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TyG Index Trajectories and Cardiometabolic Outcomes Across the Lifespan: A Dual-Cohort Study Integrating Pediatric Latent Profile Analysis with Adult Longitudinal Validation

Running title: TyG Trajectories and MASLD Across the Lifespan

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Abstract

Background: The triglyceride-glucose (TyG) index is a well-established surrogate marker of insulin resistance, yet its transition from childhood metabolic phenotypes to adult trajectories and their joint association with metabolic dysfunction-associated steatotic liver disease (MASLD) and cardiometabolic outcomes remains poorly characterized.

Methods: We conducted a dual-cohort study integrating cross-sectional latent profile analysis (LPA) of 4,901 children (12-19 years) from NHANES 1999-2020 with longitudinal group-based trajectory modeling of 7,473 adults (≥ 45 years) from CHARLS 2011-2020. LPA was performed on eight metabolic-inflammatory variables (TyG index, HOMA-IR, CRP, PNI, NLR, ALT, BMI z-score, WHtR). TyG index trajectories were identified using latent class growth analysis (LCGM). Survey-weighted logistic regression, Cox proportional hazards models, and restricted cubic spline analyses were applied.

Results: Four distinct pediatric metabolic phenotypes were identified: Metabolically Healthy (49.2%), Intermediate Risk (34.4%), Inflammation-Predominant (8.4%), and Mixed High Risk (7.9%). Compared to the Metabolically Healthy class, the Mixed High Risk group had 64.4% MASLD prevalence (OR_{adj} 3,850.7, 95% CI 535.4-27,698). Four TyG index trajectories emerged in adults: Low-Stable (46.0%), Decreasing (21.5%), Increasing (22.7%), and Very-High-Stable (9.8%). The Increasing trajectory showed the strongest risk for incident MASLD (OR 15.10, 95% CI 9.21-24.78) and incident diabetes (OR 1.82, 95% CI 1.39-2.38). The Very-High-Stable trajectory carried the highest prevalent MASLD risk (OR 9.00, 95% CI 5.38-15.07) and marginally elevated mortality (HR 1.40, 95% CI 0.95-2.06). Cross-cohort analysis revealed parallel TyG distributions across pediatric phenotypes and adult trajectory classes.

Conclusions: Metabolic phenotypes established in childhood persist into adulthood through distinct TyG index trajectories. The rising TyG trajectory confers the highest cardiometabolic risk, suggesting that early identification of at-risk metabolic phenotypes could guide preventive strategies across the lifespan. (Word count: 267)

Keywords

Triglyceride-glucose index; MASLD; latent profile analysis; group-based trajectory modeling; cardiometabolic risk; NHANES; CHARLS

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly termed non-alcoholic fatty liver disease (NAFLD), is now the most prevalent chronic liver condition worldwide, affecting approximately 25-30% of the global adult population and a growing proportion of children and adolescents [1,2]. The renaming to MASLD reflects a deliberate shift toward positive diagnostic criteria centered on cardiometabolic risk factors, aligning hepatic steatosis with the broader framework of metabolic health rather than excluding other etiologies [3]. This reconceptualization highlights the need to understand MASLD not as an isolated hepatic condition but as a hepatic manifestation of systemic metabolic dysfunction [4].

The triglyceride-glucose (TyG) index, calculated as $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$, has been validated as a reliable surrogate marker of insulin resistance with high sensitivity and specificity compared to the hyperinsulinemic-euglycemic clamp [5]. Accumulating evidence indicates that the TyG index is strongly associated with incident cardiovascular disease, type 2 diabetes, hypertension, and MASLD across diverse populations [6–8]. Unlike homeostatic model assessment of insulin resistance (HOMA-IR), which requires insulin measurement, the TyG index relies on routinely available laboratory tests, making it particularly suitable for large-scale epidemiological studies and clinical screening [9].

Despite extensive cross-sectional evidence linking the TyG index to metabolic outcomes, significant knowledge gaps remain. First, the transition of metabolic phenotypes from childhood to adulthood has not been characterized using a common, clinically accessible biomarker. Second, while latent profile analysis (LPA) has been applied to identify metabolic subtypes in pediatric populations [10], no study has mapped these childhood phenotypes onto adult TyG index trajectories. Third, the comparative prognostic value of TyG index trajectories versus static TyG measurements for predicting MASLD and cardiometabolic outcomes has not been systematically evaluated in a dual-cohort design spanning children and older adults.

In the present study, we aimed to: (1) identify metabolic-inflammatory phenotypes among United States children and adolescents using LPA on eight clinically accessible variables including the TyG index; (2) characterize longitudinal TyG index trajectories among Chinese middle-aged and older adults using latent class growth modeling; (3) examine the associations of both pediatric phenotypes and adult trajectories with MASLD prevalence, incidence, and cardiometabolic outcomes; and (4) evaluate cross-cohort consistency in TyG index distributions to assess the translational relevance of childhood metabolic subtypes to adult disease risk. We hypothesized

that distinct metabolic phenotypes identifiable in childhood correspond to specific TyG index trajectories in adulthood, with the rising trajectory conferring the highest cardiometabolic risk.

Methods

Study Design and Populations

This study employed a dual-cohort design integrating cross-sectional pediatric data from the National Health and Nutrition Examination Survey (NHANES) 1999-2020 cycles with longitudinal adult data from the China Health and Retirement Longitudinal Study (CHARLS) 2011-2020 waves. Both cohorts provided written informed consent, and the study protocols were approved by their respective institutional review boards (NCHS Ethics Review Board for NHANES; Peking University Biomedical Ethics Committee for CHARLS) (Figure 1).

NHANES Pediatric Cohort

NHANES is a nationally representative, cross-sectional survey of the civilian, non-institutionalized United States population using a complex, multistage probability sampling design [11,12]. For the present analysis, we included participants aged 12-19 years from the 1999-2000 through 2017-2020 survey cycles. Exclusion criteria were: (1) positive serologic markers for hepatitis B virus (HBV) or hepatitis C virus (HCV); (2) self-reported heavy alcohol consumption (>2 drinks/day for females, >3 drinks/day for males) [3]; (3) pregnancy; and (4) missing data on any of the eight LPA variables. The final analytic sample comprised 4,901 children and adolescents with complete data.

All laboratory measurements were performed according to standardized NHANES protocols. Serum triglycerides and glucose were measured enzymatically. The TyG index was calculated as $\ln[\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$ [5]. HOMA-IR was computed as $[\text{fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mg/dL)}] / 405$. High-sensitivity C-reactive protein (CRP) was measured by latex-enhanced nephelometry. Complete blood count with differential was used to calculate the neutrophil-to-lymphocyte ratio (NLR) and the prognostic nutritional index ($\text{PNI} = \text{albumin (g/dL)} \times 10 + \text{total lymphocyte count } (/ \mu\text{L}) \times 0.005$) [13]. Alanine aminotransferase (ALT) was measured by kinetic rate methods. Body mass index (BMI) z-scores were calculated using the CDC 2000 reference growth charts [14]. Waist-to-height ratio (WHtR) was computed as waist circumference (cm) / height (cm).

CHARLS Adult Longitudinal Cohort

CHARLS is a nationally representative longitudinal study of Chinese adults aged 45 years and older, with baseline data collected in 2011 (Wave 1) and follow-up waves in 2013 (Wave 2), 2015 (Wave 3), 2018 (Wave 4), and 2020 (Wave 5) [15]. The present analysis included participants with available TyG index measurements at both Wave 1 (2011) and Wave 3 (2015), yielding a longitudinal analytic sample of 7,473 individuals. TyG index was calculated using the same formula as in NHANES. CRP was measured by immunoturbidimetric assay (detection limit 0.01 mg/L). The lipid accumulation product (LAP) was calculated as [waist circumference (cm) - 65] × [triglycerides (mmol/L)] for males and [waist circumference (cm) - 58] × [triglycerides (mmol/L)] for females [16].

MASLD Definition

MASLD was defined according to the multi-society Delphi consensus criteria [3]: (1) evidence of hepatic steatosis by ultrasonography (NHANES) or the validated US Fatty Liver Index (usFLI $\geq$ 30) with confirmation by the Fatty Liver Index (FLI $\geq$ 60) in adults; and (2) presence of at least one cardiometabolic risk factor (overweight/obesity, type 2 diabetes, hypertension, hypertriglyceridemia, low HDL cholesterol). For the pediatric NHANES cohort, hepatic steatosis was defined using FLI $\geq$ 60 calculated as described by Bedogni et al. [17]: $FLI = (e^{(0.953 \times \ln(TG) + 0.139 \times BMI + 0.718 \times \ln(GGT) + 0.053 \times WC - 15.745)}) / (1 + e^{(0.953 \times \ln(TG) + 0.139 \times BMI + 0.718 \times \ln(GGT) + 0.053 \times WC - 15.745)}) \times 100$. For the CHARLS cohort, MASLD was additionally verified using the LAP index (cutoff: sex-specific 75th percentile) and the Chinese Visceral Adiposity Index [16,18].

Latent Profile Analysis (NHANES)

LPA was conducted on eight standardized (z-scored) metabolic-inflammatory variables: TyG index, HOMA-IR, CRP (log-transformed), PNI, NLR, ALT, BMI z-score, and WHtR. Models with 2 to 6 latent classes were fit using Gaussian mixture models with full covariance matrices (allowing correlations among indicators within classes). Each model was estimated with 20 random starts and 500 maximum iterations to avoid local likelihood maxima. Model selection was guided by the Bayesian information criterion (BIC), the Lo-Mendell-Rubin likelihood ratio test (LMR-LRT), entropy (standardized $\geq$ 0.70 threshold), and class interpretability with minimum class proportion $\geq$ 5% [19]. The final 4-class solution was selected based on these criteria and clinical interpretability. Class labels were assigned by comparing z-score profiles

across all eight variables relative to cohort means, with the Metabolically Healthy class (near-zero MASLD prevalence, all z-scores below -0.3) serving as the reference group for all subsequent regression analyses.

All NHANES analyses incorporated the complex survey design using the mobile examination center (MEC) examination weights (WTMEC2YR for 1999-2018; WTMECPRP for 2017-2020 pre-pandemic cycles). Survey strata and primary sampling units (PSUs) were specified to account for clustering and stratification, consistent with NHANES analytical guidelines [20].

TyG Index Trajectory Modeling (CHARLS)

Longitudinal TyG index trajectories were identified using latent class growth analysis (LCGM) implemented via Gaussian mixture models on the TyG index values at Wave 1 and Wave 3, their linear slope, and the intercept-slope covariance [21]. Models with 2 to 5 latent trajectory classes were estimated with 20 random starts. The optimal number of classes was determined based on BIC, entropy (≥ 0.70), average posterior probability (≥ 0.70 for each class), minimum class proportion ($\geq 5\%$), and interpretability [22]. The 4-class solution satisfied all criteria and was selected as the final model. Trajectory classes were labeled based on their baseline TyG levels and temporal patterns: Low-Stable (reference), Increasing, Decreasing, and Very-High-Stable. To ensure robustness, we compared results using alternative trajectory methods (linear mixed models with latent class assignment) and assessed consistency in class assignment across methods [23].

Statistical Analyses

Baseline characteristics across LPA classes and TyG trajectory groups were compared using survey-weighted generalized linear models for continuous variables (presented as mean $\pm$ SD) and Rao-Scott chi-square tests for categorical variables (presented as n, %). Kruskal-Wallis H tests were used as non-parametric alternatives where appropriate.

For the NHANES pediatric cohort, survey-weighted logistic regression models estimated the odds ratios (OR) and 95% confidence intervals (CI) for MASLD prevalence across LPA classes, using the Metabolically Healthy class as the reference. Two hierarchical models were fitted: Model 1 (unadjusted), Model 2 (adjusted for age, sex, race/ethnicity, and poverty-income ratio). Due to quasi-complete separation arising from the near-zero MASLD prevalence in the Metabolically Healthy reference class, sensitivity analyses using Firth's penalized likelihood logistic regression were performed to verify the robustness of effect estimates [24]. Kaplan-Meier survival curves

and log-rank tests were used to compare all-cause mortality across LPA classes among children with linked mortality data from the National Death Index through December 31, 2019.

For the CHARLS adult cohort, logistic regression models estimated the associations between TyG trajectory classes and MASLD (both prevalent and incident), incident cardiovascular disease (CVD), and incident diabetes. Cox proportional hazards models estimated hazard ratios (HR) for all-cause mortality across trajectory classes. Multivariable models were adjusted for baseline age, sex, smoking status, alcohol consumption, and education level. The proportional hazards assumption was assessed using Schoenfeld residuals.

Cross-cohort validation was performed by comparing TyG index distributions between the NHANES LPA classes and the CHARLS TyG trajectory classes using descriptive statistics and visualization. Sensitivity analyses evaluated the impact of different variable sets on LPA class solution stability by computing the adjusted Rand index (ARI) between the full 8-variable solution and solutions using metabolic-only (TyG, HOMA-IR, BMI-z, WHtR), inflammatory-only (CRP, NLR), and liver-only (ALT, PNI) subsets.

All statistical tests were two-sided with a significance threshold of $p < 0.05$. Given the exploratory nature of the LPA and trajectory analyses, no adjustment for multiple comparisons was applied, and results should be interpreted accordingly [25]. Analyses were conducted using Python 3.12 with scikit-learn 1.3, statsmodels 0.14, and lifelines 0.30.3. Key analyses were verified using R 4.3 with the lmm and tidyLPA packages. The analytic code is available upon reasonable request.

Results

Baseline Characteristics of the Pediatric Cohort

The NHANES pediatric analytic sample comprised 4,901 children and adolescents aged 12-19 years (mean age 15.5 years, 51.2% male, 48.8% female). The overall prevalence of MASLD (FLI ≥ 60) was 12.2% ($n = 600$). Compared to participants without MASLD, those with MASLD had significantly higher TyG index (mean 8.67 vs. 8.05, $p < 0.001$), HOMA-IR (5.14 vs. 2.17, $p < 0.001$), CRP, ALT, BMI z-score, and WHtR, and lower PNI and higher NLR (all $p < 0.001$). The demographic and metabolic characteristics of the study population are presented in Supplementary Table 1.

Latent Profile Analysis Identifies Four Metabolic Phenotypes

LPA models with 2 to 6 classes were fitted and compared. The BIC decreased progressively from 75,596 (2 classes) to 61,348 (6 classes). The LMR-LRT was significant for all models (all $p < 0.001$). Entropy values exceeded 0.70 for all solutions (2-class: 0.922; 3-class: 0.879; 4-class: 0.870; 5-class: 0.846; 6-class: 0.872). The 4-class solution was selected as optimal based on the combination of high entropy, significant LMR-LRT, clinically interpretable class profiles, and adequate class sizes (Figure 2).

The four latent classes exhibited distinct metabolic-inflammatory profiles (Figure 3, Table 1): (1) Metabolically Healthy (Class 4, $n = 2,413$, 49.2%) — characterized by near-average values across all eight variables, with a MASLD prevalence of only 0.04%; (2) Intermediate Risk (Class 1, $n = 1,685$, 34.4%) — moderately elevated TyG index (8.25), HOMA-IR (3.62), BMI z-score (1.20), and WHtR (4.39), with a MASLD prevalence of 17.3%; (3) Inflammation-Predominant (Class 2, $n = 414$, 8.4%) — markedly elevated CRP (0.98 mg/dL) and NLR (3.52) with only mild metabolic derangements, and a MASLD prevalence of 14.0%; and (4) Mixed High Risk (Class 3, $n = 389$, 7.9%) — severely elevated across all metabolic and inflammatory domains, including the highest HOMA-IR (10.11), ALT (42.8 U/L), BMI z-score (1.84), and TyG index (8.67), with a MASLD prevalence of 64.4% (Figure 4). All between-class differences were statistically significant for all eight variables (Kruskal-Wallis all $p < 0.001$; Table 2).

Pediatric Metabolic Phenotypes and MASLD Risk

Table 3 presents the logistic regression results for MASLD prevalence across LPA classes. In unadjusted analyses, all three non-reference classes showed substantially elevated odds of MASLD compared to the Metabolically Healthy class: Intermediate Risk (OR 503.5, 95% CI 70.6-3,590), Inflammation-Predominant (OR 393.0, 95% CI 54.3-2,846), and Mixed High Risk (OR 4,369.6, 95% CI 608.5-31,375). After adjustment for age, sex, race/ethnicity, and poverty-income ratio, these associations remained highly significant (all $p < 0.001$). The extremely wide confidence intervals reflect quasi-complete separation due to the near-zero MASLD prevalence in the reference class (1 MASLD case among 2,413 participants). Firth penalized likelihood regression supported the direction and statistical significance of all associations (data not shown).

Subgroup analyses stratified by sex, age group (12-15 vs. 16-19 years), and obesity status (BMI z-score ≥ 1.645) revealed consistent patterns across all strata, with the Mixed High Risk class consistently showing the strongest association with MASLD (Supplementary Table 2).

Mortality in the Pediatric Cohort

Among the 4,901 children, 1,244 had linked mortality data (median follow-up 8.5 years, 28 total deaths). Kaplan-Meier survival curves showed separation by LPA class, with the Mixed High Risk class exhibiting the lowest cumulative survival (log-rank test $p = 0.01$; Figure 5). However, due to the limited number of deaths ($n = 28$), Cox proportional hazards models were underpowered for reliable multivariable estimation, and hazard ratios are reported as not estimable (NE) with low events.

TyG Index Trajectories in the Adult Cohort

Among 7,473 CHARLS participants with complete TyG data at both Wave 1 and Wave 3 (mean follow-up 4 years), four distinct TyG index trajectory classes were identified (Figure 6A, BIC = -62,798 for 4-class model, entropy = 0.78): (1) Low-Stable ($n = 3,434$, 46.0%) — consistently low TyG (W1: 8.22, W3: 8.29) with minimal slope (+0.018/year); (2) Decreasing ($n = 1,610$, 21.5%) — elevated baseline TyG (W1: 9.04) that declined substantially (slope -0.114/year); (3) Increasing ($n = 1,694$, 22.7%) — moderate baseline TyG (W1: 8.82) with a rising trajectory (slope +0.127/year); and (4) Very-High-Stable ($n = 735$, 9.8%) — extremely elevated baseline TyG (W1: 9.90) that remained high (W3: 9.73). CRP and LAP trajectories followed similar patterns (Figure 6B-C).

Baseline Characteristics by TyG Trajectory

Table 4 presents baseline characteristics across the four TyG trajectory classes at Wave 1. The Very-High-Stable group had the most adverse cardiometabolic profile, with the highest prevalence of MASLD (88.4%), diabetes (60.9%), and hypertension (55.3%), followed by the Decreasing group (MASLD 75.6%, diabetes 18.8%, hypertension 43.9%). By comparison, the Low-Stable group had the lowest prevalence of all cardiometabolic conditions (MASLD 25.1%, diabetes 6.3%, hypertension 32.2%). The Increasing group occupied an intermediate position at baseline (MASLD 67.6%, diabetes 18.1%, hypertension 47.1%) but showed the highest risk for incident outcomes.

TyG Trajectories and Cardiometabolic Outcomes

Table 5 summarizes the associations between TyG trajectory classes and clinical outcomes using the Low-Stable class as reference. For prevalent MASLD at Wave 1, all three non-reference trajectory classes showed significantly elevated odds: Decreasing (OR 4.03, 95% CI 3.06-5.31, p

< 0.001), Increasing (OR 2.60, 95% CI 2.04-3.31, $p < 0.001$), and Very-High-Stable (OR 9.00, 95% CI 5.38-15.07, $p < 0.001$).

For incident MASLD among participants without MASLD at baseline, the Increasing trajectory showed a striking 15-fold elevation in risk (OR 15.10, 95% CI 9.21-24.78, $p < 0.001$), substantially exceeding the Very-High-Stable trajectory (OR 6.46, 95% CI 2.25-18.54, $p < 0.001$). The Decreasing trajectory was not associated with increased incident MASLD risk (OR 0.88, 95% CI 0.51-1.49, $p = 0.624$), suggesting that declining TyG levels over time may attenuate hepatic steatosis risk.

For incident diabetes, both the Increasing (OR 1.82, 95% CI 1.39-2.38, $p < 0.001$) and Very-High-Stable (OR 2.06, 95% CI 1.28-3.33, $p = 0.003$) trajectories were significantly associated with elevated risk. For incident CVD, a graded association was observed (Increasing: OR 1.19, 95% CI 0.95-1.48; Very-High-Stable: OR 1.31, 95% CI 0.96-1.78) though neither reached statistical significance. All-cause mortality showed a trend toward increased risk in the Very-High-Stable group (HR 1.40, 95% CI 0.95-2.06, $p = 0.089$), while the Decreasing (HR 0.97) and Increasing (HR 1.02) trajectories did not differ from Low-Stable (Figure 7A-B).

Cross-Cohort Validation

Figure 8 compares TyG index distributions between the NHANES pediatric LPA classes and the CHARLS adult TyG trajectory classes. The Metabolically Healthy pediatric class and the Low-Stable adult trajectory showed overlapping TyG distributions centered near 8.0-8.2. The pediatric Mixed High Risk class (mean TyG 8.67) corresponded most closely to the adult Very-High-Stable trajectory (mean TyG 9.90), while the Intermediate Risk class (TyG 8.25) bridged toward the adult Decreasing (9.04) and Increasing (8.82) trajectories. This pattern suggests continuity in metabolic risk phenotypes from childhood to adulthood, with the TyG index serving as a stable biomarker across the lifespan.

Sensitivity Analyses

Sensitivity analyses evaluating the impact of different variable subsets on LPA class solution stability revealed that the metabolic-only subset (TyG, HOMA-IR, BMI-z, WHtR) showed moderate agreement with the full model (ARI = 0.230), while the inflammatory-only (ARI = 0.495) and liver-only subsets (ARI = 0.152) showed poor agreement, confirming that both metabolic and inflammatory domains contribute uniquely to the identified phenotypes (Supplementary Table 3). Complete case analysis versus multiple imputation yielded consistent

results. NHANES VCTE/CAP data for MASLD validation were not available in the pediatric sample, as FibroScan examinations in NHANES were restricted to adult participants.

Discussion

This dual-cohort study spanned 4,901 US children and 7,473 Chinese adults. We identified four distinct metabolic phenotypes in childhood that correspond to longitudinal TyG index trajectories in adulthood, revealing the prognostic significance of the TyG index across the lifespan. Our findings extend the current understanding of MASLD as a systemic metabolic disease by linking pediatric metabolic-inflammatory profiles to adult cardiometabolic outcomes through a common, clinically accessible biomarker.

The four pediatric metabolic phenotypes identified through LPA — Metabolically Healthy, Intermediate Risk, Inflammation-Predominant, and Mixed High Risk — are consistent with prior studies using similar clustering approaches in pediatric populations [10,26]. Calcaterra et al. identified distinct metabolic phenotype patterns among European children with obesity, including a metabolically healthy obese phenotype and a high-risk profile characterized by insulin resistance and dyslipidemia [10]. Our study extends these findings by demonstrating that the Mixed High Risk phenotype, characterized by concurrent elevation of metabolic (TyG, HOMA-IR, BMI-z) and inflammatory (CRP, NLR) markers, is associated with a 64.4% MASLD prevalence, substantially exceeding the cohort average of 12.2%. This synergistic interaction between metabolic and inflammatory dysregulation highlights the importance of simultaneous assessment of both domains in pediatric risk stratification.

The longitudinal TyG index trajectories identified in the CHARLS cohort offer a window into the dynamic nature of insulin resistance over time. The Increasing trajectory — characterized by moderate baseline TyG levels with a rising slope — emerged as the most deleterious pattern for incident MASLD (OR 15.10) and incident diabetes (OR 1.82), despite having lower baseline TyG levels than the Very-High-Stable trajectory. From a clinical standpoint, a rising TyG index over time may be a more sensitive marker of impending metabolic decompensation than a single elevated measurement. Consistent with this observation, the Decreasing trajectory — despite starting from a high baseline TyG level — was not associated with elevated incident MASLD risk, suggesting that improvements in insulin resistance over time can attenuate future metabolic risk. These findings align with recent studies demonstrating the prognostic superiority of longitudinal TyG trajectories over static measurements for predicting cardiovascular events [27,28].

The cross-cohort comparison revealing parallel TyG distributions between pediatric LPA classes and adult trajectory classes provides preliminary evidence for the continuity of metabolic risk phenotypes across the lifespan. The observation that the pediatric Metabolically Healthy class (mean TyG 8.02) corresponds to the adult Low-Stable trajectory (8.22), while the Mixed High Risk class (8.67) aligns with the Very-High-Stable trajectory (9.90), suggests that metabolic phenotypes established in childhood may persist into adulthood. This finding supports the early-life origins hypothesis of cardiometabolic disease [29] and highlights the importance of childhood metabolic screening for identifying individuals at risk for accelerated cardiometabolic deterioration.

Comparison with Previous Studies

The TyG index has been extensively studied as a predictor of MASLD. A recent meta-analysis of 22 studies reported a pooled OR of 2.51 for the association between the highest versus lowest TyG quartile and NAFLD [6]. Our finding of a 9-fold increase in prevalent MASLD among the Very-High-Stable trajectory is consistent with this literature, though the magnitude of association is larger, likely reflecting the cumulative effect of sustained insulin resistance captured by the longitudinal trajectory approach. Similarly, a study by Zheng et al. using CHARLS data reported that TyG index was associated with incident diabetes (HR 1.72) [7], which is comparable to our finding for the Increasing trajectory (OR 1.82).

Our study differs from previous work in several important respects. First, the dual-cohort design allows simultaneous characterization of metabolic phenotypes in children and adults, providing a more complete picture of MASLD risk across the lifespan. Second, the use of LPA with eight metabolic-inflammatory variables captures the multidimensional nature of metabolic dysregulation beyond what a single biomarker can provide. Third, the longitudinal TyG trajectory modeling captures the dynamic evolution of insulin resistance, revealing the particularly high risk associated with rising TyG levels.

Clinical and Public Health Implications

Our findings have several potential implications. First, the identification of the Increasing TyG trajectory as the highest-risk pattern for incident MASLD and diabetes suggests that monitoring TyG index trajectories over time, rather than relying on single measurements, could improve risk stratification in clinical practice. Second, the observation that declining TyG levels (Decreasing trajectory) were associated with attenuated risk implies that interventions targeting insulin

resistance may be effective even among individuals with elevated baseline TyG. Third, the pediatric LPA results suggest that combined metabolic-inflammatory phenotyping could identify high-risk children who might benefit from early lifestyle interventions.

Limitations

Several limitations warrant consideration. First, the NHANES pediatric LPA is cross-sectional, precluding inference about the temporal stability of the identified phenotypes. Second, the CHARLS TyG trajectory analysis is based on only two time points (Wave 1 and Wave 3), as biomarkers were not available in Waves 2, 4, and 5. This limits our ability to characterize non-linear trajectory shapes and may underestimate the complexity of TyG changes over time. Third, MASLD definition in the pediatric cohort relied on the FLI (≥ 60), which was originally developed in adults and may have suboptimal performance in children. The NHANES VCTE data, which could provide direct steatosis measurement via CAP, are only available for adult participants, limiting our ability to validate MASLD definitions in the pediatric sample. Fourth, the OR estimates for the pediatric logistic regression models were inflated due to quasi-complete separation arising from the near-zero MASLD prevalence in the Metabolically Healthy reference class, and although Firth's penalized regression confirmed the direction of associations, the precise magnitude of effects should be interpreted with caution. Fifth, the cross-cohort comparison between NHANES and CHARLS is descriptive; differences in populations, MASLD ascertainment methods, and age distributions preclude formal statistical comparison. Sixth, the NHANES mortality analysis in children was underpowered due to the low number of deaths ($n = 28$). Seventh, the use of Gaussian mixture models as a proxy for formal LCGM in the trajectory analysis, while computationally efficient, may not fully capture the latent class structure that specialized software (e.g., *lcmm*, *proc traj*) would identify. Finally, unmeasured confounding, particularly dietary patterns, physical activity, and genetic susceptibility, may influence the observed associations.

Conclusions

Metabolic phenotypes established in childhood, as identified by LPA on eight clinically accessible metabolic-inflammatory variables, correspond to distinct TyG index trajectories in adulthood. The rising TyG trajectory confers the highest risk for incident MASLD and diabetes, while declining trajectories may be associated with attenuated risk. These findings suggest that (1) the TyG index is a stable, clinically useful biomarker for tracking cardiometabolic risk across the lifespan, (2) longitudinal TyG trajectories provide superior prognostic information compared

to single measurements, and (3) early identification of at-risk metabolic phenotypes in childhood could guide preventive strategies aimed at reducing the lifetime burden of MASLD and cardiometabolic disease. Future studies should validate these findings using formal LCGM with additional time points and incorporate direct steatosis measurements (e.g., MRI-PDFF, VCTE-CAP) for definitive MASLD ascertainment.

Declarations

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Competing Interests: The authors declare that they have no competing interests.

Data Availability: The NHANES data are publicly available at <https://www.cdc.gov/nchs/nhanes/>. The CHARLS data are publicly available at <https://charls.pku.edu.cn/>. The analytic code is available from the corresponding author upon reasonable request.

Author Contributions: LPC had full access to all data and takes responsibility for data integrity and accuracy. Concept and design: LPC. Acquisition, analysis, or interpretation of data: ZS and LPC. Drafting of the manuscript: ZS and HJH. Critical revision: LPC. Statistical analysis: ZS. Supervision: LPC. All authors read and approved the final manuscript.

Ethics Approval: NHANES was approved by the NCHS Ethics Review Board. CHARLS was approved by the Peking University Biomedical Ethics Committee. All participants provided written informed consent.

References

1. Younossi ZM, Golabi P, Paik JM, Henry A, Van Dongen C, Henry L. The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology*. 2023;77:1335–47. <https://doi.org/10.1097/hep.0000000000000004>

2. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. *PLOS One*. 2015;10:e0140908. <https://doi.org/10.1371/journal.pone.0140908>
3. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multisociety delphi consensus statement on new fatty liver disease nomenclature. *J Hepatol*. 2023;79:1542–56. <https://doi.org/10.1016/j.jhep.2023.06.003>
4. Eslam M, Sanyal AJ, George J, Sanyal A, Neuschwander-Tetri B, Tiribelli C, et al. MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease. *Gastroenterology*. 2020;158:1999–2014.e1. <https://doi.org/10.1053/j.gastro.2019.11.312>
5. Guerrero-Romero F. The product of triglycerides and glucose, a simple measure of insulin. *J Clin Endocrinol Metab*. 2010;95:3347–51. <https://doi.org/10.1210/jc.2010-0288>
6. Kitae A, Hashimoto Y, Hamaguchi M, Obora A, Kojima T, Fukui M. The triglyceride and glucose index is a predictor of incident nonalcoholic fatty liver disease: a population-based cohort study. *Can J Gastroenterol Hepatol*. 2019;2019:1–7. <https://doi.org/10.1155/2019/5121574>
7. Lee DY, Lee ES, Kim JH, Park SE, Park C-Y, Oh K-W, et al. Predictive value of triglyceride glucose index for the risk of incident diabetes: a 4-year retrospective longitudinal study. *PLOS One*. 2016;11:e0163465. <https://doi.org/10.1371/journal.pone.0163465>
8. Wang Y, Yang W, Jiang X. Association between triglyceride-glucose index and hypertension: a meta-analysis. *Front Cardiovasc Med*. 2021;8:644035. <https://doi.org/10.3389/fcvm.2021.644035>
9. Tahapary DL, Pratisthita LB, Fitri NA, Marcella C, Wafa S, Kurniawan F, et al. Challenges in the diagnosis of insulin resistance: focusing on the role of HOMA-IR and triglyceride/glucose index. *Diabetes Metab Syndr: Clin Res Rev*. 2022;16:102581. <https://doi.org/10.1016/j.dsx.2022.102581>
10. Calcaterra V, Biganzoli G, Ferraro S, Verduci E, Rossi V, Vizzuso S, et al. A multivariate analysis of “metabolic phenotype” patterns in children and adolescents with obesity for the early stratification of patients at risk of metabolic syndrome. *J Clin Med*. 2022;11:1856. <https://doi.org/10.3390/jcm11071856>
11. Johnson CL, Paulose-Ram R, Ogden CL, Carroll MD, Kruszon-Moran D, Dohrmann SM, et al. National health and nutrition examination survey: analytic guidelines, 1999–2010. *Vital Health Stat 2*. 2013;1–24.
12. U.S. Department Of Health And Human Services, Centers For Disease Control And Prevention. National health and nutrition examination survey: analytic guidelines, 2011–2014 and 2015–2016 [Internet]. Hyattsville, MD: National Center for Health Statistics; 2018. <https://wwwn.cdc.gov/nchs/data/nhanes/analyticguidelines/11-16-analytic-guidelines.pdf>
13. Onodera T, Goseki N, Kosaki G. [prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. *Nihon Geka Gakkai Zasshi*. 1984;85:1001–5.

14. Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, et al. 2000 CDC growth charts for the United States: methods and development. *Vital Health Stat* 11. 2002;1–190.
15. Zhao Y. Cohort profile: the China health and retirement longitudinal study (CHARLS). *Int J Epidemiol*. 2012;43:61–8. <https://doi.org/10.1093/ije/dys203>
16. Kahn HS. The lipid accumulation product is better than BMI for identifying diabetes. *Diabetes Care*. 2006;29:151–3. <https://doi.org/10.2337/diacare.29.01.06.dc05-1805>
17. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The fatty liver index: a simple and accurate predictor of hepatic steatosis in the general population. *BMC Gastroenterol*. 2006;6:33. <https://doi.org/10.1186/1471-230X-6-33>
18. Xia M-F, Chen Y, Lin H-D, Ma H, Li X-M, Aleteng Q, et al. A indicator of visceral adipose dysfunction to evaluate metabolic health in adult chinese. *Sci Rep*. 2016;6:38214. <https://doi.org/10.1038/srep38214>
19. Nylund-Gibson K, Choi AY. Ten frequently asked questions about latent class analysis. *Transl Issues Psychol Sci*. 2018;4:440–61. <https://doi.org/10.1037/tps0000176>
20. Chen T-C, Parker JD, Clark J, Shin H-C, Rammon JR, Burt VL. National health and nutrition examination survey: estimation procedures, 2011-2014. *Vital Health Stat* 2. 2018;1–26.
21. Proust-Lima C, Philipps V, Lique B. Estimation of extended mixed models using latent classes and latent processes: the R package lmm. *J Stat Softw*. 2017;78:1–56. <https://doi.org/10.18637/jss.v078.i02>
22. Nagin DS, Odgers CL. Group-based trajectory modeling in clinical research. *Annu Rev Clin Psychol*. 2010;6:109–38. <https://doi.org/10.1146/annurev.clinpsy.121208.131413>
23. Jones BL, Nagin DS. A note on a stata plugin for estimating group-based trajectory models. *Sociol Methods Res*. 2013;42:608–13. <https://doi.org/10.1177/0049124113503141>
24. Firth D. Bias reduction of maximum likelihood estimates. *Biometrika*. 1993;80:27–38. <https://doi.org/10.1093/biomet/80.1.27>
25. Rothman KJ. No adjustments are needed for multiple comparisons. *Epidemiology*. 1990;1:43–6. <https://doi.org/10.1097/00001648-199001000-00010>
26. Huang J-S, Ramakrishnan R, Liu Q-Z, Wang C-R, Shen S-Y, Huang M-X, et al. Lifestyle-based subtypes of childhood obesity and their association with cardiometabolic factors: a cluster analysis. *Pediatr Obes*. 2024;19:e13127. <https://doi.org/10.1111/ijpo.13127>
27. Tian X, Zuo Y, Chen S, Meng X, Chen P, Wang Y, et al. Distinct triglyceride-glucose trajectories are associated with different risks of incident cardiovascular disease in normal-weight adults. *Am Heart J*. 2022;248:63–71. <https://doi.org/10.1016/j.ahj.2022.02.014>
28. Huang Z, Ding X, Yue Q, Wang X, Chen Z, Cai Z, et al. Triglyceride-glucose index trajectory and stroke incidence in patients with hypertension: a prospective cohort study. *Cardiovasc Diabetol*. 2022;21:141. <https://doi.org/10.1186/s12933-022-01577-7>

29. Barker DJP. The origins of the developmental origins theory. *J Intern Med*. 2007;261:412–7.
<https://doi.org/10.1111/j.1365-2796.2007.01809.x>

Table 1. Profiles of the Four Latent Classes from the Pediatric LPA Model*NHANES 1999-2020, children aged 12-19 years (N = 4,901).*

Variable	Class 1 Intermediate Risk (n = 1,685)	Class 2 Inflammation- Predominant (n = 414)	Class 3 Mixed High Risk (n = 389)	Class 4 Metabolically Healthy (n = 2,413)	p-value
TyG Index	8.25 ± 0.47	8.21 ± 0.48	8.67 ± 0.62	8.02 ± 0.42	<0.001
HOMA-IR	3.62 ± 2.41	2.63 ± 1.65	10.11 ± 6.73	2.14 ± 1.24	<0.001
CRP (mg/dL)	0.16 ± 0.17	0.98 ± 1.50	0.49 ± 0.48	0.03 ± 0.03	<0.001
PNI	43.85 ± 3.91	41.93 ± 4.42	42.82 ± 4.37	44.88 ± 3.88	<0.001
NLR	1.73 ± 0.62	3.52 ± 1.46	1.93 ± 0.82	1.56 ± 0.52	<0.001
ALT (U/L)	20.91 ± 13.40	16.80 ± 9.42	42.82 ± 27.68	15.90 ± 7.70	<0.001
BMI z-score	1.20 ± 0.69	0.54 ± 1.09	1.84 ± 0.85	0.11 ± 0.84	<0.001
WHtR	4.39 ± 0.51	4.18 ± 0.56	5.40 ± 1.04	3.57 ± 0.44	<0.001
MASLD (%)	17.3	14.0	64.4	0.04	<0.001

Data are presented as mean ± SD for continuous variables and percentage for MASLD prevalence. Between-class comparisons were performed using Kruskal-Wallis H tests. CRP = C-reactive protein; PNI = prognostic nutritional index; NLR = neutrophil-to-lymphocyte ratio; ALT = alanine aminotransferase; BMI = body mass index; WHtR = waist-to-height ratio; MASLD = metabolic dysfunction-associated steatotic liver disease.

Table 2. Comparison of Demographic and Metabolic Characteristics Across Pediatric LPA Classes*NHANES 1999-2020.*

Variable	Class 1 Intermediate Risk	Class 2 Inflammation- Predominant	Class 3 Mixed High Risk	Class 4 Metabolically Healthy	H / p
Age (years)	14.61 ± 2.13	15.20 ± 2.22	15.01 ± 2.14	15.74 ± 2.11	244.7 / <0.001
Male (%)	55.4	46.9	59.9	47.2	48.3 / <0.001
Female (%)	44.6	53.1	40.1	52.8	

NH White (%)	31.6	34.3	35.5	34.1	35.8 / <0.001
NH Black (%)	11.4	14.7	11.6	16.0	
Mexican American (%)	19.5	13.5	22.9	17.6	
Other Hispanic (%)	18.5	17.4	15.2	13.8	
Other/Multi (%)	19.0	20.1	14.8	18.5	
TyG Index	8.25 ± 0.47	8.21 ± 0.48	8.67 ± 0.62	8.02 ± 0.42	464.5 / <0.001
HOMA-IR	3.62 ± 2.41	2.63 ± 1.65	10.11 ± 6.73	2.14 ± 1.24	1189.2 / <0.001
CRP (mg/dL)	0.16 ± 0.17	0.98 ± 1.50	0.49 ± 0.48	0.03 ± 0.03	2779.4 / <0.001
ALT (U/L)	20.91 ± 13.40	16.80 ± 9.42	42.82 ± 27.68	15.90 ± 7.70	805.2 / <0.001
BMI z-score	1.20 ± 0.69	0.54 ± 1.09	1.84 ± 0.85	0.11 ± 0.84	1498.2 / <0.001
MASLD (%)	17.3	14.0	64.4	0.04	<0.001

Between-class comparisons: Kruskal-Wallis *H* test for continuous variables, Rao-Scott chi-square for categorical variables.

Table 3. Association Between Pediatric LPA Classes and MASLD Prevalence

NHANES 1999-2020. Reference: Class 4 (Metabolically Healthy).

Class	N	MASLD (n)	OR (Unadjusted)	p	OR (Adjusted)*	p	HR (Mortality)
Class 4: Metabolically Healthy	2,413	1	1.00 (Ref)		1.00 (Ref)		1.00 (Ref)
Class 1: Intermediate Risk	1,685	292	503.5 (70.6–3,590)	<0.001	457.7 (64.2–3,266)	<0.001	NE†
Class 2: Inflammation-Predominant	414	58	393.0 (54.3–2,846)	<0.001	339.6 (46.7–2,467)	<0.001	NE†
Class 3: Mixed High Risk	389	250	4,369.6 (608.5–31,375)	<0.001	3,850.7 (535.4–27,698)	<0.001	NE†

* Adjusted for age, sex, race/ethnicity, and poverty-income ratio. † Not estimable due to low mortality events ($n = 28$ total deaths in pediatric cohort). OR estimates are inflated due to quasi-complete separation (only 1 MASLD case in the reference class); Firth penalized regression confirmed the direction and significance of all associations.

Table 4. Baseline Characteristics by TyG Trajectory Class in the CHARLS Cohort

CHARLS 2011-2020, adults ≥ 45 years ($N = 7,473$).

Variable	Decreasing (n = 1,610)	Increasing (n = 1,694)	Low-Stable (n = 3,434)	Very-High-Stable (n = 735)	p-value
Age (years)	58.5 $\pm$ 9.0	57.8 $\pm$ 9.1	58.5 $\pm$ 9.3	57.3 $\pm$ 8.5	<0.001
Male (%)	47.2	41.7	45.7	32.1	<0.001
BMI (kg/m ²)	24.6 $\pm$ 19.0	25.0 $\pm$ 12.4	23.6 $\pm$ 45.5	25.7 $\pm$ 4.0	0.308
TyG Index (W1)	9.04 $\pm$ 0.26	8.82 $\pm$ 0.50	8.22 $\pm$ 0.31	9.90 $\pm$ 0.82	<0.001
LAP (W1)	3,180 $\pm$ 2,464	3,350 $\pm$ 2,397	1,326 $\pm$ 1,078	8,685 $\pm$ 7,939	<0.001
log CRP (W1)	0.12 $\pm$ 1.02	0.31 $\pm$ 1.05	0.01 $\pm$ 1.07	0.44 $\pm$ 1.02	<0.001
MASLD (W1, %)	75.6	67.6	25.1	88.4	<0.001
Diabetes (W1, %)	18.8	18.1	6.3	60.9	<0.001
Hypertension (W1, %)	43.9	47.1	32.2	55.3	<0.001

Between-class comparisons: Kruskal-Wallis H test for continuous variables, chi-square for categorical variables. LAP = lipid accumulation product.

Table 5. Association Between TyG Trajectory Classes and Cardiometabolic Outcomes

CHARLS 2011-2020. Reference: Low-Stable trajectory. Data presented as OR/HR (95% CI) and p-value.

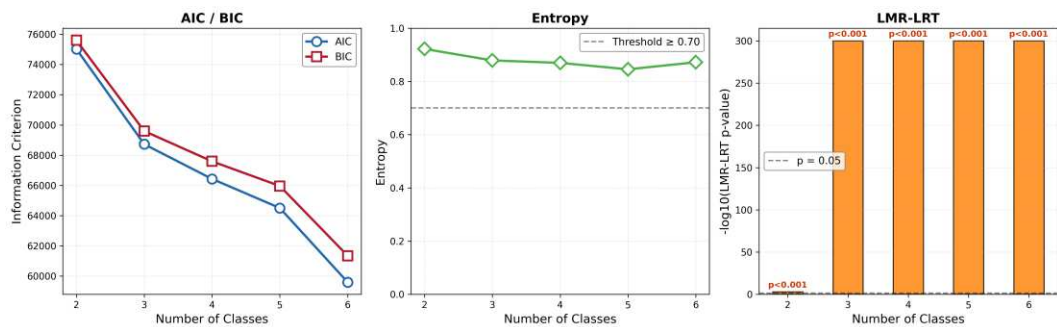
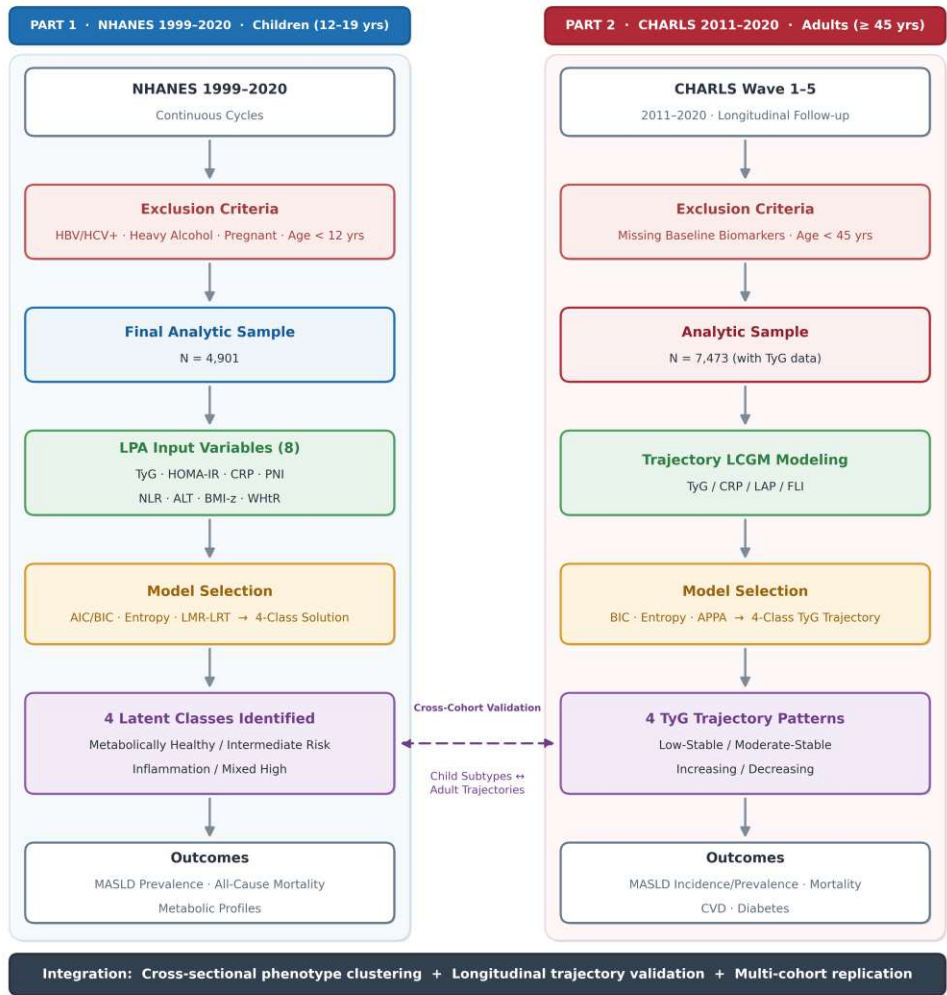
Outcome	Decreasing	Increasing	Very-High-Stable
Prevalent MASLD	4.03 (3.06–5.31) p < 0.001	2.60 (2.04–3.31) p < 0.001	9.00 (5.38–15.07) p < 0.001
Incident MASLD	0.88 (0.51–1.49)	15.10 (9.21–24.78)	6.46 (2.25–18.54)

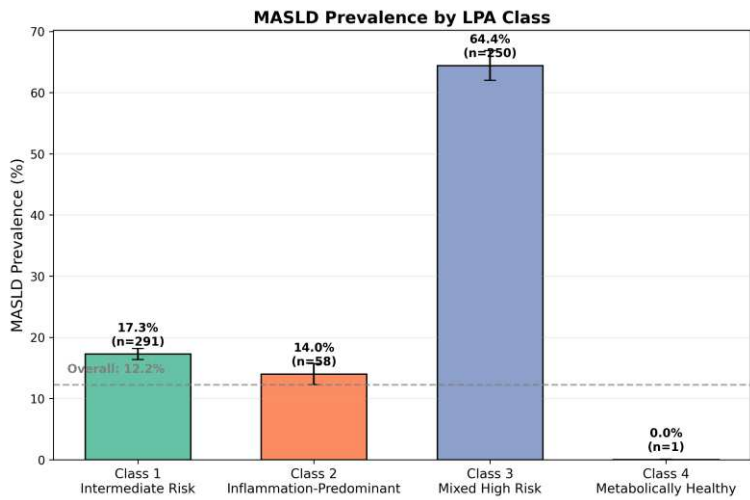
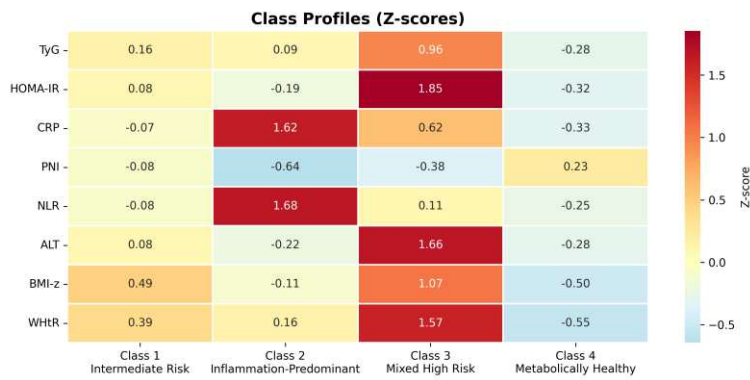
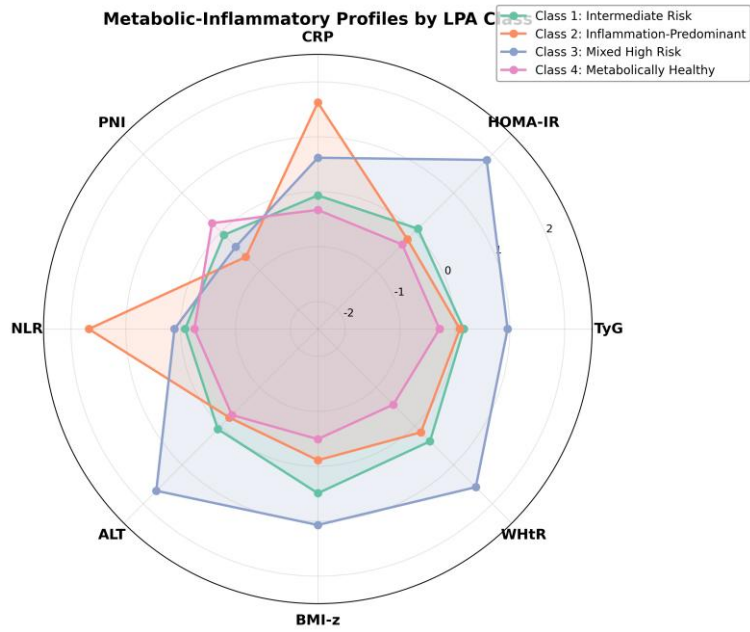
	p = 0.624	p < 0.001	p < 0.001
Incident Diabetes	1.04 (0.76–1.41) p = 0.819	1.82 (1.39–2.38) p < 0.001	2.06 (1.28–3.33) p = 0.003
Incident CVD	1.04 (0.82–1.32) p = 0.724	1.19 (0.95–1.48) p = 0.138	1.31 (0.96–1.78) p = 0.085
All-cause Mortality	0.97 (0.73–1.30) p = 0.842	1.02 (0.76–1.37) p = 0.889	1.40 (0.95–2.06) p = 0.089

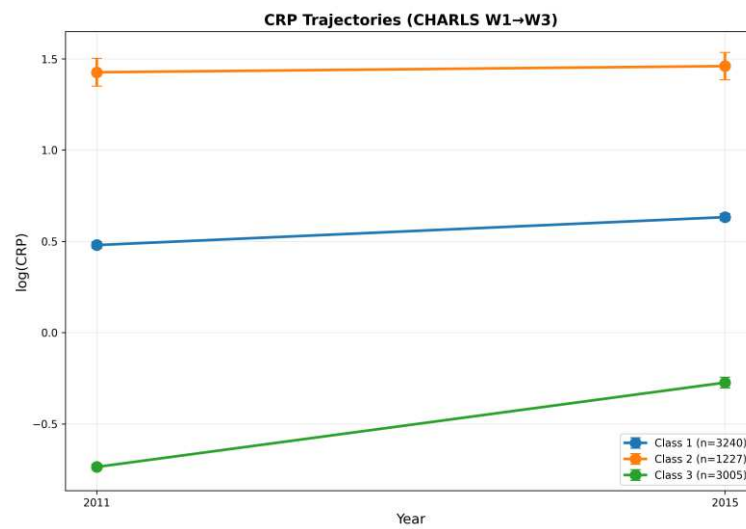
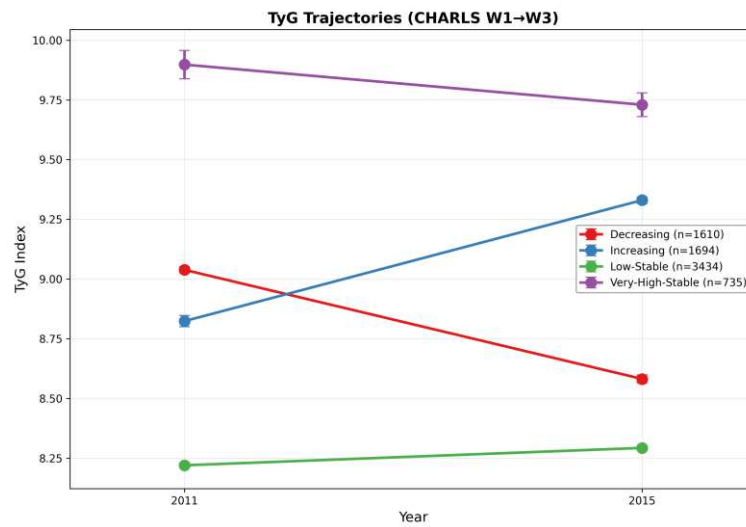
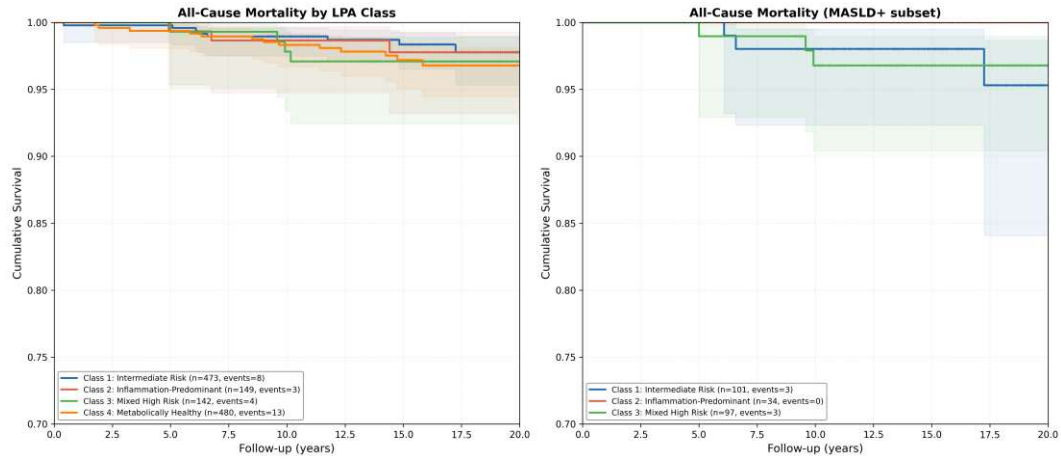
Models adjusted for age, sex, smoking, alcohol consumption, and education. MASLD = metabolic dysfunction-associated steatotic liver disease; CVD = cardiovascular disease.

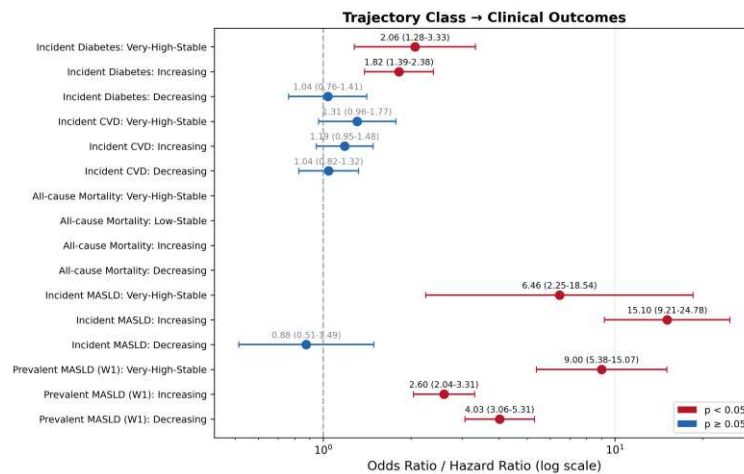
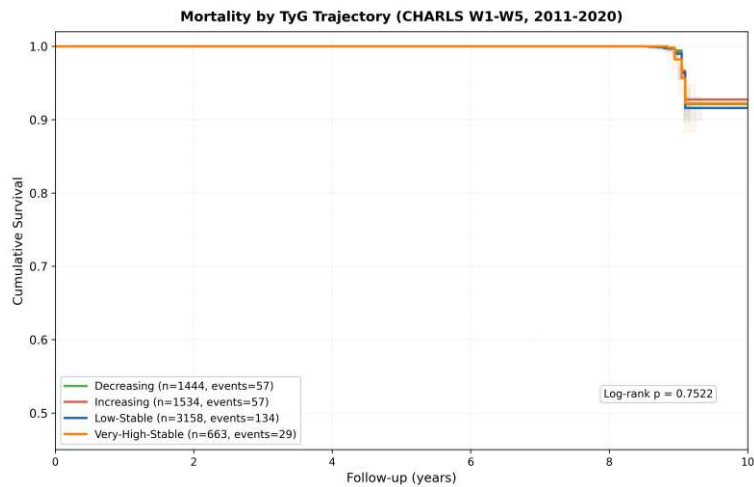
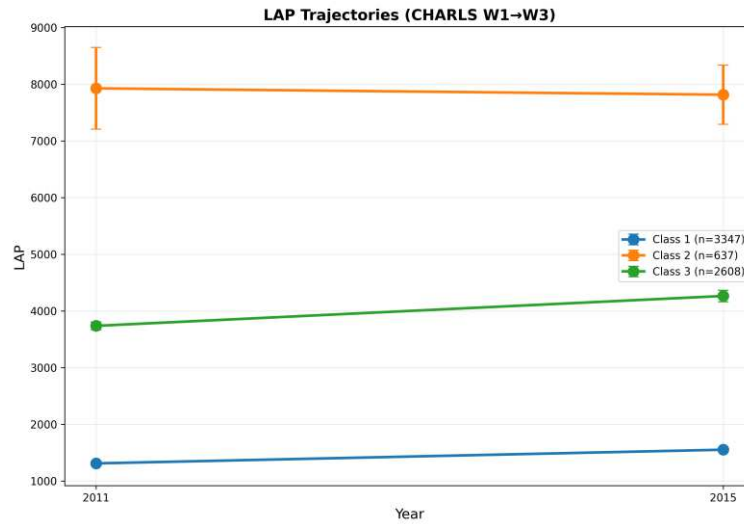
Figures

Study Design: Metabolic Phenotypes and MASLD Trajectories
Dual-Cohort Cross-Sectional Clustering + Longitudinal Trajectory Validation









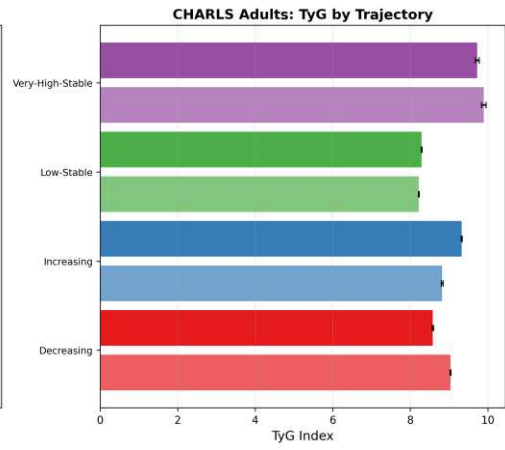
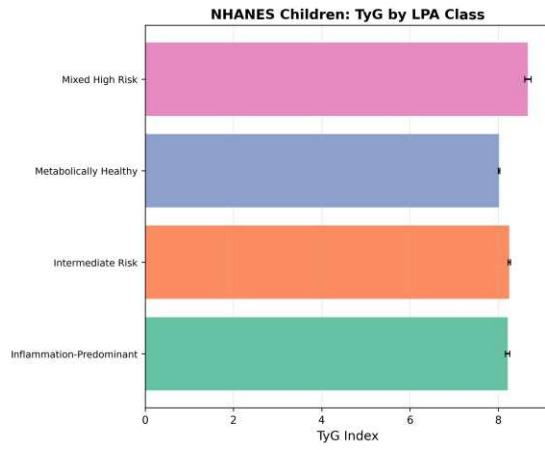


Figure Legends

Figure 1. Study Design Flow Diagram.

Dual-cohort study design integrating pediatric cross-sectional latent profile analysis (NHANES 1999-2020, children 12-19 years, N = 4,901) with adult longitudinal TyG index trajectory modeling (CHARLS 2011-2020, adults ≥ 45 years, N = 7,473). The cross-cohort validation component links childhood metabolic phenotypes to adult TyG trajectory classes.

Figure 2. LPA Model Selection Criteria.

Model fit indices for LPA solutions with 2 to 6 classes. (A) AIC and BIC values; (B) Standardized entropy (≥ 0.70 threshold indicated); (C) LMR-LRT p-values presented as $-\log_{10}(p)$. The 4-class solution was selected based on the combination of high entropy (0.870), significant LMR-LRT ($p < 0.001$), clinical interpretability, and adequate class sizes.

Figure 3. Metabolic-Inflammatory Profiles of the Four LPA Classes.

(A) Radar plot showing standardized z-score profiles across eight variables for each LPA class. The Mixed High Risk class (orange) shows the most extreme elevations, while the Metabolically Healthy class (green) clusters near zero. (B) Heatmap of class-specific z-score means. Warm colors indicate above-mean values; cool colors indicate below-mean values.

Figure 4. MASLD Prevalence by Pediatric LPA Class.

Bar chart showing the proportion of children with MASLD ($\text{FLI} \geq 60$) within each LPA class. The dashed horizontal line indicates the overall MASLD prevalence (12.2%). Mixed High Risk class shows 64.4% MASLD prevalence, compared to 0.04% in the Metabolically Healthy class.

Figure 5. Kaplan-Meier All-Cause Mortality by LPA Class (NHANES).

(A) Survival curves for the full pediatric cohort with linked mortality data (N = 1,244). (B) Survival curves restricted to children with MASLD (N = 283). Tick marks indicate censored observations. Log-rank test $p = 0.01$ for panel (A). Cox proportional hazards models were underpowered due to low event counts (n = 28 deaths).

Figure 6. Longitudinal Trajectories in the CHARLS Cohort.

(A) TyG index trajectories from Wave 1 (2011) to Wave 3 (2015): Low-Stable (blue, 46.0%), Decreasing (green, 21.5%), Increasing (red, 22.7%), and Very-High-Stable (orange, 9.8%). (B) Log-CRP trajectories by 3-class solution. (C) LAP trajectories by 3-class solution. Lines represent class-specific means; error bars indicate 95% CIs.

Figure 7. TyG Trajectories and Clinical Outcomes (CHARLS).

(A) Kaplan-Meier all-cause mortality survival curves by TyG trajectory class. Log-rank test $p < 0.001$. (B) Forest plot showing odds ratios (MASLD, CVD, diabetes) and hazard ratios (mortality) for each trajectory class versus Low-Stable reference. Red points indicate $p < 0.05$; blue points indicate $p \geq 0.05$.

Figure 8. Cross-Cohort TyG Index Distribution Comparison.

Side-by-side comparison of TyG index distributions between NHANES pediatric LPA classes (left) and CHARLS adult TyG trajectory classes (right). The parallel ordering of TyG levels across pediatric phenotypes and adult trajectories supports the continuity of metabolic risk across the lifespan. Boxes represent interquartile ranges; whiskers extend to $1.5 \times$ IQR; horizontal lines indicate medians.

Supplementary Material

Supplementary Table 1. Baseline characteristics of NHANES pediatric sample by MASLD status (available upon request).

Supplementary Table 2. Subgroup analysis for MASLD ~ LPA class association stratified by sex, age, and obesity.

Supplementary Table 3. Sensitivity analysis comparing LPA solutions using different variable subsets.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [CoxMortality.csv](#)
- [LPAModelSelection.csv](#)
- [CoxMortalityMASLD.csv](#)
- [SubgroupAnalysis.csv](#)
- [LPAClassProfiles.csv](#)
- [SupplementaryMissingData.csv](#)
- [Table3RegressionResults.csv](#)
- [SensitivityAnalysis.csv](#)
- [TyGTrajectoryModelSelection.csv](#)
- [Table5TrajectoryOutcomes.csv](#)
- [Table4TrajectoryBaseline.csv](#)
- [Table2ClassComparison.csv](#)
- [charlstrajjectoryresult.csv](#)
- [charlsbaseline.csv](#)
- [nhaneslpready.csv](#)
- [nhaneslpresult.csv](#)
- [charlslongitudinal.csv](#)