

Article

Patterns of Antidiabetic Therapy and Associated Metabolic Profiles in Routine Clinical Practice

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Abstract

Background: Contemporary antidiabetic therapy has evolved from a glucose-centered approach toward integrated cardiometabolic risk reduction. However, real-world evidence regarding treatment patterns and their association with glycemic and cardiovascular–renal profiles remain limited. **Methods:** This retrospective observational study included 250 adults with type 2 diabetes mellitus receiving non-insulin glucose-lowering therapy in routine specialist clinical practice. Demographic, clinical, biochemical, and pharmacological data were extracted from medical records. Glycemic control was assessed using HbA1c levels and HbA1c variation, while cardiovascular–renal parameters included estimated glomerular filtration rate (eGFR), C-reactive protein (CRP), lipid profile, blood pressure, and heart failure prevalence. Comparative analyses and multivariate logistic regression were performed. **Results:** The cohort had a mean age of 61.8 ± 11.3 years, and all patients had type 2 diabetes mellitus (100.0%). Obesity, metabolic syndrome, hypertension, ischemic heart disease, and chronic kidney disease were highly prevalent. Metformin was the most frequently prescribed therapy (58.8%), followed by GLP-1 receptor agonists (28.8%) and SGLT-2 inhibitors (27.6%). Patients receiving GLP-1 receptor agonists or SGLT-2 inhibitors showed numerically lower HbA1c values and greater HbA1c reductions compared with conventional therapies. However, differences in HbA1c, CRP, and eGFR were not statistically significant after correction for multiple comparisons. Longer diabetes duration independently predicted poor glycemic control, whereas increasing age was associated with a lower probability of HbA1c > 7%. **Conclusions:** Contemporary antidiabetic therapies were associated with favorable numerical cardiometabolic trends, although these associations did not remain statistically significant after multiple-comparison correction. The findings should therefore be considered exploratory and hypothesis-generating.

Keywords: diabetes mellitus; type 2 diabetes; antidiabetic therapy; SGLT-2 inhibitors; GLP-1 receptor agonists; HbA1c; cardiovascular–renal risk; real-world evidence



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1. Introduction

Diabetes mellitus represents one of the most important global health challenges, with a continuously increasing prevalence and a substantial impact on morbidity and mortality. The disease is characterized by complex metabolic disturbances involving impaired insulin secretion, insulin resistance, chronic low-grade inflammation, and progressive β -cell dysfunction. These pathophysiological mechanisms contribute not only to poor glycemic control but also to the development of cardiovascular and renal complications, which remain the leading causes of death among diabetic patients [1–3].

In recent decades, the pharmacological management of diabetes has evolved significantly, shifting from a glucose-centric approach toward a broader cardiometabolic strategy. While metformin continues to be recommended as first-line therapy due to its efficacy, safety profile, and cost-effectiveness, newer pharmacological classes have demonstrated additional benefits beyond glycemic control. In particular, sodium–glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists have shown favorable effects on cardiovascular outcomes, renal protection, body weight reduction, and systemic inflammation in large clinical trials [4–6].

Despite the availability of multiple therapeutic options, achieving optimal glycemic control in real-world clinical practice remains challenging. The heterogeneity of diabetic populations, characterized by differences in disease duration, comorbidities, obesity status, and treatment adherence, may influence pharmacological effectiveness and clinical outcomes. Furthermore, the coexistence of cardiovascular disease and chronic kidney disease complicates therapeutic decision-making and highlights the need for individualized treatment strategies [7,8].

Observational studies conducted in routine clinical settings are therefore essential to better understand the real-world impact of pharmacological therapy on metabolic control and cardiometabolic risk. Such studies may provide valuable insights into treatment patterns, therapeutic effectiveness, and the interplay between pharmacological interventions and disease progression [9,10].

Given the complexity and heterogeneity of real-world diabetic populations, the present study was designed primarily as an exploratory observational analysis. Rather than assessing comparative efficacy between pharmacological agents, the primary aim of this study was to describe real-world antidiabetic treatment patterns and to explore their associations with glycemic, inflammatory, metabolic, and renal parameters in a routine clinical setting. The study was not designed to assess comparative effectiveness or establish causal treatment effects, but rather to generate hypotheses for future prospective investigations. Additionally, the study sought to identify clinical factors associated with poor glycemic control, providing hypothesis-generating insights to inform future stratified and prospective investigations.

2. Materials and Methods

2.1. Study Design and Population

This single-center retrospective observational study included consecutive adults with type 2 diabetes mellitus evaluated between January 2023 and December 2025 in specialist outpatient diabetes clinics affiliated with the Clinical County Emergency Hospital Bihor and the University of Oradea, Romania. Data were extracted from the institutional electronic medical record database.

Patients were eligible for inclusion if they: (1) were aged 18 years or older; (2) had a physician-documented diagnosis of type 2 diabetes mellitus; (3) were receiving at least one non-insulin glucose-lowering therapy at the index visit; and (4) had the essential demographic, clinical, biochemical, and pharmacological data required for the planned analyses.

The index visit was defined as the outpatient assessment at which the pharmacological regimen and the corresponding clinical and laboratory variables were documented.

Exclusion criteria were: (1) age below 18 years; (2) type 1 diabetes mellitus, gestational diabetes, or other specific forms of diabetes; (3) treatment with insulin, either alone or in combination with non-insulin glucose-lowering agents, at the index visit; (4) absence of essential clinical, laboratory, or pharmacological information; and (5) duplicate or incomplete medical records. Patients evaluated during acute hospitalization were outside the outpatient sampling framework.

Stable chronic comorbidities, including obesity, chronic kidney disease, ischemic heart disease, heart failure, hypertension, and metabolic syndrome, were not exclusion criteria because the study was specifically designed to describe treatment patterns in a clinically complex, high-risk real-world population and to explore the distribution of cardiometabolic and cardiorenal characteristics. Consequently, these conditions were recorded as study variables rather than used as reasons for exclusion.

Patients receiving insulin were excluded because the study focused on non-insulin pharmacological treatment patterns. Although insulin exposure could be identified for eligibility assessment, detailed information regarding insulin type, dose, titration, and treatment intensity was not consistently available. The findings should therefore be interpreted only in the context of adults with type 2 diabetes managed without insulin.

2.2. Data Collection

Demographic characteristics (age, sex, area of residence), anthropometric parameters (body mass index), clinical variables (duration of diabetes, presence of metabolic syndrome and cardiovascular comorbidities), laboratory parameters (fasting glucose, HbA1c, lipid profile, inflammatory markers, and renal function indices) were extracted from medical records. HbA1c was measured in the hospital's certified clinical laboratory using a standardized high-performance liquid chromatography (HPLC) method aligned with National Glycohemoglobin Standardization Program (NGSP) recommendations. According to laboratory reference values, normal HbA1c levels were considered <5.7%, values between 5.7% and 6.4% indicated prediabetes, and values $\geq 6.5\%$ were consistent with diabetes mellitus.

Antidiabetic therapy was categorized according to pharmacological class, including metformin, sulfonylureas, GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT-2 inhibitors. When patients received multiple therapies, they were assigned to the dominant exposure category according to the presence of modern cardiometabolic agents. Combined GLP-1 + SGLT-2 therapy was prioritized over single-agent exposure categories.

Two distinct pharmacological classification approaches were used. First, individual drug classes were described as non-mutually exclusive exposures because patients receiving combination therapy could contribute to more than one class. These analyses were intended only to describe prescribing patterns.

Second, patients were assigned to one of four mutually exclusive exposure groups for comparative exploratory analyses: GLP-1 receptor agonist without SGLT-2 inhibitor, SGLT-2 inhibitor without GLP-1 receptor agonist, combined GLP-1 receptor agonist and SGLT-2 inhibitor therapy, or neither GLP-1 receptor agonist nor SGLT-2 inhibitor. Each patient contributed to only one mutually exclusive group.

2.3. Study Outcomes

The primary outcome was glycemic control, assessed by HbA1c levels and HbA1c variation. Secondary variables included the cross-sectional values of eGFR, CRP, triglycerides, blood pressure, and LDL cholesterol recorded at the index assessment, together with the prevalence of previously documented heart failure. Standardized repeated measurements

of these variables were not consistently available; consequently, they were analyzed as descriptive cross-sectional characteristics rather than longitudinal outcomes.

Heart failure was identified based on a previously documented diagnosis recorded in the electronic medical records by the treating cardiologist. No standardized NT-proBNP- or echocardiography-based reassessment was performed as part of this retrospective study.

Standard CRP measurements were available in the retrospective database and were therefore included as a routinely collected inflammatory biomarker. We acknowledge that standard CRP is less sensitive than high-sensitivity CRP (hsCRP) for evaluating chronic low-grade inflammation. Consequently, CRP findings should be interpreted as exploratory markers of systemic inflammatory status rather than precise measures of chronic low-grade inflammation.

Pharmacological exposure was defined according to the glucose-lowering regimen documented at the index clinical visit. The index visit also served as the baseline time point for the collection of demographic, clinical, biochemical, and pharmacological variables.

Comorbidities were identified from physician-documented diagnoses available in the electronic medical records. Hepatic steatosis was defined according to abdominal ultrasonography reports available in the clinical records. Ischemic heart disease was identified from a pre-existing diagnosis documented by the treating cardiologist in the electronic medical record. This category could include chronic coronary syndrome or stable angina, previously documented coronary artery disease, and a history of coronary revascularization. Previous myocardial infarction was recorded separately as a specific acute coronary event. Heart failure was also recorded as an independent cardiologist-documented diagnosis, and its etiology was not assumed to be ischemic. Stroke was considered a separate cerebrovascular comorbidity and was not included in the definition of ischemic heart disease. The specific diagnostic modality supporting the IHD diagnosis, such as coronary angiography, coronary CT angiography, or functional testing, was not consistently available in the retrospective database.

Baseline HbA1c was defined as the value documented at the index clinical visit, when the glucose-lowering treatment regimen was recorded. Follow-up HbA1c was defined as the subsequent available measurement. HbA1c change was calculated as follow-up HbA1c minus baseline HbA1c; therefore, negative values indicated a reduction and positive values indicated an increase. Treatment modifications, dose changes, and adherence during this interval were not systematically available; consequently, HbA1c change was interpreted descriptively.

2.4. Statistical Analysis

Continuous variables were summarized using mean $\pm$ standard deviation and, where relevant, median with interquartile range and minimum–maximum values. Categorical variables were presented as absolute frequencies and percentages. The combined reporting of mean-based and median-based descriptive measures was used to provide a more complete characterization of the distribution of continuous variables in this heterogeneous clinical cohort. For comparative analyses, patients were assigned to mutually exclusive analytical groups according to their dominant therapeutic strategy. This categorization was performed solely for statistical comparison purposes and does not imply that these medications cannot be prescribed in combination in routine clinical practice. Multivariate logistic regression was applied to identify independent predictors of poor glycemic control, defined as HbA1c $> 7\%$. The model included clinically relevant covariates selected a priori, including age, body mass index, duration of diabetes, and exposure to major pharmacological classes (GLP-1 receptor agonists, SGLT-2 inhibitors, DPP-4 inhibitors, metformin, and sulfonylureas).

Pharmacological-class analyses were descriptive because individual patients could receive multiple concomitant therapies. Inferential comparisons were therefore restricted to the four mutually exclusive therapeutic exposure groups. Given the multiple comparisons, Tukey-adjusted post hoc tests were applied following one-way ANOVA.

Analyses were conducted using available-case data. No missing values were imputed. The number of participants contributing to each analysis is reported in the corresponding table or table footnote. For outcomes with missing observations, denominators were based on the number of available records.

2.5. Ethical Considerations

This study was observational and involved analysis of routinely collected clinical data. No experimental interventions were performed. All data were anonymized prior to statistical analysis to ensure confidentiality. Given the non-randomized design, potential confounding due to treatment allocation bias cannot be excluded.

3. Results

3.1. Demographic and Baseline Clinical Characteristics

The cohort represents a selected high-risk specialist-care population characterized by a high prevalence of obesity, cardiovascular disease, chronic kidney disease, and metabolic syndrome.

The study included 250 patients with diabetes mellitus. The mean age of the cohort was 61.8 ± 11.3 years (median: 63 years, IQR 56.3–68.0; range: 18–84 years) (Figure 1). Regarding sex distribution, 128 patients (51.2%) were male and 122 (48.8%) were female. Most participants were from an urban area (168 patients, 67.2%), while 82 (32.8%) were from a rural area.

The mean duration of diabetes was 10.1 ± 5.9 years (median: 10 years, IQR 5.3–13.8; range: 0–30 years).

From an anthropometric perspective, the mean body mass index (BMI) was 32.9 ± 6.0 kg/m² (median: 31.6 kg/m², IQR 30.1–36.0; range: 19.5–55.2 kg/m²). Excess body weight was highly prevalent in this population. Only 16 patients (6.4%) had normal weight, 43 (17.2%) were overweight, and 190 (76.0%) were classified as obese. Among obese subjects, obesity grade I was the most frequent category (114 patients, 45.6% of the total cohort), followed by grade II (51 patients, 20.4%) and grade III (26 patients, 10.4%). In parallel, metabolic syndrome was present in 191 patients (76.4%).

The burden of associated comorbidities was high. Hypertension was the most common associated condition, affecting 220 patients (88.0%), followed by chronic kidney disease in 199 patients (79.6%), and hepatic steatosis in 180 patients (72.0%). Ischemic heart disease, defined by a previously documented cardiology diagnosis, was present in 200 patients (80.0%). Previous myocardial infarction, recorded separately as a specific acute coronary event, was documented in 18 patients (7.2%), while stroke was reported in 16 patients (6.4%). Heart failure was present in 102 patients (40.8%), although its etiology was not classified in the retrospective database. Diabetic complications were also frequent, with polyneuropathy recorded in 178 cases (71.2%) and retinopathy in 86 cases (34.4%). In addition, heart failure was present in 102 patients (40.8%), peripheral arterial disease in 68 (27.2%), hypothyroidism in 66 (26.4%), COPD in 60 (24.0%), and hyperuricemia in 115 (46.0%). A history of myocardial infarction was noted in 18 patients (7.2%), while stroke was reported in 16 cases (6.4%).

Overall, the study population was characterized by an older age profile, an almost balanced sex distribution, a predominance of urban residence and type 2 diabetes, and a

markedly increased prevalence of obesity, metabolic syndrome, and cardiovascular-renal comorbidity (Table 1).

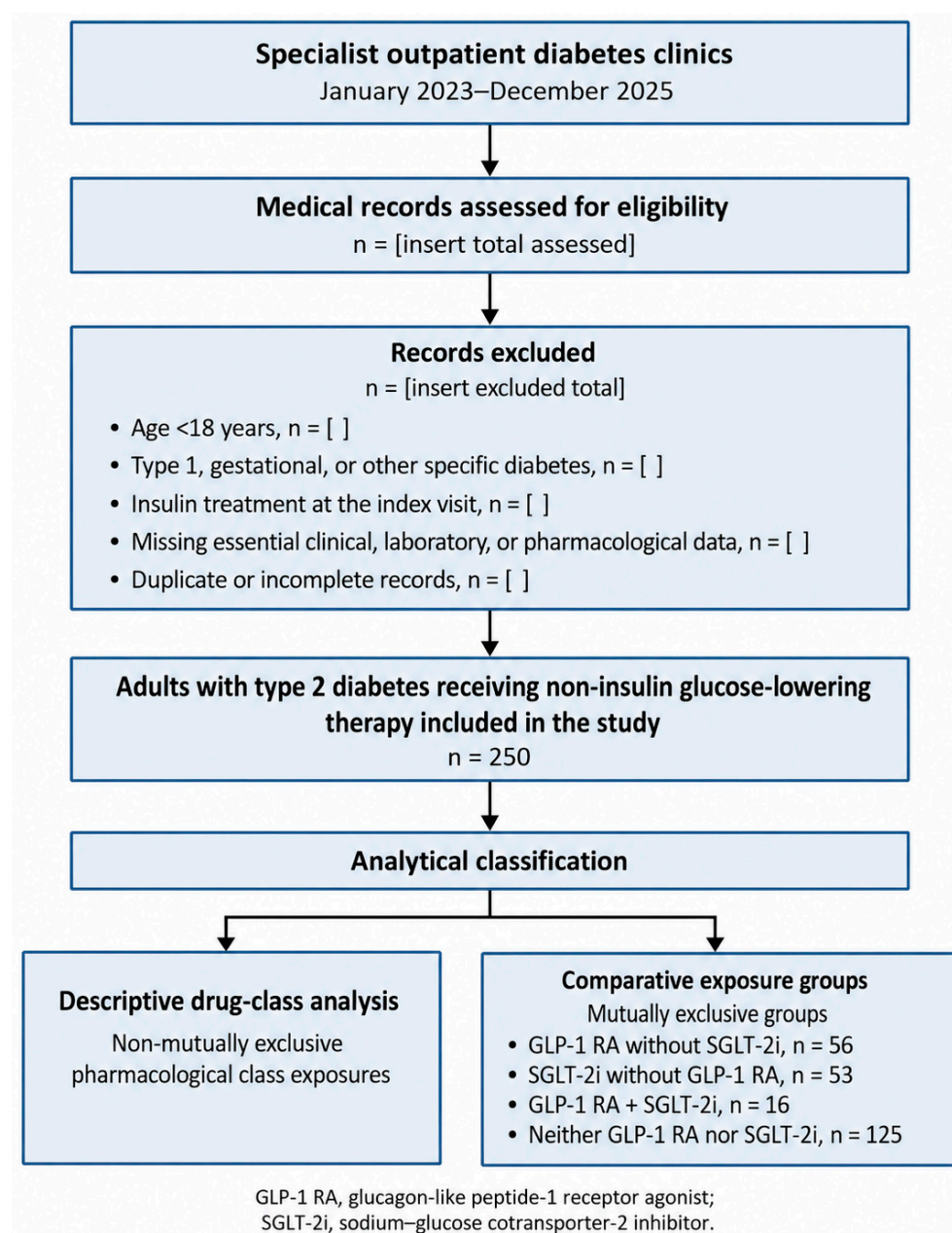


Figure 1. STROBE-style flow diagram of patient identification, eligibility assessment, inclusion, and analytical classification. GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT-2i, sodium–glucose cotransporter-2 inhibitor.

To provide additional context regarding potential confounding by indication, baseline characteristics were stratified according to the mutually exclusive therapeutic exposure groups (Supplementary Table S1). Patients receiving combined GLP-1 receptor agonist and SGLT-2 inhibitor therapy were younger and exhibited lower mean HbA1c values, whereas patients receiving no modern cardiometabolic agents showed the highest mean HbA1c levels. The prevalence of cardiovascular and renal comorbidities remained high across all groups, supporting the characterization of the cohort as a high-risk specialist-care population.

Table 1. Demographic and metabolic characteristics and comorbidities of the study population.

Variable	Value
Age (years)	61.80 ± 11.32
Male sex <i>n</i> (%)	128 (51.2%)
Urban residence <i>n</i> (%)	168 (67.2%)
Type 2 diabetes <i>n</i> (%)	250 (100.0%)
BMI (kg/m ²) <i>n</i> (%)	32.89 ± 6.01
Obesity <i>n</i> (%)	190 (76.0%)
Metabolic syndrome <i>n</i> (%)	191 (76.4%)
Comorbidity	
Hypertension <i>n</i> (%)	220 (88.0%)
Ischemic heart disease <i>n</i> (%)	200 (80.0%)
Chronic kidney disease <i>n</i> (%)	199 (79.6%)
Heart failure <i>n</i> (%)	102 (40.8%)
Myocardial infarction <i>n</i> (%)	18 (7.2%)
Stroke <i>n</i> (%)	16 (6.4%)

Values are expressed as mean ± standard deviation (SD) for continuous variables and as number (percentage) for categorical variables. BMI = body mass index; T2DM = type 2 diabetes mellitus; MetS = metabolic syndrome; CKD = chronic kidney disease; IHD = ischemic heart disease; HF = heart failure; MI = myocardial infarction. Available-case denominators were used.

3.2. Distribution of Antidiabetic Drug Classes

All patients included in the study were receiving pharmacological antidiabetic therapy, consistent with the real-world clinical setting and the predominantly type 2 diabetes profile of the cohort.

Among the non-insulin glucose-lowering therapies, metformin was the most frequently prescribed class, being recorded in 147 patients (58.8%). GLP-1 receptor agonists were used in 72 patients (28.8%), SGLT-2 inhibitors in 69 (27.6%), sulfonylureas in 64 (25.6%), and DPP-4 inhibitors in 15 (6.0%). Other oral glucose-lowering therapies were recorded in 12 patients (4.8%). Because class-level exposures were non-mutually exclusive, these percentages describe prescribing frequency rather than distinct treatment groups (Table 2).

Table 2. Distribution of antidiabetic pharmacological therapy.

Therapy	<i>n</i> (%)
Metformin	147 (58.8%)
Sulfonylureas	64 (25.6%)
GLP-1 receptor agonists	72 (28.8%)
DPP-4 inhibitors	15 (6.0%)
SGLT-2 inhibitors	69 (27.6%)
Other oral antidiabetic therapy	12 (4.8%)

Values are expressed as number (percentage) of patients receiving each pharmacological class; patients may have been treated with combination therapy. GLP-1 = glucagon-like peptide-1 receptor agonists; DPP-4 = dipeptidyl peptidase-4 inhibitors; SGLT-2 = sodium–glucose cotransporter-2 inhibitors. Patients receiving insulin, either alone or in combination with non-insulin agents, were excluded by study design. Drug-class frequencies are non-mutually exclusive; patients receiving combination therapy may be represented in more than one row. No between-class comparative-effectiveness inference should be drawn from this table. Available-case denominators were used.

Metformin was the most frequently recorded non-insulin glucose-lowering therapy, while GLP-1 receptor agonists and SGLT-2 inhibitors were also commonly used. Because these class-level categories were non-mutually exclusive, the frequencies describe prescribing exposure and not distinct treatment groups.

These findings indicate a heterogeneous pharmacological management strategy, characterized by predominant metformin use alongside an increasing adoption of newer therapeutic classes with established cardiometabolic benefits. The distribution of antidiabetic therapies is summarized in Table 2.

3.3. Therapeutic Regimen Patterns and Combination Strategies

Pharmacological treatment strategies ranged from monotherapy to dual and triple non-insulin regimens. Metformin monotherapy was documented in 66 patients (26.4%), while metformin combined with a sulfonylurea was recorded in 39 patients (15.6%). Metformin was combined with an SGLT-2 inhibitor in 31 patients (12.4%) and with a GLP-1 receptor agonist in 34 patients (13.6%). Combined SGLT-2 inhibitor and GLP-1 receptor agonist therapy was documented in 16 patients (6.4%), while 11 patients (4.4%) received triple therapy including at least one modern cardiometabolic agent. The remaining 53 patients (21.2%) received less frequently observed regimens. The mutually exclusive categories presented in Table 3 account for the entire cohort.

Table 3. Pharmacological treatment regimens in the study population.

Therapeutic Regimen	<i>n</i>	%
Metformin monotherapy	66	26.4
Metformin + sulfonylurea	39	15.6
Metformin + SGLT-2 inhibitor	31	12.4
Metformin + GLP-1 receptor agonist	34	13.6
SGLT-2 inhibitor + GLP-1 receptor agonist	16	6.4
Triple therapy including at least one modern cardiometabolic agent	11	4.4
Other pharmacological regimens	53	21.2
Total	250	100.0

Data are presented as number and percentage of the total cohort. Regimen categories are mutually exclusive, and each patient is counted once according to the complete pharmacological regimen documented at the index visit. “Other pharmacological regimens” includes all less frequently observed monotherapy and combination regimens that did not meet the prespecified categories listed separately. Modern cardiometabolic agents were defined as GLP-1 receptor agonists and SGLT-2 inhibitors. GLP-1, glucagon-like peptide-1 receptor agonist; SGLT-2, sodium-glucose cotransporter-2 inhibitor. Available-case denominators were used.

3.4. HbA1c Profiles According to Pharmacological Exposure

Glycemic profiles across pharmacological-class exposures were described using baseline HbA1c, follow-up HbA1c, and the corresponding change between the two measurements. Because these pharmacological-class exposures were non-mutually exclusive, the findings represent observed glycemic profiles rather than comparative treatment effects.

The lowest mean follow-up HbA1c values were observed among patients receiving GLP-1 receptor agonists ($7.58 \pm 1.60\%$) and SGLT-2 inhibitors ($7.62 \pm 1.50\%$), whereas the highest value was observed among patients receiving DPP-4 inhibitors ($8.50 \pm 1.50\%$). The largest mean HbA1c reductions were observed for SGLT-2 inhibitors (-0.89 percentage points) and GLP-1 receptor agonists (-0.82 percentage points). Smaller reductions were observed for sulfonylureas (-0.57 percentage points) and metformin (-0.31 percentage points), whereas the DPP-4 inhibitor group showed a mean increase of 0.44 percentage points. These class-level findings are descriptive because patients receiving combination

therapy may contribute to more than one row in Table 4. Formal comparisons based on mutually exclusive therapeutic exposure groups are reported in Section 3.7.

Table 4. Baseline and follow-up HbA1c according to non-mutually exclusive pharmacological class exposures.

Therapy	<i>n</i>	Baseline HbA1c, Mean $\pm$ SD (%)	Follow-Up HbA1c, Mean $\pm$ SD (%)	Mean HbA1c Change, Percentage Points
Metformin	147	8.16 $\pm$ 1.78	7.85 $\pm$ 1.72	−0.31
Sulfonylureas	64	8.42 $\pm$ 2.07	7.85 $\pm$ 1.63	−0.57
GLP-1 receptor agonists	72	8.40 $\pm$ 1.97	7.58 $\pm$ 1.60	−0.82
DPP-4 inhibitors	15	8.06 $\pm$ 1.07	8.50 $\pm$ 1.50	+0.44
SGLT-2 inhibitors	69	8.51 $\pm$ 1.71	7.62 $\pm$ 1.50	−0.89

Data are presented as mean $\pm$ standard deviation. Pharmacological-class exposures were non-mutually exclusive; therefore, patients receiving combination therapy may contribute to more than one row. Baseline HbA1c was recorded at the index visit, and follow-up HbA1c was the subsequent available measurement. HbA1c change was calculated as follow-up minus baseline HbA1c; negative values indicate a reduction and positive values indicate an increase. These findings are descriptive and should not be interpreted as estimates of comparative treatment effectiveness.

3.5. Glycemic Evolution and Cross-Sectional Cardiorenal Profiles According to Therapeutic Exposure

Paired baseline and follow-up measurements were available for HbA1c, whereas eGFR, CRP, triglycerides, blood pressure, LDL cholesterol, and heart failure status were available only at the index assessment. The combined GLP-1 receptor agonist and SGLT-2 inhibitor group showed the largest numerical HbA1c reduction, a higher mean eGFR, and a lower prevalence of previously documented heart failure. The remaining cardiorenal and metabolic parameters also varied across groups, but these measurements represent cross-sectional clinical profiles rather than within-patient treatment-related changes (Table 5).

Table 5. HbA1c evolution and index cardiorenal profile according to mutually exclusive therapeutic exposure groups.

Parameter	GLP-1 RA Only, <i>n</i> = 56	SGLT-2i Only, <i>n</i> = 54	GLP-1 RA + SGLT-2i, <i>n</i> = 17	No Modern Cardiometabolic Agents, <i>n</i> = 123
Glycemic measurements				
Baseline HbA1c, %	8.34 $\pm$ 2.01	8.43 $\pm$ 1.65	8.54 $\pm$ 1.97	7.98 $\pm$ 1.77
Follow-up HbA1c, %	7.71 $\pm$ 1.70	7.70 $\pm$ 1.55	7.14 $\pm$ 1.19	7.98 $\pm$ 1.62
HbA1c change, percentage points	−0.64 $\pm$ 1.95	−0.73 $\pm$ 1.70	−1.40 $\pm$ 1.17	0.00 $\pm$ 1.39
Cardiorenal and metabolic parameters recorded at the index assessment				
eGFR, mL/min/1.73 m ²	75.1 $\pm$ 23.8	75.3 $\pm$ 24.8	86.2 $\pm$ 14.3	76.2 $\pm$ 23.3
CRP, mg/dL	0.78 (0.40–2.21)	0.33 (0.17–0.83)	0.40 (0.31–0.57)	0.46 (0.19–1.21)
Triglycerides, mg/dL	146 (99–196)	145 (90–209)	159 (134–201)	144 (108–220)
Heart failure, <i>n</i> (%)	30 (53.6%)	19 (37.3%)	2 (13.3%)	51 (42.9%)
SBP, mmHg	145.0 $\pm$ 19.6	145.6 $\pm$ 19.1	138.9 $\pm$ 21.8	145.0 $\pm$ 18.6

Table 5. Cont.

Parameter	GLP-1 RA Only, <i>n</i> = 56	SGLT-2i Only, <i>n</i> = 54	GLP-1 RA + SGLT-2i, <i>n</i> = 17	No Modern Cardiometabolic Agents, <i>n</i> = 123
DBP, mmHg	85.6 ± 13.6	86.1 ± 13.2	82.8 ± 14.2	86.3 ± 12.0
LDL-C, mg/dL	109.5 (83.8–132.0)	107.0 (66.0–138.5)	141.0 (111.0–171.0)	110.0 (76.5–132.0)

Data are presented as mean ± standard deviation for approximately symmetrically distributed variables, median (interquartile range) for skewed variables, and number (percentage) for categorical variables. Therapeutic exposure groups were mutually exclusive: GLP-1 RA only, SGLT-2i only, combined GLP-1 RA + SGLT-2i therapy, and no GLP-1 RA or SGLT-2i exposure. HbA1c change was calculated as follow-up minus baseline HbA1c; negative values indicate a reduction. Paired baseline and follow-up measurements were available only for HbA1c. The remaining cardiorenal and metabolic variables were recorded at the index assessment and were analyzed cross-sectionally. One CRP value and one triglyceride value were missing; analyses were conducted using available data. GLP-1 RA, glucagon-like peptide-1 receptor agonist; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol. CRP and triglycerides each had one missing observation; the remaining analyses were performed using the available data.

3.6. Multivariate Predictors of Poor Glycemic Control

A multivariate logistic regression model was performed to identify independent clinical and therapeutic predictors of poor glycemic control (HbA1c > 7%). The model included age, sex, body mass index, diabetes duration, major cardiometabolic comorbidities (ischemic heart disease, heart failure, and chronic kidney disease), and exposure to the principal antidiabetic drug classes.

The overall model was statistically significant (Omnibus $\chi^2 = 27.55$, *df* = 12, *p* = 0.006), demonstrated acceptable calibration (Hosmer–Lemeshow $\chi^2 = 7.93$, *p* = 0.440), and explained a modest proportion of the variance in glycemic control (Nagelkerke $R^2 = 0.145$).

After multivariable adjustment, increasing age was independently associated with a lower likelihood of poor glycemic control (OR = 0.957 per year; 95% CI 0.928–0.987; *p* = 0.006). Conversely, longer diabetes duration emerged as an independent predictor of HbA1c > 7% (OR = 1.084 per year; 95% CI 1.028–1.143; *p* = 0.003).

No significant independent associations were observed for sex, body mass index, ischemic heart disease, heart failure, chronic kidney disease, metformin, sulfonylureas, DPP-4 inhibitors, SGLT-2 inhibitors, or GLP-1 receptor agonists after adjustment for potential confounders. Although GLP-1 receptor agonists showed a numerical inverse association with poor glycemic control (OR = 0.574; 95% CI 0.301–1.093), this finding did not reach statistical significance (*p* = 0.091).

Overall, these findings suggest that patient-related factors, particularly diabetes duration and age, were more strongly associated with glycemic control than pharmacological treatment class within this real-world cohort (Table 6).

Table 6. Multivariate logistic regression analysis of predictors of poor glycemic control (HbA1c > 7%).

Variable	β Coefficient	OR	95% CI	<i>p</i> -Value
Age (per year)	−0.044	0.957	0.928–0.987	0.006
Male sex	−0.321	0.725	0.411–1.280	0.268
BMI (per kg/m ²)	−0.003	0.997	0.944–1.053	0.919
Duration of diabetes (per year)	0.081	1.084	1.028–1.143	0.003
Ischemic heart disease	−0.649	0.523	0.225–1.213	0.131
Heart failure	0.339	1.403	0.748–2.631	0.291
Chronic kidney disease	0.411	1.508	0.714–3.187	0.282
Metformin	−0.054	0.948	0.518–1.735	0.862

Table 6. *Cont.*

Variable	β Coefficient	OR	95% CI	<i>p</i> -Value
GLP-1 receptor agonists	−0.555	0.574	0.301–1.093	0.091
DPP-4 inhibitors	1.165	3.205	0.656–15.666	0.150
SGLT-2 inhibitors	−0.204	0.815	0.425–1.566	0.540
Sulfonylureas	0.105	1.111	0.568–2.172	0.758

Model statistics: $\chi^2 = 27.55$, $df = 12$, $p = 0.006$; Nagelkerke $R^2 = 0.145$; Hosmer–Lemeshow goodness-of-fit test $p = 0.440$; overall classification accuracy = 68.8%. Abbreviations: BMI, body mass index; GLP-1, glucagon-like peptide-1 receptor agonists; DPP-4, dipeptidyl peptidase-4 inhibitors; SGLT-2, sodium–glucose cotransporter-2 inhibitors; OR, odds ratio; CI, confidence interval.

3.7. Comparative Analysis Across Therapeutic Exposure Groups (Revised)

Comparative analysis across the four mutually exclusive therapeutic groups (GLP-1 only, SGLT-2 only, combined SGLT-2 + GLP-1 therapy, and no modern agents) was performed using one-way analysis of variance (ANOVA) followed by Tukey’s post hoc correction for multiple comparisons.

For HbA1c, the overall ANOVA did not reveal statistically significant differences between groups ($F = 1.79$, $p = 0.149$), although numerically lower mean values were observed in the combined therapy group. In particular, the combined SGLT-2 + GLP-1 subgroup showed lower HbA1c values compared with patients receiving no modern agents (mean difference = −0.91%, adjusted $p = 0.172$), GLP-1 therapy alone (mean difference = −0.55%, adjusted $p = 0.647$), and SGLT-2 therapy alone (mean difference = −0.61%, adjusted $p = 0.578$); however, none of these comparisons reached statistical significance after Tukey correction.

Similarly, no statistically significant differences were observed for C-reactive protein (CRP) ($F = 1.22$, $p = 0.304$) or estimated glomerular filtration rate (eGFR) ($F = 1.67$, $p = 0.173$).

Post hoc analysis of renal function demonstrated a numerically higher eGFR in the combined therapy group compared with GLP-1 therapy alone (mean difference = +14.69 mL/min/1.73 m², adjusted $p = 0.129$), although this difference did not remain statistically significant after adjustment for multiple comparisons.

Overall, Tukey post hoc testing confirmed the absence of statistically significant pairwise differences across all analyzed parameters after correction for multiple testing (Table 7).

Table 7. Post hoc Tukey multiple comparison analysis of HbA1c and eGFR across mutually exclusive therapeutic groups.

Outcome	Comparison	Mean Difference	Adjusted <i>p</i> Value
HbA1c	No modern vs. SGLT2 + GLP1	−0.91	0.172
HbA1c	GLP1 vs. SGLT2 + GLP1	−0.55	0.647
HbA1c	SGLT2 vs. SGLT2 + GLP1	−0.61	0.578
eGFR	GLP1 vs. SGLT2 + GLP1	+14.69	0.129

Data are presented as mean differences between groups with Tukey-adjusted p values following one-way ANOVA. Negative values indicate lower mean values in the combined SGLT-2 + GLP-1 group.

4. Discussion

The present retrospective real-world study characterized non-insulin antidiabetic treatment patterns and their associations with glycemic and cardiorenal profiles in 250 adults with type 2 diabetes managed in specialist outpatient care. The cohort was characterized by a high prevalence of obesity, metabolic syndrome, cardiovascular disease, and chronic kidney disease, reflecting a clinically complex and high-risk population.

Metformin remained the most frequently prescribed glucose-lowering therapy, while GLP-1 receptor agonists and SGLT-2 inhibitors were also commonly used, either alone or as components of combination regimens. Patients exposed to these newer classes showed numerically lower follow-up HbA1c values and greater mean HbA1c reductions. However, comparisons across mutually exclusive exposure groups did not remain statistically significant after correction for multiple testing. Similarly, differences in CRP and eGFR were not statistically significant [11–16].

The baseline heterogeneity shown in Supplementary Table S1 provides direct evidence of confounding by indication. Patients receiving GLP-1 receptor agonists, SGLT-2 inhibitors, their combination, or neither class differed in age, body mass index, baseline HbA1c, renal function, and prevalence of ischemic heart disease, heart failure, and chronic kidney disease. These characteristics are clinically relevant determinants of treatment selection in routine practice and may also influence subsequent glycemic and cardiorenal measurements [15,16].

For example, SGLT-2 inhibitors may be preferentially prescribed to patients with established heart failure or chronic kidney disease, whereas GLP-1 receptor agonists may be selected more frequently in patients with obesity or a need for additional weight reduction. Conversely, renal impairment, treatment tolerance, reimbursement restrictions, disease duration, or physician preference may limit the use of particular therapies. Therefore, the numerically favourable profiles observed in some treatment groups cannot be separated from the clinical characteristics that influenced treatment allocation [12,13].

Although multivariable adjustment included several major covariates, the limited subgroup sizes and absence of data on treatment duration, dose, adherence, prior therapy, and treatment changes prevented comprehensive control of confounding. The results should therefore be interpreted as descriptions of clinically selected treatment groups rather than estimates of pharmacological effectiveness.

Baseline differences between therapeutic groups, presented in Supplementary Table S1, indicate substantial confounding by indication. In routine clinical practice, treatment selection is influenced by obesity, renal function, cardiovascular disease, heart failure, baseline glycemic control, treatment tolerance, reimbursement conditions, and physician preference. Therefore, the observed profiles may reflect both the clinical characteristics of the patients and the factors influencing treatment allocation.

The numerically higher HbA1c observed among patients receiving DPP-4 inhibitors may reflect the preferential use of these agents in older individuals or patients with a different clinical and metabolic risk profile rather than an unfavorable pharmacological effect [17]. Likewise, the renal profile of patients receiving metformin may partly reflect its more frequent use in individuals with better preserved kidney function [17–22].

The present findings are broadly consistent with the DIAMOND2 study, which demonstrated the continued difficulty of simultaneously achieving glycemic and weight-related targets in routine clinical practice. Although direct comparisons are limited by differences in study setting, both studies document increasing use of GLP-1 receptor agonists and SGLT-2 inhibitors and emphasize the complex relationship between glycemic control, obesity, and cardiovascular–renal risk [23].

Heart failure prevalence varied between treatment groups. These differences were likely influenced by baseline cardiovascular risk and treatment selection. Although SGLT-2 inhibitors have established benefits in heart failure populations, the cross-sectional design of the present study does not permit evaluation of treatment-related changes in heart failure risk or severity [5,24,25].

Longer diabetes duration was independently associated with poor glycemic control, consistent with progressive β -cell dysfunction and increasing treatment complexity over time [26,27]. Conversely, increasing age was associated with a lower probability of

HbA1c > 7%, potentially reflecting individualized glycemic targets, differences in treatment intensity, or greater adherence among older patients [28–30].

An additional methodological consideration is the use of conventional CRP rather than high-sensitivity CRP. Conventional CRP was the routinely available inflammatory marker in the clinical database but is less sensitive for evaluating chronic low-grade cardiometabolic inflammation. The inflammatory findings should therefore be interpreted within this analytical limitation [5,31,32].

Study Limitations

This study has several limitations. Its retrospective, single-center, and non-randomized design precludes causal inference and remains susceptible to residual confounding and confounding by indication. Patients treated with insulin were excluded; consequently, the results apply only to adults with type 2 diabetes receiving non-insulin therapy. Information on medication dose, treatment duration, adherence, prior therapy, treatment modifications, diet, and physical activity was not systematically available. The relatively small size of some exposure groups and the absence of an a priori sample-size calculation may have limited statistical power.

Ischemic heart disease was based on previously documented cardiology diagnoses, while the specific diagnostic method could not be uniformly adjudicated. Furthermore, paired measurements were consistently available only for HbA1c. Cardiorenal and metabolic variables were assessed cross-sectionally and therefore cannot be interpreted as changes caused by a particular pharmacological regimen.

Despite these limitations, the study provides a clinically relevant description of contemporary non-insulin treatment patterns in a high-risk specialist-care population. Diabetes duration, rather than exposure to a specific pharmacological class, was the principal independent determinant of poor glycemic control.

5. Conclusions

In this real-world observational study, pharmacological management of diabetes mellitus was associated with numerical differences in glycemic control and cardiovascular–renal risk profiles. The study population was characterized by advanced age, a high prevalence of obesity and metabolic syndrome, and a substantial burden of cardiovascular and renal comorbidities, reflecting the complexity of contemporary diabetic patients.

Modern antidiabetic therapies, particularly GLP-1 receptor agonists and SGLT-2 inhibitors, showed numerical trends toward more favorable glycemic and cardiometabolic profiles. However, these differences were not statistically significant after adjustment for multiple comparisons and should therefore be interpreted as exploratory observations rather than evidence of comparative effectiveness. In contrast, longer duration of diabetes emerged as a key determinant of poor metabolic control, highlighting the progressive nature of the disease and the need for timely therapeutic optimization.

These findings highlight the complexity of real-world treatment patterns and support the need for prospective, adequately powered studies to clarify the clinical impact of contemporary pharmacological strategies. Further prospective and randomized studies are required to confirm these associations and to better define individualized therapeutic approaches in complex cardiometabolic populations.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/diabetology7080145/s1>, Table S1: Baseline characteristics according to mutually exclusive therapeutic exposure.

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Abbreviations

The following abbreviations are used in this manuscript:

BMI	body mass index
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CRP	C-reactive protein
DPP-4	dipeptidyl peptidase-4
eGFR	estimated glomerular filtration rate
GLP-1	glucagon-like peptide-1
HbA1c	glycated hemoglobin
HF	heart failure
IHD	ischemic heart disease
LDL	low-density lipoprotein cholesterol
MetS	metabolic syndrome
MI	myocardial infarction
PAD	peripheral arterial disease
SD	standard deviation
SGLT-2	sodium–glucose cotransporter-2
T2DM	type 2 diabetes mellitus
SBP	systolic blood pressure
DBP	diastolic blood pressure

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