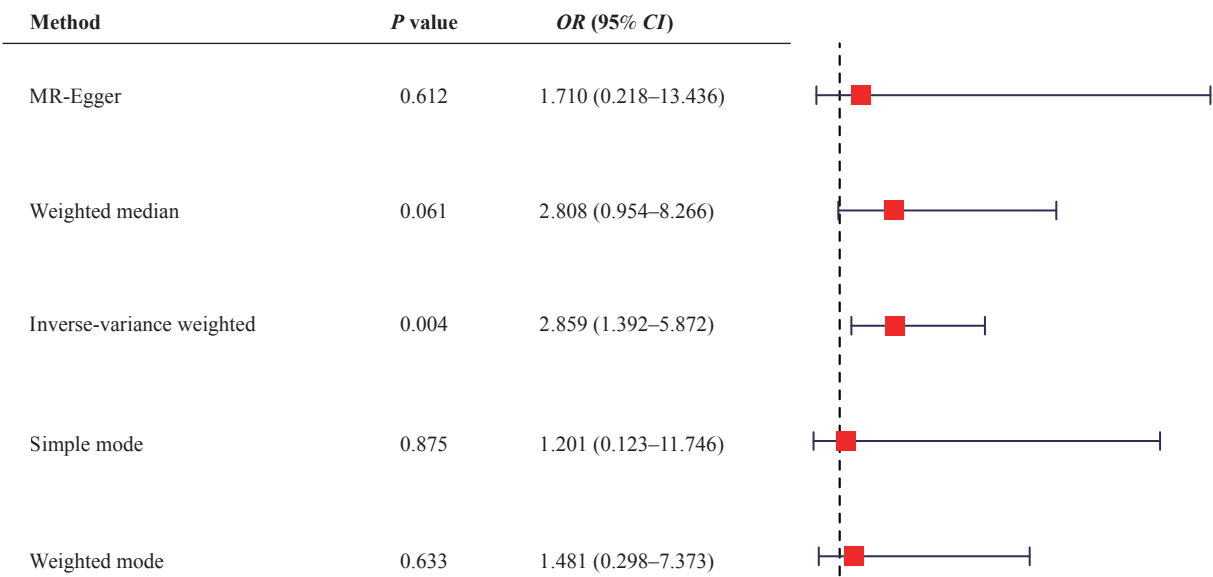


FIGURE 2. Visualization of MR analysis results. MR-Egger, weighted median, inverse-variance weighted, simple mode, and weighted mode methods were used to assess the association between BMI and malignant lymphoma. Abbreviation: OR=odds ratio; CI=confidence interval; MR=Mendelian randomization; BMI=body mass index.

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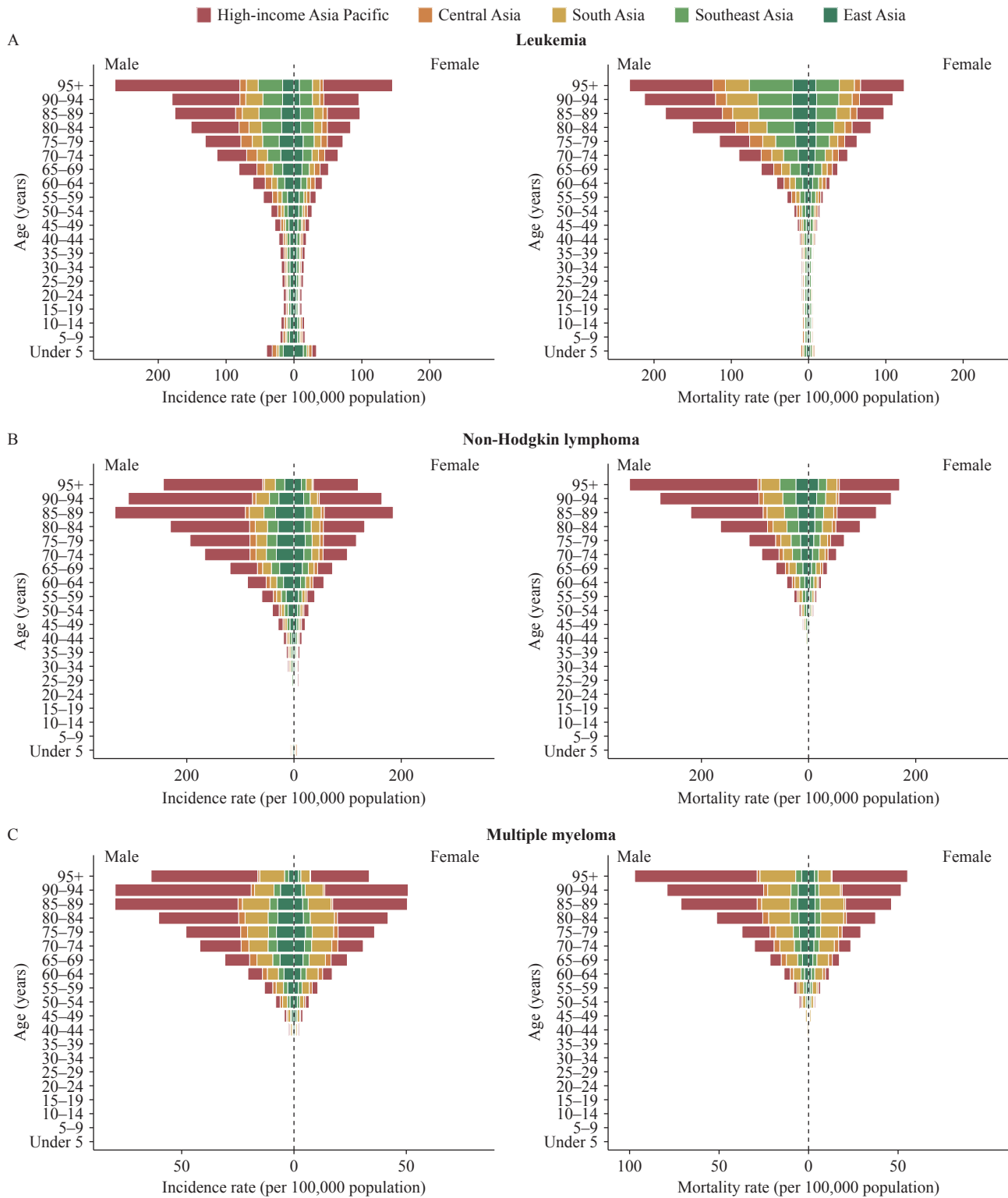
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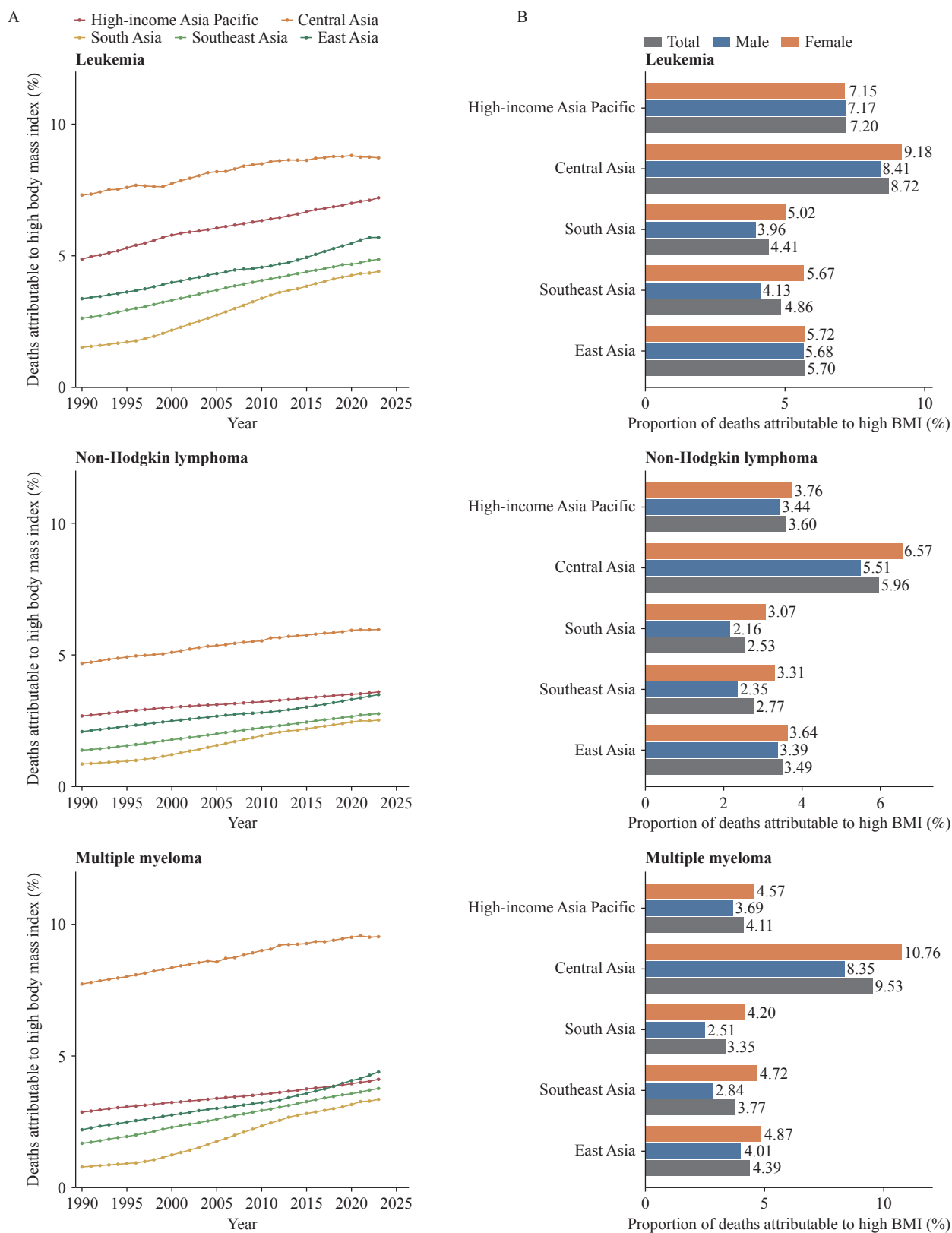
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SUPPLEMENTARY MATERIAL



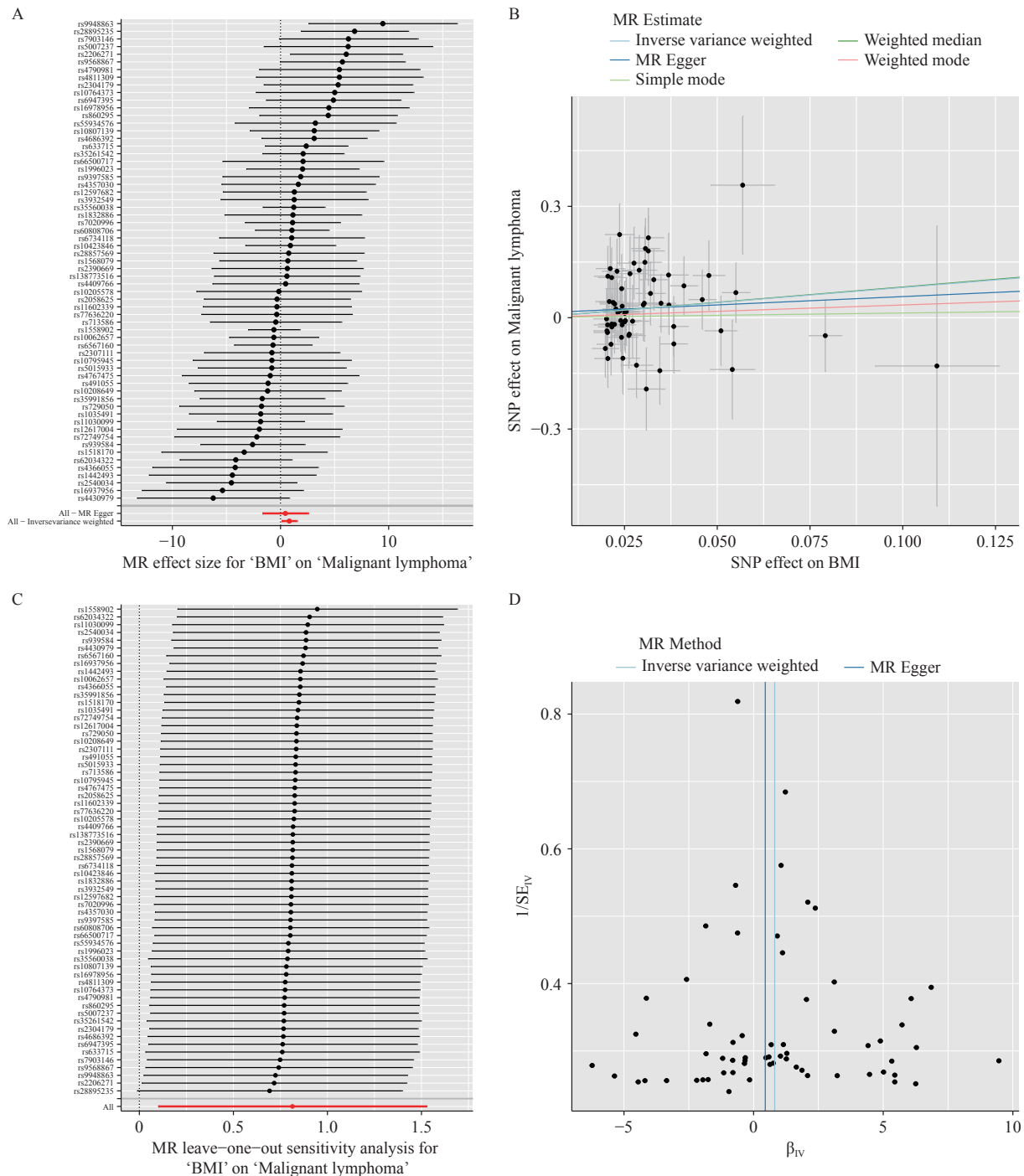
SUPPLEMENTARY FIGURE S1. Age-specific incidence and mortality rates for leukemia (A), NHL (B), and MM (C) by age and sex in five Asian subregions in 2023.

Abbreviation: NHL=non-Hodgkin lymphoma; MM=multiple myeloma.



SUPPLEMENTARY FIGURE S2. Burden of deaths from HMs attributable to high BMI. (A) Proportion of age-standardized deaths from HMs attributable to high BMI in five Asian subregions from 1990 to 2023. (B) Burden of deaths from HMs attributable to high BMI in 2023.

Abbreviation: HMs=hematologic malignancies; BMI=body mass index.



SUPPLEMENTARY FIGURE S3. Visualization of MR analysis results: (A) forest plot, (B) scatter plot, (C) leave-one-out plot, and (D) funnel plot.

Abbreviation: MR=Mendelian randomization; BMI=body mass index; SNP=single-nucleotide polymorphism; $1/SE_v$ = inverse standard error.

Note: (A) Points and horizontal lines represent single-SNP MR estimates and their 95% confidence intervals; red estimates summarize results using all SNPs with the MR-Egger and inverse-variance weighted (IVW) methods. (B) Points represent SNP associations with BMI and malignant lymphoma, with horizontal and vertical error bars indicating 95% confidence intervals; colored lines represent estimates from the five MR methods. (C) Each row shows the IVW estimate after excluding the indicated SNP; the red "All" estimate includes all SNPs. (D) Single-SNP MR estimates are plotted against their precision (inverse standard error); vertical lines indicate the overall IVW and MR-Egger estimates. MR effect estimates in panels A, C, and D are shown on the log-odds scale, where zero indicates no association.

Commentary

Smoking-Attributable Mortality in China — Epidemic Stage as a Temporal Dimension in Interpreting GBD Estimates

Gonghuan Yang^{1,2,*}; Xia Wan^{1,3}

ABSTRACT

Tobacco use remains a leading cause of preventable mortality worldwide. Estimates from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD) are widely used to quantify smoking-attributable mortality. Over recent GBD cycles, substantial methodological refinements — including improved quantification of cumulative smoking exposure and updated relative risk estimation using the Burden of Proof (BOP) Framework — have strengthened the methodological robustness of smoking-attributable mortality estimates. Nevertheless, recent GBD estimates for China remain difficult to reconcile with evidence from large national cohort studies and repeated surveys. Smoking-attributable mortality is fundamentally shaped by cumulative exposure and long latency, while the stage of the tobacco epidemic reflects the evolution of smoking exposure across successive birth cohorts and calendar periods. Evidence from China suggests that smoking-attributable mortality has not yet reached its expected plateau, whereas GBD estimates imply that smoking has accounted for approximately 30% of male deaths since around 2000. These contrasting patterns reflect different implied temporal trajectories of the tobacco epidemic, rather than simple differences in numerical estimates. We propose that the epidemic stage should be considered an essential temporal dimension when interpreting smoking-attributable mortality estimates. Incorporating the epidemic stage alongside existing modeling approaches would better reflect the differences in the timing of cumulative exposure and evolution of smoking-attributable mortality, thereby improving the interpretation, comparability, and policy relevance of model-based estimates across populations.

Tobacco use remains a leading cause of preventable mortality worldwide. Estimates from the Global

Burden of Disease, Injuries, and Risk Factors Study (GBD) are widely used by researchers and policymakers to quantify smoking-attributable mortality. The GBD framework has undergone continuous methodological refinements to improve the estimation of smoking-attributable mortality. GBD 2019 introduced important advances in quantifying cumulative smoking exposure and modeling nonlinear exposure–response relationships (1). Subsequent updates to GBD 2021 (2–3) further refined relative risk estimation by incorporating the Burden of Proof (BOP) framework and an expanded evidence base, with these improvements retained in GBD 2023. Further details are provided in the Supplementary Materials (available at <https://weekly.chinacdc.cn/>). These developments have strengthened the methodological framework underlying GBD estimates.

Despite these methodological advances, GBD estimates for China remain difficult to reconcile with the findings of large national cohort studies and repeated surveys. This Commentary addresses a different but complementary question: Rather than evaluating the GBD estimation methodology itself, we examine how smoking-attributable mortality estimates should be interpreted in populations at different stages of the tobacco epidemic. We argue that incorporating the temporal evolution of the tobacco epidemic provides an important perspective for interpreting GBD estimates and their implications for disease burden assessments and public health policies in China.

APPARENT DISCREPANCY BETWEEN GBD ESTIMATES AND EMPIRICAL EVIDENCE IN CHINA

Table 1 compares the representative model-based estimates from the GBD 2023 with major empirical evidence from China, including retrospective mortality analyses, prospective cohorts, and cohort-based projections. At comparable time points, the GBD

TABLE 1. Comparison of model-based (GBD 2023) and empirical estimates of smoking-attributable mortality among adult men in China at corresponding time points.

Year	GBD 2023 estimate		Empirical estimate	
	Deaths (million)	Proportion of male deaths (%)	Deaths (million)	Proportion of male deaths (%)
1990	1.278	20	0.606	12
2000	1.394	30	—	—
2010	1.519	30	0.845	18
2020	1.538	30	—	—
2023	1.787	30	—	—
2030–2050	—	—	2.000–3.000	25–30

Note: Estimates are presented for corresponding calendar years but are not intended to represent exact methodological equivalence across studies. GBD estimates include adults aged ≥ 25 years, whereas the empirical cohort studies included adults aged ≥ 35 years.

"—" indicates that no corresponding estimate was reported in the empirical studies. Data Sources are GBD 2023 Results Tool (4), Chen et al. (5), and Liu et al. (6).

Abbreviation: GBD=Global Burden of Disease.

estimates were consistently substantially higher than the empirical estimates. For example, GBD 2023 estimated 1.52 million smoking-attributable deaths among adult men in China in 2010 (4), compared with 0.84 million reported from the nationwide prospective cohort study (5). More importantly, these two approaches imply markedly different temporal trajectories. GBD estimates suggest that smoking accounted for approximately 30% of male deaths in China from around 2000, whereas empirical studies indicate substantially lower proportions and a continuing upward trend, with a similar level projected to be reached only from 2030 to 2050.

CUMULATIVE EXPOSURE, TEMPORAL LAG, AND TOBACCO EPIDEMIC STAGE

Smoking-attributable mortality is a cumulative and lagged process rather than an immediate response to contemporaneous exposure levels. Evidence from long-term cohort studies supports this temporal structure. In the British Doctors Study (7), excess mortality among smokers increased progressively with the duration of follow-up, reflecting an accumulation of smoking-related risks over time. Earlier initiation of smoking and greater smoking intensity result in a longer duration of smoking and greater cumulative exposure, which are associated with progressively higher smoking-related risks and, at the population level, increased smoking-attributable mortality.

At the population level, this temporal structure reflects the smoking history of successive birth cohorts. Age at smoking initiation, smoking cessation, and smoking intensity vary across birth cohorts and calendar periods, producing different cumulative

exposure profiles, and consequently, different temporal trajectories of smoking-attributable mortality. This temporal structure is reflected in an approximately 20–30-years lag between smoking uptake and smoking-attributable mortality, as observed in countries such as the United States, United Kingdom, and Australia (8–9). This delayed response is consistent with the broader temporal pattern described in the cigarette epidemic model proposed by Lopez and colleagues (10). In this model, Stage III is characterized by a rapid increase in smoking-attributable mortality, eventually reaching approximately 25%–30% of all male deaths in more mature epidemics. Populations that have not yet reached this stage are therefore expected to experience rising smoking-attributable mortality, as the effects of cumulative exposure have not yet been fully expressed.

Collectively, these findings indicate that smoking-attributable mortality is a cohort-driven outcome shaped by cumulative exposure and long latency. Consequently, populations at different stages of the tobacco epidemic are expected to exhibit different temporal trajectories of smoking-attributable mortality. This perspective provides a useful framework for interpreting the contrasting patterns presented in Table 1.

As shown in Table 1, the GBD estimates imply that smoking has accounted for approximately 30% of male deaths in China since around 2000. In contrast, empirical evidence from Chinese cohort studies suggests that smoking-attributable mortality continues to increase over time, with a comparable proportion projected only for 2030–2050. Rather than representing a simple numerical discrepancy, these contrasting patterns imply different assumptions about

the temporal evolution of tobacco epidemics. The empirical trajectory appears more consistent with the gradual accumulation of smoking exposure and associated mortality risk expected during the transition from stages III to IV of the cigarette epidemic.

Although the GBD incorporates cumulative exposure metrics and latency-related patterns, these approaches primarily characterize the relationship between smoking exposure and subsequent health outcomes. They do not explicitly characterize the population-level stage of the tobacco epidemic, which reflects the historical accumulation of exposure across successive birth cohorts. This distinction may help explain why the GBD estimates in Table 1 suggest that smoking has accounted for approximately 30% of male deaths in China since around 2000, with little further increase thereafter, whereas empirical studies indicate a continuing increase in the proportion of smoking-attributable mortality.

EPIDEMIC TIMING IN CHINA

China appears to remain at a relatively late but transitional stage of the smoking epidemic. Evidence from large-scale prospective cohort studies indicates that smoking-related risks among Chinese men have continued to increase over time, but remain below the levels observed in populations with fully mature smoking epidemics.

In a nationwide prospective cohort study conducted between 2004 and 2014, smoking relative risks and attributable fractions among Chinese men increased substantially compared to those reported in earlier nationwide studies. In urban areas, smoking-related mortality *RRs* increased from 1.32 during 1991–1999 to 1.65 during 2004–2014, while corresponding estimates in rural areas increased from 1.13 to 1.22 (5). However, these risk estimates remained below those observed in populations with fully mature smoking epidemics and were broadly comparable to those observed in the earlier phases of follow-up in the British Doctors Study. This pattern suggests that by approximately 2015, the smoking epidemic in Chinese men had not yet reached the mortality profile characteristic of a fully mature epidemic.

At the population level, since China began national epidemiological surveys on smoking in 1984, the current smoking prevalence among Chinese men has remained high (12–15), declining to below 50% only after 2020 (15). Annual per-capita cigarette production, estimated by dividing total cigarette

production by the total population, provides an indirect measure of the extent of tobacco consumption at the population level. From the 1950s to the 1970s, annual per-capita cigarette production was below 400 cigarettes per person per year, or less than one cigarette per person per day. It began to increase substantially in the 1980s and exceeded 1,700 cigarettes per person per year from 2010 to 2020, corresponding to approximately five cigarettes per person per day; the highest level, 5.23 cigarettes per person per day, was reached in 2014. Overall, these patterns suggest that the period of the highest population-level tobacco exposure among Chinese men occurred during 2010–2020, with cigarette production peaking around 2014 (Figure 1).

In summary, these findings suggest that China is still undergoing a transition from a high-exposure phase toward the period of highest smoking-attributable mortality. Consequently, the empirical evidence indicates that smoking-attributable mortality is likely to continue to increase over the coming decades before reaching a plateau.

This interpretation differs from that implied by the GBD estimates, which suggest that smoking-attributable mortality among Chinese men has remained at approximately 30% of all male deaths since 2000. The difference is therefore not merely one of the numerical magnitudes but also of the implied timing of the tobacco epidemic. Therefore, incorporating the epidemic stage into the epidemiological context may improve the interpretation of model-based estimates.

COMPETING RISKS AND CONTEXTUAL MODIFIERS

In addition to temporal dynamics, contextual factors may also modify the relationship between smoking exposure and health outcomes. Environmental and occupational exposures, such as household air pollution or workplace hazards, can influence disease risk and contribute to heterogeneity in smoking-related outcomes in high-exposure settings, such as Xuanwei in China (16). However, these factors operate primarily as effect modifiers rather than as alternative explanations for the temporal structure of smoking-attributable mortality. Although they may influence the magnitude and distribution of risk, they do not fundamentally alter the cohort-driven processes arising from cumulative exposure or long latency. As such,

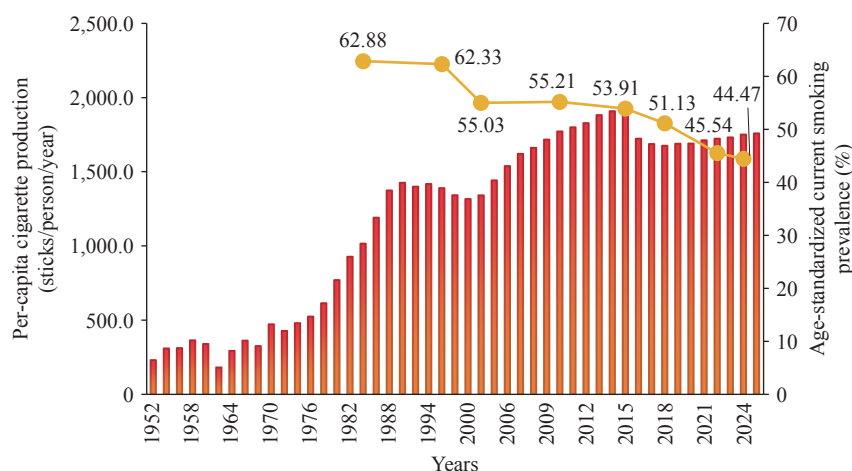


FIGURE 1. Historical trends in per-capita cigarette production and smoking prevalence among men aged 15–69 years in China, 1952–2025.

Note: Annual per capita cigarette production was calculated by dividing the total cigarette production by the total population. The smoking prevalence estimates were age-standardized for the 2020 Chinese population. The figure was compiled by the authors based on published data.

Data sources: National Bureau of Statistics of China (NBS), National Data for annual cigarette production and total population (11), and published national smoking surveys (12–15).

they add complexity to risk estimation, but do not fundamentally alter the temporal trajectory of smoking-attributable mortality driven by cumulative exposure and epidemic stages. The overall contribution of environmental exposure to smoking-attributable estimates remains uncertain and requires further empirical studies to quantify their relative effects and potential effect modification across regions and birth cohorts.

IMPLICATIONS FOR INTERPRETATION, REPORTING, AND POLICY

The evidence presented here suggests that differences between GBD estimates and empirical studies in China reflect not only differences in the estimated magnitude of smoking-attributable mortality but also different implied trajectories of the tobacco epidemic. Although the GBD framework has undergone substantial methodological refinements in recent years, including improvements in exposure assessment and relative risk estimation, model outputs should be interpreted within the epidemiological context of the populations to which they are applied. In countries such as China, where the tobacco epidemic is still evolving, the epidemic stage represents an essential temporal dimension for interpreting smoking-attributable mortality estimates.

However, empirical evidence from Chinese cohort studies has several limitations. The cohorts currently available for assessing smoking-attributable mortality were largely established several decades ago. For example, the nationwide prospective cohort reported by Chen et al. included participants born in 1971 or earlier. Therefore, continued follow-up of younger birth cohorts is important for assessing smoking-attributable mortality in populations exposed to more recent patterns of smoking initiation, intensity, and cessation. As these cohorts mature, evidence from birth cohorts born in the 1980s and later will become increasingly important for determining whether the temporal pattern of smoking-attributable mortality observed historically and summarized in the Lopez Four-Stage Model remains applicable under contemporary conditions, including changes in medical care and competing causes of death.

Methodological refinement and epidemiological interpretation are complementary approaches. Future global burden assessments could explicitly incorporate the tobacco epidemic stage into an epidemiological stratification framework. Countries at different stages of the tobacco epidemic can be analyzed within stage-specific strata while applying the same comparative risk assessment framework, allowing estimates to better reflect differences in cumulative exposure histories, epidemic timing, and the evolution of smoking-attributable mortality.

As the global burden estimation continues to evolve,

recognizing the epidemic stage as an essential temporal dimension will improve the interpretation, comparability, and policy relevance of smoking-attributable mortality estimates across populations at different stages of the tobacco epidemic. Such an approach would strengthen the integration of global modeling with national epidemiological evidence and facilitate a more appropriate application of GBD estimates in tobacco control policies and public health decision-making.

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SUPPLEMENTARY MATERIALS

Brief Overview of the GBD Approach to Estimating Smoking-Attributable Mortality

Estimation of smoking-attributable mortality in GBD is an extension of the classical epidemiological approach for estimating population-attributable risk. In conventional epidemiology, the proportion of diseases attributable to smoking is quantified using the Population Attributable Fraction (PAF), which combines smoking prevalence with the relative risk (*RR*) associated with smoking. The GBD adopts the same epidemiological principle but extends it within a comparative risk assessment (CRA) (1) framework to enable standardized and comparable estimation of attributable burden across countries, years, age groups, sexes, and risk factors.

Within the CRA framework, smoking-attributable mortality is estimated by integrating three principal components: 1) population exposure to smoking, 2) exposure–response relationships (relative risks), and 3) cause-specific mortality. Unlike conventional epidemiological studies, GBD uses a common counterfactual reference, the theoretical minimum risk exposure level (TMREL), for all risk factors, allowing comparisons of attributable burdens across diseases, populations, and time.

GBD 2019 (2) substantially refined smoking exposure assessment. Rather than relying primarily on smoking prevalence, it incorporates cumulative exposure metrics, including daily cigarette equivalents, pack-years, and years since smoking cessation, to better characterize population-level smoking exposure histories. These exposure metrics were then linked with non-linear dose–response functions derived from systematic reviews and Bayesian meta-regression, providing a more comprehensive representation of cumulative smoking-related risks.

Beginning with GBD 2021 (3), the GBD study further refined relative risk estimation by adopting the Burden of Proof Risk Function (BPRF), developed using the MR-BRT (Meta-Regression–Bayesian, Regularized, Trimmed) framework (4). This approach synthesizes evidence from systematic reviews while explicitly accounting for between-study heterogeneity and potential sources of bias. The same relative risk estimates were subsequently adopted in the GBD 2023 without further updating the smoking risk functions.

The BPRF approach extends the conventional meta-analytic estimation of relative risks by incorporating between-study heterogeneity into the uncertainty estimation, accommodating different exposure categories, identifying influential studies, and adjusting for study-level bias. In addition, the GBD introduced a risk–outcome score to summarize the strength and consistency of evidence supporting individual risk–outcome relationships. These approaches provide a more conservative characterization of the uncertainty in smoking-related risk estimates.

More broadly, the principal innovation of the GBD framework lies not in changing the epidemiological principle of attributable risk estimation, but in standardizing exposure assessment, relative risk estimation, counterfactual exposure, and disease definitions within a unified comparative risk assessment framework. Collectively, these methodological advances have substantially strengthened the scientific basis and international comparability of GBD smoking-attributable mortality estimates.

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