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).

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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/m^2 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,

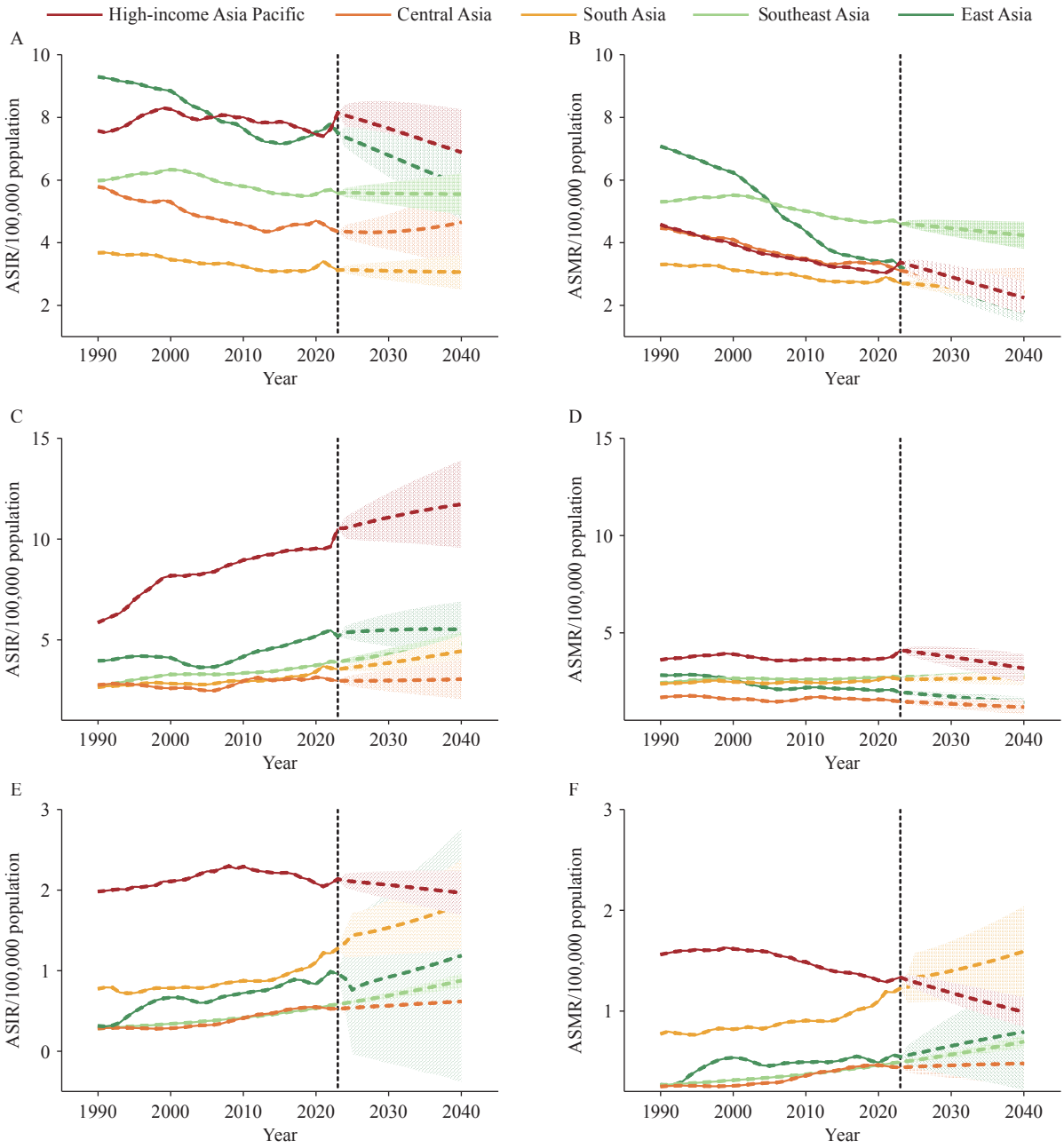


FIGURE 1. Projected trends of HM burden in five Asian subregions from 2024 to 2040. (A) Age-standardized incidence rate (ASIR) of leukemia: (B) Age-standardizedmortality rate (ASMR) of leukemia: (C) ASIR of non-Hodgkin lymphoma: (D) ASMRof non-Hodgkin lymphoma; (E) ASIR of multiple myeloma; (F) ASMR of multiplemyeloma. 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.

Ethics statement: Not applicable.

Conflicts of interest: No conflicts of interest.

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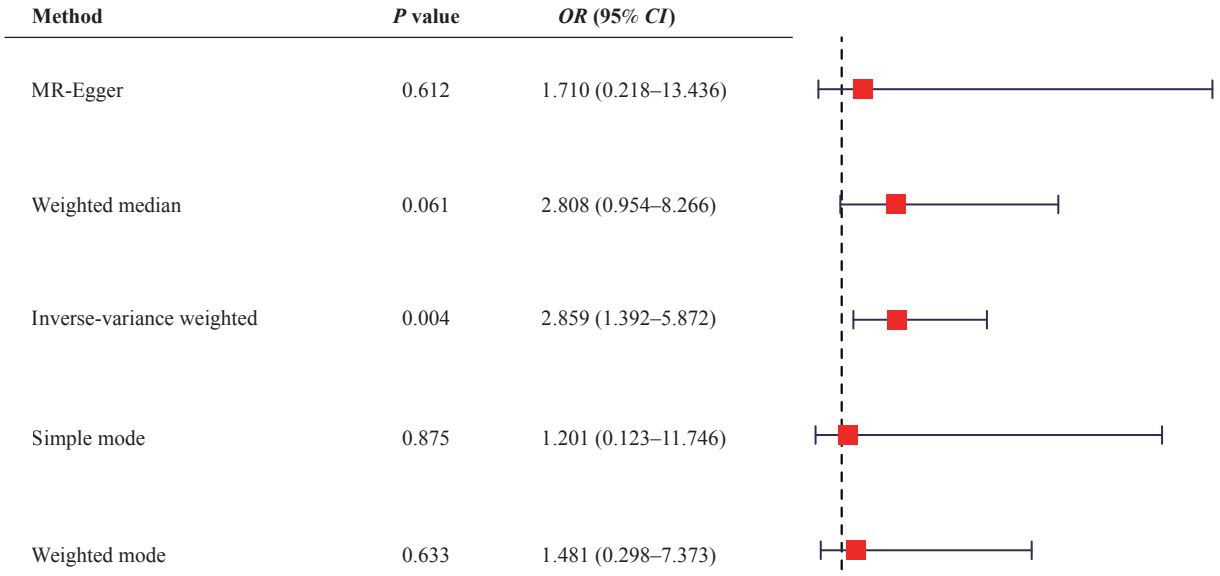


FIGURE 2. Visualization of MR analysis results. MR-Egger, weighted median, inverse-variance weighted, simple mode, and weighted mode methods were used to assess the association between BMI and malignant lymphoma.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval; MR=Mendelian randomization; BMI=body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

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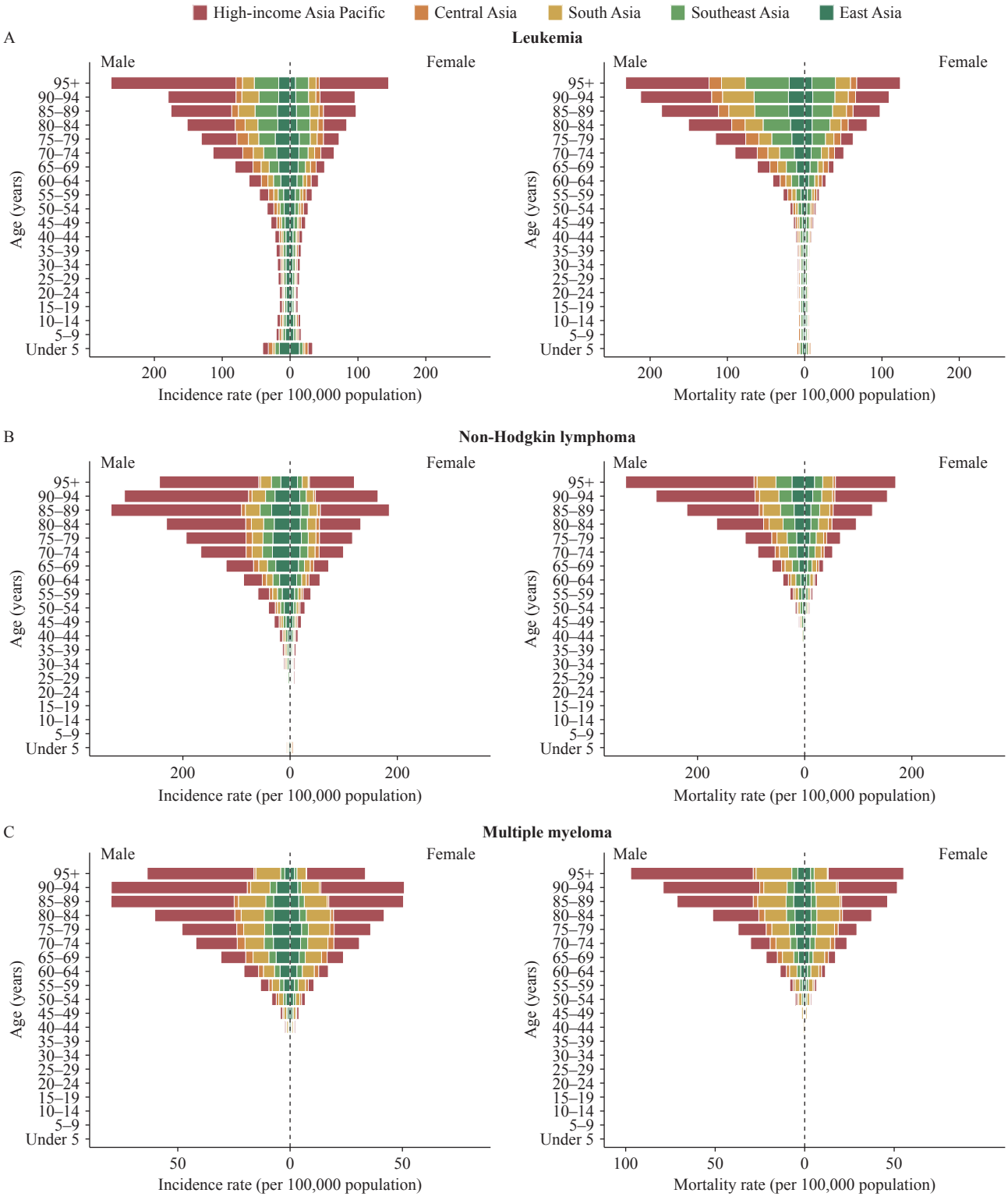
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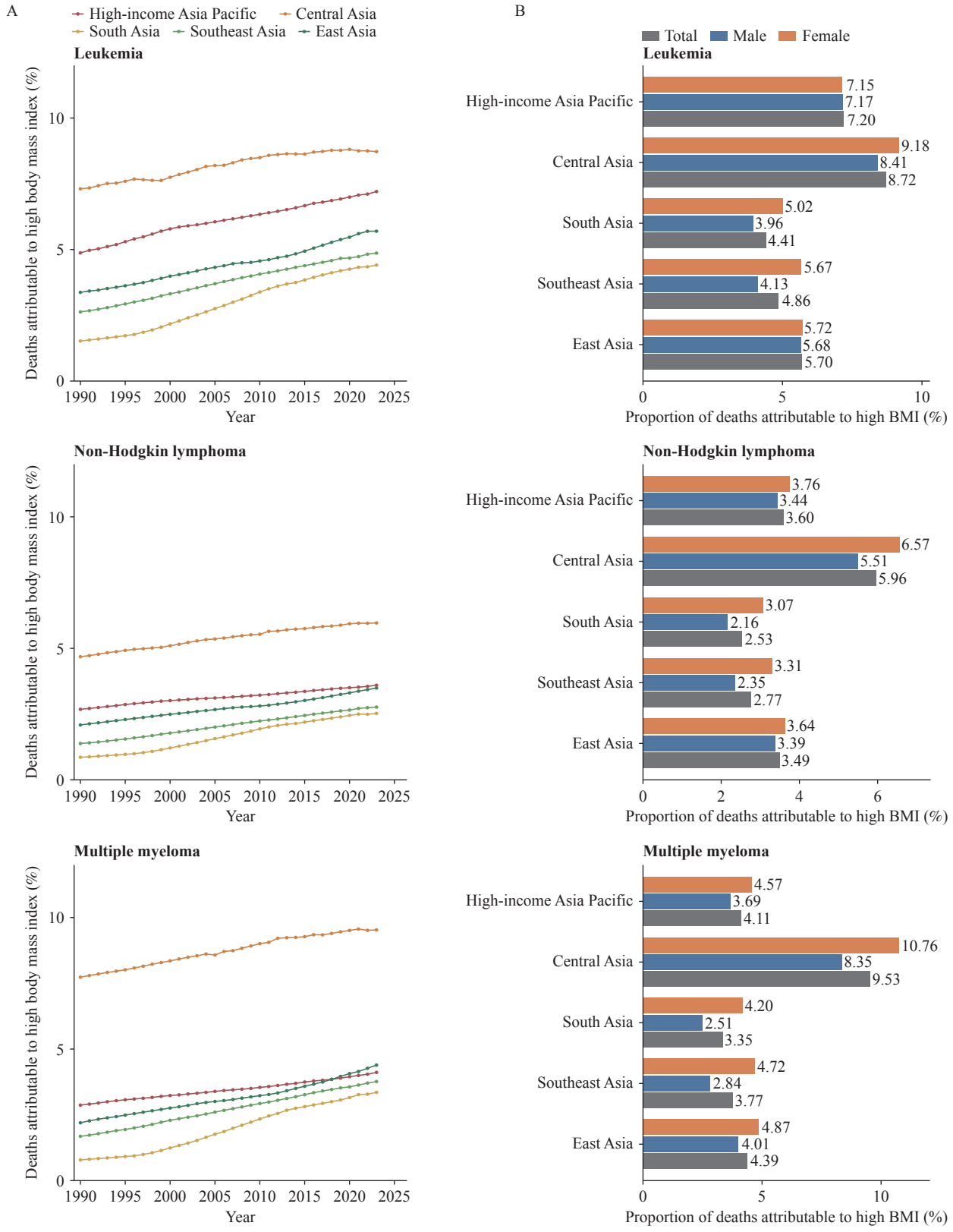
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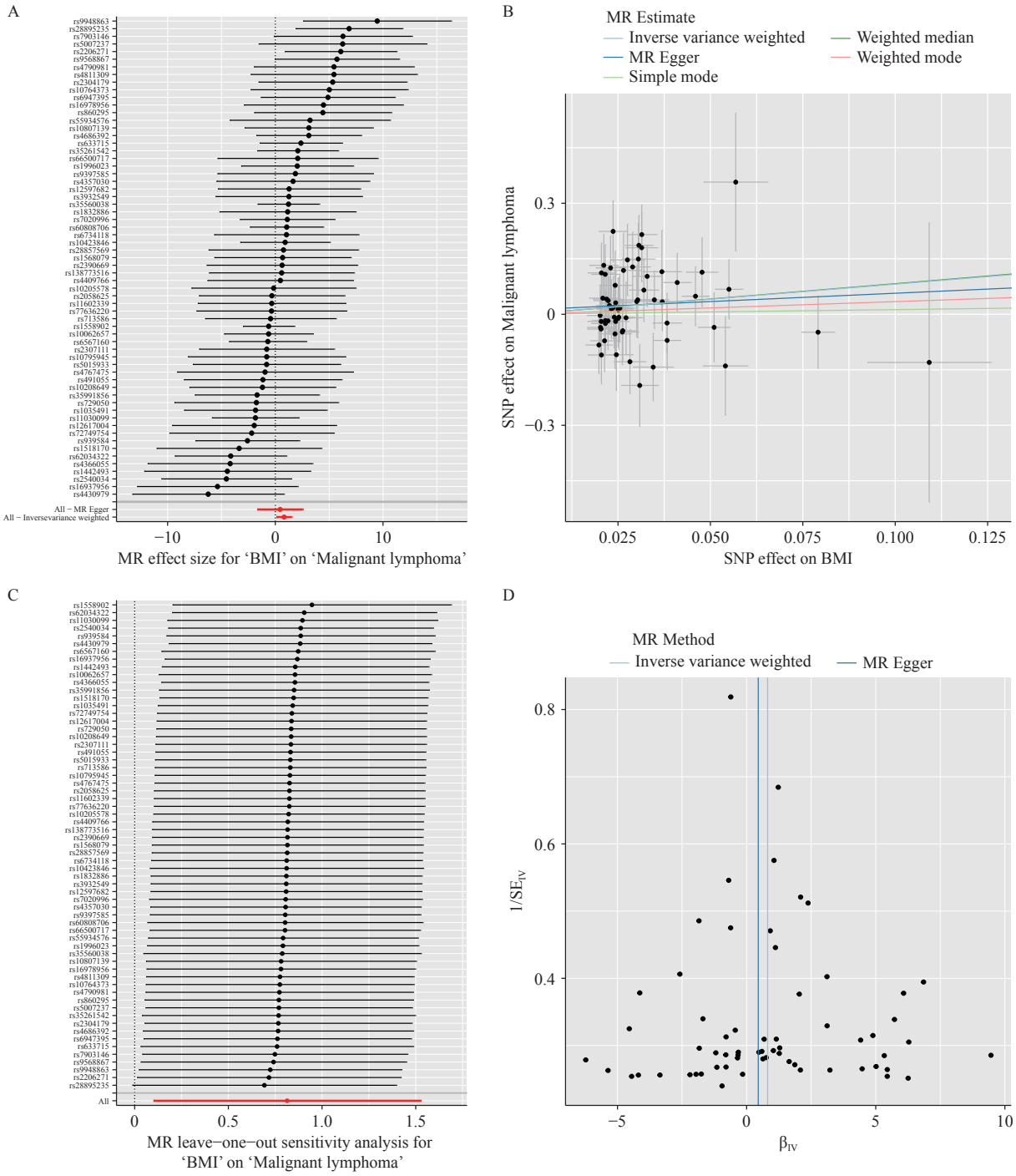
SUPPLEMENTARY MATERIAL



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.