Patient-reported outcomes of dipeptidyl peptidase-4 inhibitors: a systematic review.

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Background

- The individualization of treatment is key in type 2 diabetes mellitus (T2DM) patients according to guidelines[1].
- Besides efficacy and safety outcomes, patient preferences, treatment adherence and health-related quality of life (HRQoL) should be taken into account in treatment choice[1].
- Recent systematic reviews including dipeptidyl peptidase-4 (DPP-4) inhibitors have explored clinical or economic outcomes, but patient-reported outcomes (PROs) have not been considered.

Objective

- To synthesize the available information on the therapeutic value of DPP-4 inhibitors for T2DM treatment considering published data on PROs.

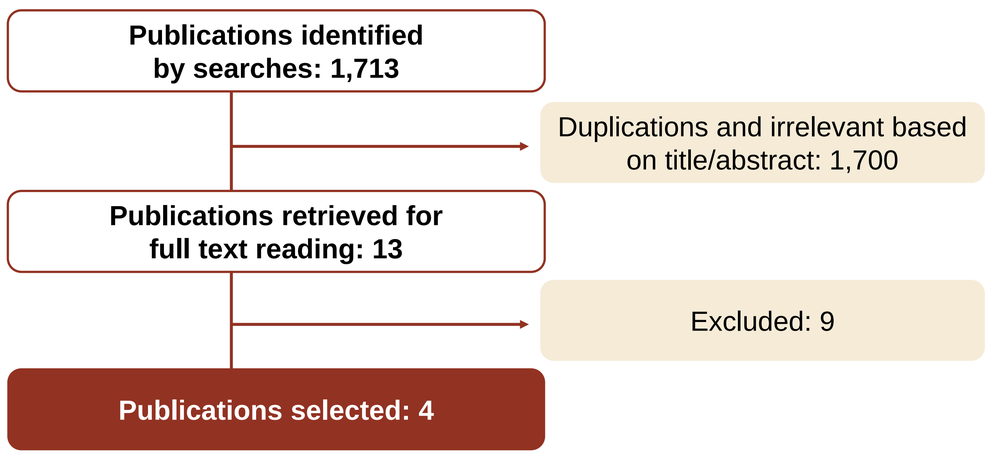
Materials and methods

- A systematic review was performed on Spanish (IBECS, MEDES) and international (PubMed, ISI WOK, Scopus, Cochrane Library) databases.
- Observational studies regarding HRQoL, adherence, persistence, satisfaction or preferences assessed in T2DM patients receiving DPP-4 inhibitors. The selected studies were published in English or Spanish until June 2013.

Results

- Of 1,713 references identified, 13 full-text articles were evaluated for eligibility and 4 publications met inclusion criteria (Figure 1).

Figure 1. Results of systematic review



- The characteristics of the selected publications are described in table 1.

Table 1. Characteristics of selected publications

First author, publication year, country, OCEBM	Design	Population	PROs evaluated
Curkendall S M, 2013[2] USA (2c)	Observational retrospective study.	79,518 T2DM patients (≥18 years old) receiving DPP-4 inhibitors, GLP-1 analogs, SU or TZD by ≥ 1 year.	**Adherence**: Proportion of days covered (adherent if PDC ≥0.8). **Persistence**: Time to discontinuation.
Genovese S, 2013[3] Italy (3b)	Observational prospective study.	1,046 T2DM patients (≥18 years old) not adequately controlled with metformin which received DPP-4 inhibitors/metformin (fixed combination) as a second step observed for up to 1 year from prescription.	**Satisfaction**: Diabetes Treatment Satisfaction Questionnaire (DTSQ): 5-6=very dissatisfied; 3-4=dissatisfied; 1-2=fairly satisfied; 0=very satisfied.
Rathmann W, 2013[4] Germany (2a)	Observational retrospective study.	19,184 T2DM patients receiving DPP-4 inhibitors and 31,110 receiving SU.	**Persistence**: Continuously refilling the prescription within 90 days of the previous dispensing.
DiBonaventura M C, 2010[5] USA, France, Italy, Germany, Spain and United Kingdom (2a)	Observational cross-sectional study.	T2DM patients receiving metformin monotherapy. n = 2,402 completed a first wave. A second wave was conducted because newer data became available after wave 1 from a head-to-head trial (sitagliptin and liraglutide) n = 1,340 participate in the second wave (56.8% of first wave).	**Preferences**: Patients were asked which medication profile they would prefer. Both profiles included 4 attributes: frequency and mode of administration; efficacy in HbA1c reduction; side effects (hypoglycemia, nausea, vomiting and diarrhea); other effects (changes in weight, blood pressure).

DPP-4: dipeptidyl peptidase 4; GLP-1: glucagon-like peptide-1; OCEBM: Oxford Centre for Evidence Based Medicine Levels of Evidence; T2DM: type 2 diabetes mellitus; TZD: thiazolidinedione; SU: sulfonylurea.

- Two studies reported information about adherence/persistence, one about satisfaction and another one about preferences. No information about HRQoL was identified.

Adherence and persistence

Curkendall *et al.*, evaluated adherence and persistence in patients receiving DPP-4 inhibitors, GLP-1 agonists, SU and TZD showing that:

- Patients receiving DPP-4 inhibitors were more likely to be adherent than those treated with GLP-1 agonists [Odds Ratio, OR=0.40; 95% CI=0.37-0.42], SU [OR=0.49; 95% CI=0.46-0.52] or TZD [OR=0.54; 95% CI=0.51-0.57].
- Patients receiving DPP-4 inhibitors were more persistent compared with GLP-1 agonists, SU and TZD (OR reported graphically).
- Compared with DPP-4, the probability of discontinuation was 71% higher for those taking GLP-1 analogs, 63% higher for those taking SU, and 55% higher for those taking TZD.
- Adherence may be better with DPP-4 inhibitors due to a better tolerability than with the other medications.

Rathmann *et al.*, evaluated treatment persistence to DPP-4 inhibitors and sulfonylureas showing that:

- DPP-4 inhibitors were associated with a lower risk of treatment discontinuation (non-persistence: 39%) compared with SU (49%) [Hazard Ratio=0.74; 95% CI=0.71-0.76].
- In this study, previous hypoglycemia was related to a future risk of hypoglycemic events. The authors suggested that this fact could contribute to non-persistence.

Patient satisfaction

The results of the study conducted by **Genovese *et al.***, showed that:

- Combination of DPP-4 inhibitors and metformin increased patient's satisfaction a 30% compared with metformin monotherapy.
- The proportion of patients 'very satisfied' with treatment increased from baseline by 44.7%; patients who perceived themselves as hyperglycemia-free increased a 37.9% from baseline (from 6.3% to 26.9%) and those who perceived as hypoglycemia-free increased a 15.2% (from 29.8% to 40.9%).
- The authors supported these figures with clinical data: improvement of HbA1c in 54% of patients and stabilization of HbA1c in 41%.

Treatment preferences

DiBonaventura *et al.*, study showed that:

- Most patients preferred the DPP-4 inhibitor profile over the GLP-1 agonist profile (wave 1: 81.9% vs. 18.1%; wave 2: 84.4% vs. 15.6%; p<0.001).
- Most patients preferred to take first the DPP-4 inhibitor profile over GLP-1 agonist profile, if they could switch later (wave 1: 82.8% vs. 17.2%; wave 2: 85.0% vs. 15.0%; p<0.001).
- Most patients believed they could take the DPP-4 inhibitor profile longer than the GLP-1 agonist profile (wave 1: 83.4% vs. 16.6%; wave 2: 86.5% vs. 13.5%; p<0.001).
- In the Spanish population (n=188), the proportion of patients preferring DPP-4 inhibitors was even higher (90.4% vs. 9.6%; p<0.001).

Conclusions

- **PROs in DPP-4 inhibitors are poorly described in the literature.**
- **Nevertheless, DPP-4 inhibitors are preferred as first option and are associated with higher persistence and satisfaction levels, mainly due to higher perception of glycemic control and lower hypoglycemia risk.**

References:

1 Inzucchi SE et al. Diabetologia. 2012;55:1577-96.

2 Curkendall SM, et al. CMRO. 2013; 29:1275-86.

3 Rathmann W, et al. Diabetes Obes Metab. 2013; 15:55-61.

4 Genovese S, et al. Adv Ther. 2013; 30:152-64.

5 DiBonaventura MC, et al. Patient Preference and Adherence. 2010;4:397-406.

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