Comparing healthcare cost among empagliflozin, DPP-4 inhibitors and GLP-1 receptor agonists in patients with type 2 diabetes mellitus: A German claims data analysis

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Background and Objective

A good risk-factor management including glycemic control reduces the risk for diabetes-related complications in patients with type 2 diabetes (T2DM). However, achieving this goal may require individualized pharmacological approaches. This study aimed to compare direct healthcare cost in prevalent T2DM patients newly treated with empagliflozin (EMPA) compared to dipeptidyl peptidase-4 inhibitors (DPP-4i) or glucagon-like peptide-1 receptor agonists (GLP-1-RA).

Methods

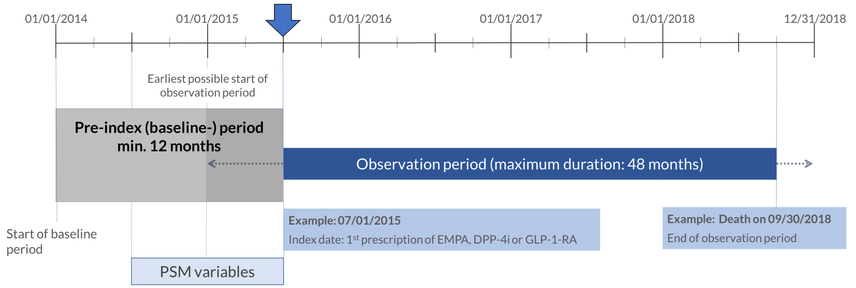
Data Sources

German claims data for over 4 million persons insured by different statutory health insurance companies across Germany over the period 01/01/2014-31/12/2018.

Selection criteria

- Patients were observed from the first day of treatment initiation until 31/12/2018, death, or therapy discontinuation (Figure 1).
- Inclusion criteria: Continuously insured (2014-2018); ≥ 18 years old; at least two outpatient diagnoses and/or one inpatient diagnosis of T2DM (ICD-10-GM code: E11) before treatment start; treatment start with EMPA, DPP-4i or GLP-1-RA in 2015-2018:
  - EMPA (ATC codes: A10BK03 [formerly A10BX12] and A10BD20)
  - DPP-4i (A10BH*, A10BD07, A10BD08, and A10BD10)
  - GLP-1-RA (A10BJ* [formerly A10BX04, A10BX07, A10BX10, or A10BX14] and A10AE56)
- Exclusion criteria: Prescription of one of the respective agents in 2014; diagnosis of other form of diabetes (type 1, gestational, or secondary diabetes), neoplasms (identified by diagnosis or prescriptions of cancer-related drugs), or one of the top three most cost-intensive diseases (sepsis, human immunodeficiency virus [HIV], or opportunistic infections) within 12 months before the start of treatment.

Figure 1. Patient selection and observation period



Propensity score matching (PSM)

A PSM approach was used to adjust for potential differences in patient characteristics and prior disease and treatment history among the cohorts:

- Patients starting EMPA versus either DPP-4i or GLP-1-RA were matched 1:1 based on a propensity score using nearest-neighbor matching without replacement and a maximum caliper of 0.001.
- The propensity scores were derived by logistic regression models estimating the probability of a patient belonging to the different treatment groups (two estimations: EMPA versus DPP-4i and EMPA versus GLP-1-RA).

Cost measurement

- The following cost items were considered from the perspective of the statutory health insurance scheme:

Outpatient cost	Inpatient cost	Medication cost
Outpatient costs were evaluated per case based on the reimbursed services in accordance with the German EBM (uniform valuation standard)	Inpatient costs were assessed per hospitalization according to the German 'diagnosis-related group' (G-DRG) reimbursement model	Medication costs refer to pharmacy sales price at the prescription date

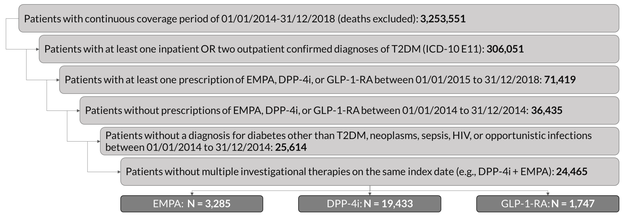
- Cost differences between the cohorts were evaluated based on an incremental cost approach using the Bang and Tsiatis estimator for censored data, as previously described by Chen et al. 2015.[1,2]

Results

Patient Selection

Of 24,465 patients included, 3,285 received EMPA, 19,443 DPP-4i, and 1,747 GLP-1-RA (Figure 2).

Figure 2. Attrition chart



Baseline characteristics

Matched cohorts were balanced on a variety of patient characteristics covering sociodemographic information, present comorbidities, as well as previous medication and healthcare resource utilization in the last 12 months. Table 1 shows only a subset of the covariates that were included in the PSM.

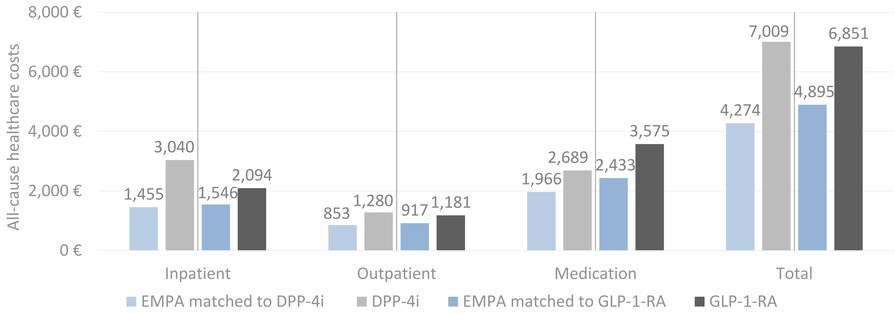
Table 1. Selected baseline characteristics of matched cohorts (EMPA vs. DPP-4i and EMPA vs. GLP-1-RA)

Variables	Matched			Matched		
	EMPA	DPP-4i	% Bias (p-value)	EMPA	GLP-1-RA	% Bias (p-value)
N	3,100	3,100		1,346	1,346	
Female - %	34.0	33.5	1.1 (0.667)	41.7	39.8	3.8 (0.327)
Age in years - mean	60.0	59.7	2.7 (0.279)	56.4	56.7	-3.1 (0.407)
CCI – mean	7.3	7.2	1.8 (0.477)	7.3	7.5	-5.5 (0.153)
With major cardiovascular disease - %	37.9	38.2	-0.7 (0.794)	27.6	30.2	-5.4 (0.148)
Previous use of insulin - %	27.1	27.7	-1.4 (0.608)	45.9	47.0	-2.3 (0.562)
Previous use of metformin - %	78.3	78.0	0.7 (0.782)	73.1	71.9	2.7 (0.490)
Previous use of sulfonylurea - %	12.1	11.8	0.9 (0.724)	9.4	9.4	0.2 (0.947)
Previous use of other antidiabetics - %	2.3	2.4	-0.4 (0.867)	3.0	2.9	-1.4 (0.725)

Healthcare cost

- Mean total costs after start of DPP-4i were €7,009 (95%-CI: 6,573-7,444) vs. €4,274 (3,982-4,566) for EMPA (Figure 3). The cost difference between DPP-4i and EMPA treatment was driven by inpatient cost (€1,585), outpatient cost (€427), and drug cost (€723).
- Costs associated with GLP-1-RA treatment were also significantly higher compared with EMPA (€6,851 [6,183-7,518] vs. €4,895 [4,345-5,445]; Figure 3). While inpatient costs did not differ significantly (€549), lower expenses resulted from lower outpatient cost (€264) and lower drug cost (€1,143).

Figure 3. Healthcare costs after matching



Conclusion

This claims data analysis demonstrated that T2DM patients who initiated EMPA therapy had lower healthcare expenses in the proceeding course of treatment than those starting DPP-4i and GLP-1-RA. While lower costs associated with EMPA versus DPP-4 mainly result from less frequent hospitalizations, cost savings in comparison to GLP-1-RA are explained by lower drug cost.

List of abbreviations

ATC: Anatomical Therapeutic Chemical, CCI: Charlson Comorbidity Index, CI: confidence interval, CVD: cardiovascular disease, ICD-10-GM: international classification of diseases version 10 (German modification), DPP-4i: dipeptidyl peptidase-4 inhibitors, EBM: Einheitlicher Bewertungsmassstab/Uniform evaluation standard, EMPA: empagliflozin, GLP-1-RA: glucagon-like peptide-1 receptor agonists, HIV: human immunodeficiency virus, PSM: propensity score matching, T2DM: type 2 diabetes mellitus

References

[1] H. Bang and A. Tsiatis, "Estimating medical costs with censored data," Biometrika, vol. 87, no. 2, pp. 329–343, Jun. ; [2] S. Chen, J. Rolfes, and H. Zhao, "Estimation of mean health care costs and incremental cost-effectiveness ratios with possibly censored data," *Stata J.*, vol. 15, no. 3, pp. 698–711, 2015.

Conflict of Interest

N. P. and S. M. participated in this study as staff members of Ingress-health; the work of IPAM and Ingress-health in this study was financed by Boehringer Ingelheim Pharma GmbH & Co. KG. A. S. and M. G. are employees of Boehringer Ingelheim Pharma GmbH & Co. KG. T. W. and A. D. participated in this study as staff members of IPAM. J. A. participated as external clinical advisor in the scientific steering committee of this study and received honoraria from Boehringer Ingelheim Pharma GmbH & Co. KG.

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