

BACKGROUND

- Sodium-glucose co-transporter 2 (SGLT2) inhibitors** demonstrate **cardiorenal benefits** in the general population
- Acutely**, **SGLT2 inhibitors** can cause a “**dip**” in **estimated glomerular filtration rate (eGFR)**
- People with HIV (PWH)** may be more **vulnerable to renal complications**
- Limited data** on renal safety of SGLT2 inhibitors in **PWH**

OBJECTIVE

Assess the **risk of acute eGFR decline** with SGLT2 inhibitors compared to other antihyperglycemic classes among PWH

METHODS

Study Design & Data Source:

- Propensity score-matched cohort study** using data from **9 sites** from the **Centers for AIDS Research Network of Integrated Clinical Systems (CNICS)**, a large, multi-center cohort of **PWH receiving routine clinical care** across the U.S.

Inclusion Criteria:

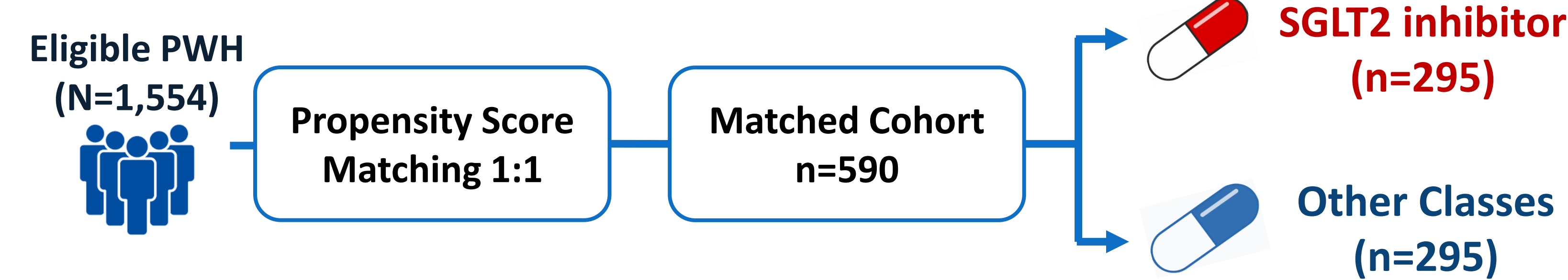
- PWH **initiating SGLT2 inhibitors or other antihyperglycemic classes**: GLP-1 receptor agonists (GLP-1RA) OR DPP-4 inhibitors (DPP4i) OR Sulfonylureas (SU) between **2013–2023**
- ≥2 eGFR measurements** (baseline + within 6 months of medication initiation)
- Baseline **eGFR ≥15 mL/min/1.73 m²**
- Follow-up**: Two approaches - **intention-to-treat (ITT)** and **on-treatment**
 - ITT: Followed until outcome occurrence, loss to follow-up, or 6 months post-medication initiation
 - On-treatment: Same as above + medication discontinuation or switching

Outcomes (within 6 months of medication initiation):

- Time to ≥30% eGFR decline**
- Time to ≥10 mL/min/1.73 m² eGFR decrease**
- Mean change in eGFR (on-treatment analysis)**

Statistical Analysis:

- 1:1 propensity score (PS) matching**; PS estimated via logistic regression using baseline age, sex, race/ethnicity, diabetes, hypertension, eGFR (categorical), viral load, CD4 count, use of ART, TDF, insulin, metformin, statins, and smoking status
- Covariate balance** was assessed using **standardized mean differences (SMD)**; Diabetes (SMD >10%) was adjusted for in multivariable models
- Time-to-event outcomes**: Analyzed using **Cox proportional hazards models**
- Continuous outcome (eGFR change)**: Analyzed using **linear mixed models**



Acute Drop in eGFR When Initiating SGLT2 Inhibitors vs. Other Antihyperglycemic Medications Among People with HIV

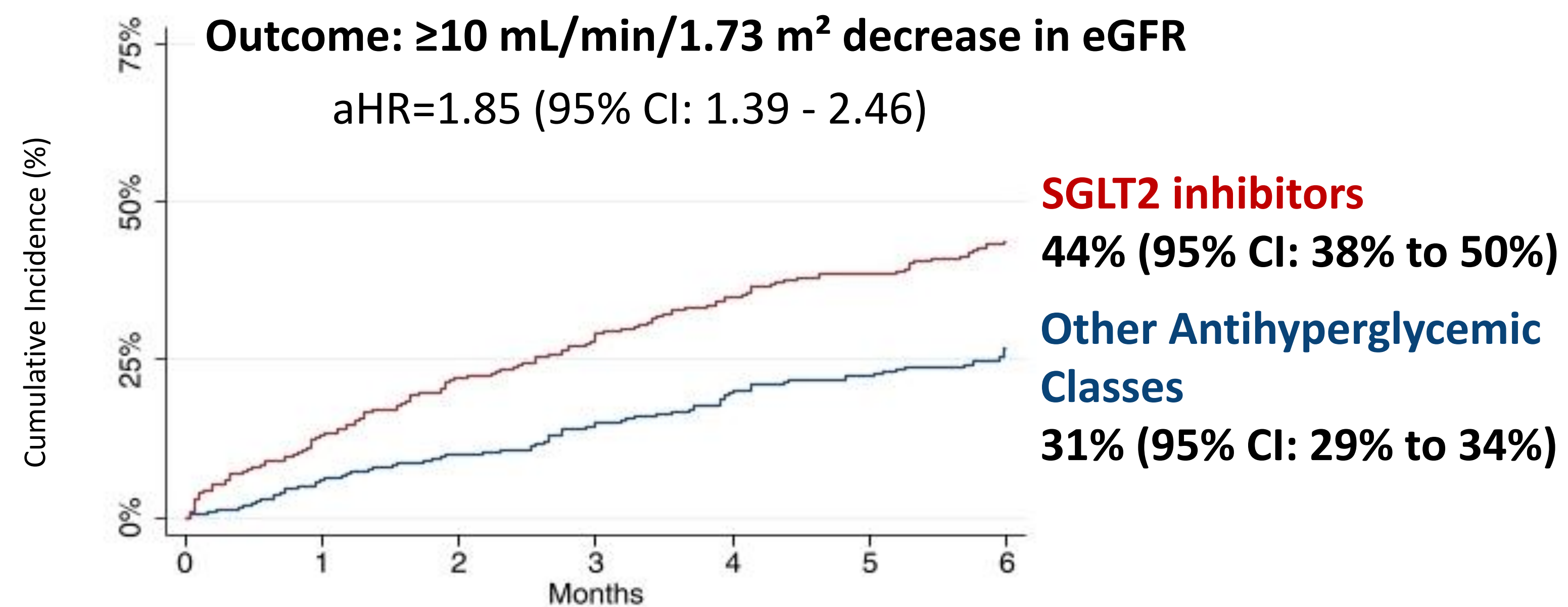
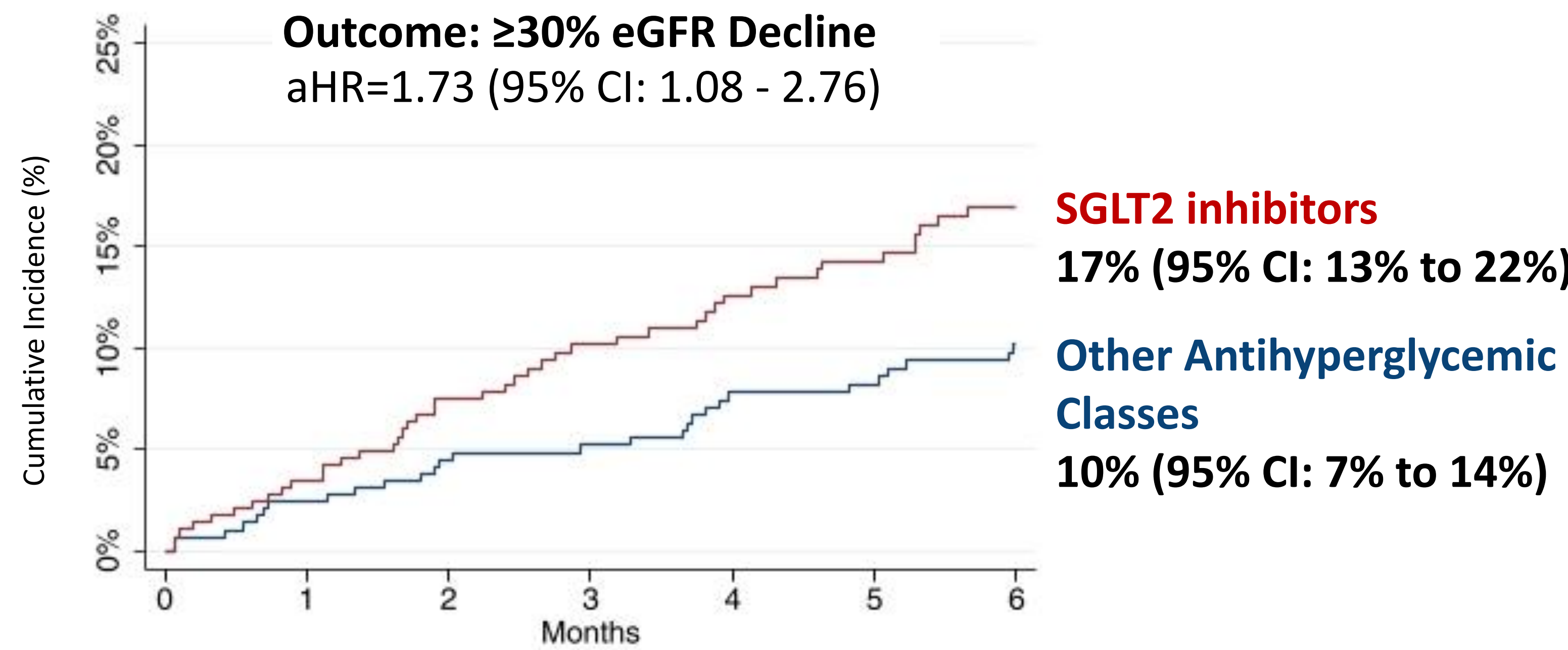
SGLT2 inhibitors increased the risk of *acute* eGFR decline in PWH, but the decline was small and comparable to the general population

Table 1. Baseline Characteristics of SGLT2 Inhibitor Users vs. Other Antihyperglycemic Classes After Propensity Score Matching

Characteristic	SGLT2i (n, %)	Others ^a (n, %)	SMD ^b (%)
Age (years) (Mean, SD)	56 (10)	57 (10)	5.5
Male	237 (80%)	245 (83%)	7.0
Race			
White	111 (38%)	106 (36%)	4.4
Black	143 (49%)	147 (50%)	
Hispanic	27 (9%)	29 (10%)	
Other	14 (5%)	13 (4%)	
eGFR (mL/min/1.73 m²) (Mean, SD)	71 (23)	71 (23)	1.7
eGFR categories			
≥ 90	70 (24%)	71 (24%)	8.3
≥ 60 to <90	129 (44%)	119 (40%)	
≥ 30 to <60	87 (30%)	97 (33%)	
≥ 15 to <30	9 (3%)	8 (3%)	
Diabetes	203 (69%)	218 (74%)	11.3
Treated Hypertension	223 (76%)	230 (78%)	5.6
CD4 Count (Mean, SD)	675 (375)	665 (347)	2.7
VL <200 copies/mL	271 (92%)	274 (93%)	3.8
Concomitant Baseline Medications			
ART	287 (97%)	286 (97%)	2.0
TDF	44 (15%)	42 (14%)	1.9
Insulin	63 (21%)	67 (23%)	3.3
Metformin	112 (38%)	124 (42%)	8.3
Statins	202 (69%)	204 (69%)	1.5

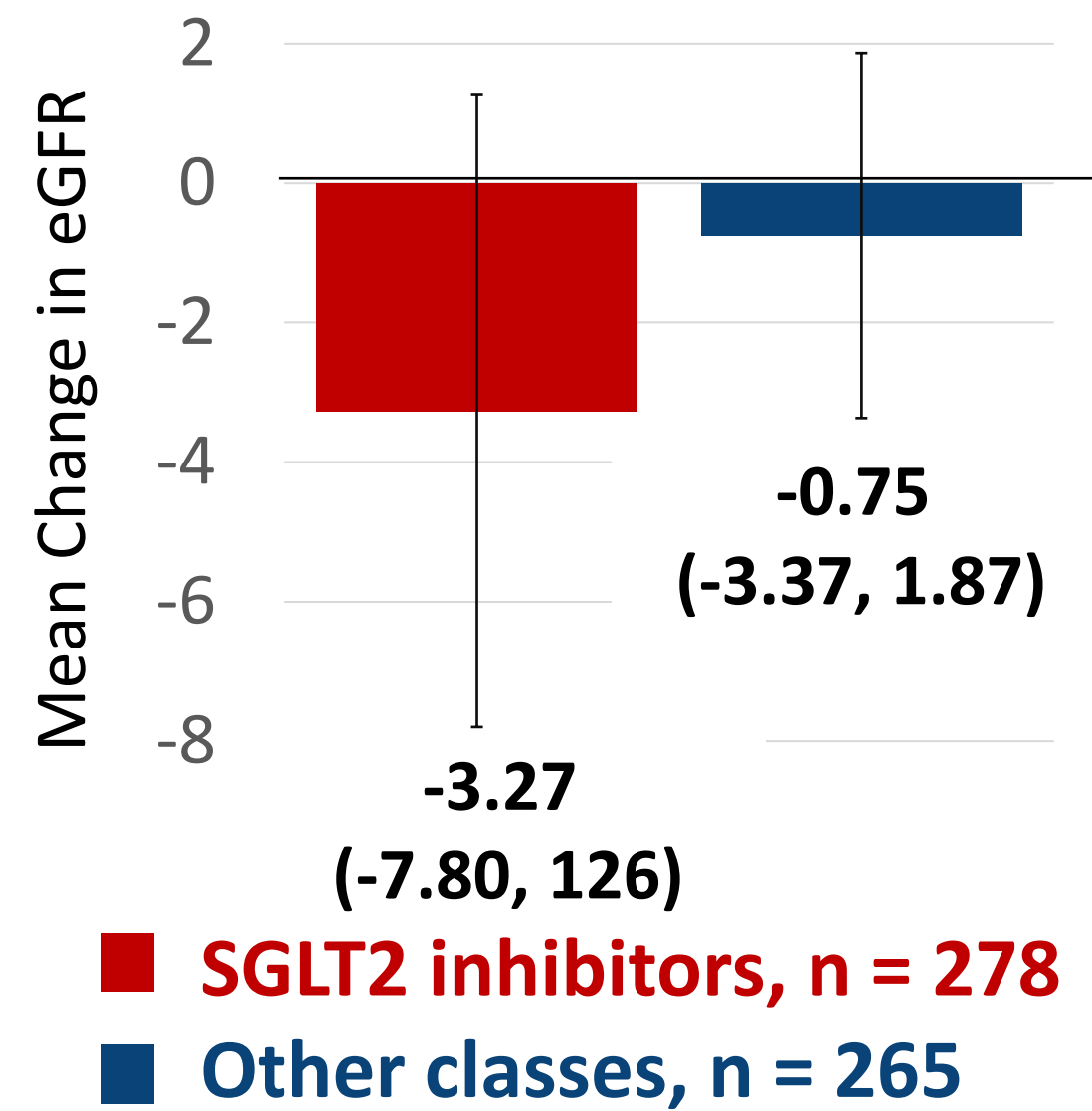
Note: ^a “Others” group consists of GLP-1 RA (n=151), DPP-4 inhibitors (n=48), and sulfonylureas (n=96).
^b SMD <10% indicates good balance between groups.
Abbreviations: SMD: Standardized mean difference, SGLT2i: Sodium-glucose cotransporter-2 inhibitor, eGFR: Estimated glomerular filtration rate, VL: Viral load, ART: Antiretroviral therapy, TDF: Tenofovir disoproxil fumarate

RESULTS



Mean change in eGFR

- On-treatment analysis approach used: only PWH with an on-treatment eGFR measurement included
- SGLT2 inhibitors showed a greater but non-significant acute eGFR decline** (-3.27; 95%CI: -7.80, 1.26; p=0.2) vs. other classes (-0.75; 95%CI: -3.37, 1.87; p=0.6), with **no significant between-group difference (p=0.3)**



CONCLUSIONS

- During the **acute phase (within 6 months)** of initiation, **SGLT2 inhibitors** were associated with a **73% higher risk of ≥30% eGFR decline** and an **85% higher risk of a ≥10 mL/min/1.73 m² absolute decline** compared to other classes. Notably, **17% of PWH experienced a ≥30% eGFR decline**, a proportion that is higher than that observed in the general population
- However, the **average eGFR decline was modest** (-3.3 mL/min/1.73 m²), similar to the general population (~3–6 mL/min/1.73 m²)
- Such declines have not negated SGLT2 inhibitors cardiorenal benefits in general population
- Further **long-term research** is needed to assess **nephroprotection**, but in the meantime, clinicians *may consider* closer renal monitoring in PWH starting SGLT2 inhibitors

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