Healthcare Utilization and Cost Associated with Empagliflozin in Older Adults with Type 2 Diabetes: Results from the EMPRISE Study

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Background

- In the **EMPA-REG OUTCOME trial**, empagliflozin reduced the risk of cardiovascular and all-cause mortality, and hospitalization for heart failure in patients with type 2 diabetes (T2D) and established cardiovascular disease.
- Simulations based on trial data showed that adding empagliflozin to the standard of care was cost-effective.
- Accumulation of real-world data on empagliflozin provides the opportunity to directly estimate the healthcare utilization and cost associated with empagliflozin in routine care compared to alternative medications.
- EMPRISE is a monitoring program aimed to assess the comparative effectiveness, safety, healthcare utilization, and cost of **empagliflozin** in T2D patients in routine care using **real-world data** in the U.S. for **5 years**.

Objective

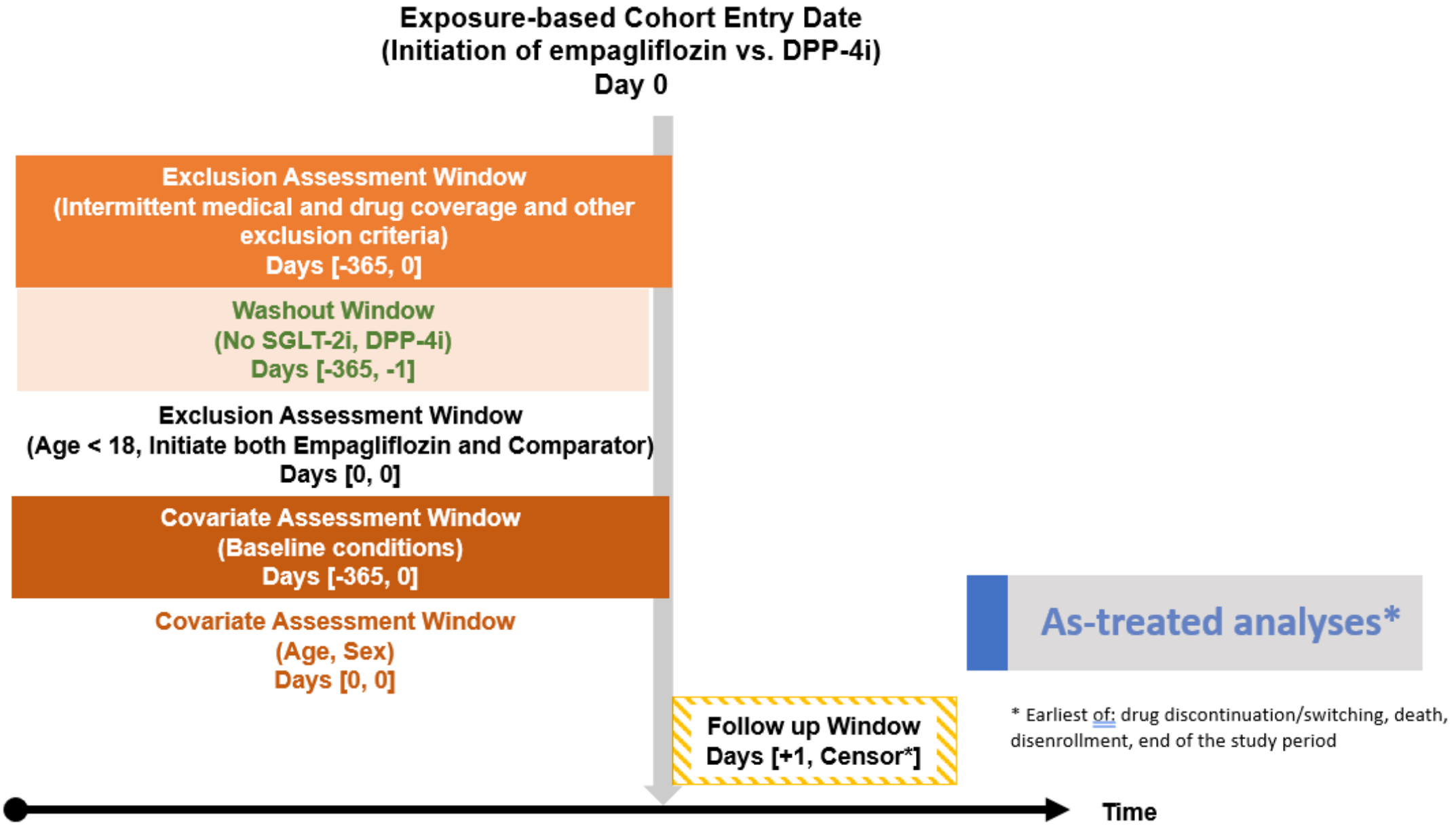
- Objective: To compare the healthcare utilization and cost of empagliflozin vs. dipeptidyl peptidase-4 inhibitors (DPP-4i) in older patients aged ≥65 years with T2D across the broad spectrum of cardiovascular disease

Methods

Methods

- **Study design:** New-user active-comparator cohort study
- **Data sources:** US Medicare (August 1, 2014-September 30, 2018).
- **Study population:** Older adults ≥65 years in Medicare with T2D
- **Exposure and comparator:** Initiators of empagliflozin compared to DPP-4i.

Overview of New-user Active-comparator Design



Outcomes

Healthcare utilization outcomes	Cost outcomes
Hospital days	Total Cost
Number of Hospitalizations	Inpatient cost
Number of Emergency Department Visits	Outpatient cost
	Pharmacy cost
	Pharmacy cost of diabetes medications

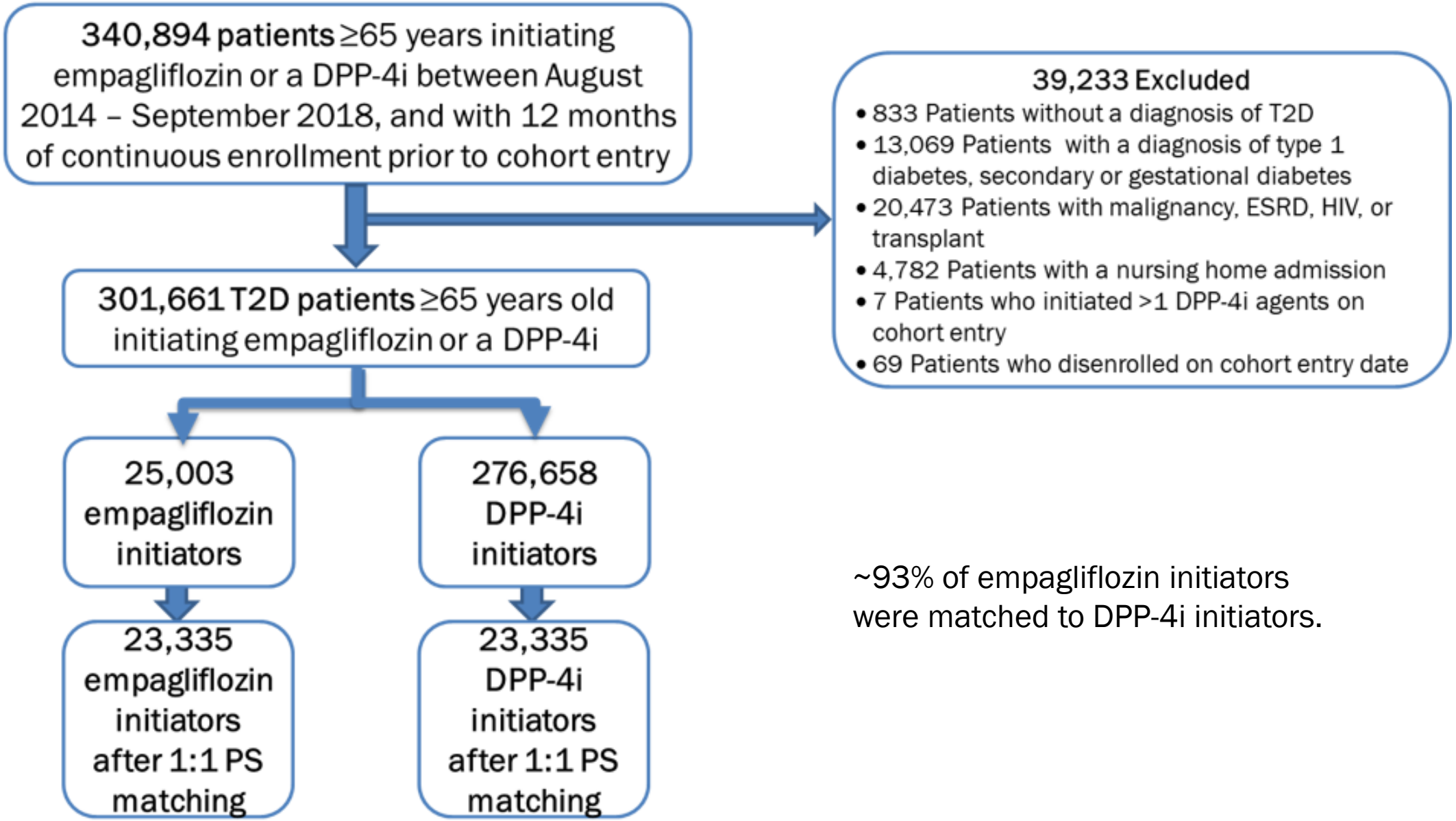
Statistical analyses

- We matched empagliflozin and DPP-4i initiators using **propensity score (PS)** adjusting for **143 covariates**
- We estimated rate ratios and differences per 1,000 person-years for healthcare utilization outcomes using zero-inflated negative binomial models, and costs per member per year (PMPY) using gamma models.
- Follow-up started from one day after drug initiation until the end of study (Sep 2018), death, gap in enrollment, or drug discontinuation/switching.

Subgroup and sensitivity analyses

- **Stratified analyses** by baseline cardiovascular disease (yes/no).
  - Defined as baseline **atherosclerotic cardiovascular disease** or **heart failure**
- **Sensitivity analyses**
  - Analyses where we did not censor for drug discontinuation or switching (up to 1 year)
  - Stabilized censoring-weighted analyses, in which censoring due to treatment discontinuation is independent of the measured covariates of interest.

Consort Flow diagram of EMPRISE Study Population (2014-2018)



~93% of empagliflozin initiators were matched to DPP-4i initiators.

Table 1. Patient characteristics during a 12-month baseline period

	Empagliflozin vs. DPP-4i (Before matching)			Empagliflozin vs. DPP-4i (After matching)		
	Empagliflozin N=25,003	DPP4i N=276,658		Empagliflozin N=23,335	DPP-4i N=23,335	
Patient characteristics	Mean (SD) or n (%)	Mean (SD) or n (%)	Stand. Diff.	Mean (SD) or n (%)	Mean (SD) or n (%)	Stand. Diff.
Age, mean (SD)	71.9 (5.0)	74.3 (6.7)	0.406	72.0 (5.1)	72.1 (5.1)	0.008
Sex female, n (%)	11,379 (45.6%)	156,503 (56.6%)	0.222	10,844 (46.5%)	10,788 (46.2%)	0.005
Race (white), n (%)	20,861 (83.4%)	208,232 (75.3%)	0.203	19,357 (83.0%)	19,471 (83.4%)	0.013
CVD history, n (%)[1]	12,843 (51.4%)	137,218 (49.6%)	0.035	11,853 (50.8%)	11,853 (50.8%)	0.000
CKD stages 3-4, n (%)	2,578 (10.3%)	50,658 (18.3%)	0.230	2,444 (10.5%)	2,512 (10.8%)	0.009
No. diabetes medications on index date, mean (SD)	1.4 (0.91)	1.2 (0.80)	0.302	1.3 (0.87)	1.3 (0.86)	0.001
Current use of metformin, n (%)	15,861 (63.4%)	162,981 (58.9%)	0.093	14,773 (63.3%)	14,824 (63.5%)	0.005
Current use of insulin, n (%)	6,056 (24.2%)	33,613 (12.1%)	0.317	5,098 (21.8%)	5,120 (21.9%)	0.002
LOS, mean (SD)[2]	0.1 (0.97)	0.5 (2.42)	0.192	0.1 (1.00)	0.1 (0.84)	0.004
Cost for T2D medications, mean (SD)	3,590 (5,269)	1,404 (2,382)	0.535	2,960 (4,334)	2,933 (4,818)	0.006

[1] CVD history includes both atherosclerotic cardiovascular diseases and heart failure.

[2] Length of stay for 30 days prior to cohort entry.

Rate ratios and differences for empagliflozin vs. DPP-4i

	Empagliflozin (n= 23,335)	DPP-4i (n= 23,335)	Empagliflozin vs. DPP-4i	Empagliflozin vs. DPP-4i
Healthcare Utilization	**Rate/1000PY**	**Rate/1000PY**	**RD (95%CI) per 1000 PY**	**RR (95%CI)**
Hospital days	1,400	1,958	-557 (-587, -528)	0.89 (0.82, 0.97)
Number of hospitalizations	240	312	-73 (-84, -61)	0.86 (0.79, 0.93)
Number of ED visits	489	617	-128 (-145, -111)	0.86 (0.82, 0.91)
Cost	**PMPY**	**PMPY**	**PMPY Difference**	**PMPY Ratio**
Total cost of care	17,369	18,478	-1,109 (-1,478, -739)	0.94 (0.92, 0.96)
Inpatient cost	3,744	4,457	-713 (-847, -579)	0.84 (0.81, 0.87)
Outpatient cost	2,273	2,471	-198 (-272, -124)	0.92 (0.89, 0.95)
Total pharmacy cost	9,222	8,867	355 (177, 532)	1.04 (1.02, 1.06)
Diabetes medication cost	6,124	5,671	454 (284, 567)	1.08 (1.05, 1.10)

ED: Emergency department
PMPY costs represent per member per year cost, which is the cost during the follow-up divided by the follow-up years
Mean follow-up ~8.9 months

Healthcare utilization outcomes by cardiovascular disease subgroups

Outcomes	Empagliflozin Rate/1000PY	DPP-4i Rate/1000PY	RD (95%CI) per 1000 PY (or PMPY Diff)	RR or PMPY Ratio (95%CI)
Patients with a history of CVD (n= 11,855 PS-matched pairs)				
Hospital days	1,881	2,712	-831 (-880, -782)	0.84 (0.76, 0.93)
Number of hospitalizations	321	428	-108 (-127, -88)	0.81 (0.73, 0.89)
Number of ED visits	641	796	-154 (-182, -127)	0.85 (0.80, 0.90)
Patients with no history of CVD (n= 11,480 PS-matched pairs)				
Hospital days	927	1226	299 (-332, -266)	0.83 (0.78, 0.88)
Number of hospitalizations	160	200	-40 (-53, -26)	0.90 (0.85, 0.95)
Number of ED visits	340	445	-105 (-125, -85)	0.84 (0.80, 0.88)

PMPY: Per-member per-year
Mean follow-up ~8.9 months

Cost outcomes by baseline cardiovascular disease subgroups

Outcomes	Empagliflozin (PMPY)	DPP-4i (PMPY)	PMPY Difference (95%CI)	PMPY Ratio (95%CI)
Patients with a history of CVD (n= 11,855 PS-matched pairs)				
Total cost of care	20,274	22,280	-2,005 (-2,451, -1,337)	0.91 (0.89, 0.94)
Inpatient cost	4,961	6,124	-1,164 (-1,409, -919)	0.81 (0.77, 0.85)
Outpatient cost	2,779	3,054	-275 (-428, -122)	0.91 (0.86, 0.96)
Total pharmacy cost	9,930	9,641	289 (96, 578)	1.03 (1.01, 1.06)
Diabetes medication cost	6,309	5,842	467 (235, 643)	1.08 (1.04, 1.11)
Patients with no history of CVD (n= 11,480 PS-matched pairs)				
Total cost of care	14,495	14,791	-296 (-740, 148)	0.98 (0.95, 1.01)
Inpatient cost	2,585	2,840	-256 (-369, -114)	0.91 (0.87, 0.96)
Outpatient cost	1,773	1,906	-133 (-210, -38)	0.93 (0.89, 0.98)
Total pharmacy cost	8,443	8,118	325 (81, 568)	1.04 (1.01, 1.07)
Diabetes medication cost	5,945	5,505	440 (220, 606)	1.08 (1.04, 1.11)

PMPY costs represent per member per year cost, which is the cost during the follow-up divided by the follow-up years. Mean follow-up ~8.9 months

Sensitivity analyses for the total cost between empagliflozin and DPP-4i

Analyses	Difference in PMPY costs (95% CI)	Ratio of PMPY costs (95% CI)
Analyses not censoring drug discontinuation/switching	-204 (-524, 122)	0.99 (0.97, 1.01)
Censoring weighted analyses	-392 (-574, -206)	0.97 (0.95, 0.98)

Conclusions

- Among older adults with T2D, initiation of empagliflozin was associated with reduced hospital days, number of hospitalizations and emergency department visits.
- Empagliflozin was also associated with lower total, inpatient, and outpatient costs compared to DPP-4i.
- Results were consistent in patients with T2D, with and without history of cardiovascular disease, though the absolute benefits of empagliflozin were larger in patients with baseline cardiovascular disease.
- Beyond superior clinical benefits, empagliflozin can also be considered a cost-efficient treatment compared to DPP-4i.

Thank you: **phtoo@bwh.harvard.edu**

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