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Association between estimated glucose disposal rate and diabetes mellitus incidence in middle-aged and elderly adults and development of predictive model: evidence from two prospective longitudinal studies

Haina Gao¹, Xiaomin Huang², Nuojin Wang², Tianrong Pan² and Xiaoyu Pan^{2*}

Abstract

Background The aim of this study was to investigate the association between estimated glucose disposal rate (eGDR) and the risk of future diabetes development in middle-aged and elderly adults, and to construct a diabetes prediction model.

Methods The present study comprised a total of 8,072 participants, with 6,965 drawn from the China Health and Retirement Longitudinal Study (CHARLS) cohort and 1,107 from the English Longitudinal Study of Aging (ELSA) cohort. The correlation between eGDR and the onset of diabetes was analysed by means of a logistic regression model, and subgroup analyses and restricted cubic spline (RCS) curve analyses were performed to verify the non-linear relationship. A predictive model was constructed based on multivariable variables, and model efficacy was assessed by subject operating characteristic curves (AUC) and calibration curves.

Results The prevalence of diabetes mellitus was 5.87% in the CHARLS cohort and 9.94% in the ELSA cohort. It was found that eGDR was significantly lower in both cohorts of diabetic patients ($P < 0.001$). Furthermore, an association was observed between eGDR reduction and an increased risk of developing diabetes. The multivariable-adjusted odds ratios (OR) for Q2–Q4 in the CHARLS cohort were 0.66 (0.51–0.84), 0.36 (0.25–0.51), and 0.31 (0.20–0.47), respectively, using the eGDR quartiles (Q1 as the reference); and for the ELSA cohort, the values were 0.40 (0.23–0.70), 0.30 (0.15–0.62), and 0.06 (0.01–0.28), respectively. RCS analyses revealed no evidence of nonlinear association between eGDR and diabetes, after adjusting for confounders. A column-line graphical model, incorporating variables of heart disease, stroke, BMI, lipids, glucose and eGDR, yielded AUCs of 0.75 (0.72–0.77) and 0.85 (0.82–0.89) in the

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CHARLS and ELSA cohorts, respectively. Calibration curves demonstrated adequate model fit, while decision curves indicated a substantial net benefit.

Conclusion Reduced eGDR is an independent risk factor for the development of diabetes mellitus in middle-aged and elderly adults, and is linearly and negatively correlated with the risk of diabetes mellitus.

Keywords Estimated glucose disposal rate, Diabetes mellitus, Middle-aged and elderly adults, Predictive model

Introduction

Diabetes represents a significant global health challenge, with the International Diabetes Federation (IDF) Diabetes Atlas 2025 reporting that in 2024, 589 million adults aged 20–79 years were living with diabetes worldwide. Projections indicate that the global prevalence of diabetes is anticipated to rise to 853 million by the year 2050 [1]. The growing prevalence of diabetes carries with it a substantial risk of morbidity and mortality for individual patients, as well as exerting a considerable economic burden on global healthcare systems. Insulin resistance is a fundamental component of the pathophysiological mechanisms of diabetes [2]. Insulin resistance, a hallmark of metabolic dysfunction, has been demonstrated to be a significant predictor of the development of prediabetes, characterised by impaired fasting glucose or impaired glucose tolerance. An accurate assessment of insulin resistance is imperative for the early detection and management of diabetes and its associated complications. The prevailing paradigm for quantifying insulin resistance is the glucose clamp technique. However, it is important to acknowledge that the technique is complex, invasive and time-consuming. It requires specialised equipment and trained personnel; as a result, its use for routine clinical testing or large-scale epidemiological studies has not been feasible.

In recent years, there has been an increased interest in the development of methods for estimating insulin resistance that are simpler, less invasive and more widely applicable. One such method is calculation of the estimated glucose discharge rate (eGDR), which incorporates readily accessible clinical factors, including waist circumference, hypertension, and glycated haemoglobin (HbA1c) levels. The validity of this metric has been established through comparison with the normoglycaemic high insulin clamp technique, demonstrating a strong correlation with insulin resistance in both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) populations [3–5]. A number of studies have demonstrated a negative correlation between eGDR and insulin resistance, with lower eGDR values indicating higher levels of insulin resistance [6–8]. It is therefore vital to clarify the relationship between eGDR and the risk of diabetes mellitus, in order to facilitate improvements in both clinical practice and public health. The identification of high-risk groups for diabetes based on eGDR facilitates

the implementation of targeted preventive interventions, including lifestyle modifications such as dietary modification, increased physical activity, weight reduction, and pharmacological treatment when necessary. The implementation of early intervention strategies targeting high-risk demographics holds the potential to postpone the onset of diabetes, and in certain cases, may even serve to prevent it. This approach has the ancillary effect of mitigating the burden of diabetes-related complications.

In the context of an ageing population, it is of particular importance to study the relationship between eGDR and diabetes risk. The prevalence of diabetes mellitus has been shown to gradually increase with age, and middle-aged and elderly adults are more susceptible to diabetes-related complications, including cardiovascular disease, neuropathy and nephropathy. Furthermore, age-related physiological changes, including a decline in muscle mass, an increase in adipose tissue, and impaired insulin secretion, may contribute to the development of insulin resistance in elderly adults [9]. Consequently, the precise estimation of insulin resistance through the utilisation of eGDR in the middle-aged and elderly population, in conjunction with the investigation of its relationship with diabetes risk, can furnish a substantial foundation for diabetes prevention and management in this susceptible group.

The objective of this study was to examine the association between eGDR and the likelihood of developing diabetes in middle-aged and elderly adults, utilising data from two prospective longitudinal studies. The analysis of longitudinal data and the construction of prediction models will facilitate a more profound comprehension of the temporal relationship between eGDR and the development of diabetes mellitus, with consideration of potential confounding factors and alterations in eGDR over time. The results of this study are expected to provide a valuable reference point for the early identification of middle-aged and elderly individuals at high risk of diabetes, as well as for the development of targeted prevention strategies.

Methods

Data source and participants

This study utilised data from two prospective longitudinal studies: the China Health and Retirement Longitudinal Study (CHARLS) and the English Longitudinal Study

of Aging (ELSA), which were conducted in the United Kingdom and China, respectively. For the CHARLS study, data from Wave 1 (2011) to Wave 5 (2020) was utilised, with Wave 1 designated as the baseline. For the ELSA study, data from Wave 2 (2004–2005) to Wave 10 (2020–2021) was utilised, with Wave 2 serving as the baseline. The present study was conducted in accordance with the guidelines established by the Peking University and London Multicentre Research Ethics Committees, with the approval of both institutions. Informed consent was obtained from all participants.

CHARLS represents a longitudinal investigation into Chinese residents over the age of 45. The database contained 17,705 participants who underwent the screening process. The subsequent period under scrutiny spanned from 2011 to 2020, with a median interval for observation amounting to 8.32 ± 0.96 years. Participants with diabetes at baseline ($N=993$) were excluded from the study. Participants with missing data were also excluded from the analysis ($N=9747$). The final sample comprised 6,965 non-diabetic participants who completed the follow-up.

The ELSA study is a longitudinal research project examining the process of ageing in individuals aged 50 years and above in England. The follow-up period is from 2004 to 2021. The median duration of follow-up was 17.52 ± 4.23 years. At the inception of the study, the database comprised 9,432 individuals. Participants with diabetes at baseline ($N=809$) were excluded from the study. Furthermore, subjects with incomplete basic clinical information were excluded from the study ($N=7525$). In the final study, 1107 individuals were included following the completion of follow-up.

Data collection

A data collection process was undertaken, with information on demographic characteristics being collated, incorporating gender, age, educational attainment, marital status, smoking and drinking status. Additionally, a range of physical parameters were measured, including waist circumference (WC), height, weight, and body mass index (BMI), which were subsequently used to calculate these values. Concurrently, a comprehensive array of blood parameters was collected, encompassing fasting blood glucose (FBG), HbA1c, haemoglobin (Hb), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c) and low-density lipoprotein cholesterol (LDL-c). Furthermore, information pertaining to hypertension, coronary heart disease and stroke was documented.

Diabetes diagnosis

Diabetic patients included in this study could be diagnosed according to any of the following criteria: (1) $\text{FBG} \geq 7$ mmol/L; (2) HbA1c level $\geq 6.5\%$; and (3) self-reported diagnosis of diabetes [10].

Definition of eGDR

The following formula is to be used to calculate eGDR: 21.158 minus $(0.551 \times \text{HbA1c})$ minus $(3.407 \times \text{HT})$ minus $(0.09 \times \text{WC})$. Within this equation, the term HbA1c is employed to denote the percentage of glycated haemoglobin. HT denotes hypertensive status, which is coded as follows: 1 for positive and 0 for negative. Hypertension is defined as two blood pressure measurements of $\geq 140/90$ mmHg, or the use of antihypertensive medications, or self-reported hypertension. The term 'WC' is an abbreviation for 'waist circumference', which is measured at the natural waistline and expressed in centimetres.

Statistical analysis

The statistical analysis of the data was conducted utilising R 4.2 software. Continuous variables are expressed as mean $\pm$ standard deviation or median (interquartile spacing). Categorical variables were expressed as percentages. A series of appropriate statistical tests were employed to facilitate the comparison of two groups. These included the t-test, the Mann–Whitney U-test and the chi-square test, the purpose of which was to ascertain any differences between the groups in question. Subgroup analyses were performed to assess the effect of eGDR on the prevalence of diabetes mellitus in several subgroups, including age ($</\geq 60$ years), sex (male/female), BMI ($</\geq 28$), marriage status (married or partnered/other status), education (below high school/high school/college or above), smoking status (yes/no) and alcohol consumption (ever drinkers/frequently drinkers/never drinkers), heart disease (yes/no) and stroke (yes/no). Univariate and multivariable logistic regression analysis was employed to investigate the potential associations between eGDR and the risk of developing diabetes. Restricted cubic spline curves (RCS) were utilised to evaluate the existence of a non-linear relationship between the two variables, and to adjust for multiple confounders, thereby determining the relationship.

The construction of predictive models was undertaken using data from the CHARLS population. Variables were screened for potential influences at $P < 0.05$ by univariate analysis with chi-square tests for categorical variables and t-tests for continuous variables. Subsequently, the univariate significant variables were incorporated into the multivariable model, and the $P < 0.05$ variables were retained in the stepwise regression method to construct the model. Following the conclusion of the model construction, an evaluation of the model was conducted in terms of discrimination, calibration, and clinical utility. The measurement of discrimination was achieved through the calculation of the area under the curve (AUC), while calibration was assessed through the utilisation of calibration plots and the Hosmer–Lemeshow test. The clinical utility of the test was analysed by decision curve analysis in order to ascertain its application value.

In conclusion, the findings of the study were subjected to external validation using ELSA population data, with the objective of evaluating the applicability and generalisation capacity of the model across a diverse spectrum of populations. A *p*-value less than 0.05 was designated as statistically significant.

Results

Characteristics of the study participants

The study comprised a total of 8072 participants, 6965 of whom were enrolled in CHARLS and 1107 in ELSA (Fig. 1). Following the conclusion of the designated follow-up period, the prevalence of diabetes was determined to be 5.87% within the CHARLS cohort, and 9.94% within the ELSA cohort. The data presented in Table 1 offers a concise overview of the sociodemographic characteristics and clinical descriptive data for all participants across the two comparison groups, namely the CHARLS and ELSA. An analysis of the CHARLS database revealed that individuals with diabetes exhibited elevated WC, BMI, FBG, HbA1c, TC, and TG levels. The prevalence of hypertension and heart disease was also found to be higher among these patients. In addition, lower HDL-C levels were observed ($P < 0.05$). Analyses of the ELSA database indicated that compared with individuals without diabetes, those with diabetes exhibited higher WC, BMI, FBG, HbA1c, and TG. They also demonstrated a higher proportion of males, higher educational attainment, and a higher prevalence of hypertension. In contrast, individuals with diabetes had lower HDL-C and lower smoking prevalence. These differences were statistically significant ($P < 0.05$). Moreover, a lower eGDR was observed in diabetic patients within both CHARLS and ELSA ($P < 0.001$).

Odds ratios for incident diabetes

The findings of the present study demonstrate a positive correlation between the incidence of diabetes and decreasing eGDR levels (Table 2). The eGDR was divided into quartiles (Q1–Q4), with Q1 serving as the reference. In the CHARLS database, univariate logistic analyses showed a significant association between a lower eGDR and an elevated risk of developing diabetes [Q2, OR (95% CI): 0.59 (0.46–0.75); Q3, OR (95% CI): 0.25 (0.18–0.34); Q4, OR (95% CI): 0.18 (0.13–0.26)]. Multivariable logistic regression analyses were utilised to ascertain that reduced eGDR is a significant predictive factor for the development of diabetes. It is evident that even in Model 3, when adjusted for potential confounders, the results remain consistent [Q2, OR (95% CI): 0.66 (0.51–0.84); Q3, OR (95% CI): 0.36 (0.25–0.51); Q4, OR (95% CI): 0.31 (0.20–0.47)].

In the ELSA database, univariate logistic analyses showed a significant association between a lower eGDR and an elevated risk of developing diabetes [Q2, OR (95% CI): 0.40 (0.25–0.64); Q3, OR (95% CI): 0.21 (0.12–0.37); Q4, OR (95% CI): 0.02 (0.01–0.10)]. Multivariable logistic regression analyses were utilised to ascertain that reduced eGDR is a significant predictive factor for the development of diabetes. It is evident that even in Model 3, when adjusted for potential confounders, the results remain consistent [Q2, OR (95% CI): 0.40 (0.23–0.70); Q3, OR (95% CI): 0.30 (0.15–0.62); Q4, OR (95% CI): 0.06 (0.01–0.28)].

To further explore the non-linear relationship of the association between eGDR and diabetes, further RCS analyses were performed. The findings of the analyses demonstrated a nonlinear correlation between eGDR and diabetes incidence; however, this nonlinear correlation was found to be non-existent following adjustment for multiple confounders (adjust: stork, sex, education, smoke, heart, age, TC, HDL-c, TG, LDL-c, haemoglobin and BMI) (Fig. 2).

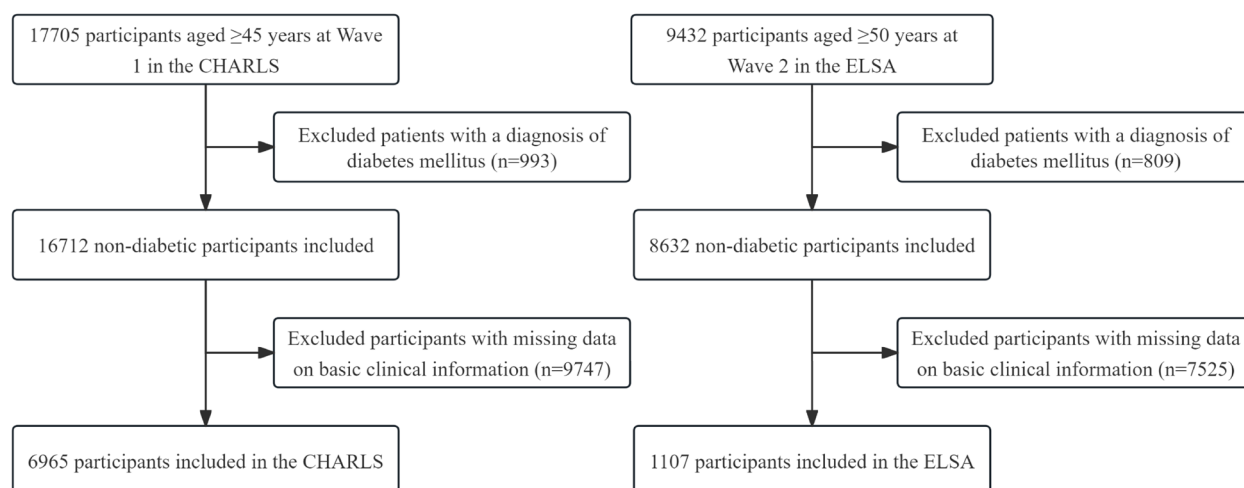


Fig. 1 Flowchart of the population included in our study

Table 1 Baseline characteristics of included participants

Variables	CHARLS				ELSA			
	Total (n = 6965)	Normal (n = 6556)	Diabetes (n = 409)	P	Total (n = 1107)	Normal (n = 997)	Diabetes (n = 110)	P
Age (y)	58.56 ± 8.83	58.53 ± 8.86	58.94 ± 8.28	0.367	60.69 ± 5.79	60.76 ± 5.74	60.03 ± 6.20	0.207
WC (cm)	84.91 ± 9.85	84.58 ± 9.68	90.31 ± 10.90	<.001	92.93 ± 12.07	91.90 ± 11.68	102.35 ± 11.59	<.001
BMI (Kg/m ²)	23.31 ± 3.48	23.21 ± 3.44	24.98 ± 3.80	<.001	27.34 ± 4.29	26.98 ± 4.05	30.63 ± 5.01	<.001
FBG (mmol/L)	105.05 ± 23.45	104.02 ± 21.44	121.71 ± 41.43	<.001	88.24 ± 9.91	87.51 ± 8.92	94.88 ± 14.83	<.001
TC (mmol/L)	193.14 ± 38.37	192.70 ± 38.29	200.19 ± 38.97	<.001	235.76 ± 43.49	235.75 ± 43.07	235.86 ± 47.38	0.980
HDL-c (mmol/L)	51.68 ± 15.27	52.01 ± 15.30	46.36 ± 13.66	<.001	61.93 ± 15.03	63.00 ± 15.00	52.28 ± 11.39	<.001
LDL-c (mmol/L)	116.16 ± 34.29	116.02 ± 34.19	118.42 ± 35.87	0.175	147.58 ± 36.19	147.58 ± 35.98	147.59 ± 38.22	0.998
TG (mmol/L)	130.38 ± 106.95	127.77 ± 103.68	172.63 ± 143.95	<.001	131.96 ± 63.65	126.44 ± 59.24	181.95 ± 79.03	<.001
HbA1c (%)	5.14 ± 0.50	5.12 ± 0.46	5.53 ± 0.84	<.001	5.41 ± 0.36	5.36 ± 0.30	5.84 ± 0.53	<.001
Hemoglobin (g/L)	14.40 ± 2.21	14.39 ± 2.22	14.59 ± 2.05	0.087	144.59 ± 15.99	144.15 ± 16.25	148.60 ± 12.72	0.006
eGDR	9.93 ± 1.89	10.01 ± 1.84	8.69 ± 2.19	<.001	9.43 ± 1.68	9.58 ± 1.60	8.08 ± 1.81	<.001
Gender, n(%)				0.069				0.007
Male	3198 (45.92)	3028 (46.19)	170 (41.56)		480 (43.36)	419 (42.03)	61 (55.45)	
Female	3767 (54.08)	3528 (53.81)	239 (58.44)		627 (56.64)	578 (57.97)	49 (44.55)	
Marry, n(%)				0.356				0.775
Married or partnered	5936 (85.23)	5581 (85.13)	355 (86.80)		721 (65.13)	648 (64.99)	73 (66.36)	
Other status	1029 (14.77)	975 (14.87)	54 (13.20)		386 (34.87)	349 (35.01)	37 (33.64)	
Education, n(%)				0.261				0.010
Below high school	1972 (28.31)	1842 (28.10)	130 (31.78)		200 (18.07)	190 (19.06)	10 (9.09)	
High school	1313 (18.85)	1242 (18.94)	71 (17.36)		178 (16.08)	164 (16.45)	14 (12.73)	
College or above	3680 (52.84)	3472 (52.96)	208 (50.86)		729 (65.85)	643 (64.49)	86 (78.18)	
Smoke, n(%)				0.080				0.034
Never smokers	2703 (38.81)	2561 (39.06)	142 (34.72)		991 (89.52)	899 (90.17)	92 (83.64)	
Ever smokers	4262 (61.19)	3995 (60.94)	267 (65.28)		116 (10.48)	98 (9.83)	18 (16.36)	
Drink, n(%)				0.299	NA			
Ever drinkers	1775 (25.48)	1684 (25.69)	91 (22.25)					
Frequently drinkers	550 (7.90)	517 (7.89)	33 (8.07)					
Never drinkers	4640 (66.62)	4355 (66.43)	285 (69.68)					
Hypertension, n(%)				<.001				0.006
Yes	1539 (22.10)	1383 (21.10)	156 (38.14)		983 (88.80)	894 (89.67)	89 (80.91)	
No	5426 (77.90)	5173 (78.90)	253 (61.86)		124 (11.20)	103 (10.33)	21 (19.09)	
Heart disease, n(%)				0.001				0.587
Yes	721 (10.35)	659 (10.05)	62 (15.16)		160 (14.45)	146 (14.64)	14 (12.73)	
No	6244 (89.65)	5897 (89.95)	347 (84.84)		947 (85.55)	851 (85.36)	96 (87.27)	
Stroke, n(%)				0.160				0.314
Yes	125 (1.79)	114 (1.74)	11 (2.69)		32 (2.89)	31 (3.11)	1 (0.91)	
No	6840 (98.21)	6442 (98.26)	398 (97.31)		1075 (97.11)	966 (96.89)	109 (99.09)	

Comparison of baseline clinical characteristics between diabetic and non-diabetic patients at the end of follow-up

Abbreviations: WC Waist circumference, BMI Body mass index, FBG Fasting blood glucose, HbA1c Glycated hemoglobin, TC Total cholesterol, TG Triglyceride, HDL-c High-density lipoprotein cholesterol, LDL-c Low-density lipoprotein cholesterol, eGDR Estimated glucose disposal rate

Subgroup analysis

The association between eGDR and diabetes incidence remained consistent across several subgroups of age, sex, BMI, hypertension, coronary heart disease, education, and marriage and other subgroups (Fig. 3; all *P* for interaction > 0.05), except in the BMI subgroup of the CHARLS database (*P* for interaction = 0.003).

Predictive model construction and validation

The model incorporates a range of variables, including heart disease, stroke, BMI, TC, LDL-C, HDL-C, FBG,

and eGDR, which function as predictors. The development of a prediction model was undertaken, and its presentation is illustrated in the form of nomograms (Fig. 4). The AUC value of the predictive model constructed using CHARLS data was 0.75 (95% CI = 0.72–0.77) (Fig. 5A). Furthermore, the predictive model was validated in this study using ELSA data, with an AUC value of 0.85 (95% CI = 0.82–0.89) (Fig. 5B). In both the CHARLS and ELSA databases, calibration curves demonstrated that the model exhibited an adequate fit (*P* = 0.077 and *P* = 0.646, respectively), and decision curves indicated that the

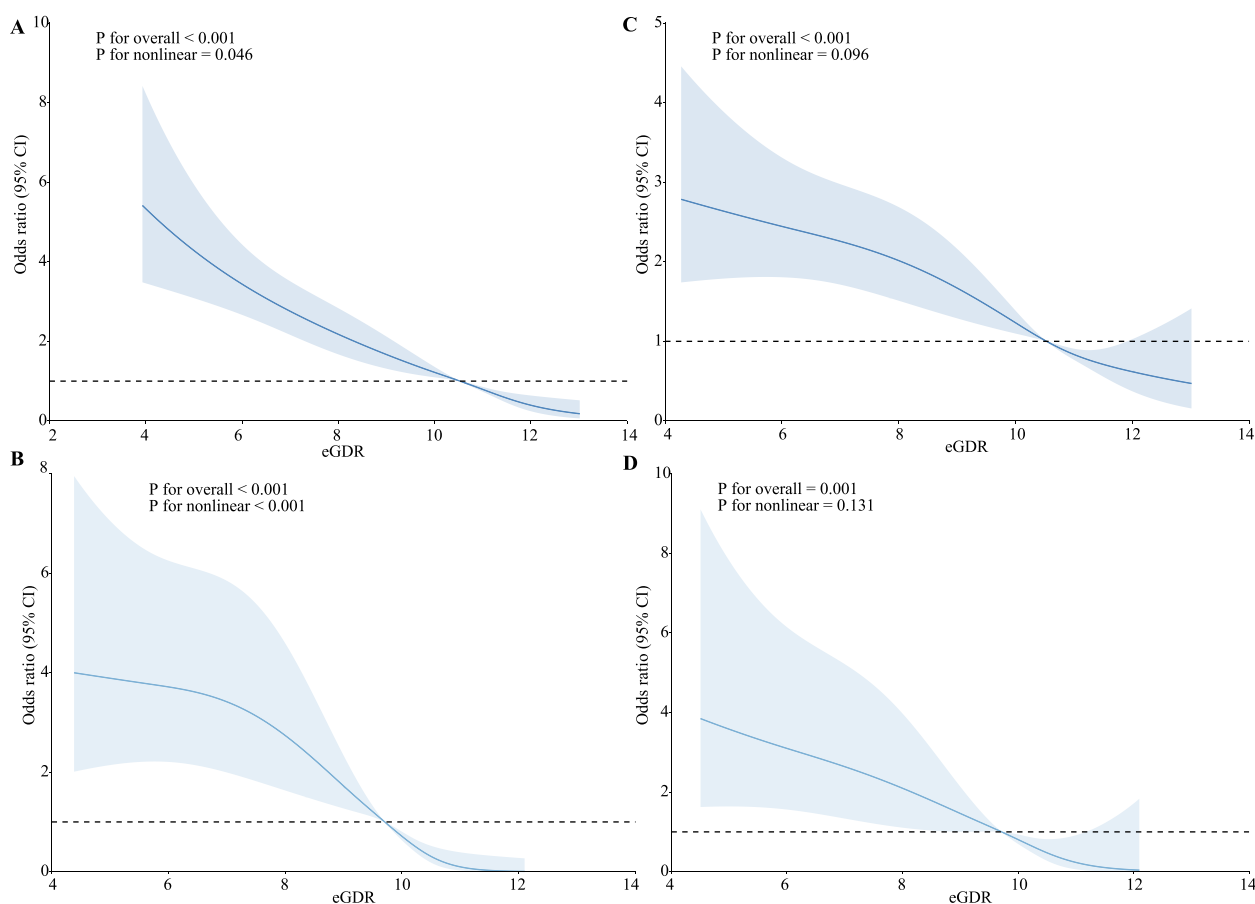
Table 2 Longitudinal association between eGDR and diabetes

Variables		Model1		Model2		Model3	
		OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
CHARLS	eGDR						
	1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	2	0.59 (0.46–0.75)	<.001	0.60 (0.47–0.77)	<.001	0.66 (0.51–0.84)	0.001
	3	0.25 (0.18–0.34)	<.001	0.25 (0.19–0.35)	<.001	0.36 (0.25–0.51)	<.001
ELSA	eGDR						
	1	1.00 (Reference)		1.00 (Reference)		1.00 (Reference)	
	2	0.40 (0.25–0.64)	<.001	0.37 (0.23–0.61)	<.001	0.40 (0.23–0.70)	0.001
	3	0.21 (0.12–0.37)	<.001	0.20 (0.11–0.36)	<.001	0.30 (0.15–0.62)	0.001
	4	0.02 (0.01–0.10)	<.001	0.02 (0.01–0.10)	<.001	0.06 (0.01–0.28)	<.001

Model1: Crude

Model2: Adjust: stroke, sex, education, smoking status and heart disease

Model3: Adjust: stroke, sex, education, smoking status, heart disease, age, total cholesterol, high-density lipoprotein cholesterol, triglycerides, low-density lipoprotein cholesterol, haemoglobin, body mass index

**Fig. 2** Results of non-linear correlation analysis between between eGDR and the risk of diabetes in middle-aged and elderly adults. **A** Unadjusted in CHARLS. **B** Unadjusted in ELSA. **C** Adjusted for stork, sex, education, smoke, heart, age, total cholesterol, high-density lipoprotein cholesterol, triglycerides, low-density lipoprotein cholesterol, haemoglobin, body mass index in CHARLS. **D** Adjusted for stork, sex, education, smoke, heart, age, total cholesterol, high-density lipoprotein cholesterol, triglycerides, low-density lipoprotein cholesterol, haemoglobin, body mass index in ELSA

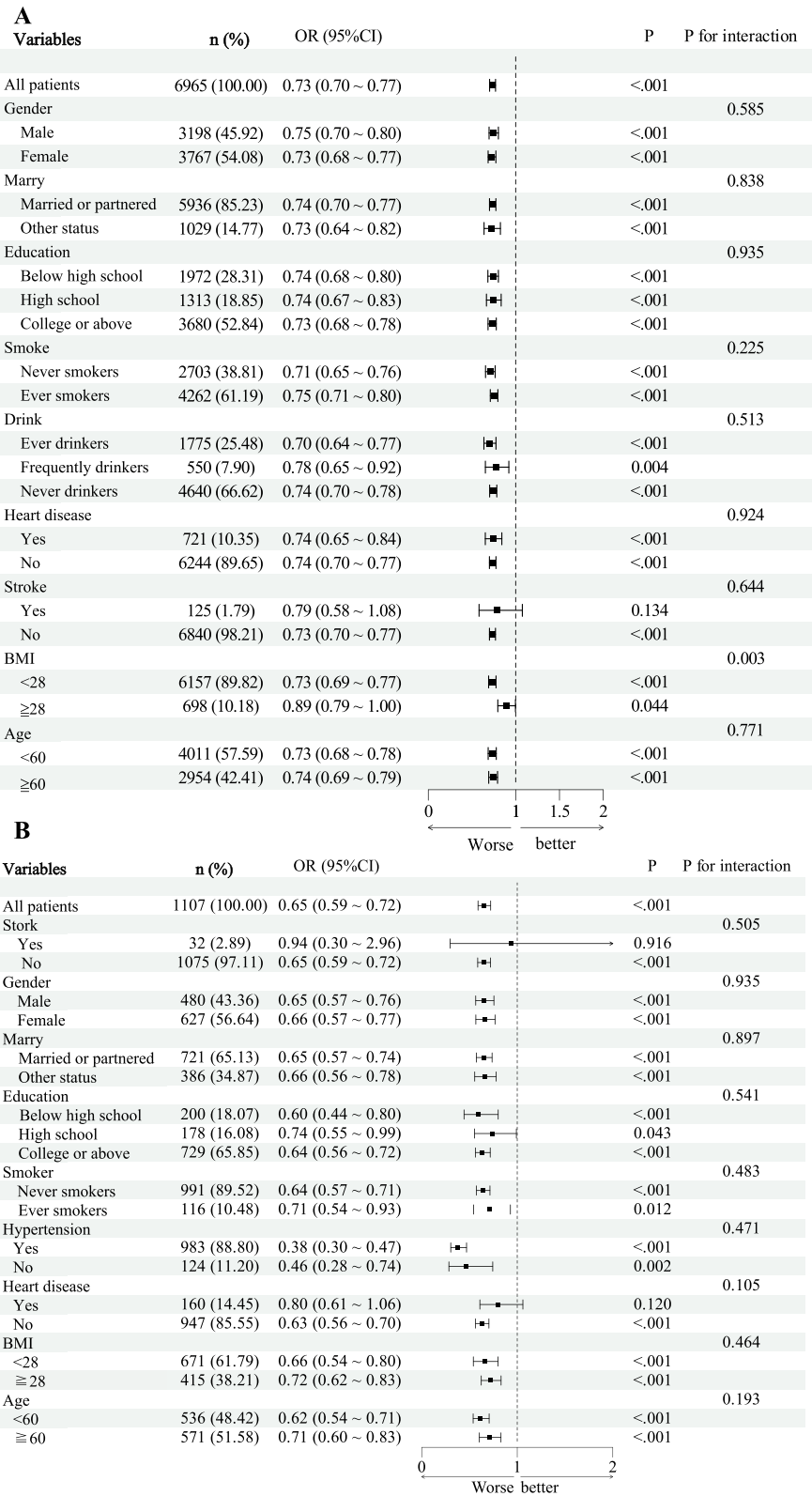


Fig. 3 A forest plot of subgroup analyses. **A** CHARLS. **B** ELSA

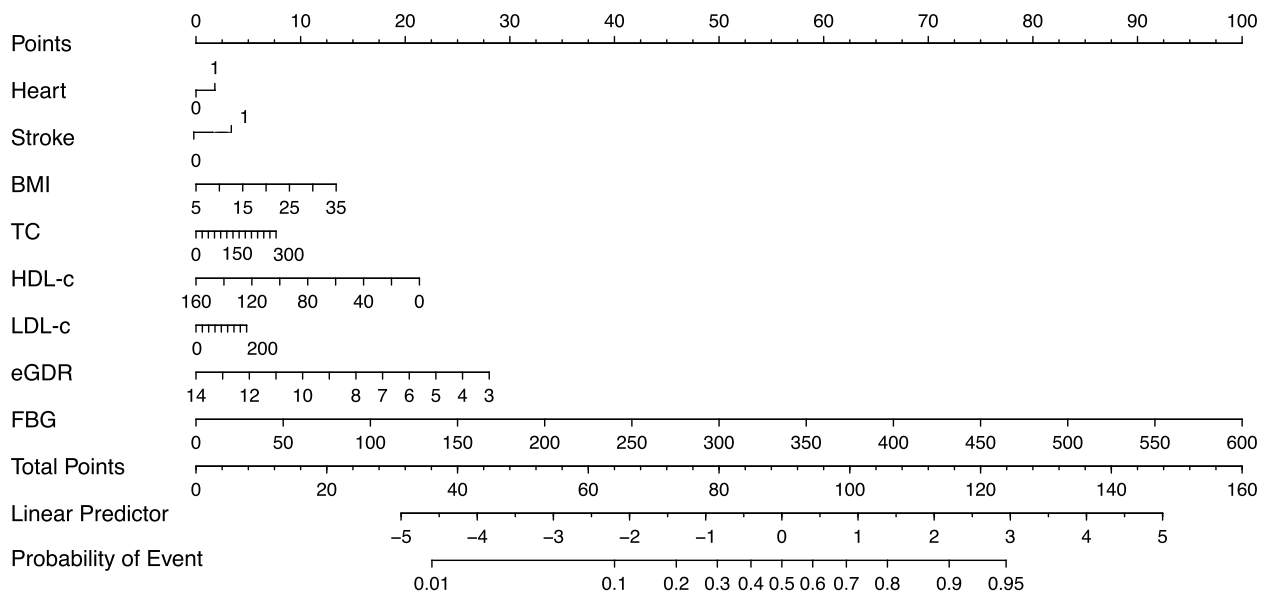


Fig. 4 A new nomogram for predicting the onset of diabetes

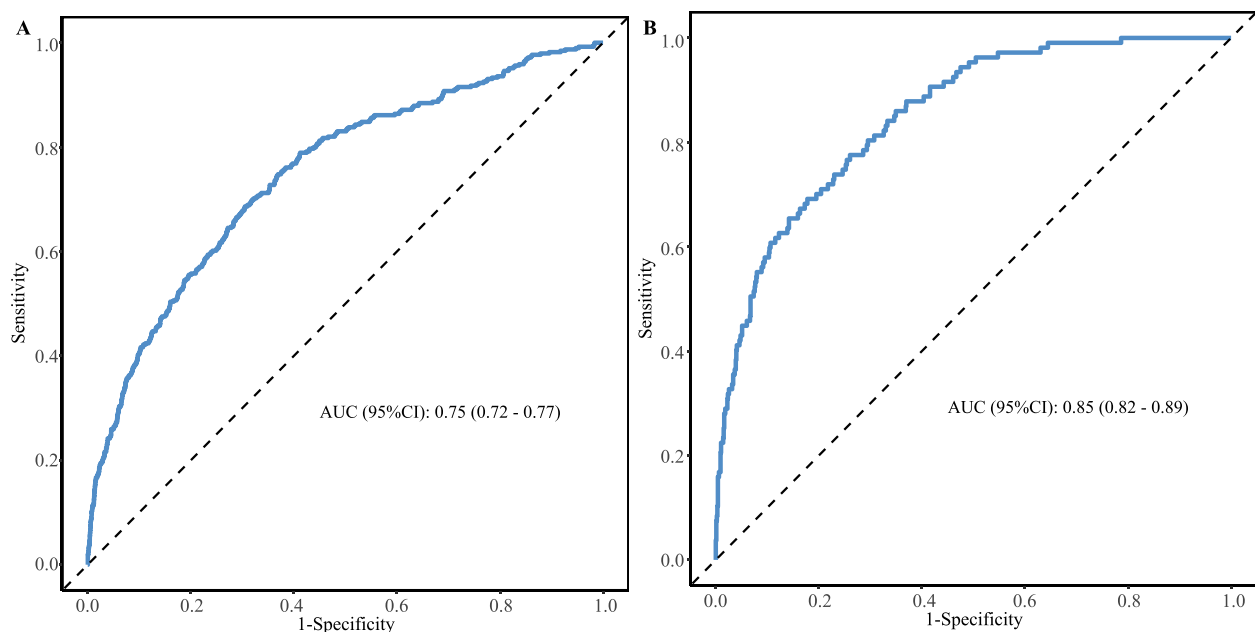


Fig. 5 ROC curves for CHARLS and ELSA to predict the onset of diabetes. **A** CHARLS. **B** ELSA

nomogram model provided superior net benefit and predictive accuracy (Fig. 6).

Discussion

The present study comprised a total of 8,072 participants, with 6,965 drawn from a cohort known as CHARLS and 1,107 from an ELSA cohort. The prevalence of diabetes was found to be 5.87% and 9.94% in the CHARLS and ELSA cohorts, respectively. Diabetic patients presented with abnormal metabolic indicators, such as elevated waist circumference and BMI, in both cohorts, and exhibited

significantly lower eGDR. Analyses demonstrated that lower eGDR was significantly associated with an increased risk of developing diabetes, and this association remained robust after multifactorial adjustment. RCS analyses demonstrated that the nonlinear relationship disappeared after adjustment for confounders. In the subgroup analyses, a significant interaction was identified only in the BMI subgroup of the CHARLS database. Furthermore, the prediction model constructed on the basis of the multivariable was validated in two cohorts, with AUCs of 0.75 and 0.85, respectively. The calibration and decision curves demonstrated that the

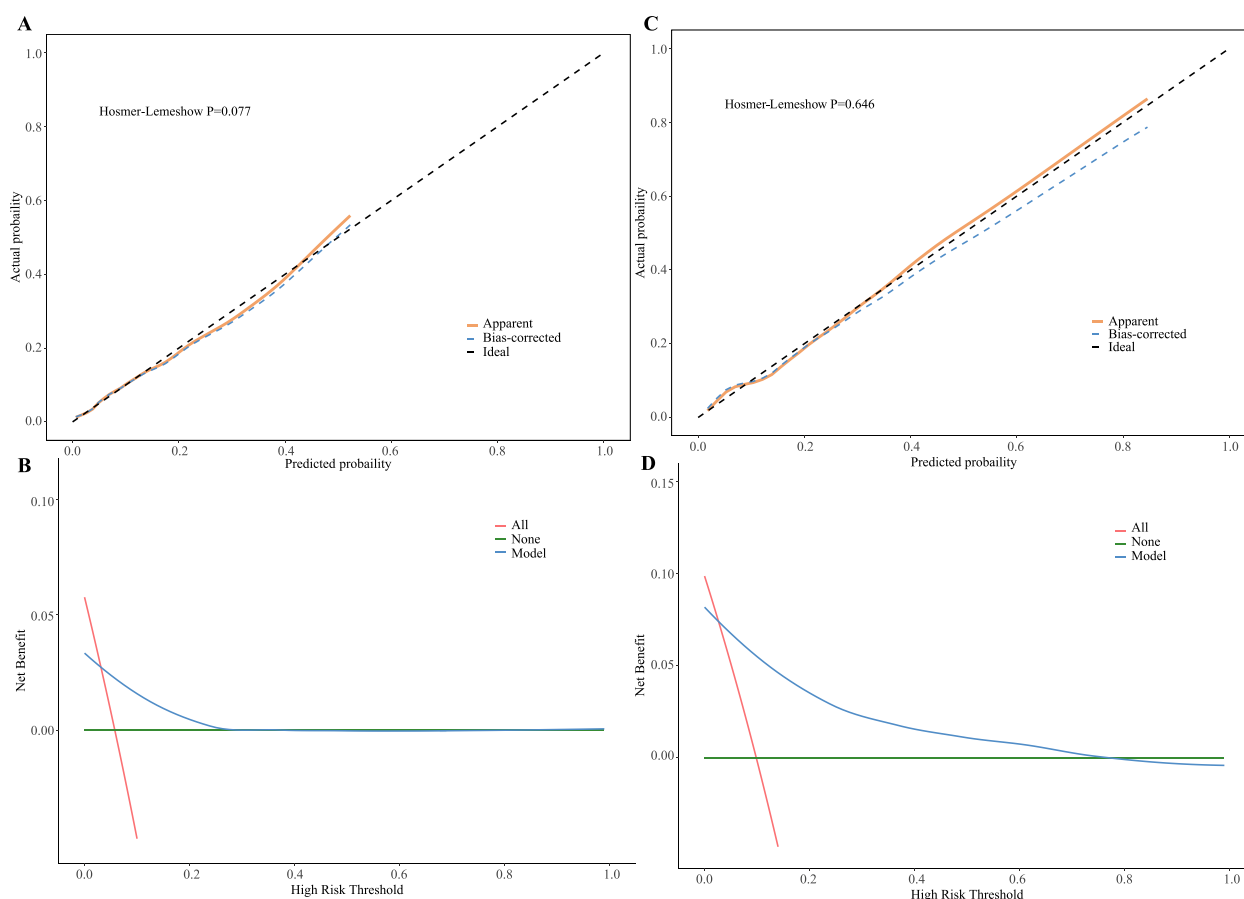


Fig. 6 Calibration curves and decision curve analysis of nomogram. **A** Calibration curves in CHARLS. **B** Decision curve analysis in CHARLS. **C** Calibration curves in ELSA. **D** Decision curve analysis in ELSA

model was well-fitted and predicted accurately. The present study utilised data from two cohorts, CHARLS and ELSA, to analyse the relationship between eGDR and the risk of developing diabetes mellitus. The findings indicated a negative association between eGDR and the risk of diabetes mellitus, suggesting that a decrease in eGDR levels is associated with an increased risk of diabetes mellitus. This association remained statistically significant after adjusting for multiple confounders, thereby underscoring the robustness of the observed relationship. This finding provides a new perspective for the early prediction of diabetes risk.

Abnormal glucose metabolism constitutes the fundamental pathological mechanism underlying the progression of diabetes mellitus, and the eGDR, as a pivotal indicator for evaluating the effectiveness of glucose metabolism in the organism, is capable of providing a visual reflection of the cooperative effect of insulin sensitivity and β -cell function [11–14]. In recent years, a growing body of research has emerged on the eGDR model. This model, constructed using serological indicators and clinical parameters, has gained significant traction within the field of metabolic diseases. The model's appeal lies in its non-invasive nature, ease of implementation, and the fact that it is capable of

reproducible results [15]. Furthermore, it serves as an indicator for the assessment of insulin resistance. A number of cross-sectional studies have demonstrated a significant correlation between eGDR and both insulin resistance and impaired glucose tolerance [16–18]. The present study utilised data from the CHARLS to conduct longitudinal analyses of the participants. A body of research has indicated that low eGDR levels are significantly associated with a higher prevalence of cardiovascular disease. For instance, previous studies have found significant reductions in cardiovascular disease risk, heart disease risk, and stroke risk for each unit increase in eGDR [19–21]. Given that insulin resistance constitutes a shared pathophysiological basis for both diabetes and cardiovascular disease, it may be hypothesized that low eGDR levels could also be associated with an augmented risk of developing diabetes among middle-aged and elderly adults. It is evident that insulin resistance contributes to elevated blood glucose levels. Prolonged insulin resistance and inadequate glycaemic control increase the risk of developing diabetes. Nevertheless, there remains a paucity of research validating the full extent of eGDR's prospective predictive value for diabetes risk, particularly in medium-sized and large prospective cohorts. Moreover, a

conspicuous absence of research exists on the longitudinal dynamic association between eGDR and the risk of diabetes development in middle-aged and elderly adults. These groups have been identified as being at high risk of developing the disease.

In both the CHARLS and ELSA cohorts, reduced eGDR was found to be associated with an elevated risk of diabetes among middle-aged and elderly adults (multi-variable ORs of 0.31 and 0.06 respectively, both $P < 0.001$). Furthermore, consistent trends were observed in all subgroups except the BMI subgroup of the CHARLS cohort, as indicated by subsequent subgroup analyses. This finding suggests that eGDR may be an independent risk factor for diabetes across diverse populations. The underlying mechanisms may be summarised as follows. Initially, the reduced eGDR may be indicative of impaired insulin clearance, which can result in hyperinsulinaemia. Hyperinsulinaemia can, in turn, induce insulin resistance, a pivotal aspect of the pathogenesis of type 2 diabetes [22]. Secondly, decreased renal function may be accompanied by a chronic inflammatory state or enhanced oxidative stress that interferes with glucose metabolic homeostasis. Furthermore, the activation of the renin-angiotensin system may play a role in the progression of diabetes by impacting pancreatic islet blood flow or β -cell function [23]. It is noteworthy that the present study found that the non-linear association between eGDR and diabetes disappeared after adjusting for confounders by RCS analysis, suggesting that there may be a linear dose–response relationship.

The findings of the present study demonstrated that the predictive efficacy of eGDR performed better in the ELSA cohort (AUC=0.85), which may be related to the inclusion of a more ageing population, longer follow-up, and higher prevalence of diabetes mellitus in this cohort. Moreover, diabetic patients in the ELSA cohort exhibited higher levels of education and lower smoking prevalence. This finding suggests that sociodemographic factors may influence the outward manifestation of the association between eGDR and diabetes, and these factors should be further adjusted in cross-population studies. The interaction of BMI subgroups in the CHARLS cohort was significant ($P=0.003$), suggesting that the predictive value of the eGDR for diabetes may vary according to the degree of obesity. In obese subjects, insulin resistance may predominate, thereby obscuring the independent contribution of eGDR. Conversely, in non-obese subjects, reduced eGDR may more directly reflect abnormalities in β -cell function or renal metabolic regulation. This finding suggests that, in order to achieve optimal outcomes in clinical applications, the predictive value of eGDR must be evaluated in conjunction with BMI stratification, particularly in populations where the prevalence of metabolic syndrome is high.

The nomogram developed in this study incorporated eGDR, BMI, blood glucose and lipid indicators, and attained AUC values of 0.75 and 0.85 in the CHARLS and ELSA cohorts, respectively, demonstrating satisfactory predictive efficacy. The subsequent calibration curve and decision curve analyses provided further validation of the clinical utility of the model, thereby suggesting that it may be employed as an auxiliary tool for the risk stratification of diabetes. In this study, two large prospective cohorts from different ethnic backgrounds confirmed a negative correlation between eGDR and the incidence of diabetes in middle-aged and elderly adults. This conclusion applies equally to both Western and Chinese populations. Furthermore, a prediction model including eGDR was constructed, which provides a new biomarker for the primary prevention of diabetes mellitus. Future studies should seek to further elucidate the physiological mechanisms underpinning eGDR, explore its direct association with insulin dynamics, and validate the model efficacy in larger samples. Furthermore, the conduction of randomised controlled trials is warranted to ascertain whether interventions targeting reduced eGDR may postpone the onset of diabetes. However, the mechanisms discussed herein are derived from hypotheses deduced through correlation analysis, rather than conclusions validated by this study.

The present study is subject to several noteworthy limitations. Firstly, The exclusion of a large number of participants due to missing data may result in selection bias. Secondly, disparities were observed in the measurement of certain indicators across the two databases, which may have constrained the extrapolation of results. Thirdly, the two databases exhibited divergent follow-up times, diets and lifestyle habits, which may have contributed to some of the observed discrepancies in findings.

Conclusion

The present study demonstrated a significant negative association between eGDR and the risk of diabetes in middle-aged and elderly adults. In other words, a lower level of eGDR was associated with a higher risk of diabetes, and this association was consistent across most subgroups. Following adjustment for multiple metabolic risk factors, eGDR was found to be an independent predictor of diabetes development. The predictive model based on eGDR demonstrated moderate to high efficacy in predicting the development of diabetes, suggesting that monitoring eGDR in clinical practice may facilitate early identification of diabetes in middle-aged and elderly adults.

Abbreviations

AUC	Area under the curve
BMI	Body mass index
CHARLS	China Health and Retirement Longitudinal Study
eGDR	Estimated glucose disposal rate

ELSA	English Longitudinal Study of Aging
FBG	Fasting blood glucose
Hb	Haemoglobin
HbA1c	Glycated haemoglobin
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
RCS	Restricted cubic spline
TC	Total cholesterol
T2DM	Type 2 diabetes mellitus
TG	Triglyceride
WC	Waist circumference

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Authors' contributions

HG, XH, NW, TP, and XP were responsible for the study's conception and design. HG, XH, and NW analyzed the data. The initial manuscript was drafted by HG and NW, with subsequent revisions by TP and XP. All authors have reviewed and approved the final manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The present study was conducted in accordance with the guidelines established by the Peking University and London Multicentre Research Ethics Committees, with the approval of both institutions. Informed consent was obtained from all participants. This study was performed in line with the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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