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# The association of serum gamma-glutamyltransferase and the incidence of type 2 diabetes mellitus based on propensity score matching: a retrospective observational cohort study

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**Research article**

**Keywords:** type 2 diabetes mellitus, serum gamma-glutamyltransferase, gender, age

**Posted Date:** September 21st, 2020

**DOI:** https://doi.org/10.21203/rs.3.rs-36902/v2

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# Abstract

**Background:** Previous studies reported that gamma-glutamyltransferase (GGT) may play an important role in the development of diabetes. The purpose of this study is to demonstrate that GGT is an independent risk factor for diabetes and to explore whether the association between GGT and the incidence of diabetes is affected by age and gender in the general Japanese population.

**Methods:** This study is a retrospective observational cohort study. The study included 15464 men and women with an average age of 43.71 years from the Japanese health checkup program at Murakami Memorial Hospital from 2004 to 2015. The serum gamma-glutamyltransferase was stratified by quartiles. Patients were stratified by gender and age.

**Results:** After adjusting for potential confounders, each additional standard deviation (SD) of GGT increases the risk of diabetes by 9%. The hazard ratio (HR) is 1.09 and the confidence interval (CI) is (1.01, 1.17). Participants in the fourth quartiles (Q4,≥ 22IU/L) had a higher risk of diabetes than the first to third quartiles (Q1-Q3) of GGT (HR: 1.47, 95 % CI: 1.15-1.87). Compared with males with lower GGT activity, males aged 40 to 50 years with GGT activity in the fourth quantile had a 53% increased risk of diabetes mellitus.

**Conclusions:** GGT was positively correlated with the incidence of diabetes in the Japanese population. Especially in males aged 40-50 y, the higher the GGT, the higher the risk of developing diabetes.


# Background

With the development of the economy, the improvement of people's living standards and changes in lifestyles, the prevalence of diabetes is increasing year by year in China and worldwide [1]. An estimate released by the International Diabetes Organization, in 2030, people with T2DM will reach 552 million[2]. As a chronic disease, type 2 diabetes mellitus can cause significant series of complications and bring a huge economic burden on society[3]. Therefore, early screening and prevention of type 2 diabetes mellitus are essential.

Serum gamma-glutamyltransferase (GGT), is an enzyme that is mainly responsible for the catabolism of the antioxidant glutathione outside the cell and is currently considered to be a sign of oxidative stress [4]. Serum GGT is considered to be a sign of endogenous fat accumulation and has a close relationship with the liver [5]. Compared with other liver markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin, GGT was still one of the main predictors of type 2 diabetes mellitus[6, 7]. A prospective study reported that even within the normal range of serum GGT, the dose-response relationship was associated with the occurrence of type 2 diabetes mellitus[8]. Some studies have shown that GGT can also independently predict the progression of type 2 diabetes mellitus[9-13]. A previous study found that among subjects with higher GGT, age was more closely related to diabetes [13]. Studies have found that men have a closer influence on the relationship between GGT and diabetes[14].

In this study, after adjusting risk factors and controlling confounding factors, we studied the relationship between GGT and type 2 diabetes. Besides, we further explored the correlation between different serum GGT levels and type 2 diabetes mellitus after stratification by age and gender.

## Methods

# Study design and participants

We downloaded the raw data from the "Dryad Digital Repository" website. The website can use the original data of published papers for free without infringing on the rights of the original author. We cited the following data packages: the Dryad data package [15]. Data from: Ectopic fat obesity presents the greatest risk for incident type 2 diabetes: a population-based longitudinal study, Dryad, Dataset, https://doi. org/10. 5061/dryad. 8q0p192. The study protocol was subject to approval by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Since the downloaded raw data is anonymous, no informed consent is required. All participants filled out questionnaires on demographics. About Japanese standards, the average weekly ethanol intake is divided into the following four groups: no or minimum alcohol consumption per day, < 40 g/week; light, 40–140 grams per week; moderate, 140–280 grams per week; or drinking heavily, > 280g/week[15]. The diagnosis of fatty liver is jointly diagnosed by a trained ultrasound technician and a gastroenterologist. According to the data filled in at the time of admission, the smoking status was divided into 3 categories: never smoke; had smoked in the past but quit smoking□currently smoking. Regular exercise is defined as the type of physical exercise performed more than once a week [16, 17]. More specific details are presented in the original report[15].

# Data source

Japanese baseline demographic data was from a medical examination program at Murakami Memorial Hospital (Gifu, Japan). Variables included in the database file were as follows: sex, age, fatty liver, body mass index (BMI), aspartate aminotransferase (AST), waist circumference(WC), body weight, exercise, high-density lipoprotein cholesterol (HDL-C), gamma-glutamyl transferase(GGT), alanine aminotransferase (ALT), total cholesterol (TC), triglyceride (TG), HbA1c, alcohol consumption, smoking status, fasting plasma glucose(FPG), diastolic blood pressure (DBP), systolic blood pressure (SBP).

# Outcomes

The outcome of the study population during follow-up (2004-2015) was the development of type 2 diabetes mellitus. Incident type 2 diabetes mellitus was defined as fasting plasma glucose≥ 7 mmol/L, HbA1c≥ 6. 5% or self-reported.

# Statistical analysis

The whole process of statistical analysis was divided into five steps. First, we grouped GGT in quartiles. Continuous variables were expressed as the means ± standard deviations, and categorical variables were expressed as a frequency or percentages. One-way ANOVA (normal distribution), Kruskal-Wallis H (skewed distribution) test and chi-square test (categorical variables) were used to determine any significant differences between the means and proportions of the groups. Second, the Kaplan-Meier method was used to draw the cumulative hazard curve, and the log-rank test was used for comparison. Third, the association between GGT and the incidence of diabetes was determined by the cox proportional hazards model. According to the recommendations of the STROBE statement [18], we also showed the results of the unadjusted, minimally adjusted analysis, and fully adjusted analysis. The adjustment of covariance is based on the following principle: after adding it to this model, the matched odds ratio would be changed by at least 10%. Schoenfeld residuals were used to test the proportional-hazards assumption. Fourth, we estimated adjusted HRs of diabetes incidence associated with GGT at baseline, stratified by age (10-y groups), sex, BMI, fatty liver, smoking status, waist circumference, exercise. We also tested the interaction effects in different subgroups. Fifth, for sensitivity analyses, propensity score matching was performed with a 1: 2 matching protocol and a caliper width equal to 0.05 of the standard deviation of the propensity score. We matched patients by sex, age, fatty liver, BMI, WC, ALT, AST, TC, TG, alcohol consumption, smoking status,exercise, FPG, DBP, SBP. After propensity score matching, paired t-test and chi-square tests were used to determine any significant differences between the non-diabetes and diabetes groups. Statistical packages R (version 3.4.3, The R Foundation; http://www.r-project.org) was used for statistical analyses.

# Results

In this study, a total of 15,464 people enrolled in the study. Female 7034 (45.49%), male 8430 (54.51%), the average age of the population was 43.71 years, the average GGT was 20.31IU/L, and the average follow-up time was 6.05y. The study population was divided into four groups according to the GGT quartiles. As can be seen from Table 1, age, BMI, WC, ALT, AST, body weight, TC, TG, HbA1c, FPG, DBP and SBP were positively correlated with GGT, and the *P* value of the trend test was significant. The proportion of fatty liver in GGTQ4 was much higher than GGTQ1-3, and this difference was statistically significant. There was also a positive correlation between alcohol intaking and GGT. For the factor of smoking, the proportion of people with high GGT was higher than that of people with low GGT in the current and past smokers. During the follow-up period, the proportion of patients diagnosed with diabetes was higher in GGTQ4 than in GGTQ1-3. The cumulative incidence of diabetes stratified by GGT quartiles was shown in Fig.1. It can be seen that the risk of diabetes mellitus in GGTQ4 was much higher than GGTQ1, GGTQ2, GGTQ3. We classified GGT into GGTQ4 (≥ 22IU/L) and GGTQ1-3 (< 22IU/), with GGT 22 IU/L as the boundary.

The COX regression analysis model was used to estimate the correlation between GGT and diabetes mellitus. As can be seen from Table 2, in the unadjusted model, there was a positive correlation between

GGT and the incident of diabetes. In Model I, we adjusted sex and age, and we found that there was still a positive correlation between GGT and the incident of diabetes. In Model II, after adjusting sex, age, fatty liver, BMI, ALT, AST, WC, exercise, smoking status, TC, TG, alcohol consumption, FPG, DBP and SBP, the risk of diabetes increased by 9% for every SD raised by GGT (per SD increase, HR: 1.09, 95%CI (1.01-1.17), *P* = 0.035). For sensitivity analysis, we converted GGT to a categorical variable (quartile). In the adjusted II model, compared with GGTQ1, the HR for diabetes in the GGTQ4 group was 1.46 (95%:1.07-2.56, *P* = 0.008). The Schoenfeld residual test for the adjusted II model was not statistically significant (p > 0.05, Table S1). For further analysis, with GGT 22IU/L as the boundary, GGTQ4 was classified into one group, and GGTQ1-3 was classified into another group. It was noted that compared to GGTQ1-3 in the adjusted model II, the HR for Q4 diabetes progression was 1.47 (95%CI: 1.15-1.87, *P* = 0.002).

After stratification, we analyzed based on the main covariates known to affect diabetes, including sex, age, BMI, smoking status, alcohol consumption, WC, exercise, fatty liver. As shown in Fig.2, the tests for interactions were significant for BMI (*P* for interaction = 0.022) and sex ( *P* for interaction = 0.047), while the tests for interactions were not statistically significant for fatty liver, exercise, waist circumference, alcohol consumption and smoking status (*P* values for interactions were larger than 0.05). For further sensitivity analysis, we stratified by age and gender. As shown in Table 3, in the adjusted model, 40–50 y males with the highest quartile (Q4) of GGT had 53% increased odds for incident diabetes, compared with males in the lower GGT. In other age groups, the risk of diabetes was not statistically significant. According to previous research, we divide BMI into three categories: underweight (BMI < 18.5 kg/$m^2$), normal weight (18.5 ≤ BMI < 25 kg/$m^2$) and obesity (BMI ≥ 25 kg/$m^2$)[19]. Compared with normal-weight participants (Table S2), GGT in obese participants was associated with higher risks of diabetes mellitus (HR: 1.51 vs. 1.44).

For propensity score matching, we matched patients by, sex, age, fatty liver, BMI, WC, ALT, AST, TC, TG, alcohol consumption, smoking status, FPG, DBP, SBP in a range of ± 0.05. As a result, we matched 746 non-diabetes patients and 373 patients diagnosed with diabetes. Their baseline characteristics are presented in Table 4. Participants finally diagnosed diabetes had higher baseline GGT activity (30.6 ± 25.8 IU/L VS 26.5 ± 22.5 IU/L, *P* < 0.001) than no diabetes participants. After further adjusted for the propensity score and ALT, compared with the participants in the first quartile of GGT, the HR for diabetes in those with the fourth quartile of GGT was 1.34 (95%CI: 1.06- 1.69, *P*< 0.05, Table S3). GGT activities remained positively associated with the incidence of diabetes. After propensity score matching, we still found that GGT was positively associated with the risk of diabetes (Table S4). The results before matching are presented in Table S5, all effect factors in the diabetes group and the non-diabetes had significant statistical differences.

# Discussion

This study mainly explored the relationship between GGT and type 2 diabetes mellitus, and confirmed that GGT was an independent risk factor for incident diabetes among participants. Male aged 40-50 years with GGT ≥ 22 IU / L were more likely to develop diabetes mellitus. Their hazard ratio was 1.53

compared with that of people with GGT < 22 IU/L. It was consistent with the results of previous investigations[20, 21].

Previous studies had shown that GGT might be one of the crucial factors to predict type 2 diabetes mellitus[22]. Some scholars mentioned that there was a dose-response relationship between GGT and diabetes mellitus. Increasing GGT concentration in its physiological range was a sensitive and early biomarker for the development of diabetes[12]. Moreover, we found that 40- 50 y males had a higher risk of incident diabetes. The mechanism of the heterogeneity of serum GGT effects of age and gender is still unclear. We speculated that it was related to visceral fat accumulation. Because 40-50-year-old men accumulate fat in their abdomen, their waist circumference was the largest of all age groups (Table S6), and the accumulated endogenous fat would affect insulin resistance. Decreased insulin secretion and decreased insulin sensitivity are the main characteristics of the pathophysiology of type 2 diabetes[23].

Misuzu Fujita[19] studied the effects of smoking, drinking, ALT, BMI, and GGT on the incidence of type 2 diabetes mellitus. We performed subgroup analysis on important covariates such as smoking, drinking, ALT, and BMI [24]. Our research found that in obese people (BMI $\geq$ 25 kg/$m^2$), high levels of GGT were more likely to develop diabetes. Previous studies have also confirmed that with the increase of BMI, the association between serum GGT and diabetes has become stronger, and even among people with BMI < 25 kg/$m^2$, serum GGT was positively correlated with diabetes[25]. Some authors speculate that this is related to visceral fat accumulation[10]. The accumulation of visceral fat in the liver produces insulin resistance[14], which may provide a reasonable explanation. The observed relationship between GGT and diabetes cannot be explained by alcohol or liver dysfunction. We have the following assumptions: GGT is an ectoenzyme that usually exists on the outside of the cell membrane. Its main function is to maintain the concentration of glutathione (GSH) in the cell, and glutathione is a key antioxidant for the cell[26-28]. The increase in serum GGT may be a response to oxidative stress, which means that the transport of glutathione into cells increases[13]. Some researchers also believed that serum GGT level was a marker of oxidative stress, which was defined by increased free radicals' presence and lipid oxidation[13, 29]. Therefore, an increase in GGT can indicate that oxidative stress is increasing at the cellular level. The pancreatic beta cells that regulate insulin secretion are particularly sensitive to oxidative stress because antioxidant enzymes (such as peroxidase) are relatively low[13]. Indeed, it is known that oxidative stress is a factor that reduces pancreatic insulin secretion by destroying pancreatic beta cells[30]. Some researches clearly showed that in the presence of Fe3 + or Cu2 +, GGT itself directly participated in the production of reactive oxygen species (ROS)[31, 32]. The reactive sulfhydryl group of cysteine-glycine derived from GGT-mediated GSH cleavage may cause the reduction of ferric iron to divalent iron, thereby starting the redox cycle process, generating active oxygen, superoxide Anions, and hydrogen peroxide. They can all induce oxidative stress in cells. The latter can cause insulin resistance and islet b-cell damage, thereby increasing the risk of insulin. Higher GGT can promote GSH catabolism and lead to more reactive oxygen species (ROS) production[33]

This study has several strengths. First, this is a large longitudinal study to confirm the relationship between GGT and type 2 diabetes mellitus. Second, for sensitivity analysis, subgroup analyses and

propensity score matching were performed. Third, this is an observational study that cannot avoid confounding factors. We used strict statistical adjustments to minimize the effects of confounding factors.

There are some limitations to our study. First, it is a secondary study and the inclusion of covariates is restricted. Many confounding factors such as high-calorie dietary habits, insulin resistance, inflammatory factors, women's pregnancy and menopause are not included. Second, the population is limited to the Japanese population, and other races are not considered. Third, due to the lack of a 75-gram oral glucose tolerance test, some type 2 diabetes may be misdiagnosed.

# Conclusion

GGT is positively correlated with the incidence of type 2 diabetes in the general population of Japan. The high GGT activities in Males aged 40-50 years were more likely to develop diabetes mellitus, compared to low GGT activities. The detection of GGT is easy to obtain in the clinic, and the cost is low. Therefore, if there are more prospective studies to confirm our results in the future, our findings may provide a reference for clinical prevention of diabetes and screening of high-risk diabetes patients.

# Abbreviations

BMI: body mass index; ALT: alanine aminotransferase; AST: aspartate aminotransferase; DBP: diastolic blood pressure; GGT: gamma-glutamyl transferase; HbA1c: hemoglobin A1c; HDL: high-density lipoprotein; TC: total cholesterol; SBP: systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; CI: confidence interval; SD: standard deviation; HR: hazard ratio.

# Declarations

### Ethics approval and consent to participate

The study protocol was subject to approval by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University. Since the downloaded raw data is anonymous, no informed consent is required.

### Consent for publication

Not applicable.

### Availability of data and material

The data analyzed in the study are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.


### Funding

Not applicable.


### Authors' contributions

RJ and SKH designed the study. BYD and ZWJ collected the data. BYD, ZWJ and LYH conducted the statistical analysis. BYD, ZWJ, HC, MXC, QF and RJ analyzed and interpreted the data. All authors wrote, reviewed and edited the manuscript. All authors read and approved the final manuscript.


### Acknowledgements

The authors thank Takuro Okamura et al for providing the raw data.



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# Tables

**Table 1** Baseline Characteristics of participants by γ-glutamyltranspeptidase quartiles (N =15464)

| Characteristics | Q1 | Q2 | Q3 | Q4 | *P*-value |
|---|---|---|---|---|---|
| | <11.00 IU/L | 11.00 to < 15.00 IU/L | 15.00 to < 22.00 IU/L | ≥22.00 IU/L | |
| No. of participants | 2885 | 2328 | 3674 | 3304 | |
| Age (years) | 42.18 ± 8.49 | 42.91 ± 8.88 | 44.22 ± 9.19 | 45.11 ± 8.64 | < 0.001 |
| BMI (kg/m^2) | 20.67 ± 2.40 | 21.27 ± 2.71 | 22.33 ± 3.04 | 23.82 ± 3.24 | < 0.001 |
| WC (cm) | 70.54 ± 7.27 | 73.64 ± 7.78 | 77.80 ± 8.26 | 82.28 ± 8.57 | < 0.001 |
| ALT (IU/L) | 12.86 ± 5.23 | 15.26 ± 5.60 | 19.56 ± 8.52 | 30.37 ± 21.87 | < 0.001 |
| AST (IU/L) | 14.96 ± 4.23 | 16.56 ± 4.83 | 18.26 ± 5.74 | 22.88 ± 13.33 | < 0.001 |
| Body Weight (kg) | 53.36 ± 8.15 | 56.78 ± 9.68 | 62.51 ± 10.88 | 67.93 ± 11.55 | < 0.001 |
| HDL (mmol/L) | 1.59 ± 0.37 | 1.54 ± 0.40 | 1.42 ± 0.41 | 1.33 ± 0.38 | < 0.001 |
| TC (mmol/L) | 4.90 ± 0.83 | 5.00 ± 0.82 | 5.14 ± 0.86 | 5.40 ± 0.87 | < 0.001 |
| TG (mmol/L) | 0.61 ± 0.31 | 0.72 ± 0.45 | 0.93 ± 0.59 | 1.31 ± 0.85 | < 0.001 |
| HbA1c (mmol/mol) | 32.33 ± 3.49 | 32.91 ± 3.36 | 33.23 ± 3.46 | 33.44 ± 3.68 | < 0.001 |
| FPG (mmol/L) | 4.95 ± 0.38 | 5.06 ± 0.39 | 5.22 ± 0.39 | 5.35 ± 0.38 | < 0.001 |
| DBP (mmHg) | 66.29 ± 8.90 | 69.06 ± 9.65 | 72.79 ± 9.97 | 76.73 ± 10.33 | < 0.001 |
| SBP (mmHg) | 107.11 ± 12.95 | 111.21 ± 13.96 | 116.06 ± 14.04 | 121.58 ± 14.80 | < 0.001 |
| Sex (male) | 418 (14.49%) | 1610 (36.90%) | 2833 (69.47%) | 3569 (86.25%) | < 0.001 |
| Fatty liver | 86 (2.98%) | 344 (7.88%) | 756 (18.54%) | 1555 (37.58%) | < 0.001 |
| Exercise | 486 (16.85%) | 779 (17.85%) | 773 (18.96%) | 671 (16.22%) | < 0.001 |
| Alcohol consumption | | | | | < 0.001 |
| None | 2699 (93.55%) | 3780 (86.64%) | 3003 (73.64%) | 2323 (56.14%) | |
| Light | 130 (4.51%) | 359 (8.23%) | 582 (14.27%) | 687 (16.60%) | |
| Moderate | 52 (1.80%) | 187 (4.29%) | 392 (9.61%) | 729 (17.62%) | |
| Heavy | 4 (0.14%) | 37 (0.85%) | 101 (2.48%) | 399 (9.64%) | |
| Smoking status | | | | | < 0.001 |
| Never | 2340 (81.11%) | 3026 (69.36%) | 2047 (50.20%) | 1618 (39.10%) | |
| Past | 277 (9.60%) | 580 (13.29%) | 962 (23.59%) | 1133 (27.38%) | |
| Current | 268 (9.29%) | 757 (17.35%) | 1069 (26.21%) | 1387 (33.52%) | |
| Year of follow up (years) | 6.87 ± 4.01 | 5.90 ± 3.65 | 5.66 ± 3.64 | 6.01 ± 3.80 | < 0.001 |
| Diabetes was diagnosed during follow-up (%) | 20 (0.69%) | 53 (1.21%) | 85 (2.08%) | 215 (5.20%) | < 0.001 |

**Table 2** Effect modification of GGT on the incident of diabetes

| Exposure | Non-adjusted | | Adjust I | | Adjust II | |
|---|---|---|---|---|---|---|
| | HR (95%CI) | *P*-value | HR (95%CI) | *P*-value | HR (95%CI) | *P*-value |
| GGT (IU/L) | 1.01 (1.01, 1.01) | < 0.001 | 1.01 (1.01, 1.01) | < 0.001 | 1.00 (1.00, 1.01) | 0.035 |
| GGT (IU/L) per SD | 1.23 (1.18, 1.27) | < 0.001 | 1.17 (1.12, 1.23) | < 0.001 | 1.09 (1.01, 1.17) | 0.035 |
| Categories | | | | | | |
| GGT Q1 | 1.0 | | 1.0 | | 1.0 | |
| GGT Q2 | 2.23 (1.33, 3.73) | 0.002 | 2.06 (1.23, 3.47) | 0.006 | 1.34 (0.74, 2.41) | 0.316 |
| GGT Q3 | 4.05 (2.49, 6.60) | < 0.001 | 3.39 (2.03, 5.67) | < 0.001 | 0.98 (0.56, 1.71) | 0.134 |
| GGT Q4 | 9.12 (5.77, 14.43) | < 0.001 | 7.35 (4.47, 12.09) | < 0.001 | 1.46 (1.07, 2.56) | 0.008 |
| Categories | | | | | | |
| GGT Q1-Q3 | 1.0 | | 1.0 | | 1.0 | |
| GGT Q4 | 3.74 (3.05, 4.59) | < 0.001 | 2.98 (2.38, 3.73) | < 0.001 | 1.47 (1.15, 1.87) | 0.002 |

Adjust I model adjust for sex, age.

Adjust II model adjust for sex, age, fatty liver, BMI, ALT, AST, WC, exercise, TC, TG, alcohol consumption, smoking status, FPG, DBP, SBP. CI, confidence interval; SD, standard deviation. (SD: 18.1)

**Table 3** Effect modification of GGT (Q4 vs. Q1–3) on the incident of diabetes, stratified by age and gender.

| Age, y | Sex | Unadjusted | | | | Adjusted | |
|---|---|---|---|---|---|---|---|
| | | Q1-Q3 (%) | Q4 (%) | HR (95%CI) | *P*-value | HR (95%CI) | *P*-value |
| 20to< 30 | | | | | | | |
| | Male | 1/108（0.93%） | 0/35（0%） | 1.00 (1.00, 1.00) | _§ | 0.00 (0.00, Inf) | _§ |
| | Female | 0/263（0%） | 0/5（0%） | 0.00 (0.00, Inf) | _§ | 0.00 (0.00, Inf) | _§ |
| 30to< 40 | | | | | | | |
| | Male | 14/1795 (0.78%) | 39/1079 (3.61%) | 4.58 (2.49, 8.44) | NS | 1.39 (0.66, 2.91) | NS |
| | Female | 15/2198(0.68%) | 2/103 (1.94%) | 3.20 (0.73, 13.98) | < 0.001 | 1.66 (0.31, 8.91) | NS |
| 40to< 50 | | | | | | | |
| | Male | 41/1626 (2.52%) | 88/1427 (6.17%) | 2.58 (1.78, 3.74) | < 0.001 | 1.53 (1.00, 2.35) | 0.047 |
| | Female | 28/2544 (1.10%) | 6/189 (3.17%) | 3.13 (1.28, 7.64) | < 0.001 | 1.42 (0.50, 4.05) | NS |
| 50to< 60 | | | | | | | |
| | Male | 28/1044 (2.68%) | 50/840 (5.95%) | 2.32 (1.46, 3.69) | < 0.001 | 1.38 (0.81, 2.34) | NS |
| | Female | 17/1260 (1.35%) | 11/231(4.76%) | 4.45 (2.08, 9.51) | < 0.001 | 2.27 (0.83, 6.21) | NS |
| ≥ 60 | | | | | | | |
| | Male | 10/288 (3.47%) | 15/188 (7.98%) | 2.54 (1.14, 5.65) | 0.023 | 1.91 (0.77, 4.74) | NS |
| | Female | 4/195 (2.05%) | 4/41 (9.76%) | 4.01 (1.00, 16.11 | 0.049 | 6.63 (0.75, 58.26) | NS |

Adjust for fatty liver, BMI, ALT, AST, WC, exercise, TC, TG, alcohol consumption, smoking status, FPG, DBP, SBP. §, The model failed because of the small sample size.

**Table 4** Baseline characteristics of participants stratified by the outcome after Propensity-Score Matching.

| | No Diabetes (n=746) | Diabetes(n=373) | *P*-value |
|---|---|---|---|
| Age (years) | 46.90 ± 8.97 | 47.14 ± 8.52 | NS |
| Sex (male) | 579 (77.61%) | 286 (76.68%) | NS |
| BMI (kg/m^2) | 25.10 ± 3.65 | 25.03 ± 3.82 | NS |
| WC (cm) | 84.75 ± 9.41 | 85.08 ± 10.20 | NS |
| ALT (IU/L) | 27.13 ± 18.29 | 31.36 ± 20.37 | 0.006 |
| Body Weight (kg) | 70.66 ± 13.11 | 69.84 ± 13.32 | NS |
| TC (mmol/L) | 5.38 ± 0.88 | 5.43 ± 0.90 | NS |
| TG (mmol/L) | 1.46 ± 1.05 | 1.50 ± 0.98 | NS |
| FPG (mmol/L) | 5.53 ± 0.4 | 5.60 ± 0.4 | NS |
| DBP (mmHg) | 77.07 ± 10.77 | 77.18 ± 10.23 | NS |
| SBP (mmHg) | 122.26 ± 15.65 | 122.03 ± 15.59 | NS |
| Fatty liver | 449 (60.19%) | 223 (59.79%) | NS |
| Exercise | 108 (14.48%) | 51 (13.67%) | |
| Alcohol consumption | | | NS |
| None | 536 (71.85%) | 266 (71.31%) | |
| Light | 94 (12.60%) | 40 (10.72%) | |
| Moderate | 77 (10.32%) | 37 (9.92%) | |
| Heavy | 39 (5.23%) | 30 (8.04%) | |
| Smoking status | | | NS |
| Never | 272 (36.46%) | 145 (38.87%) | |
| Past | 198 (26.54%) | 77 (20.64%) | |
| Current | 276 (37.00%) | 151 (40.48%) | |
| GGT (IU/L) | 26.5 ± 22.5 | 30.6 ± 25.8 | < 0.001 |

NS, no significance

# Figures

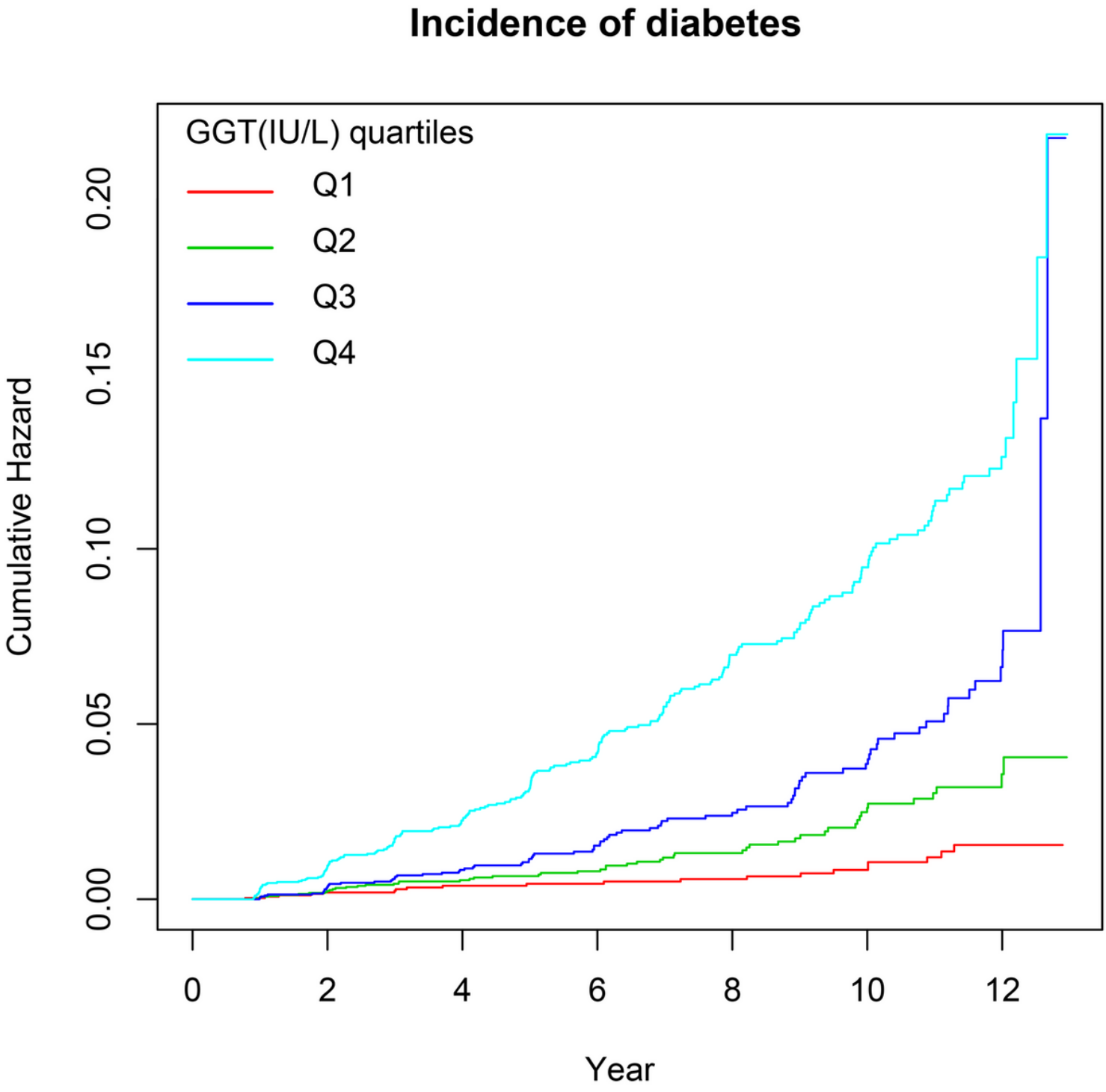


**Figure 1**

Kaplan-Meier curves stratified by GGT quartiles.

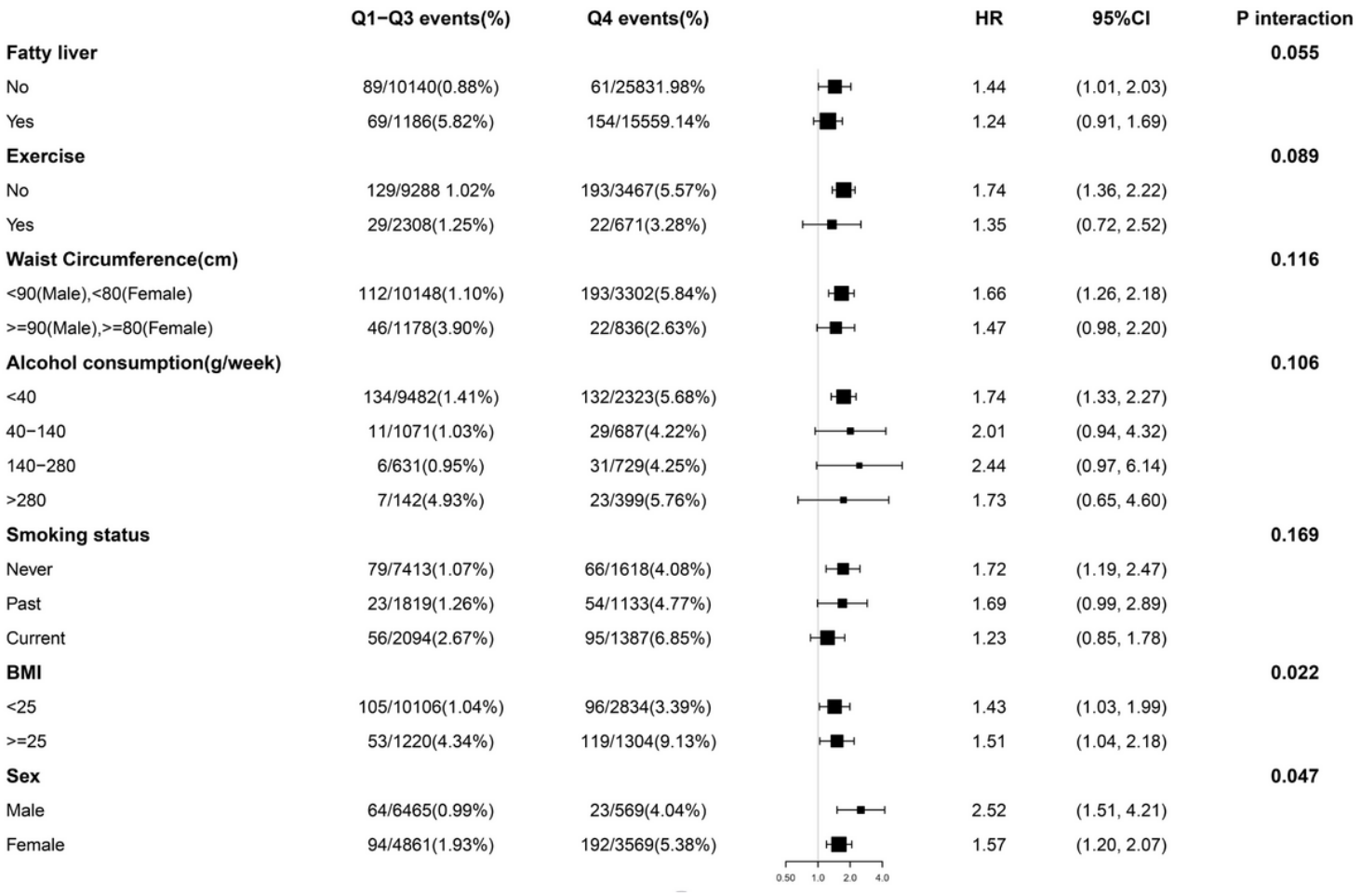


**Figure 2**

Forest plots show the effect size of GGT on incident diabetes in main subgroups.

# Supplementary Files

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

- TableS1revised.docx
- TableS2revised.docx
- TableS3revised.docx
- TableS4revised.docx
- TableS5revised.docx
- TableS6revised.docx
- TableS7revised.docx