Supplementary Materials

Cumulative metabolic, behavioral, and early-life factors for MASLD in Chinese children with validation in U.S. adolescents

Yunfei Liu[1,2], Di Shi[1,2], Ziyue Chen[1,2], Jiajia Dang[1,2], Shan Cai[1,2], Yaqi Wang[1,2], Jieyu Liu[1,2], Lipo Guo[3], Yuanyuan Li[3], Jieyun Song[1,2], Jing Li[1,2], Yanhui Dong[1,2], Yanchun Cui[4], Yi Song[1,2]

[1]Institute of Child and Adolescent Health, School of Public Health, Peking University, Beijing 100191, China.
[2]National Health Commission Key Laboratory of Reproductive Health, Beijing 100191, China.
[3]Changping Health Education Center for Primary and Secondary Schools, Beijing 100191, China.
[4]Beijing Children's Hospital, Capital Medical University, Beijing 100045, China.

Correspondence to: Prof. Yi Song, Institute of Child and Adolescent Health, School of Public Health, Peking University, Beijing 100191, China. E-mail: songyi@bjmu.edu.cn

Supplementary Table 1. Comparisons among the entire population, population included in cross-sectional analysis, and population included in longitudinal analysis

	Comparation one			Comparation two		
	Entire population	Population included in cross-sectional analysis	P	Entire population	Population included in longitudinal analysis	P
N	1500	597		1500	289	
Sociodemographic and anthropometric factors						
Age at baseline, year*	9.00 [8.00, 10.00]	9.00 [8.00, 10.00]	0.290	9.00 [8.00, 10.00]	9.00 [8.00, 10.00]	0.491
Girls**	750 (50.0)	300 (50.3)	0.956	750 (50.0)	152 (52.6)	0.457
WHtR*	0.43 [0.40, 0.48]	0.42 [0.39, 0.47]	**0.007**	0.43 [0.40, 0.48]	0.42 [0.40, 0.46]	0.084
Nutrition status**			0.098			0.149
Non-overweight/obese	895 (59.8)	386 (64.7)		895 (59.8)	186 (64.4)	
Overweight	237 (15.8)	89 (14.9)		237 (15.8)	48 (16.6)	
Obese	364 (24.3)	122 (20.4)		364 (24.3)	55 (19.0)	
Metabolic factors						
High UA**	193 (14.6)	89 (14.9)	0.925	193 (14.6)	43 (14.9)	0.984
High TG**	196 (14.8)	80 (13.4)	0.447	196 (14.8)	35 (12.1)	0.269

Early life factors						
LBW/PB	82 (15.5)	34 (16.2)	0.912	82 (15.5)	16 (16.8)	0.865
No Breastfeeding**	252 (20.5)	96 (19.6)	0.694	252 (20.5)	34 (15.5)	0.099
Behavioral factors						
Exposure to secondhand smoking**	547 (36.5)	193 (32.3)	0.082	547 (36.5)	101 (34.9)	0.671
Non-optimal PA**	1055 (70.3)	413 (69.2)	0.640	1055 (70.3)	197 (68.2)	0.505
Non-optimal SB**	756 (85.6)	280 (87.2)	0.536	756 (85.6)	143 (83.6)	0.579
Non-optimal Diet**	91 (6.5)	41 (7.4)	0.544	91 (6.5)	24 (9.0)	0.183

Note: *values are median [IQR]; **values are number (%). BMI: Body mass index; WHtR: waist-to-height ratio; UA: uric acid; TG: triglycerides; LWB: low birth weight; PB: preterm birth; PA: physical activity; SB: sedentary behavior; MASLD: metabolic dysfunction-associated steatotic liver disease.

Supplementary Table 2. Basic features for the multivariate imputation

	Cross-sectional			Longitudinal		
	Before	After	*P*	Before	After	*P*
N	597	597		289	289	
Early life factors						
LBW/PB	34 (16.2)	71 (11.9)	0.141	16 (16.8)	40 (13.8)	0.581
No Breastfeeding**	96 (19.6)	108 (18.1)	0.592	34 (15.5)	41 (14.2)	0.784
Behavioral factors						
Exposure to secondhand smoking**	193 (32.3)	193 (32.3)	1.000	101 (34.9)	101 (34.9)	1.000
Non-optimal PA**	413 (69.2)	413 (69.2)	1.000	197 (68.2)	197 (68.2)	1.000
Non-optimal SB**	117 (36.4)	223 (37.4)	0.842	56 (32.7)	99 (34.3)	0.819
Non-optimal Diet**	41 (7.4)	43 (7.2)	0.988	24 (9.0)	26 (9.0)	1.000

Note: *values are number (%). PA: Physical activity; SB: sedentary behavior.

Supplementary Table 3. Basic features of the participants by Sex

	Cross-sectional			Longitudinal		
	Boys	Girls	*P*	Boys	Girls	*P*
N	297	300		137	152	
Sociodemographic and anthropometric factors						
Age at baseline, year*	9.00 [8.00, 10.00]	9.00 [8.00, 10.00]	0.499	9.00 [8.00, 11.00]	9.00 [8.00, 11.50]	0.936
WHtR*	0.43 [0.40, 0.48]	0.41 [0.39, 0.45]	**<0.001**	0.44 [0.40, 0.48]	0.41 [0.39, 0.45]	**<0.001**
Nutrition status**			**0.038**			0.273
Non-overweight/obese	178 (59.9)	208 (69.3)		82 (59.9)	104 (68.4)	
Overweight	47 (15.8)	42 (14.0)		27 (19.7)	21 (13.8)	
Obese	72 (24.2)	50 (16.7)		28 (20.4)	27 (17.8)	
Metabolic factors						
High UA**	65 (21.9)	24 (8.0)	**<0.001**	26 (19.0)	17 (11.2)	0.090
High TG**	36 (12.1)	44 (14.7)	0.428	19 (13.9)	16 (10.5)	0.491
Early life factors						
LBW/PB	14 (15.2)	20 (16.9)	0.881	5 (13.2)	11 (19.3)	0.615
No Breastfeeding**	54 (21.3)	44 (17.2)	0.206	15 (15.0)	19 (15.8)	1.000

Behavioral factors

Exposure to secondhand smoking**	104 (35.0)	89 (29.7)	0.190	51 (37.2)	50 (32.9)	0.517
Non-optimal PA**	193 (65.0)	220 (73.3)	**0.034**	91 (66.4)	106 (69.7)	0.633
Non-optimal SB**	45 (29.0)	72 (43.4)	**0.011**	24 (32.4)	32 (33.0)	1.000
Non-optimal Diet**	26 (9.5)	15 (5.3)	0.086	13 (10.2)	11 (7.9)	0.642
Health outcomes						
MASLD**	22 (7.4)	4 (1.3)	**0.001**	14 (10.2)	8 (5.3)	0.173

Note: *values are median [IQR]; **values are number (%). BMI: Body mass index; WHtR, waist-to-height ratio; UA: uric acid; TG: triglycerides; PA: physical activity; SB: sedentary behavior; MASLD: metabolic dysfunction-associated steatotic liver disease.

Supplementary Table 4. Average of log-likelihood measured errors for different models in the 10-fold cross-validation

Model	Cross-sectional		Longitudinal	
	Independent effect	Cumulative effect	Independent effect	Cumulative effect
Model 1	0.043	0.041	0.067	0.068
Model 2	0.038	0.035	0.045	0.040
Model 3	0.036	0.034	0.049	0.045
Model 4	0.039	0.033	0.050	0.045

Note: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group; model 4, model 3 + control school cluster effect. WHtR: Waist-to-height ratio.

Supplementary Table 5. Average of log-likelihood measured errors for MASLD incidence and persistent MASLD in the 10-fold cross-validation
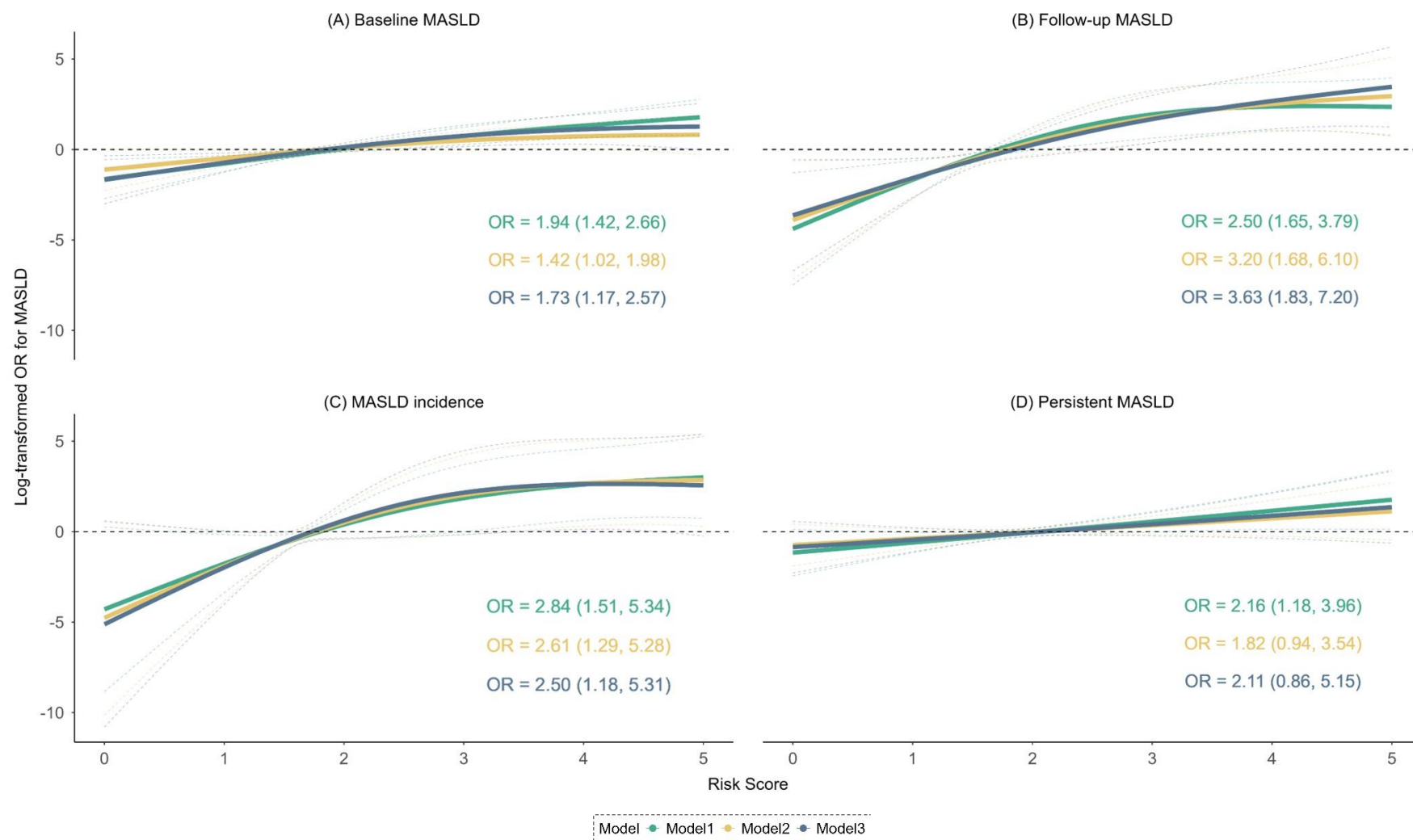
Model	MASLD incidence	Persistent MASLD
Model 1	0.037	0.033
Model 2	0.030	0.029
Model 3	0.036	0.030
Model 4	0.038	0.037

Note: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group; model 4, model 3 + control school cluster effect. WHtR: Waist-to-height ratio.
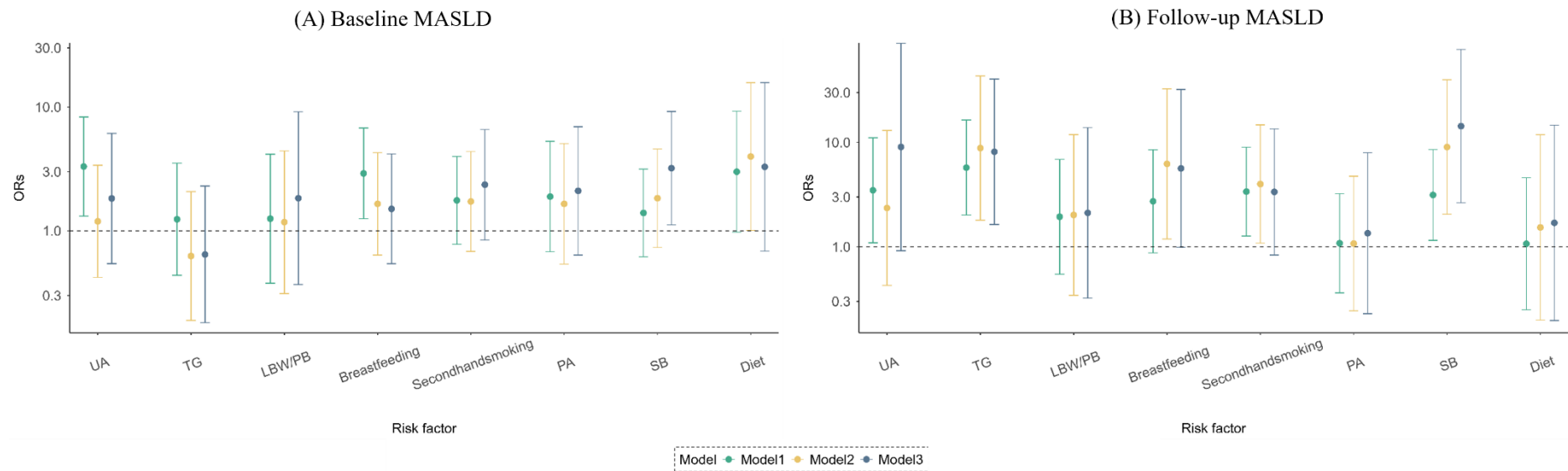
Supplementary Figure 1. Associations between metabolic, behavioral, and early life factors and (A) baseline MASLD and (B) follow-up MASLD in Chinese children, odds ratio (ORs) and 95% confidence interval (CI). Notes: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group. WHtR: Waist-to-height ratio; UA: uric acid; TG: triglycerides; PA: physical activity; SB: sedentary behavior; MASLD: metabolic dysfunction-associated steatotic liver disease. Figure is generated using R 4.2.1.
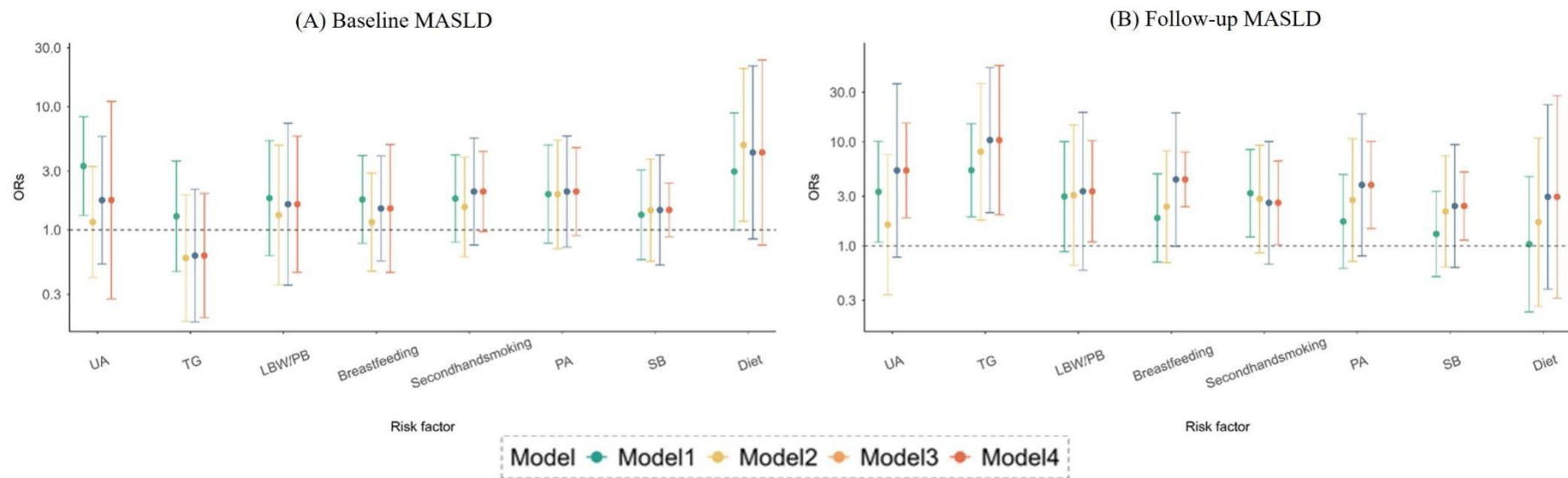
Supplementary Figure 2. Sensitivity analysis for associations between metabolic, behavioral, and early life factors and (A) baseline MASLD and (B) follow-up MASLD in Chinese children, odds ratio (ORs) and 95% confidence interval (CI). Notes: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group; model 4, model 3 + control school cluster effect. WHtR: Waist-to-height ratio; UA: uric acid; TG: triglycerides; PA: physical activity; SB: sedentary behavior; MASLD: Metabolic dysfunction-associated steatotic liver disease. Breastfeeding, PA and SB were reassigned based on the cutoff values of 12 months, 60 minutes and 360 minutes, respectively. Figure is generated using R 4.2.1.
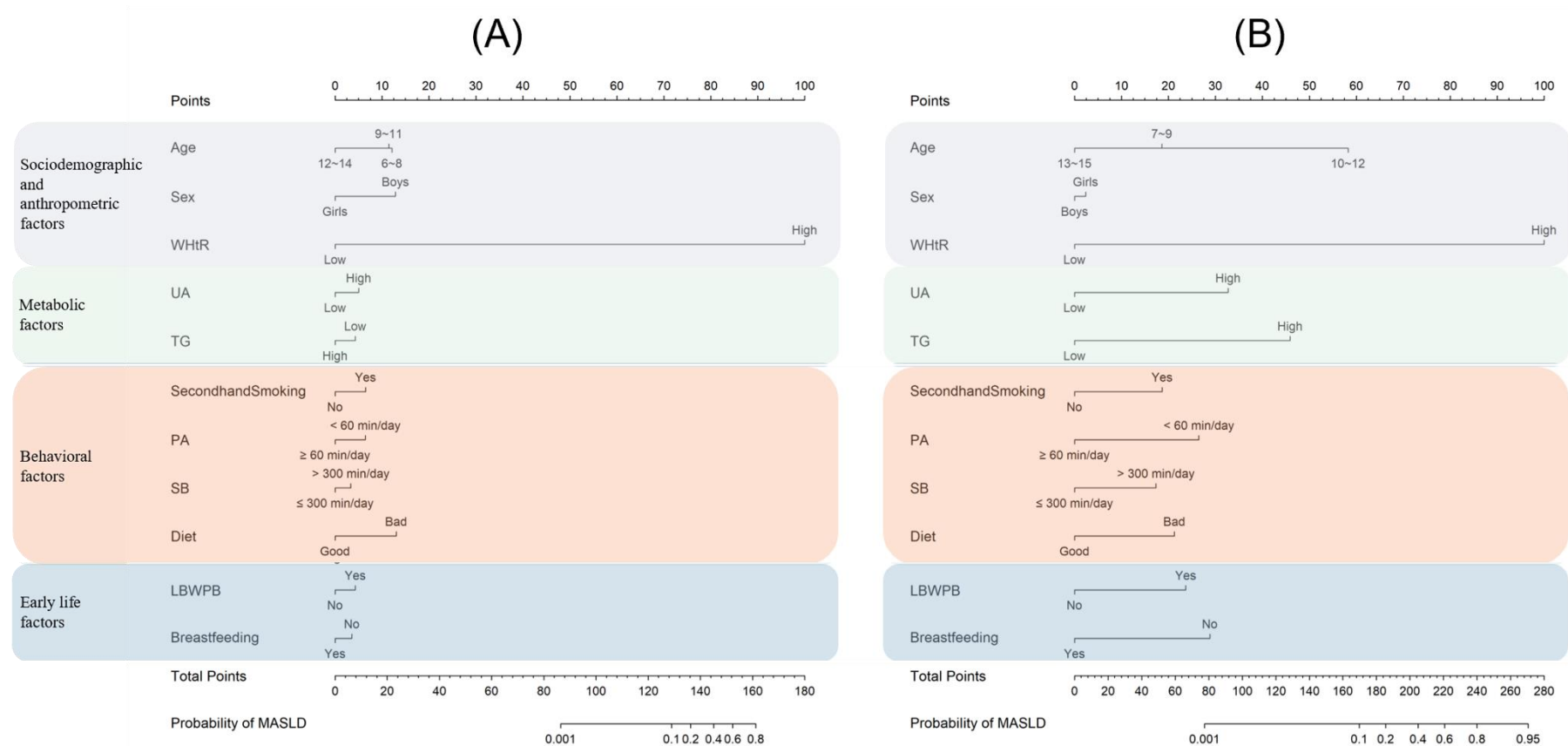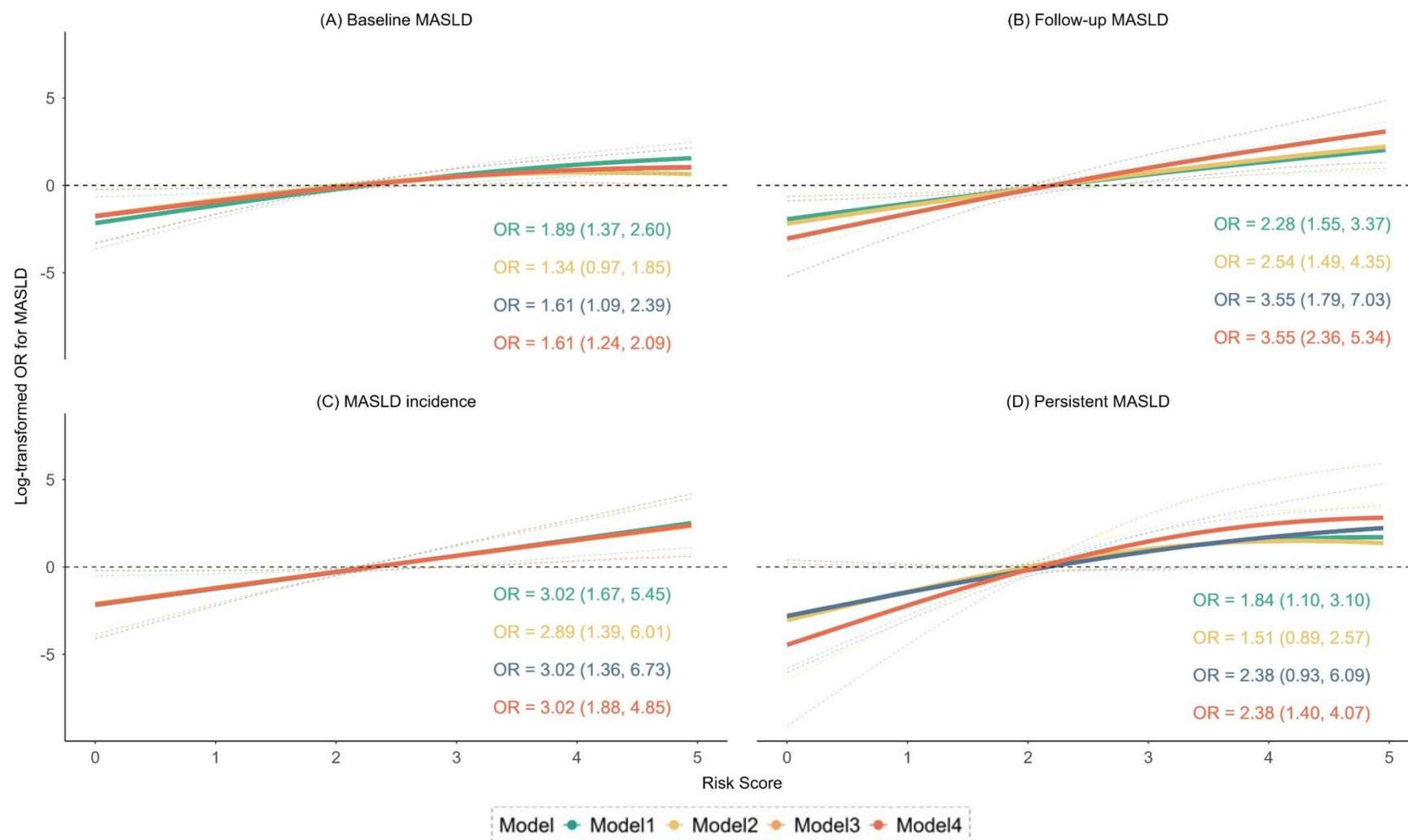
Supplementary Figure 3. Nomograms of sociodemographic and anthropometric, metabolic, behavioral, and early life factors on (A) baseline MASLD, (B) follow-up MASLD. Notes: WHtR: Waist-to-height ratio; UA: uric acid; TG: triglycerides; LBW/PB: low birth weight/ preterm birth; PA: physical activity; SB: sedentary behavior; MASLD: Metabolic dysfunction-associated steatotic liver disease. Breastfeeding, PA, and SB were reassigned based on the cutoff values of 12 months, 60 minutes and 360 minutes, respectively. Figure is generated using R 4.2.1.
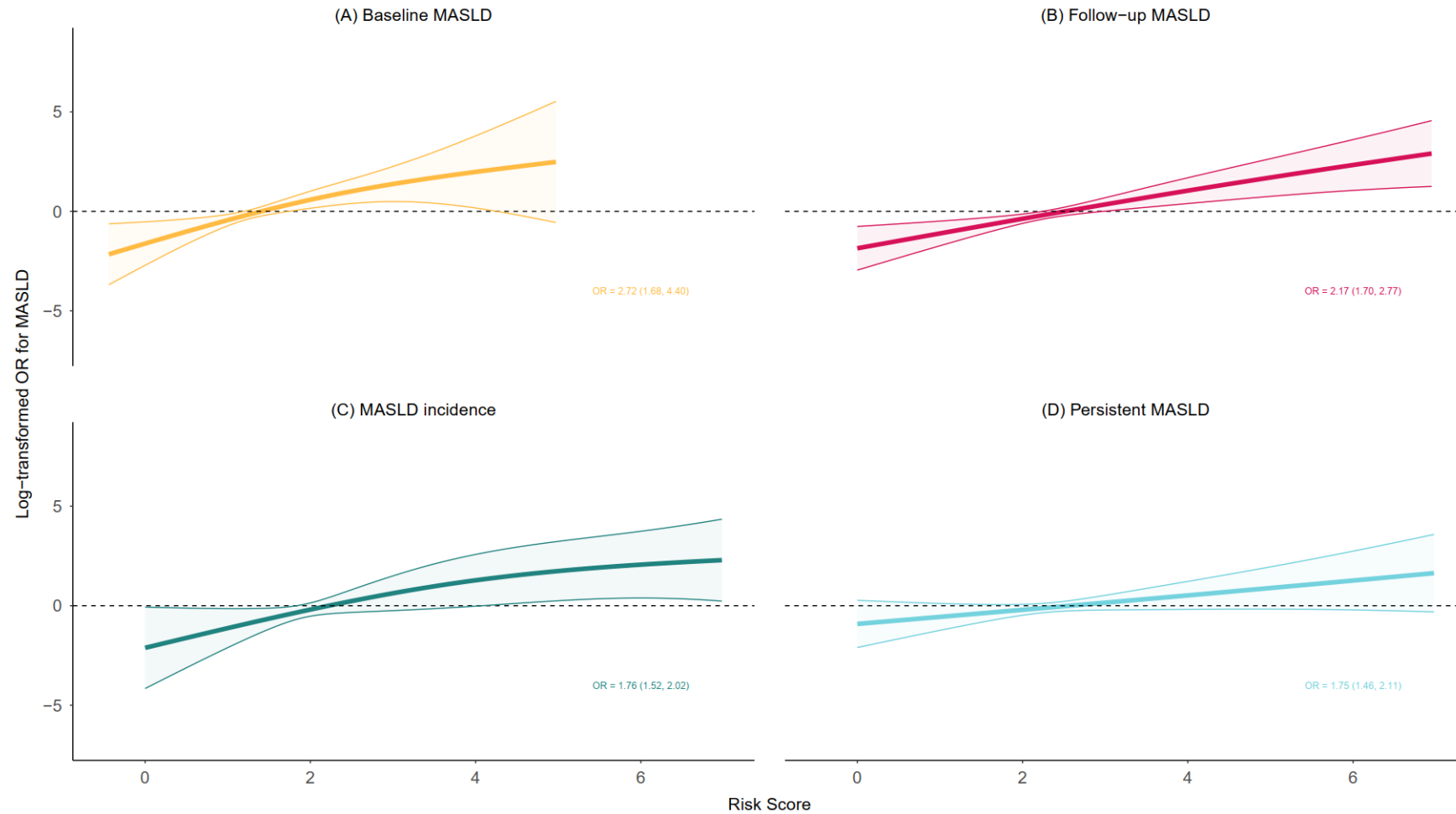
Supplementary Figure 4. Cumulative effects of metabolic, behavioral, and early life factors on (A) baseline MASLD, (B) follow-up MASLD, (C) MASLD incidence, and (D) persistent MASLD. Notes: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group. WHtR: Waist-to-height ratio; MASLD: metabolic dysfunction-associated steatotic liver disease. Figure is generated using R 4.2.1.
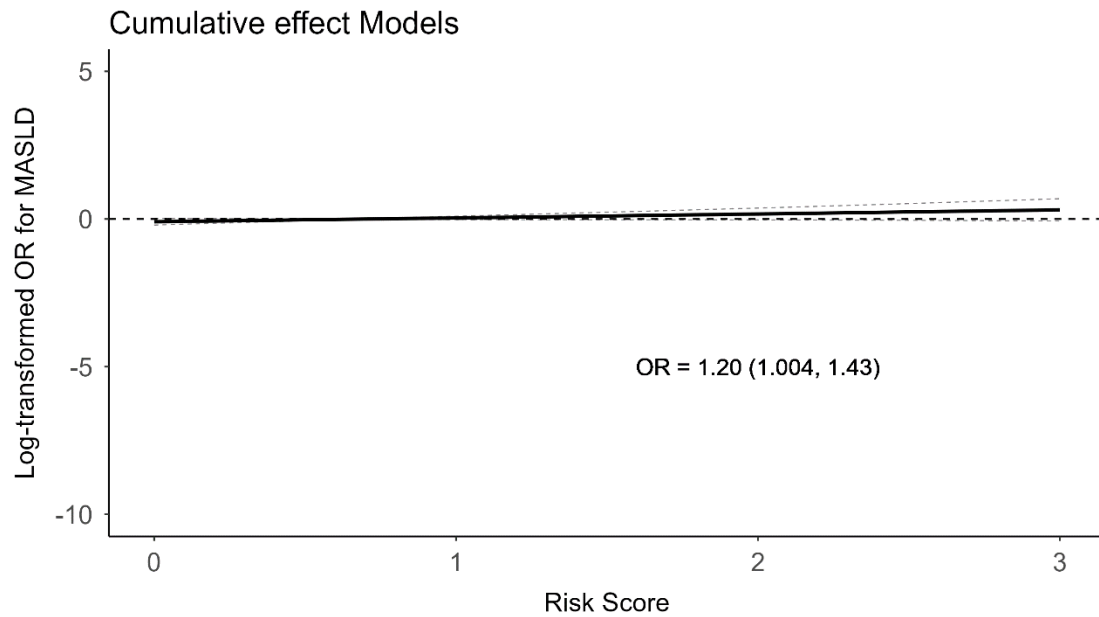
Supplementary Figure 5. Cumulative effects of metabolic, behavioral, and early life factors on (A) baseline MASLD, (B) follow-up MASLD, (C) MASLD incidence, and (D) persistent MASLD. Notes: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group; model 4, model 3 + control school cluster effect. WHtR: Waist-to-height ratio; MASLD: metabolic dysfunction-associated steatotic liver disease. PA and SB were reassigned based on the cutoff values of 60 minutes and 360 minutes, respectively. Figure is

generated using R 4.2.1.

Supplementary Figure 6. Cumulative effects of metabolic, behavioral, and early life factors on (A) baseline MASLD, (B) follow-up MASLD, (C) MASLD incidence, and (D) persistent MASLD. Notes: model 1, crude model; model 2, model 1 + control WHtR group; model 3, model 2 + control sex and age group; model 4, model 3 + control school cluster effect. WHtR: Waist-to-height ratio; MASLD: metabolic dysfunction-associated steatotic liver disease. Figure is generated using R 4.2.1.

Supplementary Figure 7. Cumulative effects of metabolic, behavioral, and early life factors on MASLD in NHANES population. Notes: TG, exposure to secondhand smoking, PA, and LBW were used to build the risk score. WHtR group, sex and age group were controlled in this model. TG: Triglycerides; PA: physical activity; LBW: low birthweight; WHtR: waist-to-height ratio; MASLD: metabolic dysfunction-associated steatotic liver disease; NHANES: national health and nutrition examination survey. Figure is generated using R 4.2.1.