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ORIGINAL RESEARCH ARTICLE

Basic medication therapy based on target glycated hemoglobin levels in patients with ischemic heart disease and diabetes

Raisa Trigulova[1†], Alisher Ikramov[2,3†*], Dilnoza Alimova[1], Shukhrat Doniyorov[1], Dilafruz Akhmedova[1], and Shakhnoza Mukhtarova[4]

[1]Scientific Laboratory of Preventive Cardiology, The Republican Specialized Scientific-Practical Medical Center of Cardiology, Tashkent, Uzbekistan

[2]Department of Mathematics, School of Humanities, Natural, and Social Sciences, New Uzbekistan University, Tashkent, Uzbekistan

[3]Laboratory of Biomedical Informatics, V.I. Romanovskiy Institute of Mathematics, Uzbekistan Academy of Sciences, Tashkent, Uzbekistan

[4]Department of Pediatric Endocrinology, Medical-Pedagogical and Medical Faculty, Tashkent Pediatric Medical Institute, Tashkent, Uzbekistan

Abstract

Introduction: Type 2 diabetes mellitus (T2DM) and ischemic heart disease (IHD) are significant medical conditions. Research indicates that patients with T2DM have a substantially increased risk of developing cardiovascular diseases, necessitating meticulous monitoring and management of both diabetes and associated cardiovascular conditions. Achieving target glycated hemoglobin (HbA1c) levels is crucial for effective T2DM treatment.

Objective: This study investigates the prescribed basic medication therapy in patients with T2DM and IHD based on target HbA1c levels.

Methods: A prospective observational study was conducted at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Uzbekistan from 2022 to 2024, involving 130 patients with T2DM and IHD. Clinical, functional, and instrumental parameters, including left ventricular ejection fraction and other metabolic indicators, were assessed. Data were collected using standardized questionnaires and analyzed using the Statistical Package for Social Sciences. Logistic and linear regression models were used to analyze the efficiency of medication treatment.

Results: Among the cohort, 56.9% achieved an HbA1c level ≤8%, while 43.1% had an HbA1c level ≥8%. Significant differences were observed in age, gender distribution, duration of diabetes, and IHD between the two groups. Medication therapy varied significantly, with higher usage of metformin and insulin in patients with an HbA1c level ≥8%. The linear regression model predicts HbA1c levels based on clinical data and dosages of prescribed medications with a root mean square error of 1.172 and a Spearman correlation coefficient of 0.826. The logistic regression model predicts achievement of target HbA1c levels with a receiver operating characteristic area under the curve value of 0.92.

Conclusion: The study highlights the importance of individualized medication therapy tailored to HbA1c levels to improve clinical outcomes in patients with T2DM and IHD. It also highlights differences in medication effects based on the target HbA1c levels in patients.

Keywords: Diabetes mellitus; Ischemic heart disease; Glycated hemoglobin; Medication therapy

†*These authors contributed equally to this work.*

***Corresponding author:**
Alisher Ikramov
(a.ikramov@newuu.uz)

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1. Introduction

Type 2 diabetes mellitus (T2DM) and ischemic heart disease (IHD) are among the most prevalent chronic conditions worldwide, posing significant challenges to healthcare systems due to their high morbidity and mortality rates. The International Diabetes Federation estimates that the global prevalence of diabetes will continue to rise, reaching alarming levels by 2030.[1] Whiting *et al.*[1] provided global estimates of diabetes prevalence, highlighting the significant burden of DM and its complications. This increase underscores the urgent need for effective management strategies to mitigate the associated health risks.

Patients with T2DM are particularly vulnerable to cardiovascular diseases, including IHD, due to the complex interplay between hyperglycemia, insulin resistance, and cardiovascular risk factors. The United Kingdom Prospective Diabetes Study (UKPDS)[2] highlighted the critical role of blood-glucose control in reducing cardiovascular complications among patients with T2DM. Achieving target glycated hemoglobin (HbA1c) levels is a cornerstone of diabetes management, as it significantly lowers the risk of cardiovascular events.

HbA1c level serves as a reliable marker for long-term glycemic control, reflecting average blood glucose levels over the past 2 – 3 months. The American Diabetes Association recommends maintaining HbA1c levels below 7% to minimize the risk of diabetes-related complications. However, individual targets may vary based on patient characteristics, comorbidities, age, and treatment goals. Older adults with complex health conditions or intermediate health are advised to reach target levels of HbA1c below 8%.[3] Similarly, the Action to Control Cardiovascular Risk in Diabetes study analyzed the trajectory of HbA1c and its impact on cardiovascular outcomes, emphasizing the importance of maintaining optimal glycemic control.[4]

Medications used for glycemic control include sodium-glucose co-transporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists,[5-8] and metformin. The results of previous studies demonstrated that SGLT2 inhibitors significantly reduced the risk of major adverse cardiovascular events, heart failure hospitalization, and all-cause mortality; their combined use with GLP-1 receptor agonists is more effective than monotherapy. Metformin remains a cornerstone in T2DM management due to its proven efficacy in lowering HbA1c and reducing cardiovascular risk, as first demonstrated by the UKPDS. Insulin therapy is reserved for patients with suboptimal control despite oral medication, a pattern reflected in both the literature and the current study's findings.

In addition to antihyperglycemic medications, the use of cardiovascular drugs in managing IHD in diabetic patients is important. Previous studies emphasize the necessity of integrating antihypertensive therapy, particularly angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, and beta-blockers, into diabetes care.[9,10] Intensive glycemic control is linked to reduced cardiovascular and renal complications.[11-13] Most of these studies used structured clinical data, such as HbA1c levels, blood pressure, lipids, creatinine, and demographic variables, to construct predictive models of treatment efficacy or complication risk.[14-16] The data are usually used to train linear and logistic regression models, but recent works incorporate machine learning and metabolomic data to refine risk stratification.[17-21]

In addition, economic and systemic factors were also considered in diabetic management. Beran *et al.*[22] conducted a cost-effectiveness analysis of expanding access to newer antidiabetic medications in low- and middle-income countries, revealing that these therapies can be viable if priced appropriately. Nelson *et al.*[23] focused on the gaps in therapy adherence among insured United States patients with T2DM and cardiovascular disease, highlighting the discrepancy between guideline recommendations and real-world practice. These findings underscore the broader systemic and socioeconomic challenges that influence therapeutic outcomes.

2. Methodology

2.1. Patient selection and data collection

This study was performed at the Republican Specialized Scientific-Practical Medical Center of Cardiology in Uzbekistan from 2022 to 2024. A total of 130 patients previously diagnosed with T2DM and IHD were included in this study. The inclusion criteria for patients with T2DM were established according to the World Health Organization classification: (i) Patients with a left ventricular ejection fraction (LVEF) ≥50%, and (ii) patients with T2DM and heart failure with LVEF between 41% and 49%.

Patients were excluded if they had any of the following conditions: (i) A recent myocardial infarction (<3 months ago), (ii) chronic heart failure of New York Heart Association class III – IV, (iii) severe liver and kidney dysfunction, (iv) respiratory failure, (v) significant arrhythmias, and (vi) heart failure with LVEF ≤40%. Patients with lower levels of LVEF were excluded because they received a different treatment regimen in accordance with national standards of care in Uzbekistan, which could affect clinical outcomes and the extent of change in measured indicators.

Data were collected using standardized questionnaires administered to the patients during their hospital visits. The questionnaires included sections on demographic information, medical history, clinical parameters, and medication usage. It also included prescriptions issued within the hospital setting. Clinical, functional, and instrumental parameters, including LVEF and other metabolic indicators, were assessed.

2.2. Outcome measurement

We employed descriptive data analysis to examine changes in clinical characteristics over time. Changes were calculated by subtracting baseline (first observation) values from follow-up (second observation) values.

The primary outcome measure was the achievement of target HbA1c levels (≤8%) in patients with T2DM and IHD. This target level was selected according to the severity of IHD in patients and in compliance with Uzbekistan's and global treatment standards. Given that the patient population consisted primarily of older adults with complex/intermediate health, many of whom have pacemakers or are at risk of hypoglycemia, a target HbA1c below 8% was considered clinically appropriate. Moreover, as the study was conducted in a cardiological hospital, all admitted patients had IHD as their primary diagnosis, with T2DM as a comorbidity. Therefore, the target HbA1c levels used were not the same as those of a healthy population.

Secondary outcome measures included comparisons of demographic characteristics, clinical parameters, and medication usage between patients who achieved target HbA1c levels and those who did not. We also compared different medication types and outcomes using statistical analysis. We randomly permuted and split our dataset into training (70%) and test (30%) sets to construct linear regression and logistic regression models.

2.3. Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences version 23.0. Continuous variables were presented as mean ± standard deviation (SD). We applied *t*-tests and the Kruskal–Wallis test to compare variables. Categorical variables were presented as percentages and compared using Chi-squared tests. For non-parametric analysis of variance, we used Python 3.7 SciPy library (v1.15). Statistical significance was accepted at $p<0.05$. In addition, the multinomial logistic regression model from the Statsmodels library (v.0.15) was used.

2.4. Ethical considerations

The study was approved by the ethics committee of the Republican Specialized Scientific-Practical Medical Center of Cardiology (decision no. П3-202007041). All patients provided informed consent to participate in the study and received a full explanation of the study's objectives and methods. Confidentiality of data and the right to withdraw from the study were guaranteed to all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki (as revised in 2013) and ethical guidelines for clinical research.

3. Results

The study included 130 patients diagnosed with T2DM and IHD. Table 1 presents the demographic and clinical characteristics of the cohort. A total of 75 patients achieved HbA1c levels ≤8% while 55 patients did not (≥8%).

3.1. Glycemic control and medication therapy

The study found significant differences in glycemic control and medication therapy between patients who achieved target HbA1c levels (≤8%) and those who did not (≥8%). The average age of participants with HbA1c levels ≤8% was significantly higher than those with HbA1c levels ≥8% (67.19 ± 9.73 years versus 63.48 ± 9.23 years, $t = 4.879$, $p=0.027$). In addition, a higher frequency of women was present in the HbA1c level ≥8% group compared to the HbA1c level ≤8% group during the second observation (62.5% vs. 48.6%, $t = 8.186$, $p=0.004$).

The duration of T2DM was higher among patients in the HbA1c level ≥8% group (11.12 ± 4.55 years) compared to the patients in the HbA1c level ≤8% group (7.04 ± 4.93 years, $t = 26.010$, $p=0.000$). Similarly, the duration of IHD was longer in the HbA1c level ≥8% group (8.38 ± 3.70 years) compared to the HbA1c level ≤8% group (6.93 ± 3.43 years, $t = 5.007$, $p=0.025$).

Table 2 shows the dosages of medications prescribed to patients. The duration of treatment before the second observation was 9.94±5.71 months (interquartile range = 6.00 – 12.00; minimum = 2.0, maximum = 31.0).

Medication therapy varied significantly between the two groups. Metformin was prescribed to 69.6% of patients with an HbA1c level ≥8%, compared to 35.1% of patients with an HbA1c level ≤8% ($t = 56.324$, $p=0.000$). Insulin therapy was also more common in the HbA1c level ≥8% group (41.1% vs. 9.5%, $t = 41.289$, $p=0.000$). Table 3 presents the distribution of antidiabetic medication prescriptions across patient groups, expressed as percentages.

Empagliflozin, a medication known for its cardiovascular benefits, was prescribed for all 130 patients in the study. Dipeptidyl peptidase-4 (DPP-4) inhibitors were more frequently prescribed to patients with an HbA1c

Table 1. Demographic and clinical characteristics of patients

Characteristic	HbA1c level ≤8% (*n*=75)	HbA1c level ≥8% (*n*=55)	*T*	*p*
Age, years (mean±standard deviation)	67.19±9.73	63.48±9.23	4.879	0.027
Female	48.6 (36)	62.5 (35)	8.186	0.004
Weight, kg (mean±standard deviation)	85.20±16.76	85.43±15.32	0.031	0.860
Height, cm (mean±standard deviation)	165.15±8.67	163.77±8.02	0.680	0.410
Body mass index, kg/m² (mean±standard deviation)	31.45±6.15	31.93±4.58	1.154	0.283
COVID-19 in anamnesis	48.6 (36)	58.9 (33)	4.366	0.037
Duration of diabetes, years (mean±standard deviation)	7.04±4.93	11.12±4.55	26.010	0.000
Duration of IHD, years (mean±standard deviation)	6.93±3.43	8.38±3.70	5.007	0.025
Atrial fibrillation	16.2 (12)	3.6 (2)	46.428	0.000
Mortality	0.0 (0)	1.8 (1)	1.818	0.178
History of myocardial infarction	35.1 (26)	35.7 (20)	0.015	0.904
History of PCI	29.7 (22)	28.6 (16)	0.066	0.798
History of CABG	10.8 (8)	7.1 (4)	2.028	0.154
History of Stroke	6.8 (5)	3.6 (2)	2.946	0.086
Proximal LAD Stenosis>50%	12.2 (9)	7.1 (4)	3.798	0.051
Complex 3-vessel disease	2.7 (2)	1.8 (1)	0.479	0.489

Note: Data are presented as *n* (%), unless stated otherwise.
Abbreviations: CABG: Coronary artery bypass grafting; HbA1c: Glycated hemoglobin; IHD: Ischemic heart disease; LAD: Left anterior descending; PCI: Percutaneous coronary intervention.

Table 2. Dosages of medications prescribed to patients during their first observation

Medication	HbA1c level ≤8% *n*=75				HbA1c level ≥8% *n*=55				*p*	Statistic
	Mean±SD	Q1 – Q3	Min; max	*n*	Mean±SD	Q1 – Q3	Min; max	*n*		
Valsartan	45.89±26.41	26.00 – 51.00	12.8; 103.0	21	34.33±11.79	26.00 – 44.75	26.0; 51.0	6	0.407	0.687
Fibrate	96.67±34.18	72.50 – 108.75	72.5; 145.0	3	96.67±34.18	72.50 – 126.88	72.5; 145.0	6	1.000	0.000
Rosuvastatin	15.54±4.85	10.00 – 20.00	5.0; 20.0	30	13.10±4.81	10.00 – 20.00	5.0; 20.0	29	0.052	3.769
Atorvastatin	15.00±5.00	10.00 – 20.00	10.0; 20.0	26	19.75±7.15	18.75 – 20.00	10.0; 40.0	20	0.023*	5.152
Beta-blockers	3.78±5.61	2.50 – 5.00	1.2; 47.5	68	3.76±2.42	2.50 – 5.00	1.2; 12.5	51	0.261	1.263
Other sartans	53.03±30.55	32.50 – 80.00	12.5; 160.0	30	48.42±37.34	21.25 – 50.00	7.5; 160.0	30	0.280	1.169
ACE inhibitors	4.07±2.15	2.50 – 5.00	1.2; 10.0	14	4.88±3.17	2.38 – 6.25	2.0; 10.0	4	0.912	0.012
GLP-1 agonists	0.60±0.00	0.60 – 0.60	0.6; 0.6	1	1.20±0.00	1.20 – 1.20	1.2; 1.2	1	0.317	1.000
Calcium channel blockers	23.50±23.97	2.00 – 37.50	2.0; 60.0	4	11.00±13.45	2.00 – 23.00	0.0; 30.0	6	0.356	0.851
Insulin	35.43±18.54	20.00 – 47.00	12.0; 64.0	7	26.87±15.78	15.00 – 37.00	8.0; 70.0	23	0.302	1.065
DPP-4 inhibitors	54.17±22.44	50.00 – 50.00	25.0; 100.0	6	72.50±26.10	50.00 – 100.00	25.0; 100.0	20	0.139	2.189
Metformin	775.00±420.81	500.00 – 850.00	250.0; 2000.0	27	1090.13±584.24	500.00 – 1,700.00	425.0; 2,000.0	38	0.012*	6.355
Empagliflozin	7.87±2.62	5.00 – 10.00	2.5; 12.5	75	8.61±4.88	5.00 – 10.00	2.5; 25.0	55	0.784	0.075

Notes: Patients are distributed in two groups based on their HbA1c levels during their second observation. The dosages are compared using the Kruskal–Wallis test. *Indicates statistical significance at $p<0.05$.
Abbreviations: ACE: Angiotensin-converting enzyme; DPP-4: Dipeptidyl peptidase-4; GLP-1: Glucagon-like peptide-1; HbA1c: Glycated hemoglobin; SD: Standard deviation.

level ≥8% (35.7%) compared to those with an HbA1c level ≤8% (8.1%). Figure 1 shows box plots for changes in fasting glucose and HbA1c levels in patients with regard to the prescribed antidiabetic medications.

3.2. Cardiovascular medications

We also analyzed the use of cardiovascular medications among the patients. ACE inhibitors were prescribed to 18.9% of patients with an HbA1c level ≤8%, compared to 7.1% in the HbA1c level ≥8% group (t = 20.908, p=0.000). Beta-blockers and loop diuretics were commonly used in both groups, with significant differences in their usage. Table 4 presents the distribution of cardiovascular medication prescriptions across patient groups, expressed as percentages.

Figure 2 shows the box plots illustrating the changes in urea, uric acid, and creatinine levels between the two observations, depending on the type of diuretics prescribed. We also calculated mean values and SDs for changes in critical clinical parameters according to the prescribed medications. Results are presented in Table 5.

The use of statins was significantly higher in the HbA1c level ≥8% group (87.5%) compared to the HbA1c level ≤8% group (75.7%, t = 12.783, p=0.000). Table 6 shows the results of this treatment on triglyceride levels, analyzed by gender across the two groups.

Table 3. Antihyperglycemic medications used in the study groups

Medication	HbA1c level ≤8% (%)	HbA1c level ≥8% (%)
Metformin	35.1	69.6
DPP-4 inhibitors	8.1	35.7
Sulfonylureas	5.4	8.9
GLP-1 agonists	1.4	1.8
Insulin	9.5	41.1

Abbreviations: DPP-4: Dipeptidyl peptidase-4; GLP-1: Glucagon-like peptide-1; HbA1c: Glycated hemoglobin.

3.3. Multinomial logistic regression and correlation of variables

Figure 3 demonstrates the cross-correlation between the study variables. The correlation between the durations of T2DM and IHD may be attributed to the simultaneous diagnosis of both conditions upon symptom presentation, resulting in the uncertainty of the actual duration of each disease. Understanding these durations is crucial for evaluating the course of treatment. Apart from the clear correlations between systolic and diastolic blood pressure, fasting glucose and HbA1c levels, and creatinine, uric acid, and urea levels, other variables exhibited sufficient independence.

We used the Statsmodels library (v.0.15) to train a multinomial logistic regression model. To enable interpretation of model coefficients as predictors of variable importance, we normalized all values before training and testing. The results are shown in Table 7. As anticipated, HbA1c levels during the first observation emerged as the most significant predictor. Although N-terminal pro-B-type natriuretic peptide (NT-proBNP) had a relatively small coefficient, its values varied significantly in the sample, even after normalization. Specifically, the maximum value of NT-proBNP reached 6.2, approximately 1.3 times higher than the maximum value of all other markers, explaining the disproportionately small coefficient. Other key predictors included urea levels, diastolic blood pressure, and duration of diabetes.

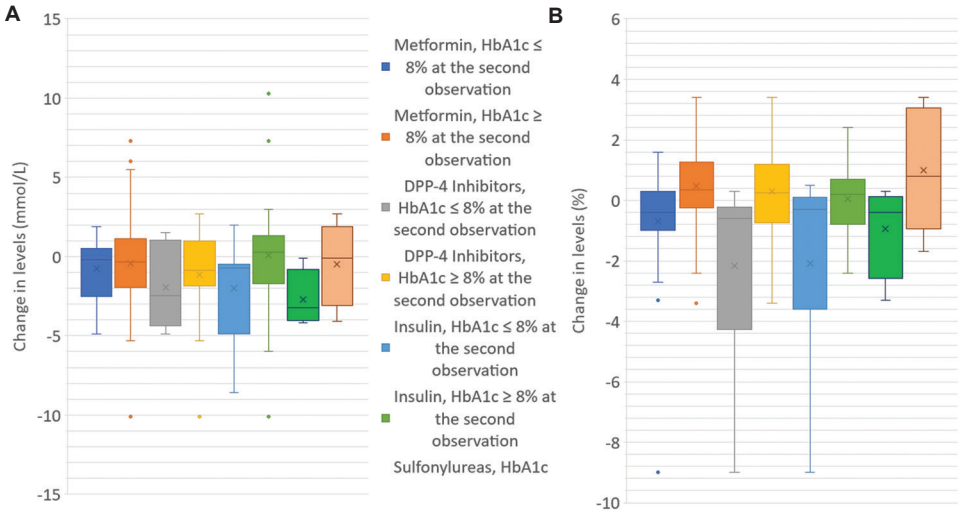

Figure 1. Box plots illustrating changes in (A) fasting glucose and (B) HbA1c levels in patients between two observations depending on the type of prescribed antidiabetic drugs. Group 1 is a group with HbA1c ≤8% during the second observation, and Group 2 consists of all remaining patients. The colors are consistent.
Abbreviations: DPP-4: Dipeptidyl peptidase-4; HbA1c: Glycated hemoglobin.

Table 4. Cardiovascular medications used in the study groups

Medication	HbA1c level ≤8% (%)	HbA1c level ≥8% (%)
ACE inhibitors	18.9	7.1
Angiotensin II receptor blockers	37.8	58.9
Beta-blockers	90.5	92.9
Mineralocorticoid receptor antagonists	68.9	51.8
Calcium channel blockers	44.6	48.2
Thiazide diuretics	9.5	16.1
Loop diuretics	71.6	46.4
Antiplatelet agents	100	100
Statins	75.7	87.5
Sacubitril/valsartan	28.4	10.7
Ivabradine	2.7	8.9

Abbreviations: ACE: Angiotensin-converting enzyme; HbA1c: Glycated hemoglobin.

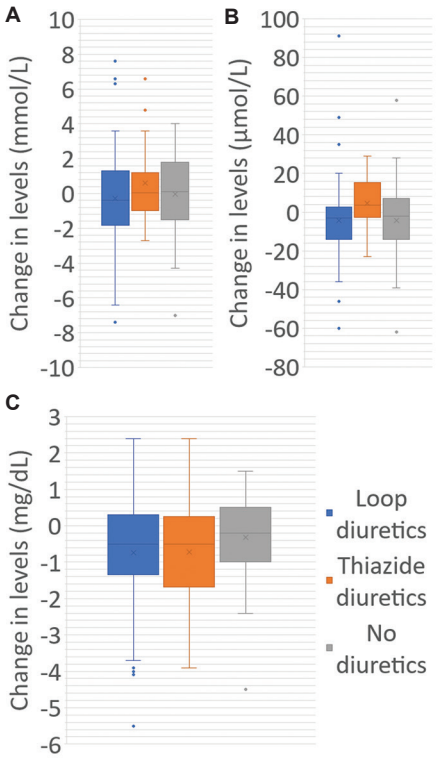

Figure 2. Box plots illustrating changes in (A) urea, (B) creatinine, and (C) uric acid levels in patients between two observations, depending on the type of prescribed diuretics. The colors are consistent.

We also constructed a linear regression model to predict HbA1c levels in patients based on their clinical data and dosages of prescribed medications. This model was trained on the training set and was tested using Spearman's correlation coefficient between predicted and actual levels of HbA1c during the second observation. This non-parametric measure was selected due to the non-linear relationship between medication dosage and glycemic response. The model achieved strong performance, with a correlation coefficient of 0.826 (p=2.3 × 10^{-22}). To understand the importance of each feature used in the model, all features were normalized before training. The description of the model is presented in Table 8. The root mean square error of the model on the test set was 1.172.

In addition, we found that patients with higher HbA1c levels (≥8%) were generally younger and had a longer duration of diabetes and IHD. These patients also required more aggressive antihyperglycemic therapy, including higher usage of metformin and insulin. The use of cardiovascular medications varied significantly between the groups, with higher usage of ACE inhibitors and statins in patients with higher HbA1c levels.

4. Discussion

The study revealed that patients with higher HbA1c levels (≥8%) were generally younger and were more likely to be female. This observation is consistent with related research indicating that younger patients with T2DM often struggle with glycemic control due to various factors, including lifestyle, adherence to treatment, and metabolic differences. Gale and Gillespie[12] discussed the impact of gender on diabetes management, noting that women may have a higher risk of poor glycemic control due to hormonal fluctuations and other physiological factors. However, we hypothesized that the primary contributing factor is the difference in life expectancy between men (72.1 years) and women (76.6 years) in Uzbekistan. The average age of women reaching the target levels was 69.2 years, whereas it was 65 years for men. The average age of women with an HbA1c level ≥8% was 66.7 years, and 58.4 years for men. Thus, the younger age in the second group is largely attributed to men with lower life expectancy. Failure to reach target levels poses a greater risk, with impaired survival being a key contributing factor to this outcome.

The longer duration of diabetes and IHD in patients with higher HbA1c levels suggests that disease duration significantly impacts glycemic control. The Diabetes Control and Complications Trial demonstrated that prolonged diabetes duration is associated with an increased risk of complications and poorer glycemic control. This study's findings underscore the importance of early and aggressive intervention to achieve and maintain target HbA1c levels. The multinomial logistic regression model revealed that the duration of T2DM has a negative impact, while the duration of IHD has a positive impact. Patients with a longer history of IHD were more likely to adhere to

Table 5. Changes in clinical characteristics by medication and HbA1c target achievement

Medication	Clinical characteristics	HbA1c level ≤8%	HbA1c level ≥8%	*H*	*p*-value
Metformin	NT-proBNP	−38.59±395.50	−121.79±207.95	0.021	0.884
	LVEF	1.62±4.23	2.11±4.37	1.192	0.275
	Systolic blood pressure	1.81±15.02	−5.39±14.16	3.880	0.049*
	Diastolic blood pressure	−2.04±9.26	−2.37±7.05	0.030	0.863
	Heart rate	−1.04±10.21	−3.79±10.96	0.010	0.920
DPP-4 inhibitors	NT-proBNP	−68.17±321.28	−98.30±226.65	0.370	0.543
	LVEF	0.93±3.48	1.75±4.38	0.675	0.411
	Systolic blood pressure	9.00±14.55	−3.50±15.58	2.700	0.100
	Diastolic blood pressure	−8.33±10.67	−3.00±7.14	1.499	0.221
	Heart rate	−1.83±5.37	−1.75±9.11	0.034	0.855
Insulin	NT-proBNP	−259.14±397.90	−86.14±780.08	0.376	0.540
	LVEF	−2.13±8.40	2.01±4.95	2.312	0.128
	Systolic blood pressure	5.57±21.92	−4.35±15.34	1.207	0.272
	Diastolic blood pressure	−7.14±17.50	−3.04±7.48	0.436	0.509
	Heart rate	1.86±6.64	−1.96±7.93	1.171	0.279
Sulfonylureas	NT-proBNP	−113.50±89.06	−44.20±82.43	1.830	0.176
	LVEF	1.94±3.42	2.12±5.19	0.000	1.000
	Systolic blood pressure	5.00±8.66	−6.00±10.20	2.055	0.152
	Diastolic blood pressure	−5.00±5.00	2.00±4.00	3.086	0.079
	Heart rate	−1.00±6.40	−8.20±11.57	0.549	0.459
ACE inhibitors	NT-proBNP	−170.64±235.10	−69.00±209.59	0.102	0.750
	LVEF	0.96±3.17	1.22±1.50	0.003	0.958
	Systolic blood pressure	6.07±17.34	5.00±20.62	0.003	0.957
	Diastolic blood pressure	3.21±10.96	0.00±7.07	0.200	0.654
	Heart rate	1.86±6.98	2.75±11.78	0.003	0.957
Angiotensin II receptor blockers	NT-proBNP	497.09±2136.96	−154.03±451.81	0.227	0.634
	LVEF	2.27±4.88	1.55±4.44	0.188	0.665
	Systolic blood pressure	−6.21±20.24	−8.75±11.25	0.498	0.480
	Diastolic blood pressure	−4.14±11.60	−2.81±6.72	0.474	0.491
	Heart rate	−2.52±10.84	−2.03±8.87	0.302	0.583
Beta-blockers	NT-proBNP	6.49±1204.74	−121.20±554.91	0.037	0.847
	LVEF	1.52±5.20	1.65±4.57	0.017	0.897
	Systolic blood pressure	−1.78±18.05	−5.29±14.93	1.498	0.221
	Diastolic blood pressure	−3.01±11.18	−2.75±7.69	0.108	0.743
	Heart rate	−1.49±9.85	−2.69±10.68	0.004	0.949
Mineralocorticoid receptor antagonists	NT-proBNP	28.02±1382.94	−233.66±470.53	0.343	0.558
	LVEF	1.72±5.92	1.57±3.83	0.261	0.610
	Systolic blood pressure	−2.08±19.42	−6.90±13.73	1.124	0.289
	Diastolic blood pressure	−3.73±11.54	−2.41±7.27	0.376	0.540
	Heart rate	−1.41±11.00	−2.86±9.05	0.003	0.960

Notes: Changes in clinical parameter levels are presented as mean±standard deviation. Kruskal–Wallis test's (non-parametric analysis of variance) results are statistics *H* and *P* value. *Indicates statistical significance at $p<0.05$.

Abbreviations: ACE: Angiotensin-converting enzyme; DPP-4: Dipeptidyl peptidase-4; HbA1c: Glycated hemoglobin; LVEF: Left ventricular ejection fraction; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

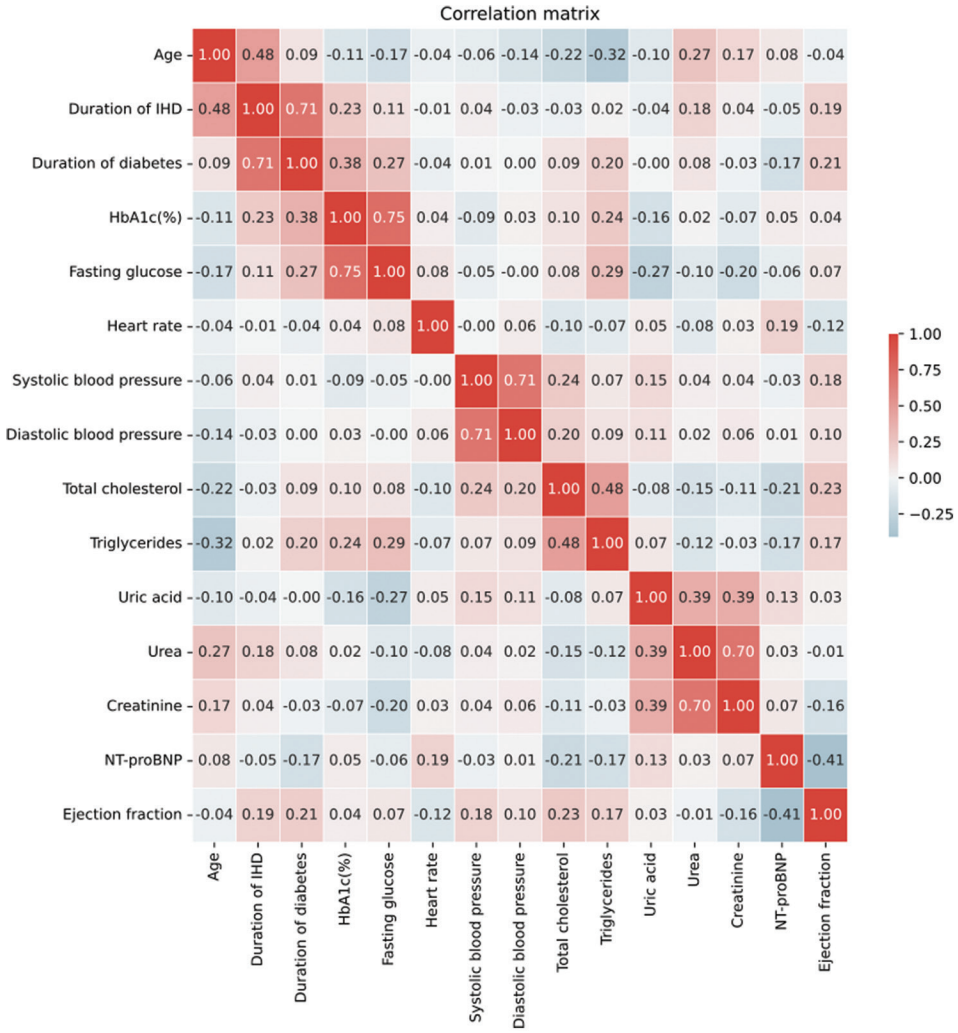

Figure 3. Correlation heatmap between primary variables in the study. Data from all patients on their first observation was used
Abbreviations: HbA1c: Glycated hemoglobin; IHD: Ischemic heart disease; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Table 6. Patients with triglyceride levels below the upper boundary based on gender

Gender	Reference value (mg/dL)	HbA1c level ≤8%		HbA1c level ≥8%		Chi-squared test	
		TG below limits (%)	TG above limits (%)	TG below limits (%)	TG above limits (%)	Statistics	*p*-value
Women	247	80.6	19.4	68.6	31.4	6.664	0.009
Men	288	74.4	25.6	55	45	29.009	0.000

Note: Pearson's Chi-squared test was used to verify the statistical significance of HbA1c control on levels of triglycerides.
Abbreviations: HbA1c: Glycated hemoglobin; TG: Triglyceride.

their prescribed medications due to their experience with the positive outcome of adherence.

4.1. Medication therapy

The significant differences in medication therapy between the two groups highlight the need for tailored treatment strategies based on individual patient characteristics and glycemic control. Patients with higher HbA1c levels required more aggressive antihyperglycemic therapy, including higher dosages of metformin and DPP-4 inhibitors (Table 2). This finding aligns with the results of Wilson et al.,[24] reporting that patients with poor glycemic control often require more complex treatment regimens.[24] We observed a statistically significant difference in the

Table 7. Multinomial logistic regression using primary variables

Variables	Coefficient	Standard error	z	$p>\|z\|$	Lower bound CI (0.025)	Upper bound CI (0.975)
Intercept	−0.4608	0.280	−1.644	0.100	−1.010	0.088
Age	−0.6777	0.393	−1.726	0.084	−1.447	0.092
Duration of IHD	−0.1246	0.506	−0.246	0.805	−1.116	0.866
Duration of diabetes	0.5746	0.445	1.292	0.196	−0.297	1.446
Heart rate	0.2971	0.302	0.983	0.326	−0.295	0.890
Systolic blood pressure	0.7056	0.417	1.693	0.091	−0.111	1.523
Diastolic blood pressure	−0.9186	0.436	−2.105	0.035	−1.774	−0.063
Fasting glucose	0.3378	0.453	0.747	0.455	−0.549	1.225
HbA1c level	1.5568	0.506	3.077	0.002	0.565	2.548
Total cholesterol	−0.3175	0.325	−0.978	0.328	−0.954	0.319
Triglycerides	0.4376	0.352	1.242	0.214	−0.253	1.128
Creatinine	−0.3337	0.418	−0.798	0.425	−1.153	0.485
Uric acid	−0.5615	0.340	−1.650	0.099	−1.229	0.106
Urea	0.9779	0.473	2.069	0.039	0.052	1.904
NT-proBNP	0.1777	0.423	0.420	0.675	−0.652	1.007
Ejection fraction	0.6635	0.338	1.963	0.050	0.001	1.326

Notes: The target was binary, indicating whether the patient failed to achieve an HbA1c level ≤8%. The receiver operating characteristic area under the curve value of the model was 0.92. The pseudo-R^2 was 0.4748.
Abbreviations: CI: Confidence interval; HbA1c: Glycated hemoglobin; IHD: Ischemic heart disease; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Table 8. Coefficients of the linear regression model

Parameters	Coefficient	Standard deviation
HbA1c level	0.81346	2.003743
Creatinine	−0.23825	36.639461
Triglycerides	0.10554	221.15185
Fasting blood glucose	0.16253	3.02244
Uric acid	0.01018	1.71296
Intercept	6.265236	-
Medication dosages		
Empagliflozin	−0.14453	3.76635
Metformin	0.19195	615.33906
DPP-4 inhibitors	−0.01531	29.76051
Insulin	0.10263	14.61167
Sulfonylureas	−0.02430	6.86299
GLP-1 agonists	0.00747	0.11685

Notes: Coefficients of linear regression model to predict levels of HbA1c in patients during their second observation based on their clinical data and dosages of hypoglycemic medications at their first observation.
Abbreviations: DPP-4: Dipeptidyl peptidase-4; GLP-1: Glucagon-like peptide-1; HbA1c: Glycated hemoglobin.

triglyceride levels between the two groups (Table 6). These results are consistent with other studies and could be attributed to dietary problems and differences in food preferences between women and men.

The use of empagliflozin, a medication known for its cardiovascular benefits, was higher in patients with better glycemic control (HbA1c levels ≤8%). This suggests that achieving target HbA1c levels may allow the use of medications with additional cardiovascular benefits, potentially improving overall patient outcomes. Our linear regression model attributed the decrease in HbA1c levels to higher dosages of empagliflozin. Sulfonylureas and DPP-4 inhibitors were also associated with decreases in HbA1c levels, albeit with smaller effect sizes. Interestingly, creatinine exhibited a negative coefficient, which may be explained by the prescription of more aggressive treatment for renal insufficiency in patients with low glomerular filtration rates, consequently leading to an improvement in their renal function by the time of the second observation.

We also found significant differences in the use of cardiovascular medications between the two groups. Patients with higher HbA1c levels were more likely to be prescribed ACE inhibitors and statins, reflecting the need for comprehensive management of cardiovascular risk factors in this patient population. Alpert *et al.*[10] emphasized the importance of controlled hypertension and lipid management in patients with diabetes to reduce cardiovascular risk.

Prescription of loop diuretics led to a decrease in creatinine levels in most patients. Ikramov *et al.*[25]

established it to be an important predictor of diastolic dysfunction in patients with T2DM.

4.2. Implications for clinical practice

The results of this study have significant implications for clinical practice. Lowering HbA1c levels below the threshold is substantial for mitigating the risk of cardiovascular complications in patients with T2DM and IHD. Healthcare providers should consider individualized treatment approaches based on patient characteristics, disease duration, and glycemic control. The use of medications with cardiovascular benefits, such as empagliflozin, should be prioritized in patients who achieve target levels of HbA1c.

The UKPDS demonstrated that intensive blood-glucose control significantly reduces the risk of cardiovascular events in patients with T2DM. The Action to Control Cardiovascular Risk in Diabetes study further emphasized the importance of maintaining optimal glycemic control to improve cardiovascular outcomes.

Recent advancements in diabetes treatment have introduced new classes of antihyperglycemic agents, such as GLP-1 receptor agonists and SGLT2 inhibitors, which have demonstrated better results in improving both glycemic control and cardiovascular outcomes. Joseph *et al.*[6] discussed management strategies for cardiovascular risk factors in adults with T2DM, underscoring the need for individualized treatment approaches. Johnson and Wang[7] and Smith and Patel[26] concluded that the combined use of these medications provides better cardiometabolic and renal outcomes than monotherapy.

4.3. Limitations

This study has several limitations that should be considered when interpreting its findings. The sample size was relatively small, and the study was conducted at a single center. Moreover, the patients in this study originate from various regions across the country, as the center serves as the primary cardiologic hospital in Uzbekistan. In addition, the observational nature of the study does not allow causal inferences to be made. The high costs of repeated laboratory tests constrained the frequency and scope of data collection.

Further limitations include potential confounding factors, such as patients' adherence, socioeconomic factors, dietary adherence, and stress. A more comprehensive analysis is required to account for these factors. However, the use of empagliflozin was well-monitored, as this medication was provided to patients by the center.

Empagliflozin was relatively recently approved by the Food and Drug Administration for the treatment of T2DM in patients with IHD. It was incorporated into the treatment standards in Uzbekistan in 2018. Consequently, the duration of observation for patients using empagliflozin was significantly limited.

5. Conclusion

This study investigated the prescribed basic medication therapy in relation to achieving target HbA1c levels in patients with T2DM and IHD. The findings revealed significant differences in demographic characteristics, duration of diabetes and IHD, and medication usage between patients who achieved target HbA1c levels (≤8%) and those who did not (≥8%). Reaching target levels of HbA1c is important for mitigating the risk of cardiovascular complications.

Patients with higher HbA1c levels had a longer duration of diabetes and IHD. Female patients with higher levels of HbA1c were older than male patients who did not reach target levels. These patients required more aggressive antihyperglycemic therapy, including higher usage of metformin and insulin. The use of cardiovascular medications varied significantly between the groups, with higher usage of ACE inhibitors and statins in patients with higher HbA1c levels.

Our logistic regression model demonstrated a very high receiver operating characteristic area under the curve value of 0.92 on the test set, effectively predicting whether the patient would achieve target HbA1c levels after treatment. In addition, the linear regression model was used to analyze the efficiency of hypoglycemic medications and their combination based on patients' data, yielding a Spearman's correlation coefficient of 0.82 on the test set.

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Conflict of interest

The authors declare they have no competing interests

Author contributions

Conceptualization: Raisa Trigulova, Alisher Ikramov
Formal analysis: Shukhrat Doniyorov
Investigation: Dilnoza Alimova, Shakhnoza Mukhtarova
Methodology: Dilafruz Akhmedova
Writing – original draft: Raisa Trigulova
Writing – review & editing: Raisa Trigulova, Alisher Ikramov

Ethics approval and consent to participate

The study was approved by the Ethics Board of the Republican Specialized Scientific-Practical Medical Center of Cardiology in Uzbekistan (Approval ID: П3-202007041). Participants provided written consent to participate in the study.

Consent for publication

The participants provided written consent to use and publish the data and results.

Availability of data

Data can be obtained by request from the corresponding author.

References

1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Res Clin Pract*. 2011;94(3):311-321.

   doi: 10.1016/j.diabres.2011.10.029

2. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK prospective diabetes study (UKPDS) Group. *Lancet*. 1998;352(9131):854-865.

3. American Diabetes Association. Glycemic goals and hypoglycemia: Standards of care in diabetes - 2025. *Diabetes Care*. 2025;48(Suppl 1):S128-S145.

   doi: 10.2337/dc25-S006

4. Wang JS, Liu WJ, Lee CL. HbA1c trajectory and cardiovascular outcomes: An analysis of data from the action to control cardiovascular risk in diabetes (ACCORD) study. *Ther Adv Chronic Dis*. 2021;12:20406223211026391.

   doi: 10.1177/20406223211026391

5. Nauck MA, Meier JJ. The incretin effect in healthy individuals and those with type 2 diabetes: Physiology, pathophysiology, and response to therapeutic interventions. *Lancet Diabetes Endocrinol*. 2016;4(6):525-536.

   doi: 10.1016/S2213-8587(15)00482-9

6. Joseph JJ, Deedwania P, Acharya T, *et al*. Comprehensive management of cardiovascular risk factors for adults with type 2 diabetes: A scientific statement from the American heart association. *Circulation*. 2022;145(9):e722-e759.

   doi: 10.1161/CIR.0000000000001040

7. Johnson L, Wang H. Cardioprotective effects of GLP-1 receptor agonists and SGLT2 inhibitors in T2DM patients. *J Diabetes Complications*. 2024;38(3):145-158.

   doi: 10.1016/j.jdiacomp.2024.01.005

8. Hou J, Ren L, Hou Q, *et al*. Efficacy and safety of sodium-glucose cotransporter 2 (SGLT2) inhibitors in patients with acute heart failure: A systematic review and meta-analysis. *Front Cardiovasc Med*. 2024;11:1388337.

   doi: 10.3389/fcvm.2024.1388337

9. Naha S, Gardner MJ, Khangura D, Kurukulasuriya LR, Sowers JR. Hypertension in Diabetes. In: Feingold KR, Ahmed SF, Anawalt B, *et al.*, editors. *Endotext*. MDText.com Inc.; 2000. Available from: https://www.ncbi.nlm.nih.gov/books/nbk279027 [Last accessed on 2024 Aug 07].

10. Alpert CM, Smith MA, Hummel SL, Hummel EK. Symptom burden in heart failure: Assessment, impact on outcomes, and management. *Heart Fail Rev*. 2017;22(1):25-39.

    doi: 10.1007/s10741-016-9581-4

11. Diabetes control and complications trial (DCCT): Results of feasibility study. The DCCT research group. *Diabetes Care*. 1987;10(1):1-19.

    doi: 10.2337/diacare.10.1.1

12. Gale EA, Gillespie KM. Diabetes and gender. *Diabetologia*. 2001;44(1):3-15.

    doi: 10.1007/s001250051573

13. Chou CL, Zheng CM, Chiu HW, *et al*. Impact of acute kidney injury, co-existing with and without chronic kidney disease on the short-term adverse outcomes following atherosclerotic cardiovascular disease events in patients with diabetes. *J Multidiscip Healthc*. 2025;18:2019-2037.

    doi: 10.2147/JMDH.S123456

14. Vloemans AF, Eilander MM, Rotteveel J, *et al*. Youth with type 1 diabetes taking responsibility for self-management: The importance of executive functioning in achieving glycemic control: Results from the longitudinal DINO study. *Diabetes Care*. 2019;42(2):225-231.

    doi: 10.2337/dc18-1143

15. Tucker B, Ong KL, Robledo K, Keech A, Patel S. Association of inflammation, triglycerides and lipoprotein(a) with cardiovascular events in the UK Biobank. *Eur Heart J*. 2024;45(Suppl 1):ehae666.2751.

    doi: 10.1093/eurheartj/ehae666.2751

16. Quispe R, Sweeney T, Varma B, Agarwala A, Michos ED. Recent updates in hypertriglyceridemia management for cardiovascular risk reduction. *Curr Atheroscler Rep*. 2022;24:52-64.

    doi: 10.1007/s11883-022-01052-4

17. Wu K, Chen J, Lin Y, Wang J. A cohort study on the correlation between serum Klotho levels and all-cause mortality in American diabetic populations. *Diabetol Metab Syndr*. 2025;17:124.

    doi: 10.1186/s13098-025-01686-9

18. Xie R, Seum T, Sha S, *et al*. Improving 10-year cardiovascular

risk prediction in patients with type 2 diabetes with metabolomics. *Cardiovasc Diabetol*. 2025;24:581.

doi: 10.1186/s12933-025-02581-3

19. Miller V, Micha R, Choi E, Karageorgou D, Webb P, Mozaffarian D. Evaluation of the quality of evidence of the association of foods and nutrients with cardiovascular disease and diabetes: A systematic review. *JAMA Network Open*. 2025;8(3):e2788634.

    doi: 10.1001/jamanetworkopen.2025.2788634.

20. Zhao C, Lin M, Yang Y, Yang H, Gao Z, Yan Z, *et al*. Association between dietary inflammatory index and cardiovascular-kidney-metabolic syndrome risk: A cross-sectional study. *Nutr J*. 2025;24:1127.

    doi: 10.1186/s12937-025-01127-3

21. Gupta A, Shah K, Gupta V. Interconnected epidemics: Obesity, metabolic syndrome, diabetes and cardiovascular diseases - insights from research and prevention strategies. *Discover Public Health*. 2025;22:106.

    doi: 10.1186/s12982-025-00496-8

22. Global Health and Population Project on Access to Care for Cardiometabolic Diseases (HPACC). Expanding access to newer medicines for people with type 2 diabetes in low-income and middle-income countries: A cost-effectiveness and price target analysis. Lancet Diabetes Endocrinol. 2021;9(12):825-836.

    doi: 10.1016/S2213-8587(21)00240-0

23. Nelson AJ, Ardissino M, Haynes K, *et al*. Gaps in evidence-based therapy use in insured patients in the United States with type 2 diabetes mellitus and atherosclerotic cardiovascular disease. *J Am Heart Assoc*. 2021;10(2):e016835.

    doi: 10.1161/jaha.120.016835

24. Wilson LM, Herzig SJ, Marcantonio ER, *et al*. Management of diabetes and hyperglycemia in the hospital: A systematic review of clinical practice guidelines. *Diabetes Care*. 2025;48(4):655-664.

    doi: 10.2337/dc24-2510

25. Ikramov A, Mukhtarova S, Trigulova R, Alimova D, Abdullaeva S. Prediction of glycosylated hemoglobin level in patients with cardiovascular diseases and type 2 diabetes mellitus with respect to anti-diabetic medication. *Front Endocrinol*. 2024;15:1305640.

    doi: 10.3389/fendo.2024.1305640

26. Smith J, Patel R. Real-world effectiveness of adding newer generation GLP-1RA to SGLT2i in T2DM patients with CHD. *Cardiovasc Diabetol*. 2024;23(4):237-250.

    doi: 10.1186/s12933-025-02737-1