Preplanned Studies

# Stage-Specific Lifestyle Effects on the Dynamic Transitions of Metabolic Multimorbidity — Jiangsu Province, China, 2019–2024

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**Summary**

**What is already known about this topic?**

The prevalence of metabolic multimorbidity is rising in China and has been linked to lifestyle factors; however, evidence characterizing the dynamic transitions across disease states and the stage-specific influence of lifestyle behaviors remains scarce.

**What is added by this report?**

At baseline, the prevalence of metabolic multimorbidity was 24.14%, with males, older adults, and individuals with adverse lifestyle behaviors bearing a disproportionately elevated risk. Hepatic steatosis was associated with a markedly increased risk of progression to multimorbidity, while smoking, high-salt diets, and irregular physical activity each showed differential associations with specific disease transition pathways.

**What are the implications for public health practice?**

Lifestyle behaviors exert meaningful influence at every stage of metabolic disease progression, identifying them as priority targets for stage-specific prevention and control strategies in China.

## ABSTRACT

**Introduction:** Metabolic multimorbidity is rising sharply in China and is closely linked to modifiable lifestyle behaviors; however, the dynamic transitions between metabolic disease states and the stage-specific effects of lifestyle factors on those transitions remain poorly understood.

**Methods:** We enrolled 9,673 participants from the Health Omics Preventive Examination Program (April 2019 – December 2024), each with at least two follow-up visits (median follow-up: 3.07 years; interquartile range: 1.09 years). A Markov multi-state model was used to evaluate the effects of eight lifestyle factors — smoking, alcohol consumption, physical activity, sleep duration, dietary oil intake, taste preference, and two dietary pattern scores — on transitions between disease states.

**Results:** At baseline, multimorbidity prevalence was 24.14%, with a substantially higher rate in males (40.92%) than in females (9.70%; $P<0.05$). Among single-disease conditions, hepatic steatosis conferred the greatest risk of progressing to multimorbidity. Lifestyle effects were markedly stage-specific: smoking [hazard ratio (HR)=2.44, 95% confidence interval (*CI*): 1.63, 3.65] and a high-salt diet (HR=2.28, 95% *CI*: 1.46, 3.55) significantly accelerated multimorbidity progression, whereas regular physical activity (HR=0.58, 95% *CI*: 0.40, 0.84) substantially reduced the risk of transitioning from single-disease to multimorbidity. These associations varied meaningfully by age and sex.

**Conclusion:** Lifestyle behaviors exhibit stage-specific associations with metabolic disease transitions, with the magnitude and direction of these effects differing by sex and age. These findings underscore the critical importance of implementing early, targeted, stage-specific lifestyle interventions to curb the growing burden of metabolic multimorbidity in China.

Metabolic diseases (MD) — including type 2 diabetes (T2D) and hypertension — share common pathophysiological mechanisms (*1*). In China, the prevalence of MD has risen steadily and frequently progresses to metabolic multimorbidity (MM; the coexistence of two or more metabolic diseases) (*2*), a condition associated with substantially higher risks of impaired physical function, cardiovascular events, and all-cause mortality (*3*).

Because metabolic diseases are largely preventable, a substantial body of research has examined associations between modifiable lifestyle factors and disease incidence (*4*). Traditional analytical frameworks, however, have concentrated on the onset of individual

diseases, overlooking the dynamic "healthy–single disease–multimorbidity" trajectory and failing to distinguish the stage-specific effects of lifestyle factors across different phases of disease progression (5–6).

To address this gap, the present study applied a Markov multi-state model (MSM) to evaluate associations between eight lifestyle factors — smoking, alcohol consumption, physical activity, sleep duration, dietary oil intake, taste preference, and two dietary pattern scores — and both the incidence of five single metabolic diseases (SMD; hypertension, T2D, dyslipidemia, hepatic steatosis, and hyperuricemia) and the subsequent development of MM among Chinese adults. Obesity was excluded from the SMD framework because it frequently co-occurs with hepatic steatosis, which more accurately reflects central or visceral adiposity (7). By capturing the full disease progression continuum, this analysis aims to provide a comprehensive understanding of how lifestyle behaviors drive SMD onset and accelerate progression to MM, thereby informing chronic disease prevention strategies in the Chinese population.

This study drew on data from the Health Omics Preventive Examination (HOPE) Program (Supplementary Material, available at https://weekly.chinacdc.cn/), which enrolled 71,010 participants between April 2019 and December 2024 and collected baseline questionnaires alongside biospecimen data. Of these, 14,423 individuals had complete baseline disease data and at least two follow-up assessments. After further excluding those with missing data on more than 2 of the eight lifestyle factors, 9,673 participants remained in the final analytic sample.

Lifestyle factors were assessed via baseline self-reported questionnaires. The five metabolic diseases were identified using a combination of clinical indicators, symptoms, self-reports, and medication use (Supplementary Material). MM was defined as the concurrent presence of two or more of these metabolic diseases. The follow-up period extended from the baseline examination to either the first diagnosis of metabolic multimorbidity or censoring on December 31, 2024. MSM was then applied to evaluate the effects of each lifestyle factor on transitions between metabolic disease states. All statistical analyses were two-sided and conducted using R software (version 4.3.1, R Core Team, Vienna, Austria).

At baseline, the prevalence of T2D, hypertension, dyslipidemia, hyperuricemia, and hepatic steatosis stood at 2.23%, 13.45%, 22.85%, 21.00%, and 26.66%, respectively (Supplementary Figure S1, available at https://weekly.chinacdc.cn/). Males demonstrated significantly higher prevalence across all five metabolic conditions compared with females ($P$<0.05). Hepatic steatosis was the most prevalent condition among males (43.46%), whereas dyslipidemia predominated among females (13.87%). Age-stratified analyses revealed distinct distributional patterns: hyperuricemia was most frequent among participants under 35 years of age (22.73%), while hypertension was most common among those over 55 years (52.74%). The prevalence of all metabolic conditions rose progressively with advancing age ($P$<0.05). Overall multimorbidity (MM) prevalence at baseline was 24.14%, markedly higher in males (40.92%) than in females (9.70%; $P$<0.05). Hepatic steatosis–related combinations represented the most common MM patterns both overall and within sex-specific strata (Supplementary Figure S1).

Table 1 summarizes the baseline sociodemographic, lifestyle, and clinical characteristics of the study population, stratified by baseline disease status. The three groups differed significantly in age, sex, education level, and lifestyle behaviors ($P$<0.05). Both median age and the proportion of male participants increased progressively from the MD-free group through the SMD group to the MM group. Unhealthy lifestyle behaviors — including smoking, alcohol consumption, physical inactivity, high dietary oil intake, and a high-salt diet — followed the same ascending pattern across these groups.

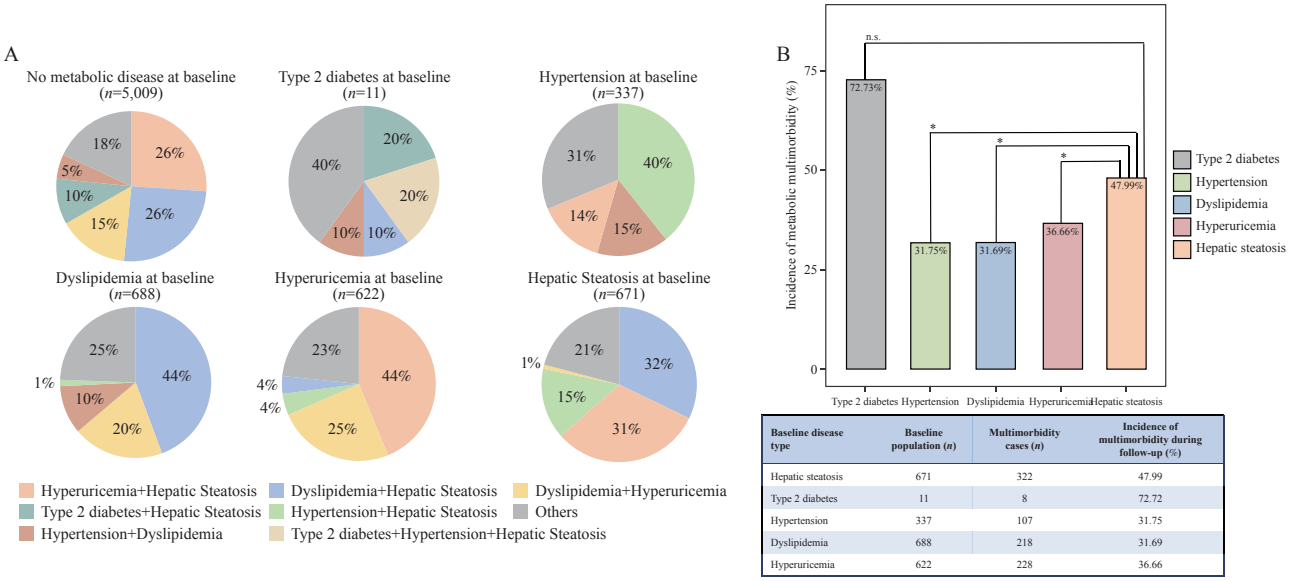
Over a median follow-up of 3.49 years [interquartile range (IQR): 2.25–5.12 years], 1,244 incident MM cases emerged, representing 16.95% of the study population. Males accounted for a disproportionate share, with 832 cases (31.47%) compared with 412 among females (8.78%; $P$<0.05), and incidence rose steadily with advancing age. Figure 1 illustrates the predominant patterns of incident MM, revealing that hepatic steatosis-related MM combinations ranked consistently as the most common, irrespective of participants' baseline disease status — whether MD-free or presenting with SMD. Among those with baseline hepatic steatosis, the MM incidence reached 47.99%, significantly exceeding rates associated with hypertension, dyslipidemia, or hyperuricemia ($P$<0.05). Although type 2 diabetes appeared to carry an even higher incidence, that estimate rested on a small sample and lacked statistical stability. Taken together, these findings position hepatic steatosis as a potentially pivotal driver in the development of MM.

To characterize disease progression, transitions

TABLE 1. Baseline characteristics of participants by metabolic disease status.

| Baseline characteristics | Total *N*=9,673 | No diseases *N*=5,009 | Single disease *N*=2,329 | Comorbidity *N*=2,335 | *P* |
|---|---|---|---|---|---|
| Sociodemographic factors | | | | | |
| Age (years) | 35.43 (30.43, 42.02) | 34.14 (29.63, 39.73) | 36.20 (30.68, 43.63) | 38.35 (32.17, 49.00) | <0.05 |
| Sex, *n* (%) | | | | | <0.05 |
| Male | 4,475 (46.26) | 1,326 (26.47) | 1,318 (56.59) | 1,831 (78.42) | |
| Female | 5,198 (53.74) | 3,683 (73.53) | 1,011 (43.41) | 504 (21.58) | |
| Educational level, *n* (%) | | | | | <0.05 |
| Below college | 338 (3.49) | 79 (1.58) | 99 (4.25) | 160 (6.86) | |
| College or above | 9,333 (96.51) | 4,929 (98.42) | 2,230 (95.75) | 2,174 (93.14) | |
| Lifestyle behavior factors | | | | | |
| Smoking status, *n* (%) | | | | | <0.05 |
| Never smoking | 8,346 (86.50) | 4,712 (94.24) | 1,959 (84.37) | 1,675 (72.01) | |
| <20 pack-years | 1,089 (11.29) | 260 (5.20) | 329 (14.17) | 500 (21.50) | |
| ≥20 pack-years | 213 (2.21) | 28 (0.56) | 34 (1.46) | 151 (6.49) | |
| Alcohol consumption, *n* (%) | | | | | <0.05 |
| Never drinking | 8,339 (86.37) | 4,610 (92.22) | 1,952 (84.03) | 1,777 (76.17) | |
| Moderate drinking (men <60 g/day, women <50 g/day) | 1,289 (13.35) | 385 (7.70) | 365 (15.71) | 539 (23.10) | |
| Heavy drinking (men ≥60 g/day, women ≥50 g/day) | 27 (0.28) | 4 (0.08) | 6 (0.26) | 17 (0.73) | |
| Regular physical activity, *n* (%) | | | | | <0.05 |
| No | 6,155 (63.68) | 3,329 (66.54) | 1,372 (58.93) | 1,454 (62.30) | |
| Yes | 3,510 (36.32) | 1,674 (33.46) | 956 (41.07) | 880 (37.70) | |
| Sleep duration, Median (IQR) | 7.00 (7.00,8.00) | 7.00 (7.00,8.00) | 7.00 (6.50,8.00) | 7.00 (6.50,8.00) | <0.05 |
| Cooking oil consumption, *n* (%) | | | | | <0.05 |
| Low | 2,382 (24.63) | 1,298 (25.92) | 625 (26.84) | 459 (19.66) | |
| Moderate | 6,326 (65.41) | 3,275 (65.40) | 1,469 (63.07) | 1,582 (67.75) | |
| High | 964 (9.96) | 435 (8.68) | 235 (10.09) | 294 (12.59) | |
| Dietary taste preference, *n* (%) | | | | | <0.05 |
| Light | 2,701 (27.93) | 1,489 (29.73) | 681 (29.25) | 531 (22.74) | |
| Moderate | 5,885 (60.85) | 3,057 (61.04) | 1,404 (60.31) | 1,424 (60.99) | |
| Salty | 1,085 (11.22) | 462 (9.23) | 243 (10.44) | 380 (16.27) | |
| Healthy dietary pattern score, Median (IQR) | 0.06 (−0.57, 0.63) | 0.10 (−0.5, 0.65) | 0.08 (−0.55, 0.69) | −0.05 (−0.74, 0.51) | <0.05 |
| High-calorie dietary pattern score, Median (IQR) | −0.16 (−0.78, 0.60) | −0.15 (−0.77, 0.58) | −0.22 (−0.81, 0.61) | −0.12 (−0.75, 0.64) | 0.15 |
| Clinical measurements | | | | | |
| SBP (mmHg), Median (IQR) | 118.00 (109.00, 129.00) | 113.00 (106.00, 122.00) | 121.00 (112.00, 131.00) | 130.00 (119.00, 140.00) | <0.05 |
| DBP (mmHg), Median (IQR) | 74.00 (67.00, 81.00) | 70.00 (65.00, 76.00) | 75.00 (68.00, 82.00) | 81.00 (74.00, 88.00) | <0.05 |
| FPG (mmol/L), Median (IQR) | 4.96 (4.67, 5.27) | 4.87 (4.61, 5.15) | 4.98 (4.69, 5.28) | 5.18 (4.86, 5.64) | <0.05 |
| HbAc1 (%), Median (IQR) | 5.30 (5.10, 5.50) | 5.21 (5.07, 5.40) | 5.30 (5.10, 5.50) | 5.44 (5.21, 5.70) | <0.05 |
| TC (mmol/L), Median (IQR) | 4.86 (4.29, 5.48) | 4.69 (4.18, 5.21) | 5.02 (4.38, 5.74) | 5.14 (4.48, 5.93) | <0.05 |
| TG (mmol/L), Median (IQR) | 1.09 (0.79, 1.58) | 0.88 (0.70, 1.15) | 1.20 (0.89, 1.61) | 1.89 (1.33, 2.65) | <0.05 |
| HDL-C (mmol/L), Median (IQR) | 1.34 (1.15, 1.56) | 1.45 (1.28, 1.65) | 1.30 (1.13, 1.53) | 1.13 (0.99, 1.31) | <0.05 |
| LDL-C (mmol/L), Median (IQR) | 2.93 (2.51, 3.39) | 2.76 (2.40, 3.14) | 3.10 (2.63, 3.61) | 3.22 (2.76, 3.76) | <0.05 |
| SUA (μmol/L), Median (IQR) | 322.00 (267.00, 394.00) | 283.00 (244.00, 326.00) | 355.00 (295.30, 406.00) | 424.00 (364.00, 473.00) | <0.05 |
| Prevalence of hepatic steatosis, *n* (%) | 2,577 (26.64) | – | 671 (28.81) | 1,906 (81.63) | <0.05 |

Note: Continuous variables are presented as median (IQR), and categorical variables as number (percentage). Differences among groups were assessed using the Kruskal–Wallis test for continuous variables and the chi-square ($\chi^2$) test for categorical variables.
Abbreviation: SBP=systolic blood pressure; DBP=diastolic blood pressure; FPG=fasting plasma glucose; HbA1c=glycated hemoglobin; TC=total cholesterol; TG=triglycerides; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; SUA= serum uric acid; IQR=interquartile range.




| Baseline disease type | Baseline population (*n*) | Multimorbidity cases (*n*) | Incidence of multimorbidity during follow-up (%) |
|---|---|---|---|
| Hepatic steatosis | 671 | 322 | 47.99 |
| Type 2 diabetes | 11 | 8 | 72.72 |
| Hypertension | 337 | 107 | 31.75 |
| Dyslipidemia | 688 | 218 | 31.69 |
| Hyperuricemia | 622 | 228 | 36.66 |

FIGURE 1. Patterns and comparisons of metabolic multimorbidity during follow-up. (A) Key metabolic multimorbidity patterns during follow-up by baseline metabolic disease status. (B) Incidence of metabolic multimorbidity by baseline single metabolic disease type.
Note: In panel A, comorbidity combinations were first identified within each baseline disease group, and the most frequent patterns were consolidated into a unified set of seven combinations displayed across all pie charts. Less frequent combinations are grouped as "Others".

across three states — MD-free, SMD, and MM — were tracked in 7,338 participants who were free of MM at baseline. The incidence rates for the MD-free–to–SMD and SMD-to–MM transitions were 97.27 and 137.03 per 1,000 person-years, respectively (Supplementary Figure S2, available at https://weekly.chinacdc.cn/). Recognizing well-established sex- and age-related differences in lifestyle behaviors and metabolic multimorbidity, we conducted sex- and age-stratified multi-state models (Figure 2 and Supplementary Table S1, available at https://weekly.chinacdc.cn/). In males, both smoking [hazard ratio (HR)=2.44, 95% confidence interval (*CI*): 1.63, 3.65] and a high-salt diet (HR=2.28, 95% *CI*: 1.46, 3.55) significantly elevated the risk of progressing directly from MD-free to MM. Among females, a high-oil diet showed a nominally significant association with increased MM risk (HR=1.76, 95% *CI*: 1.05, 2.96); conversely, regular physical activity (HR=0.58, 95% *CI*: 0.40, 0.84) and healthy dietary patterns (HR=0.83, 95% *CI*: 0.71, 0.98) were each nominally associated with a reduced risk of progression from SMD to MM. Age-stratified analyses revealed that among participants younger than 40 years, smoking (HR=2.04, 95% *CI*: 1.27, 3.30) and a high-salt diet (HR=1.74, 95% *CI*: 1.08, 2.80) accelerated the MD-free–to–MM transition, while regular physical activity offered nominal protection against SMD-to-MM progression (HR=0.77, 95% *CI*: 0.61, 0.97). In participants aged 40 years or older, the hazard estimates for both smoking (HR=3.16, 95% *CI*: 1.52, 6.55) and a high-salt diet (HR=2.27, 95% *CI*: 1.18, 4.36) were markedly stronger than those observed in the younger stratum. Additionally, alcohol consumption (HR=1.89, 95% *CI*: 1.29, 2.78) independently heightened the risk of SMD onset in this older group, and a high-oil diet (HR=1.78, 95% *CI*: 1.14, 2.77) further increased the likelihood of advancing from SMD to MM.

## DISCUSSION

Drawing on data from the HOPE cohort, this study characterized metabolic comorbidity patterns in Chinese adults, mapped disease transitions across three states, and evaluated the influence of lifestyle behaviors on those transitions. At baseline, the prevalence of five MDs and MM was higher in males than in females, and the prevalence of each MD rose with age ($P$<0.05). Hepatic steatosis-related comorbidity patterns were the most prevalent in the study population. Notably, individuals with hepatic steatosis faced a substantially elevated risk of developing metabolic comorbidity — a finding consistent with prior evidence underscoring the

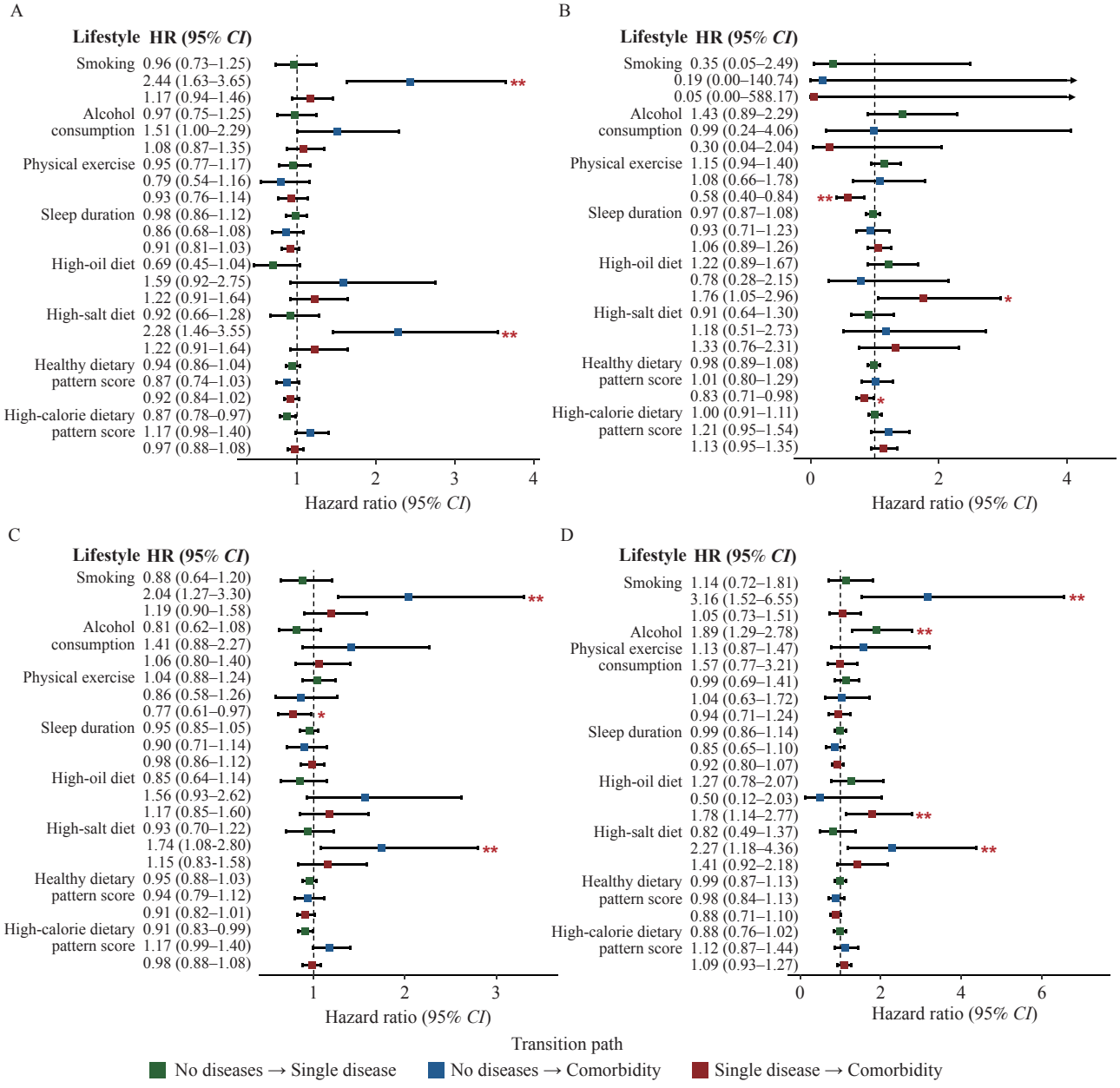



FIGURE 2. Effects of lifestyle factors on different disease transition pathways. (A) Males; (B) Females; (C) Age<40 years; (D) Age≥40 years.
Note: Forest plots present hazard ratios (HRs) and 95% confidence intervals (*CI*s) derived from multistate model analyses. Models were adjusted for education level and physical examination center.
Abbreviations: HR=hazard ratio; *CI*=confidence interval; No diseases=no metabolic diseases; Single disease=single metabolic disease; Comorbidity=metabolic multimorbidity.
* indicates *P*<0.05; ** indicates *P*_FDR<0.05.

central role of hepatic metabolic dysfunction in driving insulin resistance (*8*), which itself has been identified as a key pathological mechanism of metabolic syndrome (*9*). Taken together, these observations suggest that hepatic steatosis may serve as an early sentinel of metabolic disease progression and could help clinicians identify populations at heightened risk of metabolic multimorbidity before it fully develops.

Sex-specific differences in the associations between lifestyle factors and metabolic multimorbidity progression likely reflect, at least in part, genuine differences in lifestyle behaviors between men and women. Among the present findings, smoking was strongly associated with a higher risk of progression from SMD to MM in males, yet no comparable association emerged in females — an asymmetry

almost certainly attributable to the stark disparity in smoking prevalence between the two groups (24.32% in males versus 0.51% in females).

Prior research has demonstrated that lifestyle interventions combining healthy dietary patterns with regular moderate-intensity physical activity can reduce the prevalence of metabolic syndrome (*10*). Those studies, however, focused on the onset of individual metabolic diseases and did not account for dynamic disease progression. To address this gap, the present study employed a multi-state model to examine disease transitions over time, revealing that progression was not strictly unidirectional and, importantly, that stage-specific intervention opportunities exist. Regular physical activity and healthier dietary patterns were both associated with a lower risk of progression from SMD to MM among females, suggesting that interventions targeting these behaviors may be especially effective for women. Furthermore, a preference for high-salt diets was associated with an increased risk of progression from SMD to MM among males, and this association held consistently across both younger (<40 years) and older (≥40 years) age groups.

This study has several limitations that warrant acknowledgment. First, all lifestyle data were self-reported, introducing the potential for reporting bias. Second, restricting the analysis to participants with at least two follow-up visits may have introduced selection bias, although key baseline characteristics remained similar to those of the overall cohort. Residual confounding from unmeasured cardiometabolic family history cannot be fully excluded. Finally, the relatively short follow-up period may have constrained the observation of long-term disease trajectories and could have preferentially captured more rapid patterns of disease progression.

In sum, adopting healthier lifestyle behaviors holds meaningful potential for preventing or delaying the progression of metabolic multimorbidity. Individuals with hepatic steatosis, in particular, warrant prioritization for targeted lifestyle interventions — a finding that provides practical evidence for stage-specific prevention strategies in the broader effort to control metabolic disease.

**Conflicts of interest**: No conflicts of interest.

**Ethical statement**: The study protocol of the HOPE program was approved by the Institutional Review Board of Nanjing Medical University (Ref: 2023-278).

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# SUPPLEMENTARY MATERIAL

## The Health Omics Preventive Examination (HOPE) Program

The Health Omics Preventive Examination (HOPE) Program is a multicenter prospective cohort study conducted in Jiangsu Province, China, enrolling individuals who undergo routine health examinations (*1*). Between April 2019 and December 2024, 71,010 participants completed baseline questionnaires and provided biospecimen data. The Institutional Review Board of Nanjing Medical University approved the HOPE cohort study protocol (Ref: 2023-278), and all participants provided written informed consent. Of the 14,423 individuals with complete baseline disease data and at least two follow-up assessments, 9,673 met the inclusion criteria for analysis, each having no more than two missing values across the eight lifestyle factors examined.

## Methods

**Definitions of diseases**. This study examined five metabolic diseases: hypertension, type 2 diabetes, dyslipidemia, hepatic steatosis, and hyperuricemia. Clinicians diagnosed each condition through a comprehensive assessment integrating metabolic indicators, clinical manifestations, self-reported medical history, and current medication use (*2*–*5*).

Hypertension: Defined as systolic blood pressure (SBP) ≥140 mmHg, diastolic blood pressure (DBP) ≥90 mmHg, and/or current use of antihypertensive medication;

Type 2 Diabetes: Defined as fasting plasma glucose (FPG) ≥7.0 mmol/L (126 mg/dL), glycated hemoglobin (HbA1c) ≥6.5%, 2-hour plasma glucose during an oral glucose tolerance test (OGTT-2h) ≥11.1 mmol/L (200 mg/dL), and/or current use of insulin or antidiabetic medication;

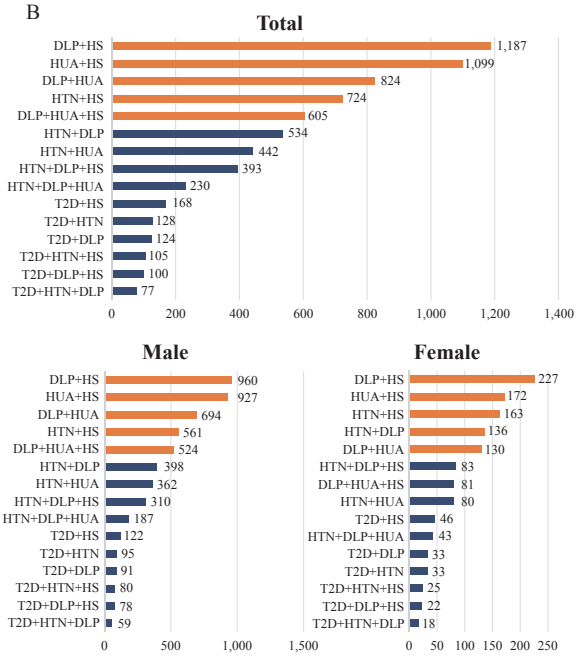
Dyslipidemia: Defined as total cholesterol (TC) ≥6.2 mmol/L, triglycerides (TG) ≥2.3 mmol/L, low-density lipoprotein cholesterol (LDL-C) ≥4.1 mmol/L, high-density lipoprotein cholesterol (HDL-C) <1.0 mmol/L, and/or current use of lipid-lowering medication;

A

| | Total population | Stratified by sex | | |
|---|---|---|---|---|
| | | Male | Female | *P* |
| *N* | 9,673 | 4,475 | 5,198 | |
| Metabolic disease | | | | |
| Type 2 diabetes | 215 (2.23) | 149 (3.33) | 66 (1.27) | <0.05 |
| Hypertension | 1,298 (13.45) | 901 (20.13) | 397 (7.64) | <0.05 |
| Dyslipidemia | 2,207 (22.85) | 1,486 (33.21) | 721 (13.87) | <0.05 |
| Hyperuricemia | 2,028 (21.00) | 1,589 (35.51) | 439 (8.45) | <0.05 |
| Hepatic steatosis | 2,577 (26.66) | 1,945 (43.46) | 632 (12.16) | <0.05 |
| Metabolic comorbidity | 2,335 (24.14) | 1,831 (40.92) | 504 (9.70) | <0.05 |

| | Stratified by age group | | | | |
|---|---|---|---|---|---|
| | <35 | (35,45] | (45,55] | >55 | *P* |
| *N* | 4,642 | 3,195 | 1,161 | 675 | |
| Metabolic disease | | | | | |
| Type 2 diabetes | 21 (0.45) | 48 (1.50) | 53 (4.57) | 93 (13.78) | <0.05 |
| Hypertension | 294 (6.33) | 357 (11.17) | 291 (25.06) | 356 (52.74) | <0.05 |
| Dyslipidemia | 816 (17.58) | 736 (23.04) | 354 (30.49) | 301 (44.59) | <0.05 |
| Hyperuricemia | 1,055 (22.73) | 607 (19.00) | 219 (18.86) | 147 (21.78) | <0.05 |
| Hepatic steatosis | 1,014 (21.84) | 861 (26.95) | 402 (34.63) | 300 (44.44) | <0.05 |
| Metabolic comorbidity | 869 (18.72) | 721 (22.57) | 373 (32.13) | 372 (55.11) | <0.05 |

B




SUPPLEMENTARY FIGURE S1. Baseline prevalence and comorbidity patterns of metabolic diseases by sex and age group. (A) Prevalence of metabolic diseases at baseline by sex and age group. (B) Baseline patterns of metabolic comorbidities in the overall population and by sex.

Note: Data are presented as number (percentage). Differences between sex and age groups were assessed using the chi-square ($\chi^2$) test.

Abbreviation: HTN=Hypertension; T2D=Type 2 diabetes; DLP=Dyslipidemia; HS=Hepatic steatosis; HUA=Hyperuricemia.

Hyperuricemia: Defined as serum uric acid ≥420 μmol/L in men or ≥360 μmol/L in women, and/or current use of uric acid–lowering medication;

Hepatic steatosis: Diagnosed based on imaging findings from ultrasonography or computed tomography.

Definitions of Lifestyle Variables

Smoking status: Current or former smokers were defined as participants who currently smoke or previously smoked and have quit; never smokers were defined as participants who never smoked.

Alcohol consumption: Alcohol consumption was defined based on self-reported questionnaire data. Participants were classified as alcohol consumers if they reported drinking at least once per month or had a history of alcohol use; non-consumers were defined as those who reported never, rarely, or only occasional drinking on special occasions.

Regular physical activity: Participants reporting consistent exercise were classified as engaging in regular physical activity, whereas those reporting occasional or no exercise were classified as not regularly physically active.

Sleep duration: Participants self-reported the average number of hours they sleep per day (hours).

High-oil diet: Participants reporting "low" or "moderate" oil intake preference were classified as "non-high-oil diet"; those reporting "high" oil intake preference were classified as "high-oil diet".

High-salt diet: Participants reporting "light" or "moderate" salt intake preference were classified as "non-high-salt diet"; those reporting "salty" preference were classified as "high-salt diet".

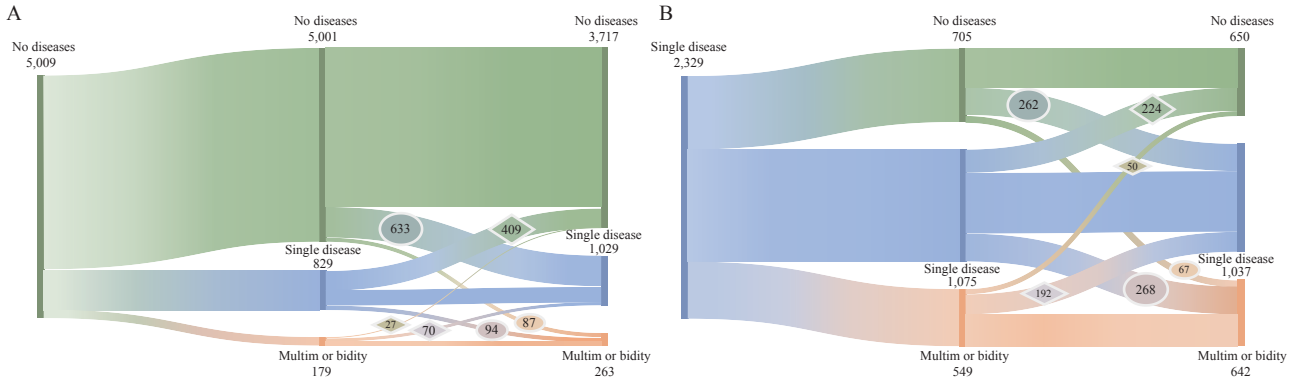
Definition of dietary pattern scores: Dietary patterns were derived from dietary questionnaire completed by participants at baseline. The questionnaire asked, "How often do you eat the following foods?" with seven response options: "Never or <1 time/month," "2–3 times/month," "1–2 times/week," "3–4 times/week," "5–6 times/week," "≥1 time/day," and "Prefer not to answer." A total of 20 food items were included in the dietary questionnaire, and each food item was assigned a frequency score ranging from 1 to 6 and treated as a continuous variable. Principal component analysis (PCA) was then conducted to identify the major dietary patterns in the study population. Two principal components were extracted:

Healthy dietary pattern: Characterized by high consumption of vegetables, fruits, whole grains, and soy products, representing a balanced and nutrient-rich diet;

High-calorie dietary pattern: Characterized by frequent consumption of fried foods, sweets, and sugar-sweetened beverages, representing a diet with higher energy density.

The two principal component scores (RC1 and RC2) derived from the PCA were standardized via z-transformation and subsequently used as individual-level dietary pattern scores in all downstream analyses.

**Markov multi-state model**. We employed a Markov multi-state model to evaluate the stage-specific associations




| | Events (*n*) | Incidence rate (per 1,000 person-years) | Follow-up time (median) |
|---|---|---|---|
| No metabolic diseases→Single metabolic disease | 1,029 | 97.27 (91.41–103.39) | 2.00 |
| No metabolic diseases→Metabolic multimorbidity | 263 | 24.31 (21.46–27.44) | 2.01 |
| Single metabolic diseases →Metabolic multimorbidity | 642 | 137.03 (126.64–148.05) | 1.99 |

SUPPLEMENTARY FIGURE S2. Transitions of metabolic disease status during follow-up. (A) No metabolic diseases at baseline. (B) Single metabolic disease at baseline.

Note: The figure illustrates state transitions occurring during follow-up. Event counts, incidence rates (per 1,000 person-years), and median follow-up time are provided for each transition pathway.

between lifestyle factors and the dynamic progression of metabolic disease. This framework enables simultaneous estimation of transition risks across multiple stages: from a disease-free state to a single metabolic condition, and subsequently to metabolic multimorbidity. The model structure accommodates transitions between all disease states, encompassing forward progression, potential reverse transitions, and direct transitions that bypass intermediate states.

The model operates under the Markov assumption, which holds that future risk depends solely on the current disease state, independent of the time previously spent in earlier states (*6*). To quantify the influence of lifestyle factors on these dynamics, we modelled the transition intensity — defined as the instantaneous risk of moving from state $r$ to state $s$ at time $t$ — using a proportional hazards specification (*7*–*8*):

$$q_{rs}(t|Z) = q_{rs,0}(t)\exp\left(\beta_{rs}^{T}Z\right)$$

where $q_{rs,0}(t)$ denotes the baseline hazard for the specific transition $r \to s$, $Z$ denotes the vector of lifestyle factors, and $\beta_{rs}$ is the corresponding vector of transition-specific regression coefficients.

SUPPLEMENTARY TABLE S1. Distribution of eight lifestyle factors by sex among study participants.

| Lifestyle factors | Male | Female | *P* |
|---|---|---|---|
| | *n*=2,644 | *n*=4,694 | |
| Smoking status, *n* (%) | | | <0.05 |
| Never smoking | 2,001 (75.68) | 4,670 (99.49) | |
| Current/former smoker | 643 (24.32) | 24 (0.51) | |
| Alcohol consumption, *n* (%) | | | <0.05 |
| Never drinking | 1,994 (75.44) | 4,568 (97.32) | |
| Current/former/occasional drinker | 649 (24.56) | 126 (2.68) | |
| Physical exercise, *n* (%) | | | <0.05 |
| No | 1,425 (53.92) | 3,276 (69.88) | |
| Yes | 1,218 (46.08) | 1,412 (30.12) | |
| Sleep duration, Median (IQR) | 7.00 (7.00, 8.00) | 7.00 (7.00, 8.00) | 0.07 |
| High-oil diet, *n* (%) | | | <0.05 |
| No | 2,368 (89.56) | 4,299 (91.60) | |
| Yes | 276 (10.44) | 394 (8.40) | |
| High-salty diet, *n* (%) | | | <0.05 |
| No | 2,309 (87.36) | 4,322 (92.09) | |
| Yes | 334 (12.64) | 371 (7.91) | |
| Healthy dietary pattern score, Median (IQR) | −0.01 (−0.63, 0.62) | 0.14 (−0.46, 0.67) | <0.05 |
| High-calorie dietary pattern score, Median (IQR) | −0.10 (−0.75,0.67) | −0.20 (−0.80,0.54) | <0.05 |

Note: Continuous variables are presented as median (IQR), and categorical variables as number (percentage). Differences among groups were assessed using the Kruskal–Wallis test for continuous variables and the chi-square ($\chi^2$) test for categorical variables.
Abbreviation: IQR=interquartile range.

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