

# Use of anti-hyperglycemic medications in patients with incident CKD and T2D by CKD severity: a descriptive study using a large US electronic health records database

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## Introduction

- Patients with type 2 diabetes mellitus (T2D) are at high risk for developing chronic kidney disease (CKD)
- Glycemic control plays a pivotal yet challenging role in disease management for patients with T2D developing CKD
- Moreover, the onset of CKD with T2D and treatment-related complications further complicates T2D management
- This study aimed to characterize treatment patterns and reveal unmet needs in T2D management among patients with new onset CKD and prior T2D to inform clinical practice

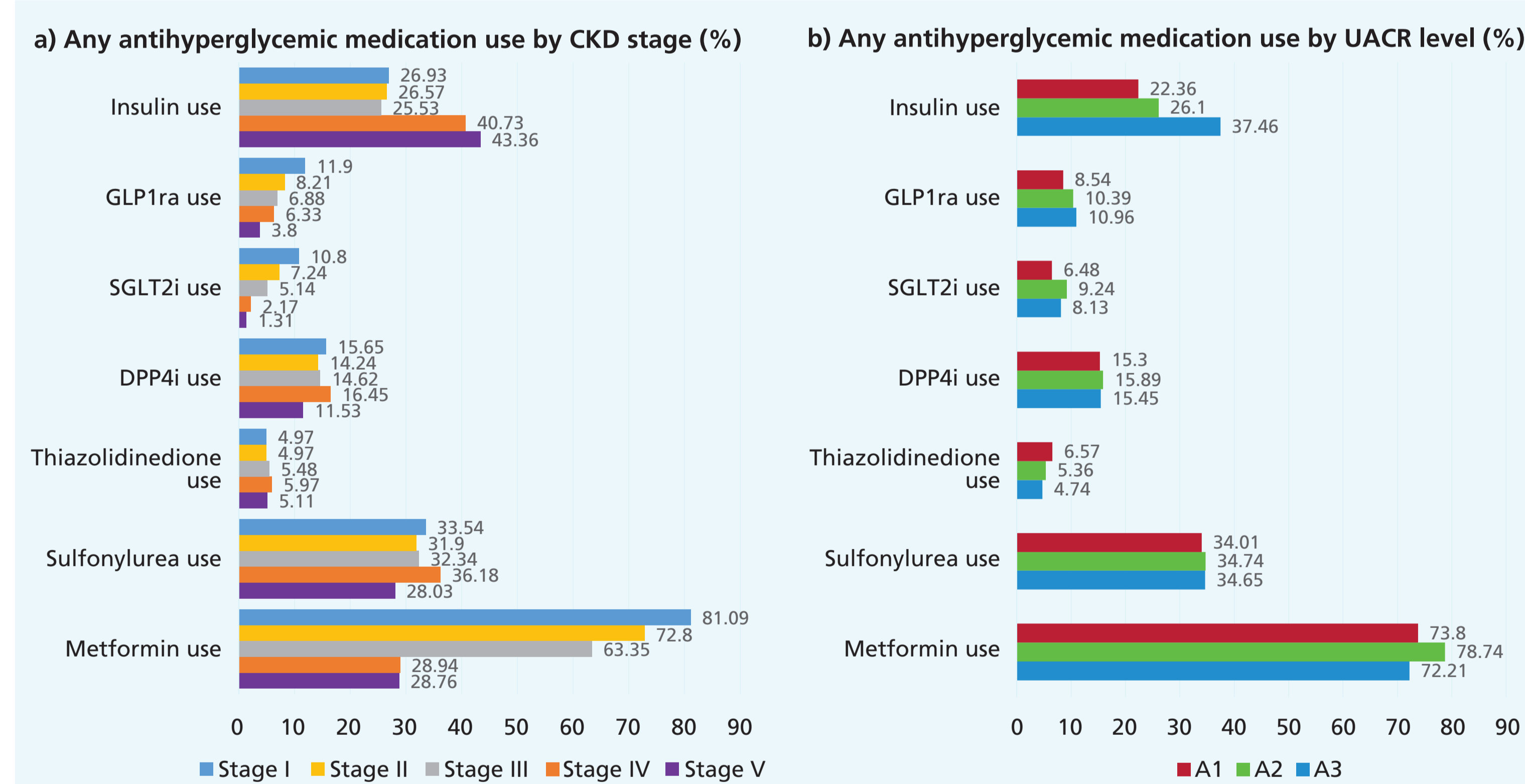
## Methods

- Adult patients with prevalent T2D and incident CKD were identified between March 2013 and September 2021 from the Optum electronic medical records (EMR) database
- CKD was defined as having either a) diagnostic codes for CKD, b) two estimated glomerular filtration rate (eGFR) values <60 mL/min/1.73m<sup>2</sup> measured 90 to 548 days apart, or c) two urine albumin-creatinine ratio (UACR) values ≥30 mg/g measured 90 to 548 days apart
- The baseline period was defined as 1 year prior to the incident CKD diagnosis (i.e., index date) and patients were followed until death, end of continuous eligibility or the end of data period
- Patterns of antihyperglycemic medication use were assessed during both the baseline and follow-up periods and described by baseline HbA1c level (controlled [ $<7\%$ ] vs. elevated [ $\geq 7\%$ ]), CKD stages (Stage I-V, defined as eGFR ≥90, 60-89, 30-59, 15-29, and <15 mL/min/1.73 m<sup>2</sup>, respectively), and UACR levels (A1-A3, defined as UACR <30, 30-300, and >300 mg/g, respectively)
- Treatment changes were assessed on a class level and defined as initiation of a new treatment relative to baseline medication
- This study was conducted in compliance with the FOUNTAIN research platform medical definitions and methods

## Results

- A total of 262,395 patients with T2D and incident CKD were included in the study (mean age: 66.5; female: 51.1%; white: 79.5%)
- Baseline CKD stage and UACR level were available for 84.3% and 61.0% of patients, respectively, with most patients (45.0%) in CKD Stage III, followed by Stage I (19.7%) and II (17.7%), and only a small proportion in Stage IV (1.6%) and V (0.3%). For UACR, 18.9%, 35.1% and 7.0% of patients were in A1, A2 and A3 categories, respectively
- Among patients with HbA1c measurements, 51.2% had an elevated HbA1c ( $\geq 7\%$ )
- Patients with elevated HbA1c tended to have elevated UACR (categories A2 [43.6%] and A3 [9.6%]) and Stage I CKD (26.3%) compared with those with controlled HbA1c ( $< 7\%$ ) (A2 UACR: 33.6%; A3 UACR: 5.6%; Stage I CKD: 16.5%) at baseline
- Patients with elevated HbA1c used more antihyperglycemics than those with controlled HbA1c (number of antihyperglycemic medication classes: 2.1 vs. 1.5) and were more likely to use DPP4i (18.7% vs. 11.3%), SGLT2i (10.2% vs. 3.8%) and GLP-1 RA (11.6% vs. 5.6%) at baseline
- Patients with advanced CKD stages tended to use less metformin, SGLT2i and GLP-1ra, but more insulin at baseline compared with its use in milder CKD stages (Figure 1a)
- In contrast, little variation was observed for the baseline prescribed drug classes across UACR categories except for insulin, which was predominantly used in patients in the most severe UACR level (A3) (Figure 1b)
- The observed utilization of modern agents (e.g., GLP-1 RA and SGLT2i) in patients with moderate to severe CKD was not high by 2021, reflecting their recent approval for CKD and non-prompt inclusion in clinical guidance

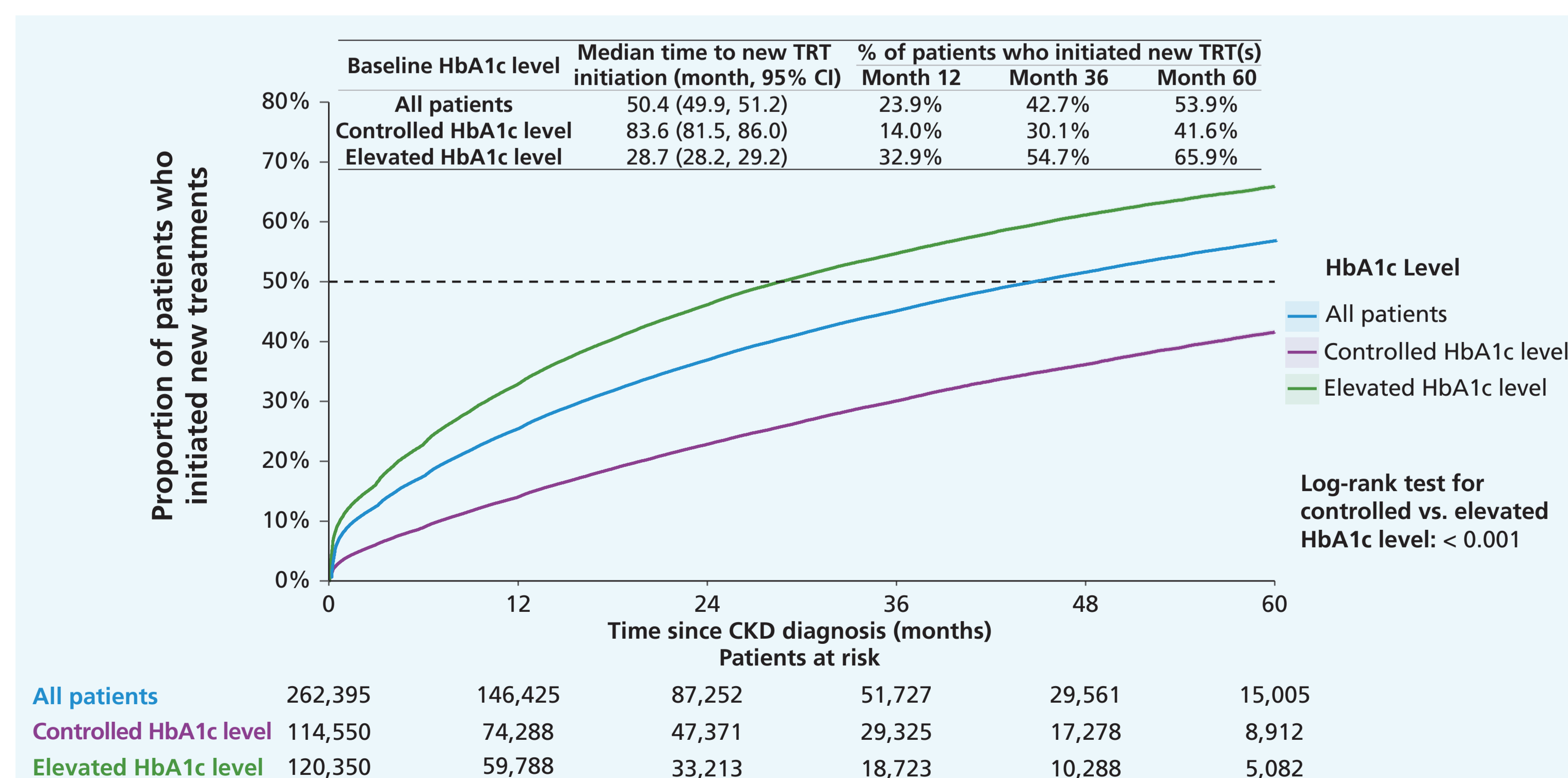
**Figure 1.** Proportion of patients using antihyperglycemics during the baseline period by CKD stage and UACR level



Abbreviations: CKD, chronic kidney disease; DPP-4i: dipeptidyl peptidase-4 inhibitor; GLP-1 RA: glucagon-like peptide 1 receptor agonist; HbA1c: hemoglobin A1c; SGLT2i: sodium-glucose cotransporter-2 inhibitor; UACR: urine albumin to creatinine ratio.

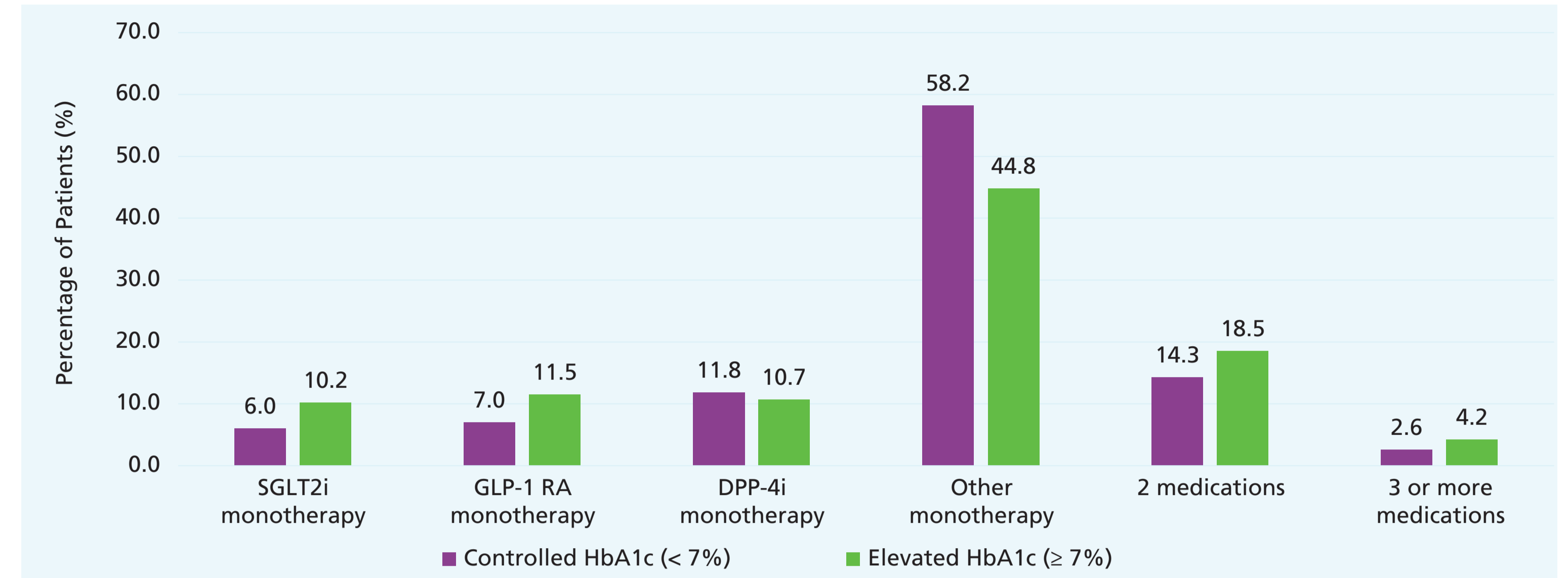
- Almost a quarter of patients initiated at least one new T2D treatment within one year after CKD onset, with a median time to new treatment initiation of 50.4 months.
- Patients with elevated HbA1c initiated a new treatment sooner (Figure 2) and tended to initiate two or more medication classes within one year after CKD onset compared with those with controlled HbA1c (Figure 3)

**Figure 2.** Cumulative incidence of new T2D treatment initiations by baseline HbA1c level



Abbreviations: CI: confidence interval; HbA1c: hemoglobin A1c; T2D: type 2 diabetes; TRT: treatment. Note: Patients without baseline HbA1c measurement (n = 27,495) were excluded from the stratified analysis by diabetes management status.

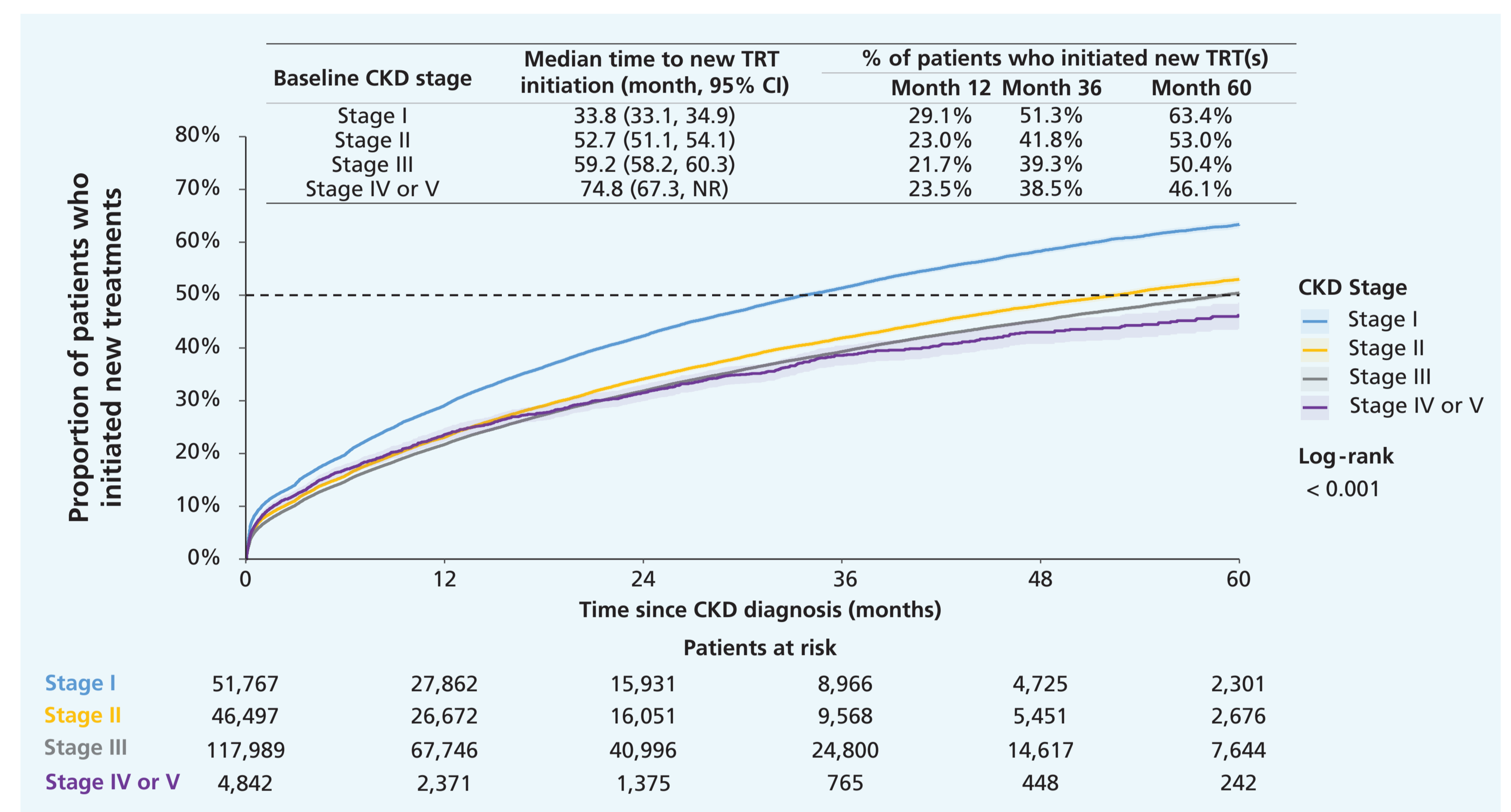
**Figure 3.** Distribution of newly initiated T2D treatments within one year among patients who initiated new T2D treatments, stratified by baseline HbA1c level



Abbreviations: DPP-4i: dipeptidyl peptidase-4 inhibitor; GLP-1 RA: glucagon-like peptide 1 receptor agonist; HbA1c: hemoglobin A1c; SGLT2i: sodium-glucose cotransporter-2 inhibitor; T2D: type 2 diabetes.

- Patients with advanced CKD stages were less likely to use new T2D treatments with longer time from CKD onset to treatment initiation (74.8 months for Stage IV/V CKD) to Stage I CKD (33.8 months). (Figure 4)

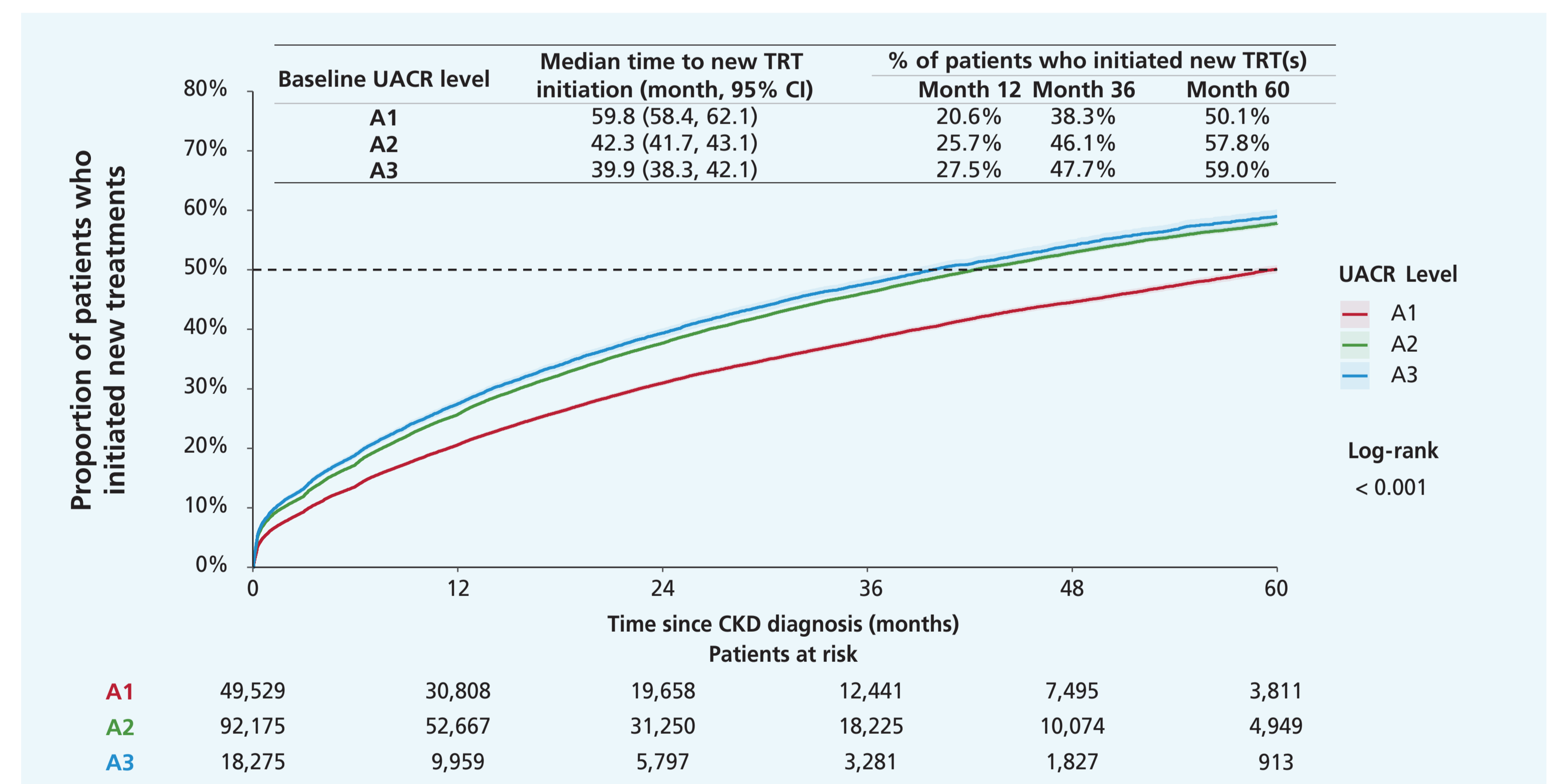
**Figure 4.** Cumulative incidence of new T2D treatment initiations by baseline CKD stage



Abbreviations: CI: confidence interval; CKD, chronic kidney disease; T2D: type 2 diabetes; TRT: treatment; NR: not reached. Note: Patients without baseline CKD stage information (n = 41,300) were excluded from the stratified analysis by CKD stage.

- On the contrary, patients with elevated UACR were more likely to initiate new T2D treatments with shorter median time to treatment initiation (42.3 and 39.9 months for A2 and A3 UACR respective) compared with those in A1 UACR (59.8 months). (Figure 5)

**Figure 5.** Cumulative incidence of new T2D treatment initiations by baseline UACR level



Abbreviations: CI: confidence interval; T2D: type 2 diabetes; TRT: treatment; UACR: urine albumin to creatinine ratio. Note: Patients without baseline UACR measurement (n = 102,416) were excluded from the stratified analysis by UACR level.

- 50.5% of patients using SGLT2i monotherapy at baseline initiated new treatment within a year after CKD onset with the median time to new treatment initiation of 11.6 months

## Limitations

- As with all EMR data, medical and pharmacy records obtained outside of the healthcare network were not captured
- Information pertaining to treatment dose and duration was lacking; treatment discontinuation and dose adjustment were therefore not assessed

## Conclusions

- The T2D treatment patterns vary by HbA1c level and CKD severity, implying complexities in T2D management when developing CKD
- Overall, the results show that T2D management was considerably heterogeneous and challenging when patients develop CKD
- Modern agents alone may not be sufficient for glucose control and disease management in patients with T2D and CKD

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## Disclosures

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