Can the triglyceride-glucose index predict the risk of stroke? A meta-analysis of high-quality studies with 12.8 million participants

Gang Xin, Huiya Li and Ji Jiang

Emergency Department, The Affiliated People's Hospital of Ningbo University, Ningbo, Zhejiang, China

ABSTRACT

Objective. The triglyceride-glucose index (TyG) has been actively researched for predicting several diseases. However, high-quality evidence assessing its ability to predict stroke is lacking. We conducted a meta-analysis of high-quality studies examining if TyG can predict stroke in the general population.

Methods. Embase, PubMed, CENTRAL, Web of Science, and Scopus databases were searched until 13th January 2025. Cohort studies on the general population, excluding those with baseline stroke or cardiovascular disease, with a minimum follow-up of four years and reporting an adjusted association between TyG and stroke were included. TyG was assessed as both a categorical and continuous variable.

Results. A total of 13 studies with 12,898,434 individuals were eligible. The overall incidence of stroke was 0.89%. Meta-analysis indicated a statistically significant increased risk of stroke between higher *vs* lower values of TyG (risk ratio (RR): 1.27 95% confidence interval (CI) [1.19–1.35] $I^2 = 66\%$). Per unit increase in TyG was also associated with a statistically significant increase in the risk of stroke (RR: 1.16 95% CI [1.07–1.27] $I^2 = 89\%$). Most results remained unchanged on subgroup analysis based on location, excluded population, stroke diagnosis, TyG data, and follow-up. Meta-regression using moderators sample size, age, male gender, diabetes mellitus, hypertension, TyG cut-off, stroke incidence, and follow-up also failed to reveal significant results.

Conclusion. High TyG is associated with increased risk of stroke in the general population.

Subjects Neuroscience, Neurology

Keywords Insulin resistance, Cerebrovascular disease, Lipids, Risk, Biomarker

INTRODUCTION

Stroke is now the second major cause of mortality worldwide leading to about 1/3rd of all disabilities (*Lozano et al., 2012*). Statistics indicate that about 13 million new incident cases of stroke were diagnosed in 2016 with about 87% being ischemic stroke (*Saini, Guada & Yavagal, 2021*). Chinese data from 2020 shows that approximately 3.4 million patients were diagnosed with first-ever stroke causing about 2.3 million deaths (*Tu et al., 2023*). About 76% of strokes develop in individuals without a prior history of the disease (*Saver et al., 2015*). The illness is a life-altering event for those who experience the disease as well as

Submitted 28 March 2025
Accepted 5 August 2025
Published 9 September 2025

Corresponding author
Gang Xin, xg00142024@163.com

Academic editor
Joao Rocha

Additional Information and Declarations can be found on page 14

DOI 10.7717/peerj.19994

for families and caregivers. About 26% of elderly experiencing stroke become dependent on activities of daily living and about 46% have cognitive impairment (*Go et al., 2014*). These findings support the fact that active and effective prevention can help in reducing the disease burden and there is an urgent need for scaling up the primary prevention programs (*Lozano et al., 2012*). In this context, the development of accurate risk prediction markers and models can help identify high-risk individuals who can be monitored and targeted by effective interventions to reduce the risk of stroke (*Xu et al., 2021*). Despite the establishment of several stroke prediction models and biomarkers in the past few decades, researchers have been unable to identify a single model or marker that is highly effective in predicting the risk of stroke (*Xu et al., 2021*; *Lu et al., 2021*; *Lip et al., 2022*; *Ihle-Hansen et al., 2023*).

Research indicates that insulin resistance could have a major role in the pathogenesis of stroke (*Ding et al., 2022*). Insulin acts as a protective agent for the brain by preventing ischemia, oxidative stress, and apoptosis-induced brain tissue damage. It also modulates cholesterol metabolism in neural tissues and astrocytes and is known to improve cognitive dysfunction in Alzheimer's disease (*Agrawal et al., 2021*; *Ding et al., 2022*). Increased insulin resistance has been linked with a higher risk of stroke in the general population (*Zheng et al., 2024*). However, the current gold standard for assessing insulin resistance, *i.e.,* the hyperinsulinemic-euglycemic clamp is too complex and expensive to be applied routinely in clinical practice (*Cersosimo et al., 2014*). A more accessible marker can be the homeostasis model assessment of insulin resistance (HOMA-IR) index (*Matthews et al., 1985*). Nevertheless, its routine clinical application is also not economical and convenient. The triglyceride-glucose (TyG) index, is considered to be a biomarker for insulin resistance which is calculated using the formula: fasting triglycerides (mg/dl) $\times$ fasting blood glucose (mg/dl)/2 (*Liao et al., 2022*). Studies have shown that high TyG levels are significantly associated with increased risk of coronary artery disease (CAD), contrast-induced nephropathy, hypertension (HT), diabetes mellitus (DM), atrial fibrillation, metabolic dysfunction associated fatty liver disease, metabolic syndrome, and stroke. Moreover, a positive association has also been demonstrated between high TyG and the prognosis of CAD and stroke (*Yin et al., 2024*; *Nayak et al., 2024*).

On the question of its predictive ability for stroke, three prior meta-analysis studies (*Liao et al., 2022*; *Feng et al., 2022*; *Yang et al., 2023*) with eight to eleven studies each have shown that high TyG may be a potential marker for stroke. However, these reviews have several limitations including inclusion of studies on specific populations (like HT, DM, CAD), use of cross-sectional data, and studies with overlapping data. Moreover, the low number of studies with a small number of participants is an additional hindrance that limits the acceptability of the evidence. To overcome the limitations of prior reviews and to present the best possible evidence in the literature, we conducted an updated meta-analysis including only high-quality cohort studies to assess the ability of TyG to predict stroke in the general population.

MATERIALS AND METHODS

Registration

Before beginning the study, all reviewers formulated a protocol which was registered and outlined on PROSPERO. The registration number was CRD42025636156. The review is presented as per the guidelines of PRISMA (*Page et al., 2021*). Ethical approval was not needed as the study was based on published literature.

Data sources and searches

Databases of Embase, PubMed, CENTRAL, Web of Science, and Scopus were searched for all observational studies evaluating the ability of TyG to predict stroke. Following Medical Subject Headings (MeSH) and free keywords were used: 'triglyceride-glucose index', 'triglyceride and glucose index', 'TyG index', 'triglyceride glucose index', 'triacylglycerol glucose index', 'Stroke', 'Cerebrovascular Accident', 'CVA', 'Brain Vascular Accident', and 'Cerebrovascular Disease'. Detailed search strategies for all databases can be found in Table S1. The bibliography for potential articles meeting the inclusion criteria and past reviews was also manually examined. Lastly, a supplemental search was run on Google Scholar for any other potential articles in gray literature. Two reviewers (GX, HL) independently performed the search which was last updated on 13th January 2025.

Eligibility criteria

A detailed criteria to include only high-quality studies was formulated by the reviewers. Studies were included in the review provided that (1) They were cohort studies conducted on the general population without a prior history of stroke or cardiovascular disease (CVD). (2) They assessed the temporal association between baseline TyG measurements and the risk of stroke. (3) They reported outcomes as a multiple covariate-adjusted effect size. (4) Mean or median follow-up was at least four years.

Exclusion criteria were: (1) Studies not reporting independent data on stroke. (2) Study on a cohort with a prespecified illness like DM, HT, CAD, *etc.* (3) Studies using the same database with overlapping study periods. In such cases, the study fulfilling the above-mentioned criteria and with the largest sample size was chosen. We also did not include articles only in abstract form, thesis, and editorials.

Study selection

The search queries were run on respective databases and all results were collated and deduplicated in EndNote software (version X9.3.3, Thomson Reuters, Philadelphia, PA, USA). The remaining studies were analyzed for eligibility by examining the titles and abstracts. Studies chosen for further analysis by either reviewer (GX, HL) were downloaded full texts were assessed. The final selection was after the agreement of both reviewers. All disagreement was resolved through discussion with the third reviewer (JJ).

Data management

Two reviewers (GX, HL) extracted information regarding the author, publication year, population included, exclusion of stroke or CVD, demographic details and comorbidities, identification of stroke, stroke incidence, TyG data (categorical, continuous), cut-off, adjusted covariates, follow-up, and outcomes. Most studies segregated TyG data as quartiles or tertiles comparing the highest with the lowest groups. Data on TyG as a continuous outcome was also extracted for the meta-analysis. If several adjusted models of the outcome were reported by the studies, the model with maximum adjustment was selected. We did not make any assumptions about missing data. The corresponding author of the study was to be contacted in such cases and case of no response, the study was to be omitted from the meta-analysis.

Risk of bias

The quality of studies was assessed using the Newcastle Ottawa Scale (NOS) (*Wells et al., 2020*). Two reviewers (GX, HL) participated in the assessment, and disagreements were resolved by consensus. The reviewers were not blinded. Each study was judged on the following domains using the prespecified questions of NOS: participant selection, group comparability, and outcomes. A score of 8–9 indicated high, 6–7 indicated medium, and <6 indicated low quality. The reviewer JJ was involved to resolve conflicts.

Statistical analysis

The software used was "Review Manager" (RevMan, version 5.3) for the primary meta-analysis. We pooled data of TyG as a categorical and continuous variable separately in an inverse variance random-effects meta-analysis model. A random effects model was chosen due to the expected baseline heterogeneity between the studies which were from different countries and variable populations. Results were generated as risk ratio (RR) and 95% confidence intervals (CI). Heterogeneity among studies was assessed through Cochran's Q statistic and the I^2 index. I^2 of over 50% and/or $P < 0.05$ indicated significant heterogeneity. The influence of individual studies was judged by sensitivity analysis which was done in the Review Manager software itself. One study at a time was removed from the meta-analysis to assess the stability of the results. Publication bias was checked using funnel plots and the Egger's test.

Assessment of the source of heterogeneity was by subgroup and meta-regression analysis. The latter was conducted using the Meta-Essentials tool (*Suurmond, Van Rhee & Hak, 2017*). Studies were divided based on location (Chinese, Asian, Western), excluded population (all CVD or all stroke), stroke diagnosis (ICD codes, medical records, physician-diagnosed), TyG data (quartile or tertile), and follow-up (≥10 or <10 years). Moderators were all continuous variables namely, sample size, age, male gender, DM, HT, TyG cut-off, stroke incidence, and follow-up.

RESULTS

Search results

We have presented the search results in Fig. 1. Of the 3,400 studies found from all databases, we removed 2,488 duplicates. A total of 1,122 studies underwent meticulous screening by the reviewers. Jointly, they selected 40 studies for further analysis. After full-text reading, 13 were selected for the review (*Hong, Han & Park, 2020*; *Zhao et al., 2021*; *Cho et al., 2022*; *Liu et al., 2022b*; *Liu et al., 2022a*; *Che et al., 2023*; *Wang et al., 2023*; *Muhammad et al.,*

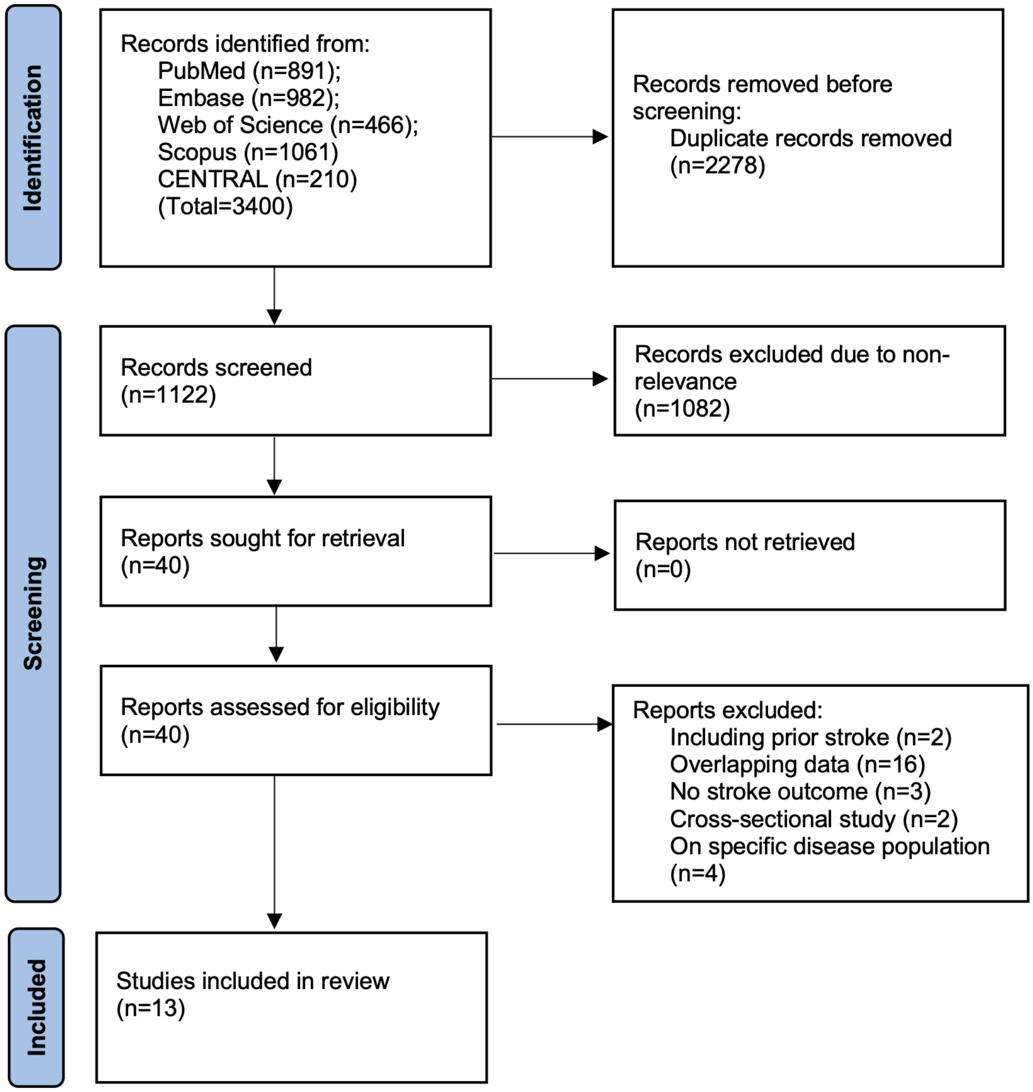

Figure 1 **Study flowchart.**

Full-size DOI: 10.7717/peerj.19994/fig-1

2023; *Wan et al., 2023*; *Yao et al., 2024*; *Li et al., 2024a*; *Li et al., 2024b*; *Rafiee et al., 2024*). Agreement between reviewers was high (kappa = 0.95). The search of additional sources did not reveal any missed study. A list of excluded studies can be found in Table S2.

Study details

As noted in Table 1, the majority of studies were from China utilizing different databases. Two studies were from Korea from the same database but with non-overlapping age of the sample (one was >40 years and the other 20–39 years). One study each was available from the UK, USA, Sweden, and Iran. Ten studies excluded all known CVD patients (including stroke) while three excluded only prior stroke patients. In total, 12,898,434 individuals were enrolled in the 13 studies. The incidence of stroke varied from 0.13 to 13.3%. Overall, the incidence of stroke was found to be 0.89% (115,068/12,989,434). Two studies excluded

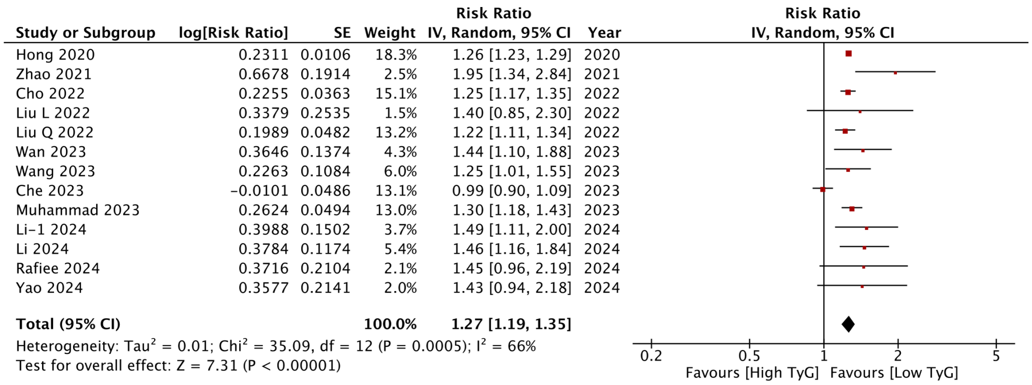

Figure 2 Meta-analysis of the association between TyG (categorical variable) and risk of stroke. Notes: *Hong, Han & Park, 2020*; *Zhao et al., 2021*; *Cho et al., 2022*; *Liu et al., 2022a*; *Liu et al., 2022b*; *Wan et al., 2023*; *Wang et al., 2023*; *Che et al., 2023*; *Muhammad et al., 2023*; *Li et al., 2024a*; *Li et al., 2024b*; *Rafiee et al., 2024*; *Yao et al., 2024*.

Full-size DOI: 10.7717/peerj.19994/fig-2

DM patients and in the remaining studies, the prevalence of baseline DM was 2.5–19%. HT ranged from 6.9–69.1%. In studies not excluding baseline CVD, the prevalence was between 5–13.4%. Data on other comorbidities was limited. Most studies used ICD codes or medical records for the identification of stroke. Eleven studies segregated TyG data as quartiles while two presented it as tertiles. Eight studies additionally used TyG as a continuous variable. Adjusted covariates varied between studies. Follow-up ranged from 4.3 to 26.6 years. All studies were high quality and received an NOS score of nine except one which got eight.

TyG as a categorical variable

Meta-analysis of all 13 studies indicated a statistically significant increased risk of stroke between higher *vs* lower values of TyG (RR: 1.27 95% CI [1.19–1.35]) (Fig. 2). I^2 was found to be 66% indicating high heterogeneity. No change in the significance of RR was found by the reviewers during sensitivity analysis. Publication bias was noted on the funnel plot (Fig. 3). Egger's test was not significant ($p = 0.69$). Subgroup analysis showed that the association between TyG and stroke persisted after dividing studies based on location, excluded population, stroke diagnosis, TyG data, and follow-up (Table 2). Heterogeneity was found to be reduced to zero in some of the subgroup analyses like studies on western cohorts, excluding only baseline stroke, using TyG as tertiles, and with follow-up ≥10 years. Meta-regression analysis found that age, male gender, DM, HT, TyG cut-off, stroke incidence, and follow-up did not have a significant effect on the meta-analysis results (Table 3).

TyG as a continuous variable

Meta-analysis of eight studies showed that a per unit increase in TyG was associated with a statistically significant increase in the risk of stroke (RR: 1.16 95% CI [1.07–1.27]) (Fig. 4). I^2 was 89%, indicating high heterogeneity again. No major asymmetry of the funnel plot was noted (Fig. 5). Egger's test was not significant ($p = 0.76$). The RR remained statistically

Table 1 **Details of included studies.**

Study	Database	Study population	Sample size	Age (y)	Male (%)	DM (%)	HT (%)	CVD (%)	CKD (%)	DL (%)	Stroke diagnosis	TyG data	TyG cut-off[^]	Adjusted covariates	Stroke incidence (%)	F/U (y)	NOS score
Hong, Han & Park (2020)	National Health Insurance Service, Korea	>40y without CVD, not on lipid-lowering or DM medication	5,593,134	52	50.5	3.7	26.9	0	6.2	11.2	ICD code	Quartiles	NR	Age, sex, smoking, alcohol consumption, regular physical activity, low socioeconomic status, BMI, hypertension, TC, HT medications, warfarin, and aspirin	1.59	8.2	9
Zhao et al. (2021)	Rural Chinese Cohort Study	≥40y without CVD and stroke	11,777	53	40.9	NR	NR	0	NR	NR	Clinical and radiological[*]	Quartiles	9.14	Age, gender, marital status, income, education level, smoking, alcohol drinking, physical activity, family history of stroke, HT, resting heart rate, BMI, waist circumference, TC, HDL-C, LDL-C	5.74	6	9
Cho et al. (2022)	National Health Insurance Service, Korea	20–39y without CVD, not on lipid-lowering or DM medication	6,675,424	31	59.6	0	6.9	0	1.9	NR	ICD code	Quartiles	8.34	Age, sex, BMI, smoking, alcohol consumption, physical activities, income, HT, andTC	0.13	7.4	9
Liu et al. (2022a)	Kailuan study, China	Without CVD	96,541	51	79.6	9	43.3	0	NR	0.75	WHO criteria	Quartiles	9.05	Age, sex, current smoking status, physical activity,education, BMI, HT, DM, HDL-C, LDL-C, hs-CRP, lipid-lowering medication, DM medication, and HTmedication	5.3	10.3	9
Liu et al. (2022b)	Eastern China cohort	Without CVD and DM	6,095	48.7	49.1	0	46.5	0	NR	NR	NR	Quartiles	8.76	Age, gender, waist-hip ratio, tobacco use, alcohol use, education, physical activity, hypertension, BMI, LDL-C, intake of fat and carbohydrates, use ofanti-hypertensive drugs, and use of antilipemic drugs	2.5	10.6	8
Che et al. (2023)	UK Biobank	40–69y without CVD	403,335	56.2	44.8	3.8	13.9	0	2	6.7	ICD code	Quartiles	9.07	Age, sex, ethnicity, region, Townsend Deprivation Index, current smoking, physical activity, BMI, HT,TC, LDL-C, uric acid, glycated hemoglobin, estimated glomerular filtration rate, hs-CRP, aspirin, insulin treatment, HT medication, cholesterol-lowering medication, prevalent retinopathy, and CKD	1	8.1	9
Muhammad et al. (2023)	Malmö Preventive Project, Sweden	Without stroke	32,920	45	67.5	2.5	5.5	NR	NR	NR	ICD code	Quartiles	4.74	Age, sex, BMI, systolic blood pressure, cholesterol, smoking status, DM, HT medication, physical activity, alcohol	13.3	16.9	9
Wan et al. (2023)	Shanghai Suburban Adult Cohort and Biobank, China	Without CVD	42,651	55.7	40.3	10.2	50	0	NR	34.6	ICD code	Quartiles	9.02	Age, sex, BMI, education level, physical activity, current smoking, current drinking, HDL-C, uric acid,HT medication and DM medication	1.6	4.7	9

(*continued on next page*)

Table 1 (*continued*)

Study	Database	Study population	Sample size	Age (y)	Male (%)	DM (%)	HT (%)	CVD (%)	CKD (%)	DL (%)	Stroke diagnosis	TyG data	TyG cut-off^	Adjusted covariates	Stroke incidence (%)	F/U (y)	NOS score
Wang et al. (2023)	ARIC Study, USA	45–64y without stroke	10,132	54.1	46	9	33	5	NR	NR	Medical records	Quartiles	NR	Age, race-center, sex, baseline smoking status, alcohol status, BMI, DM, heart failure, and peripheral artery disease, systolic blood pressure, LDL-C, estimated glomerular filtration rate, fibrinogen, lipid-lowering drugs and antihypertensive drugs	9	26.6	9
Li et al. (2024a)	Tianjin Brain Study, China	≥45Y without CVD	3,534	59	40.2	19	69.1	0	NR	NR	Medical records	Tertiles	9.04	Sex, age group, smoking status, LDL-C, andhistory of hypertension	9	10	9
Li et al. (2024b)	China Health and Retirement Longitudinal Study	Without stroke	10,569	59	47.1	6.1	39.7	12.1	5.8	9.8	Interview confirming physician-diagnosed stroke	Quartiles	9.07	Age, gender, marital status, residence, education level, BMI, smoking status, and drinking status, DM, HT, heart disease, DL, CKD, history of medication use for DM, history of medication use for HT, history ofmedication use for DL, systole blood pressure, diastolic blood pressure, glycated hemoglobin, hsCRP, and estimated glomerular filtration rate.	7.1	7	9
Rafiee et al. (2024)	Isfahan Cohort Study, Iran	≥35y without CVD	5,432	50.7	48.8	8.4	27.8	0	0	87.2	Physician diagnosis	Tertiles	NR	Age, sex, education, marital status, residency area, global dietary index, smoking status, andtotal daily physical activity, BMI, hypertension, and elevated TC	3.16	11.2	9
Yao et al. (2024)	Environment and Chronic Disease in Rural Areas of Heilongjiang, China	≥35y without stroke, cancer and transient cerebral ischemia	6,890	57	38.6	5.7	53.8	13.4	NR	NR	ICD code	Quartiles	9.06	Age, smoking status, drinking status, family history of CVD, family history of stroke, physical activity, TC, HT, DM, CVD	3.89	4.3	9

Notes.

DL, dyslipidemia; DM, diabetes mellitus; HT, hypertension; CVD, cardiovascular disease; CKD, chronic kidney disease; TyG, triglyceride glucose index; ICD, International classification of diseases; F/U, follow-up; y, year; NOS, Newcastle Ottawa scale; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; BMI, body mass index; TC, total cholesterol; hs-CRP, high sensitivity C-reactive protein; NR, not reported.

*Acute focal disturbance within 24 h thought to be due to either intracranial haemorrhage or ischaemia and confirmed by either computed tomography or magnetic resonance imaging.

^For the highest quartile or tertile.

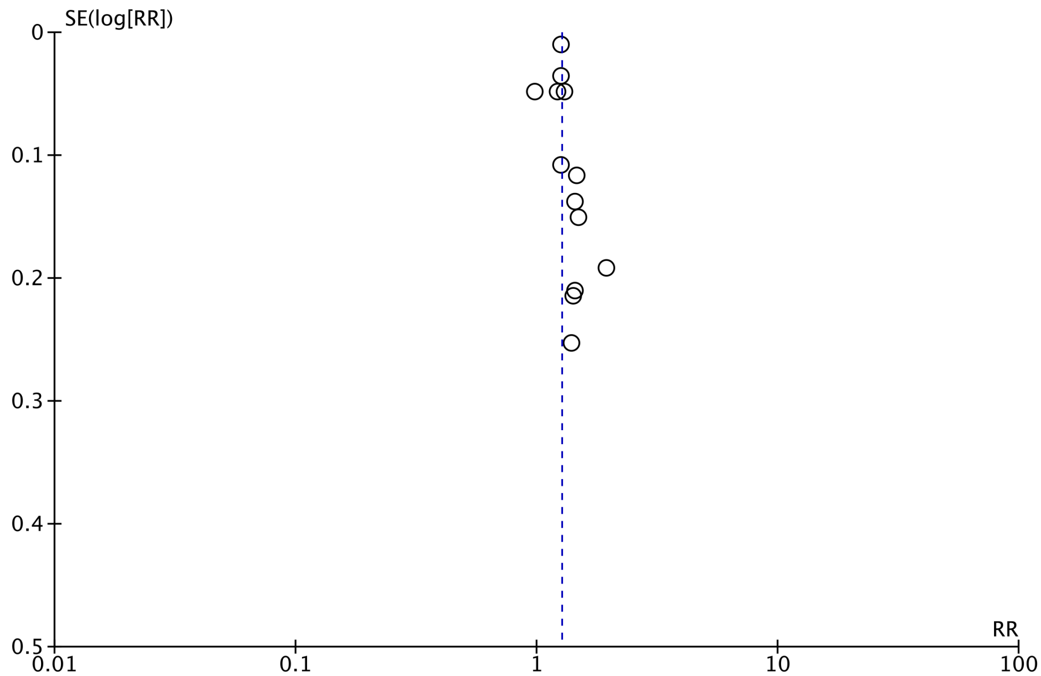

Figure 3 Funnel plot for the meta-analysis with TyG as a categorical variable.
Full-size DOI: 10.7717/peerj.19994/fig-3

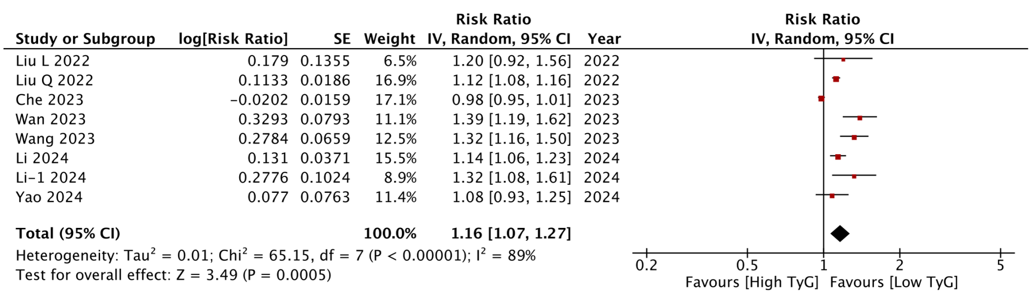

Figure 4 Meta-analysis of the association between TyG (continuous variable) and risk of stroke. Notes: *Liu et al., 2022a*; *Liu et al., 2022b*; *Wan et al., 2023*; *Wang et al., 2023*; *Che et al., 2023*; *Li et al., 2024a*; *Li et al., 2024b*; *Yao et al., 2024*.
Full-size DOI: 10.7717/peerj.19994/fig-4

significant on sensitivity analysis. Subgroup analyses revealed non-significant results for studies on the Western population and those using ICD codes for the identification of stroke. For the other subgroups, the results remained statistically significant (Table 2). On meta-regression analysis (Table 3), only sample size was found to inversely influence the effect size. A larger sample size was associated with a weaker association between TyG and stroke. None of the other moderators were found to be statistically significant.

Table 2 Subgroup analysis details.

Covariates	Groups	Number of studies	Risk ratio [95% confidence intervals]	I^2
		TyG categorical variable		
Location	Chinese	7	1.40 [1.24, 1.57]	32
	All Asian	11	1.27 [1.18, 1.37]	71
	Western	2	1.29 [1.18, 1.41]	0
Excluded population	All CVD	10	1.25 [1.16, 1.35]	72
	All Stroke	3	1.33 [1.22, 1.45]	0
Stroke diagnosis	ICD codes	6	1.22 [1.12, 1.33]	81
	Physician diagnosed	2	1.70 [1.28, 2.27]	8
TyG data	Quartile	11	1.25 [1.17, 1.34]	70
	Tertile	2	1.48 [1.16, 1.88]	0
Follow-up	≥10 years	6	1.27 [1.20, 1.35]	0
	<10 years	7	1.27 [1.15, 1.41]	81
		TyG continuous variable		
Location	Chinese	6	1.17 [1.10, 1.24]	49
	All Asian	6	1.17 [1.10, 1.24]	49
	Western	2	1.13 [0.84, 1.51]	95
Excluded population	All CVD	5	1.16 [1.04, 1.30]	92
	All Stroke	3	1.18 [1.06, 1.30]	60
Stroke diagnosis	ICD codes	3	1.13 [0.92, 1.38]	90
	Medical records	2	1.32 [1.18, 1.47]	0
Follow-up	≥10 years	4	1.22 [1.09, 1.36]	63
	<10 years	4	1.12 [0.98, 1.29]	90

Notes.
CVD, cardiovascular disease; ICD, international classification of diseases; TyG, Triglyceride glucose index.

DISCUSSION

A wide range of stroke prediction models and biomarkers have been proposed in the literature to predict the risk of stroke in the general population (*Xu et al., 2021*; *Lu et al., 2021*; *Lip et al., 2022*; *Ihle-Hansen et al., 2023*). There are several routine laboratory markers like albumin, brain natriuretic peptide, serum creatinine, red cell distribution width, total cholesterol, high-density lipoprotein, low-density lipoprotein, and non-high-density lipoprotein cholesterol which have been associated with a higher risk of stroke (*Sughrue et al., 2016*). Other non-routine markers like fibrinogen, E-selectin, interferon-γ-inducible-protein-10, resistin, and total adiponectin have also been linked with increased risk of stroke (*Prugger et al., 2013*). On the other hand, there are also complex prediction models and machine-learning-based algorithms that claim to accurately predict the risk of stroke (*Lu et al., 2021*; *Lip et al., 2022*). Lastly, specific investigation-based markers like carotid plaque scores are also linked with the risk of stroke (*Ihle-Hansen et al., 2023*). Despite a plethora of research, no single marker has been identified as the gold standard as there are issues of accuracy with simpler laboratory markers and difficulty of application with more complex models.

Table 3 **Details of meta-regression analysis.**

Variable	Beta	SE	+95% CI	−95% CI	*p*-value
TyG categorical variable					
Sample size	0.000000005	0.000000005	−0.000000006	0.00000002	0.34
Age	−0.0008	0.002	−0.005	0.003	0.64
Male (%)	−0.00002	0.001	−0.003	0.002	0.99
DM (%)	0.002	0.005	−0.008	0.014	0.59
HT (%)	0.002	0.001	−0.001	0.004	0.12
TyG cut-off	−0.004	0.003	−0.011	0.002	0.11
Stroke incidence (%)	0.007	0.004	−0.001	0.015	0.66
Follow-up (years)	0.001	0.004	−0.008	0.010	0.79
TyG continuous variable					
Sample size	−0.0000006	0.0000002	−0.0000011	−0.0000001	0.004
Age	0.0002217	0.0182591	−0.0429542	0.0433976	0.99
Male (%)	−0.0024111	0.0048529	−0.0138865	0.0090642	0.61
DM (%)	0.0193193	0.0088024	−0.0014951	0.0401336	0.20
HT (%)	0.0051778	0.0024720	−0.0006676	0.0110231	0.40
Stroke incidence (%)	0.0205690	0.0132036	−0.0106526	0.0517907	0.12
Follow-up (years)	0.0071913	0.0069041	−0.0091343	0.0235170	0.29

Notes.
SE, standard error; CI, confidence intervals; DM, diabetes mellitus; HT, hypertension; TyG, Triglyceride glucose index.

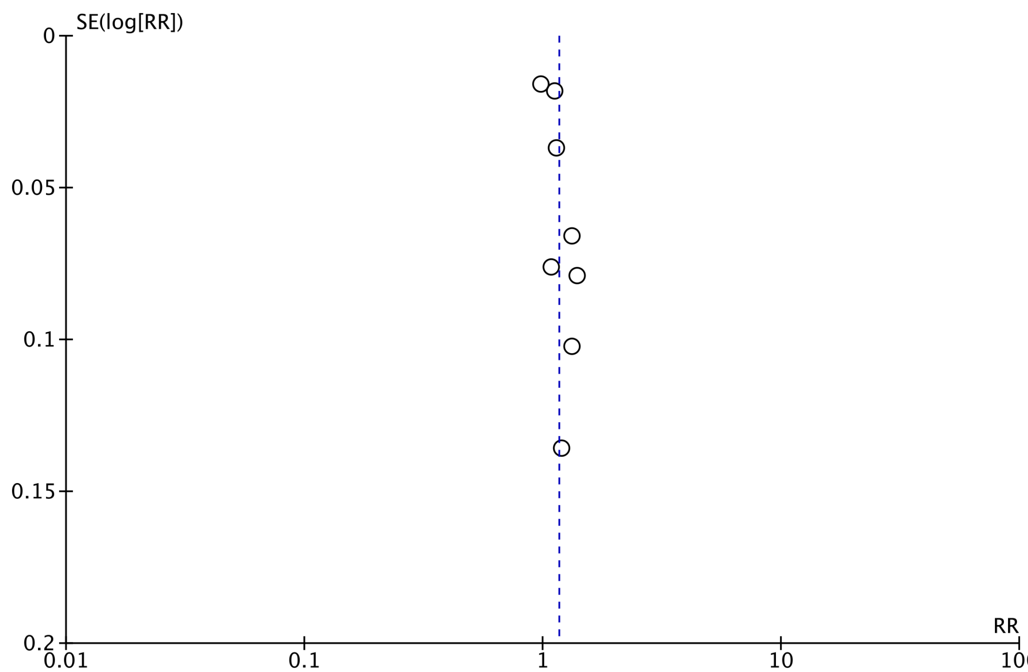

Figure 5 **Funnel plot for the meta-analysis with TyG as a continuous variable.**
Full-size DOI: 10.7717/peerj.19994/fig-5

During the search for an ideal marker, the TyG has generated considerable interest in the past few years. Its association with a large number of diseases as well as disease outcomes has prompted significant research on its ability to predict stroke in the general population (*Yin et al., 2024*; *Nayak et al., 2024*). However, despite three prior reviews (*Liao et al., 2022*; *Feng et al., 2022*; *Yang et al., 2023*), there remains uncertainty about its clinical application. One major limitation is the quality of these meta-analysis studies. *Yang et al. (2023)* in their review have not only included overlapping studies using the same dataset (Kailuan community cohort) but also have combined data of cross-sectional and cohort studies in the same meta-analysis. Repeated inclusion of the same data can overestimate the effect size generating skewed results. Also, cross-sectional studies cannot establish causality like cohort studies. Secondly, all three reviews (*Liao et al., 2022*; *Feng et al., 2022*; *Yang et al., 2023*) have also pooled studies assessing the risk of stroke in the general population with studies on specific disease cohorts like DM, HT, CAD, *etc*. The risk of stroke in the general population is considerably different compared to those with known risk factors like DM, HT, and CAD (*Saini, Guada & Yavagal, 2021*). Lastly, these reviews have not uniformly excluded studies including participants with prior stroke, which is another risk factor for recurrent stroke.

Overcoming these issues, the current systematic review and meta-analysis aimed to generate the best possible evidence on the clinical utility of TyG in predicting the risk of stroke in the general population. After the exclusion of a large number of studies with overlapping data, studies on disease populations, studies with short follow-ups, and studies including prior stroke participants, we were still left with 13 cohorts with about 12.8 million participants. Separate data analysis was conducted for TyG as a categorical as well as continuous variable. Our results revealed that high levels of TyG resulted in a 27% increase in the risk of stroke in the general population whereas a per unit increase in TyG was associated with a 16% increase of the same. We found the results to be robust on sensitivity analysis highlighting the credibility of the outcomes. Lack of publication bias also supplements the results. Our results are in agreement with the large study of *Lopez-Jaramillo et al. (2023)* which could not be included in the review as it did not exclude prior stroke patients. However, the study is worth mentioning as it was a prospective analysis of 141,243 individuals aged 35–70 years from 22 countries. After a median follow-up of 13.2 years, the authors reported an increased risk of stroke (hazard ratio: 1.16 95% CI [1.05–1.28]) with the highest TyG tertile. The association was the strongest in low-income countries followed by middle-income countries but non-significant in high-income countries.

Despite the robust results of our study, the small increase in the risk of stroke associated with high TyG may raise questions about its routine use in clinical practice. In the realm of stroke prevention, especially within the general population, establishing a precise minimal clinically important difference (MCID) is challenging due to varying baseline risks and individual patient factors. MCID represents the smallest change in the risk of disease or treatment outcome that a patient or clinician would identify as meaningful (*Salas Apaza et al., 2021*). Nevertheless, the perception of what constitutes a meaningful risk can be gauged from current CVD and stroke guidelines. For example, the American College of Cardiology and American Heart Association recommend considering statin therapy for individuals with a 10-year atherosclerotic cardiovascular disease risk of 7.5% or higher (Virani, 2022). The risk of stroke noted with high TyG in our review was much higher and therefore should be clinically relevant and prompt monitoring and risk reduction measures in high-risk individuals.

An important caveat in understanding the utility of a marker for stroke prediction is the role of confounding factors. The risk of stroke depends on numerous variables like age, gender, ethnicity, family history, physical inactivity, alcohol consumption, smoking, obesity, DM, HT, CVD, *etc* (Tu et al., 2023). Much variation was observed in the included populations in terms of such baseline characteristics which could have led to the high heterogeneity in the meta-analysis. However, we were able to somewhat circumvent this limitation by including only adjusted data and conducting several subgroup and meta-regression analyses. Most of the included studies adjusted their data for age, gender, smoking, physical inactivity, body mass index, DM, HT, and alcohol consumption thereby eliminating the impact of major confounders. On subgroup analysis, there was no change in the significance of the results especially for TyG as a categorical variable. Segregation of data based on the region of the study, exclusion of CVD or stroke, diagnosis of stroke, TyG data as tertiles or quartiles, and follow-up had no impact albeit without complete elimination of inter-study heterogeneity. This indicates that there may be other unmeasured factors at play requiring further research. Likewise, meta-regression using relevant moderators like age, male gender, DM, HT, TyG cut-off, stroke incidence, and follow-up also did not have a significant association with the pooled analysis. The only significant association noted was between sample size and TyG as a continuous variable which could have been a statistical artifact given the small number of studies in the analysis.

The underlying mechanism supporting the link between high TyG and stroke remains unclear. Substantial evidence reinforces the relationship between the TyG index and insulin resistance (Guerrero-Romero et al., 2010; Sánchez-García et al., 2020). In fact, the TyG index has been identified as one of the best markers of insulin resistance performing better than visceral adiposity indicators and other lipid parameters (Du et al., 2014). Insulin resistance has been linked with stroke *via* several mechanisms like interference with insulin signaling and sensitivity, amplification of chronic systemic inflammation, and accelerating foam cell generation causing atherosclerosis and advanced plaques (Bornfeldt & Tabas, 2011; Kosmas et al., 2023). Insulin resistance interferes with the function of insulin-like growth factors, cyclic guanosine monophosphate, and nitric oxide thereby causing adhesion, activation, and aggregation of platelet function which in turn causes vascular occlusion and stroke (Randriamboavonjy & Fleming, 2009; Guo et al., 2021). Moreover, insulin resistance may impact the cerebrovascular reserve *via* several chemical, neuronal, and metabolic mechanisms leading to reduced cerebral perfusion during stroke (Banks & Rhea, 2021; Fan et al., 2022). There is also evidence to show that admission hyperglycemia and DM can negatively impact stroke outcomes itself (Belge Bilgin et al., 2025).

Despite the robust results, there are certain major limitations of the review. Firstly, we were unable to identify the ideal cut-off of TyG to predict the risk of stroke due to a lack of sensitivity and specificity data and varied cut-offs of the included studies. Guerrero-Romero et al. (2010) have shown that the best TyG cut-off for the diagnosis of insulin resistance was 4.68. However, there remains limited data on the ideal cut-off for predicting stroke. Secondly, the studies considered only baseline glucose and triglyceride measurements and did not account for changes over time. It remains unclear how TyG changes affected the risk of stroke. Thirdly, despite the studies adjusting several potential cardiovascular and metabolic risk factors, we cannot eliminate the possibility of residual confounding due to unmeasured factors. Fourthly, data was derived from observational studies which have inherent bias. Fifthly, the large heterogeneity in the meta-analysis cannot be ignored and hence the results must be interested with caution. Lastly, the predominance of Chinese studies limits the generalization of data to other regions. More robust studies from Western countries are needed to add to current evidence.

CONCLUSIONS

High TyG is associated with increased risk of stroke in the general population. Since the index is easy to measure and calculated from routinely available laboratory values, it may be incorporated into daily clinical practice to screen individuals at high risk of stroke.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding

The authors received no funding for this work.

Competing Interests

The authors declare there are no competing interests.

Author Contributions

- Gang Xin conceived and designed the experiments, authored or reviewed drafts of the article, and approved the final draft.
- Huiya Li conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the article, and approved the final draft.
- Ji Jiang conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, and approved the final draft.

Data Availability

The following information was supplied regarding data availability:

This is a systematic review/meta-analysis.

Supplemental Information

Supplemental information for this article can be found online at http://dx.doi.org/10.7717/peerj.19994#supplemental-information.

REFERENCES

Agrawal R, Reno CM, Sharma S, Christensen C, Huang Y, Fisher SJ. 2021. Insulin action in the brain regulates both central and peripheral functions. *American Journal of Physiology. Endocrinology and Metabolism* **321**:E156–E163 DOI 10.1152/ajpendo.00642.2020.

Banks WA, Rhea EM. 2021. The blood-brain barrier, oxidative stress, and insulin resistance. *Antioxidants* **10**:1695 DOI 10.3390/antiox10111695.

Belge Bilgin G, Bilgin C, Jabal MS, Kobeissi H, Ghozy S, Senol YC, Orscelik A, Kadirvel R, Brinjikji W, Kallmes DF, Rabinstein AA. 2025. The effects of admission hyperglycemia and diabetes mellitus on mechanical thrombectomy outcomes: a systematic review and meta-analysis. *Interventional Neuroradiology* 15910199241306774 DOI 10.1177/15910199241306774.

Bornfeldt KE, Tabas I. 2011. Insulin resistance, hyperglycemia, and atherosclerosis. *Cell Metabolism* **14**:575–85 DOI 10.1016/j.cmet.2011.07.015.

Cersosimo E, Solis-Herrera C, Trautmann ME, Malloy J, Triplitt CL. 2014. Assessment of pancreatic β-cell function: review of methods and clinical applications. *Current Diabetes Reviews* **10**:2–42 DOI 10.2174/1573399810666140214093600.

Che B, Zhong C, Zhang R, Pu L, Zhao T, Zhang Y, Han L. 2023. Triglyceride-glucose index and triglyceride to high-density lipoprotein cholesterol ratio as potential cardiovascular disease risk factors: an analysis of UK biobank data. *Cardiovascular Diabetology* **22**:34 DOI 10.1186/s12933-023-01762-2.

Cho YK, Do HanK, Kim HS, Jung CH, Park JY, Lee WJ. 2022. Triglyceride-glucose index is a useful marker for predicting future cardiovascular disease and mortality in young Korean adults: a nationwide population-based cohort study. *Journal of Lipid and Atherosclerosis* **11**:178–186 DOI 10.12997/jla.2022.11.2.178.

Ding P-F, Zhang H-S, Wang J, Gao Y-Y, Mao J-N, Hang C-H, Li W. 2022. Insulin resistance in ischemic stroke: mechanisms and therapeutic approaches. *Frontiers in Endocrinology* **13**:1092431 DOI 10.3389/fendo.2022.1092431.

Du T, Yuan G, Zhang M, Zhou X, Sun X, Yu X. 2014. Clinical usefulness of lipid ratios, visceral adiposity indicators, and the triglycerides and glucose index as risk markers of insulin resistance. *Cardiovascular Diabetology* **13**:146 DOI 10.1186/s12933-014-0146-3.

Fan J-L, Nogueira RC, Brassard P, Rickards CA, Page M, Nasr N, Tzeng Y-C. 2022. Integrative physiological assessment of cerebral hemodynamics and metabolism in acute ischemic stroke. *Journal of Cerebral Blood Flow and Metabolism* **42**:454–470 DOI 10.1177/0271678X211033732.

Feng X, Yao Y, Wu L, Cheng C, Tang Q, Xu S. 2022. Triglyceride-glucose index and the risk of stroke: a systematic review and dose-response meta-analysis. *Hormone and Metabolic Research* **54**:175–186 DOI 10.1055/a-1766-0202.

Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH,

Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB, American Heart Association Statistics Committee and Stroke Statistics Subcommittee. 2014. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation* **129**:e28–e292 DOI 10.1161/01.cir.0000441139.02102.80.

Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, Martínez-Abundis E, Ramos-Zavala MG, Hernández-González SO, Jacques-Camarena O, Rodríguez-Morán M. 2010. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. *The Journal of Clinical Endocrinology and Metabolism* **95**:3347–3351 DOI 10.1210/jc.2010-0288.

Guo Y, Zhao J, Zhang Y, Wu L, Yu Z, He D, Huang H, Qu W, Luo X. 2021. Triglyceride glucose index influences platelet reactivity in acute ischemic stroke patients. *BMC Neurology* **21**:409 DOI 10.1186/s12883-021-02443-x.

Hong S, Han K, Park CY. 2020. The triglyceride glucose index is a simple and low-cost marker associated with atherosclerotic cardiovascular disease: a population-based study. *BMC Medicine* **18**:361 DOI 10.1186/s12916-020-01824-2.

Ihle-Hansen H, Vigen T, Berge T, Walle-Hansen MM, Hagberg G, Ihle-Hansen H, Thommessen B, Ariansen I, Røsjø H, Rønning OM, Tveit A, Lyngbakken M. 2023. Carotid plaque score for stroke and cardiovascular risk prediction in a middle-aged cohort from the general population. *Journal of the American Heart Association* **12**:e030739 DOI 10.1161/JAHA.123.030739.

Kosmas CE, Bousvarou MD, Kostara CE, Papakonstantinou EJ, Salamou E, Guzman E. 2023. Insulin resistance and cardiovascular disease. *The Journal of International Medical Research* **51**:3000605231164548 DOI 10.1177/03000605231164548.

Li X, Hao J, Han Q, Wang D, Lu Y, Tu J, Wang L, Wang J, Ning X, Yang C, Li Y. 2024a. Triglyceride-glucose index prediction of stroke incidence risk in low-income Chinese population: a 10-year prospective cohort study. *Frontiers in Endocrinology* **15** DOI 10.3389/fendo.2024.1444030.

Li X, Hu JG, Liao Q, Wu Y, Huo RR. 2024b. Triglyceride-glucose index mediates the association between residual cholesterol and stroke among middle-aged and older adults in China: a prospective, nationwide, population-based study. *Frontiers in Cardiovascular Medicine* **11** DOI 10.3389/fcvm.2024.1429993.

Liao C, Xu H, Jin T, Xu K, Xu Z, Zhu L, Liu M. 2022. Triglyceride-glucose index and the incidence of stroke: a meta-analysis of cohort studies. *Frontiers in Neurology* **13**:1033385 DOI 10.3389/fneur.2022.1033385.

Lip GYH, Genaidy A, Tran G, Marroquin P, Estes C, Sloop S. 2022. Improving stroke risk prediction in the general population: a comparative assessment of common clinical rules, a new multimorbid index, and machine-learning-based algorithms. *Thrombosis and Haemostasis* **122**:142–150 DOI 10.1055/a-1467-2993.

Liu Q, Cui H, Ma Y, Han X, Cao Z, Wu Y. 2022a. Triglyceride-glucose index associated with the risk of cardiovascular disease: the Kailuan study. *Endocrine* **75**:392–399 DOI 10.1007/s12020-021-02862-3.

Liu L, Wu Z, Zhuang Y, Zhang Y, Cui H, Lu F, Peng J, Yang J. 2022b. Association of triglyceride–glucose index and traditional risk factors with cardiovascular disease among non-diabetic population: a 10-year prospective cohort study. *Cardiovascular Diabetology* **21**:256 DOI 10.1186/s12933-022-01694-3.

Lopez-Jaramillo P, Gomez-Arbelaez D, Martinez-Bello D, Abat MEM, Alhabib KF, Avezum Á, Barbarash O, Chifamba J, Diaz ML, Gulec S, Ismail N, Iqbal R, Kelishadi R, Khatib R, Lanas F, Levitt NS, Li Y, Mohan V, Mony PK, Poirier P, Rosengren A, Soman B, Wang C, Wang Y, Yeates K, Yusuf R, Yusufali A, Zatonska K, Rangarajan S, Yusuf S. 2023. Association of the triglyceride glucose index as a measure of insulin resistance with mortality and cardiovascular disease in populations from five continents (PURE study): a prospective cohort study. *The Lancet Healthy Longevity* **4**:e23–e33 DOI 10.1016/S2666-7568(22)00247-1.

Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, Alvarado M, Anderson HR, Anderson LM, Andrews KG, Atkinson C, Baddour LM, Barker-Collo S, Bartels DH, Bell ML, Benjamin EJ, Bennett D, Bhalla K, Bikbov B, Bin Abdulhak A, Birbeck G, Blyth F, Bolliger I, Boufous S, Bucello C, Burch M, Burney P, Carapetis J, Chen H, Chou D, Chugh SS, Coffeng LE, Colan SD, Colquhoun S, Colson KE, Condon J, Connor MD, Cooper LT, Corriere M, Cortinovis M, de Vaccaro KC, Couser W, Cowie BC, Criqui MH, Cross M, Dabhadkar KC, Dahodwala N, De Leo D, Degenhardt L, Delossantos A, Denenberg J, Des Jarlais DC, Dharmaratne SD, Dorsey ER, Driscoll T, Duber H, Ebel B, Erwin PJ, Espindola P, Ezzati M, Feigin V, Flaxman AD, Forouzanfar MH, Fowkes FGR, Franklin R, Fransen M, Freeman MK, Gabriel SE, Gakidou E, Gaspari F, Gillum RF, Gonzalez-Medina D, Halasa YA, Haring D, Harrison JE, Havmoeller R, Hay RJ, Hoen B, Hotez PJ, Hoy D, Jacobsen KH, James SL, Jasrasaria R, Jayaraman S, Johns N, Karthikeyan G, Kassebaum N, Keren A, Khoo J-P, Knowlton LM, Kobusingye O, Koranteng A, Krishnamurthi R, Lipnick M, Lipshultz SE, Ohno SL, Mabweijano J, MacIntyre MF, Mallinger L, March L, Marks GB, Marks R, Matsumori A, Matzopoulos R, Mayosi BM, McAnulty JH, McDermott MM, McGrath J, Mensah GA, Merriman TR, Michaud C, Miller M, Miller TR, Mock C, Mocumbi AO, Mokdad AA, Moran A, Mulholland K, Nair MN, Naldi L, Narayan KMV, Nasseri K, Norman P, O'Donnell M, Omer SB, Ortblad K, Osborne R, Ozgediz D, Pahari B, Pandian JD, Rivero AP, Padilla RP, Perez-Ruiz F, Perico N, Phillips D, Pierce K, Pope CA, Porrini E, Pourmalek F, Raju M, Ranganathan D, Rehm JT, Rein DB, Remuzzi G, Rivara FP, Roberts T, De León FR, Rosenfeld LC, Rushton L, Sacco RL, Salomon JA, Sampson U, Sanman E, Schwebel DC, Segui-Gomez M, Shepard DS, Singh D, Singleton J, Sliwa K, Smith E, Steer A, Taylor JA, Thomas B, Tleyjeh IM, Towbin JA, Truelsen T, Undurraga EA, Venketasubramanian N, Vijayakumar L, Vos T, Wagner GR, Wang M, Wang W, Watt K, Weinstock MA, Weintraub R, Wilkinson JD, Woolf AD, Wulf S, Yeh

P-H, Yip P, Zabetian A, Zheng Z-J, Lopez AD, Murray CJL, AlMazroa MA, Memish ZA. 2012. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* **380**:2095–2128 DOI 10.1016/S0140-6736(12)61728-0.

Lu X, Niu X, Shen C, Liu F, Liu Z, Huang K, Wang L, Li J, Hu D, Zhao Y, Yang X, Lu F, Liu X, Cao J, Chen S, Li H, Tang W, Ren Z, Yu L, Wu X, Wu X, Li Y, Zhang H, Huang J, Hu Z, Shen H, Willer CJ, Gu D. 2021. Development and validation of a polygenic risk score for stroke in the Chinese population. *Neurology* **97**:e619–e628 DOI 10.1212/WNL.0000000000012263.

Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. 1985. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* **28**:412–419 DOI 10.1007/BF00280883.

Muhammad IF, Bao X, Nilsson PM, Zaigham S. 2023. Triglyceride-glucose (TyG) index is a predictor of arterial stiffness, incidence of diabetes, cardiovascular disease, and all-cause and cardiovascular mortality: a longitudinal two-cohort analysis. *Frontiers in Cardiovascular Medicine* **9** DOI 10.3389/fcvm.2022.1035105.

Nayak SS, Kuriyakose D, Polisetty LD, Patil AA, Ameen D, Bonu R, Shetty SP, Biswas P, Ulrich MT, Letafatkar N, Habibi A, Keivanlou M-H, Nobakht S, Alotaibi A, Hassanipour S, Amini-Salehi E. 2024. Diagnostic and prognostic value of triglyceride glucose index: a comprehensive evaluation of meta-analysis. *Cardiovascular Diabetology* **23**:310 DOI 10.1186/s12933-024-02392-y.

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. 2021. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *International Journal of Surgery* **88**:105906 DOI 10.1016/j.ijsu.2021.105906.

Prugger C, Luc G, Haas B, Morange P-E, Ferrieres J, Amouyel P, Kee F, Ducimetiere P, Empana J-P. 2013. Multiple biomarkers for the prediction of ischemic stroke. *Arteriosclerosis, Thrombosis, and Vascular Biology* **33**:659–666 DOI 10.1161/ATVBAHA.112.300109.

Rafiee H, Mohammadifard N, Nouri F, Alavi Tabatabaei G, Najafian J, Sadeghi M, Boshtam M, Roohafza H, Haghighatdoost F, Hassannejad R, Sarrafzadegan N. 2024. Association of triglyceride glucose index with cardiovascular events: insights from the Isfahan Cohort Study (ICS). *European Journal of Medical Research* **29**:135 DOI 10.1186/s40001-024-01728-4.

Randriamboavonjy V, Fleming I. 2009. Insulin, insulin resistance, and platelet signaling in diabetes. *Diabetes Care* **32**:528–30 DOI 10.2337/dc08-1942.

Saini V, Guada L, Yavagal DR. 2021. Global epidemiology of stroke and access to acute ischemic stroke interventions. *Neurology* **97**:S6–S16 DOI 10.1212/WNL.0000000000012781.

Salas Apaza JA, Ariel Franco JV, Meza N, Madrid E, Loézar C, Garegnani L. 2021. Minimal clinically important difference: the basics. *Medwave* **21**:e8149–e8149.

Sánchez-García A, Rodríguez-Gutiérrez R, Mancillas-Adame L, González-Nava V, Díaz González-Colmenero A, Solis RC, Álvarez-Villalobos NA, González-González JG. 2020. Diagnostic accuracy of the triglyceride and glucose index for insulin resistance: a systematic review. *International Journal of Endocrinology* **2020**:4678526 DOI 10.1155/2020/4678526.

Saver JL, Carroll JD, Smalling R, Thaler D. 2015. Letter by Saver et al regarding article, guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* **46**:e85-e86 DOI 10.1161/STROKEAHA.115.007311.

Sughrue T, Swiernik MA, Huang Y, Brody JP. 2016. Laboratory tests as short-term correlates of stroke. *BMC Neurology* **16**:112 DOI 10.1186/s12883-016-0619-y.

Suurmond R, Van Rhee H, Hak T. 2017. Introduction, comparison, and validation of meta-essentials: a free and simple tool for meta-analysis. *Research Synthesis Methods* **8**:537–553 DOI 10.1002/jrsm.1260.

Tu W-J, Wang L-D, Yan F, Peng B, Hua Y, Liu M, Ji X-M, Ma L, Shan C-L, Wang Y-L, Zeng J-S, Chen H-S, Fan D-S, Gu Y-X, Tan G-J, Hu B, Kang D-Z, Liu J-M, Liu Y-L, Lou M, Luo B-Y, Pan S-Y, Wang L-H, Wu J. 2023. China stroke surveillance report 2021. *Military Medical Research* **10**:33 DOI 10.1186/s40779-023-00463-x.

Virani SS. 2022. Statins and primary atherosclerotic cardiovascular disease prevention—what we know, where we need to go, and why are we not there already? *JAMA Network Open* **5**:e2228538 DOI 10.1001/jamanetworkopen.2022.28538.

Wan Y, Zhang Z, Ling Y, Cui H, Tao Z, Pei J, Maimaiti A, Bai H, Wu Y, Li J, Zhao G, Zaid M. 2023. Association of triglyceride-glucose index with cardiovascular disease among a general population: a prospective cohort study. *Diabetology and Metabolic Syndrome* **15**:204 DOI 10.1186/s13098-023-01181-z.

Wang X, Liu Q, Wang T, Tian W, Chen X, Zhang J, Li Q, Ma D, Zhao L, Chen Z, Xu H, Chen K. 2023. Triglyceride–glucose index and the risk of stroke in American adults: findings from the atherosclerosis risk in communities study. *Diabetology and Metabolic Syndrome* **15**:187 DOI 10.1186/s13098-023-01161-3.

Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. 2020. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. *Available at http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp* (accessed on 30 October 2020).

Xu W, Huang J, Yu Q, Yu H, Pu Y, Shi Q. 2021. A systematic review of the status and methodological considerations for estimating risk of first ever stroke in the general population. *Neurological Sciences* **42**:2235–2247 DOI 10.1007/s10072-021-05219-w.

Yang Y, Huang X, Wang Y, Leng L, Xu J, Feng L, Jiang S, Wang J, Yang Y, Pan G, Jiang B, Wang Y, Chen L. 2023. The impact of triglyceride-glucose index on ischemic stroke: a systematic review and meta-analysis. *Cardiovascular Diabetology* **22**:2 DOI 10.1186/s12933-022-01732-0.

Yao F, Cui J, Shen Y, Jiang Y, Li Y, Liu X, Feng H, Jiao Z, Liu C, Hu F, Zhang W, Sun D. 2024. Evaluating a new obesity indicator for stroke risk prediction: comparative cohort analysis in rural settings of two nations. *BMC Public Health* **24**:3301 DOI 10.1186/s12889-024-20631-5.

Yin J-L, Yang J, Song X-J, Qin X, Chang Y-J, Chen X, Liu F-H, Li Y-Z, Xu H-L, Wei Y-F, Cao F, Bai X-L, Wu L, Tao T, Du J, Gong T-T, Wu Q-J. 2024. Triglyceride-glucose index and health outcomes: an umbrella review of systematic reviews with meta-analyses of observational studies. *Cardiovascular Diabetology* **23**:177 DOI 10.1186/s12933-024-02241-y.

Zhao Y, Sun H, Zhang W, Xi Y, Shi X, Yang Y, Lu J, Zhang M, Sun L, Hu D. 2021. Elevated triglyceride–glucose index predicts risk of incident ischaemic stroke: the rural Chinese cohort study. *Diabetes and Metabolism* **47**:101246 DOI 10.1016/j.diabet.2021.101246.

Zheng R, Dong X, Wang T, Zhang H, Zhou Y, Wang D. 2024. Linear positive association of metabolic score for insulin resistance with stroke risk among American adults: a cross-sectional analysis of National Health and Nutrition Examination Survey datasets. *Journal of Stroke and Cerebrovascular Diseases* **33**:107994 DOI 10.1016/j.jstrokecerebrovasdis.2024.107994.