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The role of estimated glucose disposal rate in predicting cardiovascular risk among general and diabetes mellitus population: a systematic review and meta-analysis

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Abstract

Background Estimated glucose disposal rate (eGDR) is a measure of insulin sensitivity. While recent evidence suggests its role in cardiovascular risk assessment in Type 1 diabetes, its associations with cardiovascular disease (CVD), diabetic microvascular complications (DMC), and mortality across different populations remain unclear.

Methods We systematically searched Medline, EMBASE, Web of Science, and the Cochrane Library up to September 1st, 2024, following PRISMA guidelines. We examined associations between eGDR and CVD, DMC (including diabetic retinopathy, nephropathy, and peripheral neuropathy), and all-cause mortality using random-effects models. Secondary analysis assessed mean eGDR levels in diabetes populations.

Results Nineteen observational studies (185,810 participants) examined clinical outcomes, while 50 studies reported mean eGDR values. In patients with Type 1 diabetes (T1DM), each 1-unit (mg/kg/min) increase in eGDR was associated with lower risks of CVD (HR 0.78; 95% CI 0.69–0.87; $I^2 = 68\%$) and all-cause mortality (HR 0.83; 95% CI 0.79–0.88; $I^2 = 0\%$). The association between eGDR and DMC in T1DM was not statistically significant (HR 0.86; 95% CI 0.72–1.03; $I^2 = 25\%$). In patients with Type 2 diabetes (T2DM), each 1-unit (mg/kg/min) increase in eGDR was associated with reduced all-cause mortality (HR 0.90; 95% CI 0.84–0.97; $I^2 = 62\%$). Similarly, in the general population, each 1-unit (mg/kg/min) increase in eGDR was associated with decreased mortality risk (HR 0.88; 95% CI 0.82–0.94; $I^2 = 48\%$). The pooled mean eGDR was higher in patients with T1DM (8.19 mg/kg/min; 95% CI 7.81–8.57; $I^2 = 99\%$) compared to those with T2DM (7.03 mg/kg/min; 95% CI 4.89–9.17; $I^2 = 100\%$).

Conclusions Higher eGDR levels were consistently associated with lower risks of CVD and mortality in T1DM, with similar associations observed for mortality in T2DM. In the general population, higher eGDR levels were associated with reduced mortality risk. The relationship between eGDR and DMC requires further investigation, particularly in T2DM. These findings suggest eGDR's potential utility as a risk assessment tool, though its clinical application may vary across different populations.

Keywords Estimated glucose disposal rate, Insulin resistance, Cardiovascular disease, Diabetic microvascular complications, All-cause mortality, Meta-analysis

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Background

Diabetes is a chronic condition characterized by elevated blood glucose levels, closely linked to pancreatic β cell function [1]. In 2021, 529 million people worldwide were living with diabetes, with projections suggesting an increase to over 1.3 billion by 2050 [2]. This trend highlights the escalating global burden of diabetes.

Cardiovascular disease (CVD) and diabetic microvascular complications (DMC) remain the primary causes of morbidity and mortality in people with diabetes [3, 4]. CVD, including atherosclerosis, coronary artery disease, and stroke, accounts for the majority of deaths, with people with diabetes showing significantly higher risk compared to the general population [5]. This elevated risk stems from the complex interplay between chronic hyperglycemia, insulin resistance, and metabolic dysregulation [6]. Similarly, DMC—comprising diabetic retinopathy (DR), diabetic nephropathy (DN), and diabetic peripheral neuropathy (DPN)—substantially impact quality of life [7]. Early identification and management of these complications are crucial for preventing irreversible damage and improving patient outcomes.

Insulin resistance (IR) plays a fundamental role in vascular complications and adverse outcomes among people with diabetes [8–10]. While the euglycemic-hyperinsulinemic clamp technique remains the gold standard for assessing insulin sensitivity [11–13], its clinical application is limited by complexity, cost, and invasive nature. The estimated glucose disposal rate (eGDR) has emerged as a practical surrogate measure of insulin sensitivity, calculated using readily available clinical parameters: waist-to-hip ratio (WHR), waist circumference (WC), or body mass index (BMI), along with hypertension status (HTN) and glycated hemoglobin (HbA1c) [12].

The development and validation history of eGDR merit careful consideration when interpreting its applications across different populations. Initially validated against the hyperinsulinemic-euglycemic clamp in Type 1 diabetes (T1DM) [12], eGDR demonstrated a strong correlation with insulin sensitivity in this population. Subsequent clamp studies validated its utility in Type 2 diabetes (T2DM) [14]. Although direct clamp validation in the general population is currently lacking, the biological plausibility of eGDR as a marker of insulin resistance is supported by its individual components, as hypertension, anthropometric measures, and HbA1c are closely associated with insulin resistance and cardiovascular risk in non-diabetic individuals [15–20]. Recent evidence has demonstrated eGDR's utility as a risk stratification tool [21], particularly for cardiovascular outcomes in T1DM, as shown in a recent systematic review [22].

Building upon existing evidence, some important questions remain to be addressed. While recent reviews have examined eGDR's relationship with cardiovascular outcomes in T1DM, less is known about its associations with both cardiovascular and DMC across different populations, and typical eGDR values in various population groups have not been systematically summarized. Therefore, our systematic review and meta-analysis aimed to examine associations between eGDR and cardiovascular disease, DMC, and mortality in people with T1DM, T2DM, and the general population. These findings may contribute to our understanding of eGDR's utility in clinical risk assessment across different populations.

Methods

This systematic review and meta-analysis adhered to the guidelines established in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) 2020 [23] (Additional file 1: Table 1). We registered the protocol with the International Prospective Register of Systematic Reviews Database (PROSPERO) under the registration number CRD42024527263. The PRISMA flow diagram is shown in Fig. 1.

Literature search and selection

Two independent reviewers searched the Medline, EMBASE, Web of Science, and Cochrane Library databases with no linguistic constraints from inception up to Sep 1st, 2024. Both MeSH terms and free-text terms were utilized in a combination of four key term blocks:"eGDR,""CVD,""diabetic microangiopathy,"and"mortality"(Additional file 1: Table 2).

Adhering to research integrity standards, we included all observational studies that furnished insights into associations between eGDR and the risk of CVD,DMC, and mortality. Studies were included if they met the following criteria: (1) they were observational studies, including cross-sectional, retrospective and prospective cohort studies, or randomized controlled trials (RCTs); (2) they enrolled the general population or patients with DM; (3) studies presented data on the association between eGDR and the risk of CVD, DMC, and mortality. Studies were excluded if they: (1) involved nonhuman subjects; (2) were case reports (unless N > 10), editorials, protocols, commentaries, abstracts, or registered trials without results; or (3) lacked a clear methodology for data extraction.

We employed a hierarchical approach in our analysis strategy. For cohort studies reporting hazard ratios (HRs) with 95% confidence intervals (CIs), we conducted quantitative meta-analyses using either directly reported per-unit HRs or standardized HRs derived from categorical data using established dose–response methods. Cohort studies meeting inclusion criteria but lacking sufficient data for HR standardization were included in the

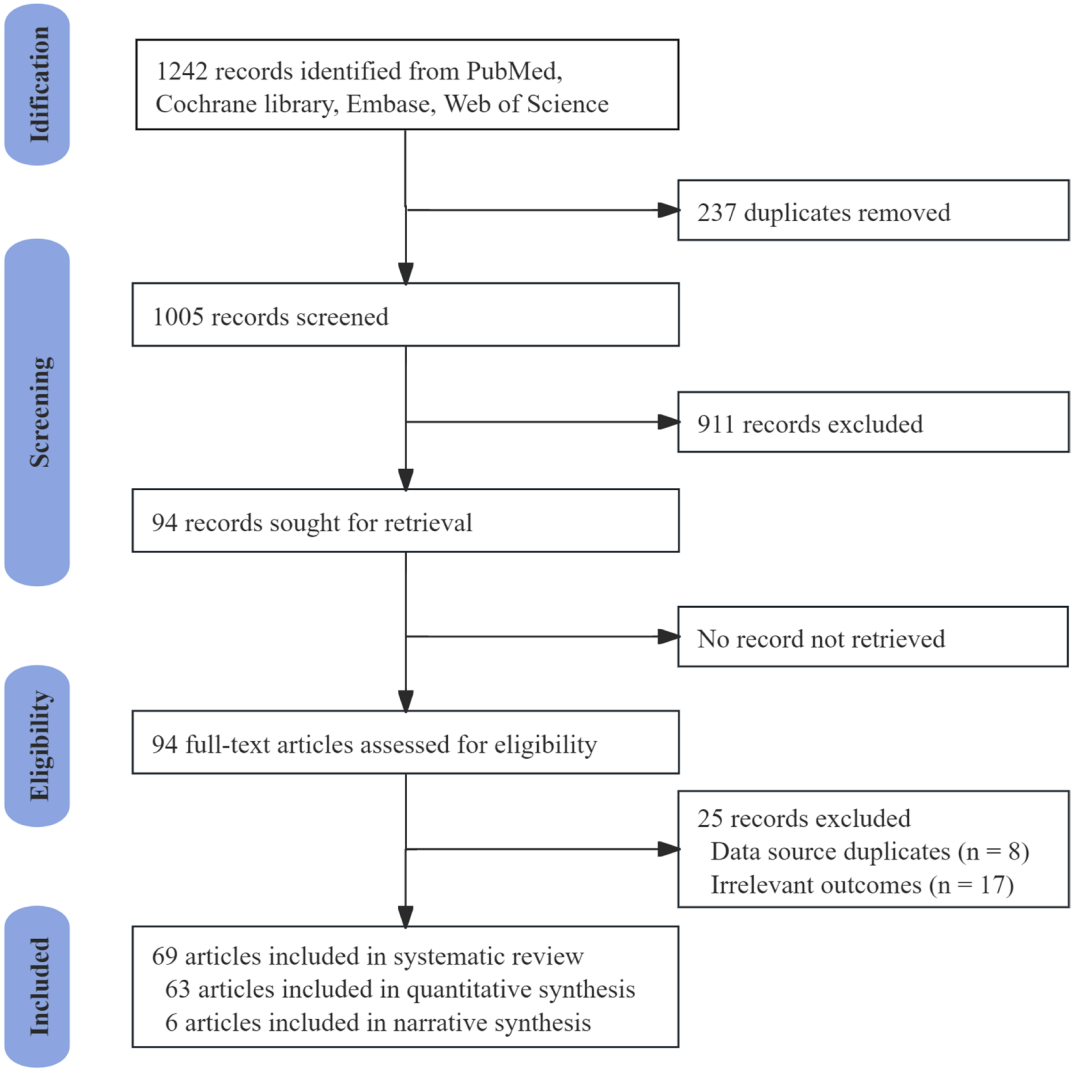

Fig. 1 The PRISMA flow diagram

narrative synthesis. Regarding cross-sectional studies, we excluded them from meta-analyses when comparable cohort data were available for the same population and outcome. However, in cases where cohort data were insufficient or unavailable, we incorporated cross-sectional studies into the narrative synthesis to provide complementary evidence on eGDR-outcome associations.

Definitions of eGDR and outcomes

The eGDR (mg/kg/min) was determined using the following formulas:

A $eGDR_{WHR} = 24.31 - (12.22 * WHR) - (3.29 * HT) - (0.57 * HbA1c)$.

B $eGDR_{WC} = 21.16 - (0.09 \times WC) - (3.41 \times HTN) - (0.55 \times HbA1c)$.

C $eGDR_{BMI} = 19.02 - (0.22 \times BMI) - (3.26 \times HTN) - (0.61 \times HbA1c)$.

The waist-to-hip ratio (WHR) is calculated by dividing the waist circumference by the hip circumference. Hypertension is a binary variable indicating the presence (1) or absence (0) of hypertension. HbA1c is expressed as a percentage. Hypertension is defined as either treatment with antihypertensive medication or systolic blood pressure (SBP) greater than 140 mm Hg or diastolic blood pressure (DBP) greater than 90 mm Hg [12, 14].

This meta-analysis focused on two primary objectives: first, to explore the association between eGDR and the risk of CVD, DMC and mortality; and second, to estimate the overall mean level of eGDR in different populations. CVD was primarily defined using

standardized diagnostic codes from the International Classification of Diseases, 10th Revision (ICD-10), encompassing coronary artery disease (CAD, I20–I25), stroke (I60–I69), and peripheral arterial disease (PAD, I70–I79). While one study included self-reported CVD outcomes [24], we systematically addressed this definitional heterogeneity through stratified analyses. DMC includes DR, diabetic nephropathy (DN), and diabetic peripheral neuropathy (DPN). Mortality was defined as all-cause mortality. Detailed definitions of clinical outcomes in each study are presented in Additional file 1: Table 3.

Data extraction and quality assessment

Two reviewers independently scrutinized the titles, abstracts, and full texts of studies to determine eligibility. Data extracted include study characteristics such as authors, study design, location, sample size, data source, timing of data collection, participant demographics (age and sex), duration of DM, duration of follow-up, and eGDR levels. Event counts, crude and adjusted HRs, along with their 95% CIs for each outcome, were also recorded. For studies using overlapping cohorts but reporting on distinct outcomes, all relevant studies were incorporated into the pooled analysis for their respective outcomes. Any discrepancies and disagreements in the data extraction process were resolved through collaborative discussion, with a third researcher examining the original data to reach a consensus.

A validated 14-item quality assessment tool developed by the National Institutes of Health (NIH) was used to assess the quality of each study (available at https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). Each item was categorized as "yes" (1 point), "no" (0 points), "not reported", or "not applicable." A score of 1 point was assigned if the item was adequately described, and 0 points if it lacked sufficient description or did not meet the quality criteria. "Not reported" was used when the item lacked a clear description, and "not applicable" when the assessment criteria could not be met. The maximum attainable score was 14 points for longitudinal studies and 11 points for observational and cross-sectional studies. For longitudinal studies, scores were categorized as high quality (> 9 points), medium quality (4–9 points), and low quality (< 4 points). For cross-sectional studies, high quality was defined as >7 points, medium quality as 3–7 points, and low quality as <3 points. Medium- and low-quality studies were considered high-risk publications. Two independent reviewers conducted the evaluations, resolving any discrepancies through discussion.

Data synthesis and statistical analyses

We conducted quantitative synthesis using R software (version 3.4.0). HRs for CVD, DMC, and all-cause mortality were pooled using random-effects models. For cohort studies reporting HRs by eGDR quantiles, we standardized the effects to represent per-unit increases in eGDR using established dose–response methodology. This transformation required the following data elements from each study: eGDR category boundaries, event counts, participant numbers per category, adjusted HRs, and their 95% confidence intervals (CIs). The methodology assumed normally distributed exposure variables and log-linear exposure-outcome relationships [25, 26].

We employed the DerSimonian-Laird random-effects method to synthesize the reported HRs and their 95% CIs [27]. For studies reporting multiple effect estimates for the same outcome, we selected the most relevant adjusted estimate to avoid unit-of-analysis errors (Additional file 1: Table 4). A separate meta-analysis was conducted to pool the mean eGDR levels across studies using untransformed means (MRAW) and standard deviations (SDs). The overall eGDR estimates and their 95% CIs were calculated using inverse variance weighting [28]. Results were visualized through forest plots, and between-study heterogeneity was quantified using I^2 statistics and tau^2 with corresponding 95% CIs [27, 29].

We conducted comprehensive subgroup analyses to investigate potential sources of heterogeneity across predefined stratification factors, including mean age (≤ 30 versus >30 years), geographical location (Europe versus North America), study site characteristics (single-center versus multicenter), sample size (≤ 1000 versus >1000 participants), follow-up duration (≤ 10 versus >10 years), diabetes duration (≤ 20 versus >20 years), and eGDR formulas ($eGDR_{WHR}$, $eGDR_{WC}$, or $eGDR_{BMI}$).

To evaluate the robustness of our findings, we performed three distinct sensitivity analyses. The first analysis examined the stability of risk estimates for CVD, DMC, and mortality across three levels of covariate adjustment: Model I (unadjusted or adjusted for age and sex only), Model II (Model I plus diabetes duration), and Model III (Model II plus demographic factors and conventional CVD risk factors at baseline). We also performed leave-one-out sensitivity analyses by sequentially excluding individual studies to examine their influence on the pooled estimates and identify potential outliers. Third, considering the variation in CVD definitions across studies, we assessed the impact of this heterogeneity by specifically addressing studies that relied on self-reported CVD. For studies included in the meta-analysis, we performed additional sensitivity analyses to evaluate their impact on the overall pooled estimates. For studies included in the narrative synthesis, we provided detailed

explanations in the corresponding sections to account for the potential limitations associated with self-reported CVD.

Reporting bias assessment and certainty assessment

A funnel plot and Egger's test were planned to assess publication bias and small-study effects if more than six studies reported data on the same outcome [30]. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach [31] was used to evaluate the certainty of the evidence, categorizing it as high, moderate, low, or very low based on evaluation criteria.

Results

Study selection

Our literature search initially identified 1,242 records. After removing duplicates and screening titles and abstracts, 94 articles were selected for full-text review. Following detailed evaluation, 25 articles were excluded: 8 due to duplicate data sources and 17 due to irrelevant outcomes (Additional file 1: Table 5). The final analysis included 69 studies for systematic review, of which 63 were eligible for quantitative synthesis and 6 were eligible for narrative synthesis (Fig. 1). Among the included studies, 19 investigated the associations between eGDR and clinical outcomes (CVD, DMC, and all-cause mortality), while 50 studies reported mean eGDR values in diabetic populations.

Study characteristics

Again, the included 19 observational studies examined the associations between eGDR and clinical outcomes (CVD, DMC, and mortality) (Table 1). These comprised 17 cohort studies and 2 cross-sectional studies, with a total enrollment of 185,810 participants. The geographical distribution of the studies was diverse: six from North America (five studies conducted in the United States and one study conducted across the United States and Canada), seven from Europe (four Swedish, one Italian, one Finnish, and one study from the Netherlands), five from Asia (all conducted in China), and one study conducted across the United States and Italy. Individual study sample sizes varied considerably, ranging from 366 to 104,697 participants. For the analysis of mean eGDR levels, we included 50 studies (Additional file 1: Table 6), with 46 studies focusing on T1DM and four on T2DM.

Study quality assessment

All 19 studies examining the associations between eGDR and clinical outcomes (CVD, DMC, and mortality) were rated as "high quality" using the NIH quality assessment tool (Additional file 1: Table 7). Among the 50 studies included in the analysis of mean eGDR levels, 28 (56%) achieved "high quality" ratings, while the remaining 22 (44%) were assessed as "medium quality"(Additional file 1: Table 8).

eGDR and the risk of CVD

Nine studies investigated the association between eGDR and CVD risk across different populations. Of these, six studies conducted in patients with T1DM (Helmink 2021 [35], Garofolo 2020 [8], Miller 2019 [36], Nystrom 2018 [37], Kilpatrick 2007 [38], Olson 2002 [39]) were included in a meta-analysis. Two studies in patients with T2DM (Zabala 2021 [41], Nystrom 2017 [47]) were included in a narrative analysis, while one study conducted in the general population (Zhang 2024 [48]) was also included in a narrative analysis (Table 1).

Our findings revealed that each unit increase in eGDR was associated with an HR of 0.78 (95% CI: 0.69–0.87, $I^2 = 68\%$, $\tau^2 = 0.0127$, $p < 0.01$), indicating a significant protective effect against CVD risk (Fig. 2A). Subgroup analyses in T1DM patients demonstrated the consistency of this protective association across various stratification factors, including age, geographical location, study center, sample size, follow-up duration, and eGDR formula. Notably, studies using the eGDR formula A exhibited higher heterogeneity ($I^2 = 80\%$, $p < 0.01$) compared to those using formula C ($I^2 = 0\%$, $p = 0.59$), suggesting that the choice of eGDR formula may be a potential source of heterogeneity (Table 2).

For T2DM, two studies (Zabala 2021 [41], Nystrom 2017 [47]) reported the association between eGDR and CVD risk using stratified eGDR levels. Both studies consistently demonstrated an inverse association between eGDR levels and CVD risk in patients with T2DM. Similarly, in the general population, Zhang Z et al. demonstrated a per-unit decrement in eGDR was associated with an aHR of 1.10 (95% CI: 1.06–1.13), further supporting the protective role of higher eGDR levels against CVD risk across broader populations (Table 3). However, it is important to note that the CVD outcomes in Zhang Z et al.'s study were self-reported, which may introduce potential bias and affect the accuracy of the observed associations.

eGDR and the risk of DMC

Six studies (total $n = 28{,}308$) examined the relationship between eGDR and DMC. Among patients with T1DM, a meta-analysis of three studies (Linn 2023 [32], Mao 2022 [33], Kilpatrick 2007 [38]) showed no statistically significant association between eGDR levels and DMC risk (HR 0.86; 95% CI 0.72–1.03; $I^2 = 25\%$) (Fig. 2B). In contrast, in T2DM populations, a narrative synthesis of three studies (Zhang Y 2024 [44], Xu 2024 [45], Meng

Table 1 Basic characteristics of studies on the risk of macrovascular and microvascular complications and mortality

Study	Design	Country	Participants	Data Source	Data collection	Baseline age, y	Duration of DM, y	Follow-up, y	Sample size	Male (%)	Degree of adjustment	eGDR formula	Outcome
Pooled Analysis													
Linn 2023 [32]	RC	Sweden	Young people with type 1 diabetes	Swedish pediatric registry for diabetes	1998 to 2017	Median, 21	Range, 6–7	Median, 4.8	22,146	57.70%	I/II/III	B	DM
Mao 2022 [33]	PC	USA	Individuals with T1DM	DCCT/EDIC	1983 to 1993	28.3 ± 6.9	Median, 6.5	Mean, 6.5	957	54.20%	II	A	DR
Harjutsalo 2021 [34]	PC	Finland	Individuals with T1DM	Finnish Diabetic Nephropathy Study	1969 to 2017	Median, 50.7	Median, 16.6	Median, 39.3	729	50.60%	III	A	All-cause mortality
Helmink 2021 [35]	PC	Netherlands	Individuals with T1DM	UCC-SMART study	1997 to 2018	38 ± 13	Median, 18	Median, 12.9	195	57%	II/III	A	CVD; All-cause mortality
Garofolo 2020 [8]	PC	Italy	Individuals with T1DM	University of Pisa	2017 to 2018	40.2 ± 11.7	19.4 ± 12.2	10.5 ± 2.6	774	52.60%	I/II/III	C	CVD; All-cause mortality
Miller 2019 [36]	PC	USA	Patients with child-hood-onset T1DM	DCCT/EDIC	1950 to 1980	Mean, 27	Median, 19	Mean, 25	604	40%	I/III	A	CVD
Nystrom 2018 [37]	RC	Sweden	Individuals with T1DM	Swedish National Diabetes Register	2005 to 2012	40.4 ± 15.1	24.8 ± 15.2	Median, 7.1	17,050	56%	I/II/III	C	CVD; All-cause mortality
Kilpatrick 2007 [38]	PC	USA and Canada	Individuals with T1DM	DCCT	NR	26.89 ± 7.04	NR	9	1337	53.33%	III	A	CVD; All-cause mortality; DMC
Olson 2002 (1) [39]	PC	USA	Individuals with child-hood-onset T1DM	Pittsburgh EDC Study	1950 to 1980	27.07 ± 7.70	18.73 ± 7.39	10	586	51.37%	III	A	CVD
Olson 2002 (2) [39]	PC	USA	Individuals with child-hood-onset T1DM	Pittsburgh EDC Study	1986 to 1988	Mean, 28	Median, 10	Median, 19	655	50.70%	III	A	All-cause mortality
Ciardullo 2023 [40]	PC	Italy and USA	Patients with T2DM	Papa Giovanni XXIII Hospital of Bergamo and NHANES	1998 to 2012	59.7 ± 9.2	9.2 ± 6.7	Median, 8.3	3553	77.90%	III	A	All-cause mortality
Zabala 2021 [41]	RC	Sweden	Adult individu-als with T2DM	Swedish National Diabetes Register	2004 to 2016	62.9 ± 11.5	4.1 ± 5.7	Median, 5.6	104,697	56.00%	I/II/III	C	All-cause mortality

Table 1 (continued)

Study	Design	Country	Participants	Data Source	Data collection	Baseline age, y	Duration of DM, y	Follow-up, y	Sample size	Male (%)	Degree of adjustment	eGDR formula	Outcome
He 2024 [42]	PC	USA	Individuals with and without DM	NHANES	2001 to 2018	45 ± 16	NA	Median, 8.92	14,628	49.70%	II/III	C	All-cause mortality
Sun 2023 [43]	PC	China	Community-dwelling elderly aged 60 years	Wanshou Road Community in Beijing	2009 to 2010	71.03 ± 7.03	NA	Median, 10.75	1826	40.36%	I/II/III	C	All-cause mortality
Narrative Synthesis													
Zhang Y 2024 [44]	PC	China	T2DM subjects without DPN	Six communities in Shanghai	2011 to 2014	62.64 ± 8.23	NR	Median, 5.91	366	45.63%	I/II/III	A	DPN
Xu 2024 [45]	CS	China	Patients with T2DM	First Affiliated Hospital of Harbin Medical University	2017 to 2022	Median, 56	Median, 8	NA	1740	60.70%	I/II/III	A	DR
Meng 2023 [46]	CS	China	Patients with T2DM	Hebei General Hospital	January to December 2020	56.68 ± 10.17	Median, 8	NA	1762	50.10%	I/II/III	C	DR
Zabala 2021 [41]	RC	Sweden	Adult individuals with T2DM	Swedish National Diabetes Register	2004 to 2016	62.9 ± 11.5	4.1 ± 5.7	Median, 5.6	104,697	56.00%	I/II/III	C	Stroke
Nystrom 2017 [47]	PC	Sweden	Patients with T2DM	Swedish National Diabetes Register	2006 to 2013	69.6 ± 7.8	10.1 ± 7.6	2.3 ± 1.9	3256	77.50%	I/II/III	C	CVD
Zhang Z 2024 [48]	PC	China	Individuals without DM	CHARLS	2011 to 2012	58.16 ± 8.82	NA	Median, 6. 6	5512	45.90%	I/II/III	C	CVD

Degree of adjustment: I for unadjusted or adjusted only for age and sex; II for I plus duration of DM, III for II plus other demographic factors and conventional CVD risk factors at baseline. The formula for calculating eGDR: A. $eGDR_{WHR} = 24.31 - 12.22*(WHR) - 3.29*(HTN) - 0.57*(HbA1c)$; B. $eGDR_{BMI} = 19.02 - 0.22*(BMI) - 3.26*(HTN) - 0.61*(HbA1c)$; C. $eGDR_{WC} = 21.158 - 0.09*(WC) - 3.407*(HTN) - 0.551*(HbA1c)$

BMI Body mass index, *CAD* Coronary artery disease, *CVD* Cardiovascular disease, *CS* Cross-sectional study, *DCCT* Diabetes Control and Complications Trial, *DMC* Diabetic microvascular complications, *DR* Diabetic retinopathy, *DN* Diabetic nephropathy, *DPN* Diabetic peripheral neuropathy, *DBP* Diastolic blood pressure, *eGDR* Estimated glucose disposal rate, *eGFR* Estimated glomerular filtration rate, *EDIC* Epidemiology of Diabetes Interventions and Complications study, *EDC* Epidemiology of Diabetes, *HDL-C* High-density lipoprotein cholesterol, *LDL-C* Low-density lipoprotein cholesterol, *MI* Myocardial ischemia, *NA* Not applicable, *NHANES* National Health and Nutrition Examination Survey, *NR* Not reported, *PC* Prospective cohort study, *RC* Retrospective cohort study, *SBP* Systolic blood pressure, *TC* Total cholesterol, *UCC-SMART* Utrecht Cardiovascular Cohort – Second Manifestations of ARTerial disease, *y* years

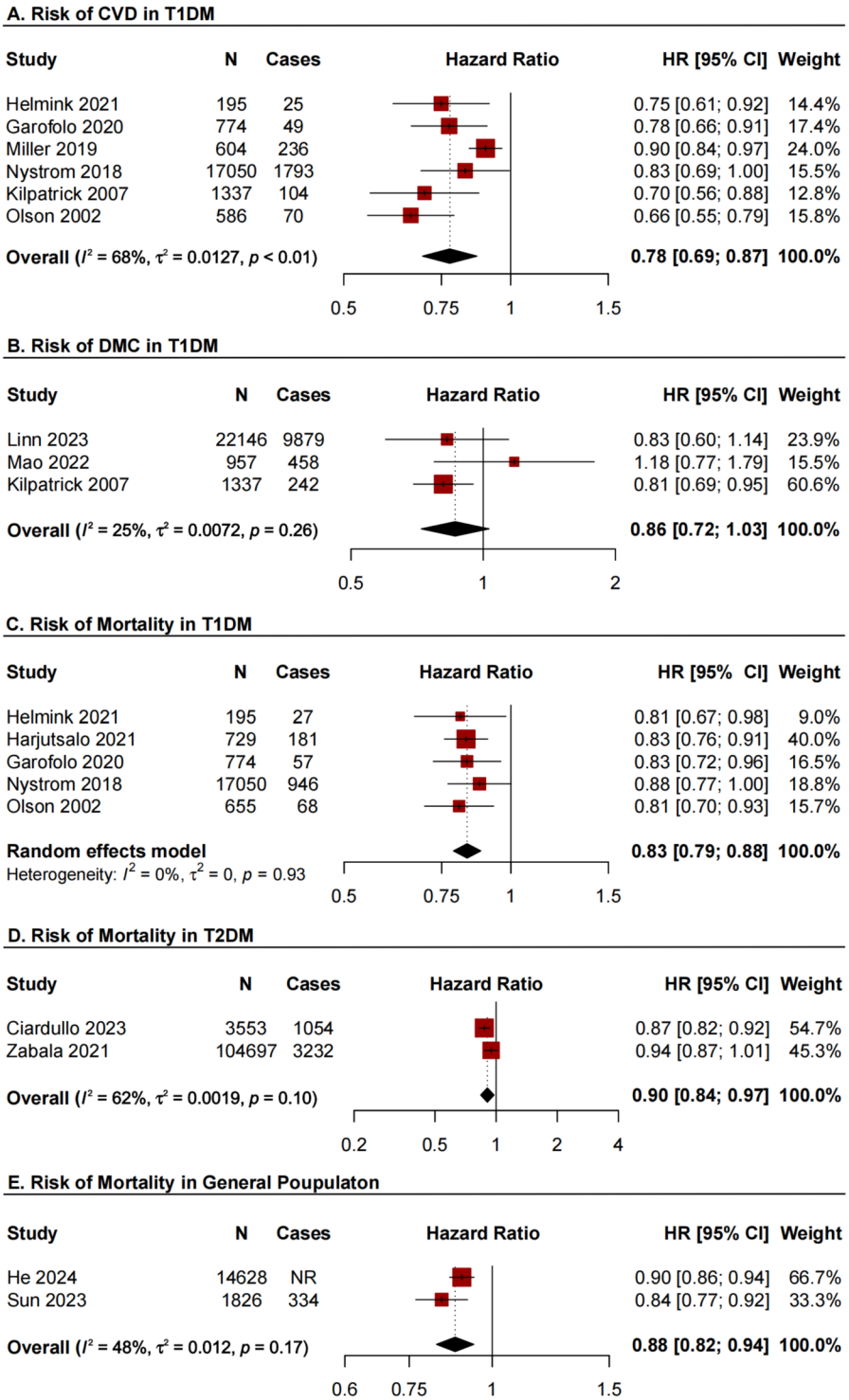

Fig. 2 Forest plots showing the association between exposure levels and various health outcomes in different populations. **A** Risk of cardiovascular disease (CVD) in type 1 diabetes mellitus (T1DM) patients (6 studies, n = 20,546). **B** Risk of microvascular complications in T1DM patients (3 studies, n = 24,440). **C** Risk of mortality in T1DM patients (5 studies, n = 19,403). **D** Risk of mortality in type 2 diabetes mellitus (T2DM) patients (2 studies, n = 108,250). **E** Risk of CVD in general population (2 studies, n = 13,779). F. Risk of mortality in general population (2 studies, n = 16,454). The forest plots show hazard ratios (HRs) with 95% confidence intervals (CIs). I^2 indicates the percentage of variation attributable to heterogeneity, τ^2 represents the between-study variance, and p-values are for heterogeneity tests. NR = Not Reported

Table 2 Subgroup analysis of eGDR on CVD and all-cause mortality in patients with T1DM

Subgroup	No. of studies	HR (95% CI)	Tests for heterogeneity			Subgroup differences
			I^2	τ^2	*P*	*P*
Outcome = CVD	6	0.78 (0.69—0.87)	68.00%	0.013	< 0.01	
Age, years						
Mean age < = 30	3	0.76 (0.60—0.95)	84.90%	0.034	< 0.01	0.79
Mean age > 30	3	0.78 (0.71–0.87)	0%	0	0.76	
Geographical location						
Europe	3	0.76 (0.60—0.95)	84.90%	0.034	< 0.01	0.79
North America	3	0.78 (0.71—0.87)	0%	0	0.76	
Single vs multicentric center						
Single-center study	4	0.78 (0.67—0.91)	77.30%	0.017	< 0.01	0.94
Multi-center study	2	0.77 (0.66—0.91)	22.40%	0.003	0.26	
Sample size						
< = 1000	4	0.78 (0.67—0.91)	77.30%	0.017	< 0.01	0.94
> 1000	2	0.77 (0.66—0.91)	22.40%	0.003	0.26	
Follow-up, years						
< = 10	3	0.73 (0.63—0.84)	36.10%	0.006	0.21	0.19
> 10	3	0.83 (0.73—0.94)	61.80%	0.008	0.07	
eGDR formula						
A	4	0.76 (0.64—0.90)	80.00%	0.025	< 0.01	< 0.01
C	2	0.80 (0.71—0.90)	0%	0	0.59	
Outcome = All-cause mortality	5	0.83 (0.79—0.88)	0%	0	0.93	
Single vs multicentric center						
Single-center study	3	0.82 (0.75—0.89)	0%	0	0.94	0.58
Multi-center study	2	0.84 (0.78—0.91)	0%	0	0.49	
Duration of diabetes						
Mean duration < = 20	3	0.81 (0.72—0.91)	0%	0	0.97	0.53
Mean duration > 20	2	0.84 (0.79—0.90)	0%	0	0.78	
Follow-up, years						
< = 10	2	0.84 (0.77—0.93)	0%	0	0.39	0.75
> 10	3	0.83 (0.77—0.89)	0%	0	0.97	
eGDR formula						
A	3	0.82 (0.77—0.88)	0%	0	0.93	0.49
C	2	0.86 (0.78—0.94)	0%	0	0.6	

The formula for calculating eGDR: A. eGDRWHR = 24.31–12.22*(WHR)–3.29*(HTN)–0.57*(HbA1c); C. eGDRWC = 21.158 – 0.09*(WC) – 3.407*(HTN) – 0.551* (HbA1c)

CVD Cardiovascular disease

2023 [46]) consistently demonstrated an inverse association between eGDR levels and the risk of DMC, with all studies analyzing eGDR as a continuous variable. Lower eGDR levels, whether expressed as per-unit or per-standard deviation decreases, were significantly associated with higher odds of DMC.

eGDR and all-cause mortality

Nine studies (total n = 144,107) investigated the association between eGDR and all-cause mortality across different populations. In T1DM patients (n = 19,403), a meta-analysis of five studies (Helmink 2021 [35], Harjutsalo 2021 [34], Garofolo 2020 [8], Nystrom 2018 [37], Olson 2002 [39]) demonstrated that each 1-unit increase in eGDR (mg/kg/min) was associated with a reduced risk of mortality (HR 0.83; 95% CI 0.79–0.88; I^2 = 0%) (Fig. 2C). Subgroup analysis revealed consistent protective effects of higher eGDR levels across different study characteristics. No significant subgroup differences were observed for study center, duration of diabetes, follow-up duration, or eGDR formula used, indicating the robustness of the observed association.

Similar associations were observed in both T2DM patients (n = 108,250; two studies: Ciardullo 2023 [40],

Table 3 Narrative synthesis of studies examining the association between eGDR and clinical outcomes in the general population and patients with T2DM

Study	Cases	N	eGDR comparison method	Effect Size
eGDR and the risk of CVD in patients with T2DM				
Zabala 2021 [41]	4,201	104,697	Per unit decrease	aHR: 1.05 (1.04–1.07)
Nystrom 2017 [47]	667	3,256	eGDR: median 3.6 (IQR:2.8–4.1) eGDR: median 5.4 (IQR: 5.0–5.9) eGDR: median 8.1 (IQR:7.5–8.8)	aHR:1.24 (1.00–1.55) aHR:1.11 (0.90–1.38) aHR: 1
eGDR and the risk of DMC in patients with T2DM				
Zhang Y 2024 [44]	198	366	eGDR < 9.15 vs. eGDR > 9.15 (ref.)	aOR: 1.75 (1.01–3.03)
Xu 2024 [45]	442	1,740	Per 1 SD decrease	aOR: 2.63 (2.27–3.13)
Meng 2023 [46]	348	1,762	Per 1 uinit decrease	aOR: 1.58 (1.31–1.89)
eGDR and the risk of CVD in general population				
Zhang Z 2024 [48]	1213	5512	Per 1 unit decrement	aHR: 1.10 (1.06–1.13)

CVD Cardiovascular disease, *DMC* Diabetic microvascular complications, *SD* Standard deviation, *aOR* Adjusted odds ratio, *aHR* Adjusted hazard ratio

Zabala 2021 [41]; pooled HR 0.90; 95% CI 0.84–0.97; I^2 = 62%) (Fig. 2D) and the general population without diabetes (n = 16,454; two studies: He 2024 [42], Sun 2023 [43]; pooled HR 0.88; 95% CI 0.82–0.94; I^2 = 48%) (Fig. 2E).

Overall eGDR levels in diabetic patients

Our meta-analysis included 50 studies examining mean eGDR levels in diabetic patients (46 studies in T1DM and 4 studies in T2DM). The pooled mean eGDR level in patients with T1DM was 8.19 mg/kg/min (95% CI 7.81–8.57; I^2 = 99%). The pooled mean eGDR level in patients with T2DM was lower (7.03 mg/kg/min; 95% CI 4.89–9.17; I^2 = 100%) (Additional file 1: Fig. S1 and Fig. S2). Subgroup analysis by eGDR formula (A, B, and C) showed pooled mean eGDR levels of 7.97 mg/kg/min (95% CI: 7.40–8.55), 8.28 mg/kg/min (95% CI: 7.44–9.12), and 8.73 mg/kg/min (95% CI: 7.84–9.61), respectively. However, the test for subgroup differences (χ^2 = 1.97, df = 2, p = 0.37) indicated that formula choice was not a source of heterogeneity (Additional file 1: Table 9).

Sensitivity and additional analyses

We performed multiple sensitivity analyses to evaluate our findings. Analyses stratified by adjustment levels (Additional file 1: Fig. S3 and Fig. S4) showed consistent results for CVD and DMC risks in T1DM patients across all adjustment levels. For T1DM mortality, results remained consistent with adjustments II and III, while adjustment I showed negative results (Additional file 1: Fig. S5). Leave-one-out sensitivity analysis demonstrated stable pooled HRs for CVD, DMC, and mortality, suggesting no single study substantially influenced the overall results (Additional file 1: Fig. S6–Fig. S10).

Publication bias assessment showed symmetrical distributions for overall eGDR levels in T1DM patients (Additional file 1: Fig. S11). However, publication bias could not be reliably assessed for other outcomes due to limited available datasets.

Using the GRADE methodology, we evaluated the certainty of evidence for each outcome. The evidence for CVD risk in T1DM patients was rated as very low due to significant inconsistency. Low certainty ratings were assigned to the evidence for DMC and all-cause mortality in T1DM patients, as well as CVD risk in the general population, the latter primarily due to notable inconsistencies. Evidence certainty for overall eGDR levels in both T1DM and T2DM patients was rated as very low due to imprecision (Additional file 1: Table 10).

Discussion

In our meta-analysis of 69 studies, we identified several key findings. First, each 1-unit (mg/kg/min) increase in eGDR was associated with a 22% reduced risk of cardiovascular disease in T1DM (HR 0.78; 95% CI: 0.69–0.87), with similar protective associations observed in T2DM. Second, while each 1-unit increase in eGDR showed no significant association with diabetic complications in T1DM (HR 0.86; 95% CI 0.72–1.03), it demonstrated consistent inverse associations with complication risk in T2DM. Third, each 1-unit increase in eGDR was associated with reduced all-cause mortality across all populations, including T1DM (HR 0.83; 95% CI 0.79–0.88), T2DM (HR 0.90; 95% CI 0.84–0.97), and the general population (HR 0.88; 95% CI 0.82–0.94). Finally, we observed distinct patterns of insulin sensitivity between diabetes types, with T1DM patients showing higher mean eGDR levels (8.19 mg/kg/min; 95% CI 7.81–8.57) compared to T2DM patients (7.03 mg/kg/min; 95% CI 4.89–9.17).

While insulin resistance is a well-established risk factor for adverse health outcomes, its clinical assessment

remains challenging. Our findings provide evidence supporting eGDR as a practical tool for risk stratification across different populations. Recent work by Sun et al. demonstrated the association between eGDR and cardiovascular outcomes specifically in T1DM [22], highlighting the need for a broader investigation. Our meta-analysis contributes to this developing area by examining eGDR's associations with multiple clinical endpoints across diverse populations. In people with T1DM, our findings align with Sun et al.'s work [22], showing that higher eGDR levels were significantly associated with lower CVD risk. This relationship may be mediated through multiple pathways, including improved endothelial function, reduced inflammation, and better metabolic control [49]. The extension of these findings to type 2 diabetes and general populations represents a novel contribution to the field. While methodological heterogeneity prevented pooling of type 2 diabetes cardiovascular outcomes, individual studies suggest similar protective associations. The significant association in the general population with minimal heterogeneity ($I^2 = 0\%$) indicates that eGDR might have broader applications beyond diabetes care.

Another finding was the difference in eGDR levels between T1DM and T2DM. The lower mean eGDR values were observed in people with T2DM compared to those with T1DM. This pattern may reflect pathophysiological differences between these diabetes types and their associated metabolic profiles. Type 2 diabetes is primarily characterized by insulin resistance and metabolic syndrome features, with approximately 85% of patients being overweight or obese [50]. The eGDR formula was initially validated in T1DM [12], and our observation of systematically lower values in T2DM suggests that population-specific thresholds might be needed for optimal risk stratification in different diabetes types.

The consistency of these associations across various populations has important clinical implications. For T1DM patients, this highlights the importance of lifestyle interventions and cardiovascular risk factor management beyond glycemic control alone. In T2DM, where insulin resistance is a primary pathophysiological feature, strategies focusing on enhancing insulin sensitivity through lifestyle modifications, weight management, and appropriate pharmacological interventions may be particularly beneficial for cardiovascular protection.

The relationship between eGDR and DMC appears more complex. While our analysis did not demonstrate a statistically significant association in T1DM (HR 0.86; 95% CI 0.72–1.03), this may reflect limitations in current evidence rather than an absence of effect. The emerging evidence in T2DM regarding specific complications suggests potential relationships that warrant further investigation.

We also investigated the all-cause mortality across different populations. In people with T1DM, higher eGDR levels were associated with significantly lower mortality risk (HR 0.83; 95% CI 0.79–0.88), with remarkable consistency across studies ($I^2 = 0\%$). Similar associations were observed in T2DM (HR 0.90; 95% CI 0.84–0.97) and general populations (HR 0.88; 95% CI 0.82–0.94), though with moderate heterogeneity. These findings suggest that eGDR may serve as a valuable predictor of mortality risk, potentially reflecting its ability to capture multiple aspects of metabolic health. The stronger association observed in T1DM compared to T2DM might indicate that insulin sensitivity plays a particularly crucial role in determining long-term outcomes in this population.

Strength and limitations

Our meta-analysis is the first comprehensive summary of research on eGDR and its associations with CVD, DMC, and all-cause mortality, providing an evidence-based foundation for clinical practice. It highlights the importance of eGDR in predicting macrovascular and microvascular complications and in prognostic assessment, not only in the general population but also among individuals with diabetes (Fig. 3). However, several important limitations of our study warrant careful consideration. First, the number of available studies was limited, particularly for analyses in T2DM and general populations, which may affect the reliability of our findings in these groups. While meta-analyses are technically feasible with as few as two studies, the interpretation of results from populations with fewer than five studies should be considered preliminary. Second, the GRADE assessment revealed varying levels of evidence certainty across outcomes. The evidence for cardiovascular risk in T1DM was rated as very low due to significant inconsistency, while evidence for microvascular complications and all-cause mortality in T1DM received low certainty ratings. These ratings reflect both the inherent limitations of observational studies and the presence of heterogeneity across studies. Additionally, publication bias assessment was limited by the small number of available studies for several outcomes, though analyses of eGDR levels in T1DM showed symmetrical distributions. While our standardization of effects to represent per-unit increases in eGDR aimed to enhance comparability across studies, the variation in reporting methods may have introduced some methodological heterogeneity. The observational nature of included studies also precludes direct causal inference, suggesting that the clinical application of eGDR requires further validation, particularly in T2DM and general populations where evidence remains limited.

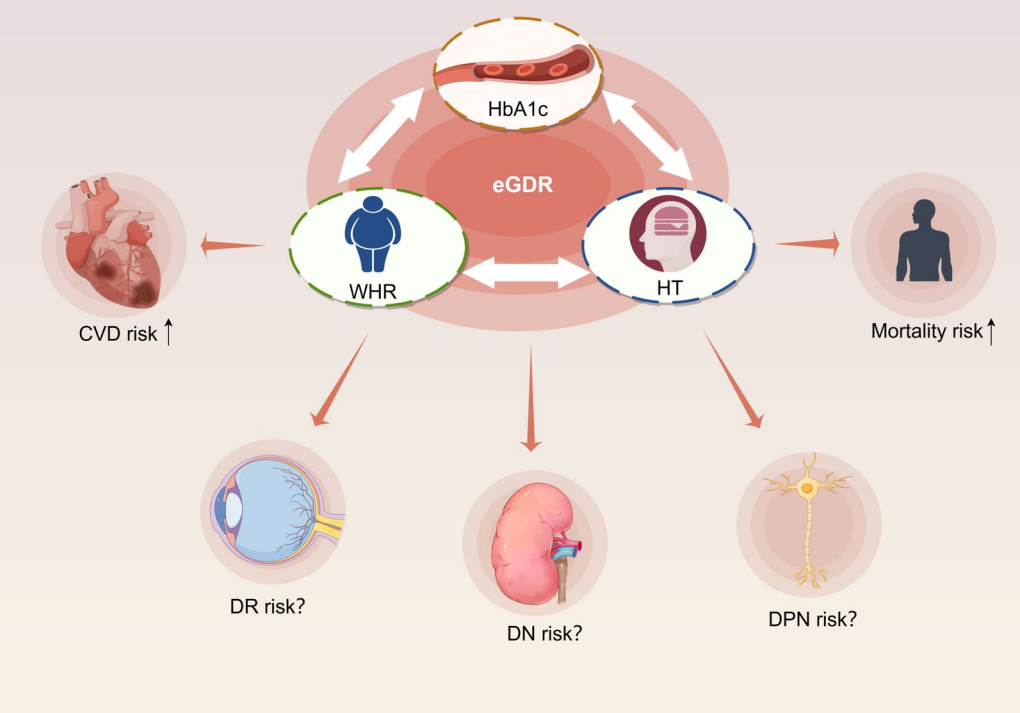

Fig. 3 Schematic diagram of the relationship between eGDR and various health outcomes. eGDR (estimated glucose disposal rate) is influenced by three key components: HbA1c (glycated hemoglobin), WHR (waist-to-hip ratio), and HT (hypertension), as shown in the central portion. Lower eGDR levels are associated with increased risks of cardiovascular disease (CVD) and all-cause mortality (shown on both sides). The potential associations between eGDR and microvascular complications including diabetic retinopathy (DR), diabetic nephropathy (DN), and diabetic peripheral neuropathy (DPN) require further investigation (shown at the bottom)

Conclusions

Our study suggests that eGDR could potentially serve as a clinical tool for risk stratification and outcome prediction. The observed associations between higher eGDR and improved outcomes indicate that strategies targeting insulin sensitivity may have beneficial effects on patient care. While these findings provide insights into the potential utility of eGDR in clinical practice, population-specific thresholds and implementation strategies need to be established through further prospective studies before widespread clinical adoption.

Abbreviations

BMI	Body mass index
CAD	Coronary artery disease
CI	Confidence interval
CS	Cross-sectional study
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DL	DerSimonian-Laird
DM	Diabetes mellitus
DMC	Diabetic microvascular complications
DN	Diabetic nephropathy
DR	Diabetic retinopathy
DPN	Diabetic peripheral neuropathy
eGDR	Estimated glucose disposal rate
eGFR	Estimated glomerular fltration rate
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HbA1c	Glycated hemoglobin A1c
HDL-C	High-density lipoprotein cholesterol
HR	Hazard ratio
HT	Hypertension
IR	Insulin resistance
LDL-C	Low-density lipoprotein cholesterol
MI	Myocardial ischemia
MRAW	Untransformed means
NA	Not applicable
NIH	National Institutes of Health
NR	Not reported
OR	Odds ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PROSPERO	International Prospective Register of Systematic Reviews Database
PC	Prospective cohort study
RC	Retrospective cohort study
SBP	Systolic blood pressure
SD	Standard deviation
TC	Total cholesterol
WHR	Waist-hip circumference

Supplementary Information

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Additional file 1: Table 1- PRISMA checklist. Table 2- Literature search strategy. Table 3- Definition of the clinical outcome. Table 4- Confounding

variable. Table 5- Excluded studies after full-text review. Table 6- Characteristics of studies included in the analysis of overall eGDR levels. Table 7- NIH Quality Assessment on the risk of CVD, DMC, and mortality. Table 8- NIH Quality Assessment of overall eGDR levels. Table 9- Subgroup analysis of overall eGDR levels. Table 10- GRADE evidence profile. FigS1- Forest plot of the eGDR in T1DM. FigS2- Forest plot of the eGDR in T2DM. FigS3- Sensitivity analysis of CVD in T1DM based on adjustment degrees. FigS4- Sensitivity analysis of DMC in T1DM based on adjustment degrees. FigS5- Sensitivity analysis of mortality in T1DM based on adjustment degrees. FigS6- Sensitivity analysis of CVD in T1DM based on leave-one-out method. FigS7- Sensitivity analysis of DMC in T1DM based on leave-one-out method. FigS8- Sensitivity analysis of mortality in T1DM based on leave-one-out method. FigS9- Sensitivity analysis of mortality in T2DM based on leave-one-out method. FigS10- Sensitivity analysis of mortality in the general population based on leave-one-out method. FigS11- Funnel plot of the overall eGDR levels in T1DM.

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Clinical Trial Number
Not applicable. This study is not a clinical trial.

Authors' contributions
LG and YQW conceived and designed the study. LG, JZ, and WRW carried out the literature search and screening of articles for the revised manuscript. LG, JZ and RA performed the updated data analysis. LG and YQW wrote and revised the manuscript. JF and YSW contributed to the initial submission version of the manuscript. All authors reviewed and approved the final manuscript.

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Declarations

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Competing interests
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References

1. Eizirik DL, Pasquali L, Cnop M. Pancreatic β-cells in type 1 and type 2 diabetes mellitus: different pathways to failure. Nat Rev Endocrinol. 2020;16(7):349–62.
2. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet 2023; 402(10397): 203–34.
3. Ali MK, Pearson-Stuttard J, Selvin E, Gregg EW. Interpreting global trends in type 2 diabetes complications and mortality. Diabetologia. 2022;65(1):3–13.
4. Ling W, Huang Y, Huang YM, Fan RR, Sui Y, Zhao HL. Global trend of diabetes mortality attributed to vascular complications, 2000–2016. Cardiovasc Diabetol. 2020;19(1):182.
5. Dal Canto E, Ceriello A, Rydén L, et al. Diabetes as a cardiovascular risk factor: An overview of global trends of macro and micro vascular complications. Eur J Prev Cardiol. 2019;26(2_suppl):25–32.
6. Li Y, Liu Y, Liu S, et al. Diabetic vascular diseases: molecular mechanisms and therapeutic strategies. Signal Transduct Target Ther. 2023;8(1):152.
7. Zakir M, Ahuja N, Surksha MA, et al. Cardiovascular Complications of Diabetes: From Microvascular to Macrovascular Pathways. Cureus. 2023;15(9):e45835.
8. Garofolo M, Gualdani E, Scarale MG, et al. Insulin Resistance and Risk of Major Vascular Events and All-Cause Mortality in Type 1 Diabetes: A 10-Year Follow-up Study. Diabetes Care. 2020;43(10):e139–41.
9. Steinberg HO, Baron AD. Vascular function, insulin resistance and fatty acids. Diabetologia. 2002;45(5):623–34.
10. Ginsberg HN. Insulin resistance and cardiovascular disease. J Clin Invest. 2000;106(4):453–8.
11. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979;237(3):E214–23.
12. Williams KV, Erbey JR, Becker D, Arslanian S, Orchard TJ. Can clinical factors estimate insulin resistance in type 1 diabetes? Diabetes. 2000;49(4):626–32.
13. Park SE, Park CY, Sweeney G. Biomarkers of insulin sensitivity and insulin resistance: Past, present and future. Crit Rev Clin Lab Sci. 2015;52(4):180–90.
14. Epstein EJ, Osman JL, Cohen HW, Rajpathak SN, Lewis O, Crandall JP. Use of the estimated glucose disposal rate as a measure of insulin resistance in an urban multiethnic population with type 1 diabetes. Diabetes Care. 2013;36(8):2280–5.
15. Ferrannini E, Balkau B, Coppack SW, et al. Insulin resistance, insulin response, and obesity as indicators of metabolic risk. J Clin Endocrinol Metab. 2007;92(8):2885–92.
16. Stefan N, Häring HU, Hu FB, Schulze MB. Metabolically healthy obesity: epidemiology, mechanisms, and clinical implications. Lancet Diabetes Endocrinol. 2013;1(2):152–62.
17. Wormser D, Kaptoge S, Di Angelantonio E, et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. Lancet. 2011;377(9771):1085–95.
18. Blood pressure-lowering treatment based on cardiovascular risk. a meta-analysis of individual patient data. Lancet. 2014;384(9943):591–8.
19. Di Angelantonio E, Gao P, Khan H, et al. Glycated hemoglobin measurement and prediction of cardiovascular disease. JAMA. 2014;311(12):1225–33.
20. Laakso M, Kuusisto J. Insulin resistance and hyperglycaemia in cardiovascular disease development. Nat Rev Endocrinol. 2014;10(5):293–302.
21. Chillarón JJ, Flores Le-Roux JA, Benaiges D, Pedro-Botet J. Type 1 diabetes, metabolic syndrome and cardiovascular risk. Metabolism. 2014;63(2):181–7.
22. Sun R, Wang J, Li M, et al. Association of Insulin Resistance With Cardiovascular Disease and All-Cause Mortality in Type 1 Diabetes: Systematic Review and Meta-analysis. Diabetes Care. 2024;47(12):2266–74.
23. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372: n71.
24. Organization WH. Title: International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10). Geneva: WHO; 2019.
25. Danesh J, Collins R, Appleby P, Peto R. Association of fibrinogen, C-reactive protein, albumin, or leukocyte count with coronary heart disease: meta-analyses of prospective studies. JAMA. 1998;279(18):1477–82.

26. Chêne G, Thompson SG. Methods for summarizing the risk associations of quantitative variables in epidemiologic studies in a consistent form. Am J Epidemiol. 1996;144(6):610–21.
27. Langan D, Higgins JPT, Jackson D, et al. A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. Res Synth Methods. 2019;10(1):83–98.
28. Balduzzi S, Rücker G, Schwarzer G. How to perform a meta-analysis with R: a practical tutorial. Evid Based Ment Health. 2019;22(4):153–60.
29. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58.
30. Drucker AM, Fleming P, Chan AW. Research Techniques Made Simple: Assessing Risk of Bias in Systematic Reviews. J Invest Dermatol. 2016;136(11):e109–14.
31. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336(7650):924–6.
32. Linn W, Persson M, Rathsman B, et al. Estimated glucose disposal rate is associated with retinopathy and kidney disease in young people with type 1 diabetes: a nationwide observational study. Cardiovasc Diabetol. 2023;22(1):61.
33. Mao Y, Zhong W. Changes of insulin resistance status and development of complications in type 1 diabetes mellitus: Analysis of DCCT/EDIC study. Diabetes Res Clin Pract. 2022;184:109211.
34. Harjutsalo V, Barlovic DP, Gordin D, Forsblom C, King G, Groop PH. Presence and Determinants of Cardiovascular Disease and Mortality in Individuals With Type 1 Diabetes of Long Duration: The FinnDiane 50 Years of Diabetes Study. Diabetes Care. 2021;44(8):1885–93.
35. Helmink MAG, de Vries M, Visseren FLJ, de Ranitz WL, de Valk HW, Westerink J. Insulin resistance and risk of vascular events, interventions and mortality in type 1 diabetes. Eur J Endocrinol. 2021;185(6):831–40.
36. Miller RG, Costacou T, Orchard TJ. Risk Factor Modeling for Cardiovascular Disease in Type 1 Diabetes in the Pittsburgh Epidemiology of Diabetes Complications (EDC) Study: A Comparison With the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC). Diabetes. 2019;68(2):409–19.
37. Nyström T, Holzmann MJ, Eliasson B, Svensson AM, Sartipy U. Estimated glucose disposal rate predicts mortality in adults with type 1 diabetes. Diabetes Obes Metab. 2018;20(3):556–63.
38. Kilpatrick ES, Rigby AS, Atkin SL. Insulin resistance, the metabolic syndrome, and complication risk in type 1 diabetes: "double diabetes" in the Diabetes Control and Complications Trial. Diabetes Care. 2007;30(3):707–12.
39. Olson JC, Erbey JR, Forrest KY, Williams K, Becker DJ, Orchard TJ. Glycemia (or, in women, estimated glucose disposal rate) predict lower extremity arterial disease events in type 1 diabetes. Metabolism. 2002;51(2):248–54.
40. Ciardullo S, Dodesini AR, Lepore G, et al. Development of a New Model of Insulin Sensitivity in Patients With Type 2 Diabetes and Association With Mortality. J Clin Endocrinol Metab. 2024;109(5):1308–17.
41. Zabala A, Darsalia V, Lind M, et al. Estimated glucose disposal rate and risk of stroke and mortality in type 2 diabetes: a nationwide cohort study. Cardiovasc Diabetol. 2021;20(1):202.
42. He HM, Xie YY, Chen Q, et al. The additive effect of the triglyceride-glucose index and estimated glucose disposal rate on long-term mortality among individuals with and without diabetes: a population-based study. Cardiovasc Diabetol. 2024;23(1):307.
43. Sun J, Wang N, Li S, et al. Estimated glucose disposal rate and risk of arterial stiffness and long-term all-acuse mortality: a 10-year prospective study. J Epidemiol Community Health. 2023;78(3):jech-2023-220664.
44. Zhang Y, Sun W, Zhang Q, et al. Estimated glucose disposal rate predicts the risk of diabetic peripheral neuropathy in type 2 diabetes: A 5-year follow-up study. J Diabetes. 2024;16(5):e13482.
45. Xu YX, Pu SD, Zhang YT, et al. Insulin resistance is associated with the presence and severity of retinopathy in patients with type 2 diabetes. Clin Exp Ophthalmol. 2024;52(1):63–77.
46. Meng C, Xing Y, Huo L, Ma H. Relationship Between Estimated Glucose Disposal Rate and Type 2 Diabetic Retinopathy. Diabetes Metab Syndr Obes. 2023;16:807–18.
47. Nyström T, Holzmann MJ, Eliasson B, Svensson AM, Kuhl J, Sartipy U. Estimated glucose disposal rate and long-term survival in type 2 diabetes after coronary artery bypass grafting. Heart Vessels. 2017;32(3):269–78.
48. Zhang Z, Zhao L, Lu Y, Xiao Y, Zhou X. Insulin resistance assessed by estimated glucose disposal rate and risk of incident cardiovascular diseases among individuals without diabetes: findings from a nationwide, population based, prospective cohort study. Cardiovasc Diabetol. 2024;23(1):194.
49. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17(1):122.
50. Daousi C, Casson IF, Gill GV, MacFarlane IA, Wilding JP, Pinkney JH. Prevalence of obesity in type 2 diabetes in secondary care: association with cardiovascular risk factors. Postgrad Med J. 2006;82(966):280–4.

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