MONASH University

Dynamics of switching, adherence, and persistence of sodium glucose co-transporter 2 inhibitors use: an Australian perspective

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Disclosures

- This work was funded by Monash University.
- I have no conflict of interest to disclose.
- However, other researchers who were involved in this study have received grants or financial assistance from pharma companies for work not related to this study.

Background

- Data from randomized clinical trials (RCTs) suggest that Sodium glucose Co-transporter 2 inhibitors (SGLT2is) significantly improve glycemic control in patients with diabetes.[1]
- SGLT2is also exhibit additional pleotropic effects such as reducing blood pressure and body weight.[2]
- However, in real world settings, suboptimal patient adherence may lead to poor drug effectiveness.[3]

[1]Wilding et al. Diabetes Care. 2016 Aug;39 Suppl 2:S154-64.
[2]Chin *et al.* Cardiovascular Research. 2019 Feb 1;115(2):266-276.
[3]Edelman and Polonksy. Diabetes Care. 2017 Nov;40(11):1425-1432.

Study aims

To characterize the patterns of **switching**, **adherence** and **persistence** to SGLT2is over a **1-year** follow-up

Data sources & inclusion criteria

- We used a 10% random sample of nationwide Australian Pharmaceutical Benefits Scheme (PBS) data.[4]
- Adults aged ≥18 years who were new users of SGLT2is between September 2015 and August 2017 were included.
- A new user was anyone without history of use in the previous 12 months.
- Only people who survived the full 12 months post-index date were included.

[4]Mellish et al. BMC Research Notes. 2015 Nov 2;8:634

Outcomes definitions

- Switching was defined as the first change from the index SGLT2i to another SGLT2i.
- Adherence was assessed as the proportion of days covered (PDC) calculated over 365 days.
- People who attained a PDC of ≥0.80 were considered adherent.[5]
- Persistence was defined as the continuous use of SGLT2i without a gap of ≥90 days.

Statistical analysis

- Generalised linear models (GLMs) were used to compare the levels of adherence (PDC = continuous) between different SGLT2is.
- Logistic regression was conducted to compare the odds of being adherent (PDC ≥0.80) across different SGLT2is.
- Switching and persistence for different SGLT2is were compared via Cox proportional hazard models.
- All models adjusted for potential confounders including age, sex, concession status (co-payment level), pre-index medication use, and whether the index therapy was a fixed-dose combination (FDC) product with metformin.

Results

- A total of 11,981 adults [mean age 60.9 years, standard deviation (SD) 11.5; 40.5% females] were included
- During the analysis period only two SGLT2is were available under the PBS (Dapagliflozin=5993; Empagliflozin=5988).
- Of the cohort, 53.6% were concession card holders (lower co-payment).
- Overall, 31.8%, 74.7%, 25.1%, 76.4%, 6.8%, and 2.7% had used insulin, lipid lowering therapy (LLT), antidepressants, blood-thinning agents, blood pressure lowering (BPL), anti-anxiety agents, and nicotine dependence therapies, respectively, prior to SGLTi initiation.
- About 29% of people were prescribed fixed dose combination (FDC) with metformin.

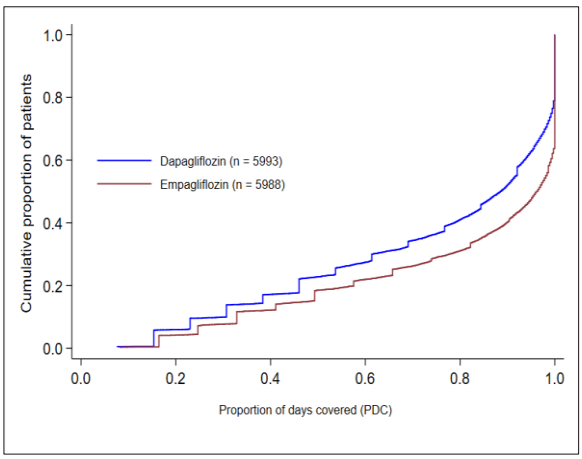
Class-level adherence and persistence

- When analysing medication use at a class level, the 1-year mean was 0.79 ± 0.27.
- The proportion adherent (PDC ≥0.80) was 65.8%.
- The proportion of persistent (no gap of ≥90 days) was 72.1%.
- The median time to non-persistence was 201 [interquartile range (IQR) 150–270] days.

Drug-level adherence

- The mean PDC for dapagliflozin was 0.75 (± 0.28).
- The mean PDC for empagliflozin was 0.81 (± 0.26).
- Cumulative PDC is presented in Figure 1

Figure 1: 1-year cumulative PDC among people prescribed dapagliflozin and empagliflozin



Comparisons of adherence, persistence and switching between people initiated on dapagliflozin and empagliflozin

Outcome	SGLT2i subtype	
	Dapagliflozin (n = 5993)	Empagliflozin (n = 5988)
Switching		
% switching	5.9	2.6
Median no. of days to switching (IQR)	222 (141-304)	132 (70-234)
HR for switching (univariate)	1.0	0.44 (0.36-0.53)*
HR for switching[a]	1.0	0.46 (0.38-0.55)*
Adherence (PDC=continuous)		
OR for adherence (univariate)	1.0	1.06 (1.05-1.07)*
OR for adherence[a]	1.0	1.04 (1.03-1.05)*
Adherent (PDC≥0.80)		
% adherent	59.3	69.4
OR of adherent (univariate)	1.0	1.56 (1.44-1.68)*
OR of adherent[a]	1.0	1.39 (1.29-1.51)*
Persistence (absence of ≥90 days gap)		
% persistent	68.6	73.3
Median number of days to non-persistence (IQR)	204.5 (150-275)	202 (150-270)
HR for persistence (univariate)	1.0	1.21 (1.13-1.29)*
HR for persistence[a]	1.0	1.14 (1.06-1.22)*

[a]adjusted for age, sex, concession status, use of fixed dose combination of SGLT2i, pre-index insulin use and all other pre-index medication use in table 1; HR= hazard ratio; OR= odds ratio; IQR=interquartile range; PDC= proportion of days covered; s.d= standard deviation.*p<0.05; [‡]proportions compared via x^2 test; [$]means by one-way analysis of variance (ANOVA); [¤]medians by Kruskal-Wallis test.

The results of persistence analysis remained similar when using 45 and 180-day gaps

Limitations

- We had no information on the underlying reasons as to why people were non-adherent to or non-persistent with their SGLT2i medication.
- We did not have records of in-hospital medication use. Thus the PDC for people hospitalised may have been underestimated.
- Moreover, given the nature of the available data, we could not verify whether people actually took the dispensed medication.
- As the PBS data set lacks information on clinical outcomes, we were unable to establish the clinical utility of the differences in adherence and persistence between empagliflozin and dapagliflozin.

Conclusions

- In this large Australian study using real-world data, we found that a considerable proportion of people prescribed SGLT2is was non-adherent or non-persistent during the first 12 months.
- Empagliflozin was associated with better adherence and persistence as well as lower switching compared with dapagliflozin.
- These data emphasize the need for increased efforts to address the potential adherence barriers to promote optimised used of prescribed medications in patients with diabetes so as to achieve the desired clinical effects

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Want to know more/collaborate?

- Let's grab coffee
- Drop me a line

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