

Supplementary Information

Metabolic Obesity Phenotypes and Their Transitions as Determinants of Multimorbidity Trajectories: Evidence from Global Aging Cohorts

Running title: Metabolic obesity phenotypes and multimorbidity trajectory

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Brief introduction to the five cohorts

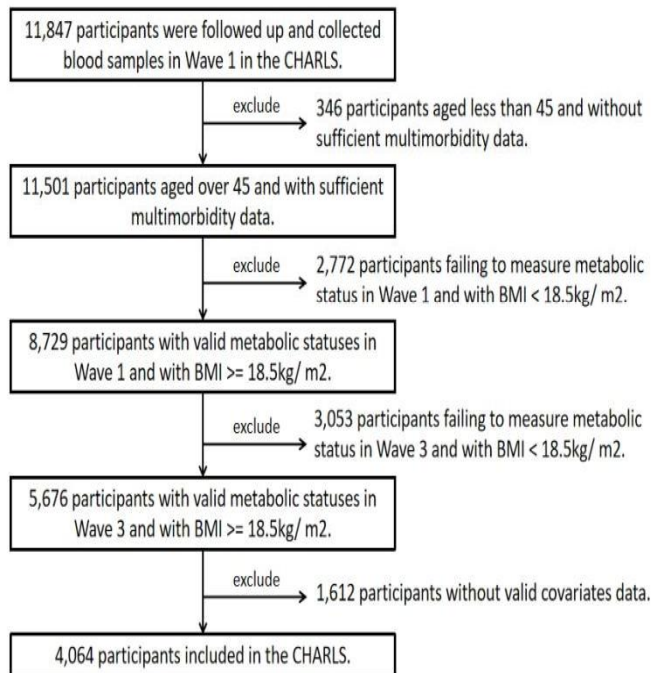
CHARLS: The purpose of the China Health and Retirement Longitudinal Study (CHARLS) is to collect a set of high-quality microdata representing families and individuals of middle-aged and elderly people aged 45 years and older in China, so as to analyze the aging problem of the Chinese population and promote interdisciplinary research on the aging problem. The survey covers 150 county-level units, 450 village-level units, and about 17,000 people in 10,000 families. The survey included basic demographic information of respondents and their families, transfer payments between family members, respondents' health status, medical care and insurance, employment, income, expenditure, and assets. CHARLS respondents are followed every 2 years, using a face-to-face computer-assisted personal interview (CAPI). Physical measurements are made at every 2-year follow-up, and blood sample collection is done once in every two follow-up periods. To ensure the adoption of best practices and international comparability of results, CHARLS was harmonized with leading international research studies in the Health and Retirement Study (HRS) model. CHARLS related data can be downloaded at the CHARLS home page at <https://charls.pku.edu.cn/>.

ELSA: The English Longitudinal Study of Ageing (ELSA) is a prospective cohort study involving the health, social, welfare and economic environmental dynamics of the UK population aged 50 years and older. The study commenced in 2002, and the sample has been followed up every 2 years. Data are collected using computer-assisted personal interviews and self-completion questionnaires, with additional nurse visits for the assessment of biomarkers every 4 years. ELSA is harmonized with ageing studies in other countries to facilitate international comparisons, and is linked to financial and health registry data. For more information about ELSA, visit <http://www.elsa-project.ac.uk/>.

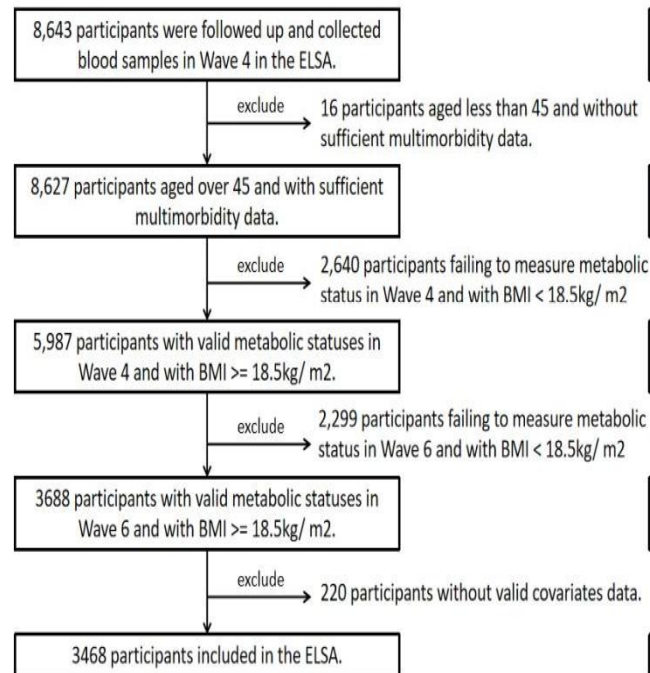
HRS: Health and Retirement Study (HRS, <https://hrs.isr.umich.edu/>), a nationally representative longitudinal study of older adults that included detailed economic and health information, surveyed a representative sample of approximately 20,000 people in the United States. The survey, which has been fielded every 2 years since 1992, was established to provide a national resource for data on the changing health and economic circumstances associated with ageing at both individual and population levels. Its multidisciplinary approach is focused on four broad topics-income and wealth; health, cognition and use of healthcare services; work and retirement; and family connections. HRS data are also linked at the individual level to administrative records from Social Security and Medicare, Veteran's Administration, the National Death Index and employer-provided pension plan information. Three categories of data-public, sensitive and restricted-can be accessed through procedures described on the HRS website <http://hrsonline.isr.umich.edu/>.

Screening process of the study

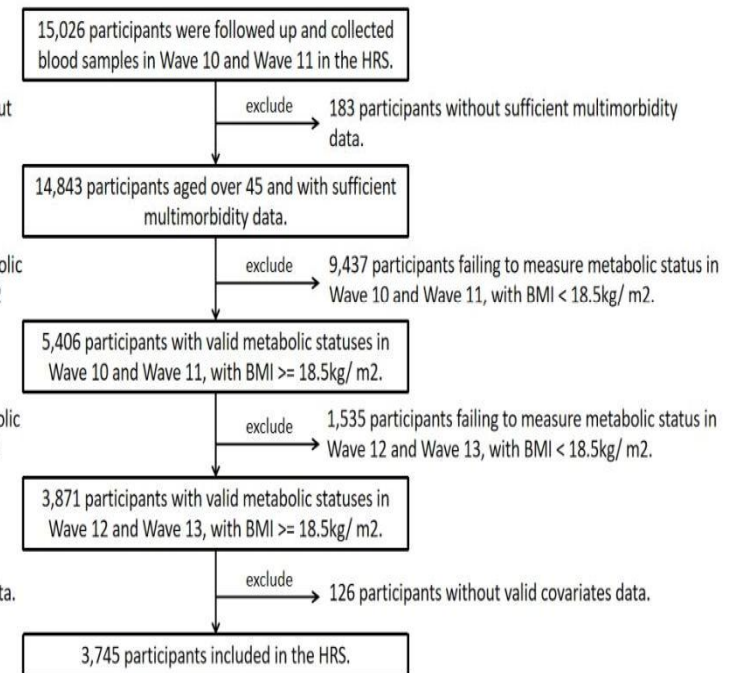
CHARLS



ELSA



HRS



Supplementary Methods Introduction to follow-up time points

For CHARLS, we used data from Wave 1 (2011) to Wave 4 (2018), with Wave 1 as the baseline for collecting data to determine individuals' baseline metabolic obesity status. In Wave 3 (2015), we collected data again to determine the changes in individuals' metabolic obesity status. For ELSA, we used follow-up data from Wave 4 (2008) to Wave 8 (2016), with Wave 4 as the baseline for collecting data to establish individuals' baseline metabolic obesity status. In Wave 6 (2012), we collected data again to determine changes in individuals' metabolic obesity status. For HRS, we used follow-up data from Wave 10 (2010) to Wave 14 (2018), collecting data from Wave 10 (2010) and Wave 11 (2012) to establish individuals' baseline metabolic obesity status, and collected data from Wave 12 (2014) and Wave 13 (2016) to construct the progression of individuals' metabolic obesity status

Supplementary Methods GBTM model introduction and trajectory selection criteria

GBTM is a latent growth model used for analyzing longitudinal data and exploring heterogeneity. Its principle assumes the existence of heterogeneity, that is, there are several potential subgroups in the population with different developmental trajectories or patterns. Its purpose is to explore how many subgroups with different development trends are contained in the population and determine the developmental trajectory of each subgroup. The GBTM model accepts a certain degree of missing data. Identifying the population's multimorbidity trajectory is a gradual iterative process, mainly relying on the assumption of the number of trajectories. When selecting a model, multiple factors need to be considered. In this study, the selection of the trajectory model was based on the following criteria for evaluation: (1) observed improvement in the Bayesian Information Criterion (2) each trajectory group contains at least 5% of the sample size in the cohort (3) the average posterior probability is higher than 70% (4) visual confirmation of the trajectory¹⁵.

Supplementary Table S1 Description of Multimorbidity Diagnosis Data from CHARLS, ELSA, HRS

Doctor Diagnosed Conditions	Description	CHARLS	ELSA	HRS
High blood pressure	High blood pressure variables include variables capturing whether the respondent has ever been diagnosed with high blood pressure (or hypertension)	YES	YES	YES
Diabetes	Diabetes questions include questions capturing whether the respondent has ever been diagnosed with diabetes (or high blood sugar)	YES	YES	YES
Cancer	Cancer questions include questions capturing whether the respondent has ever been diagnosed with cancer (or cancer or a malignant tumor of any kind except skin cancer)	YES	YES	YES
Lung disease	Lung disease questions include questions capturing whether the respondent has ever been diagnosed with chronic lung disease (except asthma) such as chronic bronchitis or emphysema	YES	YES	YES
Heart conditions	Heart conditions questions include questions capturing whether the respondent has ever been diagnosed with either heart attack, coronary heart disease, angina, congestive heart failure or other heart problems	YES	YES	YES
Stroke	Stroke questions include questions capturing whether the respondent has ever been diagnosed with stroke or transient ischemic attack (TIA)	YES	YES	YES

Psychological conditions	Psychological problems questions include questions capturing whether the respondent has ever been diagnosed with emotional, nervous, or psychiatric problems	YES	YES	YES
Arthritis	Arthritis questions include questions capturing whether the respondent has ever been diagnosed with arthritis or rheumatism	YES	YES	YES
Asthma	Asthma questions include questions capturing whether the respondent has ever been diagnosed with asthma	YES	YES	NO
High cholesterol	High cholesterol questions include questions capturing whether the respondent has ever been diagnosed with high cholesterol and whether they have taken medication for it	YES	YES	YES
Liver disease	Liver disease questions include questions capturing whether the respondent has ever been diagnosed with a liver disease	YES	NO	NO
Alzheimer's disease and Dementia	Alzheimer's disease and Dementia questions include questions capturing whether the respondent has ever been diagnosed with Alzheimer's disease and/or Dementia	YES	YES	YES
Parkinson's disease	Parkinson's disease questions include questions capturing whether the respondent has ever been diagnosed with Parkinson's disease	NO	YES	NO
Cataracts	Cataracts questions include questions capturing whether the respondent has ever been diagnosed with cataracts	NO	YES	NO
Osteoporosis	Osteoporosis questions include questions capturing whether the respondent has ever been diagnosed with osteoporosis	NO	YES	YES

Supplementary Table S2 Description of Covariates in CHARLS, ELSA, HRS

Covariates	Description
Age	The age of the individual is calculated using the year of birth and the year at the baseline of the cohort.
Sex	The gender is identified as male or female as reported in the dataset.
Education	According to the International Standard Classification of Education 1997, educational levels were a three-tier variable, including others, below high school, high school, and college and above. Different countries may have different definitions of education levels. We use the information from the harmonized dataset, which has been standardized through the Global Aging Data. This ensures that the education level information is comparable across different countries.
Drink	The level of drink is categorized into 'Yes' (including current drinkers, past drinkers, and those who used to drink but have now quit) and 'No' (those who have never consumed alcohol).
Smoke	Smoke is categorized into 'Yes' (including current smokers, past smokers, and those who used to smoke but have now quit) and No' (those who have never smoked).

hsCRP

hsCRP protein levels are extracted from the cohort blood test results, used to represent the level of chronic inflammation in individual。

SES

SES (Socioeconomic Status) is estimated by dividing the total family wealth into three quartiles within the cohort, divided into Q1: Lower, Q2: Medium, Q3: Higher.

Supplementary Table S3 Missing Data Description in CHARLS, ELSA, HRS Cohort

CHARLS										
Variables	Very low-stable		Low-stable		Low-growth		Middle-stable		High-growth	
	N	frequency	N	frequency	N	frequency	N	frequency	N	frequency
age	11	0.01	4	0.00	3	0.00	14	0.01	3	0.00
sex	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
education	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
SES	463	0.26	531	0.27	411	0.26	526	0.26	323	0.25
drink	3	0.00	4	0.00	3	0.00	1	0.00	1	0.00
smoke	2	0.00	4	0.00	1	0.00	0	0.00	0	0.00
CRP_1	1	0.00	0	0.00	0	0.00	0	0.00	0	0.00
CRP_2	638	0.35	695	0.35	401	0.25	650	0.32	324	0.26
Glu_1	2	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Glu_2	634	0.35	694	0.35	400	0.25	648	0.31	321	0.25
HDL_1	1	0.00	0	0.00	0	0.00	0	0.00	0	0.00
HDL_2	638	0.35	695	0.35	400	0.25	650	0.32	324	0.26
HbA1C_1	14	0.01	15	0.01	11	0.01	11	0.01	5	0.00
HbA1C_2	632	0.35	692	0.35	397	0.25	647	0.31	319	0.25
TC_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
TC_2	638	0.35	695	0.35	400	0.25	650	0.32	324	0.26
TG_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
TG_2	638	0.35	695	0.35	400	0.25	650	0.32	324	0.26

DBP_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
DBP_2	436	0.24	508	0.26	240	0.15	476	0.23	241	0.19
SBP_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
SBP_2	436	0.24	508	0.26	240	0.15	476	0.23	241	0.19
BMI_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
BMI_2	440	0.24	521	0.26	256	0.16	479	0.23	248	0.20
Height_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Height_2	436	0.24	515	0.26	252	0.16	473	0.23	239	0.19
Weight_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Weight_2	437	0.24	511	0.26	249	0.15	465	0.23	242	0.19
Multimorbidity_w1	2	0.00	3	0.00	1	0.00	0	0.00	0	0.00
Multimorbidity_w2	171	0.09	176	0.09	76	0.05	134	0.07	60	0.05
Multimorbidity_w3	223	0.12	225	0.11	59	0.04	224	0.11	84	0.07
Multimorbidity_w4	292	0.16	368	0.19	70	0.04	435	0.21	162	0.13

ELSA										
Variables	Low-stable		Middle-growth		High-stable		High-growth		Very high-stable	
	N	frequency	N	frequency	N	frequency	N	frequency	N	frequency
age	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
sex	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
education	118	0.06	151	0.08	33	0.09	125	0.10	50	0.09
SES	56	0.03	31	0.02	7	0.02	18	0.01	5	0.01

drink	172	0.09	159	0.08	29	0.08	107	0.09	71	0.12
smoke	3	0.00	3	0.00	1	0.00	1	0.00	0	0.00
CRP_1	0	0.00	1	0.00	0	0.00	0	0.00	0	0.00
CRP_2	634	0.34	617	0.31	144	0.41	385	0.32	257	0.45
Glu_1	609	0.32	658	0.34	159	0.46	510	0.42	319	0.56
Glu_2	1,157	0.61	1,176	0.60	254	0.73	790	0.65	441	0.77
HDL_1	0	0.00	2	0.00	0	0.00	1	0.00	0	0.00
HDL_2	635	0.34	617	0.31	144	0.41	386	0.32	257	0.45
HbA1C_1	14	0.01	18	0.01	3	0.01	13	0.01	4	0.01
HbA1C_2	646	0.34	626	0.32	150	0.43	399	0.33	257	0.45
TC_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
TC_2	634	0.34	617	0.31	144	0.41	386	0.32	256	0.45
TG_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
TG_2	634	0.34	617	0.31	144	0.41	386	0.32	256	0.45
DBP_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
DBP_2	461	0.24	364	0.19	117	0.34	226	0.19	167	0.29
SBP_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
SBP_2	461	0.24	364	0.19	117	0.34	226	0.19	167	0.29
BMI_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
BMI_2	481	0.25	397	0.20	126	0.36	245	0.20	198	0.35
Height_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Height_2	472	0.25	381	0.19	124	0.36	241	0.20	188	0.33

Weight_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Weight_2	473	0.25	384	0.20	122	0.35	225	0.18	183	0.32
Multimorbidity_w4	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Multimorbidity_w5	181	0.10	130	0.07	62	0.18	50	0.04	48	0.08
Multimorbidity_w6	277	0.15	193	0.10	93	0.27	112	0.09	104	0.18
Multimorbidity_w7	380	0.20	337	0.17	149	0.43	226	0.19	177	0.31
Multimorbidity_w8	510	0.27	480	0.24	170	0.49	335	0.28	246	0.43

HRS										
Variables	Very low-stable		Low-growth		Middle-growth		High-growth		Very high-growth	
	N	frequency	N	frequency	N	frequency	N	frequency	N	frequency
Age	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Sex	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Education	1	0.00	0	0.00	0	0.00	0	0.00	0	0.00
SES	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Drink	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Smoke	1	0.00	4	0.00	10	0.01	8	0.01	4	0.01
CRP_1	19	0.02	33	0.03	23	0.02	17	0.01	9	0.02
CRP_2	199	0.22	257	0.21	268	0.18	219	0.17	87	0.17
HDL_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00

HDL_2	240	0.26	315	0.26	355	0.24	298	0.23	122	0.24
HbA1C_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
HbA1C_2	197	0.22	241	0.20	268	0.18	215	0.17	84	0.17
TC_1	10	0.01	4	0.00	15	0.01	10	0.01	3	0.01
TC_2	202	0.22	244	0.20	281	0.19	232	0.18	90	0.18
DBP_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
DBP_2	150	0.16	194	0.16	216	0.15	169	0.13	82	0.16
SBP_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
SBP_2	150	0.16	194	0.16	216	0.15	169	0.13	82	0.16
BMI_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
BMI_2	156	0.17	203	0.16	232	0.16	174	0.14	86	0.17
Height_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Height_2	152	0.17	189	0.15	222	0.15	163	0.13	83	0.17
Weight_1	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Weight_2	154	0.17	200	0.16	227	0.15	170	0.13	82	0.16
Multimorbidity_w10	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Multimorbidity_w11	38	0.04	55	0.04	45	0.03	38	0.03	10	0.02
Multimorbidity_w12	73	0.08	80	0.06	104	0.07	65	0.05	29	0.06
Multimorbidity_w13	98	0.11	145	0.12	163	0.11	123	0.10	49	0.10
Multimorbidity_w14	170	0.19	276	0.22	305	0.21	234	0.18	88	0.18

Note: ‘_1’ represent data from baseline, ‘_2’ represent data from transition survey

SES:Socioeconomic Status, CRP:High-sensitivity CRP, HDL:high-density lipoprotein cholesterol, HbA1C:hemoglobin A1c, TC: total cholesterol, TG:triglycerides, SBP:systolic blood pressure, DBP:diastolic blood pressure, Glu:blood glucose

Supplementary Table S4 CHARLS, ELSA, HRS Cohort Trajectory Model Fitting Parameters

CHARLS										
model	1-avePP	2-avePP	3-avePP	4-avePP	5-avePP	aic	bic	caic	ssbic	hqic
traj_1	0.86730642	0.912380329	0.986352405	0.901707053	0.957026392	88547.02802	88792.38834	88821.38834	88700.22644	88625.1903
traj_2	0.960289146	1	0.911461692	0.930109636		91236.12086	91430.71697	91453.71697	91357.62305	91298.11163
traj_3	0.958424749	0.967739769	0.953648062			93233.89142	93377.72332	93394.72332	93323.69738	93279.71068
traj_4	0.979544898	0.953177018				100947.6233	101040.691	101051.691	101005.733	100977.271
traj_5	0.969792758	1	1	0.918160746	0.935208114	88696.66327	88882.79868	88904.79868	88812.88275	88755.95879
traj_6	0.958156801	1	0.918356877	0.917742184		91378.98881	91522.82072	91539.82072	91468.79478	91424.80807
traj_7	0.961024282	1	0.953590547			95326.42081	95436.40992	95449.40992	95395.09596	95361.45907
traj_8	0.978836126	0.954051575				101037.0326	101113.1789	101122.1789	101084.5769	101061.2898
traj_9	0.946340088	1	1	0.958991155	0.93447385	88974.79415	89135.54746	89154.54746	89075.16553	89026.00392
traj_10	0.958153336	1	0.916271233	0.917476993		91397.00537	91523.91587	91538.91587	91476.24592	91437.43413
traj_11	0.961170384	0.951280077	0.944585453			93198.37218	93291.43988	93302.43988	93256.48192	93228.01994
traj_12	0.978750709	0.953179049				101044.3553	101103.5802	101110.5802	101081.3342	101063.222
ELSA										
model	1-avePP	2-avePP	3-avePP	4-avePP	5-avePP	aic	bic	caic	ssbic	hqic
traj_1	1	0.957255153	0.951458152	0.948898044	0.971429556	78431.36813	78655.65129	78682.65129	78569.84564	78503.33945
traj_2	0.949974621	0.970325162	0.920196263	0.96195481		80567.40445	80750.15369	80772.15369	80680.23798	80626.04775
traj_3	0.971919575	0.965158173	0.963650917			83790.75414	83931.96947	83948.96947	83877.94369	83836.06942
traj_4	0.972395267	0.979316468				94211.81243	94303.18705	94314.18705	94268.22919	94241.13408
traj_5	1	0.956851189	0.952252315	0.948641281	0.971157713	78414.03051	78605.08653	78628.08653	78531.99283	78475.33941
traj_6	0.950031549	0.968808731	0.919518301	0.961708794		80573.62619	80731.45508	80750.45508	80671.07333	80624.27268
traj_7	0.971584963	0.965672119	0.963628565			83791.85757	83899.84576	83912.84576	83858.53193	83826.51043
traj_8	0.972104206	0.979429597				94210.82534	94285.58639	94294.58639	94256.98451	94234.81578
traj_9	1	0.971494451	0.938772231	0.951032701	0.968158206	78493.38013	78642.90223	78660.90223	78585.69847	78541.36101
traj_10	0.948573575	0.968203762	0.921812228	0.959869239		80646.67752	80771.27928	80786.27928	80723.60947	80686.66159
traj_11	0.972522423	0.961182561	0.964774261			83891.8653	83983.23992	83994.23992	83948.28207	83921.18695
traj_12	0.971558664	0.98008435				94252.72966	94310.87714	94317.87714	94288.63123	94271.38889
HRS										

model	1-avePP	2-avePP	3-avePP	4-avePP	5-avePP	aic	bic	caic	ssbic	hqic
traj_1	0.932610351	0.960080298	0.918246394	0.972321821	0.93265635	72949.48965	73179.22132	73207.22132	73090.23788	73023.56917
traj_2	0.948128515	0.963531744	0.939680511	0.963160089		75328.43733	75508.94078	75530.94078	75439.02523	75386.64267
traj_3	0.954554149	0.963757452	0.975626491			78521.35051	78660.83046	78677.83046	78606.8048	78566.32737
traj_4	0.974556108	0.96384901				88064.02098	88154.27271	88165.27271	88119.31493	88093.12365
traj_5	0.930617479	0.954465919	0.933567421	0.972204457	0.919082771	73232.44621	73429.35907	73453.35907	73353.08756	73295.94294
traj_6	0.93664658	0.959590824	0.953225567	0.96310571		75563.05499	75718.94434	75737.94434	75658.56273	75613.32324
traj_7	0.95804618	0.958540795	0.971924665			78695.12182	78809.98766	78823.98766	78765.49594	78732.16158
traj_8	0.97497231	0.963655483				88152.30765	88226.14997	88235.14997	88197.54815	88176.11892
traj_9	0.933826515	0.955503102	0.932933257	0.969307835	0.916682795	73690.06347	73845.95282	73864.95282	73785.5712	73740.33172
traj_10	0.938277012	0.959112388	0.953392773	0.959694084		75946.96674	76070.03728	76085.03728	76022.36758	75986.6522
traj_11	0.957663924	0.950046449	0.974195559			79004.76849	79095.02022	79106.02022	79060.06244	79033.87116
traj_12	0.974284278	0.963178628				88335.08568	88392.5186	88399.5186	88370.27274	88353.60556

AvePP: Average Posterior Probabilities, AIC:Akaike information criterion, BIC:Bayesian information criterion, CAIC:consistent Akaike information criterion, SSBIC:sample size adjusted BIC, HQIC:Hannan-Quinn information criterion

Supplementary Table S5 Association between Baseline Metabolic Obesity Phenotypes and Multimorbidity Trajectory using Metabolic Syndrome Definitions

CHARLS					
Variables		Model 1		Model 2	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.64 (0.52 ~ 0.78)	<.001	0.62 (0.50 ~ 0.76)	<.001
	MUNW	0.54 (0.40 ~ 0.74)	<.001	0.51 (0.38 ~ 0.70)	<.001
	MUOO	0.30 (0.24 ~ 0.39)	<.001	0.29 (0.23 ~ 0.37)	<.001
	Low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.74 (0.60 ~ 0.90)	0.003	0.74 (0.61 ~ 0.91)	0.004
	MUNW	0.67 (0.50 ~ 0.89)	0.006	0.67 (0.50 ~ 0.89)	0.007
	MUOO	0.52 (0.42 ~ 0.63)	<.001	0.51 (0.41 ~ 0.63)	<.001
Medium-Risk	Low-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.96 (0.78 ~ 1.18)	0.682	0.97 (0.79 ~ 1.19)	0.767
	MUNW	1.22 (0.93 ~ 1.59)	0.144	1.23 (0.94 ~ 1.60)	0.132
	MUOO	0.94 (0.77 ~ 1.15)	0.542	0.95 (0.78 ~ 1.16)	0.607
	Middle-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	

	MHOO	1.29 (1.05 ~ 1.58)	0.013	1.30 (1.06 ~ 1.59)	0.011
	MUNW	1.63 (1.26 ~ 2.10)	<.001	1.66 (1.28 ~ 2.15)	<.001
	MUOO	1.83 (1.52 ~ 2.21)	<.001	1.87 (1.55 ~ 2.26)	<.001
High-Risk	High-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	2.20 (1.74 ~ 2.79)	<.001	2.25 (1.77 ~ 2.85)	<.001
	MUNW	1.52 (1.10 ~ 2.10)	0.011	1.57 (1.13 ~ 2.18)	0.007
	MUOO	3.43 (2.76 ~ 4.27)	<.001	3.56 (2.86 ~ 4.44)	<.001
	OR: Odds Ratio, CI: Confidence Interval Model1: Adjust: age, sex Model2: Adjust: age, sex, education, drink, smoke, SES, CRP				

ELSA					
Variables		Model 1		Model 2	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.94 (0.78 ~ 1.15)	0.567	0.98 (0.80 ~ 1.19)	0.822
	MUNW	0.21 (0.12 ~ 0.34)	<.001	0.21 (0.13 ~ 0.36)	<.001
	MUOO	0.27 (0.22 ~ 0.34)	<.001	0.30 (0.24 ~ 0.37)	<.001
Medium-Risk	Middle-growth				

	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.08 (0.89 ~ 1.32)	0.411	1.07 (0.88 ~ 1.30)	0.483
	MUNW	1.07 (0.75 ~ 1.52)	0.706	1.09 (0.76 ~ 1.56)	0.631
	MUOO	0.88 (0.72 ~ 1.06)	0.172	0.87 (0.72 ~ 1.06)	0.175
	High-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.62 (0.36 ~ 1.06)	0.082	0.57 (0.33 ~ 0.99)	0.049
	MUNW	2.67 (1.42 ~ 5.04)	0.002	2.45 (1.28 ~ 4.70)	0.007
	MUOO	2.01 (1.31 ~ 3.10)	0.002	2.01 (1.29 ~ 3.13)	0.002
High-Risk	High-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.07 (0.81 ~ 1.40)	0.646	1.08 (0.82 ~ 1.42)	0.603
	MUNW	2.47 (1.66 ~ 3.67)	<.001	2.48 (1.66 ~ 3.70)	<.001
	MUOO	2.41 (1.89 ~ 3.08)	<.001	2.33 (1.81 ~ 3.00)	<.001
	Very high-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.88 (0.50 ~ 1.56)	0.663	0.87 (0.49 ~ 1.55)	0.628
	MUNW	2.51 (1.26 ~ 5.02)	0.009	2.19 (1.08 ~ 4.44)	0.031
	MUOO	4.93 (3.12 ~ 7.77)	<.001	4.23 (2.66 ~ 6.74)	<.001
	OR: Odds Ratio, CI: Confidence Interval				
	Model1: Adjust: age, sex				

	Model2: Adjust: age, sex, education, drink, smoke, SES, CRP
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HRS					
Variables		Model 1		Model 2	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.73 (0.59 ~ 0.92)	0.006	0.80 (0.63 ~ 1.00)	0.052
	MUNW	0.25 (0.11 ~ 0.56)	<.001	0.29 (0.13 ~ 0.66)	0.003
	MUOO	0.12 (0.09 ~ 0.17)	<.001	0.14 (0.11 ~ 0.20)	<.001
	Low-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.16 (0.93 ~ 1.43)	0.183	1.21 (0.98 ~ 1.50)	0.082
	MUNW	0.40 (0.20 ~ 0.76)	0.006	0.43 (0.22 ~ 0.84)	0.013
	MUOO	0.49 (0.39 ~ 0.62)	<.001	0.54 (0.43 ~ 0.68)	<.001
Medium-Risk	Middle-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.23 (0.98 ~ 1.54)	0.073	1.26 (1.01 ~ 1.58)	0.049
	MUNW	0.68 (0.39 ~ 1.19)	0.179	0.70 (0.40 ~ 1.23)	0.213

	MUOO	1.28 (1.03 ~ 1.60)	0.029	1.35 (1.07 ~ 1.69)	0.01
High-Risk	High-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.89 (0.68 ~ 1.17)	0.406	0.85 (0.65 ~ 1.11)	0.229
	MUNW	3.15 (1.97 ~ 5.03)	<.001	2.87 (1.79 ~ 4.62)	<.001
	MUOO	2.97 (2.33 ~ 3.79)	<.001	2.65 (2.07 ~ 3.40)	<.001
	Very high-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.65 (0.41 ~ 1.03)	0.066	0.59 (0.37 ~ 0.95)	0.03
	MUNW	4.30 (2.35 ~ 7.89)	<.001	3.37 (1.81 ~ 6.26)	<.001
	MUOO	3.33 (2.27 ~ 4.89)	<.001	2.72 (1.84 ~ 4.03)	<.001
	OR: Odds Ratio, CI: Confidence Interval Model1: Adjust: age, sex Model2: Adjust: age, sex, education, drink, smoke, SES, CRP				

MHNW:Metabolically Healthy Normal Weight, MHOO:Metabolically Healthy Obesity/Overweight, MUNW:Metabolically Unhealthy Normal Weight, MUOO: Metabolically Unhealthy Obesity/Overweight

Supplementary Table S6 Association of Baseline Metabolic Obesity Phenotypes and Multimorbidity Trajectory in Different SES Subgroups

CHARLS							
Variables		Q1		Q2		Q3	
		OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.65 (0.41 ~ 1.05)	0.078	0.77 (0.52 ~ 1.14)	0.184	0.58 (0.39 ~ 0.86)	0.006
	MUNW	0.71 (0.49 ~ 1.03)	0.068	0.61 (0.42 ~ 0.87)	0.006	0.65 (0.45 ~ 0.92)	0.016
	MUOO	0.26 (0.16 ~ 0.41)	<.001	0.40 (0.28 ~ 0.57)	<.001	0.25 (0.17 ~ 0.36)	<.001
	Low-stable						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.75 (0.48 ~ 1.16)	0.198	0.73 (0.50 ~ 1.09)	0.121	1.00 (0.68 ~ 1.49)	0.982
	MUNW	0.72 (0.50 ~ 1.03)	0.069	0.68 (0.48 ~ 0.96)	0.027	0.90 (0.63 ~ 1.30)	0.573
	MUOO	0.39 (0.27 ~ 0.58)	<.001	0.36 (0.25 ~ 0.52)	<.001	0.78 (0.56 ~ 1.09)	0.142
Medium-Risk	Low-growth						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.99 (0.62 ~ 1.57)	0.952	1.17 (0.78 ~ 1.77)	0.442	0.95 (0.63 ~ 1.44)	0.811
	MUNW	1.14 (0.80 ~ 1.62)	0.481	1.29 (0.90 ~ 1.83)	0.162	0.92 (0.63 ~ 1.35)	0.667
	MUOO	1.08 (0.76 ~ 1.54)	0.662	0.91 (0.65 ~ 1.29)	0.608	0.85 (0.60 ~ 1.20)	0.356
	Middle-stable						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	1.23 (0.81 ~ 1.86)	0.331	1.21 (0.78 ~ 1.89)	0.386	1.36 (0.84 ~ 2.21)	0.206

	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.86 (0.54 ~ 1.37)	0.522	1.04 (0.70 ~ 1.54)	0.838	1.24 (0.89 ~ 1.73)	0.204
	MUNW	1.19 (0.69 ~ 2.05)	0.533	1.30 (0.78 ~ 2.16)	0.311	0.86 (0.54 ~ 1.37)	0.531
	MUOO	0.71 (0.46 ~ 1.09)	0.118	0.92 (0.63 ~ 1.32)	0.643	1.11 (0.79 ~ 1.55)	0.542
	High-stable						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	2.45 (0.28 ~ 21.31)	0.417	0.55 (0.21 ~ 1.42)	0.215	0.54 (0.17 ~ 1.73)	0.298
	MUNW	7.16 (0.86 ~ 60.01)	0.069	1.16 (0.41 ~ 3.27)	0.777	3.92 (1.48 ~ 10.34)	0.006
	MUOO	6.29 (0.84 ~ 46.99)	0.073	1.60 (0.75 ~ 3.40)	0.225	3.07 (1.28 ~ 7.38)	0.012
High-Risk	High-growth						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	1.40 (0.71 ~ 2.74)	0.328	1.61 (0.81 ~ 3.18)	0.172	1.14 (0.68 ~ 1.89)	0.624
	MUNW	2.63 (1.29 ~ 5.34)	0.008	4.33 (2.10 ~ 8.95)	<.001	3.08 (1.76 ~ 5.39)	<.001
	MUOO	3.19 (1.75 ~ 5.81)	<.001	4.60 (2.50 ~ 8.49)	<.001	2.74 (1.72 ~ 4.36)	<.001
	Very high-stable						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.87 (0.33 ~ 2.32)	0.782	1.26 (0.23 ~ 7.04)	0.794	0.73 (0.18 ~ 3.00)	0.661
	MUNW	1.18 (0.42 ~ 3.34)	0.749	6.63 (1.38 ~ 31.97)	0.018	2.03 (0.51 ~ 7.98)	0.312
	MUOO	3.41 (1.51 ~ 7.71)	0.003	9.74 (2.31 ~ 40.97)	0.002	4.25 (1.42 ~ 12.69)	0.009

OR: Odds Ratio, CI: Confidence Interval

Model1: Adjust: age, sex

Model2: Adjust: age, sex, education, drink, smoke, CRP

HRS							
Variables		Q1		Q2		Q3	
		OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.75 (0.45 ~ 1.23)	0.256	0.84 (0.55 ~ 1.30)	0.44	0.34 (0.13 ~ 0.91)	0.032
	MUNW	0.26 (0.09 ~ 0.72)	0.009	0.28 (0.10 ~ 0.78)	0.014	1.61 (0.55 ~ 4.66)	0.383
	MUOO	0.17 (0.10 ~ 0.30)	<.001	0.13 (0.08 ~ 0.22)	<.001	1.83 (0.88 ~ 3.82)	0.105
	Low-growth						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	1.23 (0.76 ~ 2.00)	0.406	1.35 (0.89 ~ 2.06)	0.161	0.95 (0.67 ~ 1.35)	0.766
	MUNW	0.87 (0.41 ~ 1.86)	0.719	0.37 (0.15 ~ 0.94)	0.036	0.42 (0.22 ~ 0.82)	0.011
	MUOO	0.54 (0.33 ~ 0.89)	0.016	0.58 (0.38 ~ 0.89)	0.014	0.58 (0.40 ~ 0.83)	0.003
Medium-Risk	Middle-growth						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	1.07 (0.65 ~ 1.77)	0.788	0.88 (0.56 ~ 1.36)	0.563	1.55 (1.05 ~ 2.30)	0.029

	MUNW	0.72 (0.33 ~ 1.57)	0.416	0.84 (0.41 ~ 1.75)	0.648	1.09 (0.60 ~ 1.98)	0.771
	MUOO	0.95 (0.58 ~ 1.55)	0.841	1.23 (0.81 ~ 1.87)	0.328	2.05 (1.40 ~ 3.02)	<.001
High-Risk	High-growth						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	1.19 (0.65 ~ 2.21)	0.571	1.70 (0.87 ~ 3.33)	0.122	0.79 (0.47 ~ 1.34)	0.386
	MUNW	2.80 (1.30 ~ 6.02)	0.008	7.74 (3.47 ~ 17.26)	<.001	3.04 (1.65 ~ 5.59)	<.001
	MUOO	3.23 (1.81 ~ 5.77)	<.001	6.45 (3.46 ~ 12.02)	<.001	2.84 (1.79 ~ 4.53)	<.001
	Very high-growth						
	MHNW	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	MHOO	0.54 (0.22 ~ 1.32)	0.176	0.34 (0.13 ~ 0.91)	0.032	0.90 (0.26 ~ 3.13)	0.864
	MUNW	2.47 (0.94 ~ 6.47)	0.066	1.61 (0.55 ~ 4.66)	0.383	5.27 (1.61 ~ 17.28)	0.006
	MUOO	2.91 (1.36 ~ 6.22)	0.006	1.83 (0.88 ~ 3.82)	0.105	5.58 (1.96 ~ 15.87)	0.001
OR: Odds Ratio, CI: Confidence Interval							
Model1: Adjust: age, sex							
Model2: Adjust: age, sex, education, drink, smoke, CRP							

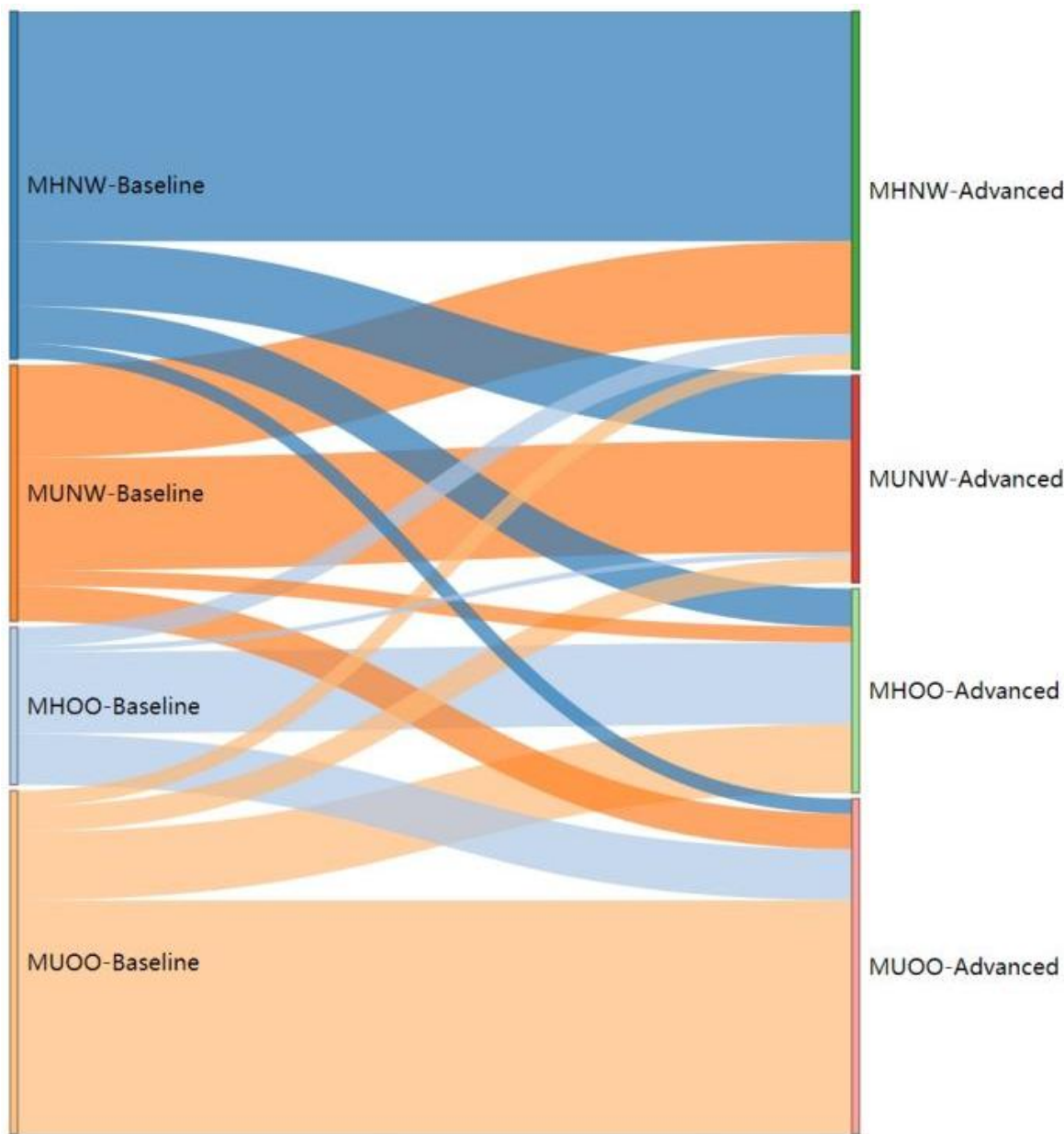
MHNW: Metabolically Healthy Normal Weight, MHOO: Metabolically Healthy Obesity/Overweight, MUNW: Metabolically Unhealthy Normal Weight, MUOO: Metabolically Unhealthy Obesity/Overweight
Q1: lower SES, Q2: medium SES, Q3: higher SES

Supplementary Table S7 Proportion of Individual Metabolic Obesity Transition Described in CHARLS, ELSA, HRS

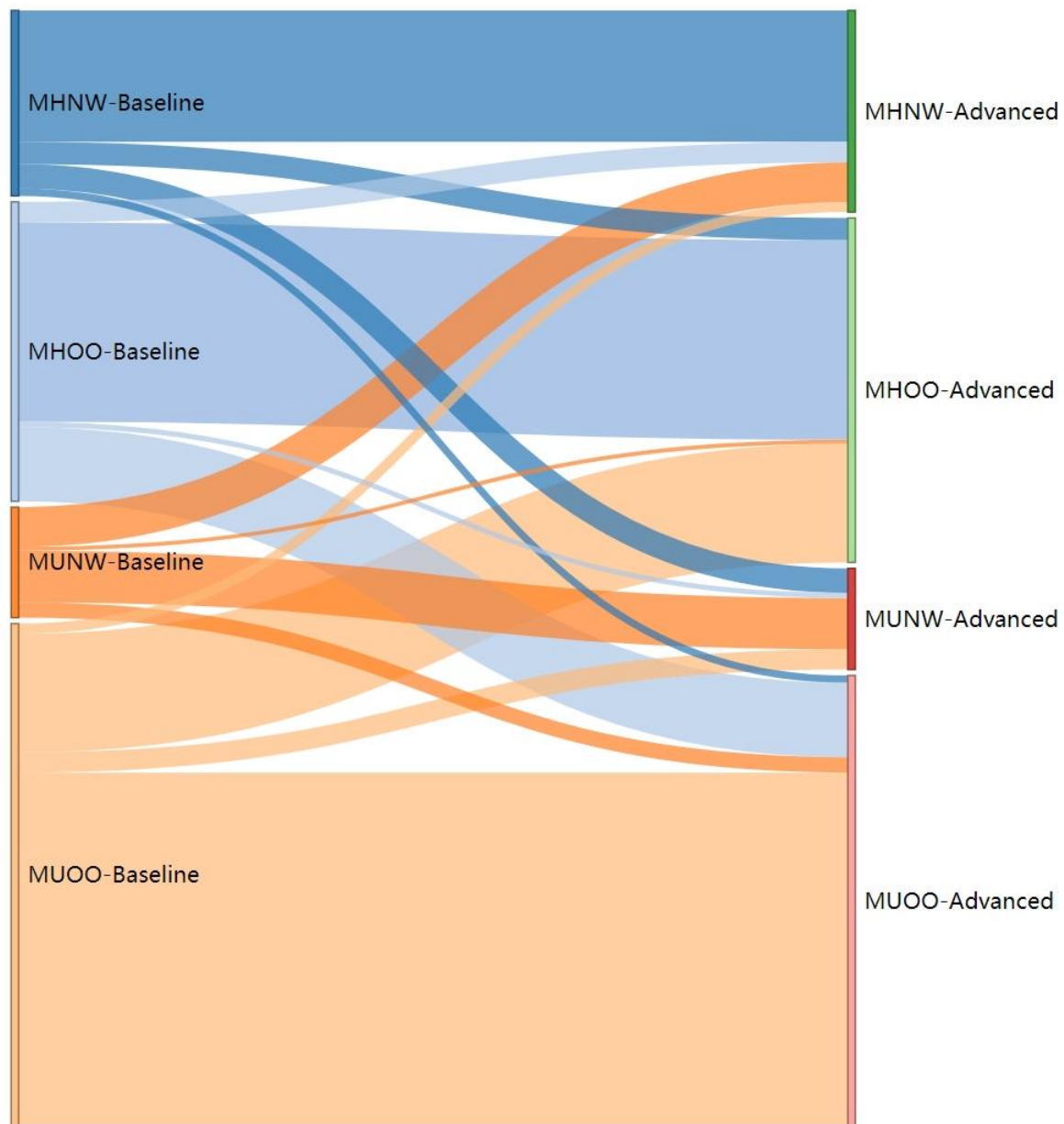
	MHN W-MH NW	MHN W-M HOO	MHN W-MU NW	MHN W-MU OO	MHO O-MH NW	MHO O-MH OO	MHO O-MU NW	MHO O-MU OO	MUN W-MH NW	MUN W-M HOO	MUN W-MU NW	MUN W-M UOO	MUO O-MH NW	MUO O-MH OO	MUO O-MU NW	MUO O-MU OO
CH AR LS	845	140	238	55	71	300	20	188	342	58	412	130	58	253	93	861
EL SA	415	70	78	23	65	630	16	235	125	13	163	49	32	375	64	1116
HR S	345	71	49	20	72	962	11	226	62	14	99	41	24	410	57	1282

MHNW: Metabolically Healthy Normal Weight, MHOO: Metabolically Healthy Obesity/Overweight, MUNW: Metabolically Unhealthy Normal Weight, MUOO: Metabolically Unhealthy Obesity/Overweight

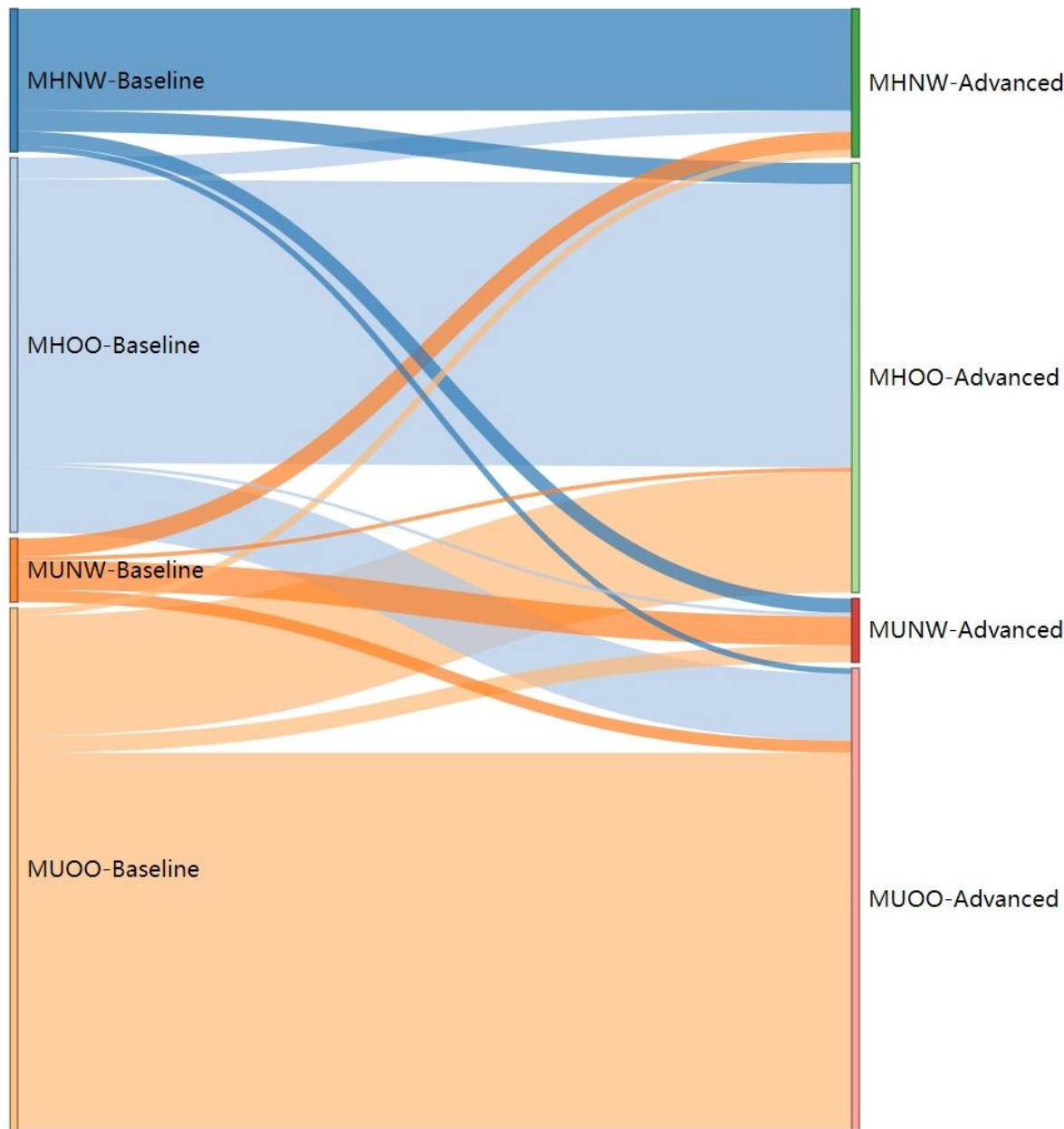
Supplementary Figure S1 Proportion of Individual Metabolic Obesity Transition Described in CHARLS (Sankey Diagram)



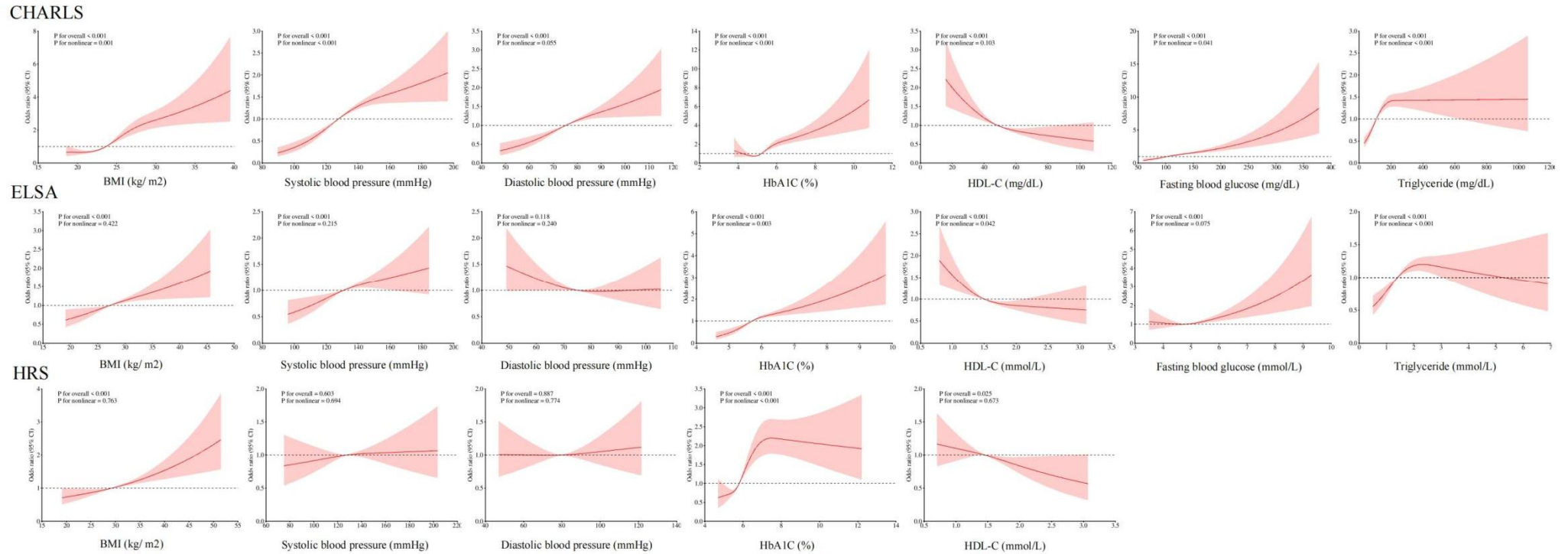
Supplementary Figure S2 Proportion of Individual Metabolic Obesity Transition Described in ELSA (Sankey Diagram)



Supplementary Figure S3 Proportion of Individual Metabolic Obesity Transition Described in HRS (Sankey Diagram)



Supplementary Figure S4 Nonlinear Relationship between Obesity Metabolic Phenotype Components and Multimorbidity Trajectories in the CHARLS, ELSA, and HRS Cohorts



Exposures are the components involved in the determination of obesity metabolic phenotypes at baseline; outcomes are the multimorbidity trajectory groups, in CHARLS as "High-growth" trajectory, in ELSA as "High-growth" trajectory, in HRS as "High-growth" trajectory. Models are adjusted according to baseline age, gender, education level, smoking, drinking, socioeconomic status (SES), and hsCRP levels. The number of nodes is selected according to the Bayesian Information Criterion (BIC), the red solid line represents the estimated nonlinear relationship curve, and light red represents the 95% confidence interval. The P-values for the Overall relationship and nonlinear relationship were calculated.

Supplementary Table S8 Subgroup Analysis Stratified by Age

CHARLS					
Variables		Age ≤ 60		Age > 60	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.67 (0.51 ~ 0.88)	0.004	0.77 (0.48 ~ 1.22)	0.263
	MUN W	0.68 (0.53 ~ 0.88)	0.003	0.57 (0.39 ~ 0.81)	0.002
	MUOO	0.30 (0.23 ~ 0.39)	<.00 1	0.30 (0.20 ~ 0.46)	<.00 1
	Low-stable				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.89 (0.68 ~ 1.17)	0.414	0.72 (0.46 ~ 1.13)	0.155
	MUN W	0.83 (0.64 ~ 1.08)	0.163	0.62 (0.44 ~ 0.87)	0.005
	MUOO	0.51 (0.40 ~ 0.66)	<.00 1	0.46 (0.32 ~ 0.65)	<.00 1
Medium-Risk	Low-growth				
	MHN	1.00 (Reference		1.00 (Reference	

ELSA					
Variables		Age ≤ 60		Age > 60	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Low-stable				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.99 (0.72 ~ 1.37)	0.967	0.77 (0.56 ~ 1.04)	0.091
	MUN W	0.28 (0.17 ~ 0.47)	<.00 1	0.24 (0.16 ~ 0.37)	<.00 1
	MUOO	0.29 (0.21 ~ 0.41)	<.00 1	0.22 (0.16 ~ 0.29)	<.00 1
Medium-Risk	Middle-growth				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.99 (0.71 ~ 1.38)	0.942	1.19 (0.88 ~ 1.60)	0.268
	MUN W	1.69 (1.03 ~ 2.78)	0.039	0.95 (0.67 ~ 1.36)	0.797
	MUOO	1.18 (0.84 ~ 1.66)	0.33	0.84 (0.63 ~ 1.10)	0.206
	High-stable				
	MHN	1.00 (Reference		1.00 (Reference	

HRS					
Variables		Age ≤ 60		Age > 60	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.75 (0.55 ~ 1.03)	0.074	0.97 (0.66 ~ 1.43)	0.892
	MUN W	0.54 (0.27 ~ 1.06)	0.075	0.19 (0.09 ~ 0.42)	<.00 1
	MUOO	0.16 (0.11 ~ 0.23)	<.00 1	0.13 (0.08 ~ 0.20)	<.00 1
	Low-growth				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.39 (1.01 ~ 1.90)	0.045	0.95 (0.68 ~ 1.34)	0.79
	MUN W	0.39 (0.17 ~ 0.90)	0.027	0.45 (0.27 ~ 0.76)	0.003
	MUOO	0.88 (0.62 ~ 1.24)	0.457	0.35 (0.25 ~ 0.49)	<.00 1
Medium-Risk	Middle-growth				
	MHN	1.00 (Reference		1.00 (Reference	

	W	)		)	
	MHOO	1.13 (0.84 ~ 1.53)	0.42	0.87 (0.56 ~ 1.35)	0.54
	MUN W	1.21 (0.92 ~ 1.60)	0.172	0.93 (0.68 ~ 1.28)	0.663
	MUOO	0.99 (0.77 ~ 1.27)	0.929	0.84 (0.60 ~ 1.17)	0.298
	Middle-stable				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.20 (0.87 ~ 1.65)	0.259	1.28 (0.84 ~ 1.95)	0.253
	MUN W	1.33 (0.99 ~ 1.78)	0.057	1.77 (1.31 ~ 2.40)	<.00 1
	MUOO	2.19 (1.71 ~ 2.81)	<.00 1	1.62 (1.19 ~ 2.21)	0.002
High-Risk	High-growth				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	2.02 (1.33 ~ 3.08)	<.00 1	1.74 (1.09 ~ 2.79)	0.021
	MUN W	1.70 (1.13 ~ 2.56)	0.011	1.56 (1.08 ~ 2.25)	0.018
	MUOO	4.81 (3.44 ~ 6.71)	<.00 1	3.31 (2.34 ~ 4.69)	<.00 1

	W	)		)	
	MHOO	0.79 (0.26 ~ 2.44)	0.687	0.61 (0.26 ~ 1.41)	0.245
	MUN W	3.11 (0.90 ~ 10.82)	0.074	2.46 (1.16 ~ 5.20)	0.019
	MUOO	3.39 (1.34 ~ 8.58)	0.01	2.12 (1.09 ~ 4.09)	0.026
High-Risk	High-growth				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.77 (0.86 ~ 3.65)	0.12	1.16 (0.78 ~ 1.73)	0.456
	MUN W	5.86 (2.59 ~ 13.27)	<.00 1	2.62 (1.72 ~ 3.97)	<.00 1
	MUOO	6.41 (3.30 ~ 12.46)	<.00 1	2.60 (1.83 ~ 3.69)	<.00 1
	Very high-stable				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.31 (0.05 ~ 1.74)	0.182	1.18 (0.52 ~ 2.68)	0.698
	MUN W	1.30 (0.22 ~ 7.64)	0.771	2.58 (1.15 ~ 5.79)	0.022
	MUOO	5.10 (1.67 ~ 15.56)	0.004	4.88 (2.43 ~ 9.79)	<.00 1

	W	)		)	
	MHOO	1.13 (0.79 ~ 1.63)	0.494	1.24 (0.87 ~ 1.77)	0.23
	MUN W	0.64 (0.28 ~ 1.45)	0.284	0.98 (0.61 ~ 1.57)	0.934
	MUOO	1.66 (1.15 ~ 2.39)	0.007	1.27 (0.91 ~ 1.78)	0.154
High-Risk	High-growth				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.26 (0.71 ~ 2.25)	0.435	0.97 (0.64 ~ 1.48)	0.892
	MUN W	6.92 (3.22 ~ 14.84)	<.00 1	3.21 (2.00 ~ 5.17)	<.00 1
	MUOO	4.84 (2.79 ~ 8.38)	<.00 1	2.99 (2.06 ~ 4.35)	<.00 1
	Very high-growth				
	MHN W	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.50 (0.20 ~ 1.22)	0.127	0.49 (0.23 ~ 1.04)	0.063
	MUN W	3.14 (1.08 ~ 9.17)	0.036	2.56 (1.24 ~ 5.24)	0.011
	MUOO	2.40 (1.10 ~ 5.23)	0.028	2.99 (1.66 ~ 5.41)	<.00 1

OR: Odds Ratio, CI: Confidence Interval	OR: Odds Ratio, CI: Confidence Interval	OR: Odds Ratio, CI: Confidence Interval
Model1: Adjust: gender	Model1: Adjust: gender	Model1: Adjust: gender
Model2: Adjust: gender, education, drink, smoke, SES, hsCRP	Model2: Adjust: gender, education, drink, smoke, SES, hsCRP	Model2: Adjust: gender, education, drink, smoke, SES, hsCRP

Supplementary Table S9 Subgroup Analysis Stratified by Sex

CHARLS					
Variables		female		male	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.67 (0.48 ~ 0.92)	0.015	0.66 (0.46 ~ 0.93)	0.018
	MUNW	0.63 (0.47 ~ 0.86)	0.003	0.67 (0.51 ~ 0.89)	0.006
	MUOO	0.31 (0.23 ~ 0.42)	<.001	0.30 (0.21 ~ 0.41)	<.001
	Low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.89 (0.65 ~ 1.21)	0.454	0.76 (0.53 ~ 1.09)	0.138
	MUNW	0.93 (0.70 ~ 1.24)	0.633	0.60 (0.44 ~ 0.81)	<.001
	MUOO	0.52 (0.39 ~ 0.68)	<.001	0.49 (0.36 ~ 0.66)	<.001
ELSA					
Variables		female		male	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.90 (0.68 ~ 1.20)	0.475	0.78 (0.54 ~ 1.13)	0.193
	MUNW	0.30 (0.19 ~ 0.49)	<.001	0.25 (0.15 ~ 0.41)	<.001
	MUOO	0.26 (0.19 ~ 0.36)	<.001	0.24 (0.17 ~ 0.34)	<.001
Medium-Risk	Middle-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.05 (0.79 ~ 1.38)	0.75	1.25 (0.86 ~ 1.81)	0.239
	MUNW	0.88 (0.61 ~ 1.29)	0.523	1.69 (1.08 ~ 2.65)	0.022
	MUOO	0.85 (0.65 ~ 1.12)	0.244	1.17 (0.83 ~ 1.66)	0.377
HRS					
Variables		female		male	
		OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.89 (0.65 ~ 1.23)	0.486	0.69 (0.47 ~ 1.02)	0.062
	MUNW	0.38 (0.20 ~ 0.73)	0.003	0.27 (0.12 ~ 0.61)	0.002
	MUOO	0.18 (0.12 ~ 0.27)	<.001	0.11 (0.07 ~ 0.18)	<.001
	Low-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.15 (0.85 ~ 1.54)	0.366	1.19 (0.80 ~ 1.77)	0.382
	MUNW	0.58 (0.35 ~ 0.97)	0.039	0.40 (0.18 ~ 0.93)	0.032
	MUOO	0.52 (0.38 ~ 0.71)	<.001	0.63 (0.43 ~ 0.94)	0.024

Medium-Risk	Low-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.16 (0.83 ~ 1.63)	0.385	0.92 (0.64 ~ 1.33)	0.649
	MUNW	1.07 (0.79 ~ 1.46)	0.664	1.14 (0.86 ~ 1.51)	0.371
	MUOO	1.07 (0.81 ~ 1.41)	0.633	0.78 (0.58 ~ 1.05)	0.1
	Middle-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.17 (0.83 ~ 1.65)	0.361	1.30 (0.89 ~ 1.91)	0.181
	MUNW	1.27 (0.94 ~ 1.72)	0.12	1.79 (1.34 ~ 2.39)	<.001
	MUOO	1.66 (1.27 ~ 2.17)	<.001	2.35 (1.77 ~ 3.11)	<.001
High-Risk	High-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.52 (0.98 ~ 2.35)	0.06	2.54 (1.63 ~ 3.94)	<.001
	MUNW	1.60 (1.09 ~ 2.36)	0.017	1.54 (1.04 ~ 2.28)	0.03
	MUOO	3.68 (2.64 ~ 5.13)	<.001	4.41 (3.13 ~ 6.22)	<.001
OR: Odds Ratio, CI: Confidence Interval					
Model1: Adjust: age					
Model2: Adjust: age, education, drink, smoke, SES, hsCRP					

	High-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.69 (0.33 ~ 1.46)	0.336	1.04 (0.20 ~ 5.41)	0.966
	MUNW	2.10 (1.01 ~ 4.40)	0.049	6.04 (1.29 ~ 28.17)	0.022
	MUOO	1.59 (0.85 ~ 2.95)	0.146	7.07 (1.70 ~ 29.37)	0.007
High-Risk	High-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.36 (0.91 ~ 2.04)	0.134	1.43 (0.73 ~ 2.82)	0.297
	MUNW	3.20 (2.05 ~ 5.00)	<.001	3.54 (1.75 ~ 7.18)	<.001
	MUOO	3.11 (2.16 ~ 4.49)	<.001	3.99 (2.16 ~ 7.37)	<.001
	Very high-stable				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.33 (0.57 ~ 3.07)	0.51	0.39 (0.09 ~ 1.63)	0.198
	MUNW	2.90 (1.25 ~ 6.73)	0.013	1.08 (0.28 ~ 4.21)	0.909
	MUOO	5.38 (2.65 ~ 10.94)	<.001	3.48 (1.23 ~ 9.83)	0.019
OR: Odds Ratio, CI: Confidence Interval					
Model1: Adjust: age					
Model2: Adjust: age, education, drink, smoke, SES, hsCRP					

Medium-Risk	Middle-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.24 (0.92 ~ 1.68)	0.155	1.22 (0.76 ~ 1.96)	0.412
	MUNW	0.80 (0.50 ~ 1.27)	0.334	1.33 (0.62 ~ 2.84)	0.461
	MUOO	1.19 (0.89 ~ 1.61)	0.244	1.95 (1.23 ~ 3.08)	0.004
High-Risk	High-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	1.13 (0.77 ~ 1.66)	0.52	1.22 (0.76 ~ 1.96)	0.412
	MUNW	3.30 (2.08 ~ 5.23)	<.001	1.33 (0.62 ~ 2.84)	0.461
	MUOO	3.03 (2.13 ~ 4.31)	<.001	1.95 (1.23 ~ 3.08)	0.004
	Very high-growth				
	MHNW	1.00 (Reference)		1.00 (Reference)	
	MHOO	0.52 (0.27 ~ 0.98)	0.043	1.32 (0.62 ~ 2.82)	0.466
	MUNW	2.20 (1.13 ~ 4.28)	0.02	6.98 (2.89 ~ 16.82)	<.001
	MUOO	2.60 (1.55 ~ 4.38)	<.001	6.43 (3.19 ~ 12.96)	<.001
OR: Odds Ratio, CI: Confidence Interval					
Model1: Adjust: age					
Model2: Adjust: age, education, drink, smoke, SES, hsCRP					

CHARLS						
Variables	Q1		Q2		Q3	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable					
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)
	MH OO	0.65 (0.41 ~ 1.05)	0.0 78	0.77 (0.52 ~ 1.14)	0.1 84	0.58 (0.39 ~ 0.86)
	MU NW	0.71 (0.49 ~ 1.03)	0.0 68	0.61 (0.42 ~ 0.87)	0.0 06	0.65 (0.45 ~ 0.92)
	MU OO	0.26 (0.16 ~ 0.41)	<.0 01	0.40 (0.28 ~ 0.57)	<.0 01	0.25 (0.17 ~ 0.36)
	Low-stable					
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)
	MH OO	0.75 (0.48 ~ 1.16)	0.1 98	0.73 (0.50 ~ 1.09)	0.1 21	1.00 (0.68 ~ 1.49)
	MU NW	0.72 (0.50 ~ 1.03)	0.0 69	0.68 (0.48 ~ 0.96)	0.0 27	0.90 (0.63 ~ 1.30)
	ELSA					
Variables	Q1		Q2		Q3	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Low-stable					
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)
	MH OO	0.91 (0.57 ~ 1.46)	0.6 97	0.94 (0.63 ~ 1.39)	0.7 4	0.79 (0.56 ~ 1.11)
	MU NW	0.27 (0.14 ~ 0.53)	<.0 01	0.20 (0.11 ~ 0.38)	<.0 01	0.36 (0.21 ~ 0.59)
	MU OO	0.22 (0.14 ~ 0.36)	<.0 01	0.26 (0.18 ~ 0.39)	<.0 01	0.28 (0.20 ~ 0.41)
Medium-Risk	Middle-growth					
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)
	MH OO	0.86 (0.54 ~ 1.37)	0.5 22	1.04 (0.70 ~ 1.54)	0.8 38	1.24 (0.89 ~ 1.73)
	MU NW	1.19 (0.69 ~ 2.05)	0.5 33	1.30 (0.78 ~ 2.16)	0.3 11	0.86 (0.54 ~ 1.37)
HRS						
Variables	Q1		Q2		Q3	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Low-Risk	Very low-stable					
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)
	MH OO	0.75 (0.45 ~ 1.23)	0.2 56	0.84 (0.55 ~ 1.30)	0.4 4	0.34 (0.13 ~ 0.91)
	MU NW	0.26 (0.09 ~ 0.72)	0.0 09	0.28 (0.10 ~ 0.78)	0.0 14	1.61 (0.55 ~ 4.66)
	MU OO	0.17 (0.10 ~ 0.30)	<.0 01	0.13 (0.08 ~ 0.22)	<.0 01	1.83 (0.88 ~ 3.82)
	Low-growth					
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)
	MH OO	1.23 (0.76 ~ 2.00)	0.4 06	1.35 (0.89 ~ 2.06)	0.1 61	0.95 (0.67 ~ 1.35)
	MU NW	0.87 (0.41 ~ 1.86)	0.7 19	0.37 (0.15 ~ 0.94)	0.0 36	0.42 (0.22 ~ 0.82)

	MU OO	0.39 (0.27 ~ 0.58)	<.0 01	0.36 (0.25 ~ 0.52)	<.0 01	0.78 (0.56 ~ 1.09)	0.1 42
Medium -Risk	Low-growth						
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)	
	MH OO	0.99 (0.62 ~ 1.57)	0.9 52	1.17 (0.78 ~ 1.77)	0.4 42	0.95 (0.63 ~ 1.44)	0.8 11
	MU NW	1.14 (0.80 ~ 1.62)	0.4 81	1.29 (0.90 ~ 1.83)	0.1 62	0.92 (0.63 ~ 1.35)	0.6 67
	MU OO	1.08 (0.76 ~ 1.54)	0.6 62	0.91 (0.65 ~ 1.29)	0.6 08	0.85 (0.60 ~ 1.20)	0.3 56
	Middle-stable						
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)	
	MH OO	1.23 (0.81 ~ 1.86)	0.3 31	1.21 (0.78 ~ 1.89)	0.3 86	1.36 (0.84 ~ 2.21)	0.2 06
	MU NW	1.33 (0.95 ~ 1.84)	0.0 94	1.54 (1.07 ~ 2.23)	0.0 21	1.76 (1.17 ~ 2.66)	0.0 07
	MU OO	1.68 (1.22 ~ 2.30)	0.0 01	2.25 (1.61 ~ 3.14)	<.0 01	1.98 (1.36 ~ 2.88)	<.0 01
High-Ri sk	High-growth						
	MH	1.00 (Refere		1.00 (Refere		1.00 (Refere	

	MU OO	0.71 (0.46 ~ 1.09)	0.1 18	0.92 (0.63 ~ 1.32)	0.6 43	1.11 (0.79 ~ 1.55)	0.5 42
	High-stable						
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)	
	MH OO	2.45 (0.28 ~ 21.31)	0.4 17	0.55 (0.21 ~ 1.42)	0.2 15	0.54 (0.17 ~ 1.73)	0.2 98
	MU NW	7.16 (0.86 ~ 60.01)	0.0 69	1.16 (0.41 ~ 3.27)	0.7 77	3.92 (1.48 ~ 10.34)	0.0 06
	MU OO	6.29 (0.84 ~ 46.99)	0.0 73	1.60 (0.75 ~ 3.40)	0.2 25	3.07 (1.28 ~ 7.38)	0.0 12
	High-growth						
High-Ri sk	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)	
	MH OO	1.40 (0.71 ~ 2.74)	0.3 28	1.61 (0.81 ~ 3.18)	0.1 72	1.14 (0.68 ~ 1.89)	0.6 24
	MU NW	2.63 (1.29 ~ 5.34)	0.0 08	4.33 (2.10 ~ 8.95)	<.0 01	3.08 (1.76 ~ 5.39)	<.0 01
	MU OO	3.19 (1.75 ~ 5.81)	<.0 01	4.60 (2.50 ~ 8.49)	<.0 01	2.74 (1.72 ~ 4.36)	<.0 01
	Very high-stable						
	MH	1.00 (Refere		1.00 (Refere		1.00 (Refere	

	MU OO	0.54 (0.33 ~ 0.89)	0.0 16	0.58 (0.38 ~ 0.89)	0.0 14	0.58 (0.40 ~ 0.83)	0.0 03
Medium -Risk	Middle-growth						
	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)	
	MH OO	1.07 (0.65 ~ 1.77)	0.7 88	0.88 (0.56 ~ 1.36)	0.5 63	1.55 (1.05 ~ 2.30)	0.0 29
	MU NW	0.72 (0.33 ~ 1.57)	0.4 16	0.84 (0.41 ~ 1.75)	0.6 48	1.09 (0.60 ~ 1.98)	0.7 71
	MU OO	0.95 (0.58 ~ 1.55)	0.8 41	1.23 (0.81 ~ 1.87)	0.3 28	2.05 (1.40 ~ 3.02)	<.0 01
	High-growth						
High-Ri sk	MH NW	1.00 (Refere nce)		1.00 (Refere nce)		1.00 (Refere nce)	
	MH OO	1.19 (0.65 ~ 2.21)	0.5 71	1.70 (0.87 ~ 3.33)	0.1 22	0.79 (0.47 ~ 1.34)	0.3 86
	MU NW	2.80 (1.30 ~ 6.02)	0.0 08	7.74 (3.47 ~ 17.26)	<.0 01	3.04 (1.65 ~ 5.59)	<.0 01
	MU OO	3.23 (1.81 ~ 5.77)	<.0 01	6.45 (3.46 ~ 12.02)	<.0 01	2.84 (1.79 ~ 4.53)	<.0 01
	Very high-growth						
	MH	1.00 (Refere		1.00 (Refere		1.00 (Refere	

