

METS-IR combined with four body shape indices and progression to diabetes or reversion to normoglycemia in middle-aged and older adults with prediabetes: a longitudinal analysis of the China Health and Retirement Longitudinal Study

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Research Article

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Abstract

Background

Combining metabolic and anthropometric information may help characterize the heterogeneous course of prediabetes. We examined four products of metabolic score for insulin resistance (METS-IR) and body shape indices in a three-state framework that included progression to diabetes and reversion to normoglycemia.

Methods

This longitudinal analysis used the 2011–2012 and 2015 examinations of the China Health and Retirement Longitudinal Study. The cohort was independently reconstructed from wave-specific source records and included adults aged ≥ 45 years with baseline prediabetes and recorded fasting blood draws at both examinations. Baseline METS-IR was multiplied by body roundness index, Chinese visceral adiposity index, weight-adjusted waist index, or a body shape index. Multinomial logistic regression estimated odds ratios with community-clustered 95% confidence intervals, using maintained prediabetes as the reference. Restricted cubic splines and model-standardized probabilities characterized nonlinear associations and the distribution of all three glycemic states.

Results

Among 2,134 participants, 329 progressed to diabetes, 467 reverted to normoglycemia, and 1,338 maintained prediabetes. The fully adjusted analysis included 2,116 participants from 343 communities. All four baseline products were associated with higher progression odds, with odds ratios per standard deviation ranging from 1.46 to 1.53 and all 95% confidence intervals excluding one. The product with a body shape index was also associated with lower reversion odds (odds ratio 0.87, 95% confidence interval 0.76–0.99). Across products, spline-standardized progression probabilities increased and reversion probabilities decreased between the lowest- and highest-quartile representative values. Probability differences ranged from 14.8 to 17.1 percentage points for progression and –9.2 to –7.7 percentage points for reversion; all contrast confidence intervals excluded zero. Progression associations remained positive under an alternative endpoint definition omitting glycated hemoglobin.

Conclusions

Baseline METS-IR–body shape products characterized glycemic progression and reversion among Chinese adults with prediabetes. Relative odds and standardized three-state probabilities describe different aspects of glycemic heterogeneity and inform further research on combined metabolic and anthropometric assessment.

Background

Prediabetes identifies glycemia above the normal range but below conventional diabetes thresholds. It is a heterogeneous state rather than a uniformly progressive disease [1, 2]. National survey data document a substantial burden of diabetes and prediabetes in China [3], while observations in older adults show that progression, regression, and death can have different frequencies across definitions and populations [4]. Reversion matters as well as progression: in the Diabetes Prevention Program Outcomes Study, participants who returned to normal glucose regulation subsequently had a lower diabetes risk [5]. The original Diabetes Prevention Program and Finnish prevention trial established that intervention can delay diabetes in selected high-risk populations [6, 7]. In China, the Da Qing trial and its long-term follow-up provide complementary prevention evidence [8, 9]. A marker that distinguishes glycemic outcomes might help describe risk heterogeneity. Its observational association does not establish an intervention effect.

Insulin resistance and impaired beta-cell compensation are linked to dysglycemia, and obesity can contribute through altered lipid flux and adipose signaling [10, 11]. In a Chinese study using magnetic resonance imaging, visceral fat was associated with newly diagnosed diabetes independently of BMI and subcutaneous fat [12]. Direct measures of insulin sensitivity and body composition are useful research tools, although the glucose clamp and insulin-based homeostasis model require information beyond routine anthropometry and basic lipid testing [13, 14]. Bello-Chavolla and colleagues developed the non-insulin-based metabolic score for insulin resistance (METS-IR) from fasting glucose, triglycerides, high-density lipoprotein cholesterol, and body mass index (BMI), validating it against insulin sensitivity measurements and evaluating incident diabetes [15]. A subsequent CHARLS study linked repeated METS-IR measurements with new-onset stroke [16], an outcome beyond glycemic conversion. Whether the score performs similarly in selected prediabetes cohorts remains uncertain.

Body roundness index (BRI), Chinese visceral adiposity index (CVAI), weight-adjusted waist index (WWI), and a body shape index (ABSI) summarize different combinations of waist, height, weight, age, and lipids [17, 18]. WWI standardizes waist for weight, whereas ABSI standardizes it for BMI and height [19, 20]. Multiplying these indices by METS-IR could emphasize different metabolic and body shape profiles. Such multiplication also reuses information already present in METS-IR, so a stronger association would not by itself demonstrate a biological interaction or superior prediction. Relevant evidence already exists: Liu and colleagues examined METS-IR and both directions of glycemic conversion in a Chinese multicenter cohort [21]. Other Chinese cohort analyses reported associations with reversion, including sex-specific analyses and comparisons of several insulin resistance surrogates [22–24]. The related clinical database settings limit treating these reports as independent replications.

Evidence from other populations supports considering glycemic severity and adiposity together. In UK Biobank, HbA1c strata and waist circumference distinguished diabetes risk among adults with prediabetes [25]. Another analysis related estimated visceral adipose tissue and Mediterranean lifestyle adherence to incident diabetes in this population [26]. In rural Chinese adults with normal BMI, the TyG

index was associated with incident diabetes [27]. These findings support joint assessment, although they do not establish whether multiplication preserves more useful information than separate component variables.

Wang and colleagues applied triglyceride–glucose (TyG)–obesity products to baseline and repeated China Health and Retirement Longitudinal Study (CHARLS) measurements, studying progression, reversion, and two-wave change patterns [28]. Related CHARLS studies examined cumulative lipid-index exposure and C-reactive protein–TyG-derived indices in relation to these glycemic outcomes [29, 30]. Our primary analysis assessed four baseline METS-IR–body shape products in relation to subsequent glycemic states among middle-aged and older Chinese adults with prediabetes in CHARLS. Baseline information was separated from summaries that included endpoint glucose, with maintained status as the reference for both terminal outcomes. We examined standardized terminal-state probabilities, compared product models with single-score references, and evaluated two-wave summaries as exploratory endpoint associations. Progression and reversion results were reported separately, including null and direction-specific findings.

Methods

Study design and data sources

This secondary observational analysis used the 2011–2012 baseline and 2015 waves of the China Health and Retirement Longitudinal Study (CHARLS). CHARLS uses multistage sampling to study middle-aged and older adults in China [31]. We linked original blood, anthropometry, health, demographic, and community files across waves. The 2015 venous blood and biomarker program has been described previously [32]. Reporting followed the STROBE framework [33]. The paired-measurement samples were not treated as nationally representative.

Identifiers were normalized as character strings, and one-to-one joins were checked within every source. Baseline diagnoses and education were taken from contemporaneous raw interviews because later harmonized histories can include retrospective corrections. Endpoint diagnosis was reconstructed from new-interview and repeat-interview branches, including preloaded diagnoses, verification responses, and reports since the preceding interview. Modern glucose-lowering medication included insulin; traditional medicine alone was not coded as a positive modern-medication response. Before model fitting, source reconstruction covered field labels, question universes, special missing values, units, and derived variables. Supplementary Tables S1A–B map the source fields. A second implementation independently rebuilt the primary cohort from the source CHARLS files. Supplementary Table S1C reports its scope and results. Current-to-historical membership differences are reported in Supplementary Tables S12C–D.

Quality control included checks of sequential exclusions, mutually exclusive endpoint states, formulas recalculated from raw fields, and boundary truth tables for glucose and HbA1c. Independent current-cohort reconstruction reproduced all 2,134 participants and the 1,338/329/467 state counts exactly.

Membership and 21 person-level diagnosis, medication, state, and two-wave index objects had zero disagreements. Checks required exact categorical and missingness agreement and an absolute numeric tolerance of 1×10^{-7} . The maximum numeric difference was zero. The retained historical-cohort audit also had zero mismatches across 18 objects for 2,107 participants. For threshold decisions, FPG was rounded to two decimal places and HbA1c to one decimal place; this prevents Stata binary-float storage from moving displayed boundary values such as 5.7% below the intended threshold. Unrounded values were retained for all continuous index calculations.

Participants and glycemic ascertainment

Eligible participants were at least 45 years old at baseline and had glucose and glycated hemoglobin (HbA1c) measured at baseline and endpoint. Because the original METS-IR formula uses fasting glucose and fasting triglycerides [15], the primary analysis required blood draws recorded as fasting at both examinations. Baseline prediabetes used the 2026 American Diabetes Association thresholds: decision-scale fasting plasma glucose ≥ 100 and < 126 mg/dL or HbA1c $\geq 5.7\%$ and $< 6.5\%$ [34]. Baseline diabetes was defined by decision-scale glucose ≥ 126 mg/dL, HbA1c $\geq 6.5\%$, reported physician-diagnosed diabetes or high blood sugar, or modern glucose-lowering medication. Participants with baseline diabetes or unascertainable baseline diagnosis/medication history were excluded.

The primary baseline cohort required only the components needed to calculate all four baseline products. Endpoint anthropometric and lipid components were not required for entry into the primary cohort. The separate two-wave exploratory cohort also required the corresponding endpoint components. Endpoint history had to be ascertainable unless a laboratory value independently satisfied a diabetes criterion. Progression was defined by endpoint glucose ≥ 126 mg/dL, HbA1c $\geq 6.5\%$, reported diabetes, or modern glucose-lowering medication. Reversion required glucose < 100 mg/dL and HbA1c $< 5.7\%$ with no positive diabetes or medication history. Maintained status comprised the remaining participants. These states describe the 2015 examination; no transition date or intervening state was observed.

Exposure definitions

METS-IR was calculated as $\ln(2 \times \text{glucose} + \text{triglycerides}) \times \text{BMI} / \ln(\text{HDL-C})$, using mg/dL for glucose, triglycerides, and high-density lipoprotein cholesterol (HDL-C), and kg/m² for body mass index (BMI) [15]. BRI, CVAI, WWI, and ABSI were calculated from their original equations [17–20]. Each product was METS-IR multiplied by the corresponding body shape index. Baseline products were the primary exposures and were standardized using the eligible baseline cohort distribution.

BMI was weight in kilograms divided by squared height in meters. With waist and height in meters, BRI was $364.2 - 365.5 \times \sqrt{1 - (\text{waist}/(\pi \times \text{height}))^2}$ [17]. WWI divided waist circumference in centimeters by the square root of weight in kilograms [19], whereas ABSI divided waist in meters by BMI to the two-

thirds power and the square root of height in meters [20]. CVAI used triglycerides and HDL-C in mmol/L and waist in centimeters: for men, $-267.93 + 0.68 \times \text{age} + 0.03 \times \text{BMI} + 4.00 \times \text{waist} + 22.00 \times \log_{10}(\text{triglycerides}) - 16.32 \times \text{HDL-C}$; for women, $-187.32 + 1.71 \times \text{age} + 4.23 \times \text{BMI} + 1.12 \times \text{waist} + 39.76 \times \log_{10}(\text{triglycerides}) - 11.66 \times \text{HDL-C}$ [18]. Triglycerides and HDL-C in mg/dL were divided by 88.57 and 38.67, respectively. Wave-specific age was used for CVAI. Continuous source values were not rounded before index calculation.

For descriptive two-wave analyses, we used the arithmetic mean of baseline and endpoint product values. These means include endpoint glucose that also contributes to endpoint classification and therefore are endpoint-informed, not prospectively available cumulative exposures. K-means used baseline and endpoint values standardized on one shared scale, three prespecified classes, 100 starts, and a fixed seed. Classes were ordered by their baseline centroids and named low initial, middle initial, and high initial. Tail-treatment sensitivity winsorized each wave-specific product at its 1st and 99th percentiles. A separate targeted analysis removed the two records with queried endpoint weights from the two-wave exposure module while retaining them in the baseline analysis. The targeted per-SD analysis retained the mean and SD estimated in the original 2,037-person two-wave eligible cohort. Repeated K-means used a subset of the original shared-scale coordinates without re-estimating the standardization constants.

Covariates, missing data, and sampling clusters

Model 1 included baseline age and sex. Model 2 additionally included education, marriage or partnership, rural residence, current smoking, alcohol consumption during the preceding year, and reported heart disease and stroke. Model 3 further included baseline low-density lipoprotein cholesterol, creatinine, HbA1c, and standardized log high-sensitivity C-reactive protein. BMI, waist, triglycerides, and HDL-C were not repeated as covariates in the primary product association models because they define the exposures; they were retained explicitly in the component-information comparison. Primary models used observations complete for their stated covariates, and model-specific outcome counts are reported.

The Harmonized CHARLS *communityID* field was linked to every participant. Point estimates came from multinomial maximum likelihood. Confidence intervals and joint Wald tests used a sandwich covariance after summing individual score contributions within communities. The finite-sample multiplier was $G/(G - 1) \times (N - 1)/(N - K)$, where G is the number of nonempty communities in the fitted sample, N is the model-specific complete-case sample size, and K is the total number of regression coefficients across both nonreference logits, including intercepts. The covariance accounts for within-community correlation; estimates were not survey-weighted national estimates.

Model 1 had no missing covariates within the eligible cohort. Model 2 and Model 3 used complete records for their respective covariates. State counts are reported separately for the full cohort and each fitted model. We did not impute exposure, outcome, or endpoint attendance. Standard chained-equation

approaches can address some covariate missingness [35, 36], but imputing a small number of baseline covariates cannot reconstruct unobserved endpoint glycemic states.

Statistical analysis

Continuous characteristics were summarized by medians and interquartile ranges; categorical characteristics by observed counts, denominators, and percentages. Descriptive group comparisons in Table 1 used the Kruskal–Wallis test for continuous variables and Pearson's chi-square test for categorical variables; these tests were unweighted. Multinomial logistic regression modeled progression and reversion relative to maintained status, yielding odds ratios (ORs) with 95% confidence intervals. ORs were not interpreted as risk ratios [37]. Products were analyzed continuously per standard deviation as the primary parameterization and by quartile as a secondary description, consistent with cautions about information loss from categorization [38]. Four-knot restricted cubic splines used the 5th, 35th, 65th, and 95th percentiles. Community-robust joint Wald tests evaluated the six spline coefficients across both nonreference logits for overall association and the four nonlinear coefficients for nonlinearity. Model-standardized terminal probabilities and cluster-robust delta-method intervals were evaluated at the observed within-quartile medians from the 2,134-person eligible baseline cohort. Those raw representative values were standardized with the same unrounded eligible-cohort mean and SD used for the exposures. Probabilities were then averaged over the 2,116-person Model 3 covariate distribution. Q4-minus-Q1 probability-difference intervals used the joint gradient contrast from the same spline model and cluster-robust covariance; they were not obtained by subtracting separate interval endpoints.

Table 1
Baseline characteristics by terminal glycemic state

Characteristic	All N = 2,134	Maintained N = 1,338	Progression N = 329	Reversion N = 467	P	Missing, n
Age, years	59.00 [53.00, 65.00]	59.00 [53.00, 65.00]	60.00 [54.00, 67.00]	57.00 [51.00, 64.00]	< 0.001	0
Male	991/2134 (46.4%)	597/1338 (44.6%)	137/329 (41.6%)	257/467 (55.0%)	< 0.001	0
Female	1143/2134 (53.6%)	741/1338 (55.4%)	192/329 (58.4%)	210/467 (45.0%)	—	0
Education: lower level	1957/2134 (91.7%)	1237/1338 (92.5%)	304/329 (92.4%)	416/467 (89.1%)	0.121	0
Education: high/vocational school	151/2134 (7.1%)	88/1338 (6.6%)	19/329 (5.8%)	44/467 (9.4%)	—	0
Education: college or higher	26/2134 (1.2%)	13/1338 (1.0%)	6/329 (1.8%)	7/467 (1.5%)	—	0
Married or partnered	1874/2134 (87.8%)	1172/1338 (87.6%)	284/329 (86.3%)	418/467 (89.5%)	0.368	0
Rural residence	1414/2134 (66.3%)	878/1338 (65.6%)	229/329 (69.6%)	307/467 (65.7%)	0.378	0
Current smoker	602/2131 (28.2%)	372/1337 (27.8%)	87/328 (26.5%)	143/466 (30.7%)	0.374	3
Alcohol in previous year	699/2134 (32.8%)	446/1338 (33.3%)	89/329 (27.1%)	164/467 (35.1%)	0.044	0
Reported heart disease	266/2124 (12.5%)	153/1331 (11.5%)	57/328 (17.4%)	56/465 (12.0%)	0.015	10
Reported stroke	39/2129 (1.8%)	25/1334 (1.9%)	9/329 (2.7%)	5/466 (1.1%)	0.223	5
BMI, kg/m ²	23.43 [21.07, 26.05]	23.24 [20.99, 25.90]	25.05 [22.53, 27.58]	22.88 [20.74, 25.25]	< 0.001	0

Values are medians [interquartile ranges] or observed n/N (%). Continuous-variable P values use the Kruskal–Wallis test; categorical-variable P values use Pearson's chi-square test and are shown once per variable. Tests are descriptive and unweighted. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C/LDL-C, high-/low-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; OR, odds ratio; CI, confidence interval; SD, standard deviation; AUC, area under the receiver operating characteristic curve.

Characteristic	All N = 2,134	Maintained N = 1,338	Progression N = 329	Reversion N = 467	P	Missing, n
Waist, cm	85.50 [79.00, 93.00]	85.00 [78.60, 93.00]	90.00 [83.40, 97.00]	83.50 [77.90, 90.00]	< 0.001	0
FPG, mg/dL	106.56 [102.78, 112.27]	106.38 [102.60, 111.96]	109.26 [104.40, 115.56]	105.48 [102.42, 110.16]	< 0.001	0
HbA1c, %	5.20 [4.90, 5.50]	5.20 [5.00, 5.50]	5.40 [5.10, 5.60]	5.00 [4.80, 5.20]	< 0.001	0
Triglycerides, mg/dL	107.53 [77.00, 157.31]	107.08 [77.00, 154.88]	115.93 [84.96, 176.12]	101.78 [72.13, 151.78]	< 0.001	0
HDL-C, mg/dL	49.10 [40.21, 60.70]	49.68 [40.98, 61.47]	46.39 [37.50, 57.60]	49.87 [40.40, 60.89]	< 0.001	0
LDL-C, mg/dL	117.91 [96.65, 141.50]	119.65 [98.20, 143.43]	121.78 [100.52, 144.98]	110.76 [89.40, 132.12]	< 0.001	1
Creatinine, mg/dL	0.75 [0.64, 0.87]	0.75 [0.64, 0.87]	0.75 [0.64, 0.85]	0.77 [0.66, 0.88]	0.155	0
hsCRP, mg/L	1.02 [0.56, 2.12]	1.01 [0.56, 2.14]	1.30 [0.73, 2.52]	0.85 [0.49, 1.88]	< 0.001	0
METS-IR	34.98 [30.23, 40.73]	34.69 [29.96, 40.20]	38.35 [33.02, 44.23]	33.86 [29.82, 39.28]	< 0.001	0
METS-IR × BRI	146.99 [101.45, 206.92]	143.85 [100.01, 201.43]	193.62 [132.90, 248.21]	131.53 [92.76, 182.09]	< 0.001	0
METS-IR × CVAI	3350.98 [2177.78, 5091.67]	3298.95 [2140.50, 4950.69]	4623.72 [3055.93, 6281.59]	2991.78 [1919.44, 4419.20]	< 0.001	0
METS-IR × WWI	391.17 [330.09, 466.42]	387.54 [327.62, 459.69]	444.29 [376.45, 522.22]	371.28 [318.40, 437.72]	< 0.001	0
Values are medians [interquartile ranges] or observed n/N (%). Continuous-variable P values use the Kruskal–Wallis test; categorical-variable P values use Pearson's chi-square test and are shown once per variable. Tests are descriptive and unweighted. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C/LDL-C, high-/low-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; OR, odds ratio; CI, confidence interval; SD, standard deviation; AUC, area under the receiver operating characteristic curve.						

Characteristic	All N = 2,134	Maintained N = 1,338	Progression N = 329	Reversion N = 467	P	Missing, n
METS-IR × ABSI	2.90 [2.50, 3.41]	2.88 [2.49, 3.37]	3.25 [2.83, 3.73]	2.75 [2.44, 3.24]	< 0.001	0
Values are medians [interquartile ranges] or observed n/N (%). Continuous-variable P values use the Kruskal–Wallis test; categorical-variable P values use Pearson's chi-square test and are shown once per variable. Tests are descriptive and unweighted. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C/LDL-C, high-/low-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; OR, odds ratio; CI, confidence interval; SD, standard deviation; AUC, area under the receiver operating characteristic curve.						

We tabulated baseline prediabetes sources as fasting-glucose only, HbA1c only, or both. Progression sources were cross-classified by glucose, HbA1c, diagnosis, and medication. A sensitivity analysis reassigned endpoint states using FPG, diagnosis, and medication without using endpoint HbA1c. Progression required decision-scale FPG ≥ 126 mg/dL, reported diagnosis, or modern medication. Participants without those criteria and with ascertainable negative history were classified as FPG-defined intermediate when decision-scale FPG was ≥ 100 and < 126 mg/dL or FPG-defined normal when decision-scale FPG was < 100 mg/dL. Participants whose history was unascertainable and whose FPG did not establish diabetes were unclassifiable. The FPG-defined normal state was not interpreted as full glycemic reversion. To examine selection, baseline-eligible participants with and without an ascertainable endpoint were compared using standardized mean differences for age, sex, glycemic measures, METS-IR, BMI, waist, heart disease, and stroke. Death was not recoded as ordinary missing glycemia, and inverse-probability weighting was not used because the available operational files did not supply a validated death-versus-other-nonattendance mechanism for this estimand.

All comparisons of product and component-information models used the same Model 3 sample. We fitted a METS-IR reference model, a METS-IR-plus-body-index model, a model retaining both main effects and their interaction, the product-only model, and a retained-components + body-index model containing fasting glucose, triglycerides, HDL-C, BMI, and the relevant body index. This last model was not a raw waist/height/weight model. Fixed four-knot spline versions gave METS-IR and each product the same nonlinear flexibility. Apparent AIC, multinomial log loss, Brier score, and one-versus-rest AUCs were descriptive. Multiclass Brier score was the participant-level sum of squared errors across the three class probabilities, averaged across participants. Each ROC used the fitted multinomial probability to contrast one nonreference state with the other two states: progression versus 1,789 other participants and reversion versus 1,654 other participants. Each curve evaluated all 2,116 participants. AUCs were computed with standard ROC methods [39, 40] and are presented as point estimates without inferential intervals because no community-resampled validation was performed. The metrics were not presented as internal or external validation, and no net-reclassification claim was made [41, 42]. Analyses used R 4.5.2 with fixed seeds; two-sided P values for secondary analyses were descriptive.

Results

Participant selection and baseline sources

The source inventory contained 25,586 identifiers. Sequential screening retained 16,931 participants aged at least 45 years, 11,114 with baseline glucose and HbA1c, 4,819 with standard-threshold prediabetes and ascertainable non-diabetes history, 3,160 with paired endpoint glycemic markers, 3,137 with ascertainable endpoint history or laboratory diabetes, 2,703 with a fasting endpoint draw, 2,482 also recorded fasting at baseline, and 2,134 with complete baseline components (Fig. 1). Requiring endpoint index components was reserved for the two-wave exploratory cohort and reduced its size to 2,037.

The primary cohort included 1,338 participants with maintained status, 329 with progression, and 467 with reversion. Among the 2,134 participants, 1,817 entered through fasting glucose alone, 97 through HbA1c alone, and 220 through both criteria (Supplementary Table S2). Progression criteria overlapped, and the evidence was grouped as follows: 140 participants met only the HbA1c criterion, 46 only the glucose criterion, 43 both laboratory criteria, 61 had diagnosis and/or medication without a laboratory threshold, and 39 had mixed laboratory and history/medication evidence; the mutually exclusive evidence groupings appear in Supplementary Table S2.

The baseline-eligible pool before endpoint requirements comprised 3,658 participants. Among those not entering the primary cohort, 1,144 lacked endpoint glucose or HbA1c, 18 had unascertainable endpoint history without laboratory diabetes, and 362 lacked a recorded fasting endpoint draw. Included and excluded participants had small standardized mean differences for the prespecified observed baseline features (absolute SMD range 0.012–0.076), although this does not exclude selection through unmeasured health, survival, or attendance processes (Supplementary Table S3).

Baseline distributions differed across terminal states for several glycemic and metabolic measures (Table 1). The products were highly correlated with METS-IR and with one another, consistent with their repeated components (Fig. 6; Supplementary Table S4). The Spearman correlation between the WWI and ABSI products was 0.99. Small differences in their ORs therefore should not be interpreted as evidence that one construction was superior.

Primary baseline associations

Model 1 included all 2,134 participants, Model 2 included 2,117, and Model 3 included 2,116 participants from 343 communities: 1,327 maintained status, 327 progressed, and 462 reverted. The METS-IR reference OR was 1.53 (95% CI 1.33–1.76) for progression and 0.91 (95% CI 0.79–1.05) for reversion. Product progression ORs per standard deviation were 1.46 (95% CI 1.27–1.67), 1.46 (95% CI 1.28–1.67), 1.53 (95% CI 1.33–1.75), and 1.51 (95% CI 1.32–1.72) for products with BRI, CVAI, WWI, and ABSI, respectively (Table 2; Fig. 2). The corresponding reversion estimates were 0.87 (95% CI 0.74–1.02), 0.90 (95% CI 0.79–1.04), 0.87 (95% CI 0.76–1.01), and 0.87 (95% CI 0.76–0.99); only the ABSI-product interval

excluded one. OR magnitudes for differently scaled composite variables were not treated as predictive rankings.

Table 2
Fasting baseline product associations with terminal glycemic states

Product	Outcome	Model 1	Model 2	Model 3	Model 3 P
METS-IR × BRI	Progression	1.553 (1.367–1.765)	1.546 (1.355–1.764)	1.456 (1.273–1.666)	< 0.001
METS-IR × BRI	Reversion	0.856 (0.742–0.987)	0.839 (0.728–0.968)	0.871 (0.744–1.021)	0.088
METS-IR × CVAI	Progression	1.526 (1.349–1.726)	1.525 (1.341–1.735)	1.463 (1.284–1.667)	< 0.001
METS-IR × CVAI	Reversion	0.908 (0.800–1.031)	0.890 (0.784–1.010)	0.904 (0.788–1.038)	0.151
METS-IR × WWI	Progression	1.596 (1.403–1.815)	1.592 (1.395–1.816)	1.527 (1.334–1.748)	< 0.001
METS-IR × WWI	Reversion	0.887 (0.778–1.012)	0.870 (0.764–0.991)	0.874 (0.758–1.008)	0.064
METS-IR × ABSI	Progression	1.570 (1.383–1.781)	1.566 (1.375–1.783)	1.510 (1.322–1.725)	< 0.001
METS-IR × ABSI	Reversion	0.890 (0.784–1.010)	0.872 (0.769–0.989)	0.868 (0.757–0.994)	0.041
ORs per eligible-cohort SD with maintained status as reference. N: Model 1 = 2,134; Model 2 = 2,117; Model 3 = 2,116 (343 communities). In the same Model 3 sample, the METS-IR reference ORs were 1.530 (1.332–1.756) for progression and 0.913 (0.793–1.051) for reversion. Model 1: baseline age and sex. Model 2: Model 1 plus education, marriage/partnership, rural residence, heart disease, stroke, current smoking, and past-year drinking. Model 3: Model 2 plus baseline LDL-C, creatinine, HbA1c, and standardized log-hsCRP. Confidence intervals use community-clustered sandwich covariance. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; BMI, body mass index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; HDL-C/LDL-C, high-/low-density lipoprotein cholesterol; hsCRP, high-sensitivity C-reactive protein; OR, odds ratio; CI, confidence interval; SD, standard deviation; AUC, area under the receiver operating characteristic curve.					

Progression odds increased across exposure quartiles, although some middle-quartile confidence intervals included one. Q4-versus-Q1 progression ORs were 3.58 for BRI, 2.71 for CVAI, 2.94 for WWI, and 2.79 for ABSI products. Q4 reversion estimates were below one; intervals excluded one for WWI (OR 0.698, 95% CI 0.495–0.986) and ABSI (OR 0.668, 95% CI 0.476–0.939). These secondary contrasts were not treated as clinical thresholds (Supplementary Table S5).

Community-robust joint Wald tests supported overall spline associations for all four products (all $P < 0.001$). Joint nonlinearity P values were < 0.001 for BRI, 0.046 for CVAI, 0.011 for WWI, and 0.041 for

ABSI products (Fig. 3; Supplementary Table S6). Spline-standardized progression probabilities rose from approximately 9–10% at Q1 medians to 24–26% at Q4 medians, corresponding to Q4-minus-Q1 differences of 14.8 to 17.1 percentage points. Reversion probabilities declined from approximately 25–26% to about 17%, with differences of -9.2 to -7.7 percentage points. All eight direction-specific contrast intervals excluded zero (Fig. 3; Table 3). The joint tests and probabilities describe model shape without establishing clinical cut points.

Table 3
Model-standardized probabilities at quartile medians

Product	State	At Q1 group median	At Q2 group median	At Q3 group median	At Q4 group median
METS-IR × BRI	Maintained	65.8 (62.0–69.4)	66.0 (63.5–68.4)	62.6 (59.8–65.4)	57.2 (53.4–61.0)
METS-IR × BRI	Progression	8.8 (6.8–11.3)	10.0 (8.5–11.7)	17.2 (15.0–19.6)	25.9 (22.7–29.5)
METS-IR × BRI	Reversion	25.4 (21.9–29.3)	24.0 (21.5–26.7)	20.2 (17.6–23.0)	16.8 (14.0–20.1)
METS-IR × CVAI	Maintained	65.4 (61.7–68.8)	65.5 (63.0–67.8)	63.2 (60.4–66.0)	58.3 (54.7–61.7)
METS-IR × CVAI	Progression	9.6 (7.5–12.2)	10.4 (8.9–12.1)	16.6 (14.4–19.1)	24.4 (21.4–27.7)
METS-IR × CVAI	Reversion	25.0 (21.7–28.7)	24.1 (21.6–26.8)	20.2 (17.5–23.0)	17.3 (14.6–20.4)
METS-IR × WWI	Maintained	65.6 (61.9–69.1)	65.3 (62.5–68.1)	62.6 (59.6–65.6)	58.0 (54.2–61.7)
METS-IR × WWI	Progression	8.6 (6.7–11.0)	10.2 (8.6–12.1)	17.8 (15.4–20.4)	25.2 (22.1–28.7)
METS-IR × WWI	Reversion	25.8 (22.3–29.6)	24.4 (21.2–27.9)	19.6 (16.9–22.5)	16.8 (13.8–20.3)
METS-IR × ABSI	Maintained	65.2 (61.5–68.6)	64.9 (62.0–67.6)	62.9 (59.9–65.8)	58.7 (55.0–62.3)
METS-IR × ABSI	Progression	8.9 (6.9–11.3)	10.6 (9.0–12.5)	17.4 (15.0–20.1)	24.5 (21.4–27.9)
METS-IR × ABSI	Reversion	26.0 (22.5–29.7)	24.5 (21.4–28.0)	19.6 (17.0–22.6)	16.8 (13.8–20.2)
Percentages (95% CIs), averaged over the 2,116-person Model 3 distribution. Points represent within-quartile median product values from the 2,134-person eligible baseline cohort (Supplementary Table S13A). Before prediction, these raw values were standardized with the same eligible-cohort mean and SD. They are not quartile cut points. Intervals use community-clustered delta-method covariance. Joint-gradient Q4-minus-Q1 contrasts are shown in Fig. 3 and Supplementary Table S13C. These are model-based probabilities, not intervention effects. Model 1: baseline age and sex. Model 2: Model 1 plus education, marriage/partnership, rural residence, heart disease, stroke, current smoking, and past-year drinking. Model 3: Model 2 plus baseline LDL-C, creatinine, HbA1c, and standardized log-hsCRP. Confidence intervals use community-clustered sandwich covariance.					

When endpoint HbA1c was omitted from state assignment, 2,133 participants remained classifiable and one participant was unclassifiable because history was unknown and FPG did not establish diabetes. Of the 140 primary progression cases identified by HbA1c alone, 85 mapped to the FPG-defined intermediate state, 54 to the FPG-defined normal state, and one was unclassifiable. The Model 3

sensitivity sample contained 2,115 participants: 622 FPG-defined intermediate, 187 progression, and 1,306 FPG-defined normal. Progression ORs remained above one for all four products, ranging from 1.29 (95% CI 1.11–1.48) to 1.35 (95% CI 1.15–1.58) (Fig. 4; Supplementary Table S7). Both the case composition and the reference-state composition changed, so the smaller ORs cannot be attributed to an isolated HbA1c contribution.

Two-wave profiles and recorded extremes

The two-wave exploratory cohort contained 2,037 participants; its Model 3 sample contained 2,020. Two-wave mean products were associated with progression and inversely associated with reversion, but they include the endpoint glucose measurement and are not prospective risk estimates (Fig. 2; Supplementary Table S8). The two largest endpoint CVAI-product values were reproduced from the source records, including weight changes from 55.3 to 147.6 kg and from 46.7 to 147.6 kg. No adjudicated correction was available, so the primary records were retained.

After 1st–99th percentile tail treatment and repeated K-means, exact class agreement was 97.9% for BRI, 92.1% for CVAI, 99.2% for WWI, and 99.1% for ABSI (Supplementary Figure S1; Supplementary Table S9). In the targeted analysis that removed only the two queried endpoint weights, 17 of 2,035 remaining participants changed CVAI class and at most three changed class for the other products. Two-wave Model 3 estimates were also similar after excluding those records on the original two-wave standardization scale. The two sensitivity analyses changed different sets of observations and addressed different questions; targeted deletion did not reproduce the larger CVAI sensitivity seen under broader tail treatment. Profiles remain secondary descriptions rather than clinical phenotypes.

Product versus retained component information

All head-to-head comparisons used the same 2,116 participants. The apparent one-versus-rest progression AUC was 0.706 for the METS-IR reference model and 0.701, 0.700, 0.704, and 0.702 for the BRI, CVAI, WWI, and ABSI product models, respectively. Reversion AUCs were 0.706 for METS-IR and 0.706–0.708 for the product models (Fig. 5; Supplementary Table S10). The reported point estimates have no inferential intervals, so small differences do not establish superiority.

Across all four body indices, the retained-components + body-index model had the lowest apparent log loss, Brier score, and AIC among the specified candidates. Relative to the linear product models, its ΔAIC ranged from -31.0 to -22.0 and its $\Delta\text{Brier} \times 1,000$ from -5.52 to -3.89 . Relative to the product splines, the corresponding ranges were -23.3 to -16.2 and -2.67 to -1.87 (Fig. 6). In matched-flexibility comparisons, neither linear nor spline products uniformly improved AIC or Brier score relative to the corresponding METS-IR specification (Fig. 5). Product, dual-index, interaction, spline, and retained-component comparisons were all evaluated in the fitting sample (Supplementary Table S11). They describe fit in this sample and do not provide a validated ranking for new participants.

Discussion

Fasting baseline METS-IR products with four body shape indices were associated with progression to diabetes relative to maintained glycemic status. The estimates remained positive after applying standard glycemic thresholds, separating the baseline cohort from the endpoint-component cohort, and accounting for community clustering. In the linear per-SD analysis, all reversion estimates were below one, but only the ABSI-product confidence interval excluded one. The weaker relative-odds evidence and the spline-standardized probability contrasts require separate interpretation.

The fasting and threshold definitions directly affected cohort membership. METS-IR was developed using fasting glucose and triglycerides [15], so documented fasting is required at baseline. The $100 \leq \text{FPG} < 126 \text{ mg/dL}$ interval follows the current ADA definition [34]. Threshold decisions were made at the source-recorded precision, preventing binary storage from moving displayed boundary values below their intended cut points. Most participants met the baseline prediabetes definition through fasting glucose alone. This helps explain the cohort median HbA1c below 5.7%, which alone does not invalidate the eligibility rule.

Earlier METS-IR studies addressed related but different questions. The original METS-IR study evaluated insulin sensitivity, visceral adiposity, and incident diabetes [15]. More recent Chinese cohorts examined glycemic conversion and reversion using different settings, eligibility rules, and comparators [21–24]. The closest comparison was Wang and colleagues' CHARLS analysis of TyG–obesity products [28]. TyG is itself a fasting glucose–triglyceride surrogate [43, 44], while METS-IR additionally incorporates BMI and HDL-C; the substitution changes the information represented by the score. Effect estimates from these studies therefore are not directly comparable. This study reconstructed a fasting cohort using standard glycemic thresholds and compared product models with models that retained component information.

Lipid measurements are relevant to the component comparisons. In PREVEND, fasting triglycerides within the normal range were associated with incident diabetes [45]. Chinese analyses evaluated nonlinear relationships between lipid-derived indices and prediabetes [46, 47]. Their outcomes concern the onset of dysglycemia, whereas our cohort already had prediabetes. These findings support examining component information and functional form. Their discrimination estimates cannot be transferred directly to our terminal-state models.

The primary and two-wave cohorts addressed different questions. The primary analysis related baseline information to the subsequent endpoint state and did not require endpoint waist, weight, triglycerides, or HDL-C. Requiring those measurements would further restrict follow-up participation without adding information needed for the baseline exposure or endpoint definition. The two-wave cohort remains appropriate for exploratory means and profiles, but it is smaller and incorporates endpoint glucose. Its stronger associations cannot be interpreted as prospective prediction because exposure and outcome use the same endpoint measurement.

Exposure timing distinguishes repeated-measure analyses. The CHARLS METS-IR stroke analysis used the 2011–2015 measurements to study subsequent stroke through 2020 [16]. By contrast, the glycemic

studies of cumulative AIP and CTI-derived indices used measurements spanning the examination at which glycemic transitions were assessed [29, 30]. Our baseline analysis keeps the exposure before the terminal state, while the two-wave summaries answer an endpoint-informed association question. Findings from cardiometabolic multimorbidity and cardiovascular studies using METS-IR or composite inflammatory-adiposity measures also concern different outcomes and comparators [48, 49].

Community-clustered covariance modestly changed uncertainty without reversing the primary progression results. Accounting for within-community correlation does not restore national representativeness, remove all selection bias, or replace survey weighting. The comparison of baseline-eligible participants showed small differences on measured features, but 1,524 otherwise baseline-eligible participants were not in the primary cohort, including 1,144 without endpoint glucose or HbA1c and 362 without documented endpoint fasting. Survival, health, and attendance may depend on variables not represented in the comparison. Death was not treated as ordinary missing glycemia; a competing-risk estimand would require a cohort and event-history structure different from the present terminal-state analysis [50, 51].

METS-IR already includes glucose, triglycerides, HDL-C, and BMI, while the body indices reuse anthropometric or metabolic components [15, 17–20, 52, 53]. Figure 6 shows the computational overlap and strong correlations among the four products; the matrix describes shared inputs and does not identify a causal pathway. A product-only coefficient is therefore not an interaction test, and attenuation after adjustment was not labeled causal mediation [54]. The comparisons examined distinct ways of retaining information: separate METS-IR and body-index terms, both main effects before an interaction, fasting glucose, triglycerides, HDL-C, BMI, and the relevant body index, or a fixed four-knot spline for METS-IR or the product. Spline terms improved the apparent fit of the product relative to its linear form, but the specified retained-components + body-index models had lower apparent loss, and product AUCs were essentially similar to the METS-IR reference. Across products, neither the linear nor spline specifications showed a consistent in-sample improvement over the corresponding METS-IR specification. These fitting-sample comparisons do not establish performance in new participants, validate the component model, or prove equivalence.

Studies of prediabetes remission have also evaluated added predictive information against reference models. In a Mexican cohort, adding selected metabolites did not significantly improve discrimination beyond age, fasting glucose, and BMI [55]. In the PREVIEW trial, novel oral glucose tolerance test metrics did not improve prediction of remission beyond conventional glycemic measures [56]. Both studies compared added information with an explicit reference model, although their populations and evaluation procedures differed. Our apparent comparisons address the narrower question of whether the specified product models fit better than their stated alternatives in this sample.

Progression and reversion were defined asymmetrically. Progression could be established by either laboratory threshold or positive diagnosis/medication history, whereas reversion required low values on both laboratory measures and no positive history. Adjustment for baseline HbA1c estimates each

product association conditional on that measured baseline marker; it does not isolate all aspects of initial glycemic severity. A confidence interval crossing one does not prove absence of a reversion association, but the linear per-SD results prevent describing the relative-odds evidence for recovery as equally strong. The continuous and Q4 ABSI reversion results, and the Q4 WWI result, should be interpreted within this broader pattern and the multiplicity of secondary comparisons.

The linear per-SD reversion OR and the spline Q4-minus-Q1 reversion probability difference answer different questions. The OR describes reversion relative to maintained status under a linear exposure parameterization, whereas the spline contrast describes the absolute change in model-standardized reversion probability between two representative exposure values. In the three-state model, $P(\text{reversion}) = \exp(\eta_R) / [1 + \exp(\eta_P) + \exp(\eta_R)]$, so the reversion probability depends on both nonreference logits rather than only the reversion coefficients. The two summaries also use different functional forms and exposure spans; whether their intervals exclude one or zero is therefore not interchangeable.

In the sensitivity analysis that omitted endpoint HbA1c, progression associations remained positive, although the estimates were smaller. Because both progression cases and the reference state were reconstituted, the change cannot be decomposed as the independent contribution of HbA1c. The direction persisted under a different endpoint definition, but laboratory misclassification remains possible and the result does not establish a preferred definition.

Definition-dependent differences also occur outside CHARLS. A UK Biobank analysis comparing ADA and WHO/IEC prediabetes criteria identified differences in cardiovascular risk stratification [57]. Although the cardiovascular outcome differs from diabetes progression, the comparison shows the relevance of the operational glycemic definition. In the Tehran Lipid and Glucose Study, regression to normoglycemia did not clearly reduce subsequent cardiovascular risk relative to persistent impaired glucose tolerance [58]. Consequently, a glycemic reversion endpoint should not be presented as evidence of cardiovascular benefit.

The nonlinear probability curves describe the associations without identifying thresholds. Community-clustered joint Wald tests combine information from progression and reversion; nonlinear terms were statistically detectable for all four products, although the CVAI and ABSI tests were close to 0.05. The curves were evaluated over the observed distribution, and higher products corresponded to higher model-standardized progression probabilities. Neither those tests nor the secondary quartile results establish a validated treatment cut point. Clinical prevention should remain grounded in established glycemic assessment and intervention evidence from the Diabetes Prevention Program, Finnish trial, and Da Qing studies [6–9], rather than a product threshold derived from this cohort.

The raw anthropometric files reproduced the two unusual endpoint weights. Without adjudicated replacements, the recorded values were retained. Excluding exactly those two records changed the two-wave associations little and changed few profile labels; wave-specific 1st/99th-percentile tail treatment produced a larger change in CVAI-product labels. The two analyses changed different sets of observations and cannot be compared participant by participant. The targeted deletion alone did not

reproduce the sensitivity to broader trait treatment. K-means uses squared distances and can be influenced by extreme values. Both checks are reported, and the profiles are treated as descriptive rather than latent biological trajectories. Two visits cannot establish a trajectory, and class membership should not guide care.

The two-wave product clusters differ from broader metabolic phenotyping. A Chinese multicohort study used multiple clinical features to identify prediabetes profiles with different future cardiometabolic risks [2]. The KORA F4/FF4 study found that phenotype-based clusters differed in diabetes risk, but high-risk clusters did not share a uniform inflammatory profile [59]. Those studies incorporated substantially richer metabolic information; their findings do not validate cluster labels derived from two measurements of a single product.

Two measurement occasions were insufficient to estimate latent trajectories or exact transition times. Machine-learning models or post hoc cutpoint searches might improve in-sample fit without answering the primary association question. The analysis focused on multinomial endpoint contrasts, with two-wave profiles retained as descriptive results.

Several limitations affect interpretation. Glycemic classifications were based on one examination per wave and were not systematically confirmed on a separate day, as clinical diagnosis generally requires in the absence of unequivocal hyperglycemia [34]. Inflammatory variation may also influence insulin resistance and glycemic progression, but the available high-sensitivity C-reactive protein measurement cannot resolve the broader causal pathways proposed in prior work [60, 61]. In the Strong Heart Study, body composition and inflammatory status accompanied incident diabetes [62]; a CHARLS study also related AIP and high-sensitivity C-reactive protein to new-onset diabetes [63]. These observational findings do not identify a causal inflammatory pathway in our analysis. Oral glucose tolerance testing was unavailable, and fasting status was recorded rather than independently timed. Self-reported diagnosis and medication may be misclassified. Model 3 conditions on baseline HbA1c, so it estimates product associations conditional on that baseline measurement rather than the total association of metabolic health. Missing-covariate complete-case analysis cannot repair missing endpoint visits. Multiple secondary comparisons remain exploratory. The multinomial OR is conditional on the maintained reference group and is neither a risk ratio nor a transition hazard [64]. Finally, all prediction metrics were apparent and require independent validation, calibration, and assessment of clinical consequences before use [65].

Measurement error may also move participants across clinical boundaries and attenuate or distort continuous associations [66]. Repeated confirmatory glycemic testing would distinguish persistent states from short-term biological and laboratory variation. Future studies should define a prediction time after all exposure measurements, preserve community or higher-level sampling structure during validation, and evaluate calibration and clinical consequences in a separate population. Resampling this endpoint-state cohort alone cannot satisfy these requirements.

The study independently reconstructed the 2,134-person cohort, separated baseline from endpoint-informed questions, accounted for community clustering, and reported unfavorable comparisons. Standard fasting and threshold definitions, individual-level source audits, outcome-source tables, analysis-set counts, and targeted sensitivity analyses document how participants, outcomes, and exposures were derived. The progression-source tables and selection comparison distinguish classification evidence from model output.

Conclusions

Among adults with prediabetes, fasting baseline METS-IR products with BRI, CVAI, WWI, and ABSI were associated with progression to diabetes compared with maintained glycemic status. Linear per-SD evidence for reversion was less consistent. The product models showed no consistent in-sample advantage over METS-IR, whereas the specified retained-components + body-index models had lower apparent loss. The two-wave means and profiles included endpoint information and remain descriptive. Deleting the two queried records changed results less than broader tail treatment, especially for CVAI. Prospective external validation and clinical-utility assessment are required before these products can be used beyond research.

Abbreviations

METS-IR, metabolic score for insulin resistance;

BRI, body roundness index;

CVAI, Chinese visceral adiposity index;

WWI, weight-adjusted waist index;

ABSI, a body shape index;

BMI, body mass index;

FPG, fasting plasma glucose;

HbA1c, glycated hemoglobin;

HDL-C/LDL-C, high-/low-density lipoprotein cholesterol;

hsCRP, high-sensitivity C-reactive protein;

OR, odds ratio; CI, confidence interval;

SD, standard deviation;

AUC, area under the receiver operating characteristic curve.

Declarations

Ethics approval and consent to participate

The original CHARLS protocol was approved by the Biomedical Ethics Review Committee of Peking University (IRB00001052-11015), and all participants provided informed consent.

Consent for publication

Not applicable.

Availability of data and materials

CHARLS data are available to qualified researchers through the official CHARLS data portal subject to registration and the study's data-use conditions.

Competing interests

The authors declare that there are no competing interests.

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Authors' contributions

Conceptualization, methodology, supervision, and project administration: YL and WX;

Software: YL;

Formal analysis and validation: YL;

Data curation: YL;

Investigation, resources and material collection: YL;

Writing-original draft preparation: YL;

Writing-reviewing and editing: WX.

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Figures

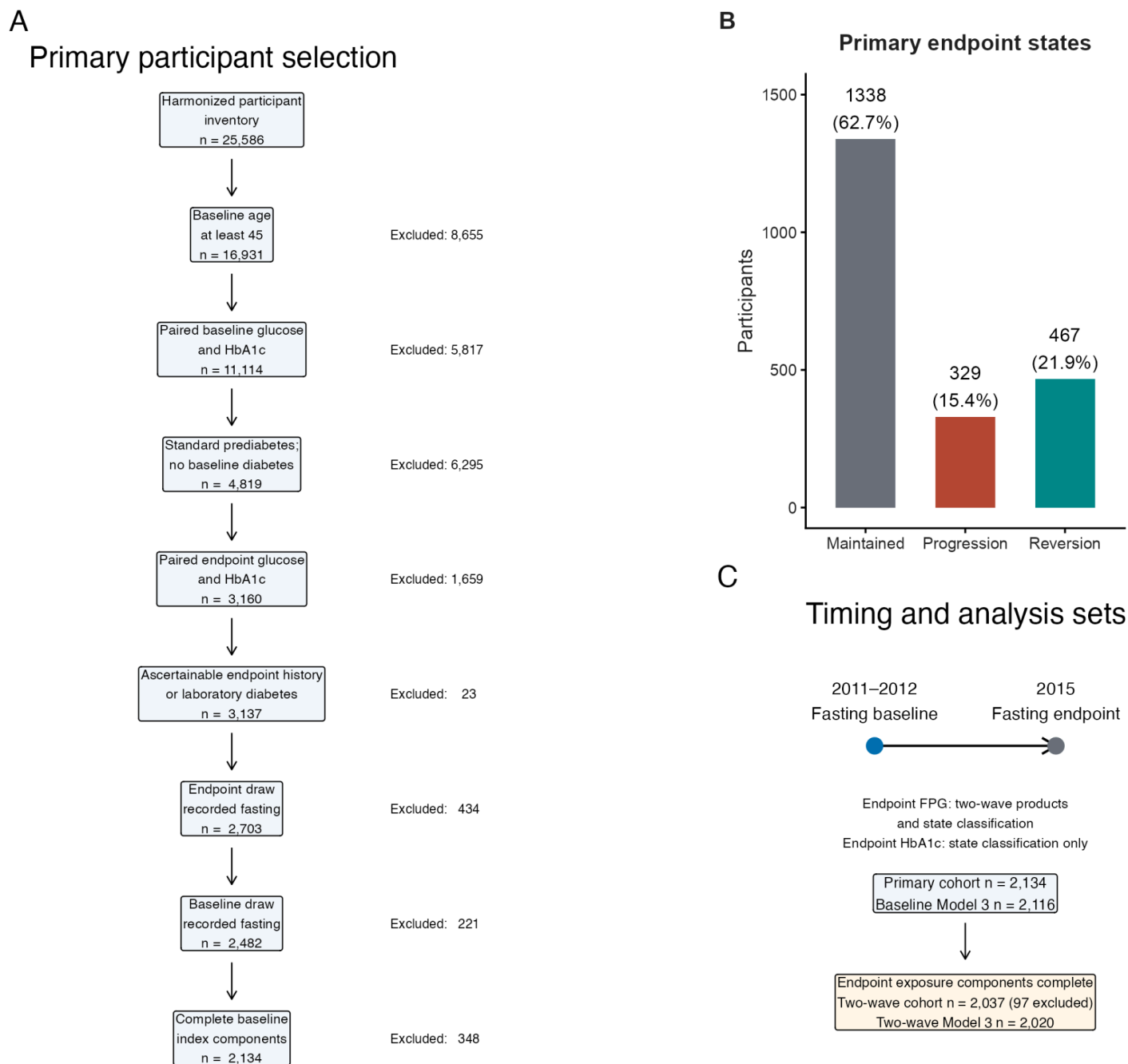


Figure 1

Participant selection and measurement timing. (A) Sequential selection of the 2,134-person primary cohort. (B) Mutually exclusive primary endpoint states. (C) Analysis branches: baseline Model 3 included 2,116 participants; requiring endpoint exposure components excluded 97 participants, leaving 2,037 for the two-wave cohort and 2,020 for two-wave Model 3. Endpoint FPG enters the two-wave products and state classification; endpoint HbA1c enters state classification only.

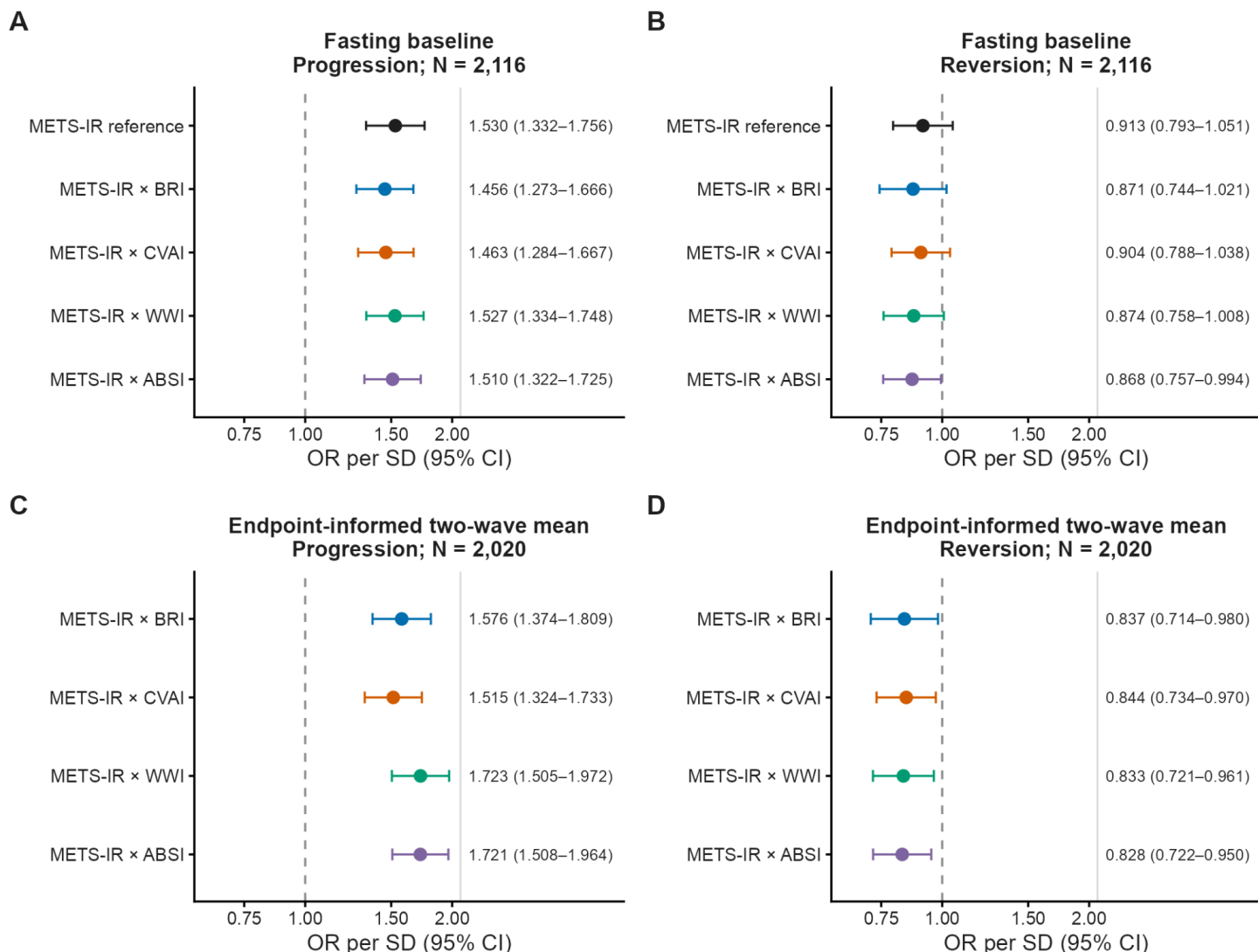


Figure 2

Community-clustered associations. (A–B) Fasting baseline progression and reversion (Model 3 N=2,116; 343 communities), including the METS-IR reference and four products. (C–D) Exploratory endpoint-informed two-wave-mean product associations (Model 3 N=2,020; 336 communities); no two-wave METS-IR reference is displayed. Labels report exact Model 3 ORs and 95% CIs per eligible-cohort SD, with maintained status as the reference. OR magnitudes across differently scaled indices are not predictive rankings. Two-wave means include endpoint glucose. Model 3 adjusted for baseline age, sex, education, marriage/partnership, rural residence, heart disease, stroke, current smoking, past-year drinking, low-density lipoprotein cholesterol, creatinine, HbA1c, and standardized log high-sensitivity C-reactive protein. Confidence intervals used community-clustered sandwich covariance. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; HbA1c, glycated hemoglobin; OR, odds ratio; CI, confidence interval; SD, standard deviation.

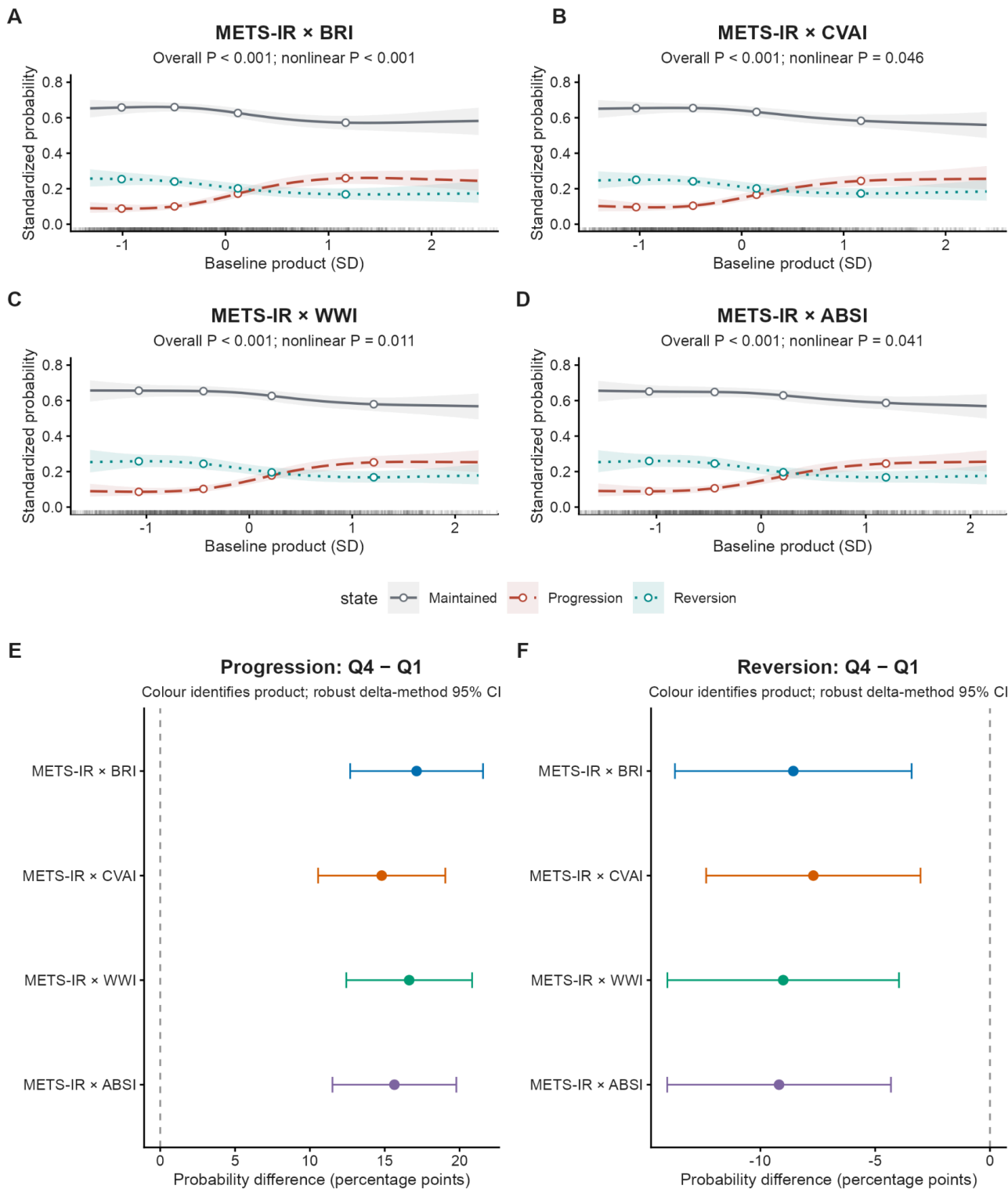


Figure 3

Fasting baseline spline-standardized terminal-state probabilities. (A–D) Products with BRI, CVAI, WWI, and ABSI in Model 3 (N=2,116); colours identify terminal states. Curves cover the 2.5th–97.5th percentile exposure range; rugs show the Model 3 exposure distribution, and open points mark predictions at eligible-baseline-cohort within-quartile medians (Supplementary Table S13). Raw representative values were standardized using the same unrounded eligible-cohort mean and SD. Probabilities were averaged

over the Model 3 distribution. (E–F) Colours identify products; points show Q4-minus-Q1 standardized progression and reversion probability differences at the same representative values. Their 95% CIs use the joint gradient contrast and the same community-robust covariance, not subtraction of separate interval endpoints. Overall and nonlinear P values are community-clustered joint Wald tests and do not identify clinical thresholds. Model 3 adjusted for baseline age, sex, education, marriage/partnership, rural residence, heart disease, stroke, current smoking, past-year drinking, low-density lipoprotein cholesterol, creatinine, HbA1c, and standardized log high-sensitivity C-reactive protein. Confidence intervals used community-clustered sandwich covariance. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; HbA1c, glycated hemoglobin; CI, confidence interval.

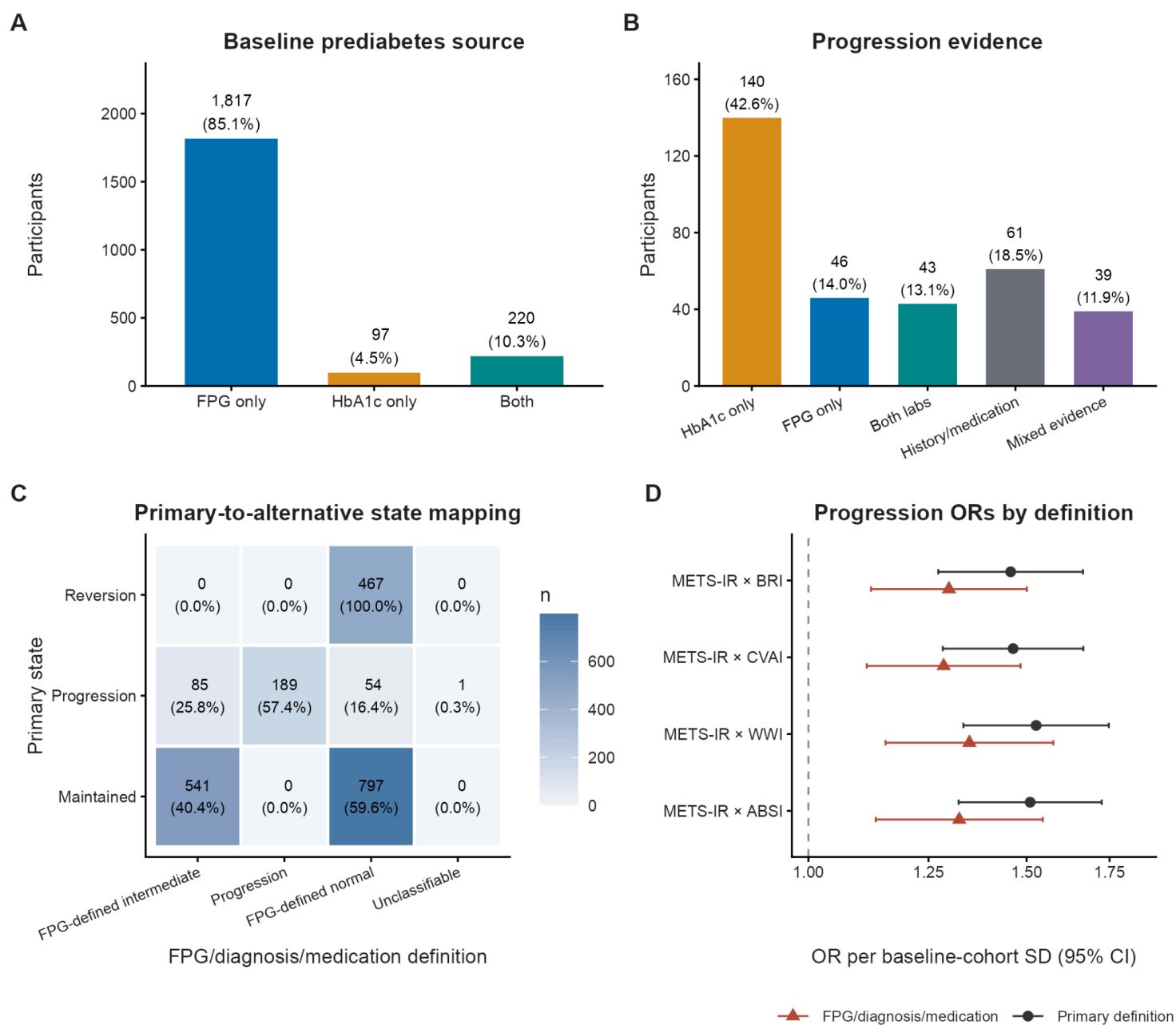


Figure 4

Glycemic classification sources and endpoint-definition sensitivity. (A) Mutually exclusive baseline prediabetes sources (N=2,134). (B) Mutually exclusive evidence groupings among 329 primary progression cases. (C) Mapping from the primary three-state definition to the endpoint FPG/diagnosis/medication definition; cells give participant counts and row percentages within each primary state, and fill colour represents the count. One primary progression participant was unclassifiable. (D) Model 3 progression ORs under the primary definition (N=2,116; reference=maintained) and alternative definition (N=2,115; reference=FPG-defined intermediate), using the same baseline-cohort SDs. Both the case group and reference group change under the alternative definition; differences therefore do not quantify an isolated HbA1c contribution. Model 3 adjusted for baseline age, sex, education, marriage/partnership, rural residence, heart disease, stroke, current smoking, past-year drinking, low-density lipoprotein cholesterol, creatinine, HbA1c, and standardized log high-sensitivity C-reactive protein. Confidence intervals used community-clustered sandwich covariance. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; OR, odds ratio; SD, standard deviation.

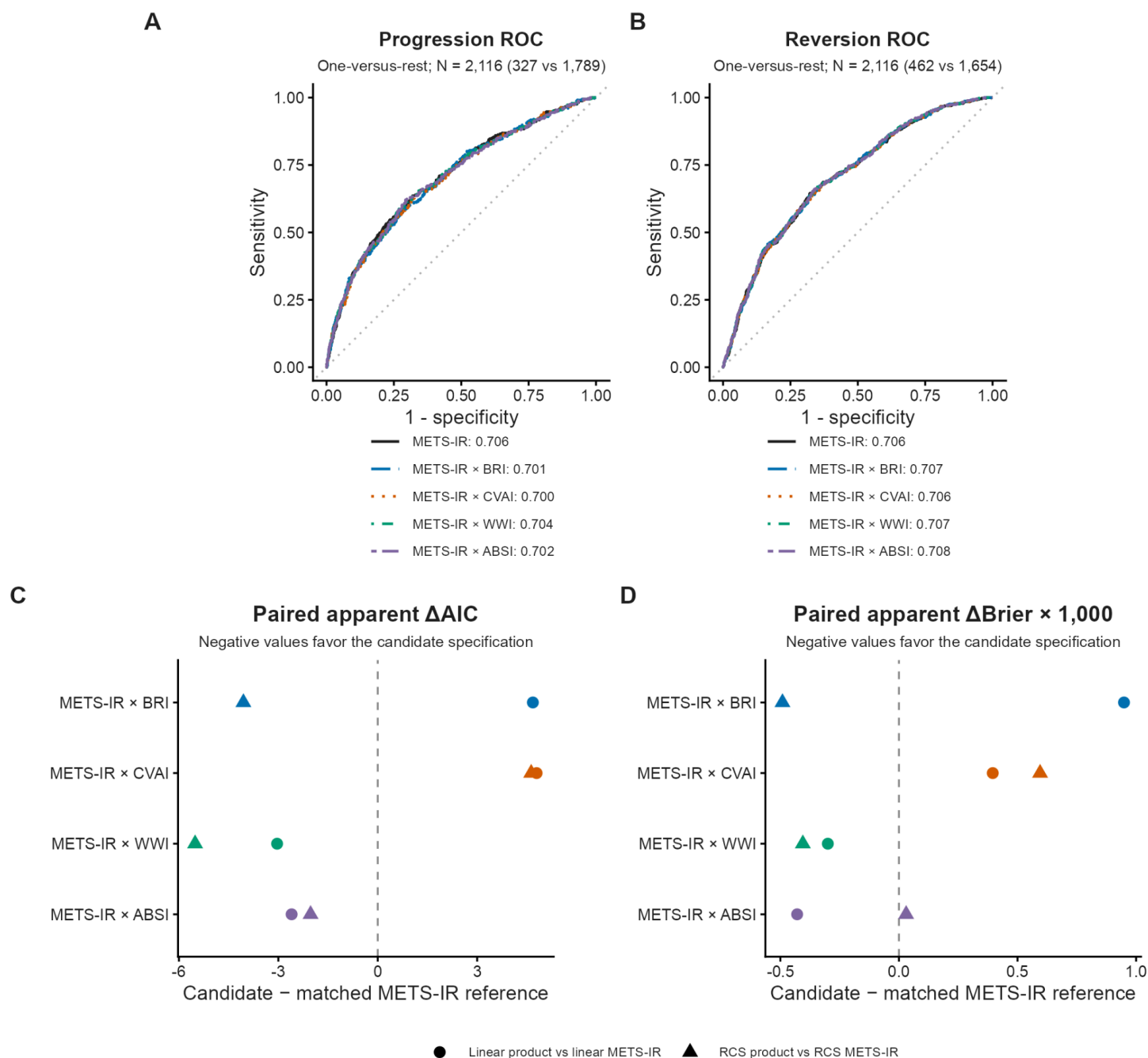


Figure 5

Apparent adjusted performance on the common 2,116-person Model 3 sample. (A) Progression one-versus-rest ROC curves (327 cases vs 1,789 others). (B) Reversion one-versus-rest ROC curves (462 cases vs 1,654 others). Legends give apparent AUC point estimates. (C–D) Candidate-minus-reference differences in AIC and multiclass Brier score ($\times 1,000$), respectively; linear products are compared with linear METS-IR, and product splines with the matched METS-IR spline. Negative differences favor the candidate specification. Retained-components + body-index models are shown in Figure 6 and Supplementary Table S11. All models were fitted and evaluated in the same sample. These comparisons do not establish validation, calibration, equivalence, or clinical utility. Model 3 adjusted for baseline age,

sex, education, marriage/partnership, rural residence, heart disease, stroke, current smoking, past-year drinking, low-density lipoprotein cholesterol, creatinine, HbA1c, and standardized log high-sensitivity C-reactive protein. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; HbA1c, glycated hemoglobin; AUC, area under the receiver operating characteristic curve; AIC, Akaike information criterion.

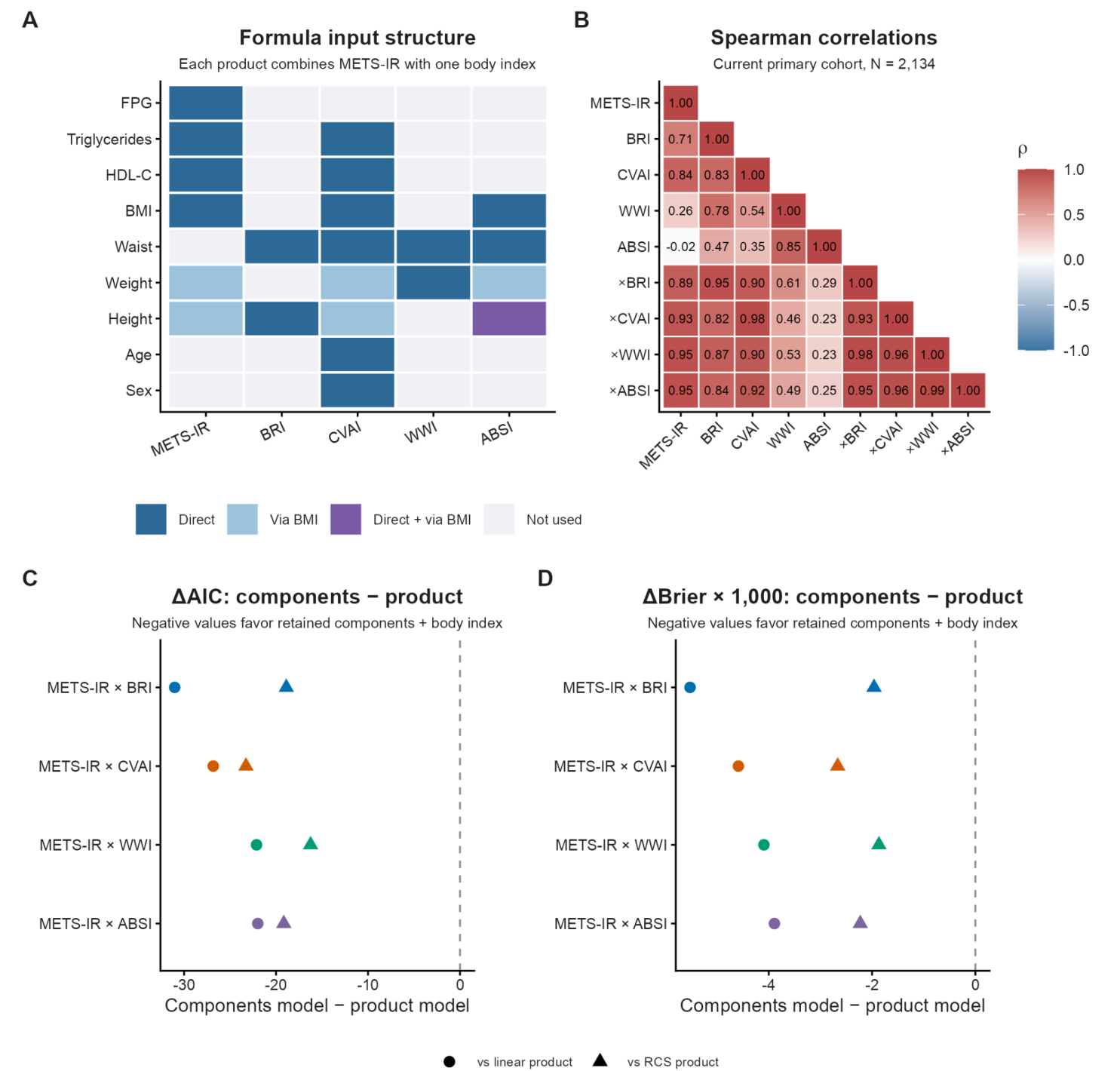


Figure 6

Shared information and apparent component-versus-product comparisons. (A) Direct formula inputs and anthropometric measurements entering through BMI; a purple cell denotes an input used both directly and through BMI. Each product combines METS-IR with one body index. The panel shows the computational structure and does not identify causal relationships. (B) Lower-triangle Spearman correlations in the current primary cohort (N=2,134). (C–D) Retained-components + body-index model minus the corresponding linear or RCS product model for AIC and multiclass Brier score ($\times 1,000$), respectively, on the common N=2,116 sample. The retained-components + body-index model contains FPG, triglycerides, HDL-C, BMI, and the relevant body index; it is not a raw waist/height/weight model. Negative values favor that model. It used 40 parameters versus 32 for linear-product and 36 for product-RCS models. All comparisons are apparent and in-sample; they do not establish validation or clinical utility. Model 3 adjusted for baseline age, sex, education, marriage/partnership, rural residence, heart disease, stroke, current smoking, past-year drinking, low-density lipoprotein cholesterol, creatinine, HbA1c, and standardized log high-sensitivity C-reactive protein. METS-IR, metabolic score for insulin resistance; BRI, body roundness index; CVAI, Chinese visceral adiposity index; WWI, weight-adjusted waist index; ABSI, a body shape index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; BMI, body mass index; AIC, Akaike information criterion; RCS, restricted cubic spline.

Supplementary Files

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- [METSIRSupplementaryv9.3.docx](#)