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# Zinc Deficiency in Patients with Type 2 Diabetes increases risk of cardiovascular diseases: A Cohort Study


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## Abstract

**Background and aim:** This study aimed to assess the prospective association between zinc (Zn) deficiency and the risk of cardiovascular diseases (CVD), CVD mortality and all-cause mortality in adults with type 2 diabetes (T2DM). **Method:** This prospective cohort study, embedded in the Tehran Lipid and Glucose Study (TLGS), including 632 adults with T2DM (mean age=59.6±12.4 years, 38% men) enrolled at 2009-2011 and followed until 2020. Serum zinc (SZn) concentrations were measured using flame atomic absorption spectrometry (FAAS), and Zn deficiency was defined as SZn <85 μg/dL. Multivariable Cox proportional hazard models were used to calculate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of outcomes in the Zn-deficient compared to Zn-sufficient group. **Results:** Mean baseline SZn concentration was 116±44.5 μg/dL, and 22% were Zn-deficient. Over a median follow-up of 9.3 years, 34.7% of participants

experienced incident CVD events, while 6.3% and 18.5% died from CVD and all causes, respectively. Zn deficiency was associated with a significantly increased risk of CVD events (HR=1.86, 95%CI=1.06-3.28, *P*=0.031) in the fully adjusted model. Each 10 μg/dL increase in SZn was associated with a borderline-significant reduced risk of CVD (HR=0.97, 95%CI=0.93-1.00, *P*=0.050). Zn status was not associated with CVD mortality or all-cause mortality. **Conclusion:** Zn deficiency is associated with a significantly increased risk of CVD events in patients with T2DM. Increased SZn concentration was associated with reduced risk of CVD events in patients with T2DM.

**Key words:** Zinc, Type 2 Diabetes, Cardiovascular Diseases, Mortality

## Introduction

Cardiovascular diseases (CVD) are major and growing contributors to global morbidity, mortality, and healthcare expenditure (1). An estimated 598 million individuals are currently living with CVD worldwide, a figure projected to rise to 1.14 billion by 2050 (1). Diabetes mellitus (DM) is a potent and prevalent risk factor for CVD, with approximately one in three individuals with DM developing cardiovascular complications and CVD remaining the leading cause of death in this population (2). Given that the global prevalence of DM is projected to increase from ~6% to nearly 13% by 2050 (3, 4), the population-level impact of CVD attributable to DM is expected to intensify substantially.

Zinc (Zn) is the second most abundant and essential trace element in the human body, with a well-known involvement in glucose and insulin homeostasis (5), pathogenesis of DM (6, 7), obesity (8, 9), and other metabolic disorders (10). DM is associated with impaired zinc absorption, dysregulated intracellular zinc transport, and excessive urinary zinc losses, resulting in persistent systemic zinc deficiency, reinforcing the need to reconsider current recommended daily allowance

(RDA) for zinc in patients with DM (11). Disruption of Zn homeostasis may contribute to endothelial dysfunction and the pathogenesis of CVD (12). Zn deficiency in DM is associated with poorer glycemic control, greater insulin resistance, and increased oxidative stress (13, 14), resulted in a higher risk of all-cause and CVD mortality, and cardiac arrhythmias (15), kidney disease progression (16), hospitalization (15, 17), and cognitive impairment (18).

The aim of this study was to examine the prospective association between Zn deficiency, as identified by serum zinc (SZn) less than 85 μg/dL, and the risk of incident CVD, CVD mortality, and all-cause mortality in adults with T2DM. We hypothesized that Zn deficiency would be independently associated with an elevated risk of incident CVD events, through its potential role in the pathophysiology of DM-related vascular complications. This study findings may address a critical gap in the literature and provides insight into the potential utility of SZn as a clinically relevant biomarker for cardiovascular risk stratification in T2DM.

**Subjects and methods**

*Study population*

This prospective cohort study was conducted as part of the Tehran Lipid and Glucose Study (TLGS), a population-based initiative that began in 1999 to investigate and prevent non-communicable diseases (NCDs) in the 13$^{th}$ district of Tehran (19). The standardized protocol evaluates the TLGS population for NCD risk factors every three years. For the current study, we included 1375 adult men and women with T2DM, who participated in the fourth examination of the TLGS (2009-2011). Among these participants, data on SZn was available for 664 individuals. The participants were followed up to March 2020 to monitor the incidence of CVD, CVD- and all-cause mortality over a median period of 9.3 years (interquartile range=2.7-10.6 years). After

excluding those who lost to follow-up (n=32), the final analysis was conducted on 632 eligible participants. **Figure 1** shows flowchart of the study participants.

*Demographic, lifestyle, anthropometric, and biochemical measurements*

Comprehensive protocols for data collection and variable assessment in the TLGS have been published previously (19-21). At each triennial examination, trained personnel updated participant information on smoking status, medication use, physical activity level, anthropometrics [weight, height, waist circumference (WC), and body mass index (BMI)], and systolic and diastolic blood pressures (SBP, DBP). Following a 12-14-hour overnight fast, venous blood samples were obtained at baseline and subsequent follow-ups to quantify fasting serum glucose (FSG), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and serum creatinine (SCr) (20). Adults aged ≥21 years who were not using glucose-lowering agents underwent a standard OGTT, consisting of ingestion of 82.5 g glucose monohydrate (equivalent to 75 g anhydrous glucose; Cerestar EP, Spain) with measurement of 2-hour post-load glucose (20). SZn concentrations were assessed using flame atomic absorption spectrometry (CTA-2000, Chem Tech Analytical Co., UK), with methodological details reported previously (22). The intra- and inter-assay coefficients of variation for all biochemical assays were below 5%.



*Definition of terms and outcomes*

According to the American Diabetes Association (ADA) criteria (23), T2D was defined as FSG≥ 126 mg/dL or 2h-SG≥ 200 mg/dL or using glucose-lowering medications. Having at least one parent or sibling with T2D was considered a positive family history.

Hypertension was defined as SBP ≥ 140 or mm Hg DBP ≥ 90 mmHg or self-reported taking blood pressure-lowering medications (24). The estimated glomerular filtration rate (eGFR) was calculated using the equation developed by Chronic Kidney Disease Epidemiology Collaboration

(25). Chronic kidney disease was defined as eGFR<60 mL/min/1.73 $m^2$, corresponding to stages 3-5 according to Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines (26).

CVD outcomes encompassed all manifestations of coronary heart disease (CHD), and both fatal and non-fatal cerebrovascular events. CHD events were classified into three categories: (1) definite myocardial infarction (MI), confirmed through electrocardiographic evidence and cardiac biomarkers; (2) probable MI, defined by characteristic electrocardiographic abnormalities accompanied by cardiac symptoms or clinical signs when biomarker data were unavailable or inconclusive; and (3) CHD verified by coronary angiography. Stroke incidence included all definite or possible strokes, as well as transient ischemic attacks (27). "Definite sudden death" was defined as an unexpected cardiac-related collapse leading to a pulseless state in an individual who had been clinically stable, while "possible sudden death" referred to an unforeseen death occurring within 24 hours of last being observed alive, without a clear non-cardiac cause of circulatory failure (28). CVD mortality comprised deaths attributable to coronary artery disease or stroke, with stroke-related deaths defined by the presence of a neurological deficit within 24 hours prior to death (29). All-cause mortality included deaths from any origin. In the TLGS, all outcome events were coded following the International Classification of Diseases, 10th Revision (ICD-10), and cardiovascular diagnoses adhered to the American Heart Association (AHA) criteria (30).

Zn-sufficiency was defined as SZn≥85 μg/dL, and Zn-deficiency was defined as SZn<85 μg/dL. SZn levels in healthy populations typically range from 70-120 μg/dL (31-33), with concentrations below 70 μg/dL generally indicating deficiency and values less than 85 μg/dL considered a marginal deficiency (33, 34). Notably, this cut-off corresponds to approximately the lowest 25% of SZn values in our study population, supporting its appropriateness for identifying individuals with relatively low zinc status.

*Statistical methods*

Statistical analyses were conducted using SPSS for Windows version 20 (SPSS Inc., Chicago, IL, USA). Baseline characteristics of the study participants were compared based on the Zn status (Zn-sufficient and Zn-deficient) using independent t-test for continuous variables or chi-square test for the categorical variables.

Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for the incidence of the outcomes in the Zn -deficient compared to the Zn-sufficient group. Potential covariates were selected based on both clinical relevance and statistical evidence (35). Initially, univariate analyses were performed to identify potential confounders, and variables with a *P*-value for entry ($P_E$) of less than 0.2 were considered for inclusion in the multivariable models. This approach is commonly applied strategy in epidemiologic modeling to avoid excluding relevant confounders that may not reach conventional significance levels in unadjusted analyses (35). In addition, clinically important covariates were retained in the models regardless of their univariate significance. Three Cox models were conducted, including model 1, which was adjusted for age and sex, model 2, additionally adjusted for WC, SBP, and TG-to-HDL-C ratio, and model 3 was further adjusted for FSG, chronic kidney disease, use of glucose-lowering drugs, physical activity and smoking. Event time was calculated from each participant's baseline examination date to the date of the first confirmed occurrence of the outcome of interest. Participants who remained free of the event were censored at the date of their last completed follow-up or at the end of the study period, whichever came first. Individuals who were lost to follow-up were censored at the date of their last verified contact. The proportional hazards assumption was evaluated using Schoenfeld residuals. Results from the global Schoenfeld residual test indicated that the fully adjusted model met the proportional hazards requirement. To assess

the robustness of the primary findings and minimize the potential influence of reverse causality, we conducted an additional sensitivity analysis excluding participants who experienced a CVD event (n=5) within the first two years of follow-up. This approach reduces the likelihood that preclinical or undiagnosed CVD at baseline influenced both SZn concentration and subsequent event risk. HRs and 95% CIs were recalculated using the same multivariable Cox proportional hazards models applied in the main analysis. The cumulative hazard of CVD event across categories of Zn status was plotted using the Kaplan-Meier method (hazard function).

**Results**

Mean age of the study participants was 59.6±12.4 years at baseline and 38% were men. Mean baseline SZn concentration was 116±44.5 μg/dL, and 22% were Zn-deficient. Over a median follow-up of 9.3 years, 34.7% of participants experienced incident CVD events, while 6.3% and 18.5% died from CVD and all causes, respectively. **Table 1** compares baseline characteristics of the study participants across Zn-sufficient and Zn-deficient groups. At baseline, participants with low SZn showed broadly similar demographic, clinical, and metabolic profiles compared with those with normal SZn concentrations. Mean of SZn concentrations in the Zn-deficient and Zn-sufficient group was 72.3±10.4 and 128±42.6 μg/dL, respectively. Mean age, sex distribution, family history of diabetes, prevalent hypertension, chronic kidney disease, smoking status, physical activity level, blood pressures, anthropometric indices, eGFR, and glycemic parameters did not differ significantly between groups. However, the Zn-deficient group had a higher prevalence of glucose-lowering medication use (63.3% *vs.* 53.3%, *P*=0.042) and BP-lowering medication use (48.2% *vs.* 37.1%, *P*=0.024).

**Table 2** presents the associations between SZn status and the risks of incident CVD, CVD mortality, and all-cause mortality among adults with T2DM. Compared with Zn-sufficient

individuals, those with Zn deficiency experienced a significantly elevated CVD risk in the fully adjusted model (HR=1.86, 95% CI=1.06-3.28, *P*=0.031). Analyses treating SZn concentration as a continuous variable further supported this finding, with each 10 μg/dL higher SZn associated with a borderline-significant lower CVD risk (HR=0.97, 95% CI=0.93-1.00, *P*=0.050). The sensitivity analysis excluding early CVD events (n= 5 occurring within the first two years of follow-up) yielded results consistent with the primary findings. Zn deficiency remained significantly associated with an increased risk of CVD events (HR= 1.81, 95% CI= 1.02-3.24, *P*= 0.044). Similarly, the inverse association between SZn concentration and CVD risk persisted, with each 10 μg/dL increment in SZn associated with a borderline-significant reduction in CVD risk (HR=0.96, 95%CI=0.93-1.00, *P*= 0.053). These findings support the robustness of the associations and suggest that they are not driven by early events or reverse causality. No significant associations were observed between Zn deficiency and CVD mortality or all-cause mortality in any of the models.

**Figure 2** shows the cumulative hazard of CVD events across categories of Zn status. The cumulative hazard of CVD events was higher in those who were Zn-deficient (SZn <85 μg/dL).



**Discussion**

This longitudinal cohort study of patients with T2DM demonstrates that Zn deficiency, characterized by SZn less than 85 μg/dL confer a significantly elevated risk of incident CVD, independent of the established demographic, metabolic, renal, and lifestyle risk factors. Although Zn status did not predict CVD or all-cause mortality, the strong association with incident events highlights Zn as a potentially important, yet under-recognized, determinant of early cardiovascular pathogenesis in T2DM. The stronger association observed when SZn was analyzed categorically, compared with the weaker borderline association in continuous models, suggests that the

relationship between zinc status and CVD risk may not be strictly linear. Specifically, excess risk appears concentrated among individuals with Zn deficiency (<85 μg/dL), while incremental increases in SZn above this threshold may confer limited additional benefit. Thus, categorical analyses may better capture clinically relevant low-zinc status, whereas continuous models estimate the average effect across the entire SZn distribution. Our study findings advance current understanding of Zn deficiency in cardiometabolic disease and underscore the clinical relevance of incorporating trace element assessment into risk stratification frameworks. By identifying SZn concentration as a modifiable biomarker associated with cardiovascular onset rather than end-stage outcomes, this study opens avenues for targeted nutritional or therapeutic interventions aimed at mitigating cardiovascular risk in this high-risk population.

The observed higher prevalence of glucose-lowering and blood pressure-lowering medication use in the Zn-deficient group likely reflects underlying baseline clinical differences between groups. Several commonly prescribed antidiabetic and antihypertensive medications, including metformin and SGLT2 inhibitors (36, 37), as well as thiazide and loop diuretics (38-40), ACEIs, and ARBs (38), have been reported to modestly influence Zn homeostasis through increased urinary Zn excretion or altered tissue Zn distribution. These pharmacotherapy-related effects may partly contribute to lower baseline SZn concentrations (41) and thus serve primarily as contextual explanatory factors rather than central mechanisms driving the associations observed in this study.

Our findings regarding the association of Zn deficiency and risk of CVD are consistent with the limited evidence from prior longitudinal cohort studies in patients with T2DM. In a prospective study, Soinio et al. reported that lower SZn concentrations were independently associated with an increased risk of MI (RR=1.37, 95% CI=1.03-1.82, *P*=0.033), and an increased risk of CHD death (RR=1.70, 95% CI=1.21-2.38, *P*=0.002) among patients with T2DM (42). Similarly, Wu et al.

demonstrated that Zn deficiency was associated to a higher incidence of major adverse CVD events (HR=1.64, 95% CI=1.27-2.10) and higher risks of all-cause mortality (HR=1.788, 95% CI=1.59-2.00) in a patients with DM (17). More recently, Lin et al. observed an elevated risk of cardiovascular outcomes (HR=1.15, 95% CI=1.08-1.24, $P$<0.001) and all-cause mortality (HR=2.08, 95% CI=1.72-2.51, $P$<0.001) among patients with DM and Zn deficiency in a large population-based cohort (15).

Unlike some previous reports, however, Zn status in our cohort was associated with incident CVD events but not CVD or all-cause mortality. Differences in Zn cut-off points, outcome definitions, population characteristics, and statistical adjustment schemes may contribute to this discrepancy. Nonetheless, our findings suggest that Zn deficiency may have a greater impact on the early stages of cardiovascular injury rather than on late-stage or fatal outcomes. A deeper exploration of biological mechanisms supports this pattern. Zn plays a pivotal role in early atherogenesis through its involvement in endothelial protection, antioxidant defense, and immune modulation. Low Zn status promotes endothelial dysfunction, enhances monocyte adhesion, increases oxidative stress, and accelerates vascular inflammation (43, 44). Such mechanisms predominantly influence the initiation and progression of atherosclerotic lesions, thereby increasing the likelihood of nonfatal CVD events. In contrast, mortality after a CVD event is typically driven by factors such as infarct size, ventricular remodeling, heart failure progression, arrhythmogenic risk, and the burden of comorbidities, processes in which zinc may have a more limited or indirect role. This biological distinction may account for the differential associations observed in our study. Notably, the mortality findings should be interpreted with caution, as the present study may not be sufficiently powered to detect modest associations with CVD or all-cause mortality given the relatively small number of death events observed during follow-up. Consequently, the absence of statistically

significant associations does not necessarily indicate the absence of a true relationship. Therefore, the clinical implications of these findings should be considered preliminary and hypothesis-generating rather than definitive. Larger prospective studies with greater numbers of mortality events, repeated assessments of Zn status, and randomized controlled trials (RCTs) are needed to clarify the potential role of Zn in CVD outcomes and to inform clinical recommendations.

To date, no RCT has directly evaluated whether Zn supplementation reduces the incidence of CVD events or mortality in individuals with T2DM. Existing RCTs, however, consistently report beneficial effects of Zn supplementation on major cardiometabolic risk factors, improving glycemic indices (45), lipid profiles (46), and markers of inflammation and oxidative stress (47), all of which are established contributors to CVD development in T2DM. Rather than focusing on specific trial effect sizes, it is most relevant to emphasize that our observational findings highlight a critical evidence gap. Well-designed RCTs are needed to determine whether optimizing zinc status can causally reduce CVD events or mortality in this population and to establish the potential clinical utility of Zn as an adjunct to current cardiometabolic therapies.



Experimental findings also support the potential vascular benefits of zinc. In animal models, Zn supplementation reduced aortic lesion area, indicating anti-atherosclerotic effects (48). Zn maintains vascular integrity through modulation of nitric oxide signaling and inhibition of phosphodiesterase-5, promoting vasodilation (43). Conversely, Zn deficiency can contribute to endothelial dysfunction, vascular inflammation, and smooth-muscle proliferation, thereby exacerbating atherosclerotic progression (43, 44).

This prospective cohort study, with its long-term follow-up, allowed for a thorough examination of the temporal relationship between Zn deficiency and the occurrence of CVD events. The study

was conducted within the framework of the TLGS population-based project, which increases the generalizability of the findings. Accurate SZn measurement with a well-defined cut-off value for identifying Zn deficiency resulted in high accuracy in classifying Zn status. Nonetheless, several limitations should be acknowledged. SZn levels were measured only at baseline, and changes over time were not captured; moreover, data on dietary Zn intake and Zn supplementation were unavailable, preventing assessment of their potential confounding effects. In addition to these factors, residual confounding cannot be ruled out, particularly given the absence of information on inflammatory markers (e.g., hs-CRP) and oxidative stress indicators, which are closely related to both Zn status and CVD risk. Finally, because SZn represents short-term Zn availability and may not fully represent long-term or tissue-level Zn status, some degree of exposure misclassification remains possible.

In conclusion, this long-term prospective analysis demonstrates that Zn deficiency is independently associated with a higher incidence of CVD events among adults with T2DM, whereas higher SZn concentrations confer a modest but significant protective effect. These findings highlight the clinical relevance of Zn status as a potentially modifiable risk factor in the cardiovascular risk profile of patients with T2DM. From a clinical perspective, routine assessment of Zn status may help identify high-risk individuals, and targeted strategies to prevent or correct Zn deficiency could complement established cardiometabolic risk-reduction approaches in T2DM. Further RCTs are warranted to determine whether optimizing Zn status can translate into meaningful reductions in CVD events and to inform evidence-based recommendations for Zn intake in this high-risk population.

**Declarations section**

*Ethical Approval and Consent to participate*

The study protocol was approved by the ethics research council of the Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran (Ethics code: IR.SBMU.ENDOCRINE.REC.1404.196). Written informed consent was obtained from all participants. The study was conducted in accordance with the guidelines outlined in the Declaration of Helsinki.

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*Clinical Trial Number*

Not applicable.

*Consent for publication*

Not applicable.

*Competing interests*

The authors declare that they have no competing interests.

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*Availability of data and materials*

Data will be presented upon forwarding the request to the corresponding author and confirming with the director of RIES (azizi@sbmu.ac.ir).

*Authors' contributions*

Z.B. and F.Gh designed the study and analyzed the data. Z.B., and F.Gh. wrote the manuscript. F.A. supervised the study design. All authors read and approved the final manuscript.

**Table 1**. Baseline characteristics of the study participants

| | Serum zinc concentration | | |
|---|---|---|---|
| | Sufficient (≥85 μg/dL) (n=493) | Deficient (<85 μg/dL) (n=139) | *P* value |
| Age (year) | 59.4±12.1 | 60.2±13.4 | 0.524 |
| Men (%) | 37.5 | 38.1 | 0.521 |
| Family history of diabetes (%) | 12.4 | 16.5 | 0.391 |
| Hypertension (%) | 55.5 | 61.9 | 0.207 |
| Chronic kidney disease (%) | 24.5 | 28.8 | 0.323 |
| Medications | | | |
| Glucose-lowering (%) | 53.3 | 63.3 | 0.042 |
| Lipid-lowering (%) | 32.3 | 29.5 | 0.853 |
| BP-lowering (%) | 37.1 | 48.2 | 0.024 |
| Current smoker (%) | 7.9 | 9.4 | 0.477 |
| Low-physical activity† (%) | 39.3 | 42.9 | 0.529 |
| SBP (mm Hg) | 130±21.7 | 131±22.1 | 0.654 |
| DBP (mm Hg) | 80.5±11.7 | 79.0±10.1 | 0.139 |
| BMI (kg/m$^2$) | 29.7±5.1 | 30.1±5.1 | 0.388 |
| WC (cm) | 100±11.3 | 102±12.3 | 0.062 |
| Serum Cr (mg/dL) | 1.07±0.23 | 1.10±0.25 | 0.340 |
| eGFR (mL/min/1.73 m$^2$) | 70.0±15.4 | 68.4±15.6 | 0.321 |
| TG-to-HDL ratio | 4.7±3.7 | 4.1±2.7 | 0.106 |
| FSG (mg/dL) | 158±57.3 | 159±59.4 | 0.888 |
| 2h-SG (mg/dL) | 247±86.2 | 230±74.5 | 0.185 |
| SZn (μg/dL) | 128±42.6 | 72.3±10.4 | 0.001 |

Data are mean ± standard error or percent

Independent sample t-test and Chi-square test were used for continuous and categorical variables, respectively.

†Physical activity level less than 600 MET (metabolic equivalent)-min/week.

BMI, body mass index; BP, blood pressure; Cr, creatinine; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FSG, fasting serum glucose; HDL-C, high-density lipoprotein cholesterol; 2h-SG, 2-hours serum glucose; SBP, systolic blood pressure; SZn, serum zinc; TG, serum triglyceride; WC, waist circumference.

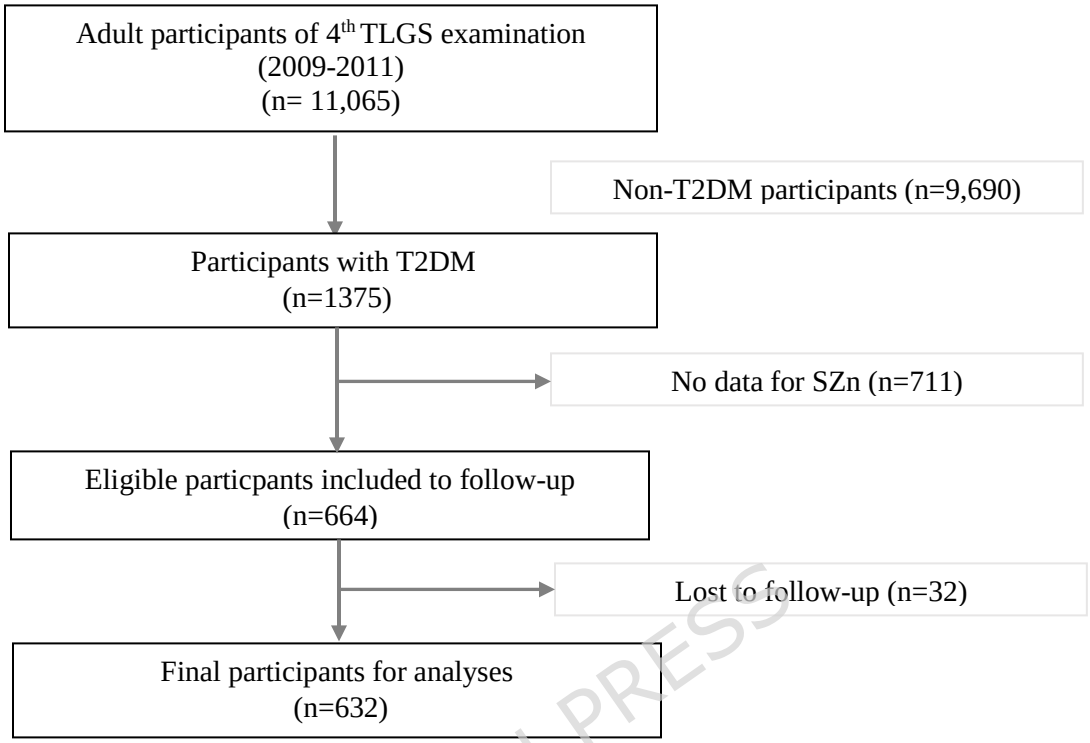


**Figure 1.** Flowchart of the study participants.

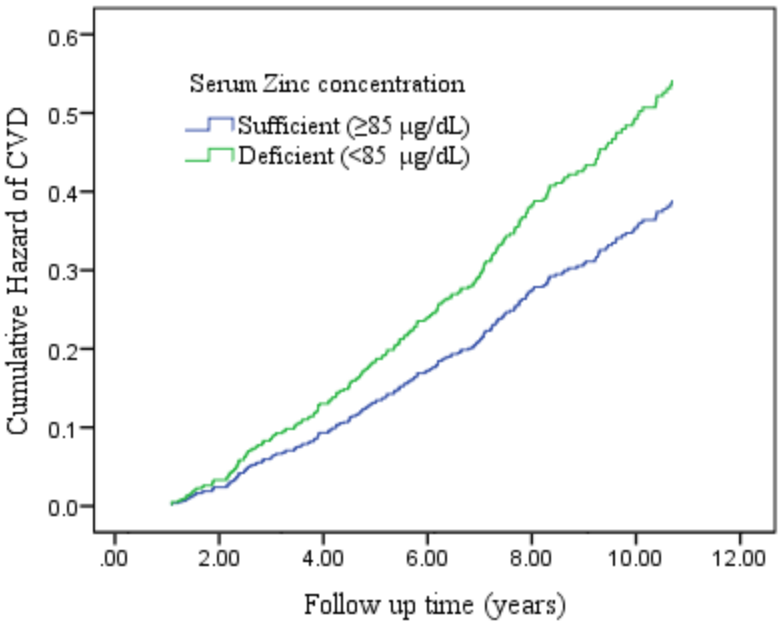


**Figure 2.** Cumulative hazard curves for cardiovascular disease (CVD) events according to serum zinc (SZn) status categories. Participants with zinc deficiency (SZn <85 µg/dL) exhibited a higher cumulative hazard of CVD events compared with those who were zinc sufficient.

**Table 2**. The association of serum zinc concentration and risk of incident CVD, CVD mortality and all-cause mortality in patients with T2DM

| | Serum zinc concentration | | |
|---|---|---|---|
| | Sufficient (≥85 μg/dL) | Deficient (<85 μg/dL) | Per 10 μg/dL increased SZn |
| **CVD** | | | |
| Case/total numbers | 162/493 | 57/139 | |
| Crude | 1.00 | 1.36 (1.01-1.84) | 0.97 (0.94-1.00) |
| Model 1 | 1.00 | 1.31 (0.97-1.77) | 0.97 (0.94-0.99) |
| Model 2 | 1.00 | 1.38 (1.02-1.89) | 0.96 (0.93-0.99) |
| Model 3 | 1.00 | 1.86 (1.06-3.28)† | 0.97 (0.93-1.00)‡ |
| **CVD mortality** | | | |
| Case/total numbers | 29/493 | 11/139 | |
| Crude | 1.00 | 1.39 (0.69-2.79) | 0.96 (0.85-1.04) |
| Model 1 | 1.00 | 1.27 (0.63-2.56) | 0.95 (0.88-1.03) |
| Model 2 | 1.00 | 1.14 (0.55-2.39) | 0.96 (0.90-1.04) |
| Model 3 | 1.00 | 1.13 (0.48-2.65) | 0.95 (0.87-1.05) |
| **All-cause mortality** | | | |
| Case/total numbers | 85/493 | 32/139 | |
| Crude | 1.00 | 1.40 (0.93-2.09) | 0.97 (0.93-1.02) |
| Model 1 | 1.00 | 1.25 (0.83-1.88) | 0.96 (0.93-1.00) |
| Model 2 | 1.00 | 1.18 (0.78-1.82) | 0.96 (0.92-1.01) |
| Model 3 | 1.00 | 1.41 (0.88-2.26) | 0.96 (0.93-1.01) |

Data are HRs and 95% CI; Cox regression was used.

†$P$=0.031

‡$P$=0.050

Model 1: age and sex; Model 2: Additionally adjusted for waist circumference, TG-to-HDL-C ratio, and SBP. Model 3 was further adjusted for FSG, use of glucose-lowering drugs, chronic kidney disease, low-physical activity and smoking.

HRs (95% CIs and $P$ values)) of covariates in the full-adjusted model for CVD events were as follow: age (1.06, 1.02-1.10, $P$=0.003), male sex (1.06, 0.58-1.93, $P$=0.851), SBP (1.00, 0.99-1.01, $P$=0.953), TG-to-HDL-C ratio (1.02, 0.92-1.12, $P$=0.737), FSG (1.00, 0.99-1.01, $P$=0.100), chronic kidney disease (1.25, 0.66-2.39, $P$=0.491), low-physical activity (1.56, 0.93-2.62, $P$=0.092), smoking (1.29, 0.37-4.47, $P$=0.680).

FSG, fasting serum glucose; HDL-C, high-density lipoprotein-cholesterol; TG, triglycerides; SBP, systolic blood pressure.

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