

Supplementary Methods. Overall framework of the main SEM and one-at-a-time sensitivity analyses

S1. Study objective and modeling strategy

To systematically evaluate the mechanistic link between glycemic dysregulation and hypercoagulability, we implemented a serial structural equation modeling (serial SEM) framework coupled with one-at-a-time (OAT) sensitivity analyses. Under a conditional SEM setting (fixed.x = TRUE), we tested the robustness of a prespecified mechanism chain:

(Tri-sugar exposure) → (four upstream pathway indices) → (two downstream coagulation nodes) → (hypercoagulability outcome),

where hypercoagulability was primarily operationalized as D-dimer positivity. Sensitivity analyses were designed to perturb one modeling dimension at a time (structure, outcome type, measurement/operational definitions, or covariate/exposure specification) while keeping all other configurations identical to the main model, thereby avoiding combinatorial explosion and ensuring interpretable contrasts.

S2. Main configuration: partial mediation serial SEM with a binary outcome (D_Pos)

S2.1 Exposures, outcome, and estimation

Main exposure configuration (Tri-sugar): three glycemic indicators were included simultaneously as competing exposures with mutual adjustment:

- FPG: fasting plasma glucose
- FA: fructosamine
- HbA1c: glycated hemoglobin

Each glycemic path coefficient represents a mutually adjusted conditional association, i.e., the association of one glycemic indicator conditional on the other two glycemic indicators and covariates. Because the aim was not to model the correlation structure among glycemic indicators, we did not explicitly specify exogenous covariances (e.g., $PG \sim FA$) in the SEM.

Primary outcome (binary):

- D_Pos = hypercoagulability status, coded as 1 if D-dimer > 0.5 µg/mL, otherwise 0.

Estimator and missingness handling:

For the binary outcome, models were estimated using WLSMV with D_Pos declared as an ordered variable (binary treated as ordered categorical under a probit link). Missing data were handled according to the default WLSMV framework (i.e., FIML was not used). FIML was only applied in the continuous-outcome sensitivity model estimated under ML/MLR (see S3.2).

S2.2 Model structure: four upstream pathways and two downstream coagulation mediators

The main SEM specifies the following modules:

(i) Tri-sugar exposures → four upstream pathway indices

- Lipid Index
- BP Index
- Inflammation Index
- Nutrition Index

The four upstream pathway indices were treated as parallel physiological modules. Because within-module causal ordering is difficult to justify, we allowed residual covariances among the

four upstream indices to reflect shared unmeasured background factors (e.g., metabolic state, inflammatory burden, lifestyle).

(ii) Upstream pathways → two downstream coagulation nodes

Two complementary downstream coagulation mediators were modeled in parallel:

A: Coagulation substrate node (reflecting substrate availability/consumption)

B: Coagulation function/time node (reflecting time-based coagulation function)

Residual covariance between the two downstream nodes was allowed to reflect coupling within the coagulation system.

(iii) Downstream nodes → D_Pos

The outcome D_Pos was regressed on both downstream coagulation nodes.

Partial mediation (main) assumptions:

The main model allows direct effects from (a) tri-sugar exposures and (b) upstream indices to D_Pos, avoiding overly restrictive constraints and improving interpretability/fit feasibility. Importantly, the baseline does not include direct paths from tri-sugar exposures to the downstream coagulation nodes; thus, glycemic effects on coagulation execution are assumed to operate primarily via the four upstream pathway modules.

S3. Composite index construction (operational definitions)

All indices are composite (observed) indices, not latent factors. We used a standardized two-step procedure: standardize each component: $z(x) = \text{scale}(x)$. form a linear composite `_raw`, then standardize again: `**Index = z(_raw)**`

S3.1 Four upstream pathway indices

- Lipid pathway (Lipid_Index):
- $\text{Lipid_Index_raw} = z(\text{TG}) + z(\text{TC}) + z(\text{LDL}) - z(\text{HDL})$
- $\text{Lipid_Index} = z(\text{Lipid_Index_raw})$
- Blood pressure pathway (BP_Index):
- $\text{BP_Index_raw} = z(\text{SBP}) + z(\text{DBP})$
- $\text{BP_Index} = z(\text{BP_Index_raw})$
- Inflammation pathway (Inflamm_Index; traditional 3-item composite):
- $\text{Inflamm_Index_raw} = z(\text{CRP}) + z(\text{SAA}) + z(\text{WBC})$
- $\text{Inflamm_Index} = z(\text{Inflamm_Index_raw})$
- Nutrition pathway (Nutrition_Index; higher values indicate poorer nutrition):
- $\text{Nutrition_Index_raw} = -z(\text{HB}) - z(\text{PAB}) - z(\text{TP})$
- $\text{Nutrition_Index} = z(\text{Nutrition_Index_raw})$

S3.2 Two downstream coagulation mediators

A. Coagulation substrate node (EndoSubstrate_Index):

- $\text{EndoSubstrate_raw} = z(\text{FIB}) + z(\text{PLT})$
- $\text{EndoSubstrate_Index} = z(\text{EndoSubstrate_raw})$

B. Coagulation function/time node (CoagTime_Index):

- $\text{CoagTime_raw} = -z(\text{APTT}) - z(\text{PT}) - z(\text{TT})$
- $\text{CoagTime_Index} = z(\text{CoagTime_raw})$

S4. Covariates included in the main conditional SEM

The following covariates were included as fixed exogenous variables (`fixed.x = TRUE`) in all main and sensitivity models to control for potential demographic, metabolic, lifestyle, and clinical

confounding factors:

Demographic and anthropometric factors

- Age
 - Gender (male) — coded as male vs. female
 - Body Mass Index (BMI)
- Metabolic comorbidity history
- Hypertension (+) — documented history of hypertension
 - Diabetes (+) — documented history of diabetes mellitus
 - Hyperlipidemia (+) — documented history of hyperlipidemia
- (The symbol “(+)” indicates presence of the corresponding condition.)

Lifestyle factors

- Smoking Status
- Alcohol Status

Clinical and physiological status

- Body Temperature (+) — presence of abnormal body temperature within ± 2 days of admission (defined as ≥ 37.4 °C)
- Psychiatric Duration — duration of psychiatric illness (years since onset)

All covariates were included only as predictors (right-hand side of regressions) for the upstream indices, downstream coagulation nodes, and the outcome; no covariate covariance terms ($Z \sim Z$) were specified to preserve the conditional SEM interpretation. Given that our primary analytical objective was to adjust for these variables to isolate the targeted structural path effects, rather than to investigate the complex interrelationships among the covariates themselves, this strategy offers a parsimonious and statistically robust method for confounding control.

S5. One-at-a-time sensitivity analyses

Sensitivity analyses were conducted by perturbing one dimension at a time while holding all other specifications identical to the main.

S5.1 Structural robustness

Direct-to-coagulation model (Partial mediation): additionally allows tri-sugar $\rightarrow$ EndoSubstrate_Index and tri-sugar $\rightarrow$ CoagTime_Index direct effects.

Full mediation model: constrains all direct effects from tri-sugar and upstream indices to D_Pos to zero (strong mechanistic constraint), preserving the serial pathway through downstream coagulation node(s).

S5.2 Outcome-type robustness

Continuous outcome sensitivity: Ddimer_log = $\log_{10}(\text{D-dimer})$, estimated with MLR + FIML, with the same main serial structure and index definitions.

S5.3 Measurement/operational robustness (index-level perturbations)

Upstream lipid index alternative:

- $\text{AIP} = \log_{10}(\text{TG} / \text{HDL})$
- $\text{Lipid_AIP} = z(\text{AIP})$ (replacing Lipid_Index)
- Inflammation alternatives:
- Winsorized Inflamm_Index_w: winsorize CRP/SAA/WBC (e.g., symmetric tails), then
- $\text{Inflamm_Index_w_raw} = z(\text{CRP_w}) + z(\text{SAA_w}) + z(\text{WBC_w})$
- $\text{Inflamm_Index_w} = z(\text{Inflamm_Index_w_raw})$

- Extended inflammation composite (Inflamm_Extended):
- $\text{Inflamm_Extended_raw} = z(\text{CRP}) + z(\text{SAA}) + z(\text{NEU}) + z(\text{MONO}) + z(\text{LDH})$
- $\text{Inflamm_Extended} = z(\text{Inflamm_Extended_raw})$
- SIRI single-index (Inflamm_SIRI):
- $\text{SIRI_raw} = \text{NEU} \times \text{MONO} / \text{LYM}$
- $\text{SIRI_log} = \log_{1p}(\text{SIRI_raw})$
- $\text{Inflamm_SIRI} = z(\text{SIRI_log})$

Nutrition/immune alternatives:

- CONUT single score (replacing Nutrition_Index)
- $\text{PNI} = \text{ALB} + 5 \times \text{LYM_abs}$ (replacing Nutrition_Index)

Downstream coagulation alternatives:

A-only: retain EndoSubstrate_Index only (remove CoagTime_Index)

B-only: retain CoagTime_Index only (remove EndoSubstrate_Index)

Composite coagulation (EndoCoag_Total):

- $\text{EndoCoag_Total_raw} = z(\text{FIB}) + z(\text{PLT}) - z(\text{APTT}) - z(\text{PT}) - z(\text{TT})$
- $\text{EndoCoag_Total} = z(\text{EndoCoag_Total_raw})$

(replacing both A and B nodes with a single summary index)

All measurement/operational robustness analyses were conducted under the binary outcome D_Pos and the main serial structure to maintain a controlled comparison set.

S5.4 Covariate and exposure robustness

Extended covariates: baseline Z plus hepatic and renal function indices (Hepatic_Index, Renal_Index), still under fixed.x = TRUE and without modeling covariate covariances.

Exposure specification perturbations:

Single-sugar models: PG-only, FA-only, HbA1c-only, and FA_ALBcorr-only, each preserving the baseline serial structure.

Tri-sugar substitution (Tri-sugar[FA-ALBcorr]): replace FA with FA_ALBcorr, i.e., PG + FA_ALBcorr + HbA1c.

Glycemic composite exposure indices:

- Gly-Composite (FA) = $z(\text{PG}) + z(\text{FA}) + z(\text{HbA1c})$
- Gly-Composite (FA-ALBcorr) = $z(\text{PG}) + z(\text{FA_ALBcorr}) + z(\text{HbA1c})$

(tested against the multi-indicator exposure specification for robustness of conclusions under information-compressed representations)

Supplementary material 1. Descriptive Summary

of Clinical Variables and Observed Laboratory Measures in Patients

With Schizophrenia, Bipolar Disorder and Major Depressive Disorder

Variable	Unit	Missing (N)			Missing (%)			Mean ± SD			Distribution		
		SCZ	BD	MDD	SCZ	BD	MDD	SCZ	BD	MDD	SCZ	BD	MDD
Glycemic Exposures													
FPG	mmol/L	0	0	0	0	0	0	7.0 ± 3.5	6.3 ± 2.6	6.1 ± 2.5	6.1 (5.3–7.3)	5.5 (4.9–6.6)	5.3 (4.8–6.3)
FA	μmol/L	0	0	0	0	0	0	1.7 ± 0.4	1.7 ± 0.3	1.7 ± 0.3	1.6 (1.5–1.8)	1.6 (1.5–1.8)	1.6 (1.5–1.8)
HbA1c	%	0	0	0	0	0	0	5.8 ± 1.2	5.6 ± 1.0	5.7 ± 0.8	5.4 (5.2–5.8)	5.3 (5.1–5.6)	5.5 (5.2–5.8)
FA-ALBcorr		0	0	4	0	0	0.21	3.93 ± 0.93	3.80 ± 0.71	3.92 ± 0.74	3.69 (3.40–4.12)	3.67 (3.36–4.02)	3.79 (3.50–4.16)
Outcomes													
D-dimer	μg/mL	230	119	314	11.89	10.71	16.27	0.4 ± 0.8	0.3 ± 1.0	0.3 ± 0.6	0.2 (0.1–0.4)	0.1 (0.1–0.3)	0.2 (0.1–0.3)
log(D-dimer)		230	119	314	11.89	10.71	16.27	0.25 ± 0.30	0.20 ± 0.28	0.24 ± 0.28	0.15 (0.07–0.31)	0.11 (0.06–0.24)	0.15 (0.07–0.29)
D-dimer (+)		230	119	314	11.89	10.71	16.27	—	—	—	258 (15.1)	111 (11.2)	253 (15.7)
Components /Derived Measures													
TG	mmol/L	2	0	1	0.1	0	0.05	1.6 ± 1.5	1.6 ± 1.4	1.7 ± 1.3	1.2 (0.8–1.9)	1.2 (0.8–1.9)	1.4 (0.9–2.1)
TC	mmol/L	35	7	28	1.81	0.63	1.45	4.5 ± 1.0	4.3 ± 0.9	4.5 ± 1.0	4.4 (3.8–5.0)	4.2 (3.7–4.8)	4.4 (3.8–5.1)
LDL-C	mmol/L	2	0	1	0.1	0	0.05	2.7 ± 0.9	2.5 ± 0.8	2.6 ± 0.8	2.6 (2.0–3.2)	2.5 (1.9–3.0)	2.5 (2.0–3.1)
HDL-C	mmol/L	2	0	1	0.1	0	0.05	1.3 ± 0.4	1.3 ± 0.4	1.3 ± 0.4	1.2 (1.1–1.5)	1.3 (1.1–1.5)	1.3 (1.1–1.6)

SBP	mmHg	1	0	0	0.05	0	0	128 ± 18	125 ± 17	123 ± 16	126 (117–137)	124 (114–135)	122 (111–133)
DBP	mmHg	1	0	0	0.05	0	0	82 ± 11	81 ± 11	78 ± 10	82 (74–89)	80 (73–88)	77 (70–85)
Hb	g/L	10	4	19	0.52	0.36	0.98	137 ± 17	137 ± 17	133 ± 14	136 (126–148)	135 (125–148)	132 (124–141)
PAB	mg/L	1	0	4	0.05	0	0.21	282 ± 75	290 ± 74	288 ± 70	273 (231–322)	283 (238–333)	279 (240–326)
TP	g/L	0	0	4	0	0	0.21	72 ± 6	71 ± 5	69 ± 6	72 (68–76)	71 (67–74)	69 (65–73)
ALB	g/L	0	0	4	0	0	0.21	45 ± 4	44 ± 4	43 ± 4	45 (42–47)	45 (42–47)	43 (40–45)
FIB	g/L	228	115	298	11.78	10.35	15.44	2.8 ± 0.7	2.6 ± 0.7	2.6 ± 0.7	2.7 (2.3–3.2)	2.5 (2.2–3.0)	2.5 (2.2–3.0)
PLT	×10 ⁹ /L	10	4	19	0.52	0.36	0.98	245 ± 70	246 ± 70	229 ± 65	237 (198–287)	240 (196–285)	223 (185–270)
APTT	s	228	115	298	11.78	10.35	15.44	28.5 ± 5.1	29.5 ± 5.1	28.8 ± 4.5	27.9 (25.5–30.5)	28.7 (26.2–31.7)	28.1 (25.9–30.8)
PT	s	228	115	298	11.78	10.35	15.44	11.4 ± 1.6	11.4 ± 0.9	11.4 ± 1.1	11.3 (10.8–11.9)	11.3 (10.8–11.9)	11.3 (10.7–11.9)
TT	s	228	115	298	11.78	10.35	15.44	15.4 ± 3.9	15.1 ± 4.0	15.2 ± 3.9	16.9 (11.1–18.5)	16.4 (10.9–18.5)	16.6 (11.2–18.6)
ALT	U/L	0	0	0	0	0	0	27 ± 27	26 ± 28	22 ± 25	19 (13–30)	18 (12–30)	16 (11–24)
AST	U/L	0	0	0	0	0	0	26 ± 24	25 ± 18	21 ± 13	20 (16–27)	20 (16–26)	18 (15–22)
GGT	U/L	35	7	31	1.81	0.63	1.61	27 ± 34	25 ± 25	23 ± 27	17 (12–29)	17 (12–28)	16 (11–24)
ALP	U/L	1	0	4	0.05	0	0.21	81 ± 27	83 ± 37	80 ± 34	76 (64–93)	75 (60–95)	74 (59–91)
TBIL	μmol/L	0	0	1	0	0	0.05	11.6 ± 7.6	9.8 ± 5.5	9.8 ± 5.2	9.5 (6.8–14.1)	8.4 (5.9–12.2)	8.7 (6.3–11.6)
DBIL	μmol/L	1	0	1	0.05	0	0.05	3.5 ± 2.9	2.9 ± 1.9	2.7 ± 1.5	2.8 (2.0–4.0)	2.4 (1.8–3.5)	2.3 (1.8–3.2)
BUN	mmol/L	1	0	0	0.05	0	0	4.8 ± 2.0	4.7 ± 1.6	4.8 ± 1.8	4.5 (3.6–5.6)	4.4 (3.6–5.4)	4.6 (3.8–5.6)
Cr	μmol/L	1	0	0	0.05	0	0	64.4 ± 17.0	63.9 ± 15.2	62.7 ± 18.1	62.0 (53.0–73.0)	62.0 (53.0–72.0)	60.0 (53.0–69.0)
WBC	×10 ⁹ /L	10	4	19	0.52	0.36	0.98	7.9 ± 2.6	7.7 ± 2.4	6.6 ± 1.9	7.4 (6.0–9.3)	7.3 (5.9–9.1)	6.3 (5.2–7.6)
CRP	mg/L	221	138	253	11.42	12.42	13.11	4.2 ± 10.4	3.1 ± 8.4	2.1 ± 7.4	1.3 (0.5–3.7)	0.8 (0.5–2.7)	0.6 (0.4–1.5)
SAA	mg/L	16	4	17	0.83	0.36	0.88	16.2 ±	13.6 ±	11.0 ±	6.3 (4.1–11.0)	5.6 (3.8–9.4)	5.5 (3.8–8.4)

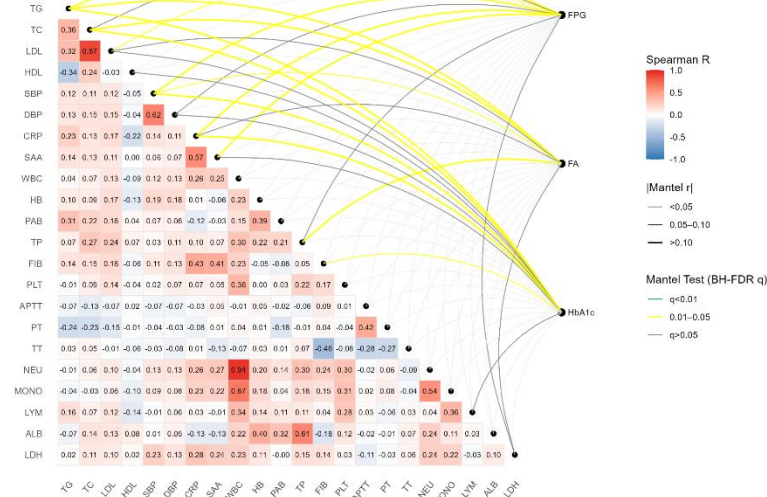
								42.6	39.6	31.8			
LDH	<i>U/L</i>	0	0	3	0	0	0.16	184 ± 56	180 ± 46	159 ± 33	173 (151–203)	171 (149–200)	154 (138–175)
NEU	$\times 10^9/L$	44	11	46	2.27	0.99	2.38	5.3 ± 2.3	4.9 ± 2.1	4.1 ± 1.7	4.9 (3.6–6.5)	4.5 (3.3–6.0)	3.8 (2.9–5.0)
MONO	$\times 10^9/L$	44	11	46	2.27	0.99	2.38	0.5 ± 0.2	0.6 ± 0.2	0.5 ± 0.2	0.5 (0.4–0.6)	0.5 (0.4–0.6)	0.4 (0.3–0.5)
LYM	$\times 10^9/L$	44	11	46	2.27	0.99	2.38	1.9 ± 0.7	2.1 ± 0.7	1.9 ± 0.6	1.8 (1.4–2.2)	2.0 (1.6–2.5)	1.8 (1.4–2.2)
AIP		2	0	1	0.1	0	0.05	0.02 ±	0.01 ±	0.04 ±	0.01	-0.03	0.02
								0.32	0.32	0.31	(-0.21–0.23)	(-0.21–0.21)	(-0.19–0.24)
SIRI		44	11	46	2.27	0.99	2.38	1.89 ±	1.58 ±	1.22 ±	1.37	1.14	0.94
								1.77	1.51	1.27	(0.87–2.23)	(0.76–1.87)	(0.61–1.42)
CONUT		44	11	50	2.27	0.99	2.59	—	—	—	—	—	—
Normal (0–1)		—	—	—	—	—	—	—	—	—	1567 (82.9)	981 (89.2)	1596 (84.9)
Mild Malnutrition (2–4)		—	—	—	—	—	—	—	—	—	323 (17.1)	119 (10.8)	279 (14.8)
Moderate Severe (5–8)		—	—	—	—	—	—	—	—	—	1 (0.1)	0 (0.0)	5 (0.3)
PNI		44	11	50	2.27	0.99	2.59	54.0 ± 5.4	54.7 ± 5.3	51.9 ± 5.3	53.8	54.8	51.6
											(50.4–57.4)	(51.2–58.3)	(48.5–55.3)
Covariates													
Age	<i>years</i>	0	0	0	0	0	0	40 ± 15	33 ± 16	46 ± 20	38 (29–51)	29 (20–44)	50 (28–62)
Gender, male		0	0	0	0	0	0	—	—	—	808 (41.8)	442 (39.8)	512 (26.5)
BMI	<i>kg/m²</i>	0	0	0	0	0	0	23.7 ± 4.4	23.7 ± 4.5	22.3 ± 3.8	23.2	23.3	21.9
											(20.5–26.3)	(20.4–26.2)	(19.6–24.4)
Hypertension (+)		0	0	0	0	0	0	—	—	—	252 (13.0)	135 (12.2)	506 (26.2)
Diabetes (+)		0	0	0	0	0	0	—	—	—	258 (13.3)	120 (10.8)	217 (11.2)
Hyperlipidemia (+)		0	0	0	0	0	0	—	—	—	74 (3.8)	38 (3.4)	98 (5.1)
Smoking Status		0	0	0	0	0	0	—	—	—	—	—	—

No history	—	—	—	—	—	—	—	—	—	1630 (84.2)	886 (79.7)	1673 (86.7)
Current	—	—	—	—	—	—	—	—	—	297 (15.3)	205 (18.5)	203 (10.5)
Former	—	—	—	—	—	—	—	—	—	8 (0.4)	20 (1.8)	54 (2.8)
Alcohol Status	0	0	0	0	0	0	—	—	—	—	—	—
No history	—	—	—	—	—	—	—	—	—	1716 (88.7)	929 (83.6)	1667 (86.4)
Current	—	—	—	—	—	—	—	—	—	215 (11.1)	173 (15.6)	241 (12.5)
Former	—	—	—	—	—	—	—	—	—	4 (0.2)	9 (0.8)	22 (1.1)
Body Temperature (+)	0	0	0	0	0	0	—	—	—	455 (23.5)	205 (18.5)	252 (13.1)
Psychiatric Duration years	0	0	0	0	0	0	10 ± 11	9 ± 10	7 ± 9	7 (1–16)	5 (2–12)	3 (1–10)

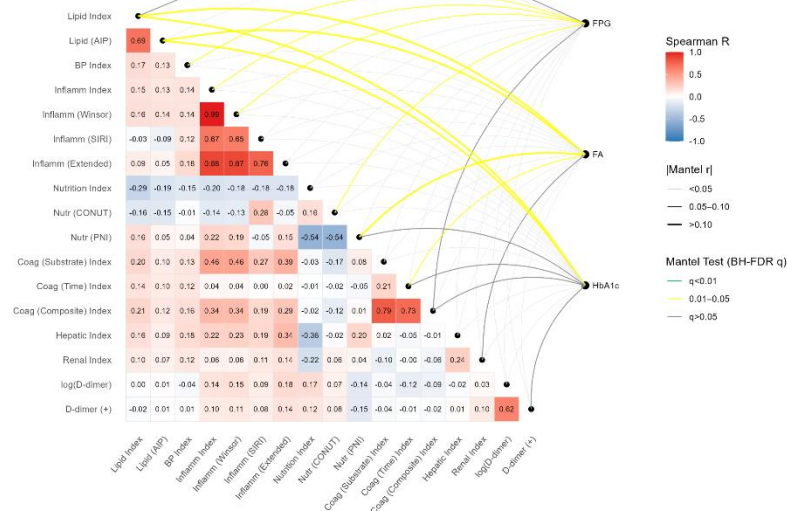
Note: This table summarizes glycemic exposures, outcomes, derived laboratory components, and clinical covariates in patients with schizophrenia (SCZ), bipolar disorder (BD), and major depressive disorder (MDD). Continuous variables are presented as mean ± standard deviation (SD) and median (interquartile range, IQR), while categorical variables are presented as number (percentage). Missing data are reported as Missing (N) and Missing (%) for each diagnostic group. Glycemic exposures include fasting plasma glucose (FPG, mmol/L), fructosamine (FA, μmol/L), glycated hemoglobin (HbA1c, %), and albumin-corrected fructosamine (FA-ALBcorr). Outcomes include D-dimer (μg/mL), log-transformed D-dimer [log(1 + D-dimer)], and D-dimer positivity [D-dimer (+)]. Observed laboratory measures include lipid profile (TG, TC, LDL-C, HDL-C), blood pressure (SBP, DBP), nutritional markers (Hb, PAB, TP, ALB), coagulation parameters (FIB, PLT, APTT, PT, TT), liver function markers (ALT, AST, GGT, ALP, TBIL, DBIL), renal function markers (BUN, Cr), and inflammatory/cell-count markers (WBC, CRP, SAA, LDH, NEU, MONO, LYM). Derived indices include the atherogenic index of plasma (AIP), systemic inflammation response index (SIRI), controlling nutritional status (CONUT) categories, and prognostic nutritional index (PNI).

Abbreviations: SCZ, schizophrenia; BD, bipolar disorder; MDD, major depressive disorder; SD, standard deviation; IQR, interquartile range; TG, triglycerides; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SBP/DBP, systolic/diastolic blood pressure; Hb, hemoglobin; PAB, prealbumin; TP, total protein; ALB, albumin; FIB, fibrinogen; PLT, platelet count; APTT, activated partial thromboplastin time; PT, prothrombin time; TT, thrombin time; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; TBIL/DBIL, total/direct bilirubin; BUN, blood urea nitrogen; Cr, creatinine; WBC, white blood cell count; CRP, C-reactive protein; SAA, serum amyloid A; LDH, lactate dehydrogenase; NEU, neutrophils; MONO, monocytes; LYM, lymphocytes.

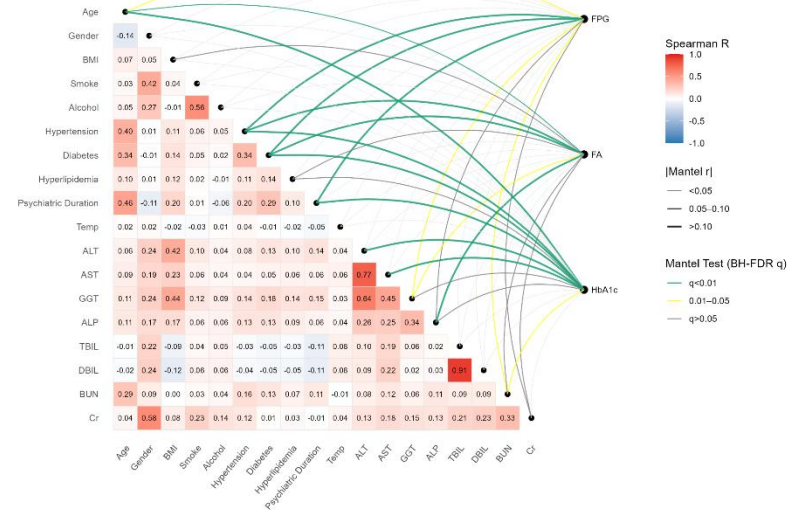
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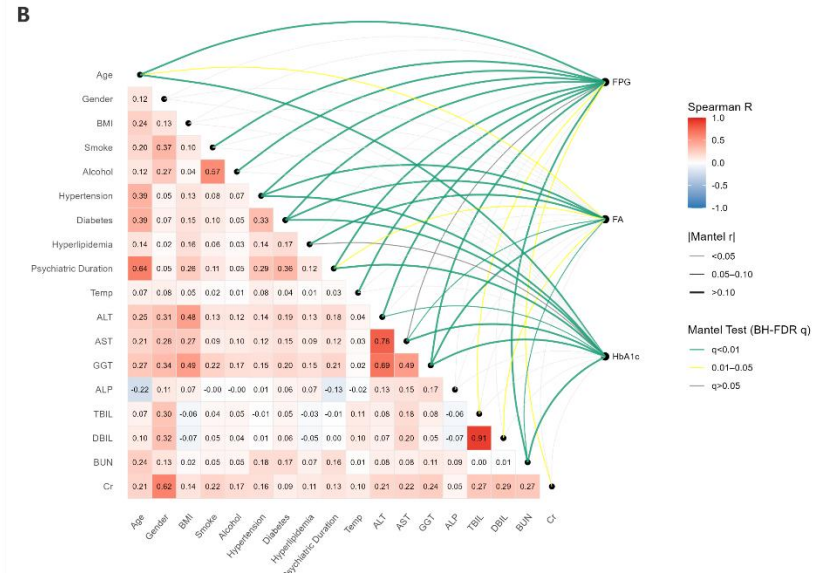
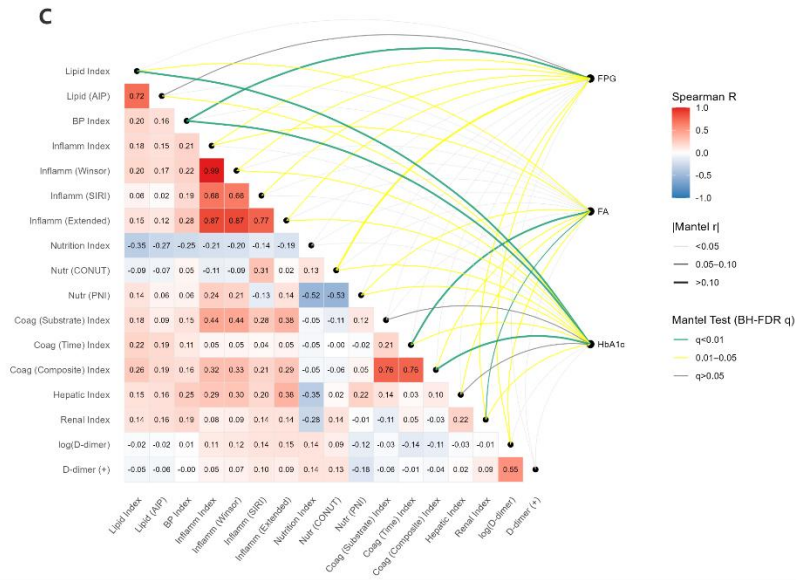
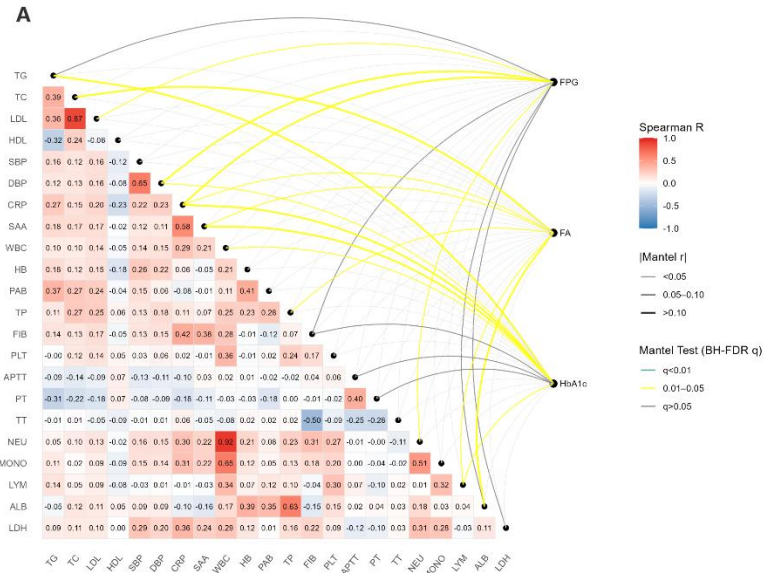


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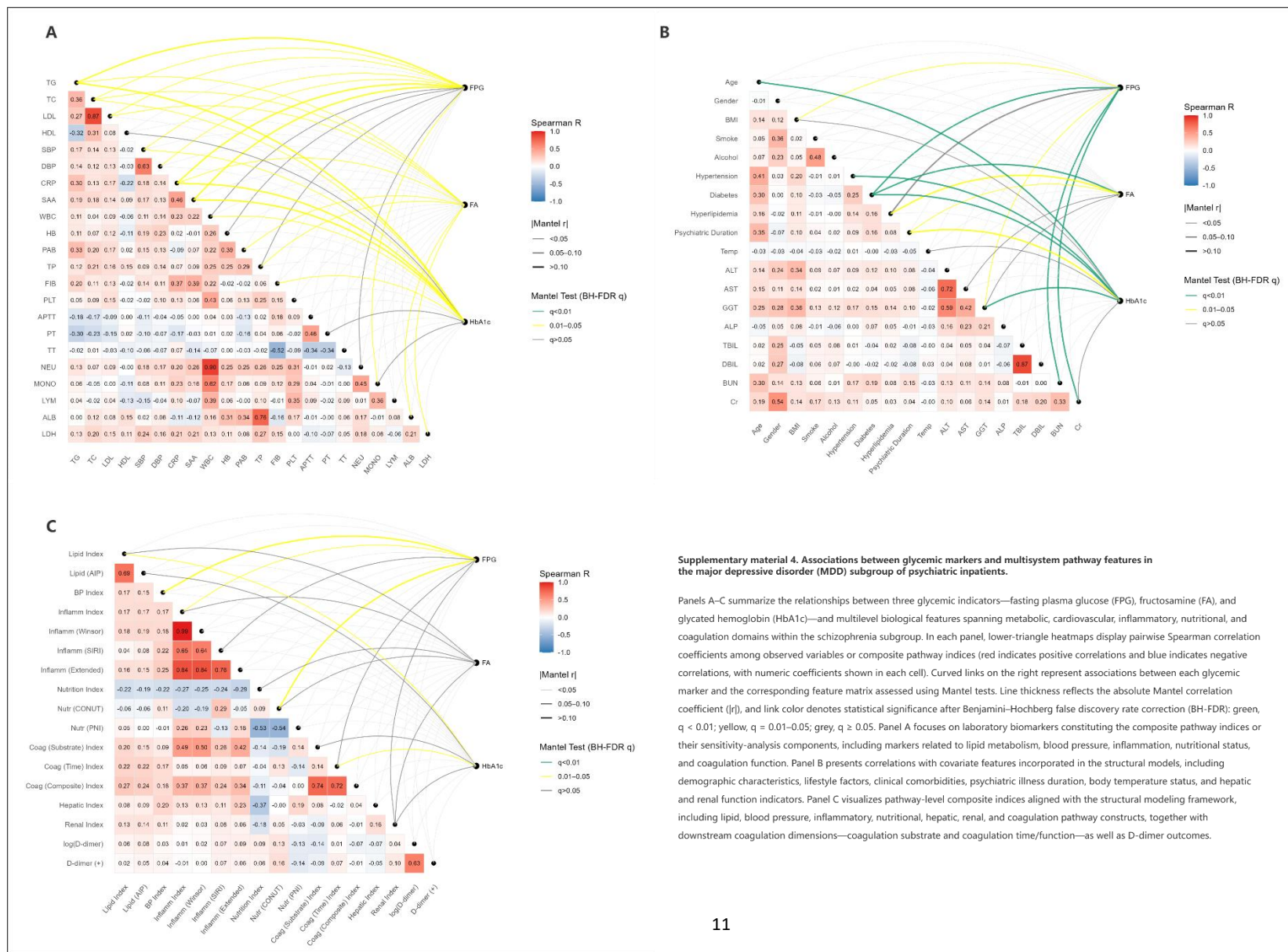
Supplementary material 2. Associations between glycemic markers and multisystem pathway features in the schizophrenia (SCZ) subgroup of psychiatric inpatients.

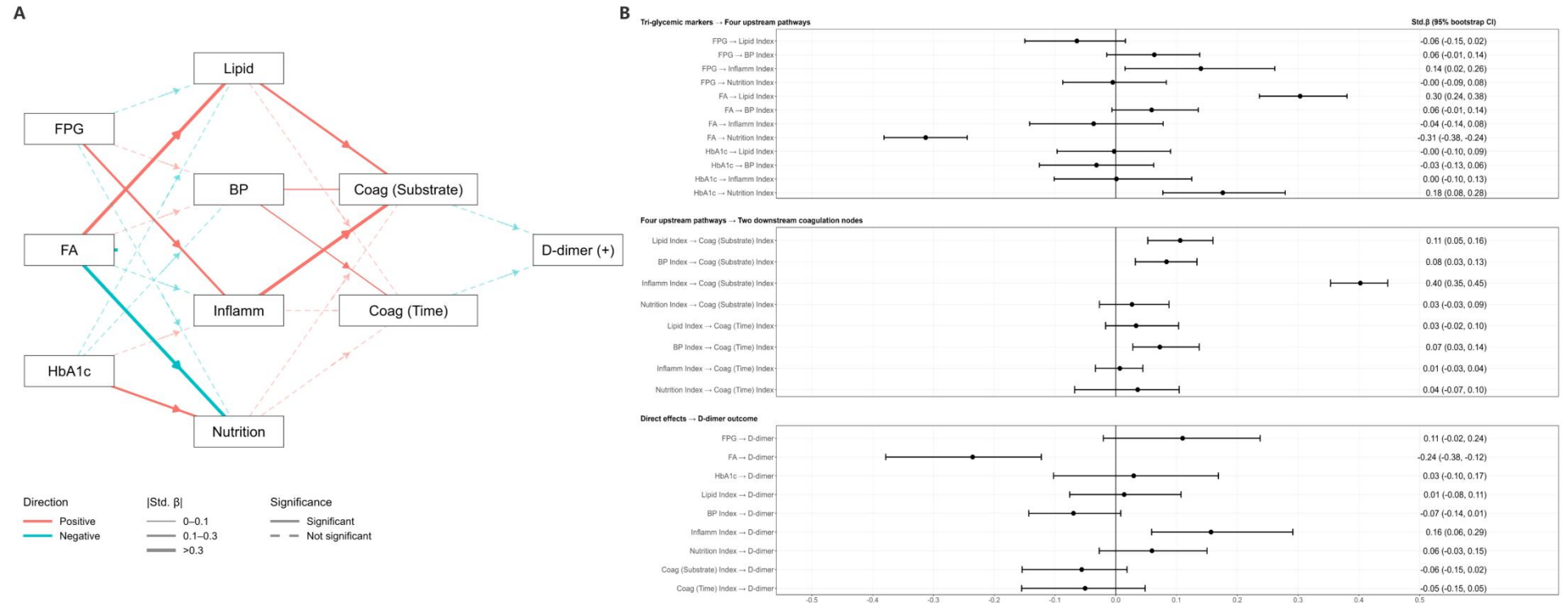
Panel A–C summarize the relationships between three glycemic indicators—fasting plasma glucose (FPG), fructosamine (FA), and glycated hemoglobin (HbA1c)—and multilevel biological features spanning metabolic, cardiovascular, inflammatory, nutritional, and coagulation domains within the schizophrenia subgroup. In each panel, lower-triangle heatmaps display pairwise Spearman correlation coefficients among observed variables or composite pathway indices (red indicates positive correlations and blue indicates negative correlations, with numeric coefficients shown in each cell). Curved links on the right represent associations between each glycemic marker and the corresponding feature matrix assessed using Mantel tests. Line thickness reflects the absolute Mantel correlation coefficient ($|r|$), and link color denotes statistical significance after Benjamini–Hochberg false discovery rate correction (BH-FDR): green, $q < 0.01$; yellow, $q = 0.01–0.05$; grey, $q \geq 0.05$. Panel A focuses on laboratory biomarkers constituting the composite pathway indices or their sensitivity-analysis components, including markers related to lipid metabolism, blood pressure, inflammation, nutritional status, and coagulation function. Panel B presents correlations with covariate features incorporated in the structural models, including demographic characteristics, lifestyle factors, clinical comorbidities, psychiatric illness duration, body temperature status, and hepatic and renal function indicators. Panel C visualizes pathway-level composite indices aligned with the structural modeling framework, including lipid, blood pressure, inflammatory, nutritional, hepatic, renal, and coagulation pathway constructs, together with downstream coagulation dimensions—coagulation substrate and coagulation time/function—as well as D-dimer outcomes.



Supplementary material 3. Associations between glycemic markers and multisystem pathway features in the bipolar disorder (BD) subgroup of psychiatric inpatients.

Panels A–C summarize the relationships between three glycemic indicators—fasting plasma glucose (FPG), fructosamine (FA), and glycated hemoglobin (HbA1c)—and multilevel biological features spanning metabolic, cardiovascular, inflammatory, nutritional, and coagulation domains within the schizophrenia subgroup. In each panel, lower-triangle heatmaps display pairwise Spearman correlation coefficients among observed variables or composite pathway indices (red indicates positive correlations and blue indicates negative correlations, with numeric coefficients shown in each cell). Curved links on the right represent associations between each glycemic marker and the corresponding feature matrix assessed using Mantel tests. Line thickness reflects the absolute Mantel correlation coefficient ($|r|$), and link color denotes statistical significance after Benjamini–Hochberg false discovery rate correction (BH-FDR): green, $q < 0.01$; yellow, $q = 0.01–0.05$; grey, $q \geq 0.05$. Panel A focuses on laboratory biomarkers constituting the composite pathway indices or their sensitivity-analysis components, including markers related to lipid metabolism, blood pressure, inflammation, nutritional status, and coagulation function. Panel B presents correlations with covariate features incorporated in the structural models, including demographic characteristics, lifestyle factors, clinical comorbidities, psychiatric illness duration, body temperature status, and hepatic and renal function indicators. Panel C visualizes pathway-level composite indices aligned with the structural modeling framework, including lipid, blood pressure, inflammatory, nutritional, hepatic, renal, and coagulation pathway constructs, together with downstream coagulation dimensions—coagulation substrate and coagulation time/function—as well as D-dimer outcomes.

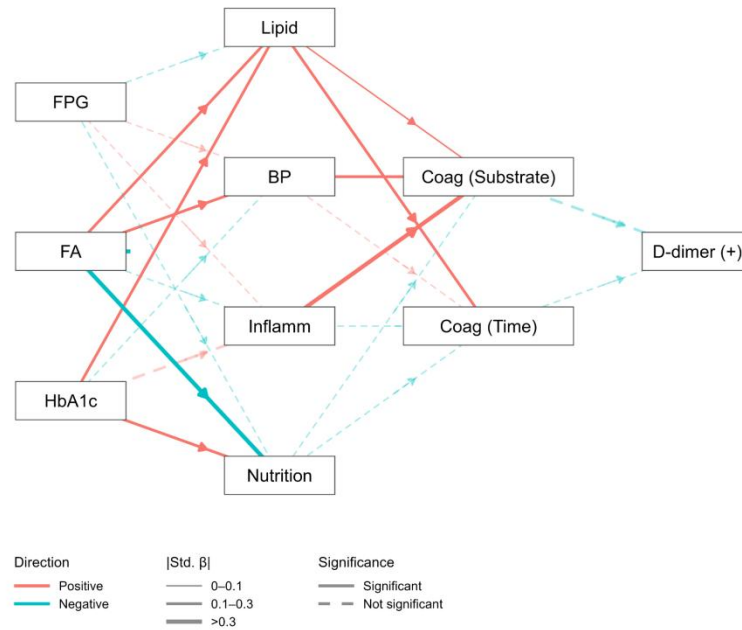




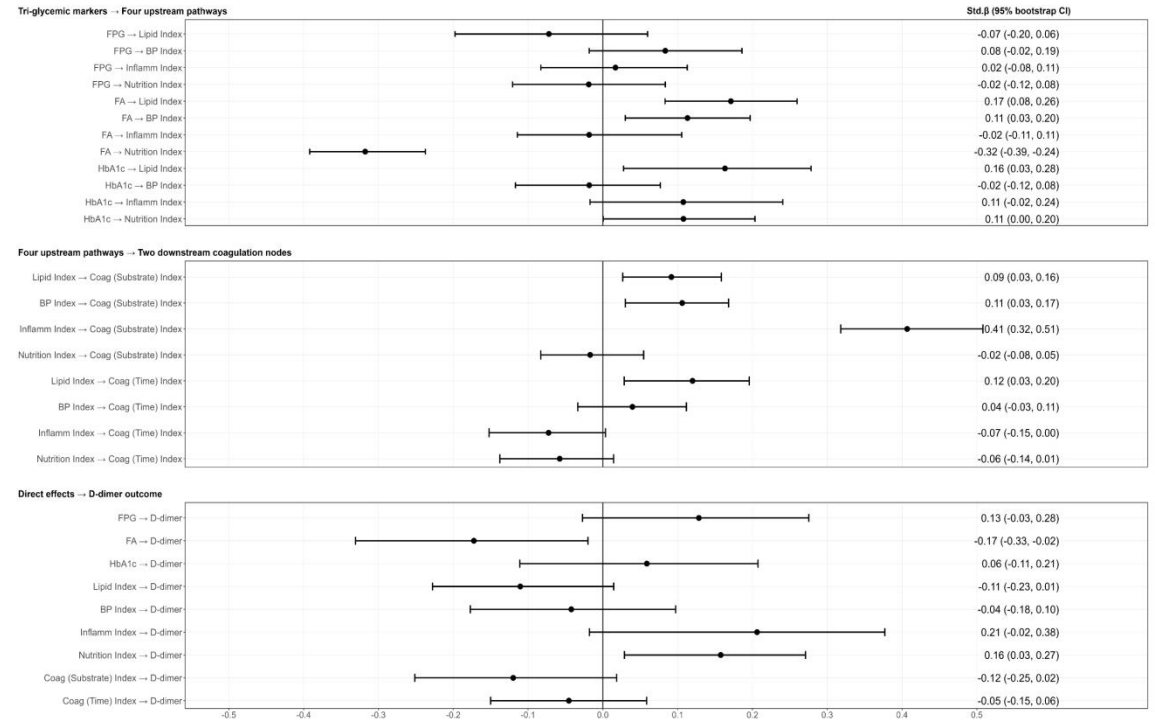
Supplementary material 5. Overview of the serial SEM pathways and standardized bootstrap-estimated effects on hypercoagulability in the schizophrenia cohort.

The left panel (A) depicts the estimated serial SEM pathways linking three glycemic indicators—fasting plasma glucose (FPG), fructosamine (FA), and glycated hemoglobin (HbA1c)—to D-dimer outcomes in the schizophrenia (SCZ) subgroup. Glycemic indicators are modeled to relate to D-dimer through four upstream pathway-level indices (Lipid Index, BP Index, Inflammation Index, and Nutrition Index) and two downstream coagulation-related nodes capturing complementary aspects of hemostasis. Red arrows indicate positive standardized associations and blue arrows indicate negative associations. Solid lines denote statistically significant paths, whereas dashed lines indicate non-significant paths. Line width reflects the magnitude of the standardized coefficient (β_{std}). Collectively, the structural component explains a non-trivial proportion of variance (R^2) in key endogenous nodes within the SCZ subgroup: Lipid Index = 0.231, BP Index = 0.209, Inflammation Index = 0.064, Nutrition Index = 0.286, Coagulation Substrate Index = 0.234, Coagulation Time/Function Index = 0.019, and D-dimer = 0.191. The right panel (B) summarizes the corresponding standardized path estimates using forest plots with 95% bootstrap confidence intervals (β_{std} [95% CI]). Effects are organized into three sequential layers aligned with the serial pathway structure: (1) glycemic indicators → upstream pathway indices, (2) upstream pathway indices → downstream coagulation nodes, and (3) direct effects on D-dimer. Points represent standardized coefficients, horizontal bars indicate bootstrap-derived 95% confidence intervals, and the vertical reference line denotes the null effect ($\beta_{std} = 0$). Together, panels A and B provide an integrated overview of the modeled multisystem associations linking glycemic markers, intermediate physiological pathways, and D-dimer outcomes within the schizophrenia subgroup.

A



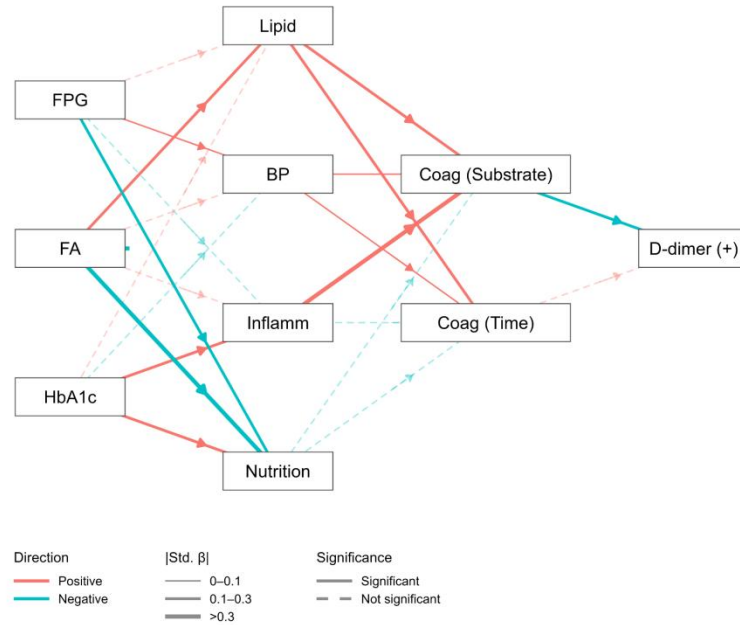
B



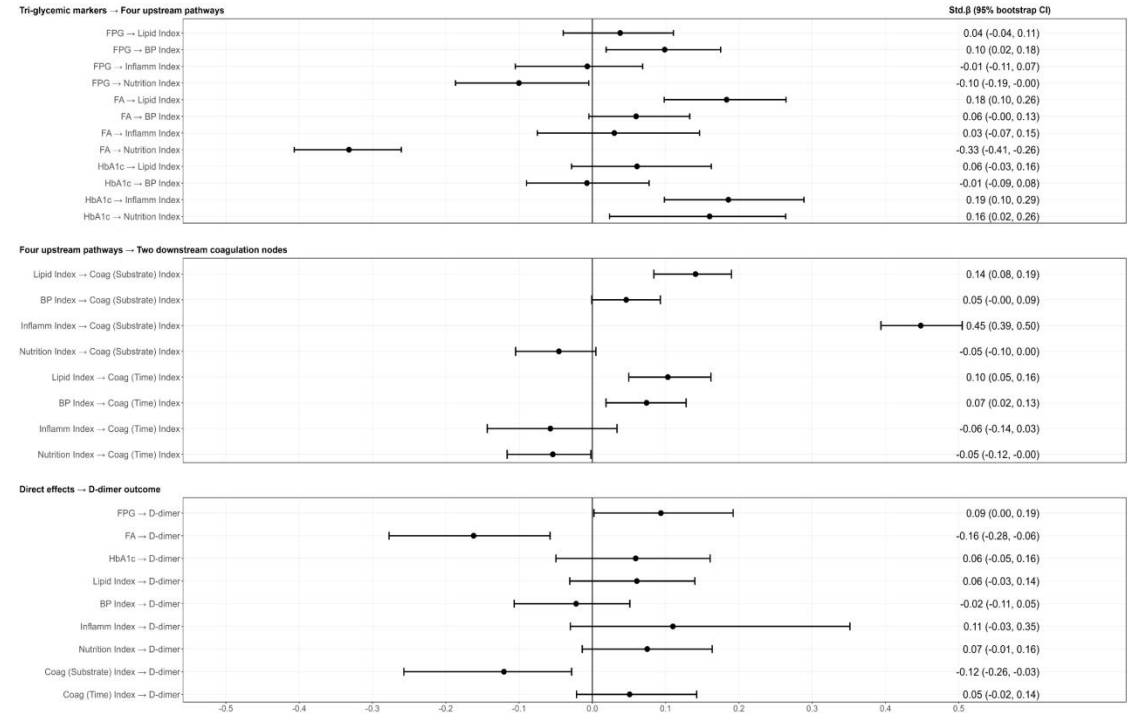
Supplementary material 6. Overview of the serial SEM pathways and standardized bootstrap-estimated effects on hypercoagulability in the bipolar disorder cohort.

The left panel (A) depicts the estimated serial SEM pathways linking three glycemic indicators—fasting plasma glucose (FPG), fructosamine (FA), and glycated hemoglobin (HbA1c)—to D-dimer outcomes in the bipolar disorder (BD) subgroup. Glycemic indicators are modeled to relate to D-dimer through four upstream pathway-level indices (Lipid Index, BP Index, Inflammation Index, and Nutrition Index) and two downstream coagulation-related nodes capturing complementary aspects of hemostasis. Red arrows indicate positive standardized associations and blue arrows indicate negative associations. Solid lines denote statistically significant paths, whereas dashed lines indicate non-significant paths. Line width reflects the magnitude of the standardized coefficient ($|\beta_{std}|$). Collectively, the structural component explains a non-trivial proportion of variance (R^2) in key endogenous nodes within the BD subgroup: Lipid Index = 0.251, BP Index = 0.275, Inflammation Index = 0.094, Nutrition Index = 0.295, Coagulation Substrate Index = 0.270, Coagulation Time/Function Index = 0.101, and D-dimer = 0.185. The right panel (B) summarizes the corresponding standardized path estimates using forest plots with 95% bootstrap confidence intervals (β_{std} [95% CI]). Effects are organized into three sequential layers aligned with the serial pathway structure: (1) glycemic indicators → upstream pathway indices, (2) upstream pathway indices → downstream coagulation nodes, and (3) direct effects on D-dimer. Points represent standardized coefficients, horizontal bars indicate bootstrap-derived 95% confidence intervals, and the vertical reference line denotes the null effect ($\beta_{std} = 0$). Together, panels A and B provide an integrated overview of the modeled multisystem associations linking glycemic markers, intermediate physiological pathways, and D-dimer outcomes within the bipolar disorder subgroup.

A



B



Supplementary material 7. Overview of the serial SEM pathways and standardized bootstrap-estimated effects on hypercoagulability in the major depressive disorder cohort.

The left panel (A) depicts the estimated serial SEM pathways linking three glycemic indicators—fasting plasma glucose (FPG), fructosamine (FA), and glycated hemoglobin (HbA1c)—to D-dimer outcomes in the major depressive disorder (MDD) subgroup. Glycemic indicators are modeled to relate to D-dimer through four upstream pathway-level indices (Lipid Index, BP Index, Inflammation Index, and Nutrition Index) and two downstream coagulation-related nodes capturing complementary aspects of hemostasis. Red arrows indicate positive standardized associations and blue arrows indicate negative associations. Solid lines denote statistically significant paths, whereas dashed lines indicate non-significant paths. Line width reflects the magnitude of the standardized coefficient (β). Collectively, the structural component explains a non-trivial proportion of variance (R^2) in key endogenous nodes within the MDD subgroup: Lipid Index = 0.171, BP Index = 0.134, Inflammation Index = 0.096, Nutrition Index = 0.265, Coagulation Substrate Index = 0.303, Coagulation Time/Function Index = 0.113, and D-dimer = 0.223. The right panel (B) summarizes the corresponding standardized path estimates using forest plots with 95% bootstrap confidence intervals (β std [95% CI]). Effects are organized into three sequential layers aligned with the serial pathway structure: (1) glycemic indicators → upstream pathway indices, (2) upstream pathway indices → downstream coagulation nodes, and (3) direct effects on D-dimer. Points represent standardized coefficients, horizontal bars indicate bootstrap-derived 95% confidence intervals, and the vertical reference line denotes the null effect (β std = 0). Together, panels A and B provide an integrated overview of the modeled multisystem associations linking glycemic markers, intermediate physiological pathways, and D-dimer outcomes within the major depressive disorder subgroup.

Supplementary material 8. Stability of SEM Structural Pathways

Under Alternative Mediation Structures and Outcome Definitions

Path	Sens. Partial Mediation (Direct-Coag) Model	Sens. Full Mediation Model	Sens. log(D-dimer) Outcome Model
FPG → Lipid Index	-0.03 (-0.08, 0.01)	-0.04 (-0.09, 0.02)	-0.03 (-0.08, 0.02)
FPG → BP Index	0.11 (0.07, 0.16)	0.11 (0.05, 0.16)	0.11 (0.07, 0.16)
FPG → Inflamm Index	0.10 (0.04, 0.16)	0.08 (0.02, 0.15)	0.10 (0.04, 0.15)
FPG → Nutrition Index	-0.04 (-0.10, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)
FA → Lipid Index	0.22 (0.18, 0.27)	0.23 (0.18, 0.27)	0.22 (0.18, 0.26)
FA → BP Index	0.08 (0.04, 0.13)	0.09 (0.05, 0.13)	0.08 (0.04, 0.12)
FA → Inflamm Index	-0.00 (-0.07, 0.06)	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)
FA → Nutrition Index	-0.32 (-0.36, -0.28)	-0.32 (-0.37, -0.29)	-0.32 (-0.37, -0.28)
HbA1c → Lipid Index	0.06 (-0.00, 0.11)	0.06 (0.01, 0.13)	0.06 (-0.00, 0.11)
HbA1c → BP Index	-0.06 (-0.12, -0.01)	-0.05 (-0.11, -0.00)	-0.06 (-0.11, -0.01)
HbA1c → Inflamm Index	-0.01 (-0.06, 0.05)	0.04 (-0.01, 0.11)	-0.01 (-0.06, 0.05)
HbA1c → Nutrition Index	0.17 (0.12, 0.23)	0.17 (0.11, 0.23)	0.17 (0.12, 0.23)
Lipid → Coag(Substrate)	0.11 (0.07, 0.14)	0.12 (0.09, 0.15)	0.12 (0.09, 0.15)
BP → Coag(Substrate)	0.09 (0.06, 0.12)	0.08 (0.05, 0.11)	0.09 (0.05, 0.12)
Inflamm → Coag(Substrate)	0.42 (0.38, 0.45)	0.43 (0.39, 0.47)	0.42 (0.39, 0.46)
Nutrition → Coag(Substrate)	-0.02 (-0.05, 0.02)	-0.01 (-0.04, 0.03)	-0.02 (-0.05, 0.02)
Lipid → Coag(Time)	0.06 (0.03, 0.11)	0.07 (0.03, 0.12)	0.09 (0.05, 0.13)
BP → Coag(Time)	0.07 (0.04, 0.11)	0.07 (0.04, 0.11)	0.08 (0.04, 0.11)
Inflamm → Coag(Time)	-0.02 (-0.06, 0.01)	-0.03 (-0.07, 0.01)	-0.02 (-0.06, 0.01)

Nutrition → Coag(Time)	-0.01 (-0.05, 0.04)	-0.01 (-0.08, 0.03)	-0.03 (-0.08, 0.02)
FPG → D-dimer	0.11 (0.03, 0.18)	—	0.07 (0.01, 0.12)
FA → D-dimer	-0.19 (-0.26, -0.11)	—	-0.12 (-0.16, -0.08)
HbA1c → D-dimer	0.05 (-0.03, 0.13)	—	0.03 (-0.03, 0.08)
Lipid → D-dimer	-0.00 (-0.05, 0.05)	—	0.03 (-0.01, 0.06)
BP → D-dimer	-0.03 (-0.08, 0.02)	—	-0.02 (-0.05, 0.02)
Inflamm → D-dimer	0.16 (0.08, 0.28)	—	0.14 (0.10, 0.18)
Nutrition → D-dimer	0.08 (0.03, 0.14)	—	0.06 (0.02, 0.10)
Coag(Substrate) → D-dimer	-0.09 (-0.15, -0.02)	0.07 (-0.02, 0.24)	-0.08 (-0.12, -0.03)
Coag(Time) → D-dimer	-0.02 (-0.08, 0.05)	-0.07 (-0.16, -0.00)	-0.04 (-0.07, -0.01)

Supplementary Material 9. Stability of SEM Structural Pathways

Under Alternative Upstream Pathway Operationalizations

Path	Sens. Lipid (AIP) Model	Sens. Inflamm (Winsor) Model	Sens. Inflamm (SIRI) Model	Sens. Inflamm (Extended) Model	Sens. Nutr (CONUT) Model	Sens. Nutr (PNI) Model
FPG → Lipid Index	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.02)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.02)	-0.04 (-0.09, 0.02)
FPG → BP Index	0.11 (0.06, 0.16)	0.11 (0.06, 0.15)	0.11 (0.06, 0.15)	0.11 (0.06, 0.16)	0.11 (0.06, 0.15)	0.11 (0.06, 0.16)
FPG → Inflamm Index	0.08 (0.01, 0.14)	0.08 (0.02, 0.15)	0.08 (0.02, 0.15)	0.08 (0.02, 0.15)	0.08 (0.02, 0.14)	0.08 (0.02, 0.15)
FPG → Nutrition Index	-0.04 (-0.08, 0.01)	-0.04 (-0.09, 0.00)	-0.04 (-0.10, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)
FA → Lipid Index	0.23 (0.18, 0.27)	0.23 (0.17, 0.27)	0.23 (0.18, 0.28)	0.23 (0.18, 0.27)	0.23 (0.18, 0.27)	0.23 (0.18, 0.28)
FA → BP Index	0.09 (0.04, 0.14)	0.09 (0.05, 0.13)	0.09 (0.05, 0.14)	0.09 (0.05, 0.14)	0.09 (0.04, 0.14)	0.09 (0.05, 0.13)
FA → Inflamm Index	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)
FA → Nutrition Index	-0.32 (-0.37, -0.29)	-0.32 (-0.37, -0.29)	-0.32 (-0.37, -0.29)	-0.32 (-0.36, -0.29)	-0.32 (-0.37, -0.29)	-0.32 (-0.36, -0.28)
HbA1c → Lipid Index	0.06 (0.00, 0.12)	0.06 (0.01, 0.12)	0.06 (-0.00, 0.12)	0.06 (0.01, 0.12)	0.06 (0.01, 0.12)	0.06 (0.01, 0.12)
HbA1c → BP Index	-0.05 (-0.11, 0.00)	-0.05 (-0.11, -0.00)	-0.05 (-0.11, 0.01)	-0.05 (-0.11, 0.01)	-0.05 (-0.10, 0.00)	-0.05 (-0.10, -0.00)
HbA1c → Inflamm Index	0.04 (-0.02, 0.10)	0.04 (-0.02, 0.11)	0.04 (-0.01, 0.11)	0.04 (-0.02, 0.10)	0.04 (-0.01, 0.11)	0.04 (-0.02, 0.10)
HbA1c → Nutrition Index	0.17 (0.12, 0.23)	0.17 (0.12, 0.23)	0.17 (0.12, 0.23)	0.17 (0.12, 0.23)	0.17 (0.11, 0.23)	0.17 (0.11, 0.23)
Lipid → Coag(Substrate)	0.12 (0.09, 0.15)	0.12 (0.08, 0.16)	0.12 (0.08, 0.15)	0.12 (0.09, 0.15)	0.12 (0.08, 0.15)	0.12 (0.08, 0.15)
BP → Coag(Substrate)	0.08 (0.05, 0.11)	0.08 (0.05, 0.11)	0.08 (0.05, 0.11)	0.08 (0.05, 0.11)	0.08 (0.05, 0.12)	0.08 (0.05, 0.11)
Inflamm → Coag(Substrate)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)
Nutrition → Coag(Substrate)	-0.01 (-0.04, 0.03)	-0.01 (-0.04, 0.03)	-0.01 (-0.05, 0.03)	-0.01 (-0.04, 0.03)	-0.01 (-0.04, 0.03)	-0.01 (-0.04, 0.03)
Lipid → Coag(Time)	0.07 (0.03, 0.12)	0.07 (0.03, 0.11)	0.07 (0.03, 0.12)	0.07 (0.03, 0.11)	0.07 (0.03, 0.11)	0.07 (0.03, 0.11)

BP → Coag(Time)	0.07 (0.04, 0.11)	0.07 (0.04, 0.10)	0.07 (0.04, 0.11)	0.07 (0.04, 0.11)	0.07 (0.04, 0.11)	0.07 (0.04, 0.10)
Inflamm → Coag(Time)	-0.02 (-0.07, 0.01)	-0.02 (-0.06, 0.01)	-0.02 (-0.06, 0.01)	-0.02 (-0.06, 0.01)	-0.02 (-0.07, 0.01)	-0.02 (-0.06, 0.01)
Nutrition → Coag(Time)	-0.01 (-0.08, 0.03)	-0.01 (-0.07, 0.04)	-0.01 (-0.07, 0.04)	-0.01 (-0.07, 0.04)	-0.01 (-0.07, 0.04)	-0.01 (-0.07, 0.03)
FPG → D-dimer	0.12 (0.05, 0.18)	0.12 (0.04, 0.18)	0.12 (0.05, 0.19)	0.12 (0.05, 0.18)	0.12 (0.04, 0.19)	0.12 (0.05, 0.18)
FA → D-dimer	-0.19 (-0.27, -0.12)	-0.19 (-0.26, -0.12)	-0.19 (-0.27, -0.12)	-0.19 (-0.27, -0.13)	-0.19 (-0.26, -0.13)	-0.19 (-0.27, -0.12)
HbA1c → D-dimer	0.03 (-0.05, 0.11)	0.03 (-0.04, 0.11)	0.03 (-0.05, 0.11)	0.03 (-0.05, 0.11)	0.03 (-0.05, 0.10)	0.03 (-0.04, 0.11)
Lipid → D-dimer	0.00 (-0.05, 0.05)	0.00 (-0.05, 0.05)	0.00 (-0.06, 0.05)	0.00 (-0.06, 0.05)	0.00 (-0.06, 0.05)	0.00 (-0.05, 0.06)
BP → D-dimer	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)	-0.03 (-0.09, 0.02)	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)
Inflamm → D-dimer	0.16 (0.09, 0.25)	0.16 (0.09, 0.27)	0.16 (0.09, 0.25)	0.16 (0.08, 0.23)	0.16 (0.08, 0.24)	0.16 (0.08, 0.26)
Nutrition → D-dimer	0.08 (0.03, 0.14)	0.08 (0.03, 0.13)	0.08 (0.03, 0.14)	0.08 (0.02, 0.14)	0.08 (0.03, 0.14)	0.08 (0.03, 0.13)
Coag(Substrate) → D-dimer	-0.09 (-0.15, -0.02)	-0.09 (-0.16, -0.03)	-0.09 (-0.16, -0.02)	-0.09 (-0.15, -0.03)	-0.09 (-0.15, -0.03)	-0.09 (-0.15, -0.03)
Coag(Time) → D-dimer	-0.02 (-0.08, 0.04)	-0.02 (-0.08, 0.04)	-0.02 (-0.08, 0.04)	-0.02 (-0.07, 0.04)	-0.02 (-0.09, 0.04)	-0.02 (-0.08, 0.03)

Supplementary material 10. Stability of SEM Structural Pathways Under Alternative Downstream Coagulation Operationalizations and Covariate Specifications

Path	Sens. Coag (Substrate) Model	Sens. Coag (Time) Model	Sens. Coag (Composite) Model	Sens. Covars (Extended) Model
FPG → Lipid Index	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.08, 0.02)	-0.04 (-0.09, 0.02)
FPG → BP Index	0.11 (0.06, 0.15)	0.11 (0.05, 0.16)	0.11 (0.06, 0.16)	0.11 (0.06, 0.15)
FPG → Inflamm Index	0.08 (0.03, 0.15)	0.08 (0.02, 0.14)	0.08 (0.02, 0.15)	0.08 (0.02, 0.14)
FPG → Nutrition Index	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)	-0.04 (-0.09, 0.01)
FA → Lipid Index	0.23 (0.18, 0.27)	0.23 (0.18, 0.27)	0.23 (0.18, 0.27)	0.23 (0.18, 0.27)
FA → BP Index	0.09 (0.05, 0.13)	0.09 (0.05, 0.13)	0.09 (0.04, 0.14)	0.09 (0.05, 0.14)
FA → Inflamm Index	-0.00 (-0.06, 0.06)	-0.00 (-0.06, 0.06)	-0.00 (-0.07, 0.07)	-0.00 (-0.06, 0.07)
FA → Nutrition Index	-0.32 (-0.37, -0.29)	-0.32 (-0.37, -0.28)	-0.32 (-0.37, -0.28)	-0.32 (-0.37, -0.28)
HbA1c → Lipid Index	0.06 (0.01, 0.12)	0.06 (0.01, 0.12)	0.06 (0.01, 0.12)	0.06 (0.00, 0.13)
HbA1c → BP Index	-0.05 (-0.11, -0.00)	-0.05 (-0.10, 0.01)	-0.05 (-0.11, 0.00)	-0.05 (-0.11, -0.00)
HbA1c → Inflamm Index	0.04 (-0.02, 0.11)	0.04 (-0.02, 0.11)	0.04 (-0.02, 0.11)	0.04 (-0.02, 0.11)
HbA1c → Nutrition Index	0.17 (0.12, 0.23)	0.17 (0.12, 0.23)	0.17 (0.11, 0.23)	0.17 (0.11, 0.24)
Lipid → Coag(Substrate)	0.12 (0.08, 0.15)	0.12 (0.08, 0.15)	0.12 (0.09, 0.15)	0.12 (0.08, 0.15)
BP → Coag(Substrate)	0.08 (0.05, 0.12)	0.08 (0.05, 0.11)	0.08 (0.05, 0.11)	0.08 (0.05, 0.11)
Inflamm → Coag(Substrate)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)	0.42 (0.39, 0.46)
Nutrition → Coag(Substrate)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.03)	-0.01 (-0.04, 0.03)
Lipid → Coag(Time)	0.07 (0.03, 0.11)	0.07 (0.03, 0.12)	0.07 (0.03, 0.11)	0.07 (0.03, 0.11)
BP → Coag(Time)	0.07 (0.04, 0.10)	0.07 (0.04, 0.10)	0.07 (0.04, 0.11)	0.07 (0.04, 0.10)
Inflamm → Coag(Time)	-0.02 (-0.06, 0.01)	-0.02 (-0.06, 0.01)	-0.02 (-0.06, 0.01)	-0.02 (-0.06, 0.01)

Nutrition → Coag(Time)	-0.01 (-0.07, 0.04)	-0.01 (-0.08, 0.04)	-0.01 (-0.07, 0.04)	-0.01 (-0.07, 0.03)
FPG → D-dimer	0.12 (0.04, 0.19)	0.12 (0.05, 0.19)	0.12 (0.05, 0.18)	0.12 (0.05, 0.19)
FA → D-dimer	-0.19 (-0.26, -0.12)	-0.19 (-0.26, -0.12)	-0.19 (-0.27, -0.12)	-0.19 (-0.27, -0.12)
HbA1c → D-dimer	0.03 (-0.04, 0.12)	0.03 (-0.06, 0.12)	0.03 (-0.05, 0.11)	0.03 (-0.04, 0.11)
Lipid → D-dimer	0.00 (-0.05, 0.06)	0.00 (-0.06, 0.06)	0.00 (-0.05, 0.05)	0.00 (-0.05, 0.06)
BP → D-dimer	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)	-0.03 (-0.08, 0.02)
Inflamm → D-dimer	0.16 (0.08, 0.25)	0.16 (0.08, 0.25)	0.16 (0.09, 0.27)	0.16 (0.09, 0.25)
Nutrition → D-dimer	0.08 (0.03, 0.14)	0.08 (0.03, 0.15)	0.08 (0.02, 0.14)	0.08 (0.02, 0.14)
Coag(Substrate) → D-dimer	-0.09 (-0.15, -0.02)	-0.09 (-0.15, -0.03)	-0.09 (-0.15, -0.03)	-0.09 (-0.16, -0.04)
Coag(Time) → D-dimer	-0.02 (-0.08, 0.03)	-0.02 (-0.07, 0.04)	-0.02 (-0.08, 0.04)	-0.02 (-0.08, 0.05)

Supplementary material 11. Stability of SEM Structural Pathways

Under Single-Indicator Glycemic Exposure Specifications

Path	Sens. Single-Sugar (FPG) Model	Sens. Single-Sugar (FA) Model	Sens. Single-Sugar (FA-ALBcorr) Model	Sens. Single-Sugar (HbA1c) Model
FPG → Lipid Index	0.12 (0.08, 0.17)	—	—	—
FPG → BP Index	0.13 (0.09, 0.17)	—	—	—
FPG → Inflamm Index	0.10 (0.06, 0.14)	—	—	—
FPG → Nutrition Index	-0.13 (-0.17, -0.09)	—	—	—
FA → Lipid Index	—	0.24 (0.20, 0.27)	—	—
FA → BP Index	—	0.12 (0.09, 0.16)	—	—
FA → Inflamm Index	—	0.05 (0.01, 0.10)	—	—
FA → Nutrition Index	—	-0.26 (-0.31, -0.23)	—	—
HbA1c → Lipid Index	—	—	—	0.19 (0.15, 0.23)
HbA1c → BP Index	—	—	—	0.08 (0.04, 0.12)
HbA1c → Inflamm Index	—	—	—	0.10 (0.06, 0.15)
HbA1c → Nutrition Index	—	—	—	-0.07 (-0.11, -0.03)
Lipid → Coag(Substrate)	0.12 (0.09, 0.15)	0.12 (0.09, 0.15)	0.12 (0.09, 0.16)	0.12 (0.09, 0.15)
BP → Coag(Substrate)	0.09 (0.06, 0.11)	0.09 (0.05, 0.12)	0.09 (0.06, 0.12)	0.09 (0.05, 0.12)
Inflamm → Coag(Substrate)	0.42 (0.38, 0.45)	0.42 (0.38, 0.46)	0.42 (0.39, 0.45)	0.42 (0.39, 0.46)
Nutrition → Coag(Substrate)	-0.01 (-0.05, 0.02)	-0.01 (-0.05, 0.03)	-0.01 (-0.05, 0.03)	-0.01 (-0.05, 0.02)
Lipid → Coag(Time)	0.08 (0.05, 0.12)	0.07 (0.03, 0.12)	0.07 (0.04, 0.14)	0.08 (0.04, 0.13)
BP → Coag(Time)	0.07 (0.04, 0.11)	0.07 (0.04, 0.11)	0.07 (0.04, 0.12)	0.07 (0.04, 0.11)
Inflamm → Coag(Time)	-0.02 (-0.07, 0.01)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.01)

Nutrition → Coag(Time)	-0.03 (-0.08, 0.02)	-0.01 (-0.07, 0.04)	-0.04 (-0.08, 0.01)	-0.03 (-0.08, 0.02)
FPG → D-dimer	0.04 (-0.02, 0.09)	—	—	—
FA → D-dimer	—	-0.12 (-0.19, -0.05)	—	—
HbA1c → D-dimer	—	—	—	-0.02 (-0.07, 0.05)
Lipid → D-dimer	-0.02 (-0.07, 0.03)	-0.00 (-0.06, 0.06)	0.00 (-0.05, 0.06)	-0.00 (-0.07, 0.04)
BP → D-dimer	-0.03 (-0.08, 0.02)	-0.02 (-0.07, 0.03)	-0.02 (-0.07, 0.03)	-0.03 (-0.08, 0.03)
Inflamm → D-dimer	0.16 (0.07, 0.44)	0.17 (0.08, 0.26)	0.17 (0.09, 0.32)	0.44 (0.06, 0.43)
Nutrition → D-dimer	0.12 (0.05, 0.17)	0.09 (0.03, 0.14)	0.12 (0.07, 0.18)	0.11 (0.05, 0.17)
Coag(Substrate) → D-dimer	-0.08 (-0.22, -0.01)	-0.08 (-0.15, -0.02)	-0.08 (-0.17, -0.02)	-0.20 (-0.22, 0.00)
Coag(Time) → D-dimer	-0.04 (-0.16, 0.02)	-0.02 (-0.07, 0.04)	-0.02 (-0.08, 0.04)	-0.02 (-0.17, 0.03)

Supplementary material 12. Stability of SEM Structural Pathways

Under Alternative Fructosamine Corrections and Glycemic Composite Definitions

Path	Sens. Tri-Sugar (FA-ALBcorr) Model	Sens. Gly-Composite (FA) Model	Sens. Gly-Composite (FA-ALBcorr) Model
FPG → Lipid Index	0.00 (-0.05, 0.05)	—	—
FPG → BP Index	0.14 (0.10, 0.19)	—	—
FPG → Inflamm Index	0.07 (0.01, 0.13)	—	—
FPG → Nutrition Index	-0.19 (-0.23, -0.14)	—	—
FA → Lipid Index	—	—	—
FA → BP Index	—	—	—
FA → Inflamm Index	—	—	—
FA → Nutrition Index	—	—	—
HbA1c → Lipid Index	0.08 (0.03, 0.14)	—	—
HbA1c → BP Index	-0.00 (-0.06, 0.05)	—	—
HbA1c → Inflamm Index	0.01 (-0.04, 0.08)	—	—
HbA1c → Nutrition Index	-0.08 (-0.14, -0.03)	—	—
Lipid → Coag(Substrate)	0.12 (0.08, 0.16)	0.12 (0.09, 0.16)	0.12 (0.08, 0.16)
BP → Coag(Substrate)	0.08 (0.06, 0.11)	0.09 (0.06, 0.12)	0.09 (0.06, 0.12)
Inflamm → Coag(Substrate)	0.42 (0.39, 0.46)	0.42 (0.38, 0.46)	0.42 (0.39, 0.46)
Nutrition → Coag(Substrate)	-0.01 (-0.04, 0.02)	-0.01 (-0.05, 0.02)	-0.01 (-0.05, 0.02)
Lipid → Coag(Time)	0.06 (0.03, 0.11)	0.07 (0.04, 0.13)	0.07 (0.04, 0.13)
BP → Coag(Time)	0.07 (0.04, 0.11)	0.07 (0.04, 0.11)	0.07 (0.04, 0.11)
Inflamm → Coag(Time)	-0.03 (-0.07, 0.01)	-0.02 (-0.06, 0.02)	-0.02 (-0.06, 0.02)

Nutrition → Coag(Time)	-0.04 (-0.09, 0.01)	-0.02 (-0.07, 0.03)	-0.03 (-0.08, 0.02)
FPG → D-dimer	0.11 (0.04, 0.17)	—	—
FA → D-dimer	—	—	—
HbA1c → D-dimer	0.06 (-0.02, 0.14)	—	—
Lipid → D-dimer	0.01 (-0.05, 0.06)	-0.01 (-0.07, 0.04)	-0.01 (-0.07, 0.04)
BP → D-dimer	-0.03 (-0.09, 0.01)	-0.03 (-0.08, 0.02)	-0.03 (-0.07, 0.02)
Inflamm → D-dimer	0.16 (0.10, 0.35)	0.17 (0.02, 0.48)	0.17 (0.08, 0.47)
Nutrition → D-dimer	0.14 (0.09, 0.20)	0.11 (0.05, 0.17)	0.11 (0.06, 0.17)
Coag(Substrate) → D-dimer	-0.08 (-0.16, -0.02)	-0.08 (-0.23, 0.01)	-0.09 (-0.23, -0.01)
Coag(Time) → D-dimer	-0.03 (-0.10, 0.03)	-0.03 (-0.14, 0.03)	-0.04 (-0.13, 0.03)