

Table S1. Individual and joint effect of trehalose and glutamate on the odds of diabetic retinopathy before missing value filling.

Metabolites > median	Model 1		Model 2		Model 3	
	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
Trehalose						
Per IQR	0.41(0.26,0.65)	<0.001	0.33(0.19,0.59)	<0.001	0.11(0.04,0.31)	<0.001
Quartiles						
Q ₁	1.00(1.00,1.00)	Ref.	1.00(1.00,1.00)	Ref.	1.00(1.00,1.00)	Ref.
Q ₂	0.57(0.21,1.51)	0.257	0.26(0.07,0.91)	0.035	0.09(0.02,0.59)	0.012
Q ₃	0.72(0.27,1.92)	0.509	0.42(0.12,1.42)	0.162	0.06(0.01,0.41)	0.004
Q ₄	0.10(0.03,0.32)	<0.001	0.04(0.01,0.19)	<0.001	0.01(0.00,0.03)	<0.001
P for trend		<0.001		<0.001		<0.001
Glutamate						
Per IQR	1.62(1.15,2.30)	0.006	1.66(1.11,2.48)	0.014	1.98(1.21,3.24)	0.006
Quartiles						
Q ₁	1.00(1.00,1.00)	Ref.	1.00(1.00,1.00)	Ref.	1.00(1.00,1.00)	Ref.
Q ₂	1.76(0.66,4.69)	0.257	1.28(0.40,4.11)	0.684	1.30(0.33,5.16)	0.705
Q ₃	3.14(1.17,8.41)	0.023	2.13(0.68,6.66)	0.193	2.64(0.65,10.75)	0.174
Q ₄	3.38(1.25,9.16)	0.017	3.66(1.09,12.33)	0.036	5.57(1.31,23.75)	0.020
P for trend		0.008		0.023		0.010
Trehalose Glutamate						
Yes No	1.00(1.00,1.00)	Ref.	1.00(1.00,1.00)	Ref.	1.00(1.00,1.00)	Ref.
No No	0.89(0.34,2.35)	0.813	0.82(0.25,2.65)	0.738	1.75(0.37,8.20)	0.480
Yes Yes	0.89(0.34,2.35)	0.813	0.73(0.23,2.29)	0.590	0.76(0.20,2.88)	0.689
No Yes	10.23(2.89,36.18)	<0.001	10.04(2.52,40.05)	0.001	29.85(5.19,171.89)	<0.001
Interaction	12.93(2.68,62.40)	0.001	16.82(2.69,105.26)	0.003	22.43(2.45,205.04)	0.006
(Trehalose*Glutamate)						
RERI (95% CI)	9.45(-2.84,21.74)		9.49(-3.74,22.73)		28.35(-22.49,79.18)	

Abbreviation: IQR, interquartile range; Q₁, the first quartile; Q₂, the second quartile; Q₃, the third quartile; Q₄, the fourth quartile; RERI, relative excess risk of interaction; OR, odds ratio.

Model 1 was unadjusted.

Model 2 was adjusted for SBP and duration of diabetes.

Model 3 was adjusted for the confounders chosen by LASSO regression, including TG, SBP, DBP, duration of diabetes, residence, degree of education, smoking status, history of hypertension, ITIADM and therapy or not.