Patterns of adherence, persistence, and switching among Australians prescribed Dipeptidyl peptidase 4 inhibitors

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Introduction

- Despite increased availability of pharmacological therapies, several patients with type 2 diabetes mellitus (T2DM) do not achieve glycaemic control.[1]
- Poor adherence and persistence in medication use is ubiquitous among patients with T2DM in real world settings.[2]
- In Australia, Dipeptidyl peptidase 4 inhibitors (DPP4is) are increasingly being prescribed to people with T2DM, yet there is limited insight into patients' patterns of use of these drugs.
- We examined the patterns of switching, adherence, and persistence in use over 12-months among Australians dispensed DPP4is.

Methods

- We analysed data from a 10% random sample of the Australian pharmaceutical benefits scheme (PBS) datasets.
- Switching was defined as the first change from the index DPP4i to another.
- Non-adherence was defined as a proportion of days covered (PDC) <0.80.[3]
- Non-persistence was defined as a gap of ≥90 days.[4]
- Logistic regression model was used to compare non-adherence and Cox models were used to compare switching and non-persistence between different DPP4is.

Results

- A total of 15,915 adults (mean age 62.7±13.3 years; 42.8% female) newly initiated with DPP4is (sitagliptin=9576; vildagliptin=1130; saxagliptin=1126; linagliptin=3560; alogliptin=523) between January 2015 and August 2017 were included (**Table 1**).
- The mean PDC over 1-year was 0.76±0.32 and the cumulative PDC for each DPP4i is presented in **Figure 1.**
- Overall, 3.2% switched between different DPP4is (**Table 2**), 36.0% were non-adherent while 30.0% were non-persistent at 1-year follow up.
- Switching was lowest amongst users of sitagliptin.
- Compared to sitagliptin, people dispensed vildagliptin, alogliptin, and linagliptin were no more likely to be non-adherent or non-persistent (**Table 3**).
- Compared to sitagliptin, saxagliptin was associated with higher non-adherence and non-persistence.

Figure 1: One-year cumulative PDC among the people prescribed various DPP4is

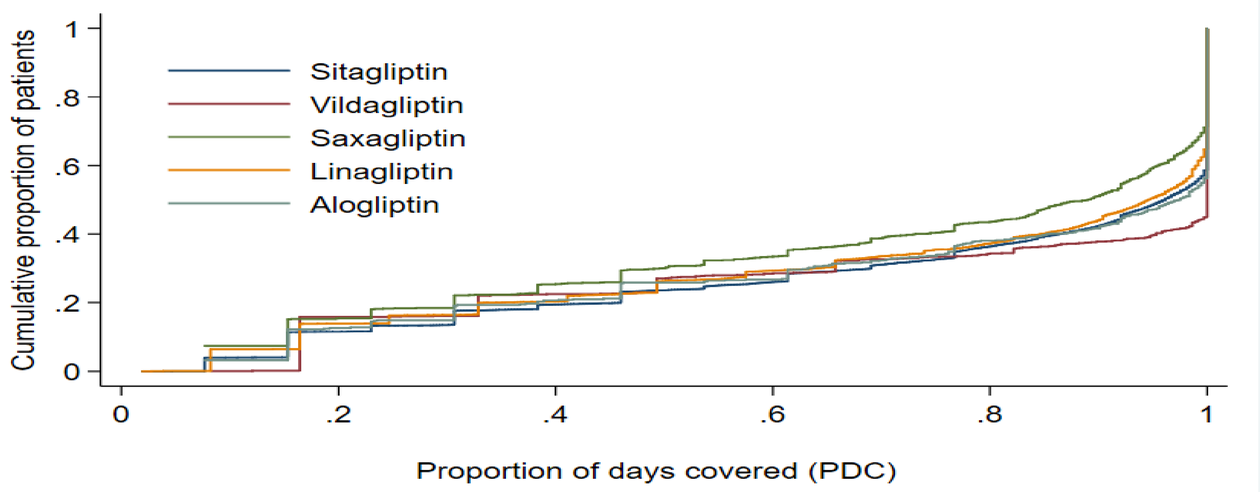


Table 1: Baseline characteristics of the study cohort initiating DPP4is between January 2015 and August 2017

Variable	All	DPP4i type					P-value[a]
		Sitagliptin	Vildagliptin	Saxagliptin	Linagliptin	Alogliptin	
Total no. of people	15,915	9576	1130	1126	3560	523	-
Mean age (± s.d)	62.7 (13.3)	61.6 (13.1)	60.8 (13.1)	61.7 (12.9)	66.8 (13.1)	62.0 (12.9)	0.926
Female Gender (n, %)	6804 (42.8)	4,078 (43.6)	498 (44.1)	446 (39.6)	1568 (44.0)	214 (40.9)	0.072
Pre-index Medication use (n, %)							
Insulin	2381 (15.0)	1345 (14.1)	113 (10.0)	100 (8.9)	763 (21.4)	60 (11.5)	<0.001
Blood pressure lowering agents	11497 (72.2)	6785 (70.9)	738 (65.3)	794 (70.5)	2815 (79.1)	365 (69.8)	<0.001
Blood thinning agents	3596 (22.6)	1995 (20.8)	209 (18.5)	212 (18.8)	1096 (30.8)	84 (16.1)	<0.001
Antidepressants	3894 (24.5)	2386 (24.9)	253 (22.4)	247 (21.9)	896 (25.2)	112 (21.4)	0.025
Anti-anxiety agent	1187 (7.5)	715 (7.5)	81 (7.2)	73 (6.5)	280 (7.9)	38 (7.3)	0.632
Anti-dementia	87 (0.6)	44 (0.5)	4 (0.4)	8 (0.7)	30 (0.8)	1 (0.2)	0.047
Lipid-lowering therapy	10729 (67.4)	6296 (65.8)	747 (66.1)	729 (64.7)	2620 (73.6)	337 (64.4)	<0.001
Drugs for reactive airway disease	1909 (12.0)	1131 (11.8)	114 (10.1)	136 (12.1)	476 (13.4)	52 (9.9)	0.013
Anti-epilepsy	507 (3.2)	312 (3.3)	26 (2.3)	30 (20.7)	122 (3.4)	17 (3.3)	0.319
Drugs for malignancy	230 (1.5)	127 (1.3)	14 (1.2)	9 (0.8)	75 (2.1)	5 (1.0)	0.003
Thyroid-related medication	1214 (7.6)	705 (7.4)	85 (7.5)	83 (7.4)	307 (8.6)	34 (6.5)	0.134
Antipsychotics	697 (4.4)	429 (4.5)	39 (3.5)	40 (3.6)	161 (4.5)	28 (5.4)	0.218
Nicotine dependence therapies	404 (2.5)	256 (2.7)	41 (3.6)	32 (2.8)	62 (1.7)	13 (2.5)	0.003
Concessional beneficiary (n, %)	9326 (58.6)	5442 (56.8)	618 (54.7)	658 (58.4)	2297 (64.5)	311 (59.5)	<0.001
Prescribed as FDC with metformin[b]	9968 (62.6)	6555 (68.5)	936 (82.8)	791 (70.3)	1315 (36.9)	371 (70.9)	<0.001

FDC = fixed dose combination; s.d=standard deviation; [a]means compared by one-way analysis of variance, proportions compared with chi-square test and medians are compared using Kruskal Wallis rank test; [b]based on the index script.

Table 2: Patterns of in-class switching during 12 months among people prescribed DPP4is

		Switch to (n, %)				
		Sitagliptin	Vildagliptin	Saxagliptin	Linagliptin	Alogliptin
Switch from (index DPP4is)	Sitagliptin (n=221)		28 (12.7%)	45 (20.3%)	126 (57.0%)	22 (10.0%)
	Vildagliptin (n=44)	25 (56.8%)		5 (11.4%)	13 (29.5%)	1 (2.3%)
	Saxagliptin (n=63)	39 (61.9%)	3 (4.8%)		17 (27.0%)	4 (6.3%)
	Linagliptin (n=144)	109 (75.7%)	9 (6.3%)	16 (11.1%)		10 (6.9%)
	Alogliptin (n=36)	21 (58.3%)	2 (5.6%)	3 (8.3%)	10 (27.8%)	

Table 3: Comparison of switching, adherence, and persistence between people initiated on various DPP4is over 12 months follow up

Outcome	DPP4i subtype					P-value[a]
	Sitagliptin	Vildagliptin	Saxagliptin	Linagliptin	Alogliptin	
Total no. of people	9576	1130	1126	3560	523	-
Switching						
Number switched	221	44	63	144	36	
% switched	2.3	3.9	5.6	4.0	6.9	<0.001
Univariate HR (95% CI) for switching	1.0	1.58 (1.07-2.33)*	2.45 (1.77-3.40)*	1.49 (1.15-1.93)*	2.43 (1.55-3.83)*	
Multivariable HR (95% CI) for switching[b]	1.0	1.60 (1.08-2.37)*	2.44 (1.76-3.39)*	1.38 (1.05-1.81)*	2.42 (1.53-3.82)*	
Non-adherent (PDC<0.80)						
Number non-adherent	3478	386	489	1,324	199	
% non-adherent	36.3	34.2	43.4	37.2	38.0	<0.001
Univariate OR (95% CI) for being non-adherent	1.0	0.85 (0.74-0.96)*	1.35 (1.19-1.52)*	1.04 (0.96-1.13)**	1.07 (0.90-1.28)**	
Multivariable OR of being non-adherent[b]	1.0	0.99 (0.86-1.13)**	1.41 (1.23-1.60)*	0.93 (0.85-1.01)**	1.13 (0.93-1.36)**	
Non-Persistence (≥90 gap)						
Number non-persistent	2837	358	404	1,112	159	
% non-persistent	29.6	31.7	35.9	31.2	30.4	<0.001
Univariate HR (95% CI) for non-persistence	1.0	1.06 (0.95-1.19)**	1.26 (1.14-1.41)*	1.07 (0.99-1.14)**	1.03 (0.88-1.21)**	
Multivariable HR for non-persistence[b]	1.0	1.11 (0.98-1.24)**	1.27 (1.15-1.42)*	1.01 (0.94-1.09)**	1.06 (0.90-1.24)**	

*p<0.05; **p>0.05; PDC= proportion of days covered; [a]proportions were compared via a chi-square test; [b]all logistic regression and cox models were adjusted for age, sex, concession status, pre-index medication use and whether the index therapy was a fixed-dose combination (FDC) with metformin; HR=hazard ratio; OR= odds ratio; CI=confidence interval

Conclusions

- About 1 in 3 people dispensed with DPP4is were non-adherent or non-persistent at 12-months follow-up.
- There were no significant differences in the adherence and persistence rates between alogliptin, vildagliptin or linagliptin and sitagliptin. However, saxagliptin was associated with greater likelihoods of being non-adherent or non-persistent compared to sitagliptin.
- Switching was lowest among the users of sitagliptin.

Declarations

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Conflict of interest: Danny Liew reports past participation in advisory boards and/or receiving honoraria from Abbvie, Astellas, AstraZeneca, Bristol-Myers Squibb, Novartis, Pfizer, Sanofi, and Shire for work unrelated to this study. Ella Zomer reports receiving study funds from Amgen, AstraZeneca, Pfizer and Shire for work unrelated to this study. Dianna J Magliano reports past participation in advisory boards and/or receiving honoraria from AstraZeneca, and Bayer for work unrelated to this study. All others have nothing to disclose.

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