GLP-1 Use in Non-Diabetics Associated with Trivial Increase in Creatinine

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Key Findings

- Among non-diabetic patients without chronic kidney disease (CKD), there was a minimal increase of 0.01 mg/dL to 0.02 mg/dL in serum creatinine in the months following initiation of semaglutide, liraglutide, or tirzepatide. Of note, creatinine values can vary up to 0.6 mg/dL and still be considered within the normal range.[1]
- In patients diagnosed with CKD, there were no statistically significant changes in creatinine associated with any of the three GLP-1 medications studied.

GLP-1s are increasingly prescribed for weight management and metabolic health in patients without diabetes. While renal benefits of these medications have centered on diabetic populations,[2,3] limited data exist on kidney function changes in non-diabetic patients using GLP-1s. Lab tests to measure creatinine levels are often used to measure kidney function, and higher levels indicate poorer kidney function.[3]

To understand the relationship between GLP-1 medications and kidney function, as measured by creatinine lab results, we studied 108,439 adult patients who started semaglutide, liraglutide, or tirzepatide between 2021 and 2024 and had one or more creatinine labs in the months leading up to and following the new medication. Their change in creatinine was compared to patients with no GLP-1 exposure who had office visits in the same period. Patients prescribed GLP-1s were compared to patients who did not take GLP-1s but had similar patient demographics, baseline creatinine levels, follow-up period durations, and BMIs.

Among patients diagnosed with CKD, no statically significant changes in creatinine were seen for any of the medications, as shown in Figure 1. Among patients without CKD, minimal increases in serum creatinine were observed for patients on a GLP-1 compared to those who were not prescribed a GLP-1: 0.01 mg/dL for semaglutide, 0.01 mg/dL for liraglutide, and 0.02 mg/dL for tirzepatide. Normal creatinine levels are 0.5 to 1.1 mg/dL for females and 0.6 to 1.2 mg/dL for males.[1]

Change in Creatinine Levels on GLP-1s

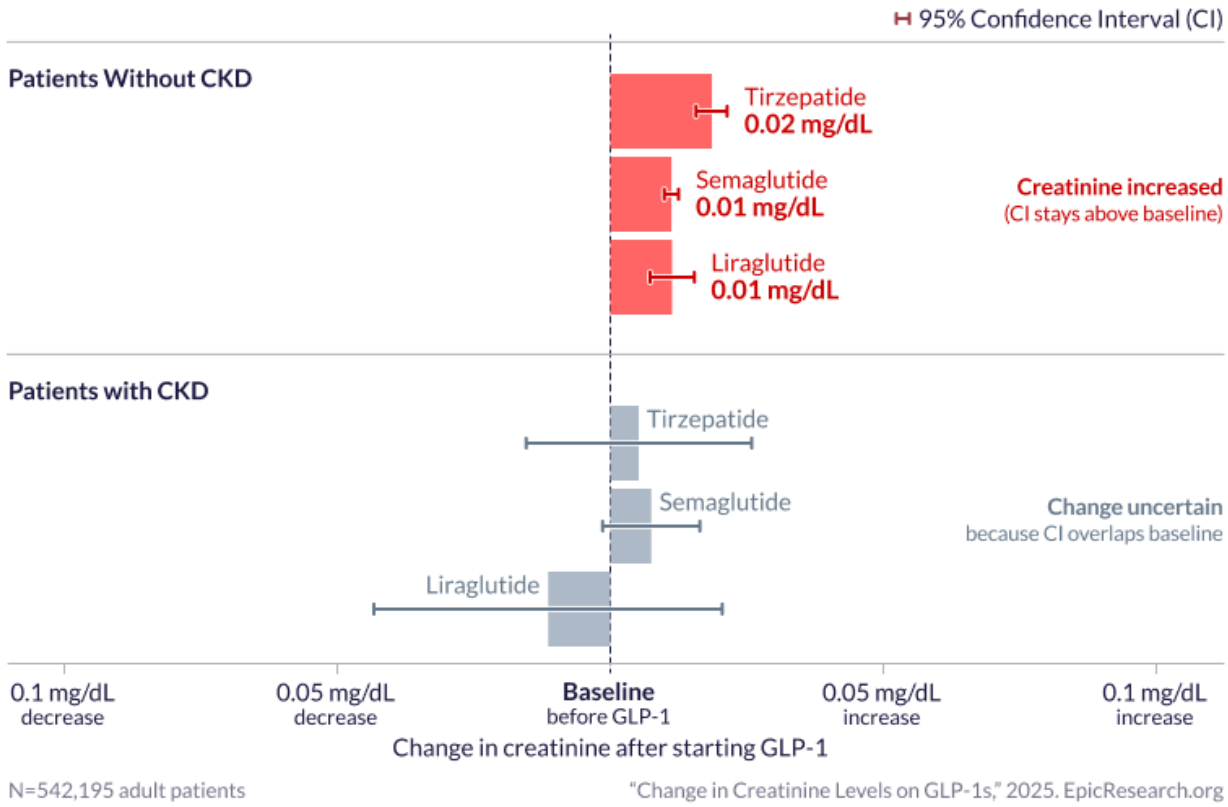

Figure 1. The change in creatinine levels from the three months before GLP-1 was started compared to levels one to three months after, split by whether the patient had pre-existing CKD.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 41,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Devkota, B. P. (2024, June 28). Creatinine. Medscape. https://emedicine.medscape.com/article/2054342-overview. Accessed August 1, 2025.
2. Li X, Song Y, Guo T, Xiao G, Li Q. Effect of glucagon-like peptide 1 receptor agonists on the renal protection in patients with type 2 diabetes: A systematic review and meta-analysis. Diabetes Metab. 2022;48(5):101366. doi:10.1016/j.diabet.2022.101366
3. Simental-Mendía M, Linden-Torres E, Sánchez-García A, Sahebkar A, Simental-Mendía LE. Effect of glucagon-like peptide-1 receptor agonists on renal function: A meta-analysis of randomized controlled trials. Br J Clin Pharmacol. 2022;88(8):3566-3576. doi:10.1111/bcp.15304

Data Definitions

Term	Definition
Study period	Patients prescribed a **GLP-1 medication** for the first time in 2021– 2024
Study population: inclusion	Adult patients with: • At least one **creatinine** lab within three months prior to their **index date** (the closest is designated as the baseline level) • At least one **creatinine** lab between one and three months following their **index date** • Patients returned from **evaluated sex filter** with a value of male or female • A body mass index of 30+ in the year prior to the **index date** Index date: • For exposure patients, their first order for a **GLP-1** medication • For non-exposure patients, a random office visit encounter for a patient with no documentation of a GLP-1 prescription at any time
Study population: exclusion	Diabetes: ICD-10-CM code E08*-E13* Pregnancy during the window of **creatinine** labs
GLP-1 medications	Medications with a simple generic name of "semaglutide," "liraglutide," or "tirzepatide" Patients who received multiple forms of a GLP-1 concurrently or in succession or who received any other medication with a pharmaceutical class of "ANTIHYPERGLY,INCRETIN MIMETIC(GLP-1 RECEP.AGONIST)," "ANTIHYPERGLY,INSULIN,LONG ACT-GLP-1 RECEPT.AGONIST," "ANTIHYPERGLYCEMIC – INCRETIN MIMETICS COMBINATION," or "ANTI-OBESITY GLUCAGON-LIKE PEPTIDE-1 RECEP AGONIST" were excluded
Creatinine	Lab with LOINC code 2160-0 or 38483-4 Creatinine results less than 0.1 and greater than 15.0 are ignored Creatine results from an inpatient admission are ignored
Confounders	**Evaluated sex filter** Age group: • <50 • 50-64 • 65+ Baseline **creatinine** level • <0.7 • 0.7-0.9 • 1.0-1.2 • 1.3-1.5 • 1.6-2.0 • 2.1+ Time between **creatinine** results • 45–90 day • 91–125 days • 126–160 days • 161–182 days BMI classification (at index date) • Class 1 obesity: 30–<35

	• Class 2 obesity: 35–<40
	• Class 3a obesity: 40–<45
	• Class 3b obesity: 45+
	Start or stop of a renally active or nephrotoxic medication between creatinine results:
	• Analgesic combination products
	  ○ Acetaminophen + Aspirin (+ caffeine): RxNorm code 209468
	• Nonsteroidal anti-inflammatory drugs (NSAIDs)
	  ○ Diclofenac: RxNorm code 855926
	  ○ Ibuprofen: RxNorm code 5640
	  ○ Indomethacin: RxNorm code 5781
	  ○ Meloxicam: RxNorm code 41493
	  ○ Naproxen: RxNorm code 198013
	• Calcineurin inhibitors
	  ○ Cyclosporine: RxNorm code 3008
	  ○ Tacrolimus: RxNorm code 235991
	• Mood stabilizers
	  ○ Lithium: RxNorm code 6448
	• Aminoglycoside antibiotics
	  ○ Gentamicin: RxNorm code 1596450 (IV route)
	  ○ Streptomycin: RxNorm code 10109
	  ○ Tobramycin: RxNorm code 10627
	• Other antimicrobial agents
	  ○ Vancomycin: RxNorm code 11124
	  ○ Foscarnet: RxNorm code 33562
	  ○ Cidofovir: RxNorm code 199388
	  ○ Tenofovir disoproxil fumarate: RxNorm code 322248
	  ○ Tenofovir DF + Emtricitabine: RxNorm code 639888
	  ○ Atazanavir: RxNorm code 343047
	• Bisphosphonates
	  ○ Zoledronic Acid (IV route): RxNorm code 1546014
	• Chemotherapy agents
	  ○ Cisplatin: RxNorm code 1546014

Race and ethnicity	Patients were categorized into mutually exclusive categories, first for “Hispanic” and then “non-Hispanic White,” “non-Hispanic Black,” “non-Hispanic Asian,” or “non-Hispanic Other.”
Stratifications	Diagnosis with CKD at baseline: ICD-10-CM code N18*
Matching	Exposure patients were matched to non-exposure patients 1:4 based on: Baseline creatinine levels • < 0.7 mg/dL • 0.7 to 0.99 mg/dL • 1.0 to 1.29 mg/dL • 1.3 to 1.59 mg/dL • 1.6 to 2.09 mg/dL • 2.1+ mg/dL **Evaluated sex filter** Days between baseline and follow-up creatinine labs • 45 to 90 days

	• 91 to 125 days • 126 to 160 days • Over 160 days
Evaluated sex filter	Uses documentation across a patient's record, including the legal sex, sex assigned at birth, gender identity, OB history, and organ inventory, to determine whether the patient has an unambiguous sex
Model Specifications	Linear regression of the change in creatinine levels between the baseline and follow-up labs

Table 1a. Change in Creatinine Levels on GLP-1s Without CKD

Cohort	Coefficient	Lower CI	Upper CI
Liraglutide	-0.01	-0.04	0.02
Semaglutide	0.01	0.00	0.02
Tirzepatide	0.01	-0.02	0.03
Female	-0.03	-0.04	-0.02
Asian	0.02	-0.02	0.06
Black	0.03	0.02	0.04
Hispanic	0.01	-0.01	0.02
Other race	0.00	-0.01	0.01
Age <50	0.00	-0.01	0.01
Age 65+	0.01	0.00	0.02
Baseline creatinine <0.7	0.03	0.01	0.05
Baseline creatinine1.0-1.2	-0.04	-0.05	-0.03
Baseline creatinine 1.3-1.5	-0.07	-0.08	-0.06
Baseline creatinine 1.6-2.0	-0.11	-0.12	-0.10
Baseline creatinine 2.1+	-0.08	-0.09	-0.06
Follow up days 91-125	0.00	0.00	0.01
Follow up days 126-160	0.01	0.00	0.02
Follow up days 161-182	0.00	-0.02	0.02
BMI obese level 2	0.01	0.00	0.02
BMI obese level 3	0.01	0.00	0.02
BMI obese level 4	0.03	0.02	0.04
Confounding medication active	-0.01	-0.02	0.00
Confounding medication stopped	0.00	-0.01	0.01
Confounding medication started	-0.03	-0.05	-0.02

Table 1b. Change in Creatinine Levels on GLP-1s with CKD

Cohort	Coefficient	Lower CI	Upper CI
Liraglutide	0.01	0.01	0.02
Semaglutide	0.01	0.01	0.01
Tirzepatide	0.02	0.02	0.02
Female	-0.04	-0.04	-0.04
Asian	-0.01	-0.01	-0.01
Black	0.01	0.01	0.01
Hispanic	-0.01	-0.02	-0.01
Other race	0.00	0.00	0.00
Age <50	-0.01	-0.01	-0.01
Age 65+	0.01	0.01	0.01
Baseline creatinine <0.7	0.05	0.05	0.05
Baseline creatinine1.0-1.2	-0.06	-0.06	-0.06
Baseline creatinine 1.3-1.5	-0.14	-0.15	-0.14
Baseline creatinine 1.6-2.0	-0.27	-0.28	-0.26
Baseline creatinine 2.1+	-0.68	-0.70	-0.66
Follow up days 91-125	0.00	0.00	0.00
Follow up days 126-160	0.00	0.00	0.00
Follow up days 161-182	0.00	0.00	0.00
BMI obese level 2	0.00	0.00	0.00
BMI obese level 3	0.00	0.00	0.00
BMI obese level 4	0.00	0.00	0.00
Confounding medication active	0.00	0.00	0.00
Confounding medication stopped	0.00	0.00	0.00
Confounding medication started	0.00	0.00	0.00