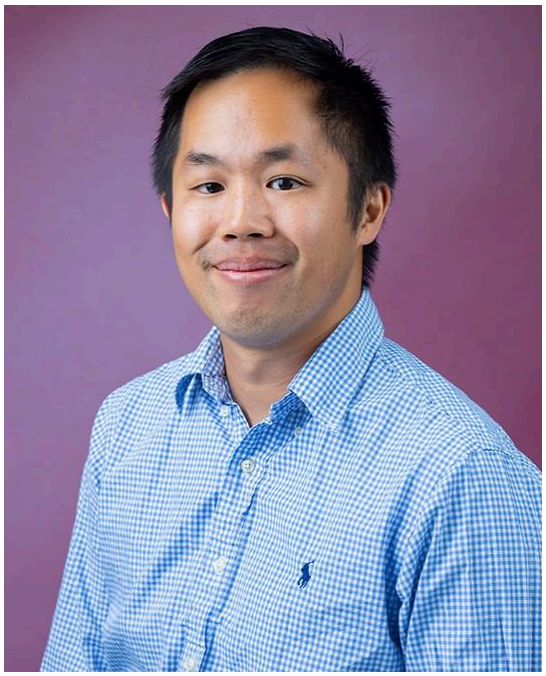
Article
https://www.sciencedirect.com/science/article/pii/S2468024926028500

🧵 Tweetorial Alert 🧵

1/
Hey #NephTwitter!
Welcome to a 🆕 #tweetorial #xtorial brought to you by @KIReports

2/
Our author is Melvin @MChanMD (pediatric nephrologist)
Our topic: GLP1 in Hemodialysis

#MedTwitter #nephtwitter @ISNkidneycare #XTwitter



3/
There are no conflicts of interest. Please also check out #KIReportsCommunity educational #blogposts at https://www.kireportscommunity.org/. FOLLOW US at @KIReports for more expert #MedEd in #kidneydisease. #FOAMed @MedTweetorials

4/ Intro

⚕There are limited treatments for diabetic patients on HD.

⚕Metformin is not used in HD;; SGLT2 use has expanded at low eGFR but remains unstudied in HD.

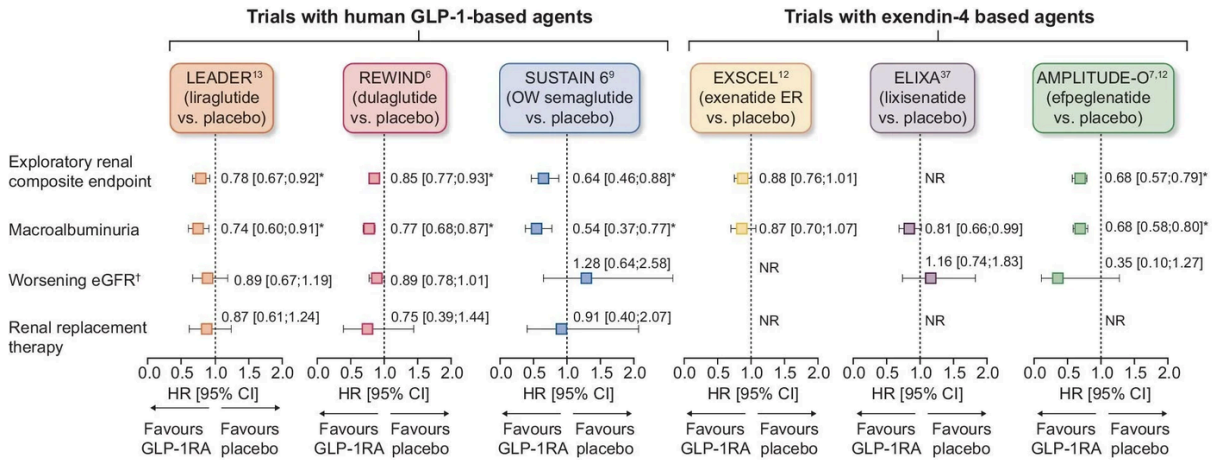
⚕Dialysis patients weren't included in landmark trials.

⚕<5% in this cohort are on GLP-1s.

5/ Introduction

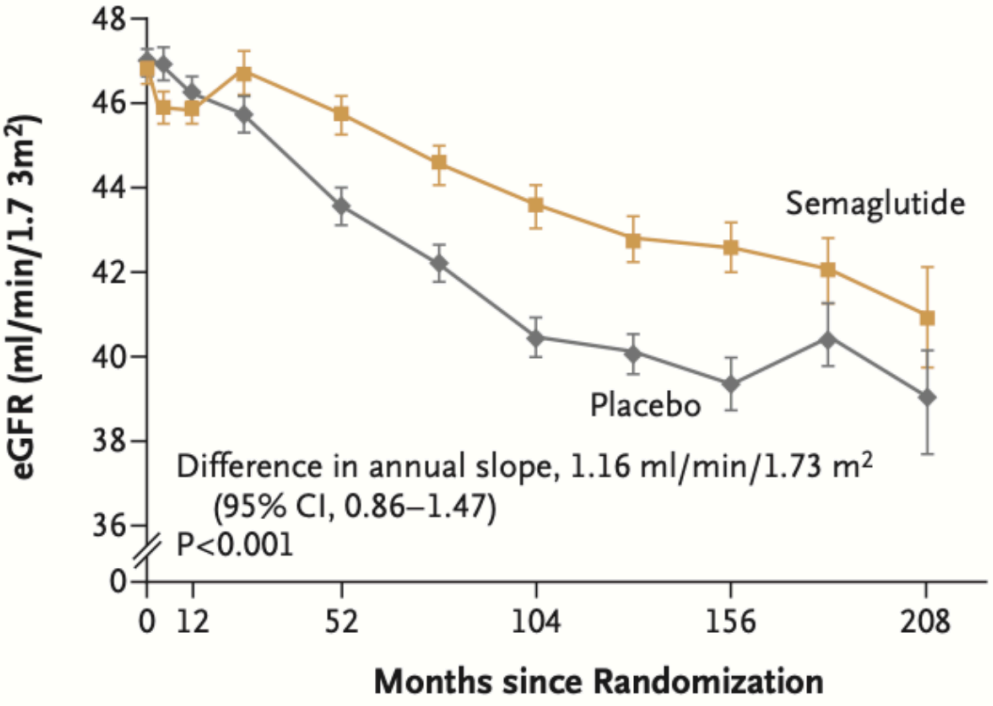
Multiple studies have demonstrated improvement in albuminuria with GLP-1 receptor agonists. DPP-4 inhibitors, oral medications that inhibit the breakdown of endogenous GLP-1, show less robust benefits.

PMID: 38033315



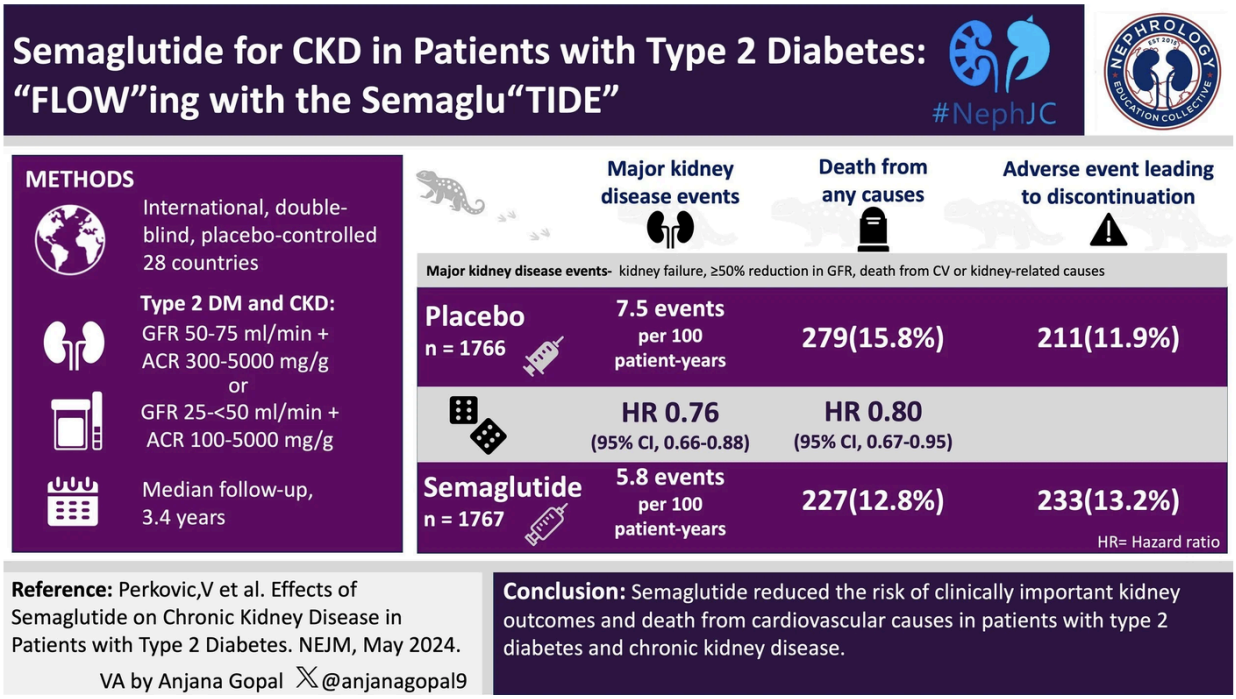
6/ Introduction
The most exciting study is the FLOW trial that showed slower eGFR decline for those taking GLP1s compared to placebo. For a great review, check out
👉https://www.nephjc.com/news/flow

D **Total eGFR Slope**



No. at Risk

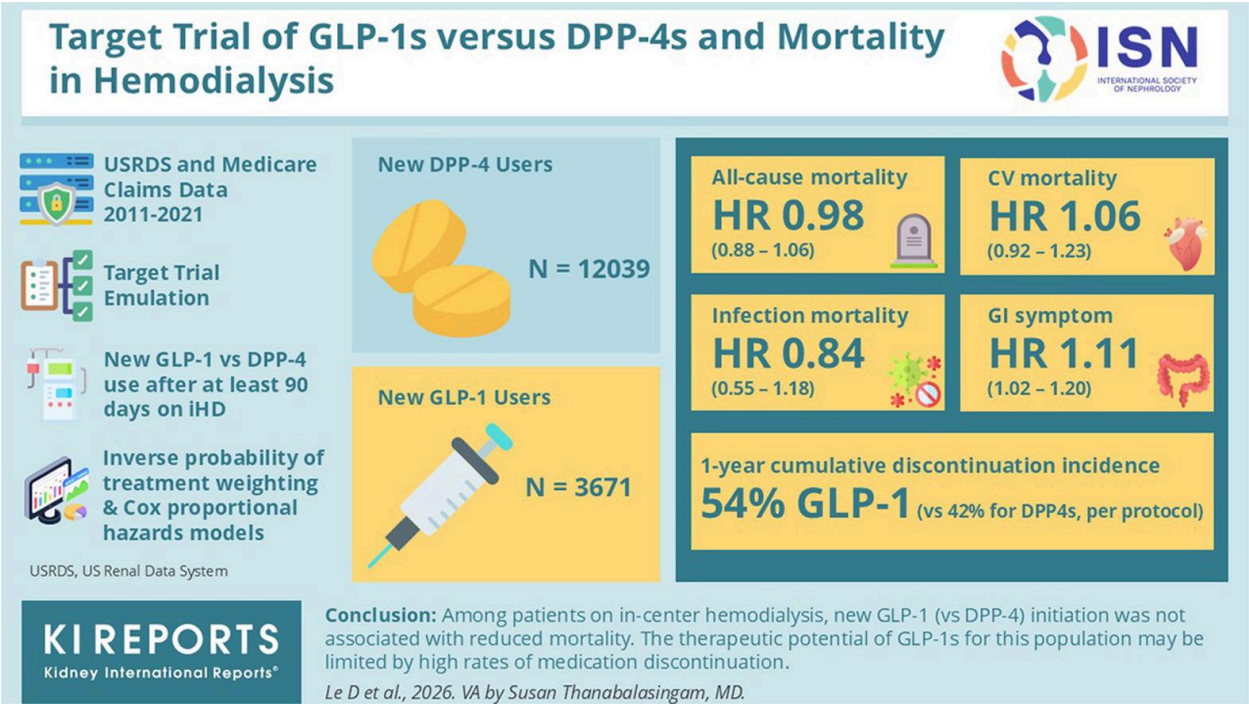
Placebo	1766	1663	1573	1609	1490	1441	1284	876	609	199
Semaglutide	1766	1665	1590	1606	1521	1468	1345	952	651	218



7/ Our #Tweetorial is based on a recent publication by Dr. Lel and VA by @susanthana.bsky.social:
GLP1 in Hemodialysis Patients

It looks at outcomes for T2D patients on GLP1 vs DPP-4s and on maintenance HD.

🔗https://www.kireports.org/article/S2468-0249(26)02850-0/fulltext



8a/ Methods

💽Data: US Renal Data Systems with Medicare claims

🕐January 2011-December 2021

🫘Compares those on GLP1s vs DPP-4s receiving in-center HD

8b/

🎗️Inclusion: >= 18 years old, survived >=90 days on HD, and did not have GLP1/DPP-4 in previous 180 days

❌Exclusion: Simultaneous dispense of GLP1 and DPP-4 at study start, no longer on in-center dialysis, <180 days of continuous Medicare Part A, B, and D primary payer, absence of T2DM

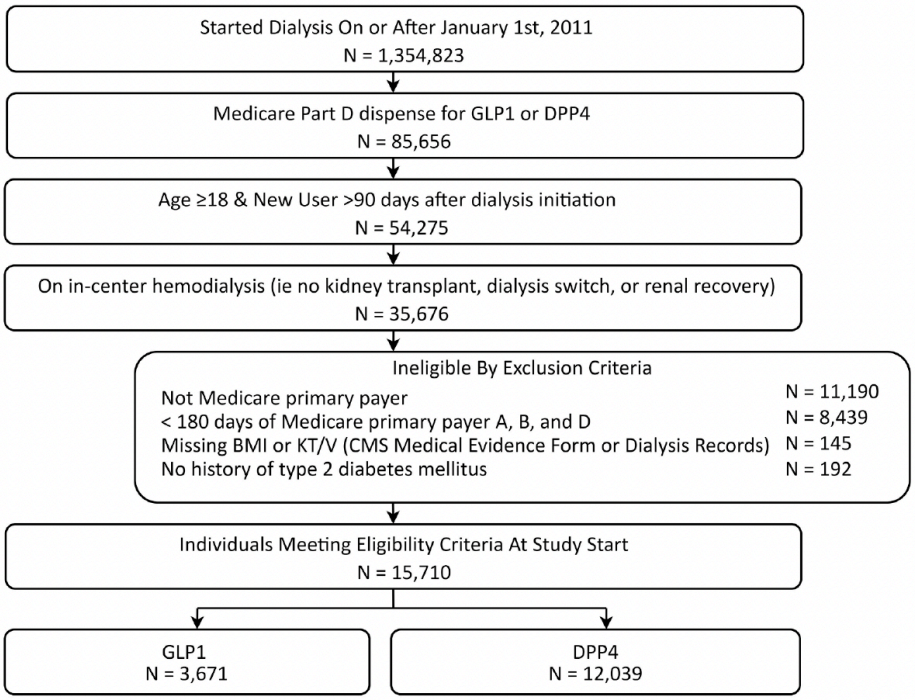


Figure 1. Study flow diagram. BMI, body-mass-index; CMS, Centers for Medicare & Medicaid services; DPP4, dipeptidyl peptidase 4 inhibitors; GLP1, glucagon like peptide-1 receptor agonists; sHR, subdistribution hazard ratio. KT/V, (quantitative measurement of dialysis adequacy).

9/ Inverse Probability of Tx Weighting (IPTW)

⚡RCTs randomize tx regardless of confounders, but observational studies don't.

⚡IPTW emulates an RCT by creating a weighted pseudo-population where confounders no longer drive tx, using probabilities of treatment based on baseline factors.

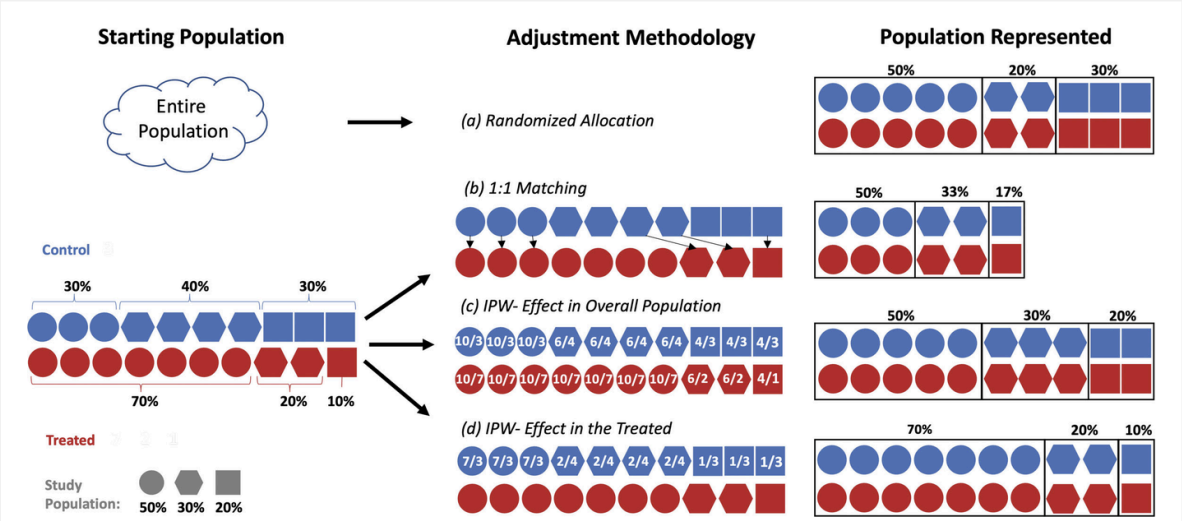


Figure. **Conceptual model of propensity scores analytic populations.** This figure illustrates the pseudo-population formed from (**A**) randomized allocation vs (**B–D**) different propensity score methods. Each shape represents a certain set of characteristics and thus probability of being allocated to the respective study arm. The percentages underneath the gray shapes represent the overall proportion for each shape type in the study population sample before applying any propensity score method. For example, there are 30% (3/10) circles in the control group and 70% (7/10) circles in the treated group averaging 50% (10/20) circles in the overall study population. The fractions in white are the weights applied to each shape to develop the final weighted cohorts. For example, as the inverse probability weighting (IPW) effect in overall forms a cohort distribution of characteristics that reflects the average in the overall study population, we can expect that 50% will be circles. In the control group, there are only 3 circles, so you would apply a weight of 10/3×3 circles to get 50% circle representation in the weighted cohort.

PMID: 38189126

10a/ Statistical Methods

🎛️IPTW-weighted analysis with 2 cohorts

👉ITT: follow patients regardless of discontinuation

👉PP: censor at discontinuation

⚠️Fine-Gray: models competing risks (death, transplant) without treating them as simple censoring

10b/ Outcomes

🎯Primary: all-cause mortality

➕Secondary: CV + infection mortality, plus safety (GI, hyper/hypoglycemia, pancreatitis, retinopathy, etc.)

11/ Results: Clinical Characteristics

Most common GLPs include dulaglutide > liraglutide > semaglutide,

with GLP1s users being:

🔬Younger

🔬Caucasian

🔬Longer dialysis vintage

🔬Higher BMI

🔬Non-diabetic cause of CKD

After IPTW, the clinical characteristics were similar between GLP1 and DPP4 cohort.

Table 1. Baseline characteristics of new GLP-1 versus new DPP-4 users pre- and post-IPTW

	Pre-IPTW			Post-IPTW		
	GLP-1	DPP-4		GLP-1	DPP-4	
Baseline characteristics	*n* = 3671	*n* = 12,039	SMD	*n* = 3517	*n* = 12,155	SMD
Age, SD	60 (12)	65 (12)	0.39	63 (12)	63 (13)	0.03
Male	1853 (50)	6374 (53%)	0.05	1815 (52%)	6338 (52%)	0.01
Race			0.14			0.08
White	2382 (65%)	7282 (60%)		2277 (65%)	7523 (62%)	
Black/African American	1035 (28%)	3646 (30%)		990 (28%)	3596 (30%)	
Asian	122 (3%)	705 (6%)		140 (4%)	628 (5%)	
Native Hawaiian or Pacific Islander	64 (2%)	205 (2%)		55 (2%)	205 (2%)	
American Indian or Alaska Native	50s[a] (2%)	150 (1%)		40[a] (1%)	159 (1%)	
Other or Multiracial	< 11[a] (0%)	51 (51%)		< 11[a] (0%)	45 (0%)	
Year of medication initiation			0.69			0.08
2011	< 11[a] (0%)	86 (1%)		22 (1%)	71 (1%)	
2012	20s[a] (1%)	342 (3%)		92 (3%)	283 (2%)	
2013	53 (1%)	576 (5%)		109 (3%)	484 (4%)	
2014	87 (2%)	925 (8%)		206 (6%)	776 (6%)	
2015	151 (4%)	1290 (11%)		310 (9%)	1105 (9%)	
2016	205 (6%)	1497 (12%)		399 (11%)	1309 (11%)	
2017	362 (10%)	1683 (14%)		402 (11%)	1561 (13%)	
2018	542 (15%)	1682 (14%)		511 (15%)	1724 (14%)	
2019	873 (24%)	1712 (14%)		623 (18%)	2006 (17%)	
2020	850 (23%)	1532 (13%)		556 (16%)	1823 (15%)	
2021	517 (14%)	714 (6%)		287 (8%)	1012 (8%)	
Dialysis vintage	2.3 [1.2–2.6]	1.9 [0.9–3.5]	0.19	2.0 [1.0–3.7]	2.0 [0.9–3.6]	0.02
KTV, median [IQR]	1.6 [1.4–1.7]	1.6 [1.4–1.8]	0.01	1.6 [1.4–1.8]	1.6 [1.4–1.8]	0.01
Smoking status at dialysis initiation	183 (5%)	585 (5%)	0.01	191 (5%)	601 (5%)	0.02
Medicare Part D low-income subsidy	2953 (80%)	9518 (79%)	0.03	2765 (79%)	9671 (80%)	0.02
ESKD from diabetes	2943 (80%)	9106 (76%)	0.11	2735 (78%)	9339 (77%)	0.02
USRDS network region			0.10			0.03
West	985 (27%)	3042 (25%)		910 (26%)	3190 (26%)	
Northeast	687 (19%)	2740 (23%)		733 (21%)	2615 (22%)	
South	1307 (36%)	4128 (34%)		1218 (35%)	4183 (34%)	
Midwest	692 (19%)	2129 (18%)		657 (19%)	2167 (18%)	
Nephrology care before dialysis initiation			0.14			0.03
None	1198 (33%)	4694 (39%)		1298 (37%)	4505 (37%)	
< 6 mos	557 (15%)	1821 (15%)		531 (15%)	1840 (15%)	
> 12 mos	1089 (30%)	3,137 (26%)		979 (28%)	3264 (27%)	
6–12 mos	827 (23%)	2387 (20%)		709 (20%)	2546 (21%)	
Initial dialysis access via catheter	2748 (75%)	9231 (77%)	0.04	2709 (77%)	9308 (77%)	0.01
BMI, median [IQR]	34 [29–40]	29 [25–34]	0.65	31 [26–36]	30 [25–36]	0.01
Arrhythmia	702 (19%)	2894 (24%)	0.12	789 (22%)	2823 (23%)	0.02
Atherosclerosis	896 (24%)	4029 (33%)	0.20	1080 (31%)	3770 (31%)	0.01
Cancer	213 (6%)	928 (8%)	0.08	270 (8%)	869 (7%)	0.02
Congestive heart failure	1146 (31%)	4751 (39%)	0.17	1333 (38%)	4537 (37%)	0.01
Dementia	33 (1%)	432 (4%)	0.18	101 (3%)	357 (3%)	< 0.01
Diabetic retinopathy	1140 (31%)	2789 (23%)	0.18	924 (26%)	3068 (25%)	0.02
Gastrointestinal bleed	157 (4%)	889 (7%)	0.13	217 (6%)	798 (7%)	0.02
Hypertension	3313 (90%)	10,917 (91%)	0.01	3203 (91%)	11,026 (91%)	0.01
Nonambulatory status	209 (6%)	769 (6%)	0.03	238 (7%)	762 (6%)	0.02
Liver disease	217 (6%)	1434 (12%)	0.21	344 (10%)	1269 (10%)	0.02
Other cardiac disease	472 (13%)	2092 (17%)	0.13	562 (16%)	1962 (16%)	< 0.01
Peripheral vascular disease	1372 (37%)	5861 (49%)	0.23	1549 (44%)	5544 (46%)	0.03
Respiratory disease	450 (12%)	1634 (14%)	0.04	494 (14%)	1607 (13%)	0.02
Cerebrovascular disease	645 (18%)	2720 (23%)	0.13	743 (21%)	2586 (21%)	< 0.01
Number of hospitalizations, < 6 mos			0.40			0.05
0	2274 (62%)	5356 (44%)		1725 (49%)	5954 (49%)	
1	775 (21%)	2916 (24%)		808 (23%)	2832 (23%)	
2	330 (9%)	1731 (14%)		434 (12%)	1583 (13%)	

(Continued on following page)

Table 1. (Continued) Baseline characteristics of new GLP-1 versus new DPP-4 users pre- and post-IPTW

	Pre-IPTW			Post-IPTW		
	GLP-1	DPP-4		GLP-1	DPP-4	
Baseline characteristics	*n* = 3671	*n* = 12,039	SMD	*n* = 3517	*n* = 12,155	SMD
3	150 (4%)	952 (8%)		244 (7%)	843 (7%)	
4+	145 (4%)	1095 (9%)		312 (9%)	953 (8%)	
Outpatient primary care visit, ≥ 1	2175 (59%)	6835 (57%)	0.05	2011 (57%)	6948 (57%)	< 0.01
Outpatient endocrinology visit, ≥ 1	929 (25%)	2882 (24%)	0.03	806 (23%)	2924 (24%)	0.03
Hyperglycemia hospitalization, ≥ 1	298 (8%)	1226 (10%)	0.07	365 (10%)	1174 (10%)	0.02
Hypoglycemia hospitalization, ≥ 1	89 (2%)	695 (6%)	0.17	181 (5%)	604 (5%)	0.01
Number of Unique Medications, < 90 d	11 [8–15]	10 [7–14]	0.14	11 [8–14]	11 [8–14]	0.04
ACE/ARB	1115 (30%)	4321 (36%)	0.12	1277 (36%)	4190 (34%)	0.04
Aldosterone	46 (1%)	146 (1%)	< 0.01	39 (1%)	142 (1%)	< 0.01
Antiplatelet	694 (19%)	2458 (20%)	0.04	732 (21%)	2485 (20%)	0.01
Alpha glucosidase inhibitors	< 11[a] (0%)	18 (0%)	0.01	< 11[a] (0%)	21 (0%)	0.01
Beta blocker	2028 (55%)	7146 (59%)	0.08	2123 (60%)	7087 (58%)	0.04
Calcium channel blocker	1520 (41%)	5777 (48%)	0.13	1575 (45%)	5623 (46%)	0.03
Diuretics	1172 (32%)	3137 (26%)	0.13	1007 (29%)	3334 (27%)	0.03
DOAC	260 (7%)	683 (6%)	0.06	220 (6%)	795 (7%)	0.01
History of any Epo use	2948 (80%)	9025 (75%)	0.13	2685 (76%)	9268 (76%)	< 0.01
Insulin	2591 (71%)	4975 (41%)	0.62	1777 (51%)	5900 (49%)	0.04
Phosphate binders	2300 (63%)	7306 (61%)	0.04	2119 (60%)	7374 (61%)	0.01
SGLT2	18 (0%)	20 (0%)	0.06	< 11[a]	31 (0%)	< 0.01
Sulfonylurea	247 (7%)	1558 (13%)	0.21	378 (11%)	1389 (11%)	0.02
Thiazolidinediones	84 (2%)	358 (3%)	0.04	131 (4%)	348 (3%)	0.05
Warfarin	217 (6%)	834 (7%)	0.04	217 (6%)	808 (7%)	0.02

ACE/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BMI, body mass index; DOAC, direct oral anticoagulant; DPP-4, dipeptidyl peptidase-4 inhibitor; Epo, erythropoietin; ESKD, end-stage kidney disease; GLP-1, glucagon-like peptide-1 receptor agonist; Kt/V, fractional urea clearance; SD, standard deviation; SGLT2, sodium-glucose cotransporter-2 inhibitor; SMD, absolute standardized mean difference; USRDS, United States Renal Data System.
[a]Cells with < 11 were censored per USRDS reporting policy or rounded down (if multiple categories).
Data reported as mean (SD), number (percent), or median (interquartile interval).

12/ Results

💊Median follow-up of 1.5 years

💊High rates of medication discontinuation in both GLP1 and DPP-4 (>50%), with median use of 120 and 160 days, respectively

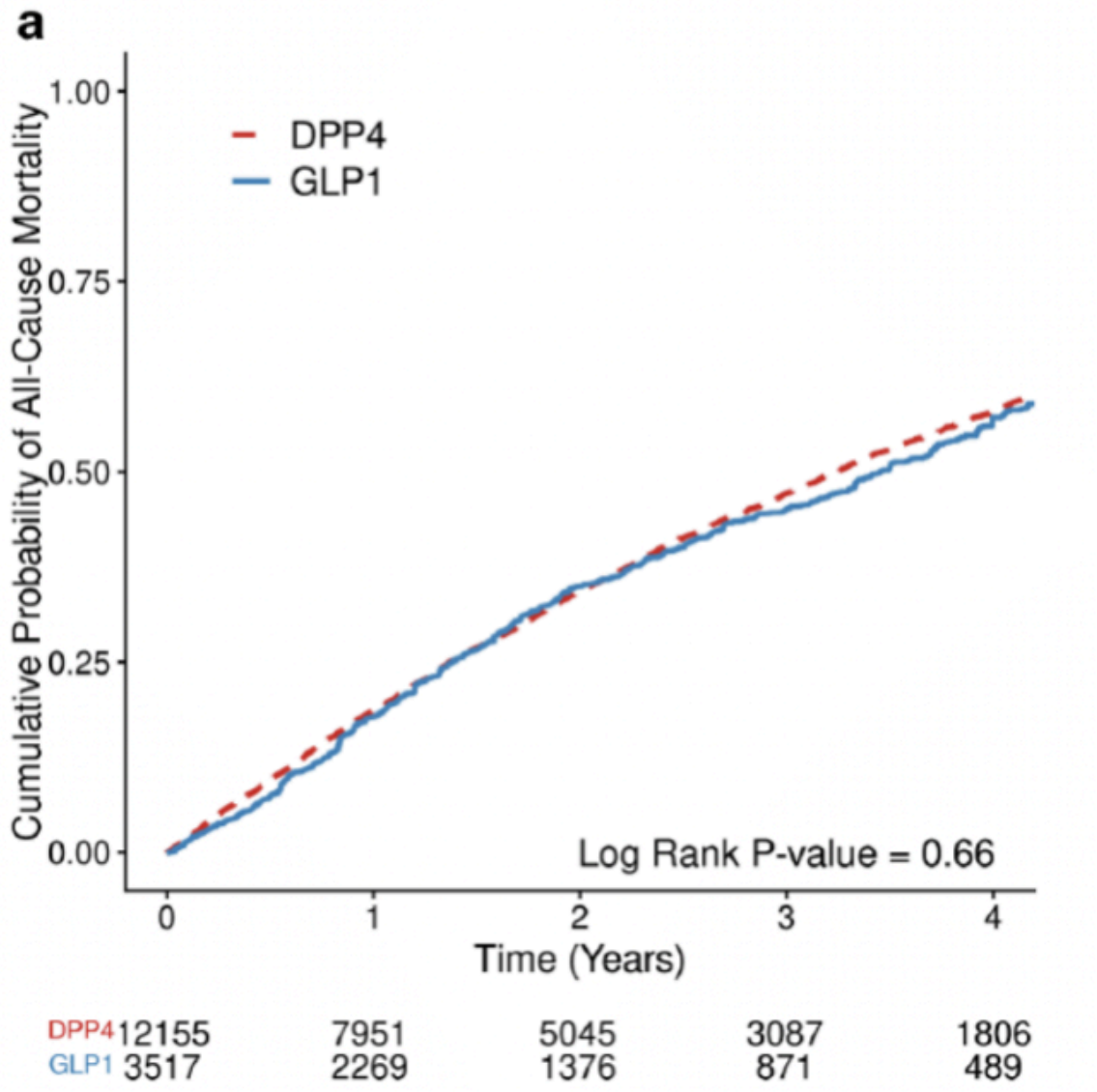
13a/ Results: Intention to Treat

💊No difference between GLP1 and DPP-4 on all primary outcomes, likely from high rates of discontinuation

Table 2. HR of mortality by GLP-1 (vs. DPP-4) use in Medicare beneficiaries receiving hemodialysis

Causes of mortality	IPTW-No. of events		Effect estimate—hazard ratios	
Intention to treat	GLP-1 *N* = 3517	DPP-4 *N* = 12,155	IPTW-HR	IPTW-sHR
All-cause	1531	5588	0.98 (0.89–1.07)	
Cardiac	677	2276	1.06 (0.92–1.23)	1.07 (0.93–1.23)
Infection	90	387	0.83 (0.54–1.26)	0.83 (0.54–1.26)

DPP-4, dipeptidyl peptidase-4 inhibitors; GLP-1, glucagon-like peptide-1 receptor agonists; HR, hazard ratio; IPTW, inverse probability of treatment weighting; sHR, subdistribution hazard ratio.
IPTW-HRs were estimated using Cox proportional hazards regression, and IPTW-sHRs were estimated using Fine-Gray models accounting for competing risk of mortality and kidney transplantation.



13b/ Results: Per Protocol

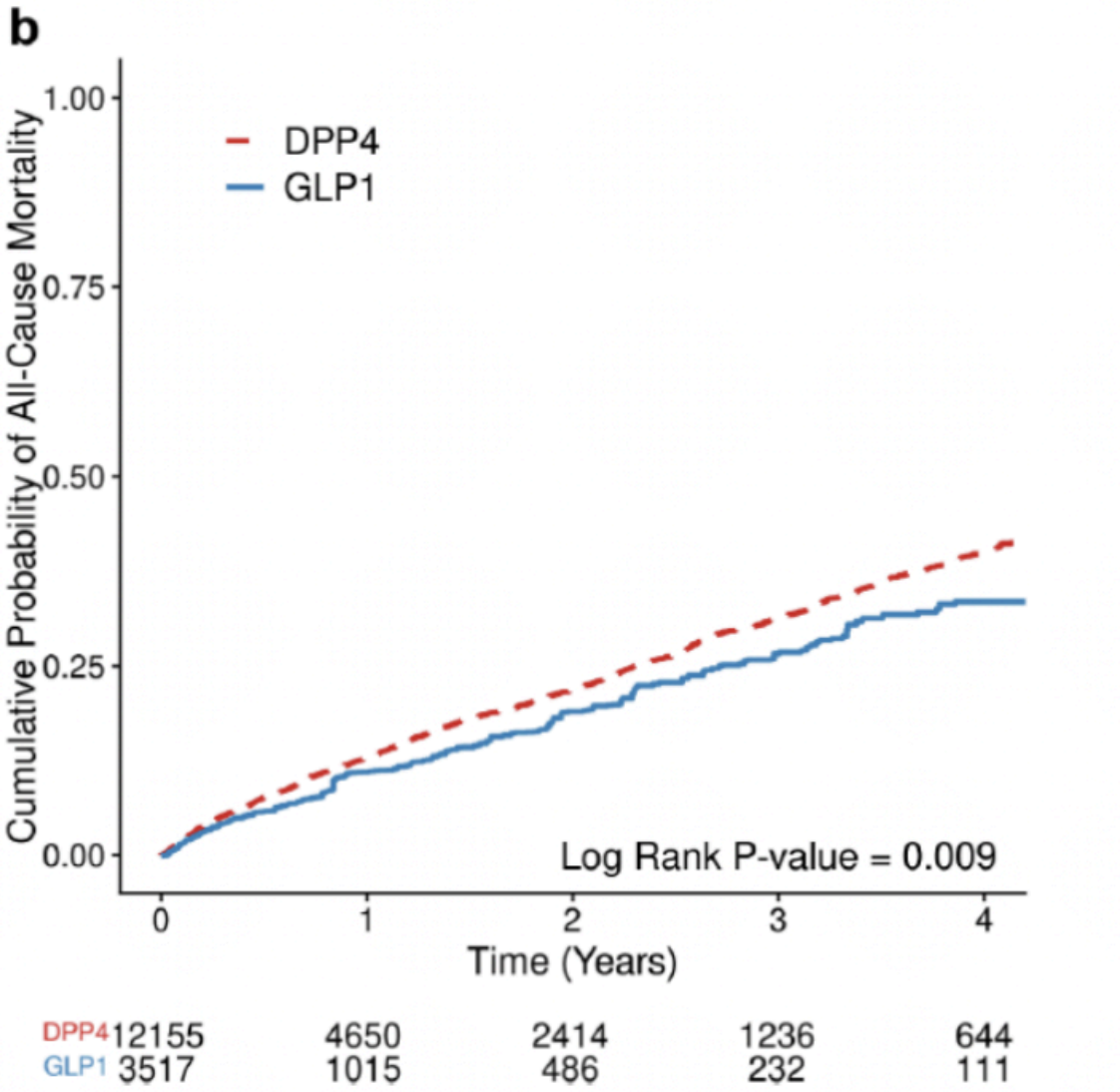
💊GLP1 patients had decreased all cause mortality versus DPP-4 patients

💊No other difference in other primary outcomes

Table 2. HR of mortality by GLP-1 (vs. DPP-4) use in Medicare beneficiaries receiving hemodialysis

Causes of mortality	IPTW-No. of events		Effect estimate—hazard ratios	
Intention to treat	GLP-1 $N = 3517$	DPP-4 $N = 12,155$	IPTW-HR	IPTW-sHR
Per-protocol				
All-cause	361	1962	0.81 (0.68–0.96)	
Cardiac	174	862	0.89 (0.69–1.13)	0.87 (0.68–1.11)
Infection	18	121	0.65 (0.37–1.14)	0.65 (0.37–1.14)

DPP-4, dipeptidyl peptidase-4 inhibitors; GLP-1, glucagon-like peptide-1 receptor agonists; HR, hazard ratio; IPTW, inverse probability of treatment weighting; sHR, subdistribution hazard ratio.
IPTW-HRs were estimated using Cox proportional hazards regression, and IPTW-sHRs were estimated using Fine-Gray models accounting for competing risk of mortality and kidney transplantation.



14/ Results: Safety

💊Overall adverse events were similar; hyperglycemia was higher with GLP-1s in the per-protocol analysis.

💊There is greater GLP-1 discontinuation throughout follow-up (≈55% vs ≈45% by year 1; ≈76% vs ≈66% by year 5), limiting on-treatment inference.

Table 3. HR of secondary outcomes associated with GLP-1 use (vs. DPP-4s) in Medicare beneficiaries receiving hemodialysis

Secondary outcomes	IPTW-No. of events		Effect estimate—hazard ratios	
Intention to treat	Events/IPTW-GLP-1	Events/IPTW-DPP-4	IPTW-HR	IPTW-sHR
Cholecystitis	50/3448	185/11,999	1.02 (0.68–1.53)	0.99 (0.66–1.49)
Hyperkalemia	644/2944	2400/9612	0.92 (0.91–1.04)	0.91 (0.80–1.02)
Hyperglycemia	419/1464	2284/7845	1.10 (0.95–1.27)	1.06 (0.92–1.23)
Hypoglycemia	310/2857	1222/10,182	0.98 (0.81–1.18)	0.95 (0.80–1.15)
Pancreatitis	68/3425	281/11,830	0.91 (0.64–1.29)	0.89 (0.62–1.26)
Retinopathy	382/1536	1981/7710	1.04 (0.90–1.20)	1.02 (0.89–1.19)
Per-protocol				
Cholecystitis	23/3448	98/11,999	1.04 (0.88–1.24)	1.01 (0.54–2.12)
Hyperkalemia	334/2944	1419/9612	0.95 (0.81–1.11)	0.94 (0.81–1.11)
Hyperglycemia	236/1464	1405/7845	1.27 (1.06–1.52)	1.22 (1.02–1.46)
Hypoglycemia	111/2857	617/10,182	0.81 (0.64–1.02)	0.81 (0.64–1.03)
Pancreatitis	38/3425	161/11,830	1.03 (0.66–1.61)	1.02 (0.65–1.60)
Retinopathy	208/1536	1536/7710	1.04 (0.88–1.24)	1.06 (0.89–1.26)

DPP-4, Dipeptidyl peptidase 4 inhibitors; GLP-1, Glucagon Like Peptide - 1 Receptor Agonists; HR, hazard ratio; IPTW, inverse probability of treatment weighting; sHR, subdistribution hazard ratio.
For each outcome, we excluded individuals who had a claim for the specific outcome at any time before study initiation. IPTW-HRs were estimated using Cox proportional hazards regression, and IPTW-sHRs were estimated using Fine-Gray models accounting for competing risk of mortality and kidney transplantation.

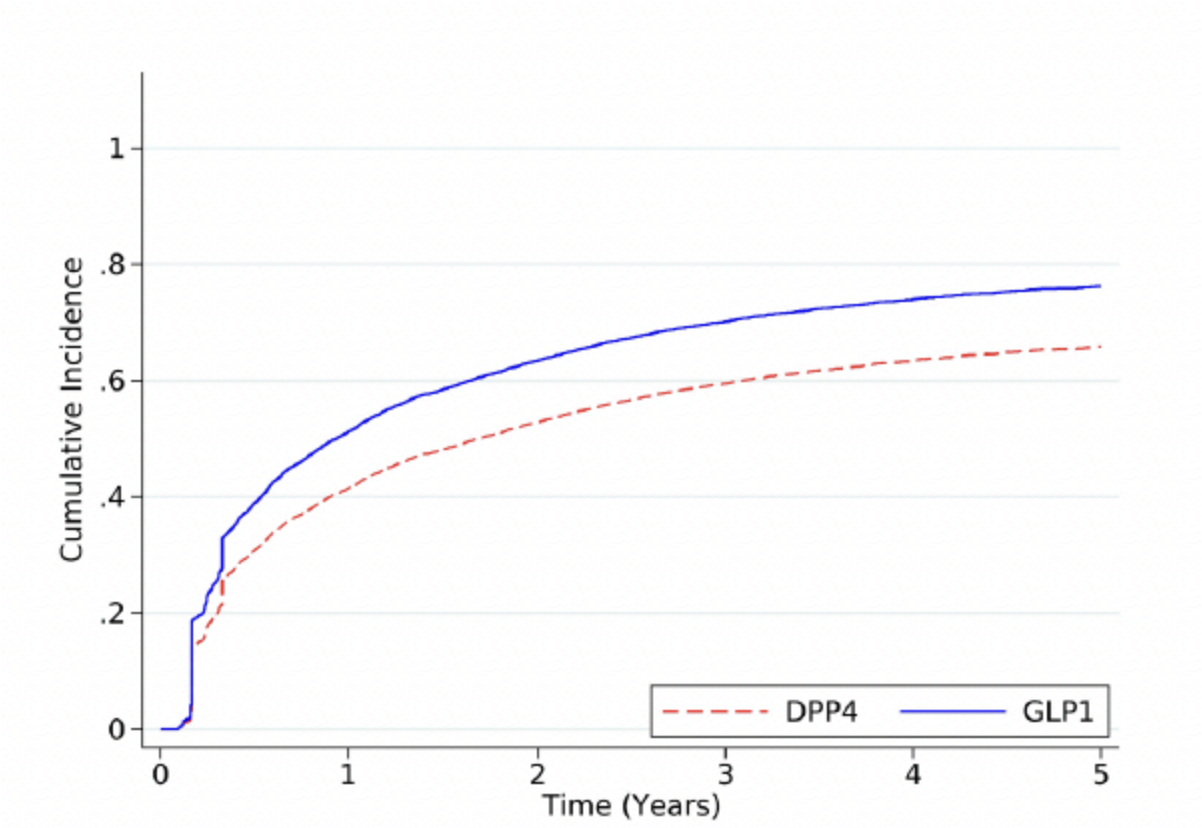


Figure 3. IPTW-cumulative incidence curve of GLP-1 versus DPP-4 discontinuation in per-protocol analysis. Estimated via Fine-Gray models accounting for competing risk of all-cause mortality and kidney transplantation. DPP4, dipeptidyl peptidase 4 inhibitors; GLP-1, glucagon like peptide - 1 receptor agonists; IPTW, inverse probability of treatment weighting.

15/ Summary

⚡In the ITT analysis, GLP-1 vs DPP-4 use showed **no difference** in primary or secondary outcomes.

⚡High discontinuation limits interpretation of the per-protocol analysis, where sustained GLP-1 use was associated with lower mortality but more hyperglycemia.

16/ Limitations

👎High discontinuation (>50% at 1 yr)

👎Claims data, with residual confounding and no randomization

👎Limited clinical granularity (no A1c, weight, dosing)

👎Class-level analysis (older GLP-1s dominate; newer agents underrepresented)

17/ Based on this evidence, does this change your thought on the effectiveness and safety of GLP1s for HD patients? Please comment!

18/ The topic remains developing. We hope this #tweetorial has improved your knowledge on the effects of GLP1s on HD patients. Please share this #tweetorial with your followers and friends! Thanks to @MChanMD for authoring & *** for great feedback! @ISNkidneycare @KIReports